Department of Clinical Sciences, Ophthalmology, 2026

Microinvasive Trabecular Surgery in Glaucoma

Anna Barkander

UMEÅ UNIVERSITY

ISBN: 978-91-8070-845-6 (print)
ISBN: 978-91-8070-846-3 (pdf) no. Umeå University Medical Dissertations New Series
Electronic version available at: http://umu.diva-portal.org/
Printed by: Scandinavian Print Group, Skarpnäck, 2026

“Have no fear of perfection, you `ll never reach it.” – Marie Curie

Table of Contents

ABSTRACT

To manage the increasing prevalence of glaucoma, we need access to effective and safe medical and surgical treatments that can lower the intraocular pressure (IOP) – so far the only proven strategy to slow disease progression. Treatment typically starts with eye drops or a laser procedure, but many patients will eventually require surgery. Traditional surgery is time-consuming and carries significant risks, whereas microinvasive glaucoma surgery (MIGS) has emerged as a safer, earlier option that could potentially prevent or delay more invasive procedures such as a trabeculectomy. Additionally, many patients with glaucoma develop cataract, and MIGS procedures can be conveniently performed together with the cataract operation. Although MIGS is now widely adopted, concerns about bias remain as many studies are industry-funded. The benefit of combining MIGS with cataract surgery is also debated, especially in advanced glaucoma. Moreover, research is scarce for pseudoexfoliation glaucoma (PEXG), common in the Nordic countries and harder to treat, with a poorer prognosis than other open-angle glaucoma types.

In this thesis, we evaluate the efficacy and safety of the trabecular MIGS procedures iStent inject® (iStent) and Kahook Dual Blade® (KDB) across various stages and subtypes of glaucoma. We show that KDB is effective and safe when combined with cataract surgery, whereas its efficacy as a stand-alone procedure is lower. Therefore, we do not recommend the stand-alone approach in patients with advanced or uncontrolled glaucoma.

Furthermore, iStent and KDB demonstrate comparable outcomes, showing effectiveness not only in mild to moderate disease but also in advanced stages and in PEXG. Our results show that trabecular MIGS combined with cataract surgery is effective even in patients with markedly elevated IOP and/or on maximum tolerated therapy. These patients, previously considered candidates for bleb-forming surgery, may instead begin with trabecular MIGS combined with cataract surgery.

Many patients undergoing trabecular surgery have previously received laser trabeculoplasty (LTP), and we show that LTP does not seem to negatively affect the surgical outcomes of cataract surgery combined with KDB.

Finally, surgical success can be enhanced if iStent or KDB is added to the cataract operation, and in stable glaucoma patients this will mainly be due to greater medication reductions. Postoperative IOP spikes can also be reduced by more than half by adding iStent or KDB.

In summary, this thesis demonstrates that trabecular MIGS as a stand-alone procedure offered only moderate success and often required further interventions. Therefore, we do not recommend the stand-alone approach in patients with advanced or uncontrolled glaucoma. When performed together with cataract surgery, our data show that trabecular MIGS is both effective and safe – even in patients with markedly elevated IOP and/or on maximum tolerated therapy. In more stable glaucoma patients with lower preoperative IOP levels and a low rate of progression, combining trabecular MIGS with cataract surgery can be considered when medication reduction is a clinical goal. This approach also lowers the risk of early IOP spikes, and both iStent and KDB perform equally well, with comparable outcomes in PEX and non-PEX eyes.

SVENSK SAMMANFATTNING

Glaukom är den främsta orsaken till permanent blindhet globalt. I takt med den demografiska utvecklingen och en växande andel äldre i befolkningen förväntas sjukdomens förekomst öka under kommande decennier. För att möta denna utmaning krävs effektiva och säkra medicinska och kirurgiska behandlingar som sänker ögontrycket, vilket är den enda bevisade metoden för att bromsa sjukdomens fortskridande.

Glaukombehandling inleds oftast med ögondroppar eller laser, men många patienter behöver på sikt kirurgi. Traditionella kirurgiska metoder är dock tidskrävande och medför betydande risker. Mikroinvasiv glaukomkirurgi har därför väckt stort intresse som ett mindre riskabelt alternativ som kan användas tidigare i sjukdomsförloppet. Mikroinvasiv glaukomkirurgi kan med fördel även kombineras med kataraktkirurgi, vilket är relevant då katarakt och glaukom ofta förekommer samtidigt.

Även om mikroinvasiv glaukomkirurgi numera används brett finns det oro för att forskningen kan vara snedvriden, eftersom många studier är finansierade av industrin. Det råder också delade meningar om nyttan med att utföra denna typ av kirurgi vid avancerade stadier av glaukom. Därtill finns det begränsad forskning om pseudoexfoliationsglaukom – en form av glaukom som är vanlig i Norden och som ofta är svårare att behandla och har sämre prognos än andra typer av öppenvinkelglaukom.

Denna avhandling utvärderar de mikroinvasiva metoderna iStent inject® (iStent) och Kahook Dual Blade® (KDB) – vid olika stadier och former av glaukom. Båda metoderna verkar genom att öka utflödet av vätska genom ögats utflödeskanaler i det så kallade trabekelverket.

Vi visar att KDB är en effektiv och säker metod i kombination med kataraktkirurgi, medan dess effekt som fristående ingrepp är lägre och därför inte bör rekommenderas vid avancerat eller okontrollerat glaukom.

Vidare uppvisar iStent och KDB i kombination med kataraktkirurgi jämförbara resultat och är effektiva inte bara vid milda till måttliga glaukom, utan även vid mer avancerade stadier, liksom vid pseudoexfoliationsglaukom. Mikroinvasiv glaukomkirurgi i kombination med kataraktkirurgi förefaller vara effektivt och säkert även hos

patienter med kraftigt förhöjda ögontryck och/eller maximal medicinering. Baserat på avhandlingens resultat kan mikroinvasiva ingrepp i kombination med kataraktkirurgi övervägas även hos dessa patienter, som tidigare ofta bedömts behöva mer omfattande kirurgi.

Många glaukompatienter som genomgår kataraktkirurgi har tidigare fått laserbehandling mot trabekelverket, och våra resultat visar att detta inte påverkar utfallet av ett kombinerat ingrepp med kataraktoperation och mikroinvasiv glaukomkirurgi. Dessutom ser vi att hos patienter med stabilt glaukom kan fler läkemedel sättas ut när iStent eller KDB kombineras med kataraktoperation, och risken för höga ögontryck dagen efter operationen mer än halveras jämfört med när kataraktoperation utförs som enskilt ingrepp.

Sammanfattningsvis visar avhandlingen att de mikroinvasiva glaukomkirurgiska metoderna iStent och KDB är likvärdiga och båda har en god effekt och hög säkerhet när de kombineras med kataraktoperation – även hos patienter med höga ögontryck och/eller maximal medicinering. Våra resultat visar att dessa patienter kan börja med ett mikroinvasivt ingrepp i samband med kataraktkirurgi. Som enskilt ingrepp är resultaten sämre och vi rekommenderar därför inte denna form av kirurgi hos patienter som redan är kataraktopererade sedan tidigare. Vidare är resultaten jämförbara hos patienter med och utan pseudoexfoliationer och, oavsett om ett mikroinvasivt ingrepp läggs till eller ej, så ser vi att livskvaliteten förbättras av att operera katarakt hos patienter med glaukom.

ABBREVIATIONS

ALT	argon laser trabeculoplasty
ANOVA	analysis of variance
BCVA	best corrected visual acuity
dB	decibels
EGS	European Glaucoma Society
GAT	Goldmann applanation tonometry
IOP	intraocular pressure
IQR	inter-quartile range
iStent	iStent inject
iStent W	iStent inject W
KDB	Kahook Dual Blade
KDB Glide	Kahook Dual Blade Glide
logMAR	logarithm of the minimum angle of resolution
LTP	laser trabeculoplasty
MD	mean deviation
MIGS	Micro Invasive Glaucoma Surgery
mmHg	millimeter mercury
OCT	optical coherence tomography
OHT	ocular hypertension
PEX	pseudoexfoliation

PEXG	pseudoexfoliation glaucoma
POAG	primary open-angle glaucoma
SD	standard deviation
SLT	selective laser trabeculoplasty
SMIGS	Swedish Micro Invasive Glaucoma Surgery Study
TCP	transscleral cyclophotocoagulation
TGF-β	transforming growth factor beta
TM	trabecular meshwork
QoL	quality of life
YAG	Yttrium Aluminum Garnet

ORIGINAL PAPERS

The thesis is based on the following papers, which are referred to in the text by their Roman numerals:

I. Barkander A, Economou MA, Jóhannesson G. Kahook Dual-Blade Goniotomy with and without Phacoemulsification in Medically Uncontrolled Glaucoma. *Clin Ophthalmol*. 2023;17:1385-1394. Published 2023 May 12. doi:10.2147/OPTH.S409375

II. Barkander A, Economou MA, Jóhannesson G. Outcomes of iStent Inject Versus Kahook Dual Blade Surgery in Glaucoma Patients Undergoing Cataract Surgery. *J Glaucoma*. 2023;32(10):e121-e128. doi:10.1097/IJG.0000000000002243

III. Barkander A, Nolan AS, Jóhannesson G, Economou MA. Influence of Laser Trabeculoplasty on Combined Phacoemulsification/Kahook Dual Blade Goniotomy. *Clin Ophthalmol*. 2024;18:1811-1817. Published 2024 Jun 24. doi:10.2147/OPTH.S468809

IV. Barkander A, Economou MA, Jóhannesson G. Randomized Controlled Trial Comparing Cataract Surgery Alone versus Combined With iStent Inject W or Kahook Dual Blade Glide. Manuscript sent to journal.

INTRODUCTION

Background

Glaucoma is a chronic, progressive eye disease characterized by optic nerve damage, thinning of the retinal nerve fiber layer and corresponding visual field defects. It is the leading cause of irreversible blindness worldwide, and its prevalence is expected to rise in the coming decade due to an aging population.[1] By 2040, approximately 112 million people are expected to be affected by the disease.[2] Glaucoma is a heterogenous disease that can present with either open- or closed-angle mechanisms and exhibits a wide range of clinical phenotypes. This thesis focuses exclusively on open-angle glaucoma.

Primary open-angle glaucoma (POAG) is the most common form of glaucoma and is often associated with elevated intraocular pressure (IOP), although IOP can also be within the normal range, then called normal-tension glaucoma. Pseudoexfoliation glaucoma (PEXG) and pigmentary glaucoma are additional subtypes of secondary open-angle glaucoma.

PEXG develops from pseudoexfoliation syndrome, a condition characterized by the accumulation of abnormal fibrillo-granular protein material (pseudoexfoliations, PEX) both within the eye and systemically. In the eye, this PEX material deposits on the anterior lens capsule, pupillary margin, trabecular meshwork (TM), and zonules, obstructing aqueous humor outflow and elevating IOP, thereby increasing the risk of glaucoma development.[3,4] In eyes with PEXG, IOP levels tend to be higher than in POAG, and optic nerve damage often progresses more rapidly.[5,6] PEXG is particularly prevalent in the Nordic countries,[7–10] where it is considered a subtype of POAG, whereas in other regions it is classified as a secondary glaucoma.

Pigmentary glaucoma is a secondary form of open-angle glaucoma, accounting for approximately 1-1.5% of cases.[4,11] In pigmentary glaucoma, melanin pigment from the iris pigmented epithelium is released due to rubbing between the lens zonules and posterior

surface of the iris. These melanin granules obstruct aqueous humor outflow through the TM, leading to elevated IOP and an increased risk of glaucomatous optic nerve damage.[12,13] Clinical features of pigmentary glaucoma include dense TM pigmentation, mild myopia, and iris transillumination defects.[12,14]

The trabecular outflow system

The IOP is regulated by the balance between aqueous humor production by the ciliary body (2-3 µL/min) and its outflow through the TM and the supraciliary space, although the latter is believed to play only a minor role.[15] TM dysfunction is a key contributor to glaucoma, making it a central target for treatment.

The TM separates the anterior chamber from Schlemm's canal and consists of three layers: the uveal meshwork, the corneoscleral layer, and the juxtacanalicular tissue (Figure 1). TM cells exhibit phagocytic activity, helping maintain outflow by clearing debris.[16] Aqueous humor passes through these layers into Schlemm's canal, which encircles the limbus and connects to collector channels. Outflow occurs segmentally,[17] with high-flow regions near collector channels, especially in nasal and inferior quadrants – also preferred sites for microinvasive glaucoma surgeries (MIGS).

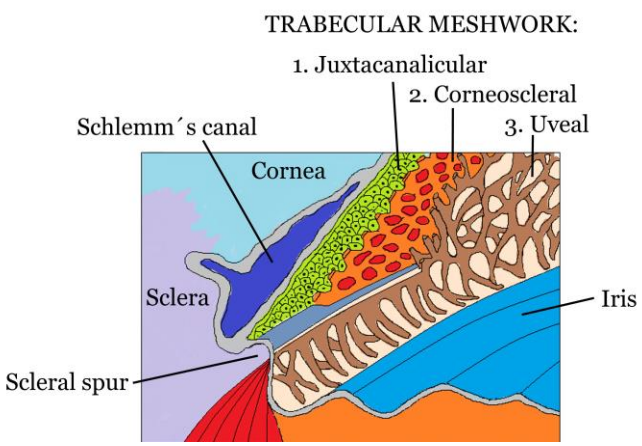

Figure 1. The trabecular meshwork and surrounding structures seen from within the eye. Illustration by Anna Barkander.

Trabecular outflow is a dynamic process influenced by ocular pulse, blinking, and eye movements. The TM expands and recoils in synchrony with the cardiac cycle, facilitating aqueous humor movement into Schlemm's canal. This pump-like mechanism depends on the TM's elasticity and recoil capacity. In glaucoma, the TM becomes stiffer and loses its natural flexibility, impairing this function.[18–20] Excessive production and crosslinking of extracellular matrix components further increase tissue rigidity and reduce aqueous humor permeability in glaucoma. Furthermore, trabecular outflow resistance is driven by cellular and molecular changes, including the overexpression of specific growth factors such as transforming growth factor beta (TGF-β). Elevated levels of TGF-β have been consistently observed in glaucoma patients, underscoring its role in promoting fibrosis within the trabecular outflow pathway.[21–23]

Effective IOP regulation depends not only on a functional TM but also on an episcleral venous pressure within normal limits. In healthy individuals, episcleral venous pressure typically ranges from 8-10 mmHg, while in glaucoma patients it is often elevated to 10-14 mmHg.[24] Episcleral venous pressure acts as a counterpressure, preventing IOP from dropping too low. Since episcleral venous pressure restricts trabecular outflow, treatments targeting the TM cannot lower IOP below the episcleral venous pressure.

For trabecular surgeries to be effective, both a patent outflow system and a normal episcleral venous pressure are necessary. However, downstream structures such as collector channels and aqueous veins may be compromised by chronic conjunctival inflammation, long-term topical glaucoma therapy, or previous ocular surgeries. It has been hypothesized that in advanced or long-standing glaucoma, dysfunction of the distal collector system may occur, potentially limiting the efficacy of trabecular MIGS; although this hypothesis remains unproven.

The effect of IOP on the trabecular meshwork

Already in the 1980s, Rosenquist et al demonstrated that complete removal of the TM in enucleated human eyes reduced resistance by

49% at an IOP of 7 millimeter mercury (mmHg), with this effect increased to 71% at 25 mmHg.[25] These findings suggest that the impact of trabecular surgery may be more pronounced at higher IOP levels. However, studies have shown that when IOP exceeds 30 mmHg, Schlemm's canal can collapse, obstructing the collector channels.[26,27]

Studies on trabecular MIGS have found that eyes with higher preoperative IOP levels often experience better postoperative outcomes compared to those with lower preoperative IOP levels.[28,29] However, some studies have also reported an increased incidence of surgical failure and a need for additional glaucoma procedures when baseline IOP has been high.[30] This may be due to chronic damage to the outflow system, affecting long-term efficacy.[31]

Glaucoma diagnostics

Since IOP is the only modifiable risk factor for glaucoma,[4,6,32] IOP measurement is a cornerstone in glaucoma care. While direct measurements are invasive and not used in routine practice, current methods estimate true IOP using techniques such as applanation and rebound tonometry.[33] The most widely used applanation method is Goldmann Applanation Tonometry (GAT). To measure IOP with GAT, a drop of anesthetic and fluorescein is applied to the ocular surface, and an optical prism is gently pressed against the cornea. The force required to applanate the cornea is then directly proportional to the IOP. Noncontact tonometry also uses the applanation method but does not require anesthetics since an air pulse is used instead of a probe. Due to its noninvasive nature, noncontact tonometry is widely used by opticians. Rebound tonometry with Icare® is another widely used method that uses a small probe which briefly touches the cornea, making it ideal for children and patients with disabilities due to its portability and ease of use.[34]

Functional assessment of glaucoma is primarily performed through visual field testing (Figure 2). In Sweden, the most widely used device for this purpose is the Humphrey Field Analyzer (Carl Zeiss Meditec AG®). Humphrey utilizes standard automated

perimetry, a computerized, static threshold test that evaluates the patient's ability to detect white light stimuli presented against a white background. Humphrey is highly sensitive and capable of detecting glaucomatous visual field defects even in the early stages of the disease, before noticeable symptoms arise.[35,36] It provides detailed information about the location, depth, and progression of visual field loss, which is crucial for guiding treatment decisions and evaluating the effectiveness of therapy over time. The test results are typically presented in grayscale and pattern deviation plots, which help distinguish true glaucomatous damage from other causes of visual field loss. Regular and consistent visual field testing is essential for tracking disease progression and preventing significant vision impairment.

