New and Emerging Trabecular Meshwork Bypass Stents

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Minimally invasive glaucoma surgery procedures are newly developed surgical modalities for the management of glaucoma. Their target is to lower intraocular pressure with minimal eye trauma and fewer complications. The first-generation iStent® (Glaukos Corp, Laguna Hills, CA, USA) is the first minimally invasive glaucoma surgery device to be approved for the treatment of open-angle glaucoma. It allows aqueous humour to be drained directly from the anterior chamber to Schlemm's canal, bypassing the trabecular meshwork, which is believed to be the main site of outflow resistance. The second-generation iStent inject® (Glaukos Corp, Laguna Hills, CA, USA) is a smaller implant that allows simultaneous implantation of two stents, which could theoretically result in lower intraocular pressure. The Hydrus® Microstent (Alcon, Geneva, Switzerland) is another trabecular implant that dilates and scaffolds Schlemm's canal. This articles reviews publications about all trabecular meshwork bypass stents, comparing them in terms of their efficacy and safety.

Keywords

Hydrus, iStent, iStent inject, iStent infinite, minimally invasive glaucoma surgeries, trabecular microbypass

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Glaucoma is a major cause of irreversible blindness worldwide.[1,2] High intraocular pressure (IOP) is one of the major risk factors for the development and progression of open-angle glaucoma (OAG) but is not an essential criterion for diagnosis.[3,4] Nonetheless, lowering the IOP is considered the only proven intervention to decelerate disease progression.[3–5] IOP can be reduced using topical hypotensive medications, laser treatment or filtration surgery, including trabeculectomy and glaucoma drainage devices.[6,7] However, poor compliance and tolerability are known issues with medications,[8,9] and vision-threatening complications could follow filtration surgeries.[10] Recently, minimally invasive glaucoma surgery (MIGS) has emerged as a safer and more effective IOP-lowering approach.[11]

Since the US Food and Drug Administration (FDA) approval of the iStent® (Glaukos Corp, Laguna Hills, CA, USA) in 2012, MIGS has provided more glaucoma surgical options.[12] Mechanisms of IOP reduction in MIGS procedures include drainage of aqueous humour through Schlemm's canal (trabecular MIGS) or to the subconjunctival space (subconjunctival MIGS).[11,13] The American Glaucoma Society published a position statement to define MIGS as procedures associated with rapid recovery, less impact on usual daily activities and lower risk of ocular tissue damage compared with traditional incisional glaucoma surgery.[14] Other potential advantages of MIGS over traditional glaucoma procedures include faster recovery, less impact on leisure activities (such as swimming), and reduced risk of damaging other structures in the eye, which may necessitate additional ocular surgeries.

Trabecular microbypass stents are commonly used MIGS implants. They work by augmenting the conventional aqueous outflow through Schlemm's canal,[15–17] bypassing the trabecular meshwork, which is thought to be the main site of aqueous outflow resistance in OAG.[18,19] Trabecular stents include the first-generation iStent, or iStent classic (Glaukos Corp, Laguna Hills, CA, USA), the second-generation iStent inject® (Glaukos Corp, Laguna Hills, CA, USA), and Hydrus® Microstent (Alcon, Geneva, Switzerland).

iStent classic

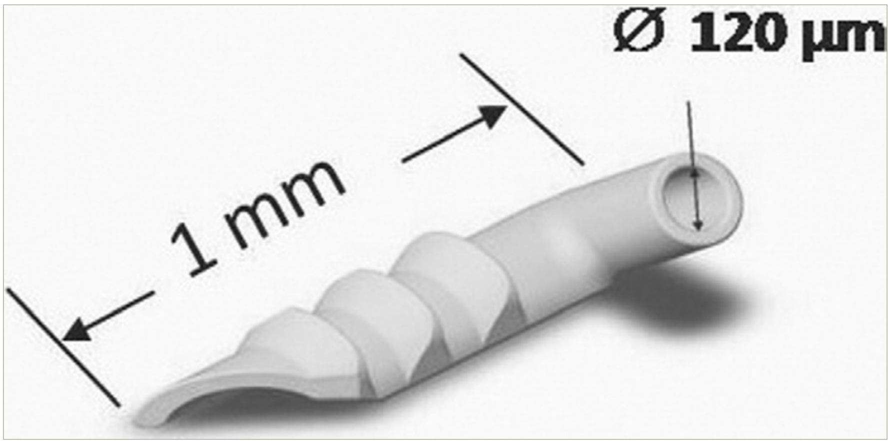
Design

The iStent classic is the first trabecular microbypass stent to be approved in the United States.[15] It is a heparin-coated, non-ferromagnetic titanium stent measuring 1 mm in length and 0.33 mm in height, with a snorkel length of 0.25 mm and a nominal snorkel bore diameter of 120 µm (*Figures 1 and 2*), making it the smallest implantable medical device ever approved for use in humans by the FDA at the time of approval.

Surgical technique

Intracameral viscoelastic is introduced through a corneal incision to deepen and maintain the anterior chamber.[15] The patient's head is turned 45° away from the surgeon, and the microscope is turned 45° toward the surgeon. Viscoelastic is placed on the cornea, and the handheld prism

Figure 1: Dimensions of the iStent® classic (Glaukos Corp, Laguna Hills, CA, US)



Courtesy of Glaukos Corporation.

is aligned so that the trabecular meshwork is visible. The device should be inspected and visualized in the inserter tip. The inserter (*Figure 3*) and the device should be advanced through a temporal clear corneal incision. The self-trephining tip of the iStent classic is used to penetrate the trabecular meshwork. Once the device is placed in Schlemm's canal, the inserter button is depressed to release the device. The inserter tip is used to fully drive the iStent classic into the canal.

