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Cataract & Refractive Surgery Today | *EUROPE EDITION*

iSTENT TECHNOLOGIES: Long-Term Evidence, Real-World Experience, and Systematic Reviews

Early intervention in glaucoma made simple.

Long-Term Evidence With iStent *inject*

A 7-year study supports the positive impact of the device on glaucoma care.

WATCH IT NOW

BY FRITZ HENGERER, MD, PHD

In 2016, the University of Heidelberg embarked on a long-term, real-world study of the iStent *inject*® (Glaukos) as both a standalone procedure and combined with cataract surgery.[1] **Now, 7 years later, our data highlights more than just the success of the procedure—it confirms that the outcomes can have a profound impact on the quality of life of our patients.**

REAL-WORLD OUTCOMES DATA

A total of 125 patients were enrolled. A combined procedure was performed in 81 eyes, and a standalone iStent *inject* procedure was performed in 44 eyes. IOP before surgery was slightly lower in the combined group, but these patients had undergone prior glaucoma surgery and were on multiple medications to manage their condition.

After 7 years, IOP decreased to 14 mm Hg, the mean IOP decreased by about 9 mm Hg, and patients had sustained a 59% reduction in medications (Figure), **demonstrating the sustained efficacy of the iStent *inject* technology**. There were **no intraoperative or early postoperative complications,** including anterior synechiae, a dislocated stent, hypotony, or choroidal hemorrhage. Seven eyes, two from the combined surgery group and five from the standalone iStent *inject* group, underwent a nonfiltering glaucoma procedure due to disease progression unrelated to stent implantation. **No filtering surgery was required over the 7-year follow-up.**

Our study found that even **higher IOP values can be managed effectively with the iStent *inject*.** Additionally, the procedure can **mitigate the need for future, more invasive procedures**. These findings underscore the **importance of early intervention** and point to the promise of sustained reduction of IOP and medication use for our **patients' quality of life.**

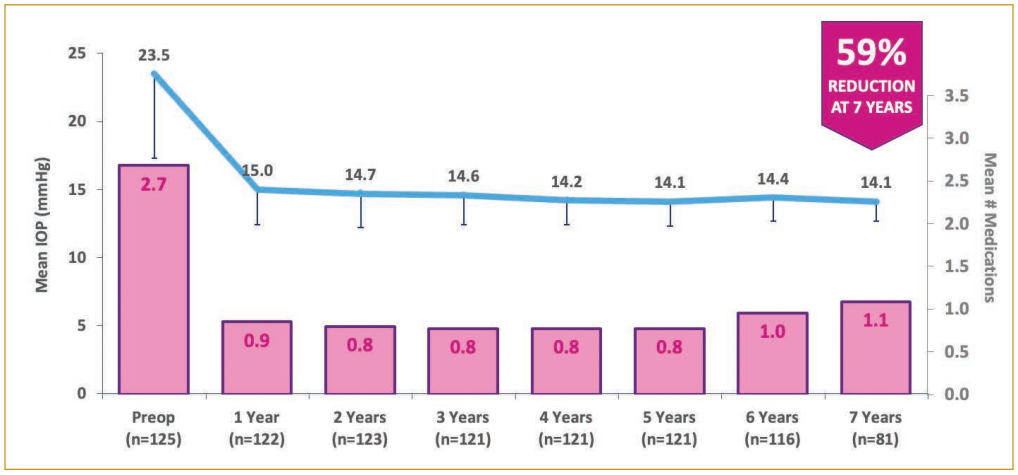

Figure. Sustained IOP reduction was seen at 7 years.

CONCLUSION

Whether combined with cataract surgery or as a standalone procedure, the iStent *inject*® W challenges the traditional norms in glaucoma management. Our 7-year journey with the iStent *inject* at the University of Heidelberg reinforces the **importance of both patient selection and early intervention.** Future advancements, such as the iStent infinite technology, offer hope for addressing more advanced glaucoma in a single session. ■

1. Hengerer FH, Auffarth GU, Conrad-Hengerer I. Sustained 7-Year Glaucoma Control after Second-Generation Trabecular Micro-Bypass with or without Cataract Surgery. Presentation at the Annual Meeting of the European Society of Cataract and Refractive Surgeons (ESCRS); September 8-12, 2023: Vienna, Austria

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iStent *inject* W: A Game Changer for Clinical Practice

Preserving patients' visual function and acuity.

BY FAISAL AHMED, MBBS, BSC(HONS), FRCOPHTH

WATCH IT NOW

MIGS devices have come to the forefront of the glaucoma landscape, challenging the paradigm of patient care. Notably, the **iStent *inject*® W (Glaukos) has emerged as a valuable tool for interventional glaucoma**, transforming the way we approach patients with mild to moderate disease.

It is tempting to think about the ideal patient for the iStent *inject* W, focusing primarily on aspects of the disease and treatment targets and goals. My experience with the iStent® technologies in clinical practice has been transformative to the way I care for patients. **Rather than thinking about the treatment first, I now think about treating the patient first.** This, in my opinion, includes **considering the iStent *inject* W for all glaucoma patients undergoing cataract surgery** who have no contraindications for the procedure. **We must think about patients' best long-term interests and involve them in the treatment decision**.

BENEFITS OF COMBINED PROCEDURES

Combining the iStent *inject* W with cataract surgery in patients with mild to moderate glaucoma can help **reduce their medication burden, improve their quality of life, and reduce the progression of their functional disease.**[1] Performing a trabecular microbypass procedure earlier in the disease state helps curb the progression of functional disease over time.

The iStent technologies have traditionally been reserved for patients with mild to moderate glaucoma, especially those taking medications for other conditions such as ocular surface disease and those patients who have difficulty instilling their eye drops such as those with arthritis.

Combining procedures also shifts patients from a moderate to low-risk category for disease progression.

Regardless of the target glaucoma patient population, including a trabecular microbypass strategy such as the iStent *inject* W technologies as a routine procedure is important in the current management landscape.

LONG-TERM SAFETY AND STABILITY

iStent *inject*® W has an overall high safety profile similar to standalone cataract surgery.[2]

Long-term studies also demonstrate that the iStent technologies effectively lower IOP and ultimately preserve visual function and acuity. In a 5-year prospective, longitudinal case series of standalone and combined iStent *inject* procedures in 125 patients with a high preoperative treatment burden, the visual field, retinal nerve fiber layer thickness, and cup:disc ratio were positive (Table 1).[3] **Patients who underwent combined cataract and iStent procedures exhibited stable visual fields and reduced reliance on glaucoma medications over 5 years.** In another study of 41 patients in low- and high-risk subgroups, only five patients required further surgery during a 7-year follow-up period. Four of the five were in the high-risk group (Table 2).[4]

PERSONAL EXPERIENCE

I have been implanting iStents for over 10 years. I recently performed an observational,