Evaluation of the optic nerve head is another key component of glaucoma diagnostics and can be performed using indirect fundoscopy at the slit lamp. Structural assessment may also include fundus photography and optical coherence tomography (OCT), which measures the optic nerve head, retinal nerve fiber layer, and ganglion cell layer. While OCT can support a glaucoma diagnosis, it must be interpreted alongside visual field findings, as an abnormal OCT alone is not sufficient for diagnosis.[4]

Additional diagnostic tools include gonioscopy and pachymetry. Gonioscopy is essential for evaluating the anterior chamber angle, confirming the presence of open-angle glaucoma, and identifying features such as TM pigmentation, abnormal blood vessels, and peripheral anterior synechiae. Pachymetry, commonly performed using OCT, measures central corneal thickness. Central corneal thickness plays an important role in the interpretation of IOP readings. Variations in corneal thickness can significantly influence IOP measurements: thicker corneas may produce falsely elevated IOP values, while thinner corneas may result in underestimation of the true IOP. Beyond its role in glaucoma assessment, corneal thickness measurement is also valuable in detecting corneal decompensation,[37] which may arise following intraocular surgery or as a consequence of corneal pathology.

Glaucoma staging and target IOP

Glaucoma staging is crucial since disease severity influences target IOP levels and the aggressiveness of treatment. Generally, the more advanced the disease, the lower the IOP should be to prevent further visual field deterioration.

Glaucoma staging is typically based on visual field mean deviation (MD). The Hodapp-Parrish-Anderson classification is one of the most commonly used staging criteria in glaucoma research and is also recommended by the European Glaucoma Society.[4] According to the Hodapp classification:[38]

- Mild glaucoma: MD ≥-6 decibels (dB)
- Moderate glaucoma: MD -6.01 to -12 dB
- Advanced glaucoma: MD <-12 dB

If visual field defects are absent and the optic nerve appears normal in the presence of elevated IOP, the condition is classified as ocular hypertension (OHT). If visual field defects are absent but optic nerve cupping is observed, the condition is classified as suspected glaucoma, as structural changes may precede functional loss.[4]

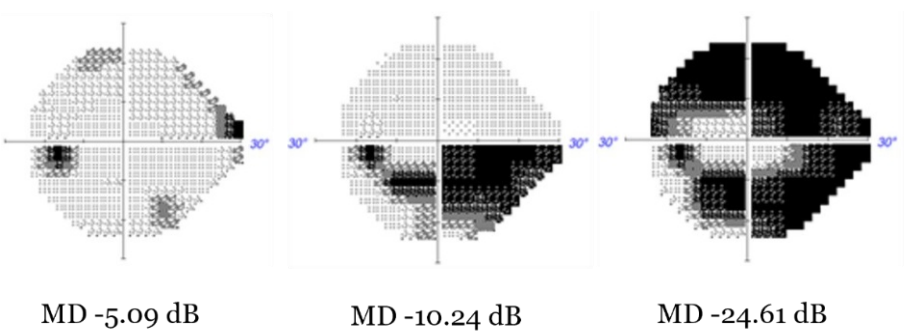

Figure 2. Examples of mild, moderate and advanced glaucoma (left eye) from three different glaucoma patients. dB = decibels; MD = mean deviation.

Target IOP refers to the maximum pressure considered acceptable for an individual with glaucoma. For newly diagnosed patients, the target IOP is a qualified guess by the treating clinician, based on disease severity and baseline IOP. In mild glaucoma, an IOP of up to 21 mmHg is generally acceptable, whereas moderate glaucoma requires a target of 15-17 mmHg. In advanced cases, IOP should be kept below 15 mmHg and often reduced to as low as 10-12 mmHg.[36] For OHT or suspected glaucoma, higher IOP levels may be tolerated, but even in these cases, IOP should remain well below 30 mmHg. Due to disease progression and potential comorbidities, the target IOP must be continuously reassessed.[39]

Treatment in glaucoma

The goal of glaucoma treatment

The primary goal of glaucoma treatment is to halt disease progression and preserve the patient's quality of life (QoL).[4,40] Research has shown that QoL is significantly impaired when the visual field in the worst-seeing eye declines below 50%.[41] Given the often slow progression of glaucoma, IOP is commonly used as a surrogate endpoint in surgical trials. This approach is both practical and ethically sound, as waiting for substantial visual field loss would require many years and expose patients to irreversible harm.

QoL can also be negatively impacted by the side effects of glaucoma medications or the development of cataract.[42] These factors can result in ocular discomfort and reduced functional vision, even in the absence of significant visual field loss.

Medical therapy

Topical eye drops are, alongside laser procedures, typically the first-line treatments for glaucoma. These medications either reduce aqueous humor production or increase aqueous humor outflow:

- Reduction of aqueous humor production: beta-blockers, carbonic anhydrase inhibitors, and alpha-2 selective adrenergic agonists.

- Increase in aqueous humor outflow: prostaglandin analogues, parasympathomimetics, and Rho kinase inhibitors. Prostaglandin analogues enhance uveoscleral outflow, while parasympathomimetics increase TM outflow by stimulating ciliary muscle contraction. Rho kinase inhibitors, a relatively new treatment, lower resistance in the TM and reduce episcleral venous pressure.

Glaucoma treatment usually follows a stepwise approach, beginning with a prostaglandin analogue or beta-blocker as monotherapy. If IOP remains above target, additional medications are introduced. However, the Glaucoma Intensive Treatment Study (GITS) has challenged this strategy, suggesting that intensive initial treatment may be beneficial in newly diagnosed cases with higher IOP levels.[43,44] If a patient requires more than three medications or suffers from intolerable side effects, surgery should be considered. Oral carbonic anhydrase inhibitors can temporarily be added while awaiting surgical intervention, but they are seldom tolerated as long-term treatment.

Laser trabeculoplasty

Laser trabeculoplasty (LTP) can be used as either a primary treatment or an adjunctive therapy when topical medications are insufficient, and its effect has been shown to be comparable to IOP-lowering eye drops.[45–47]

LTP consists of two main techniques:

- Argon Laser Trabeculoplasty (ALT): targets both pigmented and non-pigmented cells but causes coagulative tissue damage.

- Selective Laser Trabeculoplasty (SLT): acts specifically on pigmented cells, avoiding collateral damage to the TM. SLT is nowadays the laser treatment of choice, and its efficacy is similar to that of ALT.

Both ALT and SLT involve applying laser spots to the TM, triggering mechanical and cellular changes that enhance

permeability and promote aqueous outflow, thereby reducing IOP.[48]

LTP is generally safe, with mild inflammation and temporary IOP spikes as the most common adverse effects.[49] Despite its safety profile, LTP may not be effective for all patients and should preferably be used in mild to moderate glaucoma.[50]

Transscleral cyclophotocoagulation

Transscleral cyclophotocoagulation (TCP) is applied over the sclera, penetrating the tissue to reach the ciliary body, where it impairs the function of the secretory epithelium, thereby reducing aqueous humor production. Due to potential severe adverse effects such as persistent hypotony, prolonged intraocular inflammation, and deterioration of visual acuity, TCP is primarily reserved for eyes with advanced glaucoma and poor visual function,[51] although recent studies indicate that serious complications are rare.[52]

Bleb-forming surgery

When medical therapy and/or LTP can no longer provide sufficient IOP control, surgical intervention is recommended. Traditionally, trabeculectomy has been considered the gold standard for glaucoma surgery. This procedure involves the creation of a fistula to connect the anterior chamber with the subconjunctival space, establishing an alternative pathway for aqueous humor drainage. The long-term IOP control following a trabeculectomy is largely dependent on wound healing, which is managed using antifibrotic agents such as mitomycin-C. While mitomycin-C significantly improves surgical success, it carries risks including excessive drainage, scarring and endophthalmitis.[53] Despite procedural refinements that have improved trabeculectomy safety, major complications remain, and the surgery requires frequent postoperative follow-up visits and adjustments, such as suture manipulation and needling.

Long-tube glaucoma drainage devices such as Molteno®, Ahmed®, Baerveldt® and Paul® are alternatives to trabeculectomy. In Europe, they have traditionally been used after failed trabeculectomy, but recent trials suggest their potential also as primary procedures, especially when trabeculectomy success rates

are expected to be low.[54] However, like trabeculectomy, long-tube surgery carries risks of early or late hypotony, infection, scarring, corneal decompensation, and diplopia.[55–57]

Over the past decade, less invasive bleb-forming surgeries have entered the market, and currently, two devices are available – Xen Gel Stent® and PreserFlo® microshunt. These surgeries use the same mechanism as traditional bleb-forming surgeries with the creation of an external subconjunctival filtration, but with potentially faster recovery.[58] However, their efficacy seems to be inferior to traditional bleb-forming surgeries and serious complications such as hypotony and excessive scarring remain.[59,60]

History of trabecular meshwork surgery

Trabecular meshwork surgery in glaucoma has a long history. In 1938, Otto Barkan introduced goniotomy (from Greek: *gonio* = angle; *tomein* = cut), a procedure designed to surgically incise and open the TM in infants with congenital glaucoma.[61] In the 1960s, Hermann Burian and Redmond Smith adapted the technique for adults, using an ab externo approach, i.e from outside the eye.[62] Although goniotomy appeared to be effective in adult glaucoma, results were better in congenital glaucoma.[63] In the 1960s, trabeculectomy emerged as a surgical option, and goniotomy nearly disappeared as a treatment for adult glaucoma.[64,65]

By the early 2000s, surgical advancements using ab interno techniques again renewed interest in goniotomy for adult glaucoma. An ab interno approach – i.e. from within the eye without disrupting the conjunctiva – offers a less invasive surgical option, with reduced risks and faster recovery compared to earlier techniques. These new techniques performed ab interno form the foundation of the modern paradigm of MIGS.

MIGS

MIGS is a group of surgical techniques designed to lower IOP and/or reduce the need for topical medications, while being minimally traumatic to the eye. These procedures are characterized by a favorable safety profile and a fast postoperative recovery.[66,67]

The possibility of intervening earlier in the disease course has led to a growing adoption among surgeons, and the use of MIGS continues to expand. All MIGS devices enhance aqueous humor outflow from the anterior chamber, either by directly accessing the TM or by diverting aqueous humor to the suprachoroidal space (Figure 3).

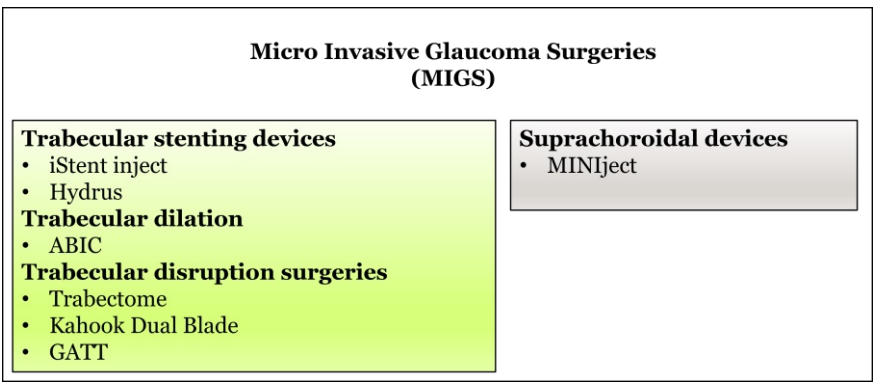

Figure 3. Overview of microinvasive glaucoma surgeries. ABIC= Ab interno canaloplasty; GATT= Gonioscopy assisted transluminal trabeculotomy.

Suprachoroidal devices work by creating controlled cyclodialysis and increasing uveoscleral outflow via the suprachoroidal space.[68] While ongoing studies continue to assess their efficacy and safety, long-term data are limited.

Trabecular MIGS include stenting devices, trabecular dilation, and trabecular disruption, all of which improve conventional trabecular outflow. This thesis focuses on one stenting device – iStent inject® (iStent), and one disruptive device – Kahook Dual Blade® (KDB).

The iStent®, developed by Glaukos Corporation and FDA-approved in 2012, was the first trabecular micro-bypass stent introduced to the market. Implanted through a clear corneal incision, it is inserted into Schlemm´s canal to bypass the TM, facilitating aqueous humor outflow. It was originally launched as a single snorkel-shaped device but has undergone refinements over the years (Figure 4). The iStent inject®, introduced in 2018, features a dual stent coated with heparin and made of non-ferromagnetic

titanium. Measuring 360 µm in length and 230 µm in diameter, it is the smallest medical implant approved for human use. In 2019, the iStent inject W® was developed; with a broader neck, it improves implantation precision and prevents over-insertion. The most recent version, the iStent infinite®, was introduced in 2022 as a three-stent model. However, long-term comparative studies evaluating its efficacy and safety are still awaited.

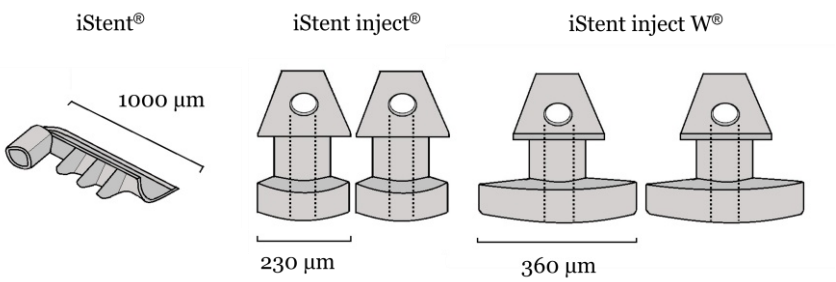

Figure 4. First, second and third generation iStent stents. Illustration by Anna Barkander.

The KDB, developed by New World Medical and approved by the FDA in 2015, features a knife with a dual-sided tip designed for precise incisions in the TM. By lifting and excising a strip of TM tissue, it facilitates aqueous humor drainage into Schlemm´s canal. The KDB Glide®, introduced in 2020 as a second-generation instrument, features beveled edges and rounded corners designed to enhance usability (Figures 5 and 6). Despite these ergonomic improvements, it retains the original KDB's ramp technology and 230 µm blade distance. Given the minor design changes, KDB and KDB Glide are expected to demonstrate comparable efficacy.

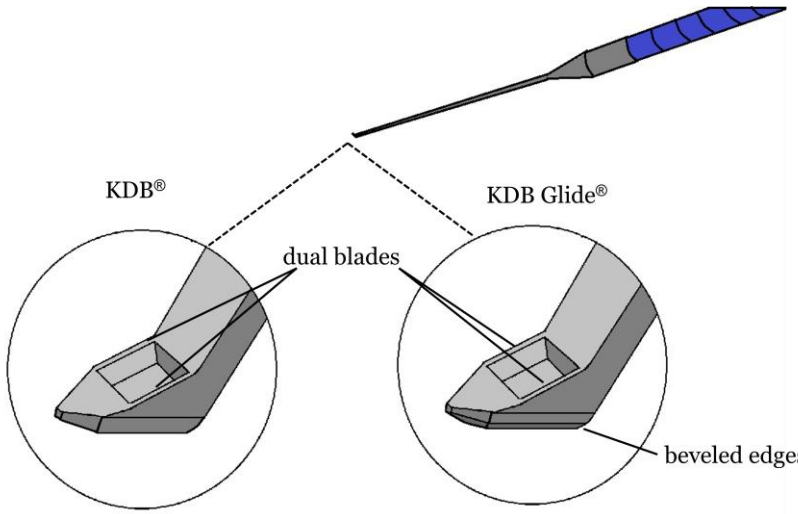

Figure 5. Kahook Dual Blade and Kahook Dual Blade Glide. Illustration by Anna Barkander.

Comparative studies between the first generation iStent and KDB suggest that KDB may be slightly more effective.[69] The second-generation iStent inject and iStent inject W appear to offer improved efficacy compared to the single-stent version, though few direct comparisons between iStent inject/iStent inject W and KDB have been conducted.[70–72] Additionally, long-term studies remain sparse. Moreover, studies including PEXG patients are few,[73–75] and this glaucoma type is especially common in the Nordic countries.[7–10]

The most common postoperative complications after iStent and KDB are transient IOP spikes and hyphema. Although a hyphema does not appear to negatively impact surgical outcomes,[76] it can temporarily impair visual acuity, which is particularly problematic for patients who are blind in one eye. IOP spikes are typically managed with additional IOP-lowering medications. However, delayed or insufficient treatment can result in irreversible optic nerve damage.[77] Cases of cyclodialysis cleft have also been reported with both iStent and KDB.[69]

Conducting comparative studies on trabecular MIGS poses significant challenges due to variations in glaucoma severity,

baseline IOP levels, and medication regimens among study patients. Additionally, the use of different outcome measures further complicates comparisons. The frequent combination of MIGS with cataract surgery adds another layer of complexity when interpreting outcomes, as it can be challenging to separate the effect of the cataract procedure from the effect of the MIGS procedure.