In combined surgery, the timing of iStent implantation relative to phacoemulsification may vary according to the surgeon's preference and patient-related factors.[15] The iStent classic could be implanted prior to cataract surgery to take advantage of a clearer cornea and higher scleral rigidity and to ensure correct positioning before any potential intraoperative complications of cataract surgery. Nonetheless, implanting the device following phacoemulsification could provide a wider view of the angle and avoid the accidental touch of the anterior lens capsule. The surgeon may also choose to employ a trypan blue or indocyanine green stain at the time of cataract surgery to clearly outline the trabecular meshwork for better visualization prior to stent placement.

iStent inject

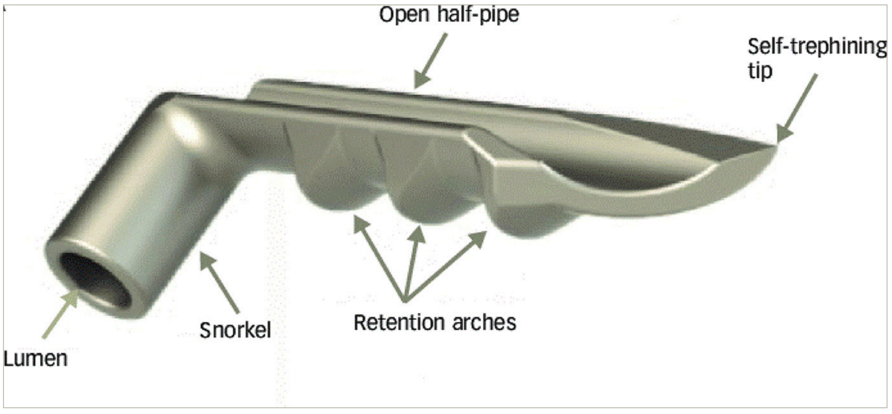
Design

The iStent inject contains two preloaded heparin-coated, biocompatible, implant-grade titanium stents.[16] The stent has a single-piece design measuring 230 µm in diameter and 360 µm in height (*Figure 4*). The central inlet and outlet lumens have a diameter of 80 µm, and the head has four side outlets of 50 µm each. The iStent inject is composed of three parts: the flange, which faces the anterior chamber; the head, which resides in Schlemm's canal; and the thorax, which is retained by the trabecular meshwork. Two stents are preloaded in the injector (*Figure 5*). Each stent is designed to allow smooth outflow of the whole amount of aqueous humour produced by the human eye per minute (average: 2.5 µl/min).[16] This multiple-stent implantation was developed to allow access to a higher number of collector channels and create arcs of outflow that can span up to six clock hours. Prior studies have shown that the nasal segment of the eye has more collector channels;[20,21] accordingly, nasal implantation of trabecular stents would provide better outflow. However, the distal post-canalicular outflow system is complex and may be controlled by other factors affecting IOP, even if the stents are patent in the nasal part of the canal.[20,21] Imaging the Schlemm's canal and collector channel system could help in evaluating the variation of aqueous outflow through the trabecular stents implanted in different angle locations.[22–24]

Surgical technique

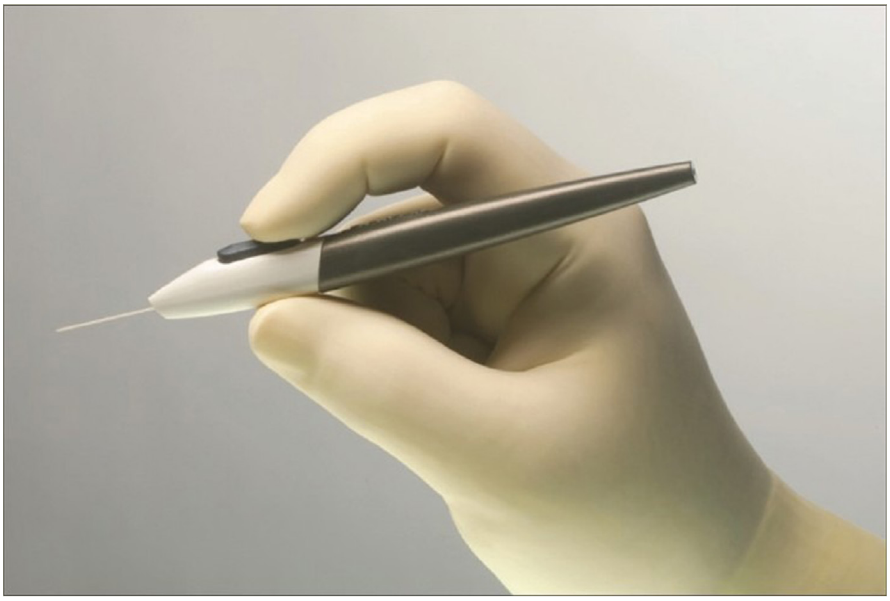
Intracameral viscoelastic is introduced through a corneal incision to deepen and maintain the anterior chamber. The patient's head is turned 45° away from the surgeon, and the microscope is turned 45° toward the surgeon. Viscoelastic is placed on the cornea, and the handheld prism is aligned so that the trabecular meshwork is visible. The injector is advanced through a temporal clear corneal incision, and the nasal angle and device are visualized. The sleeve of the injector is retracted,

Figure 2: Parts of the iStent® classic (Glaukos Corp, Laguna Hills, CA, USA)



Courtesy of Glaukos Corporation.

Figure 3: The insertor of iStent® (Glaukos Corp, Laguna Hills, CA, USA)



Courtesy of Glaukos Corporation.