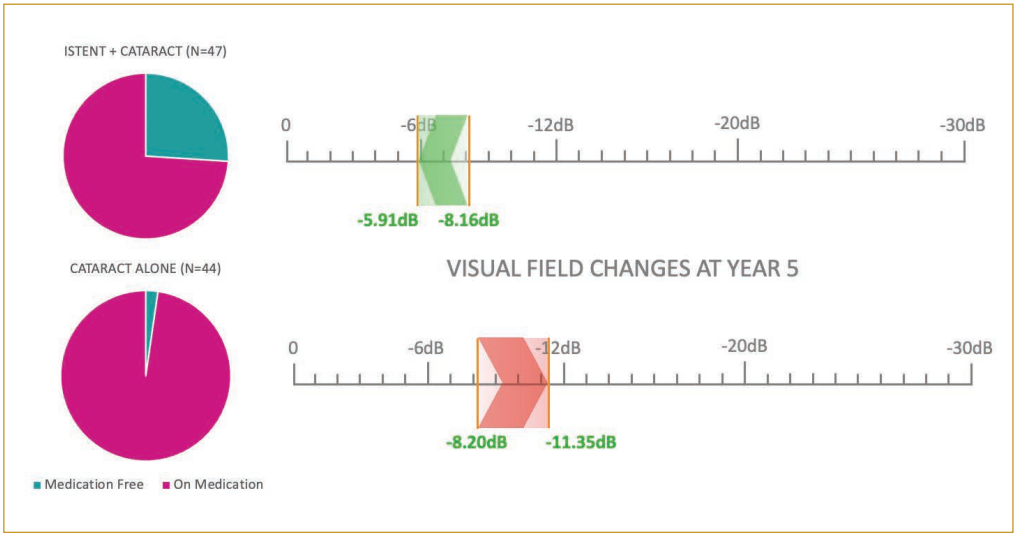

Figure. Data from Dr. Ahmed's practice showing the visual field changes and medication burden 5 years after iStent implantation.

TABLE 1. Disease Stability: Standalone Versus Combined iStent *inject* Procedures

	STAND ALONE (N=44)	COMBINED WITH CATARACT (N=81)
VF MD	-7.0 vs -7.1 (*P* = 0.502)	-6.6 vs -6.7 (*P* = 0.462)
RNFL	82.1 vs 80.9 (*P* = 0.194)	81.4 vs 80.2 (*P* = 0.497)
C:D RATIO	0.78 vs 0.79 (*P* = 0.386)	0.74 vs 0.76 (*P* =0.324)

TABLE 2. Disease Stability: Low-Risk Versus High-Risk Groups

	LOW RISK SUBGROUP (N=27)	HIGH RISK SUBGROUP (N=14)
VF MD	-7.58 vs -8.16 (*P* = 0.44)	-10.31 vs -10.79 (*P* = 0.67)
IOP (mmHg)	19.5 vs 17.9 (*P* = 0.05)	24.7 vs 17.9 (*P* = 0.0006)
C:D RATIO	0.63 vs 0.67 (*P* = 0.01)	0.75 vs 0.79 (*P* = 0.04)

retrospective, longitudinal cohort study of 91 well-matched patients with open-angle glaucoma or ocular hypertension who underwent either cataract surgery plus the first-generation iStent (n = 47) or cataract surgery alone (n = 44).

The results showed that **patients who received the iStent had statistically significantly less visual field progression and were better controlled on fewer medications.** Further, 26% were medication-free at 5 years. At that time, the mean IOP reduction was 6.8 mm Hg in the combination group but only 4 mm Hg in the standalone group. Patients in the combination group also had a mean reduction in medications at 5 years postoperative (2.36 to 1.39) whereas the standalone group experienced an increase in medication use (1.65 medications). Visual field changes are found in the Figure.

CONCLUSION

In my practice, **the iStent *inject* W is an important treatment modality for the management of glaucoma.** It can be seamlessly integrated into our cataract surgery workflow, **helping patients reduce the medication burden and maintain stable visual function at both mild to moderate stages of disease.** ■

1. Husain R, Liang S, Foster PJ, et al. Cataract surgery after trabeculectomy: the effect on trabeculectomy function. *Arch Ophthalmol*. 2012;130(2):165-170.
2. Samuelson TW, Sarkisian SR Jr, Lubeck DM, et al. Prospective, randomized, controlled pivotal trial of an ab interno implanted trabecular micro-bypass in primary open-angle glaucoma and cataract: two-year results. *Ophthalmology*. 2019;126(6):811-821.
3. Hengerer FH, Auffarth GU, Conrad-Hengerer I. iStent inject trabecular micro-bypass with or without cataract surgery yields sustained 5-year glaucoma control. *Advances in Therapy*. 2022;39(3):1417-1431.
4. Ziaei H, Leon A. Manchester iStent study: long-term 7-year outcomes. *Eye*. 2021;35(8):2277-2282.

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The Real-World Impact of iStent *inject* W on Patients' Quality of Life

Shifting focus to quality of life outcomes is transformative.

BY GOK RATNARAJAN, MD

WATCH IT NOW

Our primary goal as glaucoma surgeons is to improve the lives of our patients. Trabecular micro-bypass devices like **the iStent *inject*® W (Glaukos) provide an opportunity for patients to experience a better quality of life.** It can improve their visual function and ease their fears about glaucoma-related sight loss, as data from more than 300 studies show.

Traditionally, the success of glaucoma surgery was measured by the reductions in IOP and medications. **Today, however, the focus is shifting to quality of life outcomes. iStent *inject*® is the first and only MIGS device to show significant durable vision-related quality of life improvements in a pivotal trial.[1]**

PIVOTAL TRIAL RESULTS

The pivotal study of 505 patients evaluated patient-reported outcomes after iStent *inject* plus phacoemulsification (n = 387) or phacoemulsification alone (n = 118).[1] The Visual Functioning Questionnaire-25 (VQF-25) and the Ocular Surface Disease Index (OSDI) were used to assess the impact of surgery on patients' overall quality of life at 1, 6, 12, and 24 months.

Patients in both groups reported improvements in their quality of life, but the **improvements were greater in patients who underwent phacoemulsification combined with the iStent *inject* procedure.**

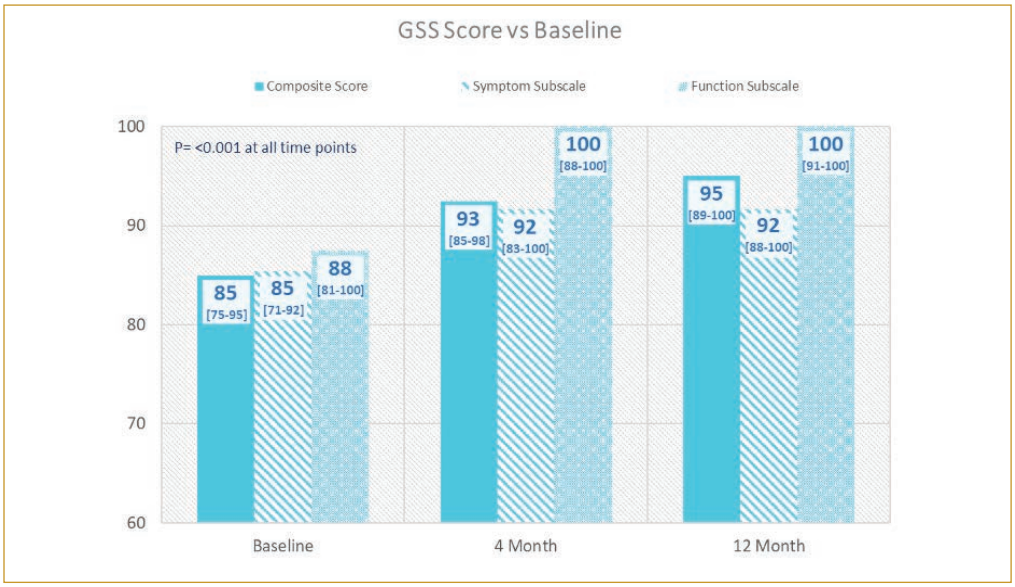

Figure 1. Patient-reported quality of life outcomes at Dr. Ratnarajan's practice.