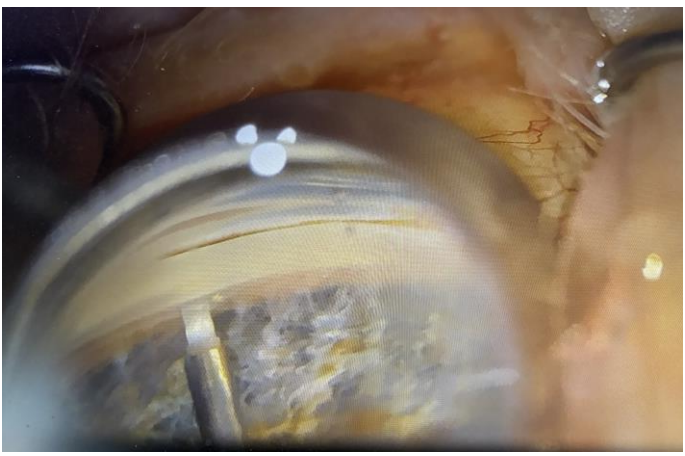

Figure 6. Kahook Dual Blade surgery performed by Anna Barkander. From the operating room at the Eye Clinic in Östersund.

Glaucoma and cataract surgery

Many glaucoma patients develop cataract, and early cataract surgery is often beneficial for these individuals. Beyond improving visual acuity and QoL,[78] cataract surgery can contribute to a modest reduction in IOP, typically averaging 2-4 mmHg.[79–82] In patients with PEX, the IOP-lowering effect is often at the higher end of the range,[83–85] and it has even been shown that cataract surgery in PEX patients can reduce the risk of developing glaucoma.[86]

Having a pseudophakic patient – one who has undergone cataract surgery – is beneficial if bleb-forming surgery is later required. Pseudophakia simplifies surgical planning and reduces the risk of lens-induced complications. In phakic patients – those with their natural lens – bleb-forming surgery accelerates cataract

development,[87] and if cataract surgery is performed after a bleb-forming procedure, the likelihood of failure can increase due to inflammation and scarring.[88,89] This underscores the importance of performing cataract surgery at an earlier stage.

When cataract surgery is performed in both study arms of a comparative MIGS trial, it becomes difficult to assess the true effect of the MIGS procedure. Additionally, some postoperative complications may result from the cataract operation rather than the MIGS procedure.

Cataract surgery is generally considered safe, but it can nonetheless have complications such as infection, corneal edema and prolonged postoperative inflammation. In glaucoma patients, and especially if PEX is present, cataract surgery can be more challenging due to small pupils or weak zonules.[90,91]

Compliance and adverse effects of treatment

Eye drops and laser procedures are usually first-line treatments for glaucoma, while traditional bleb-forming surgery is the most effective treatment. However, bleb-forming surgery carries risks such as inflammation, hypotony, bleeding and infection.[92] They also require longer operating times and more frequent postoperative follow-up visits. Additionally, the lifelong risk of bleb-related complications, such as bleb dysesthesia, leakage, and infection, must be considered when deciding upon surgery.

Treatment with eye drops and laser procedures also has limitations. Topical medications can cause both ocular and systemic side effects,[93] and patient adherence is often suboptimal.[94] Despite using multiple medications or undergoing repeated laser treatments, many patients still experience glaucoma progression. By the time surgery is performed, patients have often been on several medications for years, leading to increased postoperative inflammation and a higher risk of scarring and surgical failure.[93,95,96]

Given the side effects of topical therapy and the potential complications associated with traditional surgery, MIGS has

emerged as an alternative to control the disease at an earlier stage, while simultaneously reducing topical medications.[97]

Need for further MIGS research?

Interest in MIGS has grown over the past decade, yet a clear consensus on its optimal use is still lacking. Although numerous publications have reported results on MIGS outcomes, most are retrospective and show considerable variability in the definition of outcome measures.[72,98–104] Non-industry sponsored studies that stratify results by glaucoma severity are limited, and most of the existing research focuses on patients with mild to moderate disease.[104–106] There is a notable lack of studies involving patients with PEXG and those with advanced-stage disease. Furthermore, no head-to-head comparisons have been made between iStent W and KDB. Additionally, nearly all existing studies on KDB are retrospective in nature, limiting the strength of the evidence.[99]

KDB has been less extensively studied than iStent, but its lower cost suggests it may be a more cost-effective alternative. However, further research is essential to determine the comparative efficacy, safety, and long-term impact of these procedures.

HYPOTHESES AND AIMS

The overall purpose of this project was to provide insights into the role of trabecular MIGS in contemporary glaucoma management. The general aim was to study the efficacy and safety of the trabecular MIGS procedures iStent inject/iStent inject W and KDB/KDB Glide.

Based on prior studies and clinical experience, we hypothesized that iStent and KDB, when performed in combination with cataract surgery, would lead to a reduction in IOP and/or a decreased need for glaucoma medications compared to cataract surgery alone. We also hypothesized that these MIGS procedures would be effective and safe across various glaucoma subtypes and severities. To evaluate their overall effectiveness, stand-alone trabecular MIGS procedures were also included in the retrospective analysis alongside combined MIGS and cataract surgery.

The specific aims of this project were:

- To evaluate the efficacy and safety of stand-alone KDB versus KDB combined with cataract surgery in patients with medically uncontrolled glaucoma.

- To compare KDB and iStent in mild to moderate versus advanced glaucoma and evaluate the effect of preoperative IOP levels and number of medications on surgical outcomes.

- To assess the efficacy and safety of KDB and iStent in patients with and without PEX.

- To investigate a possible association between the effect of LTP and the effect of subsequent surgery with cataract-KDB.

- To evaluate if adding iStent W or KDB Glide to cataract surgery affects surgical outcomes and QoL compared to performing cataract surgery as a stand-alone procedure.

MATERIALS AND METHODS

Subjects

Studies I-IV included patients from the Eye Clinic in Östersund, located in the Region of Jämtland Härjedalen in northern Sweden (Figure 7). Studies I-III were retrospective analyses of medical records from patients who underwent surgery with iStent or KDB between 2019 and 2021. To minimize bias, only the first operated eye was included for patients who had both eyes eligible for surgery.

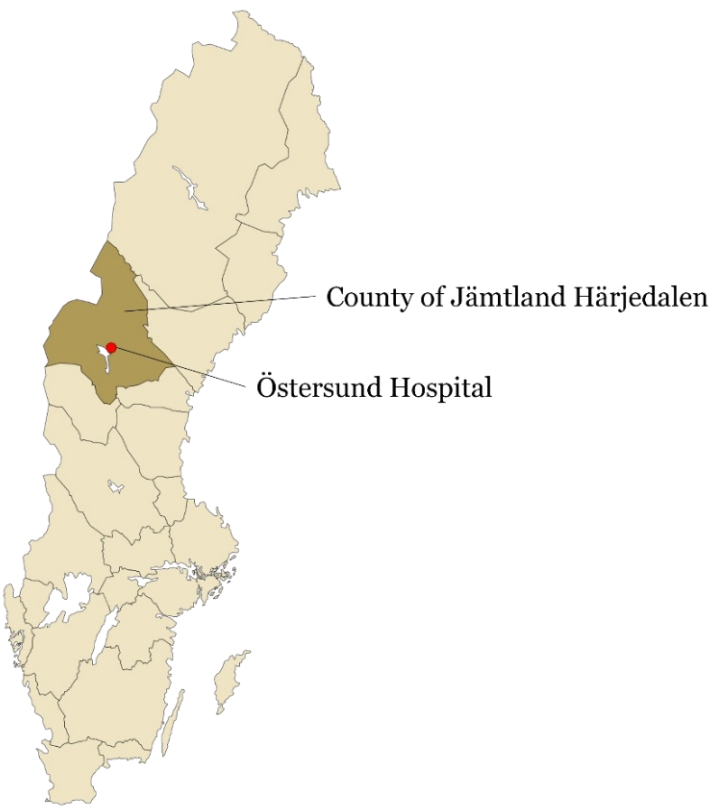

Figure 7. Map of Sweden with the County of Jämtland Härjedalen marked. Image adapted from Wikimedia Commons.

Study I included 90 patients who had undergone goniotomy with KDB, either as a stand-alone procedure or in combination with cataract surgery, between September 1, 2019, and December 31, 2020. The inclusion criteria were mild to advanced open-angle glaucoma that was uncontrolled, i.e., having visual field progression and/or elevated IOP despite treatment with three or more medications.

Study II included 153 patients who had undergone cataract surgery combined with iStent or KDB between March 1, 2019, and August 31, 2020. The inclusion criteria were mild to advanced open-angle glaucoma.

Study III included 250 open-angle glaucoma patients who had undergone cataract surgery combined with KDB between October 1, 2019, and December 31, 2021. Among these, 111 patients had previously undergone LTP at some point before the cataract-KDB operation.

Study IV, referred to as the SMIGS (Swedish MicroInvasive Glaucoma Surgery) study, included 120 adult patients receiving medical treatment for glaucoma or OHT, all of whom had clinically significant cataract.

The inclusion criteria in Study IV were:

- Age over 18 years
- Clinically significant cataract
- Glaucoma or OHT treated with one to four medications and no need for additional glaucoma surgery at the time of study enrollment
- Open chamber angle with Shaffer grading three to four in at least two quadrants

The exclusion criteria in Study IV were:

- Prior glaucoma surgery, including TCP

- SLT within 90 days prior to the planned surgery

- Exudative age-related macular degeneration, proliferative diabetic retinopathy, clinically significant corneal dystrophy, or any eye disease that could potentially affect IOP or the visual field

- Inability to participate or provide written consent due to other medical conditions

Patients likely to be eligible for the trial were identified at their regular consultation for glaucoma and provided with a patient information leaflet. The principal investigator was responsible for deciding whether a patient was eligible for inclusion in the study. Eligible patients, who agreed to take part, signed a consent form before being randomized into one of three treatment arms: cataract surgery alone, cataract surgery combined with iStent W, or cataract surgery combined with KDB Glide.

IOP measurements

In Studies I, II and III, IOP measurements were generally performed using GAT. However, due to the retrospective design, occasional IOP measurements were performed with iCare or noncontact tonometry.

In Studies I and II, we used IOP measurements at baseline and postoperatively at one week, one month, three months (Study I only), six months, 12 months and 24 months. In Study III, we used IOP measurements taken three months after LTP and one year after cataract-KDB surgery. Since Studies I-III were retrospective analyses of medical records, the closest available time point to the scheduled measurement was selected.

In Study IV, all IOP measurements were obtained using GAT. Since this prospective study was not masked, the *two-person method* was used, wherein the investigator performed the GAT measurement while an assistant recorded the IOP. Before randomization to surgery, two IOP measurements were taken on separate days and averaged before calculation. Postoperatively,

IOP measurements were taken on day one, week six, months three, six, 12, and 24. Additional measurements were performed when necessary, such as after a change in therapy.

Best corrected visual acuity

Best corrected visual acuity (BCVA) was measured as decimal acuity using the Snellen chart. In Studies I-III, data were collected from medical records. In Study IV, BCVA was measured before pupil dilation, tonometry, gonioscopy, or any other procedure that could affect visual acuity. Decimal acuity values were converted into logMAR to allow for statistical analysis. A high logMAR value corresponds to low BCVA, and vice versa. In cases of very poor visual acuity, BCVA was documented as counting fingers, hand movements, light perception, or amaurosis.

Slit lamp biomicroscopy

In Studies I-III, slit lamp biomicroscopy findings were collected from medical records. In Study IV, slit lamp biomicroscopy was performed in a standardized manner, examining the anterior segment first and progressing posteriorly. In Study IV, examinations were conducted within three months preoperatively and at postoperative intervals on day one, week six, months three, six, 12, and 24. The presence of hyphema, intraocular inflammation, and corneal edema was recorded.

Gonioscopy

In Study IV, preoperative gonioscopy was conducted in all patients to confirm an open chamber angle. Shaffer grading was used, requiring an angle grade of three or four in at least two quadrants to exclude closed-angle glaucoma.

Pachymetry

In Study IV, pachymetry was performed within six months prior to surgery and reassessed three months after surgery to exclude surgery-related corneal decompensation.

Optical Coherence Tomography (OCT)

In Study IV, preoperative OCT (DRI OCT Triton®, Topcon) of the optic nerve and macula was conducted to strengthen the diagnosis, differentiate suspected glaucoma from OHT, and detect any pathology affecting BCVA or visual field. Postoperative OCT was allowed at any time point if BCVA declined, investigating potential complications such as postoperative macular edema or epiretinal membrane formation.

Visual field testing

In Studies I and II, the last visual field before surgery was evaluated and reassessed after one and two years.

In Study IV, visual field testing was conducted before surgery (within three months) and at six and 12 months postoperatively. Standard automated perimetry using the Humphrey® Field Analyzer (SITA Faster) was utilized, with the technician monitoring the patient throughout.

Cataract surgery

In Studies I-IV, cataract surgery was performed in a standardized manner by an experienced surgeon (Figure 8). When iStent/iStent W or KDB/KDB Glide were added, these procedures were performed after cataract removal and intraocular lens placement. In Study IV, patients were randomized to cataract surgery alone or combined with iStent W or KDB Glide.

Figure 8. Cataract surgery performed by Anna Barkander at the Eye Clinic in Östersund.

iStent inject and Kahook Dual Blade surgery

In Studies I-IV, implantation with iStent/iStent W or goniotomy with KDB/KDB Glide was performed after cataract surgery (Figures 9 and 10). The anterior chamber was filled with additional cohesive viscoelastic, and the operating microscope was tilted approximately 35°, while the patient´s head was turned 35° away from the surgeon to optimize the view of the chamber angle.

The previously made temporal cataract incision was utilized. After implanting iStent stents or performing goniotomy with KDB, all viscoelastic was removed using an irrigation-aspiration instrument, and the eye was filled with balanced salt solution. At the end of surgery, intracameral cefuroxime (1 mg) and ampicillin (0.1 mg) were administered.

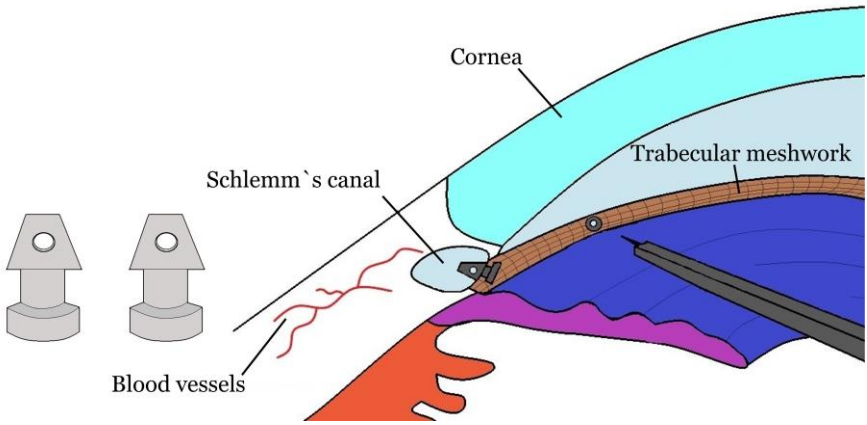

Figure 9. iStent inject. Illustration by Anna Barkander.

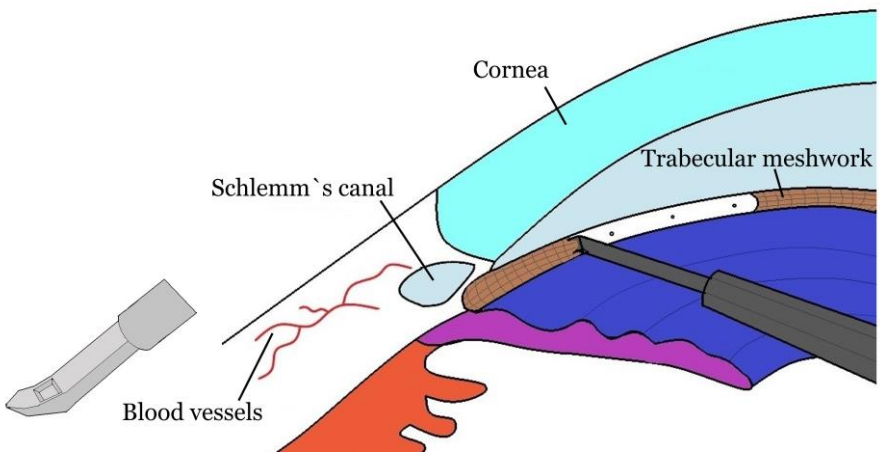

Figure 10. Kahook Dual Blade. Illustration by Anna Barkander.

Postoperative care and follow-up

In Studies I-III, patients received topical dexamethasone (1 mg/ml) three times daily for three weeks postoperatively. In Study IV, this regimen was supplemented with topical nepafenac (3 mg/ml) once daily for three weeks to reduce postoperative inflammation and minimize the risk of macular edema.

Glaucoma medications were generally continued for the first three postoperative weeks. After this period, medications were discontinued if the disease remained stable and target IOP was achieved. Generally, IOP levels ≤21 mmHg were acceptable in medically treated OHT or suspected glaucoma, ≤18 mmHg in mild glaucoma, ≤15 mmHg in moderate glaucoma, and ≤12 mmHg in advanced glaucoma. The Hodapp-Parrish-Anderson criteria were used to classify glaucoma severity. If visual field progression occurred or IOP became unacceptably elevated, medications were adjusted, or LTP was performed. To ensure patient safety, further glaucoma surgery was permitted if necessary during follow-up.

Vision-related quality of life

Patients in the SMIGS study (Study IV) were asked to complete a vision-related QoL assessment preoperatively and after six months, using the National Eye Institute Visual Function Questionnaire (NEI VFQ-25, 25 items). NEI VFQ-25 is one of the most commonly used patient-reported outcome measures in ophthalmology studies, and its purpose is to measure both vision- and health-related QoL.[107,108]

Vision-related QoL measurements have been advocated in glaucoma trials but also questioned as glaucoma's impact on vision-related QoL is often only detectable once the disease reaches an advanced stage.[109] However, side effects associated with glaucoma medications can also negatively affect vision-related QoL, and reducing medication dependency through MIGS has been shown to improve ocular symptoms.[110] Since MIGS surgeries are commonly combined with cataract surgery, which itself enhances vision-related QoL,[111] it is essential that QoL assessments in MIGS studies include a comparative cataract control group.