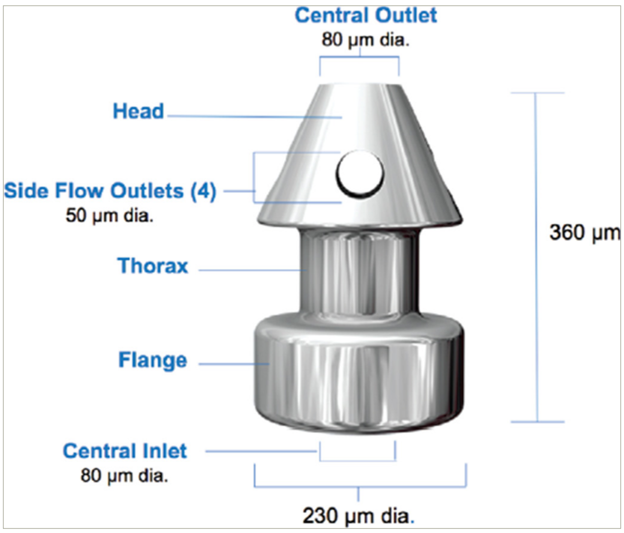
revealing the trocar and micro-insertion tube. The trabecular meshwork is penetrated by the trocar, and the delivery button is depressed to implant the first stent. The trocar is then moved two to three clock hours away, and the second stent is implanted. After confirmation of the correct stent placement, the viscoelastic is irrigated out. The timing of the stent implantation relative to cataract surgery is the same as in the first-generation iStent.

iStent infinite

Design

The iStent infinite® (Glaukos Corp, Laguna Hills, CA, USA) is the first FDA-cleared microinvasive implantable device indicated as a standalone treatment option for patients with OAG or patients undergoing concomitant cataract surgery.[25,26] It contains three heparin-coated, implant-grade, titanium, wide-flange stents (i.e. iStent inject® W [Glaukos Corp, Laguna Hills, CA, US], which measure 360 µm in diameter versus 230 µm in the regular iStent inject). The stents help to enhance visibility and facilitate implantation (*Figure 6*), and are preloaded in a sterile, single-use injector system (*Figure 7*). Each stent measures 360 µm in length, and the diameter of the rear flange is 360 µm. The thorax retains the stent within the trabecular meshwork, whereas four lateral outlet lumens on the head of the device facilitate multidirectional aqueous outflow from the anterior chamber into Schlemm's canal. Following implantation, only 3% of the angle is occupied by the three stents, while the remaining 97% is left untouched. The three stents are distributed over at least four clock hours of the angle, providing access to up to 240° of collector channels for aqueous outflow.[25]

Figure 4: Parts and dimensions of iStent inject® (Glaukos Corp, Laguna Hills, CA, USA)



Courtesy of Glaukos Corporation.
dia = diameter.

Surgical technique

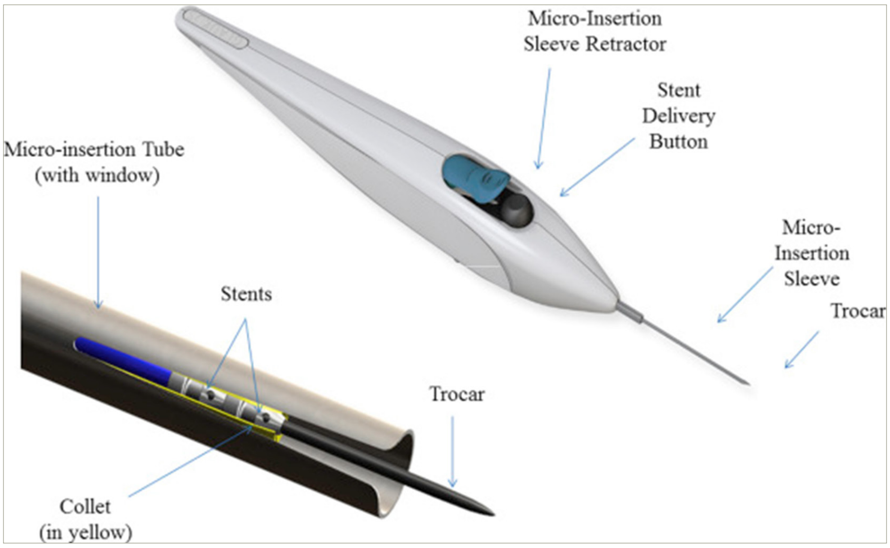
Intracameral viscoelastic is introduced through a corneal incision to deepen and maintain the anterior chamber. The patient's head is turned 45° away from the surgeon, and the microscope is turned 45° toward the surgeon. Viscoelastic is placed on the cornea, and the handheld prism is aligned so that the trabecular meshwork is visible. The iStent infinite injector is advanced under direct gonioscopy to the nasal trabecular meshwork, where the first stent is implanted. The injector tip is then repositioned to implant the second stent two clock hours away from the first stent. Additional viscoelastic is placed in the anterior chamber, and the surgeon then positions the third stent two clock hours away from either of the first two stents. Following confirmation of proper placement and seating, the viscoelastic is then removed.[25]

Hydrus Microstent

Design

The Hydrus Microstent is an 8 mm long, curved device that contains alternating spines for structural support and openings for aqueous outflow.[17] The scaffold design of the stent allows it to occupy Schlemm's canal without blocking the collector channel ostia in its posterior wall (*Figure 8*). The stent is made of nitinol, a nickel and titanium alloy with super-elastic properties, which enable it to return to its original shape following deformation. After insertion, the Hydrus Microstent can increase the diameter of Schlemm's canal up to four- to five-fold, which facilitates aqueous outflow and counteracts the luminal collapse induced by high IOP.[27,28]

Figure 5: iStent inject® (Glaukos Corp, Laguna Hills, CA, USA) delivery system



Courtesy of Glaukos Corporation.

Surgical technique

The delivery system is designed for both right- and left-handed surgeons. Currently, the Hydrus is inserted at the time of cataract surgery. It has a rotatable sleeve to facilitate the alignment of the cannula according to the surgeon's preference (*Figure 9*). A 1.5 mm long clear corneal incision is made, and the preloaded injector is placed through the paracentesis adjacent to the main wound. The cannula tip is advanced through the trabecular meshwork until it enters Schlemm's canal with the bevel flush against the entry point. The target tissue is then visualized using gonioscopy with a handheld prism. Once the distal cannula tip is confirmed to be positioned properly, the tracking wheel is used to advance and release the microstent. Following injection, the device occupies about two clock hours, or 90°, of Schlemm's canal and has a 1 mm inlet portion within the anterior chamber. Following confirmation of the appropriate device positioning, the injector is withdrawn, and the viscoelastic is removed from the anterior chamber.

