10 YEARS & COUNTING: THE TRUE TEST OF TIME!

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WHEN DID YOUR EXPERIENCE WITH ISTENT® START?

I implanted my first iStent® nearly 15 years ago, during a time when the technology was not widely accepted and regarded as largely unproven. At that time the technology available was the first generation iStent®, and the attraction was the possibility of providing IOP control and/or medication reductions in patients where the potential complications of traditional surgery may make it difficult to justify. My use of the iStent® device in 2010 was not in the context of a clinical trial, and so was not influenced by inclusion or exclusion criteria. **The iStent® procedure was considered in any patients who were comorbid with a cataract where there was a desire by the patient to reduce topical medication and/or the surgeon wanted a low-risk surgical option.** As a result, I ended up with a heterogenous group of patients, including ocular hypertension, primary open-angle glaucoma and pseudoexfoliation. Secondary or post-traumatic glaucoma were not recommended.

WHAT HAS YOUR EXPERIENCE BEEN?

Over the last decade I have published several papers on my outcomes with iStent®. My first publication in 2015 provided three-year outcomes for 41 patients with the first-generation device. It showed **IOP reductions from 24mmHg under topical therapy down to around 15mmHg after 3 years without medication[1]. However, the reassuring thing at this time was the safety.** The pivotal study for the iStent® had already been published in 2011 showing similar overall safety to cataract surgery alone[2], and it was reassuring to find that this was reflected in my real-world practice. As all of these early procedures were combined with phacoemulsification, it was important to see that the outcomes of the cataract surgery would not be compromised. **I didn't experience any intraoperative complications during this early period and found the outcomes of the procedure to be very predictable.** In some cases, I saw in the early postoperative phase a hyphema. It compromised in the early postoperative phase visual acuity only for some days but never needed a surgical intervention. Some years later, **I also published a 5-year analysis of this same cohort of patients demonstrating very similar results at 5 years[3].** This was one of the earliest publications to show that the efficacy of iStent® could be sustained in the long term. The **long-term safety was a very interesting element of this publication,** because it showed that not only were there no sight-threatening or device related adverse events over the long term, but also that the cataract outcomes were preserved, and relatively few patients (7 eyes) went on to require further IOP lowering surgery.

ARE YOU STILL FOLLOWING THIS COHORT, AND IF SO, WHAT ARE THE RESULTS LIKE NOW?

During this time Glaukos launched the second-generation device, the iStent *inject*®, and so naturally I progressed onto using this device. As it happens, Germany was the first country in the world to launch the iStent *inject*® and so, once again, our real-world experience was breaking new ground. As a result, although we did

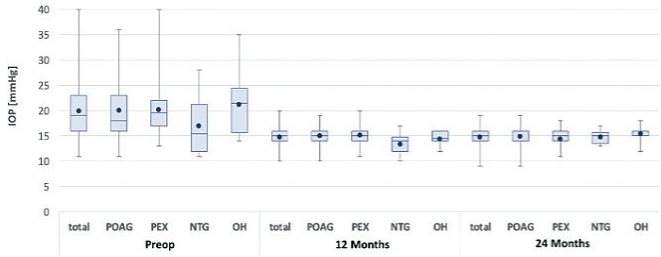

Figure 1: Intraocular pressure through 12 and 24 months of follow-up.

try to follow the original cohort of patients from the first-generation study, we were also keen to share our results with the **iStent *inject*®**. Our first publication came in 2020 when we shared our experience in a cohort of **164 eyes over 24 months** (88 eyes at 2 years)[4]. Reassuringly we were able to **show extremely predictable results once again, with mean postoperative IOPs of around 15mmHg and 80% reduction in medication at 2 years. 73% of our two-year cohort were completely medication free at the 24-month timepoint with no postoperative complications.** An interesting observation from this publication was the predictability of the results; as in the first-generation study, we did not have inclusion/exclusion criteria, and as a result our cohort consisted of various subtypes of glaucoma including primary open angle glaucoma, pseudoexfoliation, ocular hypertension, and even normal tension glaucoma. Whilst there was a lot of variation in the baseline IOPs, at both postoperative follow-ups the **consistency and predictability of the results with the iStent *inject*® device was remarkable, regardless of the glaucoma subtype (fig 1).**

Then more recently we published our **ten-year results** with the first-generation iStent® (which I believe is **currently the longest follow up in the world to date)[5]**. Due to difficulties following up, some attrition, and some deaths, the cohort is not exactly the same cohort as the 3- and 5-year publications, although there is some overlap. Once again, **the study reports postoperative IOPs around 16mmHg at the 10-year timepoint in addition to a 50% reduction in medication.** Preoperatively over half of the patients were on two or more topical medications; **at 10 years, a third of the patients were completely medication free, and a further 50% were only reliant on a single topical medication.**

HOW HAVE THESE RESULTS IMPACTED ON CLINICAL PRACTICE?