Statistical methods

In Studies I-IV, subject demographics and outcomes were descriptively summarized using means and standard deviations (SD) for continuous, symmetric variables and medians and inter-quartile ranges (IQR) for continuous skewed variables. Categorical variables were presented as frequencies and percentages. Group

comparisons were performed using independent-samples t-tests for parametric data and Mann-Whitney U tests for nonparametric data. In Study IV, comparisons across the three treatment arms were performed using one-way ANOVA for parametric data and Kruskal-Wallis tests for nonparametric data. Categorical variables were analyzed using chi-square tests or Fisher's exact tests. For paired data, dependent-samples t-tests (parametric) or Wilcoxon signed-rank tests (nonparametric) were used. Kaplan-Meier survival analysis was used to assess failure rates over time. Postoperative comparisons included IOP measurements, changes in visual field MD, and the number of IOP-lowering medications.

A P-value <0.05 was considered statistically significant. Snellen visual acuity was converted into logMAR for statistical analysis. If a patient required additional surgery, their BCVA and IOP data were excluded from further analysis.

In Study IV, a power calculation was performed based on the assumption of a 4 mmHg difference in IOP between cataract surgery alone and cataract surgery combined with either iStent W or KDB Glide.[81] The study was not designed to detect a significant difference in efficacy between iStent W and KDB Glide. To achieve a statistical power greater than 80% at a significance level of 0.05, a sample size of 37 eyes per group was required. To account for a potential dropout rate of up to 10%, 40 eyes were included in each group.

Outcome measures and adverse events

In Study I, surgical success was defined as:

- A reduction in IOP of ≥20% and/or a reduction of ≥1 medication at 24 months.

In Study II, we chose to report IOP- and medication reduction as separate outcomes to enable comparisons between patients with varying glaucoma severity, as well as between iStent and KDB. Surgical success was defined as:

- A reduction in IOP of ≥20% with a postoperative IOP ≤18 mmHg at 24 months.

- A reduction of ≥1 medication at 24 months.

Results were stratified according to glaucoma severity – mild to moderate versus advanced.

In Study III, the primary outcome was to examine whether previous LTP treatment influenced subsequent surgery with cataract surgery combined with KDB. The secondary outcome was to examine whether there was an association between LTP success and cataract-KDB success. A successful outcome of LTP and cataract-KDB was defined as:

- A reduction in IOP of ≥20% and/or a reduction of ≥1 medication after three months (± two months) and one year (± six months) respectively. If further glaucoma surgery occurred within the follow-up period, the cataract-KDB procedure was considered a failure.

In Study IV, the primary outcome measures were:

- Number of patients in each group achieving a reduction in IOP of ≥20% and/or a reduction of ≥1 medication at 12 months.

- Changes in IOP and number of medications compared to baseline.

In Study IV, the secondary outcome measures were:

- Number of patients reaching IOP thresholds of ≤12 mmHg, ≤15 mmHg, ≤18 mmHg, and ≤21 mmHg at 12 months.

- Number of patients requiring additional surgery or TCP during follow-up.

- Number of patients requiring additional medications or SLT during follow-up.

In Studies I-IV, for outcomes to be classified as successful, they had to be achieved without additional medical therapy, SLT, TCP, or further glaucoma surgery. In Studies I, II, and IV, the number of patients requiring additional glaucoma surgery or TCP during follow-up was documented, along with adverse events such as hyphema, IOP spikes, and excessive inflammation, including rebound iritis and postoperative macular edema. We also assessed any potentially serious adverse events that could result in permanent and significant visual impairment, such as endophthalmitis or suprachoroidal hemorrhage.

Study dropout rates

- In Study I, two-year data were unavailable for eight patients due to death (n=4), comorbidities preventing examination (n=3), or relocation to another city (n=1).

- In Study II, two-year data were unavailable for four patients due to death (n=3) or relocation to another city (n=1).

- In Study III, patients were excluded due to lack of IOP and/or medication data (n=12), death (n=9), presence of another eye disease affecting the IOP (n=4), or prior glaucoma surgery before the cataract-KDB operation (n=8).

- In Study IV, there were no dropouts at the one-year follow-up.

Ethical considerations

All studies adhered to the Declaration of Helsinki and were approved by the Swedish Ethical Review Authority.

In Studies I-III, data was collected from medical records, and no new interventions were introduced that could potentially harm patients. In Study IV, patients were monitored at regular postoperative intervals, with additional follow-up visits as needed. If patients in any treatment arm exhibited visual field progression

or elevated IOP, adjustments were made through medication changes, laser therapy, or further glaucoma surgery.

Consent

In Study IV, all patients provided written informed consent before inclusion. Consent was obtained after patients received both oral and written study information and were given the opportunity to ask questions.

Risk of harm

In Studies I-III, surgery had already been completed, and no additional harm was expected from retrospectively collecting and analyzing the data.

In Study IV, patients were closely monitored in accordance with the study protocol. All measurements used in the study are standard in glaucoma care. IOP measurements and anterior chamber angle grading require a local anesthetic drop and are routinely performed in clinical practice. Other assessments, including perimetry, pachymetry, and OCT, are non-invasive.

Cataract surgery carries potential risks such as infection, inflammation, bleeding, and IOP spikes, but all patients in Study IV had clinically significant cataract and an indication for surgery. KDB and iStent have demonstrated an acceptable safety profile, with hyphema being the most common postoperative complication. Patients underwent regular follow-up visits, and adverse events were managed according to standard clinical practice.

Study results were presented at the group level, and all data were handled securely to ensure the protection of sensitive personal information.

RESULTS

Baseline characteristics

Across all studies, patient characteristics including age, gender and the presence of PEX were similar (Table 1). In Study I, patients were specifically selected due to uncontrolled glaucoma; therefore, baseline IOP levels and the number of medications were higher compared to the other studies. Additionally, Study I included patients with a history of previous glaucoma surgery, which was an exclusion criterion in Studies II-IV.

In contrast, patients in Study IV were required to be stable enough to undergo cataract surgery alone. Consequently, baseline IOP levels and medication use were lower, and advanced glaucoma was less common in this cohort.

Study	I	II	III	IV
Number of patients	90	153	250	120
Age (years), mean ± SD	77 ± 6.9	75 ± 6.4	75 ± 6.5	76 ± 5.5
Female, % (n)	48% (43)	46% (71)	50% (124)	48% (57)
PEX, % (n)	62% (56)	59% (90)	57% (143)	55% (66)
Advanced glaucoma, % (n)	50% (45)	49% (75)	35% (88)	5% (6)
IOP, mean ± SD	23.1 ± 7.0	20.2 ± 6.1	21.1 ± 6.5	18.6 ± 4.0
Range	12 to 54	8 to 44	11 to 44	11.5 to 28.5
Medications, median [IQR]	3 [3-4]	3 [2-3]	3 [1-3]	2 [1-3]
Previous glaucoma surgery*, % (n)	10% (9)	-	-	-

*Table 1. Patient characteristics from Studies I-IV. *Including transscleral photocoagulation. IOP = intraocular pressure; IQR = interquartile range; PEX = pseudoexfoliations; SD = standard deviation.*

Success rates and change in IOP and medications

At month 12, the largest reductions in IOP were observed in Study I, where patients also had the highest IOP levels at baseline (Table 2). In both Studies I and II, IOP reductions remained stable from month 12 to 24. Although the average IOP reduction ranged from approximately 4 to 8 mmHg, there was considerable variation among the included eyes. Some eyes experienced an IOP reduction of up to 41 mmHg, whereas others had the same or even higher IOP after 12 and 24 months.

The reduction in medication use was greater at 12 than at 24 months, especially in the KDB-alone group, where the number of medications was actually higher at month 24 compared to baseline.

Across Studies I-II, the highest success rates – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication – were seen in the cataract-KDB groups at month 12, while the lowest success rate was seen in the KDB-alone group at month 24. In this group, 28% of patients required additional glaucoma surgery within 24 months. These eyes were excluded from the IOP- and medication reduction analysis, but their outcomes were reflected in a lower success rate.

Study		I		II	
		KDB-alone	Cataract-KDB	Cataract-iStent	Cataract-KDB
Month 12	Number of patients	29	46	43	88
	IOP change, mean ± SD	-8.3 ± 8.8	-7.7 ± 6.3	-5.0 ± 6.0	-4.4 ± 6.3
	Range	-41 to 3	-28 to 2	-23 to 8	-28 to 9
	Meds change, mean ± SD	-0.4 ± 1.1	-1.4 ± 1.3	-0.4 ± 0.7	-1.2 ± 1.3
	Range	-3 to 1	-4 to 1	-3 to 1	-4 to 2
	Success rate month 12	57%	85%	55%	83%
Month 24	Number of patients	22	43	47	91
	IOP change, mean ± SD	-7.8 ± 6.8	-8.0 ± 4.7	-5.2 ± 7.3	-5.3 ± 5.5
	Range	-23 to 2	-22 to -1	-27 to 13	-26 to 5
	Meds change, mean ± SD	0.5 ± 1.0	-1.1 ± 1.1	-0.4 ± 0.9	-0.9 ± 1.2
	Range	-3 to 1	-4 to 1	-3 to 1	-4 to 2
	Success rate month 24	47%	76%	65%	75%

Table 2. Success rates and change in intraocular pressure and number of medications. Success defined as an IOP reduction of ≥20% and/or a reduction of ≥1 medication at 12 and 24 months. Eyes having further glaucoma surgery within follow-up were excluded from the IOP- and medication reduction analysis, but their outcomes were reflected in a lower success rate. IOP = intraocular pressure (in mmHg); iStent = iStent inject; KDB = Kahook Dual Blade; Meds = medications; SD = standard deviation.

To further illustrate the variability in the IOP-lowering effect, we combined 12-month data from Studies I-IV in a scatterplot (Figure 11). As illustrated in the scatterplot, most eyes had a 12-month IOP level between 10 mmHg and 21 mmHg, regardless of whether the preoperative IOP was as low as 10 mmHg or as high as 40 mmHg.

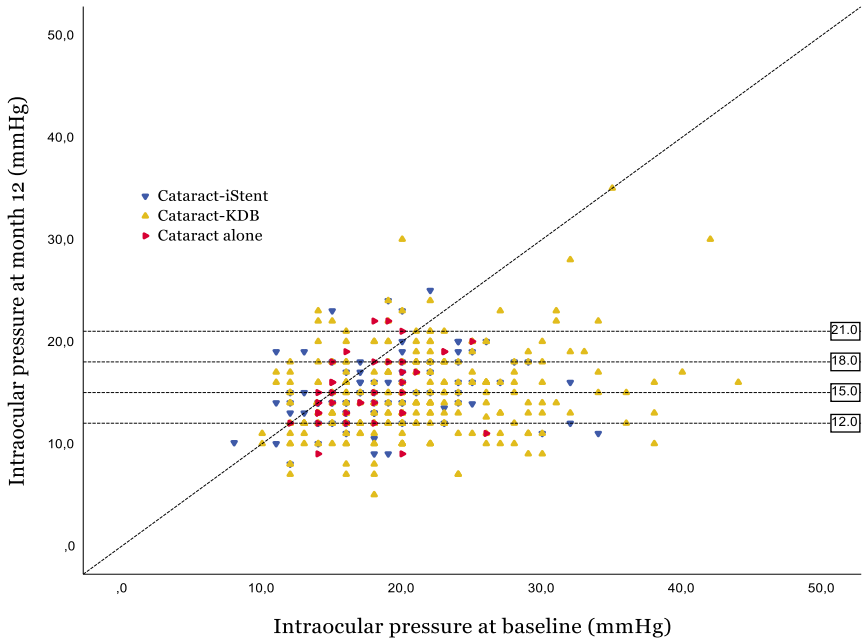

Figure 11. Scatterplot showing combined data from Studies I-IV. iStent = iStent inject/iStent inject W; KDB = Kahook Dual Blade/Kahook Dual Blade Glide.

Target IOP levels at baseline and at month 12

After combining data from Studies I-IV, we found that baseline IOP levels ≤12 mmHg were achieved in only up to 8% of patients (Table 3). At month 12, this proportion had increased in all groups, even so in the cataract-alone group, thus reflecting the IOP-lowering effect of cataract surgery. Notably, target IOP levels were overall similar between groups. However, it is important to consider that patients who required further surgery within 24 months were excluded from the IOP- and medication analyses. Additionally, some patients may have needed additional medications to reach their target IOP, which could improve IOP control without necessarily qualifying as a surgical success.

		Study I	**Studies I-IV**	**Studies II & IV**	**Study IV**
IOP levels	Timepoint	KDB-alone, % (n)	Cataract-KDB, % (n)	Cataract-iStent, % (n)	Cataract, % (n)
≤12 mmHg	Baseline	-	6% (19)	8% (8)	3% (1)
	Month 12	24% (7)	33% (96)	19% (18)	18% (7)
≤15 mmHg	Baseline	8% (3)	18% (53)	24% (23)	30% (12)
	Month 12	52% (15)	63% (182)	59% (49)	59% (23)
≤18 mmHg	Baseline	21% (8)	40% (120)	48% (46)	55% (22)
	Month 12	79% (23)	86% (251)	84% (70)	82% (32)
≤21 mmHg	Baseline	38% (15)	62% (184)	65% (62)	83% (33)
	Month 12	86% (25)	95% (276)	95% (79)	95% (37)

Table 3. Target IOP levels at baseline and at month 12. Combined data from Studies I-IV. IOP = intraocular pressure; iStent = iStent inject/iStent inject W; KDB = Kahook Dual Blade/Kahook Dual Blade Glide. ***Note:*** *Patients that lacked 12-month data or had further surgery are not included in the 12-month follow-up.*

Medication use at baseline and at month 12

When KDB was performed as a stand-alone procedure, patients were unlikely to become medication-free postoperatively. Only one patient in the KDB-alone group was able to discontinue all medications within the first 12 months (Study I, Table 4). In contrast, when iStent or KDB were combined with cataract surgery, nearly one-third of patients became medication-free postoperatively (Studies I-IV, Table 4). Notably, following cataract surgery alone, 23% of patients were medication-free at 12 months (Study IV, Table 4).

		Study I	Studies I-IV	Studies II & IV	Study IV
Meds	Timepoint	KDB-alone, % (n)	Cataract-KDB, % (n)	Cataract-iStent, % (n)	Cataract, % (n)
0	Baseline	-	4% (12)	-	-
	Month 12	3% (1)	30% (88)	27% (22)	23% (9)
1	Baseline	-	23% (69)	30% (29)	35%(14)
	Month 12	7% (2)	14% (42)	19% (16)	31% (12)
2	Baseline	-	31% (92)	20% (19)	31% (12)
	Month 12	3% (1)	21% (61)	20% (17)	15% (6)
≥3	Baseline	100% (39)	42% (124)	50% (48)	35% (14)
	Month 12	86% (25)	21% (60)	34% (28)	31% (12)

Table 4. Medication use at baseline and at month 12. Combined data from Studies I-IV. Meds = medications; iStent = iStent inject/iStent inject W; KDB = Kahook Dual Blade/Kahook Dual Blade Glide.

Trabecular MIGS as stand-alone

In Study I, we retrospectively compared KDB as a stand-alone procedure to KDB combined with cataract surgery. Patients included in this study had glaucoma progression or risk thereof due to uncontrolled IOP, despite treatment with three or more glaucoma medications. In the KDB-alone group, 21% of patients had a previously failed glaucoma operation compared to 2% in the cataract-KDB group (P=0.004). Patients in the KDB-alone group were older (80 versus 75 years, P <0.001), but advanced glaucoma was equally common in both groups (47% versus 54%, P=0.523). All patients in the KDB-alone group were pseudophakic, and the cataract operation had been performed on average 7.4 ± 6.6 years prior to the KDB operation.

The primary success rate – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication at month 24 – was 47% (15 eyes) in the KDB-alone group and 76% (37 eyes) in the cataract-KDB group, a statistically significant difference favoring the combined approach (P = 0.009).

Medication reduction was modest in the KDB-alone group, and the main treatment effect was seen in IOP reduction, where mean IOP decreased from 24.8 ± 8.3 mmHg at baseline to 15.0 ± 5.3 mmHg at 24 months (P <0.001). However, it is important to note that data from patients who underwent further glaucoma surgery were excluded from this analysis.

Furthermore, after KDB-alone, only 24% of patients achieved IOP levels below 12 mmHg – often considered necessary in advanced glaucoma – suggesting limited efficacy in this subgroup. Additionally, 28% of patients in this group required additional glaucoma surgery within two years compared to 12% in the combined cataract-KDB group. This was a statistically significant difference in cumulative survival rate between the two groups (Figure 12).