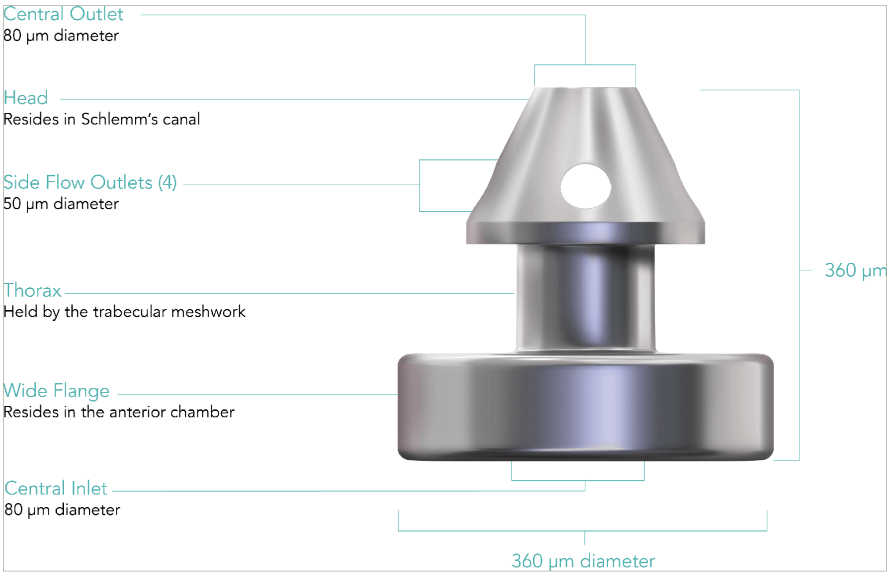
A comparison of trabecular stents

A summary of the studies comparing all trabecular stents is presented in *Table 1*.[29–44]

iStent classic versus iStent inject

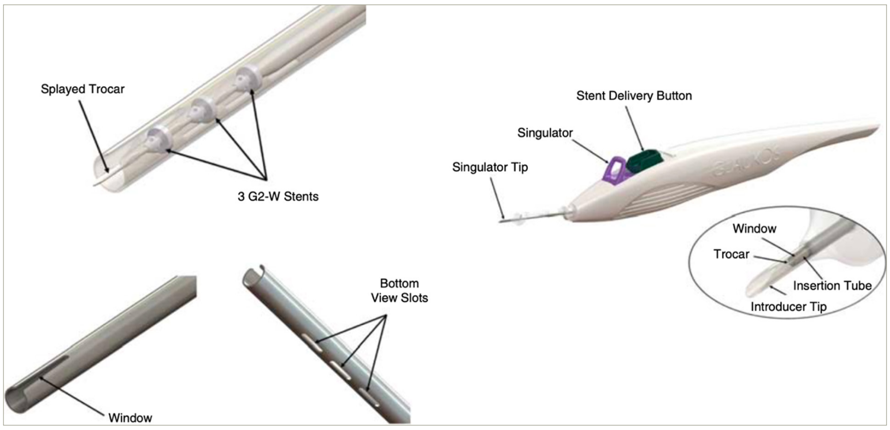
The efficacy of a single iStent classic was compared with double iStent inject combined with phacoemulsification in patients with OAG in a prospective case series conducted in two centres in Australia.[29] A total of 245 eyes from 148 patients with mild-to-moderate OAG were included, of whom 145 were treated with iStent classic and 100 with iStent inject. The mean baseline IOP and medication number were similar in both groups. After 1 year, the primary success rate (IOP ≤18 mmHg with no medications) was 56.0% versus 51.3%. The secondary success rate (IOP ≤18 mmHg with reduced medications number) was 63.1% versus 57.7% in the iStent classic group versus the iStent inject group, respectively. At 12 months, IOP was comparable in both groups

Figure 6: Parts and dimensions of iStent infinite® (Glaukos Corp, Laguna Hills, CA, USA)



Courtesy of Glaukos Corporation.

Figure 7: iStent infinite ® (Glaukos Corp, Laguna Hills, CA, USA) delivery system



Courtesy of Glaukos Corporation.

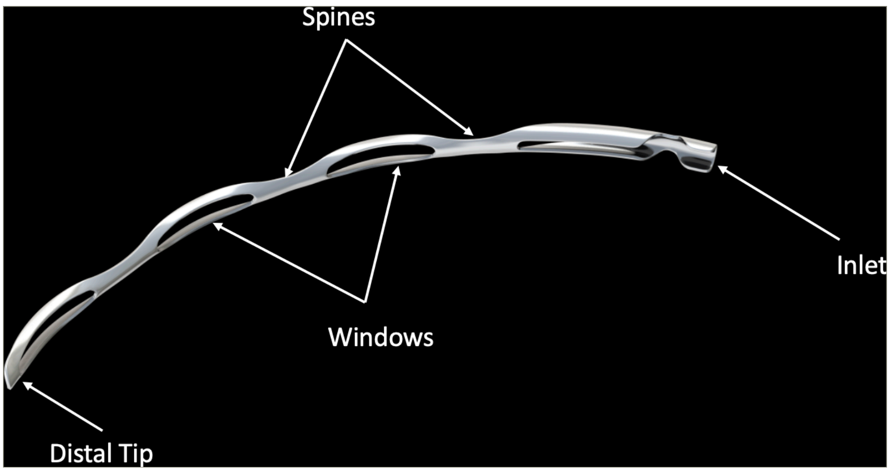
(16.6 mmHg versus 16.9 mmHg). There was a significant reduction in the medication number in both groups. After 1 year, 64.0% of iStent classic eyes and 68.0% of iStent inject eyes restarted hypotensive medications. The time needed before restarting glaucoma therapy was shorter for iStent inject (7 months) than for iStent classic (12 months). Such findings suggest that the first- and second-generation iStent treatments have comparable efficacy in terms of IOP and medication reduction. However, iStent inject was shown to require an earlier restart of topical glaucoma therapy.