In my practice, the majority of my **iStent® & iStent *inject*® procedures have been performed along with cataract surgery** – and I believe that this is the **ideal opportunity for the patient both from a convenience and a safety perspective.** In the wider population, this presents a couple of challenges; firstly, that the majority of cataracts (even in glaucoma patients) are not performed by glaucoma surgeons. Secondly, **combining these procedures often means intervening earlier with a glaucoma procedure than we might if we were treating the two diseases separately** - although taking the opportunity to intervene early with a glaucoma procedure also has many advantages. And thirdly, if these procedures are going to be adopted by non-glaucoma surgeons, then they must be easy to learn, predictable, and not compromise the outcomes of the cataract procedure in any way.

My results have shown that the **iStent® devices provide excellent safety & predictability,** and this is reinforced by the other 300+ peer reviewed

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publications on the various iStent® devices. Consequently, **I think that cataract surgeons feel comfortable to adopt this procedure and offer it to their patients at an earlier point in the treatment pathway.**

IS EARLIER INTERVENTION NECESSARY?

As glaucoma surgeons, we have many options available to us, and the challenge is to use the right procedure at the right time; there is no one-size-fits-all approach to glaucoma, because every patient is different, and it is important to treat each patient individually. We acknowledge that every treatment has its advantages and disadvantages, and **our challenge is to find the treatment that will work for each individual patient – because this is the only way we can prevent sight loss, and this of course is the end goal of all treatments!**

It is well published that topical medications are associated with compliance and tolerability issues, and we know that this leads to patients not taking their medication properly, or not taking it at all[6]. We also know that adding in more and more medications not only impacts on the patient's quality of life, but leads to diminishing returns or benefits in terms of treatment success. **By intervening procedurally at an earlier stage, we can feel more reassured that the disease is being adequately controlled 24 hours a day, 7 days a week.**

The missing piece in the jigsaw was to have a device or procedure which cataract surgeons feel comfortable adopting, both from a technical and a safety perspective, and one which has high-quality peer reviewed evidence supporting its clinical outcomes. I think that **iStent *inject*® W fulfills all of these criteria and therefore gives surgeons an opportunity to take compliance out of the patients' hands and slow the progression of the disease.** A recent meta-analysis of visual field change and functional progression following iStent® implantation showed that **the rate of progression after iStent® / iStent *inject*® was less than medically treated glaucoma or ocular hypertension, at only 0.03dB per year![7]**

WHAT DOES THE FUTURE OF GLAUCOMA TREATMENT LOOK LIKE?

The last 10 years have offered us many new options in treating glaucoma, although it is important to remember that **there are differences in efficacy and safety** – and therefore we must hold **the manufacturers accountable to provide us with high quality evidence, particularly for safety, so that we can provide the best care for our patients.** The next 10 years look equally promising, and companies like Glaukos have a very strong pipeline. Following their track record of providing us with first-in-class, disruptive technologies, **the next decade will surely be an exciting time as we enter an era of interventional glaucoma and continue to pursue our ultimate goal of preventing sight loss.** ■

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2. Samuelson, Thomas W., et al. "Randomized evaluation of the trabecular micro-bypass stent with phaco-emulsification in patients with glaucoma and cataract." *Ophthalmology* 118.3 (2011): 459-467
3. Neuhann, Tobias H., et al. "Long-term effectiveness and safety of trabecular microbypass stent implantation with cataract surgery in patients with glaucoma or ocular hypertension: five-year outcomes." *Journal of Cataract & Refractive Surgery* 45.3 (2019): 312-320.
4. Neuhann, Raphael, and Tobias Neuhann. "Second-generation trabecular micro-bypass stent implantation: retrospective analysis after 12-and 24-month follow-up." *Eye and Vision* 7 (2020): 1-10.
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6. Tsai, James C., et al. "Compliance barriers in glaucoma: a systematic classification." *J of glaucoma* 12.5 (2003): 393-398.
7. Gillmann, Kevin, and Dana M. Hornbeak. "Rates of visual field change and functional progression in glaucoma following trabecular microbypass implantation of iStent technologies: a meta-analysis." *BMJ Open Ophthalmology* 9.1 (2024): e001575.

iStent® Important Safety Information
INDICATIONS FOR USE: The iStent® Trabecular Micro-Bypass System is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma. The device is safe and effective when implanted in combination with cataract surgery in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma medications and conventional glaucoma surgery. **CONTRAINDICATIONS:** The iStent® Trabecular Micro-Bypass Stent is contraindicated under the following circumstances or conditions: • In eyes with primary angle closure glaucoma, or secondary angle-closure glaucoma, including neovascular glaucoma, because the device would not be expected to work in such situations • In patients with retrobulbar tumor, thyroid eye disease, Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure. **WARNINGS/PRECAUTIONS:** For prescription use only. This device has not been studied in patients with uveitic glaucoma. Do not use the devices if the Tyvek® lid has been opened or the packaging appears damaged. In such cases, the sterility of the device may be compromised. iStent is MR-Conditional; see MRI Information below. Physician training by Glaukos personnel is required prior to use of this device. Do not re-use the stent(s) or inserter, as this may result in infection and/or intraocular inflammation, as well as occurrence of potential postoperative adverse events as shown below under "Potential Complications." There are no known compatibility issues with the iStent and other intraoperative devices (e.g., viscoelastics) or glaucoma medications. Unused product & packaging may be disposed of in accordance with facility procedures. Implanted medical devices and infected products must be disposed of as medical waste.