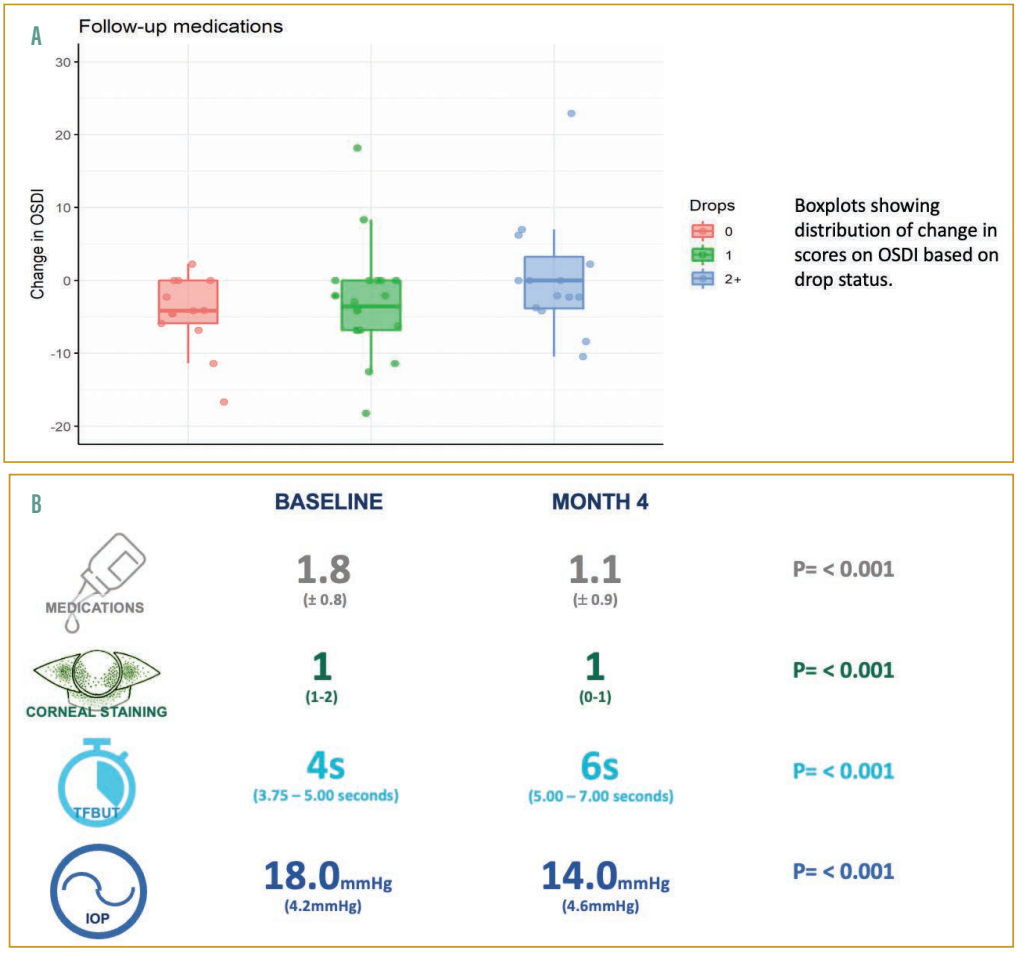

Figure 2. Mean change in OSDI (A) and changes in medications, corneal staining, tear breakup time, and IOP (B) at Dr. Ratnarajan's practice.

Overall, patient-reported improvements in the iStent *inject* group were not confined to the immediate postoperative period and **were sustained through 24 months.** Patients experienced **statistically significant improvements in general vision, ocular pain, and driving ability, indicating a positive impact on quality of life**.

PERSONAL RESULTS

I recently reviewed the patient-reported outcomes at 4 and 12 months from 57 patients who underwent cataract surgery combined with iStent *inject* W using a range of questionnaires, including the European Quality of Life in Five Dimensions, Glaucoma Quality of Life - 15, Glaucoma Symptom Severity Score, and OSDI. Patient-reported improvements in ocular surface disease were also assessed.

My results (Figures 1 and 2) mirrored the trends observed in larger studies, demonstrating **consistent improvements in general health, quality of life, and ocular surface signs at 4 months, and these were maintained at 12 months**. The improvement in the OSDI was more pronounced in patients who were medication-free after surgery, underscoring the importance of considering not only glaucoma control but also the overall enhancement of patients' lives when opting for procedures like combined phacoemulsification and iStent *inject* W.

CONCLUSION

Being aware of quality of life outcomes, in addition to the traditional metrics of IOP and glaucoma drop reduction has benefitted the care I can provide my patients. In general, **patients' eyes are more comfortable and they express high satisfaction after cataract surgery combined with iStent *inject* W.** ■

1. Samuelson TW, Singh IP, Williamson BK, et al. Quality of life in primary open-angle glaucoma and cataract: an analysis of VFQ-25 and OSDI from the iStent inject® pivotal trial. *Am J Ophthalmol.* 2021;229:220-229.

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Long-Term Safety and Efficacy of the iStent Technologies

WATCH IT NOW


Looking beyond IOP when measuring the efficacy of trabecular micro-bypass procedures.

BY IQBAL IKE K. AHMED, MD, FRCSC, AND TICIANA DEL FRANCESCO, MD

Glaucoma management has always been complex. Balancing the best combinations of eye drops to help the patient's disease state while avoiding the comorbidities, intolerances, and side effects can be extremely challenging. The advent of MIGS triggered a transformative shift in glaucoma treatment with an emphasis on early noninvasive surgical treatment. It still can be challenging, however, to know which medicines and procedures to use and in what order.

The original aim of MIGS surgery has not changed. These procedures have four clear advantages: (1) they are minimally traumatic, requiring only an ab interno microincision, (2) they have at least modest efficacy, (3) they have a favorable safety profile, and (4) patients typically experience rapid recovery.[1] Of these, long-term safety is key to allow early intervention with beneficial risk-benefit ratio.

MIGS is typically used to treat early-stage glaucoma. It can be combined with cataract surgery to maintain safety, reduce the medication burden for patients, and preserve their refractive outcomes, which is especially crucial for patients who elect an advanced technology IOL. In a retrospective consecutive case series of 106 eyes, the **iStent *inject*® (Glaukos) procedure was refractively neutral by 4 weeks postoperative, and 74% and 99% of eyes were within ±0.50 D and ±1.00 D of the target refraction, respectively.**[2]

The **iStent *inject* W has a very similar safety profile to standalone cataract surgery, including no significant difference in the rate of endothelial cell loss over 5 years.**[3] Studies have shown no reports of myopic shift, flat anterior chamber, choroidal hemorrhage or effusion, cyclodialysis, hypotony for 1 or more months, hypotony maculopathy, stent dislocation, significant hyphema, and corneal decompensation at up to 24 months after the iStent *inject* procedure.[3-5]

MEASURING EFFICACY BEYOND IOP

It is important to **look beyond IOP when measuring the efficacy of trabecular micro-bypass procedures**. While IOP reduction remains a primary goal, factors such as medication reduction, quality of life improvement, visual field stability, and reduced need for secondary glaucoma interventions should be considered. More studies are needed to look at these important parameters.