Manning conducted a real-world retrospective case series in Australia that included 137 eyes with mild to moderate OAG, 67 of which were treated with iStent classic and 70 with iStent inject, with 1 year follow-up.[30] There was a significant reduction in IOP at month 12 in both the iStent classic and iStent inject groups compared with baseline (p<0.001 for both). However, iStent inject was shown to have a significantly greater IOP-lowering effect than iStent classic (6.0 mmHg versus 4.2 mmHg; p=0.034). Effectiveness endpoints, defined as IOP ≤18 mmHg, were achieved in 95.7% of iStent inject eyes versus 92.5% of iStent classic eyes. Both groups experienced significant medication reduction at month 12 compared with baseline (p<0.001 for both). However, iStent inject was shown to have greater a reduction of medication number (94.7%) compared with iStent classic (84.0%) (p<0.001 for both). More iStent inject eyes were medication free at 1 year (92.9%) compared with iStent classic eyes (76.1%) (p=0.0068). This study concluded that, while both iStent classic and Stent inject were effective through 1 year in terms of IOP and medication reduction, iStent inject demonstrated greater efficacy than iStent classic.

A smaller retrospective consecutive case series (N=58) on eyes with OAG also indicated the superiority of iStent inject.[31] Uneventful cataract surgery was performed in all eyes combined with either iStent classic (n=35) or iStent inject (n=23). The mean follow-up duration was 12 months. At month 12, IOP was reduced from 16.1 ± 3.6 mmHg at baseline to 15.4 ± 2.4 mmHg in iStent classic eyes (p=0.201). On the other hand, iStent inject eyes showed significant IOP reduction from 16.2 ± 3.1 mmHg to 13.1 ± 2.2 mmHg (p<0.001). Between-group comparison showed significantly greater IOP reduction in iStent inject eyes (19.1%) than in iStent classic eyes (4.3%) (p<0.001), even though preoperative IOP was comparable in both groups (p=0.882). Similarly, both groups had a comparable medication number at baseline (1.8 ± 0.8 versus 1.7 ± 3.1; p=0.565), and both groups achieved significant medication reduction at month 12 (p<0.001 for all). However, medication reduction was significantly greater in iStent inject eyes than in iStent classic eyes (p=0.023). Additionally, more iStent inject eyes became medication free at month 12 compared with iStent classic eyes (95.7% versus 71.4%, respectively; p=0.021).[31]

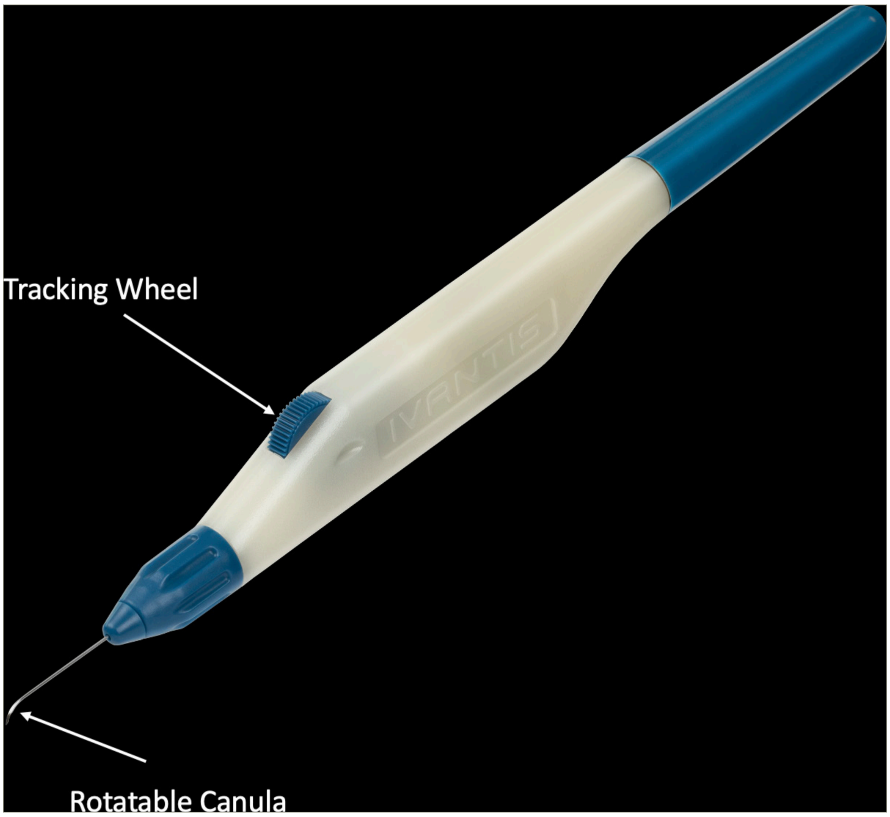
The intermediate 6-month results of the same study were published in a separate cohort, as more eyes were available for the analysis

Figure 8: Parts of Hydrus® Microstent (Alcon, Geneva, Switzerland)



Courtesy of Alcon.

Figure 9: Hydrus® Microstent (Alcon, Geneva, Switzerland) delivery system



Courtesy of Alcon.

(N=73; iStent classic: n=38; iStent inject: n=35).[32] Both groups achieved significant IOP reduction at month 6 compared with baseline (p<0.001 for all). However, IOP reduction was still significantly greater in the iStent inject group than in the iStent classic group (26.6% versus 15.8%; p=0.005). The number of eyes that reached IOP ≤18 mmHg at 6 months was significantly higher in the iStent inject group than in the iStent classic group (100.0% versus 86.8%; p=0.033). Significant medication reduction was achieved in both groups (p<0.001 for all), but iStent inject showed significantly higher medication reduction compared to iStent classic. No additional glaucoma surgery was required for iStent inject eyes; however, two iStent classic eyes required reoperation for glaucoma at month 6, one of whom was included in the 12 month analysis. In conclusion, the superiority of iStent inject over iStent classic was shown at both 6 and 12 months in this study.