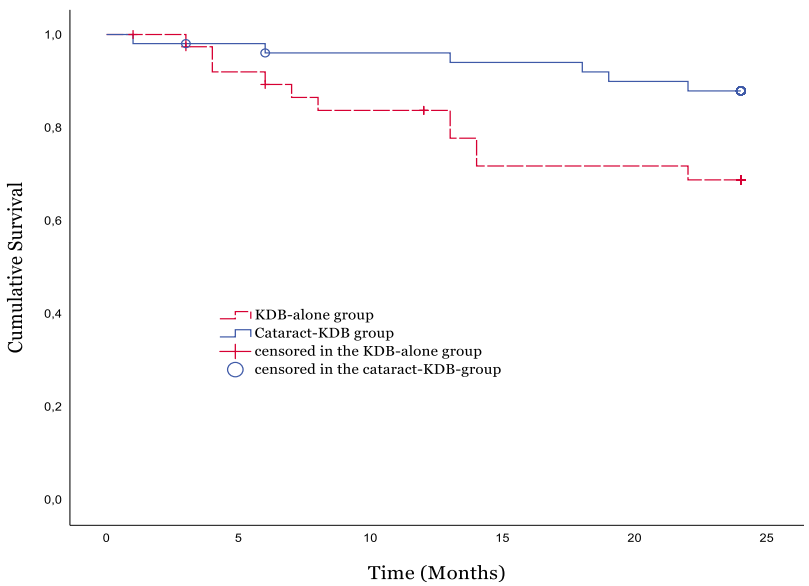

Figure 12. Kaplan-Meier cumulative survival in the KDB-alone and cataract-KDB groups. Patients in the cataract-KDB group were less likely to undergo further surgical procedures within 24 months (P = 0.026, log-rank test). From Study I. KDB = Kahook Dual Blade.

Trabecular MIGS across glaucoma stages

In Study II, we evaluated the efficacy and safety of cataract surgery combined with either iStent or KDB in patients with mild to moderate glaucoma versus advanced glaucoma. A total of 153 eyes were included, of which 49% had advanced glaucoma.

Among eyes with mild to moderate glaucoma, 52% in the cataract-iStent group and 54% in the cataract-KDB group achieved a reduction in IOP of ≥20% with a postoperative IOP ≤18 mmHg. In eyes with advanced glaucoma, the same outcome was achieved by 42% in the cataract-iStent group and by 46% in the cataract-KDB group. Although a higher percentage of eyes with mild to moderate glaucoma met the success criterion compared with those with advanced glaucoma, the difference was not statistically significant.

At month 24, a reduction of ≥1 glaucoma medication was more common in the cataract-KDB group compared with the cataract-iStent group (53% versus 32%, P = 0.013), whereas no significant differences were found between mild to moderate and advanced glaucoma within either group (Study II).

After combining data from Studies I-IV and including eyes that had either iStent/iStent W or KDB/KDB Glide, a statistically significant difference in success rate at month 12 was observed between mild to moderate and advanced glaucoma (Figure 13). Among patients undergoing cataract surgery combined with these trabecular MIGS procedures, the success rate was 86% in those with mild to moderate glaucoma compared to 73% in those with advanced glaucoma.

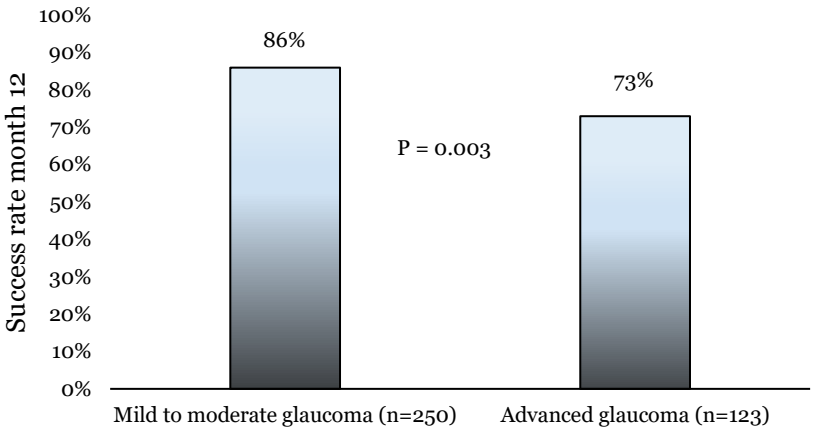

Figure 13. A comparison of success rates between mild to moderate and advanced glaucoma, where success is defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication at month 12. Combined data from Studies I-IV on patients who had cataract surgery combined with iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide.

In Study II, we found that target IOP levels had improved at 24 months compared with baseline. For mild to moderate glaucoma, IOP levels up to 18 or 21 mmHg are generally considered acceptable, while for advanced glaucoma, targets are typically below 12 or 15 mmHg. However, these thresholds are individual. Some patients with mild to moderate glaucoma may require pressures lower than 18 mmHg, while some patients with advanced disease can remain stable even with IOP levels above 15 mmHg.

In mild to moderate glaucoma (Study II):

- IOP levels ≤18 mmHg increased from 30% to 74% in the cataract-iStent group and from 35% to 90% in the cataract-KDB group.

- IOP levels ≤21 mmHg increased from 39% to 90% in the cataract-iStent group and from 56% to 94% in the cataract-KDB group.

In advanced glaucoma (Study II):

- IOP levels ≤12 mmHg increased from 12% to 50% in the cataract-iStent group and from 5% to 44% in the cataract-KDB group.

- IOP levels ≤15 mmHg increased from 27% to 82% in the cataract-iStent group and from 31% to 74% in the cataract-KDB group.

Stratified results based on IOP levels and preoperative medication burden

After combining 12-month data from all operations with cataract-iStent/iStent W and cataract-KDB/KDB Glide (Studies I-IV), we stratified outcomes based on preoperative IOP levels and number of medications. The success rate – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication – was comparable across varying preoperative IOP levels and number of medications (Figures 14 and 15).

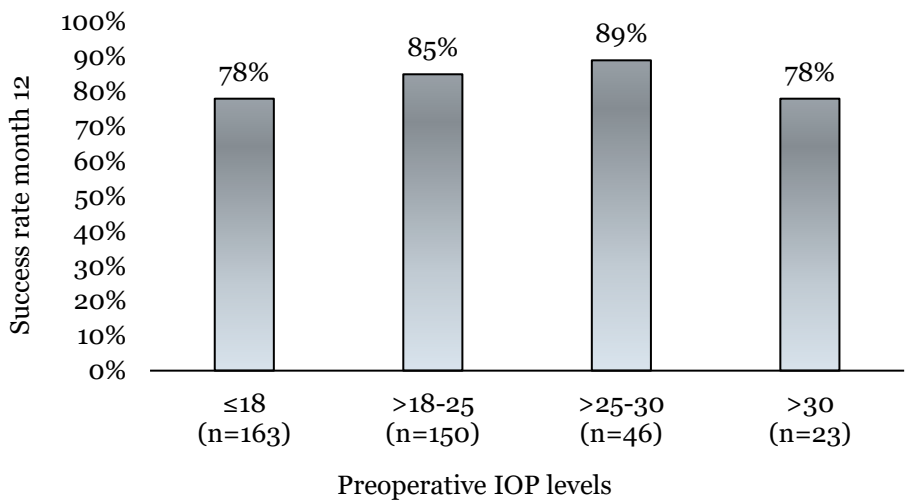

Figure 14. Success rates stratified by preoperative IOP levels in mmHg. Success defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication at month 12. Combined data from patients in Studies I-IV who had cataract surgery combined with either iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide.

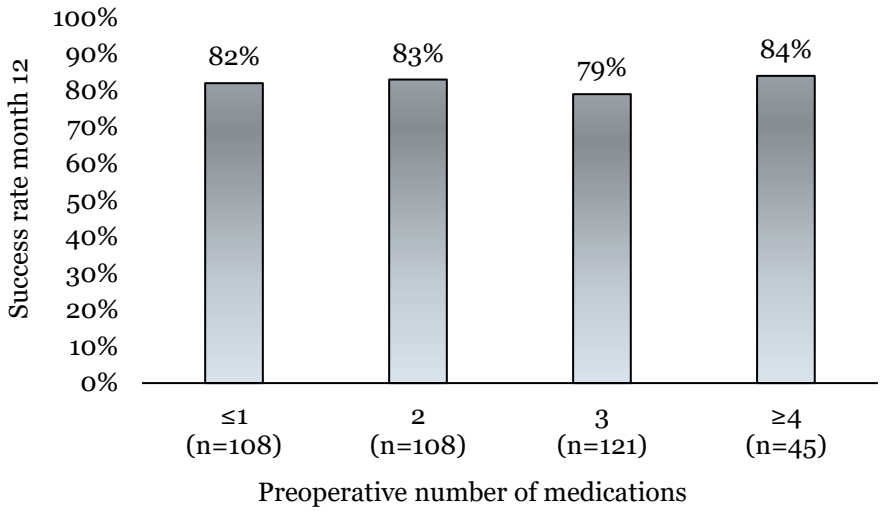

Figure 15. Success rates stratified by preoperative number of medications. Success defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication at month 12. Combined data from patients in Studies I-IV who had cataract surgery combined with either iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide.

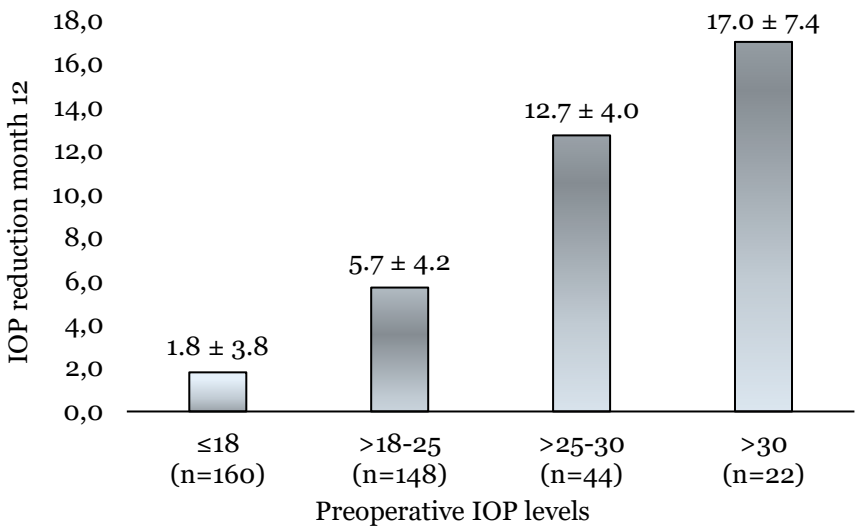

Figure 16. Mean IOP reductions (± standard deviation) in mmHg at month 12 stratified by preoperative IOP levels. Combined data from patients in Studies I-IV who had cataract surgery combined with either

iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide. IOP = intraocular pressure.

IOP reductions at month 12 were greater in eyes with higher preoperative IOP levels, with reductions from 1.8 mmHg in eyes with lower IOP levels to 17 mmHg in eyes with higher IOP levels (Figure 16).

Medication reductions were greater in eyes with lower preoperative IOP levels, although eyes with higher preoperative IOP levels also demonstrated a modest reduction in medication use (Figure 17). Interestingly, the reduction in medication use was comparable between eyes with preoperative IOP levels of >18-25 mmHg and >25-30 mmHg. Medication reductions were also greater in eyes with a higher number of medications prior to surgery (Figure 18).

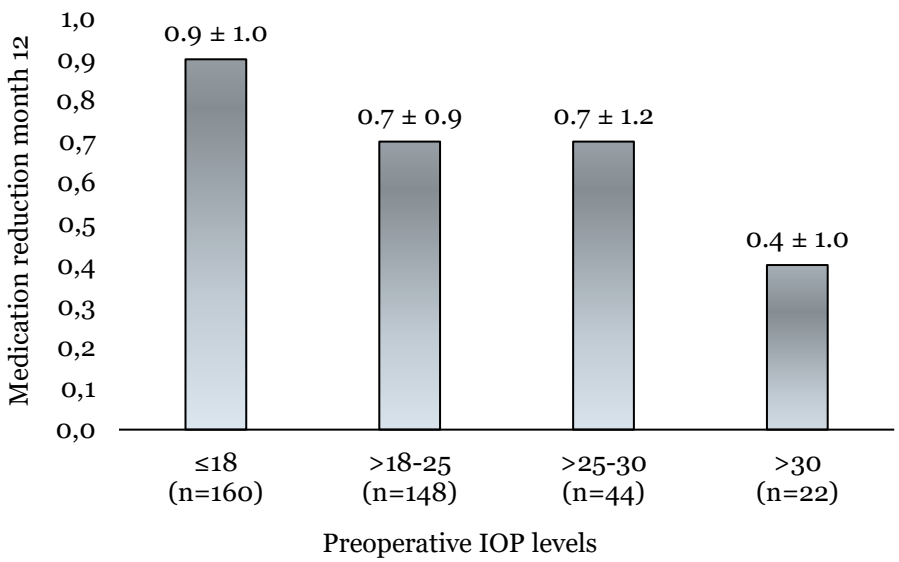

Figure 17. Mean medication reduction (± standard deviation) at month 12 stratified by preoperative IOP levels in mmHg. Combined data from patients in Studies I-IV who had cataract surgery combined with either iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide. IOP = intraocular pressure.

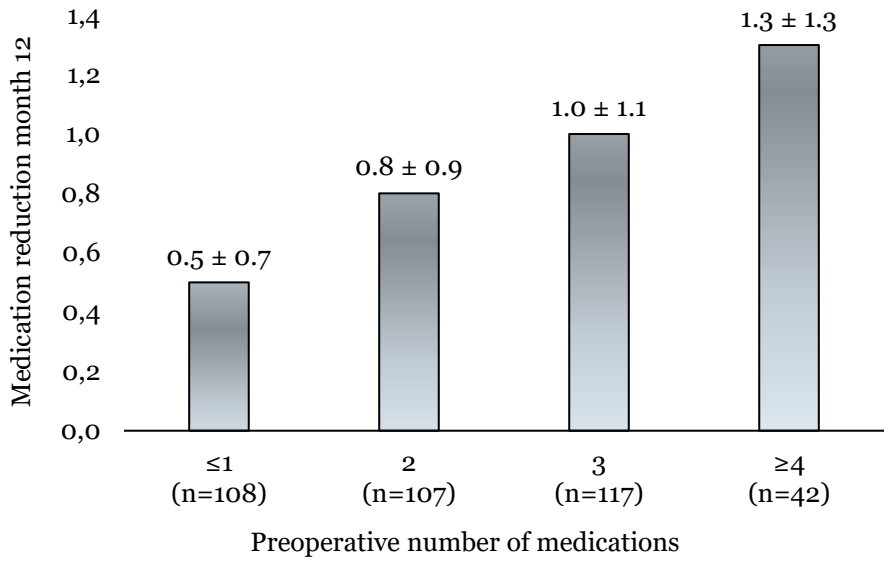

Figure 18. Mean medication reduction (± standard deviation) at month 12 stratified by preoperative number of medications. Combined data from patients in Studies I-IV who had cataract surgery combined with either iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide.

Trabecular MIGS in eyes with PEX

In Study I, the success rate at month 24 – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication – was similar in eyes with and without PEX (65% versus 63%). Notably, 20 eyes demonstrated IOP reductions of ≥40%, 75% of which had PEX. Furthermore, IOP reductions of ≥50% and ≥60% were observed in 11 and 7 eyes, all of which had PEX.

Similarly, in Study IV, success rates at month 12 were comparable between eyes with and without PEX across all three treatment groups (cataract-alone, cataract-iStent W and cataract-KDB Glide). The success rate – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication – was met by 55%, 84% and 90% of PEX eyes in the cataract, cataract-iStent and cataract-KDB groups. In non-PEX eyes the same success criterion were met by 44%, 93%, and 86%, respectively.

After combining data from Studies I-IV on cataract surgery combined with either iStent/iStent W or KDB/KDB Glide, we found a significant difference in success rate at month 12 between eyes with and without PEX. The predefined success criterion – a reduction in IOP of ≥20% and/or a reduction of ≥1 medication was met by 87% of PEX eyes compared to 75% of non-PEX eyes (P = 0.006). This higher success rate observed in PEX eyes was primarily driven by a greater reduction in IOP rather than a reduction in medication use. The mean IOP reduction was 6.3 ± 6.2 mmHg in PEX eyes compared to 4.4 ± 6.0 mmHg in non-PEX eyes (P = 0.004). The mean medication reduction was 0.9 ± 1.0 in PEX eyes and 0.7 ± 1.0 in non-PEX eyes (P = 0.203).

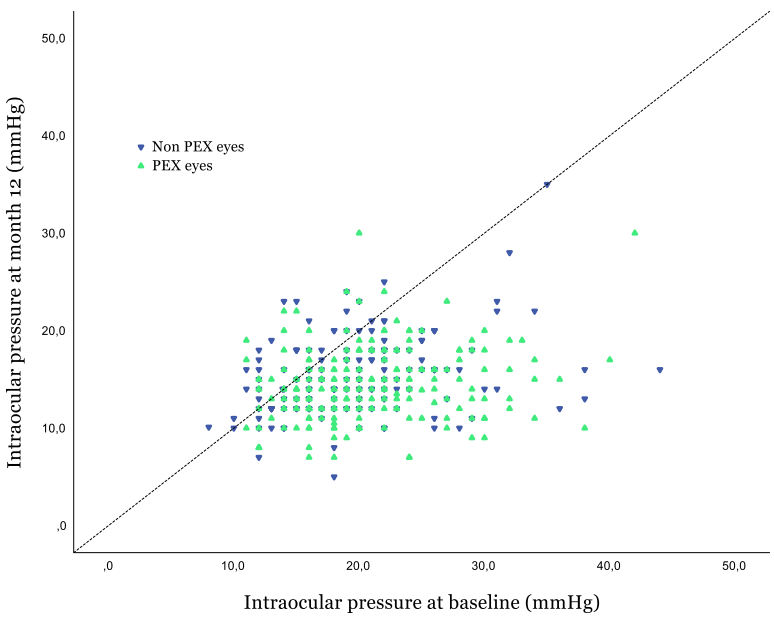

Figure 19. Scatterplot showing intraocular pressure levels at baseline and at month 12. Combined data from patients in Studies I-IV who had cataract surgery combined with iStent inject/iStent inject W or Kahook Dual Blade/Kahook Dual Blade Glide. PEX = pseudoexfoliations.