According to **the long-term outcomes** (up to 9 years) from multiple independent, real-world studies, **iStent® technologies provide efficacy.**[6-10] Although the IOP reductions often differ from study to study, it is likely due to differences in baseline, demographics, and surgical approach.

A systematic review and **meta-analysis of 778 eyes from 13 studies** showed the **efficacy of iStent devices as a standalone procedure.**[11] Patients were followed for 6 months to 5 years. All studies showed a level of IOP consistency across the duration of the follow-up (Figure).

CONCLUSION

A key feature of MIGS is safety. Long-term data supports iStent as a safe procedure that combines well with phacoemulsification. Although there are few comparative studies, iStent appears to be one of the safest MIGS options, with rapid recovery and a side effect profile similar to phacoemulsification alone. Data supports the IOP-lowering and medication-reduction impact of iStent, which in turn can improve quality of life after surgery. ■

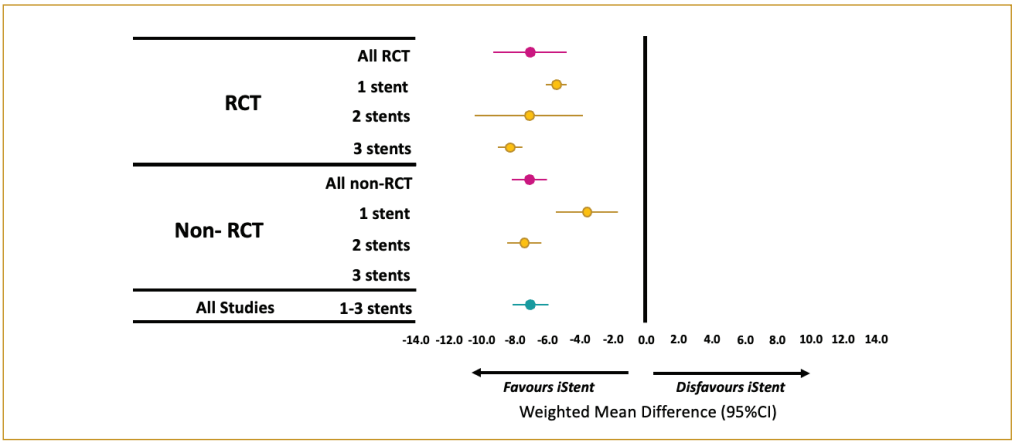

Figure. IOP outcomes with the iStent technologies as a standalone procedure.

1. Saheb H, Ahmed IIK. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol*. 2012;23(2):96-104.
2. Ioannidis AS, Töteberg-Harms M, Hamann T, Hodge C. Refractive outcomes after trabecular micro-by-

pass stents (iStent inject) with cataract extraction in open-angle glaucoma. *Clin Ophthalmol*. 2020;14:517-524.
3. Samuelson TW, Singh IP, Williamson BK, et al. Quality of life in primary open-angle glaucoma and cataract: an analysis of VFQ-25 and OSDI from the iStent inject® pivotal trial. *Am J Ophthalmol*. 2021;229:220-229.
4. Shalaby WS, Patel S, Lam SS, et al. Hemorrhagic complications following trabecular bypass microstent surgery in the setting of antithrombotic therapy. *J Glaucoma*. 2023;32(5):389-395.
5. Ahmed IIK, Sheybani A, De Francesc T, et al. Long-term endothelial safety profile with iStent inject in patients with open-angle glaucoma. *Am J Ophthalmol*. 2023;252:17-25.
6. Berdahl JP, Voskanyan L, Myers JS, Katz JL, Samuelson TW. iStent inject trabecular micro-bypass stents with topical prostaglandin as standalone treatment for open-angle glaucoma: 4-year outcomes. *Clin Exp Ophthalmol*. 2020;48(6):767-774.
7. Hengerer FH, Auffarth GU, Conrad-Hengerer I. iStent inject trabecular micro-bypass with or without cataract surgery yields sustained 5-year glaucoma control. *Advances in Therapy*. 2022;39(3):1417-1431.
8. Ferguson TJ, Mechels KB, Dockter Z, et al. iStent trabecular microbypass stent implantation with phacoemulsification in patients with open-angle glaucoma: 6-year outcomes. *Clin Ophthalmol*. 2020;14:1859-1866.
9. Ziaei H, Leon A. Manchester iStent study: long-term 7-year oucomes. *Eye*. 2021;35(8):2277-2282.
10. Salimi A, Watt H, Harasymowycz P. Long-term outcomes of two first-generation trabecular micro-bypass stents (iStent) with phacoemulsification in primary open-angle glaucoma: eight-year results. *Eye and Vision*. 2021;8(1):1-12.
11. Healey PR, Clement CI, Kerr NM, Tilden D, Aghajanian. Standalone iStent trabecular micro-bypass glaucoma surgery: a systematic review and meta-analysis. *J Glaucoma*. 2021;30(7):606-620.

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A Meta-Analysis of the Effect of iStent Technologies on Visual Field Progression

A closer look at the device's role in preserving visual function.

BY KEVIN GILLMANN, MD, PHD, MBBS, MBA, FEBO, MARCH, PGCERT

WATCH IT NOW

Over the past decade or more, the landscape of glaucoma management has changed profoundly. One of the biggest changes was the introduction of less invasive and traumatic procedures. The idea was that MIGS options could provide a procedural solution to the management of glaucoma at the milder end of the disease spectrum—before more invasive procedures such as trabeculectomy were indicated. The first of these devices was the iStent® (Glaukos), and it was clear from the randomized controlled studies carried out more than 10 years ago that the device had the ability to reduce both the IOP and the medication burden.[1] **What was less clear at the time was whether the device would have an effect on structural or functional endpoints, which is of course the ultimate goal in treating glaucoma.**

A NEEDED SHIFT IN FOCUS

While IOP is an important factor in glaucoma management, several groups advise a shift in the focus of glaucoma clinical trials toward biomarkers that better represent disease stability, such as structural, functional, and composite endpoints.[2] **iStent technologies have well-documented IOP-reducing potential and favorable safety profiles**, but no study concluded on their effect on the rates of functional progression in glaucoma.

In the first systematic review of the effect of iStent technologies on functional glaucoma progression, 15 studies were analyzed, encompassing a total of 1,115 eyes with a mean follow-up of 37.9 months (range, 12-96 months; personal data under review). At the end of the follow-up period, a weighted mean 26.6% IOP reduction was achieved (range, 15.2% to 42.3%).

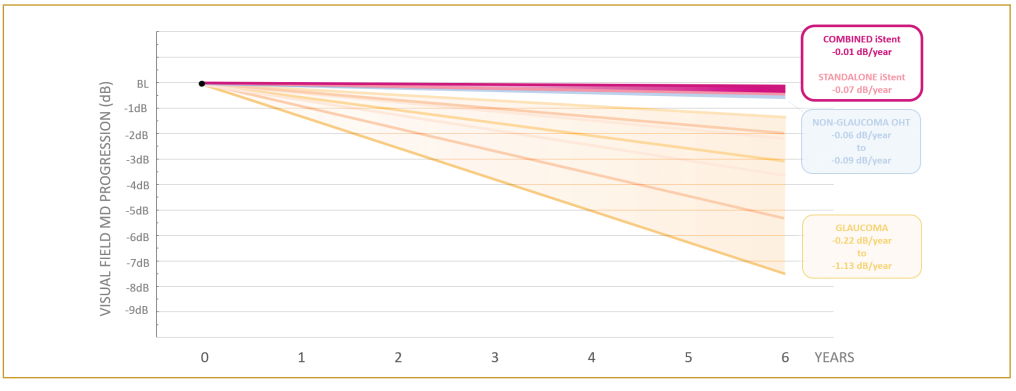

Figure. Observed visual field mean deviation progression following standalone and combined iStent technologies implantation (pink lines) compared to the rates of progression reported in the literature for ocular hypertension (blue lines) and treated glaucoma (yellow lines). Abbreviations: BL, baseline; MD, mean deviation; OHT, ocular hypertension.