iStent *inject*® Important Safety Information
INDICATIONS FOR USE: The iStent *inject*® is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudo-exfoliative glaucoma or pigmentary glaucoma. The iStent *inject*® can deliver two (2) stents on a single pass, through a single incision. The implant is designed to stent open a passage through the trabecular meshwork to allow for an increase in the facility of outflow and a subsequent reduction in intraocular pressure. The device is safe and effective when implanted in combination with cataract surgery in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma medications and conventional glaucoma surgery. **CONTRAINDICATIONS:** The iStent *inject*® System is contraindicated under the following circumstances or conditions: • In eyes with primary angle closure glaucoma, or secondary angle-closure glaucoma, including neovascular glaucoma, because the device would not be expected to work in such situations • In patients with retrobulbar tumor, thyroid eye disease, Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure. **WARNINGS/PRECAUTIONS:** • For prescription use only. • This device has not been studied in patients with uveitic glaucoma. • Do not use the devices if the Tyvek® lid has been opened or the packaging appears damaged. In such cases, the sterility of the device may be compromised. • Due to the sharpness of certain injector components (i.e. the insertion sleeve and trocar), care should be exercised to grasp the injector body. Dispose of device in a sharps container. • iStent *inject*® is MR-Conditional; see MRI Information below. • Physician training is required prior to use of the iStent *inject*® System. • Do not re-use the stent(s) or inserter, as this may result in infection and/or intraocular inflammation, as well as occurrence of potential postoperative adverse events as shown below under "Potential Complications." • There are no known compatibility issues with the iStent *inject*® and other intraoperative devices (e.g., viscoelastics) or glaucoma medications. • Unused product & packaging may be disposed of in accordance with facility procedures. Implanted medical devices and contaminated products must be disposed of as medical waste. • Due to the sharpness of certain injector components (i.e. the insertion sleeve and trocar), care should be exercised to grasp the injector body • The surgeon should monitor the patient postoperatively for proper maintenance of intraocular pressure. If intraocular pressure is not adequately maintained after surgery, the surgeon should consider an appropriate treatment regimen to reduce intraocular pressure.

iStent *inject*® W Important Safety Information
INDICATION FOR USE: The iStent *inject*® W, is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudo-exfoliative glaucoma or pigmentary glaucoma. The iStent *inject*® W, can deliver two (2) stents on a single pass, through a single incision. The implant is designed to stent open a passage through the trabecular meshwork to allow for an increase in the facility of outflow and a subsequent reduction in intraocular pressure. The device is safe and effective when implanted in combination with cataract surgery in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma medications and conventional glaucoma surgery. **CONTRAINDICATIONS:** The iStent *inject*® W System is contraindicated under the following circumstances or conditions: • In eyes with primary angle closure glaucoma, or secondary angle-closure glaucoma, including neovascular glaucoma, because the device would not be expected to work in such situations. • In patients with retrobulbar tumor, thyroid eye disease, Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure. **WARNINGS/PRECAUTIONS:** • For prescription use only. • This device has not been studied in patients with uveitic glaucoma. • Do not use the device if the Tyvek® lid has been opened or the packaging appears damaged. In such cases, the sterility of the device may be compromised. • Due to the sharpness of certain injector components (i.e. the insertion sleeveand trocar), care should be exercised to grasp the injector body. Dispose of device in a sharps container. • iStent *inject*® W is MR-Conditional; see MRI Information below. • Physician training is required prior to use of the iStent *inject*® W System. • Do not re-use the stent(s) or injector, as this may result in infection and/or intraocular inflammation, as well as occurrence of potential postoperative adverse events as shown below under "Potential Complications." • There are no known compatibility issues with the iStent *inject*® W and other intraoperative devices. (e.g., viscoelastics) or glaucoma medications. • Unused product & packaging may be disposed of in accordance with facility procedures. Implanted medical devices and contaminated products must be disposed of as medical waste. • The surgeon should monitor the patient postoperatively for proper maintenance of intraocular pressure. If intraocular pressure is not adequately maintained after surgery, the surgeon should consider an appropriate treatment regimen to reduce intraocular pressure. • Patients should be informed that placement of the stents, without concomitant cataract surgery in phakic patients, can enhance the formation or *progression* of cataract. **ADVERSE EVENTS:** Please refer to Directions For Use for additional adverse event information. **CAUTION:** Please reference the Directions For Use labelling for a complete list of contraindications, warnings and adverse events.
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