PEXG is typically more aggressive and challenging to manage than POAG. Despite this, findings from Study II showed that although 59% of eyes had PEXG, these eyes accounted for only 27% of the cases requiring additional surgery. A similar pattern was observed

in the cataract-KDB group in Study I, where 60% of included eyes had PEX, but only 33% of the eyes that needed further surgery had PEX. In the KDB-alone group, on the other hand, 72% of the eyes requiring further glaucoma surgery had PEX.

Trabecular MIGS and laser trabeculoplasty

LTP is widely used in clinical practice, and many patients undergoing cataract surgery have previously undergone LTP. In Study III, we evaluated 250 patients with open-angle glaucoma who underwent cataract surgery combined with KDB between 2019 and 2021. Of these, 111 patients had received one or more previous LTP treatments (43 ALT and 68 SLT).

The surgical success after cataract-KDB – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 medication – was similar regardless of whether previous LTP treatment had been performed or not (83% with previous LTP and 89% without previous LTP) and also similar regardless of whether previous LTP treatment had been successful (81% after successful LTP and 83% after unsuccessful LTP). Comparable results were seen, regardless of whether ALT or SLT had been performed.

IOP- and medication reductions were also comparable in LTP- and non-LTP-treated patients. One year after cataract-KDB, the mean IOP reduction in LTP-treated patients was 6.3 ± 6.2 mmHg compared to 6.9 ± 6.5 mmHg in non-LTP-treated patients. Similarly, the reduction in glaucoma medications was 0.8 ± 1.1 in LTP-treated patients and 0.9 ± 1.1 in non-LTP-treated patients.

The effect of cataract surgery on the IOP

To evaluate the IOP-lowering effect of cataract surgery compared to cataract surgery combined with either iStent W or KDB Glide, we conducted a randomized controlled study including 120 patients. Although the study aimed to include patients across all stages of glaucoma, patients with an unstable disease were excluded due to the requirement that further glaucoma surgery should not be needed at the time of study enrollment. Consequently, Study IV primarily reflects the outcomes of adding

iStent W or KDB Glide in patients with a stable disease, and few of the included patients had advanced glaucoma.

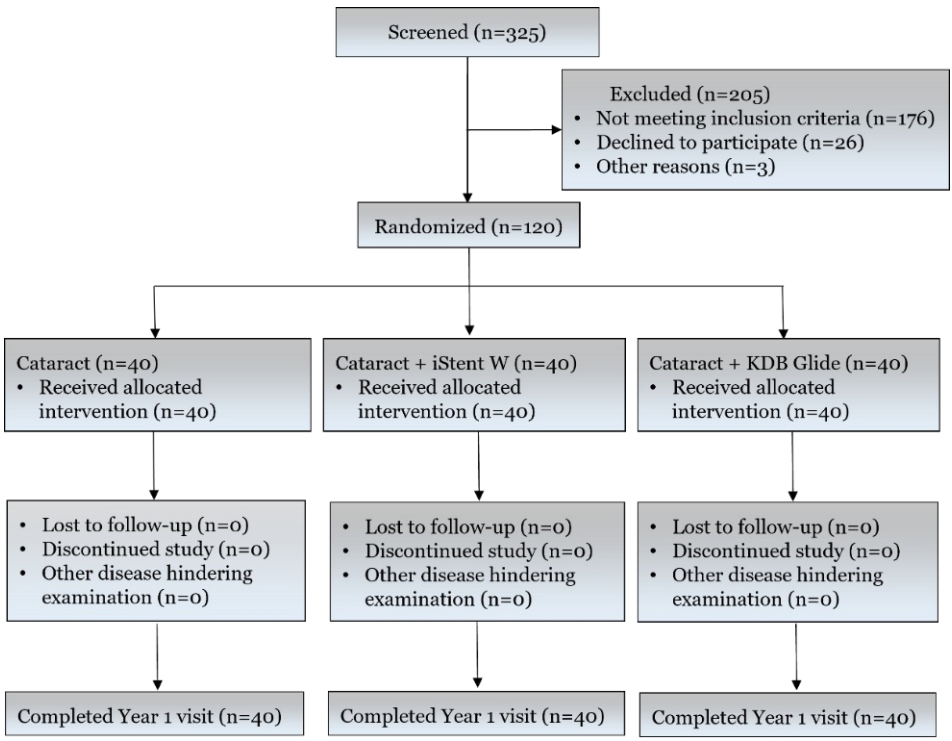

Figure 20. Flow diagram outlining the phases of the SMIGS Study (Study IV). iStent W = iStent inject W; KDB Glide = Kahook Dual Blade Glide.

Patients in the SMIGS study will be followed for five years, but the results so far – after one year – show that the primary success (a reduction in IOP of ≥20% and/or a reduction of ≥1 medication) was achieved by 53% after cataract surgery alone and by 88% after cataract surgery combined with iStent W or KDB Glide (P<0.001). IOP reductions were similar between groups (Table 5), whereas medication reductions were greater in the groups receiving iStent W or KDB Glide. In the cataract group, 23% of patients were medication-free at one year compared to 53% in the cataract-iStent W group and 43% in the cataract-KDB Glide group.

	Cataract	Cataract-iStent W	Cataract-KDB Glide	P-value
Number of patients	40	40	40	
IOP change,* mean ± SD	-3.0 ± 4.2	-3.5 ± 3.8	-2,8 ± 4.3	0.755
Range	-17.5 to 4	-13.5 to 4.5	-10.5 to 10	
Meds change,* mean ± SD	-0.4 ± 0.8	-0.8 ± 0.7	-0.9 ± 0.7	0.01
Range	-3 to 1	-3 to 0	-3 to 1	
Success rate	53%	88%	88%	<0.001

*Table 5. Success rates and change in intraocular pressure and number of glaucoma medications at month 12. From the SMIGS study (Study IV). Success defined as an IOP reduction of ≥20% and/or a reduction of ≥1 medication at 12 months. IOP = intraocular pressure in mmHg; iStent W = iStent inject W; KDB Glide = Kahook Dual Blade Glide; Meds = medications. ***Note:** Intraocular pressure- and medication changes are not included for one patient (in the cataract group) that had further glaucoma surgery within the specified time-period.*

Safety and adverse events

Hyphema

Definition of hyphema varied in the different studies, as did the time of evaluation. In Study I, hyphema was defined as layered blood in the anterior chamber at week one after surgery. Since small layered hyphemas are generally harmless, in Study II, we also evaluated presence of complete hyphemas, defined as total filling of blood in the anterior chamber, resulting in a postoperative BCVA <20/200 within the first postoperative week. Presence of blood cells visible at the slit lamp at week one was also assessed in the same study. In Study IV, hyphema was again defined as layered blood in the anterior chamber (as in Study I), but the assessment was performed on postoperative day one rather than at week one.

In Study I, a layered hyphema at week one was observed in 26% (n=9) of eyes after KDB-alone and in 4% (n=2) of eyes after cataract-KDB. In Study II, blood cells in the anterior chamber were, as expected, more common than layered hyphema and found in 14% (n=8) of cataract-iStent eyes and in 62% (n=60) of cataract-

KDB eyes. A total 5% of eyes (n=7) developed a complete hyphema – one in the cataract-iStent group and six in the cataract-KDB group. All complete hyphemas occurred in eyes with PEX and two of these patients (both in the cataract-KDB group) required an anterior chamber washout in the operating room. Both these two patients later also underwent Yttrium Aluminum Garnet (YAG) laser capsulotomy because of blood staining on the posterior lens capsule.

In Study IV, the rate of hyphema was lower than in the other studies, despite the assessment being performed on day one rather than at week one, when many hyphemas would typically have resolved. All hyphemas found in Study IV were small and self-limiting and observed only in the cataract-KDB Glide group (15%, n=6).

In Studies I and II, we investigated a potential association between anticoagulation therapy and hyphema. Although 44% and 29% of patients were on anticoagulants, we found no association between anticoagulation therapy and hyphema at week one when KDB or iStent were combined with cataract surgery. However, when KDB was performed as a stand-alone procedure (in Study I), a statistically significant association was observed between hyphema and anticoagulation therapy (P = 0.005). Still, the number of patients in this subgroup was only 39, making it difficult to draw firm conclusions.

IOP spikes

An IOP spike was defined as an IOP elevation of ≥10 mmHg from baseline or an absolute IOP of ≥30 mmHg. In Studies I and II, IOP spikes were assessed at postoperative week one, whereas in Study IV, the evaluation was performed on day one.

In Study I, an IOP spike was observed in 11% (n=4) of eyes in the KDB-alone group and in 8% (n=4) of eyes in the cataract-KDB group. One patient in each group required an aqueous tap through the existing paracentesis at the slit lamp due to elevated IOP (and concurrent hyphema). In both cases, IOP normalized within one month.

In Study II, an IOP spike at week one was seen in 5% (n=3) of eyes in the cataract-iStent group and in 14% (n=14) of eyes in the cataract-KDB group (P = 0.120).

In Study IV, where patients were evaluated on postoperative day one instead of week one, an IOP spike was observed in 38% (n=15) of eyes in the cataract-alone group, 10% (n=4) in the cataract-iStent W group, and 15% (n=6) in the cataract-KDB Glide group. This represented a statistically significant difference between the cataract-alone group and the two MIGS groups (P = 0.006).

Postoperative inflammation

Postoperative inflammation is an expected consequence of intraocular surgery. Following cataract surgery, with or without trabecular MIGS, the standard three-week course of anti-inflammatory therapy is sometimes insufficient and must be extended due to persistent or rebound iritis or macular edema. In our studies, we examined the number of patients who, due to prolonged inflammation, required extended anti-inflammatory therapy beyond the third postoperative week.

In Study I, one patient (with PEX) in the cataract-KDB group developed rebound iritis, and one patient (without PEX) postoperative macular edema. These inflammatory conditions both resolved within three months on topical treatment.

In Study II, rebound iritis occurred in four eyes in both the cataract-iStent and cataract-KDB groups. Notably, 88% of these cases were in eyes with PEX. One patient (without PEX) in the cataract-KDB group experienced transient postoperative macular edema, resolving within two months on topical treatment.

In Study IV, surgical complications were also more common in eyes with PEX. Rebound iritis (two cases in the cataract-alone group) and transient macular edema (one case in the cataract-alone group and three in the cataract-KDB group) were exclusively observed in PEX eyes, and resolving within four months on topical treatment.

No serious adverse events were found in any of the studies.

Corneal edema

In Study IV, corneal edema was observed on day one in 5% (n=2) of eyes in the cataract-alone group compared to 35% (n=14) in the cataract-iStent W group and 38% (n=15) in the cataract-KDB Glide group (P = 0.001). All cases were spontaneously resolved. One patient in the cataract-iStent W group also had pre-existing corneal guttata, but even in this patient, the corneal edema was resolved by the six-month visit.

Surgical complications

In Study IV, one eye developed transient aqueous misdirection with posterior fluid pressure, resulting in iris prolapse and subsequent loss of iris tissue at the wound site. Another eye had a posterior capsule rupture, although without vitreous prolapse. Despite these events, the assigned procedures were completed as planned (in both cases cataract-KDB Glide), and no further interventions were needed.

Mechanical pupil dilation was required in 8% (n=5) of eyes (all with PEX) – three in the cataract-alone group and one in the cataract-iStent W group. None of these cases resulted in postoperative complications. Additionally, due to PEX and zonular weakness, one eye in the cataract-KDB Glide group required the use of capsule retractors during surgery.

Vision and visual field status

In Study I, visual field status at month 24 showed a statistically significant worsening in the KDB-alone group. The MD declined from -13.7 ± 5.6 at baseline to -16.6 ± 6.7 at month 24 (n=14, P = 0.019). However, this deterioration was observed only in patients with advanced glaucoma; those with mild or moderate disease showed stable MD values. In contrast, the cataract-KDB group demonstrated overall stability in visual field status, with MD changing from -11.4 ± 7.8 preoperatively to -10.8 ± 8.3 at month 24 (n=39, P = 0.129). Even among patients with advanced glaucoma in this group, MD remained stable (-17.9 ± 6.5 at baseline versus -17.8 ± 1.5 at month 24; n=18, P = 0.955).

In Study II, both BCVA and MD at month 24 were either improved or unchanged across all treatment subgroups.

In Study IV, BCVA was improved or unchanged in all three treatment groups (cataract-alone, cataract-iStent W, and cataract-KDB Glide). At the group level, both MD and BCVA remained stable or improved across all groups. No patient experienced a reduction in BCVA of ≥2 lines at month 12 compared to baseline. However, a worsening in MD by ≥2 dB at month 12 was observed in two patients in the cataract-alone group (from -6.0 to -12.4 and from -6.6 to -9.4), and in one patient in the cataract-iStent W group (from -4.1 to -6.2). One patient underwent additional glaucoma surgery at month eight (in the cataract-alone group) and was excluded from the visual field analysis at month 12, as were three patients who were unable to perform a reliable visual field test at that time point (two in the cataract-alone group and one in the cataract-KDB Glide group).

Further interventions

In Study I, additional glaucoma surgery or TCP was performed in 28% (n=11) of eyes in the KDB-alone group and in 12% (n=6) of eyes in the cataract-KDB group within 24 months. Kaplan-Meier analysis showed a higher likelihood of requiring additional surgical intervention in the stand-alone group. However, it is important to note that eight patients in the KDB-alone group had previously undergone a failed glaucoma surgery, and five of these patients required an additional surgical intervention following the KDB procedure.

In Study II, a total of 7% (n=11) of patients required a further surgical intervention within 24 months – seven in the cataract-iStent group and four in the cataract-KDB group. This difference was statistically significant ($P < 0.046$, log-rank test), although the groups were not matched at baseline, and the second-generation iStent was used rather than the updated W-model.

Interestingly, although a total of 23 patients across all studies had preoperative IOP levels >30 mmHg, only one of these patients required additional glaucoma surgery within the first year.

In Study IV, follow-up is currently limited to 12 months. During this period, one patient in the cataract-alone group required further glaucoma surgery, performed at month eight. Additional interventions, defined as the initiation of glaucoma medications or SLT, were required in four eyes: three in the cataract-alone group (one SLT and two with added medications) and one in the cataract-KDB Glide group (added medications).

Vision-related quality of life

There were no significant differences in patient-reported outcomes, as measured by the NEI VFQ-25, between the cataract-alone, cataract-iStent W, and cataract-KDB Glide groups at baseline or at month six.

The composite score improved in all three groups at month six, indicating a perceived enhancement in vision-related QoL following surgery.

Composite score	**Baseline**	**Month 6**	**P-value**
Cataract surgery alone, mean ± SD	77.7 ± 13.9	88.4 ± 10.0	<0.001
Cataract surgery & iStent W, mean ± SD	79.9 ± 13.1	87.2 ± 9.6	<0.001
Cataract surgery & KDB Glide, mean ± SD	79.0 ± 12.0	89.0 ± 10.8	<0.001
P-value	0.634	0.522	

Table 6. Composite scores at baseline and at month six using the Visual Field Questionnaire 25 (VFQ-25). From the SMIGS study (Study IV). iStent W = iStent inject W; KDB Glide = Kahook Dual Blade Glide; SD = standard deviation.