ISTENT TECHNOLOGIES AND GLAUCOMA STABILITY

The rate of **visual field progression over the entire cohort was -0.02 ±0.34 dBs per year**, ranging from -0.01 ±0.42 dBs per year in combined procedures to -0.07 ±0.62 dBs per year in standalone iStent device implantations. To put these data into context, if a blind eye is considered to have a mean deviation between -25 and -30 dBs, **it would take a healthy eye more than 1,000 years to become blind at this rate of progression**. In comparison, large international cohorts of medically and surgically treated glaucoma exhibited mean progression rates ranging from -0.22 to -0.67 dBs per year (Figure).[3-5]

CONCLUSION

iStent technologies have well-documented IOP-reducing potential and favorable safety profiles. In this meta-analysis of 1,115 eyes, the device achieved a mean rate of progression of -0.02 dBs per year with serial standard automated perimetry, which is **similar to that reported in non-glaucomatous eyes and slower than that reported in medically treated glaucoma**. While specifically designed and powered trials would be useful to confirm these results, the present findings suggest that early trabecular bypass surgery may be beneficial in stabilizing glaucoma progression. ■

1. Healey PR, Clement CI, Kerr NM, Tilden D, Aghajanian L. Standalone iStent trabecular micro-bypass glaucoma surgery: a systematic review and meta-analysis. *J Glaucoma*. 2021;30(7):606-620.
2. Weinreb RN, Ramulu P, Topouzis F, Park KH, Mansouri K, Lerner F. 2019. 11th Consensus Meeting: Glaucoma Surgery.
3. Heijl A, Bengtsson B, Hyman L, Leske MC. Natural History of Open-Angle Glaucoma. *Ophthalmology*. 2009;116(12):2271-6.
4. Heijl A, Buchholz P, Norrgren G, Bengtsson B. Rates of visual field progression in clinical glaucoma care. *Acta Ophthalmologica*. 2013;91(5):406-12.
5. Aptel F, Aryal-Charles N, Giraud JM, El Chehab H, Delbarre M, Chiquet C, et al. Progression of visual field in patients with primary open-angle glaucoma - ProgF study 1. *Acta Ophthalmol*. 2015;93(8):e615-20.

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The Role of Early Intervention in Glaucoma Management

WATCH IT NOW

Interventional glaucoma is better for both patients and clinicians.

BY JULIÁN GARCÍA FEIJOO, MD, PHD

Glaucoma patients are seeking not only a reduction of their IOP but a substantial decrease to their medication burden and even an improvement in their visual quality and quality of life. We must manage their expectations while providing a safe, effective, and cost-beneficial procedure. The challenge lies in aligning such varied needs to create a cohesive approach to early glaucoma surgical intervention.

PATIENT SCENARIOS

Consider the following patient scenarios.

Patients A and B. Patient A has 20/20 vision but is on two glaucoma medications to treat her primary open-angle glaucoma (POAG). Patient B also has POAG and 20/20 vision but experienced a severe visual field defect. From the surgeon's perspective, the first patient should be the happier patient.

But what about the patient perspective? The true measure of success for patients extends beyond IOP reduction. It includes a decrease in medication, long-term stability, ocular and systemic side effects, and cost effectiveness. Medical treatment is therefore not always the best option for patients. In some cases, surgical intervention is a more appropriate choice, especially for those with mild disease. The two patient scenarios illustrate this point, and, for Patient A, severe OSD was triggered by her glaucoma medication and had a considerable negative impact on her quality of life.

Patient C. A 70-year-old patient with POAG presented with a mild cataract and mild glaucoma. He had suboptimal IOP control ranging from 16 to 25 mm Hg with medications because of poor compliance. He also suffers from OSD.

We tend to think that patients with early glaucoma are relatively happy, but, like this patient, that is not always the case. The aim of the intervention for Patients A and C therefore is to decrease medications, which should result in an improved ocular surface and quality of life. For patient C, one option was cataract surgery alone, but the **more appropriate option**, in my opinion, was to perform a **combined procedure with a trabecular micro-bypass device like the iStent *inject*® W (Glaukos). For patient A standalone iStent *inject* W procedure is a good option.**

Patient D. A 62-year-old patient diagnosed with early glaucoma presented with a BCVA of 20/20. Her IOP was controlled at 17 mm Hg. She was, however, on maximum medications and experienced mild problems with the medication schedule. For these reasons, she asked for alternatives. Again, **an iStent *inject* W procedure was selected because it was the best opportunity for improving her quality of life**.

WHY EARLY INTERVENTION MATTERS

Surgeons are shifting away from the classic and rigid treatment algorithms that recommend medications and selective laser trabeculoplasty (SLT) as first-line treatments for glaucoma. Now, however, we have more long-term data on the efficacy and safety of trabecular MIGS procedures, especially on the iStent® technologies, so early surgery is an option that should be discussed with patients.

The efficacy of early trabecular surgery is not only about IOP reduction. Disease stability over the long term is also important. IOPs can be expected to drop to the mid-teens. Studies consistently show a **significant decrease in IOP, even up to 7 years after surgery, with the iStent technologies.**[1-7] Results from the first- and second-generation iStents extend to **8 years and demonstrate a sustained decrease in IOP and medication use of up to 30%,**[8] **further establishing the effectiveness of early intervention.** Now, with newer generation iStents like the **iStent *inject*® and iStent *inject* W, the decrease in medication use is even more substantial with an excellent IOP-lowering effect even after 4 to 5 years.**

Additionally, when patients experience a decrease in their medication burden, typically there is an **improvement in ocular surface health** as well.[9,10] In my experience, **ocular surface health after iStent *inject W* surgery improves in about 50% to 60% of patients.**

The impact on patients' subjective experiences is also evident with the iStent technologies. **A pivotal trial found improvements in general vision, ocular pain, and even driving abilities after the procedure.**[9]

CONCLUSION

Early glaucoma intervention with trabecular micro-bypass surgery is a patient-centric strategy with a focus on quality of life, ocular surface health, and long-term disease stability. When making a treatment recommendation, clinicians should consider the benefits of early trabecular surgery in the context of medical and nonmedical patient characteristics. ■