Shalaby et al. retrospectively compared the outcomes of iStent classic versus iStent inject when combined with cataract surgery in subjects with OAG in the United States.[33] A total of 197 eyes of 148 patients were included (iStent classic: n=122; iStent inject: n=75). Significant IOP and medication reduction was achieved in both groups at months 6 and 12 compared with baseline (p<0.05 for all). At month 6, IOP was significantly lower in iStent inject eyes compared with iStent classic eyes (p=0.003); however, the difference was nonsignificant by month 12 (p=0.172). Medication number was comparable in both groups at months 6 and 12 (p>0.05). More iStent inject eyes achieved IOP ≤15 mmHg at month 6 (p=0.003) and 12 (p=0.047). Surgical success, defined as a 20% IOP reduction from baseline, was comparable in both groups at months 6 and 12 (p>0.05). The cumulative rate of surgical failure was found to be similar in both groups at year 1 (p=0.644) using the Kaplan–Meier survival analysis. Multivariate regression analysis was conducted to identify factors predicting surgical failure. The model identified older age (p=0.017) and lower baseline IOP (p=0.002) as the strongest predictors of surgical failure.

Efficacy of iStent infinite

Sarkisian et al.[25] evaluated the safety and efficacy of iStent infinite as a standalone procedure in patients with uncontrolled OAG on maximum medical therapy or with prior failed glaucoma surgery in a prospective multicentre clinical trial. Seventy-two eyes of 72 patients were enrolled. A total of 76.1% of eyes met the effectiveness endpoint (i.e. a 20% IOP reduction on the same or fewer medications) at month 12. For patients on the same or fewer medications as baseline, 53.0% achieved a ≥30% IOP reduction without surgical interventions. The safety findings were favourable, with no major complications.

iStent classic versus Hydrus Microstent

The COMPARE study prospectively compared the outcomes of standalone Hydrus Microstent with two standalone first-generation iStents in eyes with OAG up to 1 year.[34] It included 152 eyes from 152 patients, who were randomized to either the Hydrus group (n=75) or the iStent classic group (n=77). The original study design included medication washout at baseline and postoperative month 12 to allow a direct comparison between the two devices in terms of non-medicated IOP reduction. However, this protocol was altered per the investigators' recommendations, as 20% of eyes developed uncontrolled IOP on maximum tolerated medical therapy, which did not allow for medication washout at postoperative month 12. Compared with baseline, IOP reduction was significantly lower throughout the first year postoperatively, with no difference between groups (p=0.300). However, the medication number was significantly lower in the Hydrus group compared with the iStent classic group (p=0.004). Additionally, the Hydrus group showed a significant reduction in the number of eyes at IOP ≤21, 18 and 15 mmHg at postoperative

Table 1: Summary of studies comparing trabecular stents

Author	Year	Site	Journal	Design	Number of eyes	Comparison	OAG severity	Follow-up period (months)	IOP reduction	Medication reduction	Effectiveness endpoint	Rate	Notes
Hooshmand et al.[29]	2019	Australia	*Clinical and Experimental Ophthalmology*	Prospective comparative case series	245	iStent classic versus iStent inject	Mild to moderate	12	Comparable	Comparable	IOP ≤18 mmHg	63.1% versus 57.7%	iStent inject required earlier restart of topical glaucoma therapy
Manning[30]	2019	Australia	*Ophthalmology and therapy*	Retrospective case series	137	iStent classic versus iStent inject	Mild to moderate	12	iStent inject was superior	iStent inject was superior	IOP ≤18 mmHg	92.5% versus 95.7%	More iStent inject eyes were medication free at 1 year versus iStent classic eyes
Guedes et al.[31]	2019	Brazil	*Advances in Therapy*	Retrospective consecutive case series	58	iStent classic versus iStent inject	Mild to moderate	12	iStent inject was superior	iStent inject was superior	IOP ≤18 mmHg	80.0% versus 100.0%	More iStent inject eyes were medication free at 1 year versus iStent classic eyes
Guedes et al.[32]	2019	Brazil	*Ophthalmology and therapy*	Retrospective case series	73	iStent classic versus iStent inject	Mild to moderate	6	iStent inject was superior	iStent inject was superior	IOP ≤18 mmHg	86.8% versus 100.0%	2 iStent classic eyes versus 0 iStent inject eyes required reoperation for glaucoma at month 6
Shalaby et al.[33]	2021	United States	*Indian Journal of Ophthalmology*	Single-centre retrospective comparative case series	197	iStent classic versus iStent inject	Mild to severe	12	Comparable	Comparable	IOP ≤15 mmHg	46.7% versus 61.4%	Multivariate regression analysis identified older age and lower baseline IOP as the strongest predictors of surgical failure
Ahmed et al.[34]	2020	United States, Canada, Europe, Asia	*Ophthalmology*	Prospective, multicentre, randomized clinical trial	152	iStent classic versus Hydrus Microstent	Mild to moderate	12	Comparable	Hydrus was superior	IOP ≤18 mmHg + 0 medications	9.3% versus 30.1%	More Hydrus eyes were medication free at 1 year versus iStent classic eyes; 2 iStent classic eyes versus 0 Hydrus eyes required reoperation for glaucoma at 1 year

Continued

Table 1: Continued

Author	Year	Site	Journal	Design	Number of eyes	Comparison	OAG severity	Follow-up period (months)	IOP reduction	Medication reduction	Effectiveness endpoint	Rate	Notes
Alcon[35]	2019	United States, Canada, Europe, Asia	Unpublished	Prospective randomized clinical trial	152	iStent classic versus Hydrus	Mild to moderate	24	Comparable	Hydrus was superior	20% IOP reduction	40.0% versus 63.0%	Double the number of Hydrus eyes were medication free versus iStent classic eyes at 2 years; 9% of iStent classic eyes versus 0 Hydrus eyes required reoperation for glaucoma at 2 years
Hu et al.[36]	2022	United States, Europe	*BMJ Open*	Systematic review and network meta-analysis	1,397	iStent classic versus Hydrus	Mild to moderate	12 to 24	Hydrus was superior	Comparable	IOP ≤21 mmHg + 0 medications	Hydrus and 2-iStent classic had a higher complete success compared with 1-iStent classic	Focal peripheral anterior synechiae was more shown with Hydrus
Holmes et al.[37]	2022	Australia	*Clinical & Experimental Ophthalmology*	Retrospective case series	344	iStent inject versus Hydrus	Mild to moderate	24	Comparable	Comparable	IOP ≤18 mmHg	37.9% versus 38.3%	5.4% of iStent inject eyes versus 7.5% of Hydrus eyes required reoperation for glaucoma at 2 years
Favre et al.[38]	2021	United States	*Investigative Ophthalmology & Visual Science*	Retrospective case series	73	iStent inject versus Hydrus versus Kahook	Mild to moderate	6	Comparable	iStent inject was superior	N/A	N/A	iStent inject had significantly lower medication number at baseline
Toris et al.[39]	2020	United States	*Ophthalmology Glaucoma*	Experimental, randomized design	36 pairs of dissected anterior segments	iStent classic versus iStent inject versus Hydrus	Non-glaucomatous human eyes	N/A	Hydrus was superior (outflow facility)	N/A	N/A	N/A	The longer the stent, the more the Schlemm's canal dilation, the greater the outflow facility