DISCUSSION AND CLINICAL IMPLICATIONS

Trabecular MIGS as stand-alone

We found the success rate after KDB alone to be 47% (compared with 76% after cataract-KDB) and almost a third of patients required further glaucoma surgery within two years. Consistent with our findings, previous studies have reported less favorable outcomes after KDB alone compared with KDB combined with cataract surgery.[98,112] Wakil et al. found a significant reduction in medication after 12-18 months in patients who underwent cataract-KDB, whereas patients who underwent KDB alone were unable to reduce their medications. IOP levels were similar between groups, but the re-operation rate within 18 months was 22% after KDB alone compared with only 2% after combined cataract-KDB.[112] The re-operation rate after trabecular MIGS as stand-alone is an important measure on the overall effectiveness, and due to inclusion of patients with different preoperative characteristics, the re-operation rate has varied from 12% to 44% within 12 to 24 months postoperatively.[112–115] Duong et al. reported the highest re-operation rate – 44% within 24 months – and patients in that study were using four or more glaucoma medications preoperatively, had IOP levels exceeding 25 mmHg, and more than one-third had severe glaucoma.[115]

In our studies, we did not evaluate iStent as a stand-alone procedure, but previous studies have shown iStent to have an effect in a stand-alone setting.[116,117] A meta-analysis including 17 studies and 978 eyes, reported that 86% (95% CI: 74% to 93%) of eyes achieved an IOP reduction ≥20% at the study endpoint (up to 42 months). The mean difference in IOP between baseline and endpoint was -2.6 (95% CI: -3.2 to -2.1), and the mean difference in medication use was -1.7 (95% CI: -2.2 to -1.2).[116] Another meta-analysis on stand-alone iStent (including 13 studies and 778 eyes) reported a mean IOP reduction of 31%, corresponding to a mean decrease of 7.0 mmHg (95% CI: 5.9 to 8.1) at six to 12 months. For studies with longer follow-up periods (36 to 60 months), IOP

reductions remained consistent, ranging from 30% to 33%.[117] Medications were reduced by approximately 1.0 medication at six to 18 months and by 1.2 medications at 36 to 60 months. Overall, 3% of eyes included in the analysis required secondary glaucoma surgery, such as trabeculectomy, during the follow-up period. The relatively low rate of subsequent surgical interventions likely reflects that 92% of included eyes had mild to moderate glaucoma, and therefore a reduced need for additional procedures.[117]

Based on our findings and supported by other studies,[116,117] we suggest that trabecular MIGS as a stand-alone procedure may be an appropriate option for patients with mild to moderate glaucoma and inadequately controlled IOP. Conversely, for patients with advanced disease who require lower target IOP levels, bleb-forming surgery should remain the preferred approach.

iStent versus KDB

IOP reductions were similar in patients undergoing cataract surgery combined with either iStent or KDB. However, in Study II, we found that medication reduction was significantly greater in the cataract-KDB group compared with the cataract-iStent group, with 53% versus 32% of patients achieving a reduction of ≥1 medication at 24 months (P = 0.013). This finding is consistent with results from Lee et al., who reported that a higher proportion of eyes undergoing cataract-KDB achieved a reduction of ≥1 medication at six months compared with those undergoing cataract-iStent (43% versus 17%, P = 0.004).[118] Similarly, ElMallah et al. observed a greater medication reduction with KDB compared with iStent (first generation), although the difference was not statistically significant (80% versus 77%, P = 0.522).[102]

Furthermore, we found an increased occurrence of further surgery after cataract-iStent compared with cataract-KDB (Study II). However, the groups were not matched at baseline, which may have influenced the results. Additionally, the iStent model used in Study II was an earlier version; the currently used iStent W is likely more effective.

It is important to note that comparative studies between iStent and KDB have not evaluated the iStent W model, and studies comparing iStent W with the earlier versions have demonstrated higher success rates with the W model.[119,120] In Study IV, we found the efficacy of iStent W and KDB Glide to be similar, likely due to the broader neck of the iStent W, which helps prevent over-implantation. Based on these findings, we believe that KDB may offer slightly greater efficacy compared with the first- and second-generation iStent stents (iStent and iStent inject), whereas KDB/KDB Glide and iStent W are likely equally effective.

This conclusion is supported by a recent meta-analysis (including 14 studies with a total of 1959 eyes) that found similar IOP reductions at 12 and 24 months following cataract surgery combined with either iStent/iStent W or KDB/KDB Glide.[72] Additionally, the same study found similar rates of glaucoma re-operations between the cataract-KDB and cataract-iStent groups. Rates of hyphema and IOP spikes were also comparable between KDB and iStent, although these events were evaluated together (21% versus 12%, P = 0.140).[72] Likewise, we did not observe a statistically significant difference in the incidence of IOP spikes between KDB and iStent. However, the rate of hyphema was consistently higher following cataract-KDB compared with cataract-iStent in both Studies II and IV.

An increased incidence of hyphema after KDB compared with iStent is an expected finding, since KDB opens a larger area of the TM, thereby raising the likelihood of blood reflux into the anterior chamber. Given this elevated risk of hyphema after KDB, iStent may be the preferable option in one-eyed patients, where minimizing postoperative complications that could cause transient vision loss is particularly important.

Trabecular MIGS across glaucoma stages

While prospective MIGS studies mainly evaluate patients with mild to moderate glaucoma,[98,121,122] retrospective studies often involve a broader range of disease severities,[100,123] although few studies have stratified results according to glaucoma grade.

We found that surgical success was slightly higher in eyes with mild to moderate glaucoma compared with advanced glaucoma, although this difference reached statistical significance only after combining data from Studies I-IV (Figure 13). Nevertheless, the success rate regarding reduction in IOP and/or medications in eyes with advanced glaucoma was still 73% (combined data from Studies I-IV). Importantly, we found that among patients with advanced glaucoma, target IOP levels were improved. IOP levels ≤15 mmHg went from 27% to 82% in the cataract-iStent group and from 31% to 74% in the cataract-KDB group.

A case series (n=59) by Ferguson et al. evaluated the outcomes of cataract surgery combined with the first generation iStent in eyes with advanced glaucoma.[124] They found that 63% of eyes achieved an IOP ≤15 mmHg at 36 months compared with 31% at baseline. In another small case series (n=117), the same authors reported outcomes stratified by glaucoma severity in patients with PEXG undergoing cataract surgery combined with iStent implantation.[73] In eyes with mild PEXG (n=49), the mean IOP reduction at 24 months was 4.7 mmHg, and medication reduction 0.7. In eyes with severe PEXG (n=12), the mean IOP reduction was 9.6 mmHg, and medication reduction 0.7 over the same period. These findings suggest that even in more advanced cases, iStent combined with cataract surgery can provide meaningful reductions in both IOP and medication burden.

Conversely, Chansangpetch et al. evaluated 104 eyes undergoing cataract surgery with iStent implantation and found that surgical success at 12 months – defined as achieving an IOP of ≤18 mmHg without medications – was significantly lower in eyes having advanced glaucoma (6%) compared with those having mild (72%) and moderate (23%) glaucoma.[125] While informative, the study included only 33 eyes from 29 patients with advanced glaucoma, limiting the strength of its conclusions.

The effect of preoperative IOP levels and number of medications on surgical outcomes

Experimental studies on enucleated and animal eyes have shown that Schlemm´s canal can collapse when IOP exceeds 30 mmHg,

potentially contributing to increased outflow resistance.[26,27] However, high preoperative IOP levels do not seem to negatively affect outcomes after trabecular MIGS combined with cataract surgery. [126,127]

After stratifying results from Studies I-IV according to preoperative IOP levels and number of medications (Figure 14-19), the greatest IOP reductions were observed in patients with the highest preoperative IOP levels – those exceeding 25 and 30 mmHg. Similarly, Samuelson et al. reported that patients with baseline IOP levels ≥30 mmHg and on ≥3 medications achieved the greatest IOP reductions and the highest surgical success rates when iStent (inject) was added to cataract surgery.[126] Likewise, Ferguson et al. reported that patients with PEXG and preoperative IOP levels of 22-24 mmHg experienced a mean IOP reduction of 7.6 mmHg – more than twice the reduction observed in patients with baseline IOP levels of 16-18 mmHg.[74] Among patients with preoperative IOP levels >24 mmHg, the mean IOP reduction was 14.1 mmHg, and 100% of patients had a reduction in IOP.

IOP reductions varied across our studies, with the greatest reductions observed in Study I, where patients had a more unstable disease and higher preoperative IOP levels. In contrast, in Study IV, patients had a stable disease preoperatively and lower preoperative IOP levels, resulting in smaller IOP reductions. However, a high proportion of patients in Study IV were instead medication-free at follow-up: 53% in the cataract-iStent W group and 43% in the cataract-KDB Glide group (compared with 23% in the cataract-alone group). Our data show that in our cohort of patients with stable glaucoma and mean preoperative IOP levels <19 mmHg (Table 5, Study IV), more medications could be reduced when trabecular MIGS was added to the cataract operation compared with when cataract surgery was performed as a stand-alone procedure.

Trabecular MIGS combined with cataract surgery had favorable outcomes – even in patients with advanced and/or uncontrolled glaucoma and markedly elevated IOP levels (sometimes >40 mmHg). We therefore suggest that trabecular MIGS combined with cataract surgery is both a safe and effective strategy to start with, even in patients that may previously have been considered

candidates for bleb-forming surgery. Our data show that in patients with IOP levels >30 mmHg (n=23), only one needed further surgical intervention within the first year.

While further surgical interventions were rare within the first 12-24 months, consistent with findings from other studies,[124] long-term outcomes beyond this period remain uncertain. However, a key advantage of trabecular MIGS procedures is that they preserve the conjunctiva, allowing for bleb-forming surgery if needed in the future.

Trabecular MIGS in eyes with PEX

Overall, IOP reductions were greater in eyes with PEX, although these eyes often presented with higher preoperative IOP levels. This trend is in agreement with previous studies, which have also reported more substantial IOP reductions following cataract surgery combined with iStent or KDB in PEX eyes compared with non-PEX eyes.[73,75,128]

Although our studies individually did not show a statistically significant difference in success between PEX and non-PEX eyes (Studies I and IV), the success rate reached significance when combining data from Studies I-IV. Specifically, 87% of PEX eyes achieved a reduction in IOP of ≥20% and/or a reduction of ≥1 medication compared with 75% of non-PEX eyes (P = 0.006). Although both PEX and non-PEX eyes had clinically relevant IOP reductions, our data suggest that combining cataract surgery with trabecular MIGS may be particularly beneficial for patients with PEX. However, cataract surgery alone can result in higher IOP reductions in PEX eyes,[83,84] so this approach may be sufficient in certain cases, especially when glaucoma progression is stable.

Despite favorable outcomes, PEX eyes were more susceptible to both peri- and postoperative complications. These included a higher incidence of large hyphemas, persistent postoperative inflammation, and increased surgical complexity due to small pupils and zonular instability. These findings were expected to some extent and consistent with previous literature.[90,129,130]

Interestingly, despite the fact that PEXG is often harder to treat and is known to progress more rapidly compared with POAG, the need for additional glaucoma surgery was unexpectedly low in PEX eyes following combined cataract surgery and trabecular MIGS. Ferguson et al. similarly reported a low rate of further surgical interventions (4%, n=5) in a retrospective case series involving 117 PEX eyes treated with cataract surgery and iStent.[73] This low rate of further surgery may be attributed to the enhanced IOP-lowering effect of cataract extraction in PEX eyes, potentially reducing the necessity for subsequent procedures.

Notably, this advantage was not observed when trabecular MIGS was performed as a stand-alone procedure (Study I), suggesting that the synergistic benefit may be specific to the combined surgical approach.

Previous LTP treatment and trabecular MIGS

Previous LTP treatment does not seem to impair the outcomes of subsequent cataract surgery combined with trabecular MIGS. Eyes that were unresponsive to LTP still demonstrated favorable responses to further surgery with cataract-KDB (Study III). Our methods were not designed to assess structural changes that could explain the observed outcomes, but we hypothesize that in cases where LTP is ineffective, the TM may be stiffened or fibrotic, thereby limiting the laser's ability to enhance aqueous outflow. In such instances, the KDB may still be effective by mechanically excising a segment of the TM, thereby bypassing the dysfunctional tissue and facilitating outflow through a more direct pathway.

The lack of an observed association between prior LTP and subsequent cataract surgery combined with trabecular MIGS is consistent with findings from most previous studies.[131–134] However, a recent registry-based study reported that prior LTP was linked to an increased likelihood of requiring additional glaucoma surgery within 12 months following trabecular MIGS.[135] It is important to interpret these findings with caution, as such analyses may be influenced by confounding factors. For example, patients who previously underwent LTP might have had a more

advanced or aggressive disease, making them more prone to further surgical intervention.

Although existing studies report mixed findings regarding the impact of prior LTP on subsequent MIGS procedures, our data suggest that previous LTP does not negatively affect the efficacy of surgeries targeting the TM. Furthermore, responsiveness to LTP does not appear to be a reliable predictor of surgical success with trabecular MIGS.

Trabecular MIGS combined with cataract surgery versus cataract surgery alone

We found improved efficacy when trabecular MIGS was combined with cataract surgery, compared with cataract surgery performed alone. In Study IV, the overall success rate – defined as a reduction in IOP of ≥20% and/or a reduction of ≥1 glaucoma medication – was 88% when iStent W or KDB Glide was added, versus 53% with cataract surgery alone. Using the same success criterion, although without including a cataract-alone group, Sieck et al. reported a 72% success rate at 12 months after cataract-KDB,[98] while Falkenberry et al. reported a 94% success rate after cataract-KDB, and 83% after cataract-iStent (first generation single iStent).[122]

In our study, the primary benefit of adding iStent W or KDB Glide was a greater reduction in medication use, and more patients became medication-free after the combined surgeries. The lack of a significant difference in IOP reduction between cataract surgery alone and cataract surgery combined with iStent W or KDB Glide may be attributed to the fact that patients in our prospective study (Study IV) had well-controlled IOP preoperatively. A more pronounced IOP reduction is expected when baseline IOP is high or following a medication washout.[126] Since our study included patients with advanced glaucoma, we deemed it unethical to perform a medication washout or include patients with unstable disease who might require additional surgery within the first postoperative months.

Previous studies have consistently demonstrated superior IOP-lowering outcomes when trabecular MIGS procedures have been

combined with cataract surgery compared with cataract surgery performed alone.[105,136,137] A meta-analysis (including 26 studies and 1659 patients) comparing cataract surgery combined with KDB to cataract surgery alone reported a significantly greater IOP reduction in the combined group (23% versus 10%).[137] Similarly, a meta-analysis (including 10 studies) evaluating iStent combined with cataract surgery (n=853) versus cataract surgery alone (n=600) found a greater IOP reduction in the combined group (4.7 ± 2.0 versus 2.8 ± 1.9 mmHg).[105] Additionally, patients in the combined group experienced a larger reduction in glaucoma medications (1.2 ± 0.3 versus 0.6 ± 0.6). Registry data from Clement et al (including 1420 patients) further support these findings.[136] Cataract surgery combined with iStent (inject) resulted in higher efficacy and a reduced need for secondary IOP-lowering procedures at 12 months compared with cataract surgery alone.

In addition to increased success rates, we also found reduced incidence of postoperative IOP spikes when iStent W or KDB Glide was added to the cataract operation. This aligns with previous studies showing a lower frequency of IOP spikes on postoperative day one following cataract surgery combined with trabecular MIGS compared with cataract surgery alone.[138,139] A sub-analysis of a prospective multicenter study (including 556 patients) demonstrated that adding a trabecular MIGS procedure to cataract surgery reduced the incidence of IOP spikes (>40 mmHg on postoperative day 1) from 14% to 1%.[139] Similarly, another study reported IOP spikes in 23% of patients undergoing cataract surgery alone compared with only 6% in those receiving combined cataract surgery and trabecular MIGS.[138]

These findings suggest that incorporating a trabecular MIGS procedure may not only enhance IOP control and reduce medication burden but also improve postoperative safety. However, for patients with stable disease and a low requirement for topical therapy, it is important to recognize that the additional benefit of a MIGS procedure may be limited. Given that cataract surgery alone often results in reduced IOP levels, these patients may be adequately managed without trabecular MIGS. However, if medication reduction is a clinical goal, there could be a benefit to adding a trabecular MIGS procedure also in patients with stable preoperative IOP levels and mild to moderate disease.

The safety of trabecular MIGS

No serious adverse events were observed in our studies. As expected, hyphema and IOP spikes were the most frequently observed transient complications. The hyphemas were often subclinical, but a few patients had complete hyphemas with markedly reduced visual acuity within the first postoperative week. Interestingly, all of these patients had PEX, which may not be coincidental given that PEX is known to affect vessel walls.[140–142] However, due to the small number of patients with complete hyphemas, we cannot conclude that PEX is a true risk factor for excessive bleeding in this context.

Anticoagulation therapy is theoretically associated with an increased risk of hyphema. However, previous studies have not demonstrated a significant association between anticoagulation use and hyphema following MIGS procedures, although included number of patients has been relatively small (64 to 164 patients).[122,143] Our findings align with these results, reinforcing the clinically important observation that anticoagulant therapy can be safely continued when planning combined cataract and trabecular MIGS surgery. This is particularly relevant given that many glaucoma patients are elderly and commonly prescribed anticoagulants.

Postoperative IOP spikes are another expected finding and can also occur following cataract surgery alone.[144,145] The reported incidence of IOP spikes varies across studies, largely due to differences in definitions and the timing of IOP measurements. The underlying cause of these IOP spikes may also vary depending on the timing of assessment. Within the first 24 hours after surgery, IOP spikes are typically attributed to inflammation or retained viscoelastic material, and thereafter they are more likely related to corticosteroid use. In Study IV, we observed a reduced incidence of early IOP spikes when either iStent W or KDB Glide was combined with cataract surgery compared with cataract surgery alone. This finding further supports the safety profile of trabecular MIGS when performed in conjunction with cataract surgery.

Corneal edema on the first postoperative day was more frequently observed following trabecular MIGS combined with cataract

surgery than after cataract surgery alone (Study IV). However, the clinical relevance of this finding remains uncertain. Previous studies have shown minimal differences in corneal endothelial cell loss between cataract surgery alone and cataract surgery combined with trabecular MIGS.[146,147] A prospective study comparing iStent (inject) combined with cataract surgery versus cataract surgery alone reported a mean percentage decrease in endothelial cell density at 60 months of 14% ± 13% in the iStent group (n=178) and 15% ± 10% in the cataract group (n=49, P = 0.8112).[146] The annualized rate of endothelial cell density change from 3 to 60 months was neither clinically nor statistically significant between the groups.

Although KDB has been less extensively studied in this context, a fellow-eye comparison (21 eyes) by Dorairaj et al. found less endothelial cell loss following cataract surgery combined with KDB compared with cataract surgery combined with iStent.[147] Nonetheless, longer-term follow-up is needed to fully evaluate the potential long-term effects of trabecular MIGS on corneal endothelial health.

Increased or prolonged postoperative inflammation is a recognized concern following both cataract surgery alone and cataract surgery combined with trabecular MIGS. Interestingly, a lower rate of postoperative inflammation was observed in Studies I and II compared with Study IV, likely attributable to under-reporting and the absence of predefined follow-up visits. OCT examinations were not routinely performed in Studies I and II, and subclinical cases of inflammation-induced macular edema were likely undetected.