1. Ahmed IIK, Sheybani A, De Francesc T, et al. Long-term endothelial safety profile with iStent inject in patients with open-angle glaucoma. *Am J Ophthalmol*. 2023;252:17-25.
2. Berdahl JP, Voskanyan L, Myers JS, Katz JL, Samuelson TW. iStent inject trabecular micro-bypass stents with topical prostaglandin as standalone treatment for open-angle glaucoma: 4-year outcomes. *Clin Exp Ophthalmol*. 2020;48(6):767-774.
3. Hengerer FH, Auffarth GU, Conrad-Hengerer I. iStent inject trabecular micro-bypass with or without cataract surgery yields sustained 5-year glaucoma control. *Advances in Therapy*. 2022;39(3):1417-1431.
4. Ferguson TJ, Mechels KB, Dockter Z, et al. iStent trabecular microbypass stent implantation with phacoemulsification in patients with open-angle glaucoma: 6-year outcomes. *Clin Ophthalmol*. 2020;14:1859-1866.
5. Ziaei H, Leon A. Manchester iStent study: long-term 7-year outcomes. *Eye*. 2021;35(8):2277-2282.
6. Salimi A, Watt H, Harasymowycz P. Long-term outcomes of two first-generation trabecular micro-bypass stents (iStent) with phacoemulsification in primary open-angle glaucoma: eight-year results. *Eye and Vision*. 2021;8(1):1-12.
7. Healey PR, Clement CI, Kerr NM, Tilden D, Aghajanian. Standalone iStent trabecular micro-bypass glaucoma surgery: a systematic review and meta-analysis. *J Glaucoma* 2021;30(7):606-620.
8. Salimi A, Watt H, Harasymowycz P. Long-term outcomes of two first-generation trabecular micro-bypass stents (iStent) with phacoemulsification in primary open-angle glaucoma: eight-year results. *Eye and Vision*. 2021;8(1):1-12.
9. Samuelson TW, Singh IP, Williamson BK, et al. Quality of life in primary open-angle glaucoma and cataract: an analysis of VFQ-25 and OSDI from the iStent inject® pivotal trial. *Am J Ophthalmol*. 2021;229:220-229.
10. Schweitzer JA, Hauser WH, Ibach M, et al. Prospective interventional cohort study of ocular surface disease changes in eyes after trabecular micro-bypass stent(s) implantation (iStent or iStent inject) with phacoemulsification. *Ophthalmology and Therapy* 2020;9(4):941-953.

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Clinical Results From Randomized Controlled Trials

Breaking down myths and facts about the iStent *inject* W.

BY ANA MIGUEL, MD

WATCH IT NOW

There are several myths surrounding the safety and effectiveness of trabecular micro-bypass procedures. There is also, however, evidence supporting the benefits of these devices, especially as an early intervention strategy for mild to moderate glaucoma. This article challenges common misconceptions and further establishes the need for devices such as the iStent *inject*® W (Glaukos).

FIVE COMMON MYTHS

Myth No. 1: iStent *inject* W is minimally effective. A pivotal randomized controlled trial of 505 patients dispelled doubts about the device's efficacy.[1] Patients were randomized to undergo cataract surgery alone or in combination with the iStent *inject*®. **All endpoints were met, including at least a 20% reduction in unmedicated diurnal IOP and a mean reduction in unmedicated diurnal IOP** (Figure 1). More than 75% of patients in the iStent® group were medication-free and attained the primary endpoint of more than 20% reduction in any medicated IOP. The mean IOP reduction from baseline was 7 mm Hg, which was a statistically significant difference versus the cataract surgery only group. Additionally, the **IOP was consistent across all time points** (6, 12, and 24 months) without additional medication. When performed as a standalone procedure, iStent can decrease IOP by up to 8 mm Hg.[2]

A study by Ahmed et al showed **the iStent *inject* had long-term safety,**[3] and sustained effectiveness has been shown for up to 7 years.[1,2,4]

Myth No. 2: Patients do fine with eye drops. The two biggest challenges in preventing disease progression are late presentation and patient noncompliance with topical medication.[5-10] According to Market Scope, worldwide glaucoma medical treatment is about 40 times more common than surgical treatment with MIGS. Yet glaucoma

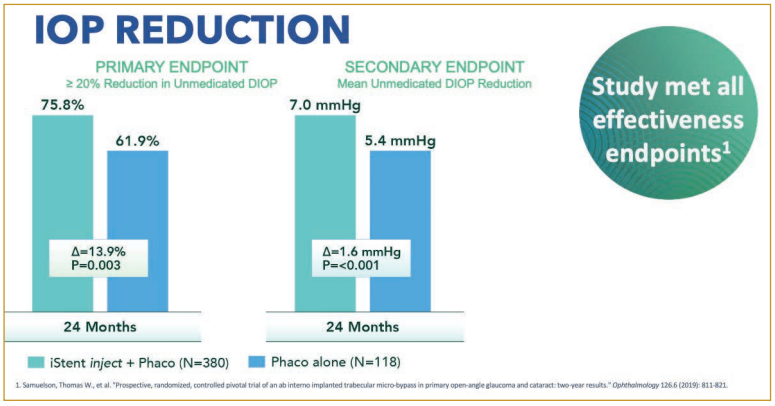

Figure 1. IOP reduction was sustained through 24 months.

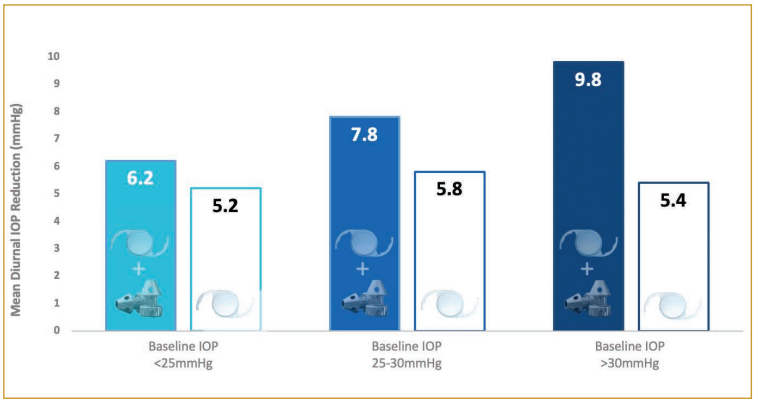

Figure 2. Pivotal data outcomes stratified by baseline IOP.

patients on prolonged medication often experience side effects such as inflammation and ocular surface disease. **Quality of life is a critical factor in the decision-making process. The iStent *inject* is the first MIGS device to show significant durable Vision Related Quality of Life improvements from a pivotal trial by reducing ocular pain and improving general vision.[1]**

Myth No. 3: iStent *inject* W doesn't work when the baseline IOP is elevated. A post-hoc analysis of Samuelson et al's pivotal trial demonstrated the device's effectiveness of iStent *inject* even in patients with elevated baseline IOP exceeding 30 mm Hg[11] **with a mean diurnal IOP reduction of 9.8 mm Hg.** In the study, patients were divided into three groups, those with low (< 25 mm Hg), mid (25 to 30 mm Hg), and high baseline (> 30 mm Hg) diurnal IOPs after washout (Figure 2).