Continued

Table 1: Continued

Author	Year	Site	Journal	Design	Number of eyes	Comparison	OAG severity	Follow-up period (months)	IOP reduction	Medication reduction	Effectiveness endpoint	Rate	Notes
Shalaby et al.[40]	2023	United States	*Journal of Glaucoma*	Retrospective case series	435	iStent classic versus iStent inject versus Hydrus	N/A	3	Comparable	Comparable	N/A	N/A	Hyphema was most common with Hydrus microstent versus iStent classic and iStent inject
Gonnermann et al.[41]	2017	Germany	*Graefes Archive for Clinical and Experimental Ophthalmology*	Retrospective case series	54	iStent inject versus Trabectome	Mild to moderate	12	Comparable	Comparable	IOP ≤21 mmHg + 20% IOP reduction	Comparable	Trabectome was implanted in one eye versus iStent inject in the contralateral eye of the same patient
Pantalon et al.[42]	2020	Europe	*British Journal of Ophthalmology*	Retrospective case series	109	2 iStents-cataract extraction-ICE2 versus phacoemulsification-iStents inject	Mild to moderate	12	ICE2 group was superior	ICE2 group was superior	N/A	N/A	
Gandolfi et al.[43]	2016	Italy	*Journal of Ophthalmology*	Retrospective case series	45	Hydrus versus canaloplasty	Mild to moderate	24	Comparable	Comparable	0 medications	33.3% versus 50.0%	
Shalaby et al.[44]	2021	United States	*Journal of Cataract and Refractive Surgery*	Retrospective case series	436	iStent classic versus iStent inject versus Hydrus versus gel stent versus goniotomy	Mild to severe	3	N/A	N/A	N/A	N/A	Trabecular stent group has lowest proportion of reoperation versus gel stent and goniotomy

ICE2 = iStent-cataract extraction-endocyclophotocoagulation; IOP = intraocular pressure; N/A = not applicable; OAG = open-angle glaucoma.

month 12 versus baseline, while the iStent classic group showed no significant changes. Moreover, the Hydrus group had a higher percentage of patients who were medication free at month 12 compared with the iStent classic group (p=0.006), as well as a significantly lower percentage of eyes on three or more medications in the Hydrus versus the iStent classic group (p=0.001). Similarly, the number of eyes with a medication reduction of three or more was significantly higher in the Hydrus group compared with the iStent classic group (p=0.002). The study speculated that stretching the trabecular meshwork by the Hydrus scaffold to prevent the collapse of Schlemm's canal may be the reason behind the improved aqueous drainage and superiority of Hydrus over the iStent classic. Although the study showed better outcomes for Hydrus in terms of medication reduction, there is a debate about the validity of these outcomes since the study investigators were reluctant to conduct a month-12 medication washout.[34]

The superiority of Hydrus in treating OAG was also shown in the COMPARE study. Twice the number of eyes of the iStent classic group were medication free in the Hydrus group at postoperative month 24.[35] Medication use was lowered on average by 52% in the Hydrus eyes compared with 29% in the iStent classic eyes. Reoperation for glaucoma was required in 9% of the iStent classic eyes versus 0% of the Hydrus eyes. A 20% IOP reduction was achieved in 63% of Hydrus eyes versus 40% of the iStent classic eyes. Despite these differences, both groups were shown to have a more stable IOP and medication reduction at 24 months compared with the earlier outcomes at month 12.

Hu et al. compared the efficacy and safety of iStent classic and Hydrus Microstent combined with phacoemulsification in subjects with OAG in a systematic review and network meta-analysis.[36] Effectiveness was estimated using IOP reduction, the percentage of IOP reduction, and the proportion of medication-free eyes by the end of follow-up. Six prospective randomized clinical trials with 1,397 patients were included. Both devices combined with phacoemulsification were significantly more effective than phacoemulsification alone. Hydrus was shown to be a better option for IOP reduction using rank probability analysis, and the proportion of medication free eyes was found to be equal in the two groups. Compared with 1-iStent classic implantation or phacoemulsification alone, Hydrus and 2-iStent classic implantation were more likely acquire a medication-free status. In terms of safety, both devices had a good profile. Focal peripheral anterior synechiae was more shown with Hydrus, perhaps due to its larger size.

iStent inject versus Hydrus

Holmes et al. compared 2-year results of iStent inject versus Hydrus Microstent combined with phacoemulsification.[37] They included 344 eyes with OAG (iStent inject: n=224; Hydrus Microstent: n=120), and patients were matched for baseline characteristics. At 2 years, IOP and medication reduction were similar in both groups. iStent inject achieved a 3.1 mmHg reduction and Hydrus a 2.3 mmHg reduction (p=0.530). The mean medication reduction was 1.0 for iStent inject versus 0.5 for Hydrus (p=0.081). Reoperation for glaucoma was required in 5.4% of iStent inject eyes and in 7.5% of Hydrus eyes. Complications were infrequent and similar in both groups.[37]