Myth No. 4: iStent *inject* W is not safe or well known. In the **more than 300 published papers** on iStent technologies with up to 8 years of follow-up, more than 20,000 eyes studied, and more than 1 million implanted devices worldwide, there have been **no serious adverse events** such as myopic shift, flat anterior chamber, choroidal hemorrhage, and corneal decompensation.[1] Endothelial cell loss, a significant concern in other glaucoma surgeries, is with iStent *inject* nearly similar to phacoemulsification (6.3% and 9.4%, respectively, after 5 years).[3]

CONCLUSION

From its **proven safety and efficacy in diverse patient populations** to its **ability to enhance quality of life, iStent *inject* W offers many advantages to glaucoma patients and can be considered early in the disease state.** ■

1. Samuelson TW, Singh IP, Williamson BK, et al. Quality of life in primary open-angle glaucoma and cataract: an analysis of VFQ-25 and OSDI from the iStent inject® pivotal trial. *Am J Ophthalmol*. 2021;229:220-229.
2. Healey PR, Clement CI, Kerr NM, Tilden D, Aghajanian. Standalone iStent trabecular micro-bypass glaucoma surgery: a systematic review and meta-analysis. J Glaucoma 2021;30(7):606-620.
3. Ahmed IIK, Sheybani A, De Francesco T, et al. Long-term endothelial safety profile with iStent inject in patients with open-angle glaucoma. *Am J Ophthalmol*. 2023;252:17-25.
4. Ziaei H, Au L. Manchester iStent study: long-term 7-year outcomes. *Eye (London)*. 2021;35(8):2277-2282.
5. Boodhna, Trishal, and David P. Crabb. "Disease severity in newly diagnosed glaucoma patients with visual field loss: trends from more than a decade of data." *Ophthalmic and Physiological Optics* 35.2 (2015): 225-230.
6. Nordstrom BL, Friedman DS, Mozaffari E, Quigley HA, Walker AM. Persistence and adherence with topical glaucoma therapy." *Am J Ophthalmol*. 2005;140(4):598-606.
7. Fechtner RD, Godfrey DG, Budenz D, Stewart JA, Steward WC, Jasek MC. Prevalence of ocular surface complaints in patients with glaucoma using topical intraocular pressure-lowering medications. *Cornea* 2010;29(6): 618-621.
8. Li G, Akpek EK, Ahmad S. Glaucoma and ocular surface disease: more than meets the eye. *Clinical Ophthalmology*. 2022:3641-3649.
9. Skalicky SE, Goldberg G, McCluskey P. Ocular surface disease and quality of life in patients with glaucoma. *Am J Ophthalmol*. 2012;153(1):1-9.
10. Tsai JC, McClure CA, Ramos SE, Schlundt DG, Pichert JW. Compliance barriers in glaucoma: a systematic classification. *J Glaucoma*. 2003;12(5):393-398.
11. Singh IP, et al. Treatment success across different levels of preoperative disease burden: stratified two-year outcomes from the pivotal trial of iStent inject® trabecular micro-bypass in primary open-angle glaucoma and cataract. *Clin Ophthalmol*. 2021;15:3231.

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Trabecular Micro-Bypass for the Treatment of Glaucoma

The iStent *inject* W plays a major role in early intervention.

BY VINCENT QIN, MD

WATCH IT NOW

The population is aging, and the prevalence of glaucoma is on the rise. In Western Europe alone, diagnosed and undiagnosed primary open-angle glaucoma (POAG) are projected to increase by 8.6% and 13.7%, respectively, from 2020 to 2026.[1] The challenge with glaucoma management lies not only with the growing number of diagnosed cases overall but also with late-stage diagnoses. Patients with advanced disease often have irreversible visual field loss.

Traditionally, the first-line treatment for glaucoma is medication, followed by laser and then more invasive surgery. Unfortunately, this treatment paradigm comes at a steep cost. Less than 50% of patients adhere to their prescribed medication regimen after 12 months,[2] and intervention for advanced disease is more costly.[3] The economic costs of glaucoma management outside the health and social care system constitute about 85% of total expenses.[4] **Shifting to an early interventional mindset therefore is key to reduce health care costs, prevent disease progression, and improve the overall quality of life for glaucoma patients.**

MIGS procedures, including devices like the **iStent *inject*® W** (Glaukos), **address the challenges associated with late-stage glaucoma diagnosis and noncompliance with topical medications**. These procedures can be performed in patients with mild to moderate glaucoma, offering a more efficient approach to disease management.

THE LATEST-GENERATION ISTENT

The evolution of iStent® spans 2 decades. The first-generation device was relatively complicated to implant in the trabecular meshwork, but the latest generation, iStent *inject* W, is more straightforward. In my hands, I can perform the procedure elegantly due to the device's enhanced visibility. The **iStent *inject* W** also **includes observable positioning confirmation to ensure the device is implanted safely, efficiently, and seamlessly.**

The iStent *inject* W is implanted into the trabecular meshwork. There are four outflow pathways on the sides and one at the tip of the implant. The flange, visible during injection, stabilizes the implant in the trabecular meshwork. The injection system is very straightforward to use; two stents are included in each injector. The injector has two buttons; the first and second buttons are depressed to retract the sleeve of the trocar when the anterior segment is entered and deliver the stents perpendicularly into the trabecular meshwork, respectively. Once the first stent is delivered, the injector is moved 2 clock hours away on the nasal side of the trabecular meshwork, and the second one is implanted, again perpendicular to the trabecular meshwork. Only a small tenting of the sclera is required for implantation.

The anterior segment OCT scans in Figure 1 show the location of the iStent *inject* W in the trabecular meshwork. Note the **improvement in the diameter of the Schlemm canal both nasally as well as**

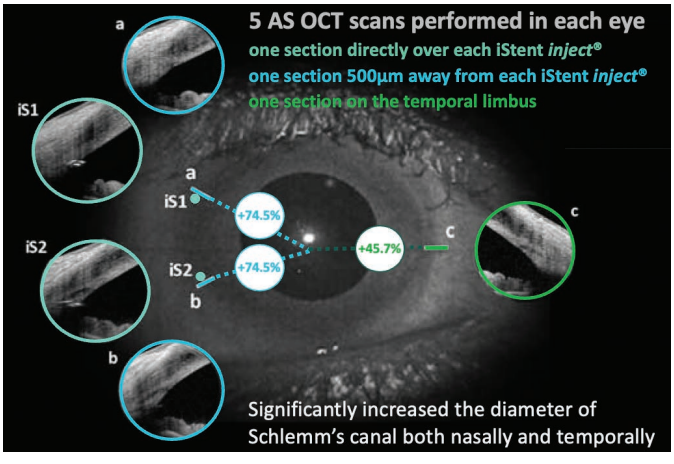

Figure 1. The location of the iStent *inject* in the trabecular meshwork as seen on anterior segment OCT.

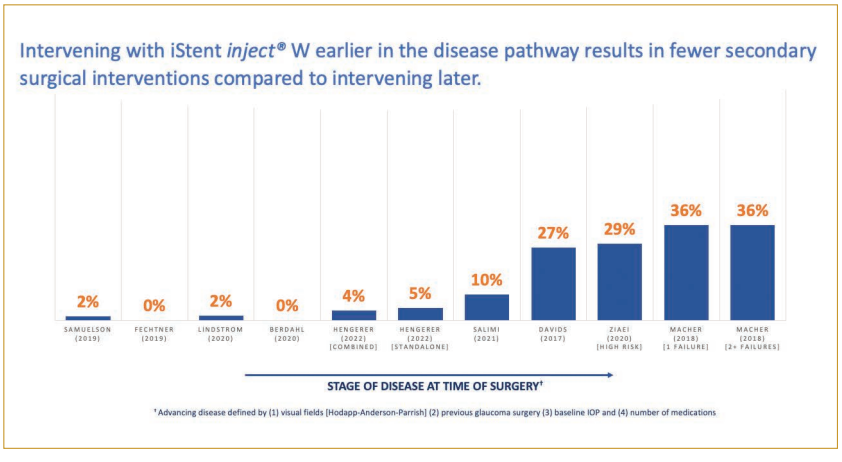

Figure 2. Intervening with iStent *inject* W earlier in the disease pathway results in fewer secondary surgical interventions compared to intervening later.

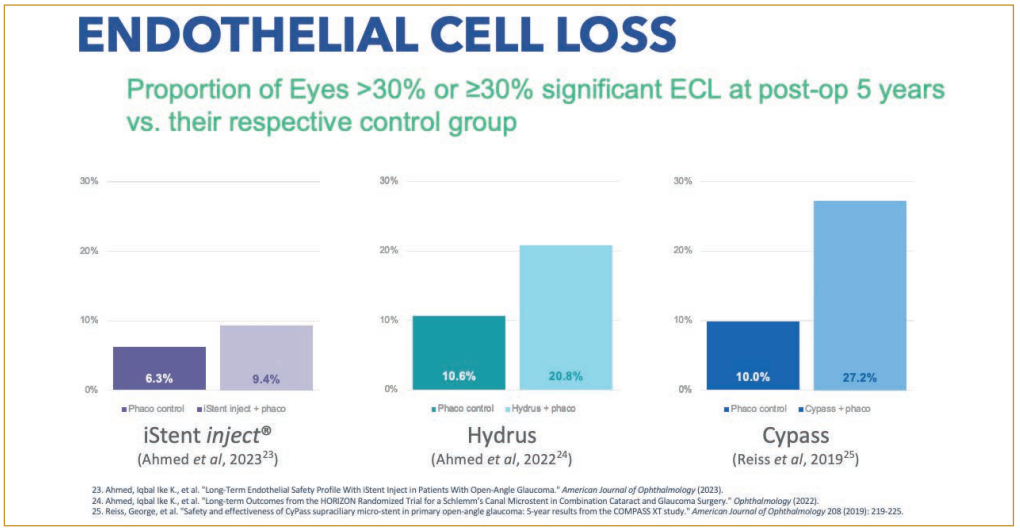

Figure 3. Endothelial cell loss at 5 years.

temporally, signifying an increased pathway for aqueous outflow.[5] Additionally, an angiography study **found improved drainage of aqueous fluid in the episcleral veins immediately after surgery when the stents are placed 2 to 3 clock hours apart.**[6]

The **iStent technologies** can achieve a **significant decrease in IOP across various stages of glaucoma** disease as a standalone procedure and in combination with cataract surgery.[7,10] Long-term studies on the iStent technologies show the **stability of visual fields over 7 years regardless of glaucoma stage, optic nerve cupping, and retinal nerve fiber layer thickness.**[11,12]

Intervening with iStent *inject*® W earlier in the disease pathway results in fewer secondary surgical interventions compared to intervening later (Figure 2). In a retrospective study of 333 patients undergoing trabecular bypass surgery, the rate of postoperative hyphema was four times greater with the Hydrus Microstent (Alcon) than the iStent *inject* in the setting of antithrombotic therapy.[13]

Additionally, the rate of postoperative peripheral anterior synechiae in the Hydrus pivotal trial[14] was almost 10 times greater than in the iStent *inject* pivotal trial.[15] Evidence from pivotal trials also showed the proportion of **patients experiencing more than 30% endothelial cell loss at 5 years was lower in the iStent versus other microbypass stent procedures** (Figure 3).[8,16,17]

CONCLUSION

The iStent technologies have evolved from an unproven technology in 2012 to an efficient solution for glaucoma. **Long-term data have showed predictable reduction in IOP,[10] visual outcomes,[18] and safety.**[8,14] The device is **proven to stabilize visual fields over the long term**[11,12] with a **low rate of secondary surgical interventions** when used early in the disease state.[11,14,19] **This device is playing a crucial role to improve patients' quality of life as we continue to move toward early glaucoma intervention and navigate an aging population.** ■

1. Market Scope Glaucoma Device Report. Market Scope. 2021.
2. Nordstrom BL, Friedman DS, Mozaffari E, Quigley HA, Walker AM. Persistence and adherence with topical glaucoma therapy. *Am J Ophthalmol*. 2005;140(4): 598-e1.
3. Traverso CE, et al. Direct costs of glaucoma and severity of the disease: a multinational long term study of resource utilisation in Europe. *Br J Ophthalmol*. 2005;89(10):1245-1249.
4. Time to Focus Report (Fight for Sight).
5. Gillmann K, Mansouri K, Ambresin A, Bravetti GE, Mermoud A. A prospective analysis of iStent inject microstent implantation: surgical outcomes, endothelial cell density, and device position at 12 months. *J Glaucoma*. 2020;29(8):639-647.
6. Huang AS, Penteado RC, Papoyan V, Voskanyan L, Weinreb RN. Aqueous angiographic outflow improvement after trabecular microbypass in glaucoma patients. *Ophthalmology Glaucoma*. 2019;2(1):11-21.
7. Samuelson TW, Singh IP, Williamson BK, et al. Quality of life in primary open-angle glaucoma and cataract: an analysis of VFQ-25 and OSDI from the iStent inject® pivotal trial. *Am J Ophthalmol*. 2021;229:220-229.
8. Ahmed IIK, Sheybani A, De Francesc T, et al. Long-term endothelial safety profile with iStent inject in patients with open-angle glaucoma. *Am J Ophthalmol*. 2023;252:17-25.
9. Boodhna, Trishal, and David P. Crabb. "Disease severity in newly diagnosed glaucoma patients with visual field loss: trends from more than a decade of data." *Ophthalmic and Physiological Optics* 35.2 (2015): 225-230.
10. Healey PR, Clement CI, Kerr NM, Tilden D, Aghajanian. Standalone iStent trabecular micro-bypass glaucoma surgery: a systematic review and meta-analysis. *J Glaucoma* 2021;30(7):606-620.
11. Hengerer FH, Auffarth GU, Conrad-Hengerer I. iStent inject trabecular micro-bypass with or without cataract surgery yields sustained 5-year glaucoma control. *Advances in Therapy*. 2022;39(3):1417-1431.
12. Ziaei H, Leon A. Manchester iStent study: long-term 7-year outcomes. *Eye*. 2021;35(8):2277-2282.
13. Shalaby WS, Patel S, Lam, S, et al. Hemorrhagic complications following trabecular bypass microstent surgery in the setting of antithrombotic therapy. *J Glaucoma*. 2023;32(5):389-395.
14. Samuelson TW, et al. Prospective, randomized, controlled pivotal trial of an ab interno implanted trabecular micro-bypass in primary open-angle glaucoma and cataract: two-year results. *Ophthalmology*. 2019;126(6):811-821.
15. Samuelson TW, et al. A Schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: the HORIZON study. *Ophthalmology*. 2019;126(1):29-37.
16. Ahmed IIK, De Francesco T, Rhee D, et al. Long-term outcomes from the HORIZON randomized trial for a Schlemm's canal microstent in combination cataract and glaucoma surgery. *Ophthalmology*. 2022;129(7):742-751.
17. Reiss G, Clifford B, Vold S, et al. Safety and effectiveness of CyPass supraciliary micro-stent in primary open-angle glaucoma: 5-year results from the COMPASS XT study. *Am J Ophthalmol*. 2019;208:219-225.
18. Ioannidis AS, Töteberg-Harms M, Hamann T, Hodge C. Refractive outcomes after trabecular micro-bypass stents (iStent inject) with cataract extraction in open-angle glaucoma. *Clin Ophthalmol*. (2020):517-524.
19. Ali S, Watt H, Harasymowycz P. Long-term outcomes of two first-generation trabecular micro-bypass stents (iStent) with phacoemulsification in primary open-angle glaucoma: eight-year results. *Eye and Vision*. 2021;8(1):1-12.

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