Another retrospective study compared the efficacy of phacoemulsification combined with either iStent inject (n=38), Hydrus Microstent (n=24) or Kahook Dual Blade® goniotomy (New World Medical, Rancho Cucamonga, CA, USA) (n=31) to treat OAG in a Hispanic population from the United States.[38] Although the percent IOP reduction at month 6 did not statistically differ across groups (10.55%, 4.24%, and 7.74%, respectively; p=0.75), a lower number of glaucoma medications was significantly associated with the iStent inject. All complications were mild in severity and self-limiting in all groups.

iStent classic versus iStent inject versus Hydrus

Toris et al. studied the effect of 3 trabecular stent devices on outflow facility in a randomized design. Thirty-six pairs of dissected anterior segments from non-glaucomatous human eyes were included.[39] Outflow facility was measured at baseline and following implantation of a trabecular stent (1 iStent, 2 iStent, 2 iStent inject versus Hydrus Microstent) or sham procedure. Significant increase in the outflow facility was observed with Hydrus compared with 2 iStent inject (p=0.018). The 1 iStent group showed higher outflow facility from baseline compared with the sham procedure (p=0.042). The study concluded that the longer the MIGS device, the more the Schlemm's canal dilation and the greater the outflow facility.

A retrospective study compared the incidence of postoperative haemorrhagic complications in patients on antithrombotic therapy (ATT) and controls following combined trabecular stent implantation and phacoemulsification within the 3-month postoperative period in a single centre.[40] They included 333 patients (435 eyes), of whom 161 patients (211 eyes) were in the ATT group and 172 patients (224 eyes) in the control group. Hyphema was the only observed hemorrhagic complication and was seen in 84 eyes (19.3%). Stent type significantly affected the incidence of hyphema (19.9% in iStent classic, 8.5% in iStent inject and 36.4% in Hydrus; p=0.002). However, ATT intake was not significantly associated with hyphema (p=0.827). Hyphema associated with IOP spike was similar between groups (p=0.878). Reoperations for hyphema or associated IOP spike were not required. At month 3, visual outcomes, IOP reduction and medication reduction were similar between groups (p<0.001 for all). The higher rate of hyphema with Hydrus may be related to its relatively large size compared with iStent and iStent inject. While both iStent and Hydrus bypass the trabecular meshwork, iStent penetrates approximately 1 mm into Schlemm's canal, while Hydrus dilates approximately 90 degrees of the Schlemm's canal.[34] Although the wider surface area of Hydrus Microstent has been shown to enhance the outflow facility in laboratory experiments[45] and may have led to greater surgical success in clinical trials as compared to two iStents,[34] it may also lead to a higher incidence of hyphema as the device involves a larger part of the Schlemm's canal. Additionally, a higher rate of hyphema in the Hydrus group was not associated with a greater incidence of IOP spikes, possibly due to its greater outflow facility. Although hyphema was most common following Hydrus and least common following iStent inject, the results were not conclusive given the small sample size of Hydrus included in the study.[40]

Trabecular stents versus other minimally invasive glaucoma surgeries

A retrospective study conducted by Gonnermann et al.[41] compared two trabecular MIGS combined with phacoemulsification in the same patient: Trabectome® (NeoMedix Corporation, Tustin, CA, USA) in one eye versus iStent inject in the contralateral eye. A total of 54 eyes of 27 patients were included in this intra-individual eye comparison with similar baseline characteristics. At month 12, both devices achieved significant IOP reduction compared with baseline (p<0.001). However, there was no significant difference in postoperative IOP between the two groups (p>0.05). Likewise, a significant reduction of medication number compared with baseline was observed in both groups (p<0.05), with no significant difference between groups except at postoperative week 6, as the medication number was higher in the Trabectome group compared with the iStent group, which may be related to the use of pilocarpine 1% eye drops in the first postoperative 6 weeks in the Trabectome group only.

A retrospective case series compared the outcomes of two iStent-cataract extraction-endocyclophotocoagulation (ICE2 group) versus phacoemulsification-iStents inject alone (phaco-iStent group).[42] Significant IOP and medication reduction was observed in both groups at months 6 and 12 compared with baseline. The IOP percentage reduction at month 12 in the ICE2 group (35%) was significantly higher than the phaco-iStent group (21%) (p=0.03). Likewise, the IOP (13.0 ± 2.1 mmHg versus 14.0 ± 1.8 mmHg) and medication number (1.2 ± 1.0 versus 1.3 ± 1.0) at month 12 were lower in the ICE2 group than ihe phaco-iStent group (p<0.05 for all). Both groups had similar outcomes in terms of safety profile. However, the conclusion was in favour of the ICE2 procedure over phaco-iStent alone in terms of efficacy.

The results of canaloplasty versus Hydrus Microstent were investigated retrospectively over 2 years in patients with uncontrolled IOP in OAG.[43] Both canaloplasty and Hydrus Microstent implantation achieved significant IOP reductions and a similar rate of surgical success and safety outcomes.[43]

Shalaby et al. described reoperations that occurred within 90 days of different MIGS procedures in a single centre retrospective study over a follow-up duration of 30 months.[44] A total of 448 MIGS procedures were performed on 436 eyes of 348 patients. Of these, 206 (46.0%) were trabecular microbypass stents (198 iStent/iStent inject and 8 Hydrus), 152 (33.9%) were gel microstents, and 90 (20.1%) were goniotomy procedures. Cataract surgery was combined with MIGS in 256 eyes (58.7%). Reoperation within 90 days was required in 23 (5.3%) of 436 eyes, with the lowest proportion in the trabecular stent group (4 [2.0%] of 198 eyes) versus 16 (10.5%) of 152 eyes in the gel microstent group, and 3 (3.3%) of 90 eyes in the goniotomy group. High IOP (two eyes) and lens-related complications (two eyes) were the main indications for reoperation in the trabecular stent group.

Conclusions

Trabecular stents have been shown to be safe and effective procedures in the management of OAG, either as a standalone procedure or combined with phacoemulsification. The iStent inject is suggested to be superior to the first-generation iStent classic in both pressure-lowering ability and medication use. Whether Hydrus Microstent is superior over the iStent classic and iStent inject remains a controversial question, and more large randomized clinical trials are required to answer this. ❑

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