Preserving visual field is a key goal in glaucoma management. Still, most studies on trabecular MIGS do not report visual field outcomes. Among those that do, studies on the iStent have demonstrated stable visual fields for up to seven years postoperatively.[121,127,148] It is important to acknowledge that visual field progression has rarely been the primary outcome in studies evaluating MIGS surgeries, and our studies were likewise not specifically designed to detect visual field changes over time.

Therefore, while the findings should be interpreted with appropriate caution, our data suggest that the combined surgical

approach – cataract extraction with either iStent or KDB – is associated with stable visual field outcomes over the first 12-24 months (Studies I, II and IV). By contrast, Study I demonstrated that stand-alone MIGS using KDB in patients with advanced glaucoma was associated with a progressive decline in MD. However, the strength of this finding is limited by the high proportion of patients lacking reliable visual field data, largely due to advanced age and comorbidities that impaired their ability to perform consistent visual field testing. Both advanced glaucoma and older age are known risk factors for disease progression, and even bleb-forming surgery may not be sufficient in some of these cases. While stand-alone KDB may be considered when bleb-forming surgery is not feasible, its long-term efficacy – particularly in advanced disease – appears limited. Notably, previous studies on stand-alone KDB in advanced glaucoma have not reported visual field outcomes.[98,101,113,114,149,150]

Overall, the need for additional glaucoma surgery was low when trabecular MIGS was combined with cataract extraction, even in patients with preoperative disease progression despite treatment with maximum number of glaucoma medications (Study I). These findings support the use of combined surgery as a safe and effective first-line surgical option in patients with uncontrolled glaucoma and coexisting cataract.

Vision-related QoL

Vision-related QoL improved following surgery. However, no significant difference was observed between cataract surgery alone and cataract surgery combined with either iStent W or KDB Glide. This finding is in agreement with a previous study by van Gaskin et al., which did not either find a significant difference in QoL between cataract surgery alone and cataract surgery combined with iStent.[148] In contrast, Samuelson et al. reported a measurable improvement in vision-related QoL following cataract surgery combined with iStent compared with cataract surgery alone.[42]

Detecting changes in QoL after glaucoma surgery can be challenging, as glaucoma progresses gradually over many years, often without immediate impact on central vision. The

improvements observed in some MIGS studies are likely attributable to reduced reliance on topical glaucoma medications, which can improve ocular surface health and patient comfort, rather than direct enhancements in visual acuity or preservation of visual function.

Clinical relevance of trabecular MIGS in glaucoma management

Trabecular MIGS demonstrated a high rate of surgical success across various stages and subtypes of glaucoma (Studies I-IV). Higher baseline IOP levels were generally associated with greater absolute IOP reductions, with eyes having preoperative IOP levels >25 mmHg and >30 mmHg showing the most substantial decreases (Figure 17). Additionally, eyes with PEXG exhibited greater IOP reductions than those with POAG, although their postoperative IOP levels were similar. In patients with a more stable disease and lower preoperative IOP, the primary benefit was often a reduction in the number of medications rather than a reduction in IOP (Study IV).

These findings suggest that trabecular MIGS can provide meaningful reductions in IOP and/or medication use, particularly in patients taking multiple medications and with elevated baseline IOP levels (Studies I and II). The additive effect of iStent or KDB appears most pronounced in these patients. However, even patients with stable glaucoma may benefit from trabecular MIGS when a reduction in medication burden is a clinical goal (Study IV).

When performed as a stand-alone procedure, trabecular MIGS still resulted in IOP reductions, but many patients remained dependent on multiple glaucoma medications (Study I). A significant proportion also required additional surgical interventions or experienced visual field progression. Therefore, in pseudophakic patients requiring further glaucoma surgery, a bleb-forming procedure is likely more appropriate.

Although it has been hypothesized that prior LTP treatment may induce TM fibrosis,[151] which could reduce the efficacy of

subsequent trabecular interventions, our findings did not support this concern (Study III). Therefore, we suggest that prior LTP does not need to be considered when planning combined cataract and trabecular MIGS surgery.

Furthermore, iStent and KDB were found to be equally effective and safe. Given the lower cost of KDB, it may represent a promising alternative to iStent. However, while cost-effectiveness is a critical factor in evaluating MIGS options, it falls outside the scope of this thesis.

Study population and patient selection

In Studies I-III, a high proportion of patients had advanced glaucoma. In contrast, Study IV included fewer advanced cases, as patients were required to be stable enough to be randomized to cataract surgery alone. The study populations were generally of advanced age, which aligns with the increasing prevalence of glaucoma in elderly individuals.[152,153] This age distribution may influence both the outcomes and the long-term durability of trabecular MIGS. Younger glaucoma patients tend to have more aggressive scarring after bleb-forming surgery,[154] and whether this is also the case after trabecular MIGS surgery is so far unknown.

The populations studied were relatively homogeneous, which may limit the generalizability of our findings to more diverse ethnic groups. Of particular interest was the high prevalence of PEX – present in approximately 50% of patients across all studies. PEX is especially common in Scandinavian populations and is often associated with a worse prognosis and more challenging glaucoma management.[6,155] The favorable response of trabecular MIGS in combination with cataract surgery in PEX eyes is therefore a clinically relevant finding.

Strengths and limitations

The studies presented in this thesis each have different strengths and limitations.

Studies I-II were retrospective in design, which inherently introduces a higher risk of bias. These studies lacked a cataract control group and relied on a single preoperative IOP measurement, increasing the risk of regression to the mean affecting the results. Additionally, the absence of predefined follow-up intervals may have led to underreporting of postoperative complications. Other limitations include missing data at certain time points, unmatched comparison groups, and limited follow-up beyond 24 months. Additionally, due to limited clinical experience with stand-alone iStent procedures during the study period, we were unable to assess the outcomes of stand-alone iStent implantation or directly compare them with those of stand-alone KDB. The number of patients in the KDB-alone group was also quite few (n=39), and all had uncontrolled glaucoma, which may have underestimated the potential efficacy of stand-alone trabecular MIGS in patients with a more stable disease.

Despite these limitations, a key strength of Studies I-III is their reflection of real-world clinical practice. Patients were included regardless of comorbidity or glaucoma severity, allowing us to assess the performance of trabecular MIGS in a broader and more clinically relevant population – including patients with advanced and uncontrolled glaucoma. Another strength is the relatively large sample size, with a total of 476 patients included, and a low rate of loss to follow-up.

Study IV was a prospective randomized study with a fixed protocol and included a cataract control group, which strengthens the study design and enhances comparability between groups. However, the study was not masked, which may have influenced both patient-reported outcomes and investigator assessments. The sample size calculation was based on a difference in IOP, while the difference observed was in medication reduction. A medication washout period could have strengthened the validity of the findings, as could the use of a fixed protocol for tapering or introducing medications. Furthermore, only a limited number of patients in this cohort had advanced or uncontrolled glaucoma.

CONCLUSIONS

- Stand-alone KDB offered limited efficacy and should not be recommended as a primary surgical option for patients with uncontrolled or advanced glaucoma.

- KDB and iStent demonstrated comparable efficacy at 12 and 24 months postoperatively, especially when the iStent W version was used.

- Combining iStent or KDB with cataract surgery was both safe and effective across all stages of glaucoma – including advanced cases.

- In patients with uncontrolled glaucoma despite maximal treatment, trabecular MIGS combined with cataract surgery can be considered as a first surgical option.

- Patients with PEX demonstrated a favorable response to combined cataract surgery and trabecular MIGS, although peri- and postoperative complications must be considered.

- Adding trabecular MIGS to cataract surgery improved surgical success compared with cataract surgery alone, primarily by reducing the need for IOP-lowering medications. While hyphema and corneal edema were more common on the first postoperative day, the addition of trabecular MIGS markedly reduced the incidence of IOP spikes.

EPILOGUE

The journey so far

It all began with a desire to understand how well the newly introduced microinvasive glaucoma surgeries actually worked. These procedures held great promise, but when colleagues at other clinics began to question their efficacy, I felt a strong responsibility to take a closer look. At our clinic, we were performing these surgeries on a large scale, and I knew we had a unique opportunity – and perhaps even an obligation – to evaluate their outcomes more systematically.

What started as a clinical curiosity soon evolved into something more. One conversation led to another, and the idea of pursuing a doctoral project was suggested by Gauti, who would later become my supervisor. His encouragement and belief in the value of this work planted a seed that would grow into this research journey.

At first, the path felt uncertain. I struggled with doubts – about my English, my academic writing, my ability to conduct quality research, and especially whether I could manage the time and energy required. But through hard work and persistence, I began to see real progress. What once felt impossible gradually became deeply rewarding. Learning new things is truly one of life's greatest joys.

Through doctoral courses, presentations, and countless articles and books, my understanding deepened, and new perspectives opened. Along the way, I made discoveries and realizations that challenged what I thought I knew. Time and again, I found that things are often far more complex than they first appear. This fosters humility – something I have not always been great at but have come to value deeply.

This project has taken me to new places and introduced me to people I would not otherwise have met. I have learned a great deal – not only about the research subject and the scientific process, but also about myself, my beliefs, and my limits. This project has also

been a constant in an otherwise changing life and world. I have watched my daughters grow from small children into pre-teens. I've experienced the loss of my beloved father – who encouraged me in the beginning but wasn't there to see the work continue. Around me, the world has shifted too – with the escalation of the climate crisis, growing political instability, and the increasing influence of AI. But change can also hold potential for something better – if we cooperate, keep hope alive, and recognize that we're all part of a bigger puzzle, where every contribution can make a difference. Just like in research, where each individual effort may seem small, but together, they can lead to something much greater.

At times, this journey has been stressful. Balancing the roles of researcher, surgeon, ophthalmologist, department head – and parent – has not always been easy. Yet, these years of research have been rewarding, and I've found great joy in the scientific process. It has offered a welcome contrast to the daily demands of meetings, strategic decisions, personnel matters, and the constant stream of responsibilities.

And now, as this thesis comes to an end, there will be some emptiness, like a small black hole in my universe. But I'm also proud and happy to have completed this work, and I look forward to the new challenges that await.

ACKNOWLEDGEMENT

My deepest appreciation goes to all the study participants from the Region of Jämtland and Härjedalen. Your willingness to contribute to this research has been essential – this thesis would not have been possible without you. I would also like to express my heartfelt thanks to all of you that have supported me throughout this journey. In particular, I would like to thank:

Gauti Jóhannesson, my main supervisor, for your support and for encouraging me to pursue this work from the very beginning. Thank you for always making time for me despite your busy schedule, and for guiding me with your wise and thoughtful advice throughout this journey.

Mario Economou, my co-supervisor, for your valuable feedback and for generously sharing your expertise. Your contributions have been invaluable to the development of this work.

The Unit of Research, Education and Development (FoU), Region Jämtland-Härjedalen, for the financial and institutional support that made this thesis possible and enabled me to combine clinical work with research.

Anna Lindam, statistician, for your expert guidance with statistical analyses and for so generously sharing your knowledge.

Elisabeth Liljekvist, my boss, for your patience and for giving me the flexibility to pursue this research alongside my other responsibilities.

Andrew Nolan, my former colleague, for your inspiring attitude, your kindness, and for the collaboration in the third study.

Maria Eriksson, for your help with coordinating the booking of study appointments.

Carina Mårtensson, for keeping track of my research hours and helping to manage the schedule. Thank you for keeping everything running smoothly.

Erling Streman, my former colleague and supervisor, for introducing me to the fascinating – and at times daunting – world of cataract and glaucoma surgery. Your mentorship laid an important foundation for this work.

The booking coordinators at the Eye Clinic, thank you for arranging the surgical schedule and finding time for all of the study participants.

All wonderful colleagues at the Eye Clinic in Östersund, both past and present. I am proud and grateful to be part of such a dedicated and supportive team. Thank you for your help in recruiting and following up with study participants, and for your patience when I have been away due to research activities.

Gun, my mother, and Anders, my brother – for always being there, and especially for helping with the children.

Per, my father, for everything you have taught me and for making me believe that anything is possible. I wish you could have stayed longer to see this work completed.

My friends and family, including my parents-in-law, brother and sisters-in-law with families and all children. I am grateful to be part of such a warm and caring extended family.

Alicia and Elina, the lights of my life. You remind me every day of what really matters. Thank you for filling my life with joy and love. You are the best thing that has ever happened to me, and I love you more than anything.

And finally, **Niklas** – thank you for your support, love, and friendship. For all the incredible experiences we have shared, for the life and the place we have together. Everything we have been through has made us stronger. We are truly the best team.

REFERENCES

1. Stuart K V., de Vries VA, Schuster AK, et al. Prevalence of Glaucoma in Europe and Projections to 2050. *Ophthalmology*. 2025;132(10):1114-1124. doi:10.1016/j.ophtha.2025.06.002

2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. *Ophthalmology*. 2014;121(11). doi:10.1016/j.ophtha.2014.05.013

3. Holló G, Katsanos A, Konstas AG. Management of exfoliative glaucoma: Challenges and solutions. *Clinical Ophthalmology*. 2015;9. doi:10.2147/OPTH.S77570

4. Pazos M, Traverso CE, Viswanathan A. European Glaucoma Society – Terminology and guidelines for glaucoma, 6th Edition. *British Journal of Ophthalmology*. 2025;109(Suppl 1):1-212. doi:10.1136/bjophthalmol-2025-egsguidelines

5. Ayala M. Comparison of visual field progression in new-diagnosed primary open-angle and exfoliation glaucoma patients in Sweden. *BMC Ophthalmol*. 2020;20(1). doi:10.1186/s12886-020-01592-w

6. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M. Reduction of intraocular pressure and glaucoma progression: Results from the Early Manifest Glaucoma Trial. *Archives of Ophthalmology*. 2002;120(10). doi:10.1001/archopht.120.10.1268

7. Åström S, Stenlund H, Lindén C. Incidence and prevalence of pseudoexfoliations and open-angle glaucoma in northern Sweden: II. Results after 21 years of follow-up. *Acta Ophthalmol Scand*. 2007;85(8). doi:10.1111/j.1600-0420.2007.00980.x

8. Ringvold A. Epidemiology of the pseudo-exfoliation syndrome. A review. *Acta Ophthalmol Scand*. 1999;77(4). doi:10.1034/j.1600-0420.1999.770401.x

9. Arnarsson A, Damji KF, Sverrisson T, Sasaki H, Jonasson F. Pseudoexfoliation in the Reykjavik Eye Study: Prevalence and related ophthalmological variables. *Acta Ophthalmol Scand*. 2007;85(8). doi:10.1111/j.1600-0420.2007.01051.x

10. Hirvelä H, Tuulonen A, Laatikainen L. Intraocular pressure and prevalence of glaucoma in elderly people in Finland: a population-based Study. *Int Ophthalmol*. 1994;18(5). doi:10.1007/BF00917834

11. Niyadurupola N, Broadway DC. Pigment dispersion syndrome and pigmentary glaucoma - A major review. *Clin Exp Ophthalmol*. 2008;36(9). doi:10.1111/j.1442-9071.2009.01920.x

12. Campbell DG, Schertzer RM. Pathophysiology of pigment dispersion syndrome and pigmentary glaucoma. *Curr Opin Ophthalmol*. 1995;6(2). doi:10.1097/00055735-199504000-00015

13. Sugar HS, Barbour FA. Pigmentary Glaucoma. *Am J Ophthalmol*. 1949;32(1):90-92. doi:10.1016/0002-9394(49)91112-5

14. Bustamante-Arias A, Ruiz-Lozano RE, Carlos Alvarez-Guzman J, Gonzalez-Godinez S, Rodriguez-Garcia A. Pigment dispersion syndrome and its implications for glaucoma. *Surv Ophthalmol*. 2021;66(5). doi:10.1016/j.survophthal.2021.01.002

15. Maus TL, Brubaker RF. Measurement of aqueous humor flow by fluorophotometry in the presence of a dilated pupil. *Invest Ophthalmol Vis Sci*. 1999;40(2).

16. Keller KE, Peters DM. Pathogenesis of glaucoma: Extracellular matrix dysfunction in the trabecular

meshwork-A review. *Clin Exp Ophthalmol*. 2022;50(2). doi:10.1111/ceo.14027

17. Hann CR, Fautsch MP. Preferential fluid flow in the human trabecular meshwork near collector channels. *Invest Ophthalmol Vis Sci*. 2009;50(4). doi:10.1167/iovs.08-2375

18. Keller KE, Peters DM. Pathogenesis of glaucoma: Extracellular matrix dysfunction in the trabecular meshwork-A review. *Clin Exp Ophthalmol*. 2022;50(2). doi:10.1111/ceo.14027

19. Hann CR, Fautsch MP. Preferential fluid flow in the human trabecular meshwork near collector channels. *Invest Ophthalmol Vis Sci*. 2009;50(4). doi:10.1167/iovs.08-2375

20. Vahabikashi A, Gelman A, Dong B, et al. Increased stiffness and flow resistance of the inner wall of Schlemm's canal in glaucomatous human eyes. *Proc Natl Acad Sci U S A*. 2019;116(52). doi:10.1073/pnas.1911837116

21. Prendes MA, Harris A, Wirostko BM, Gerber AL, Siesky B. The role of transforming growth factor β in glaucoma and the therapeutic implications. *British Journal of Ophthalmology*. 2013;97(6). doi:10.1136/bjophthalmol-2011-301132

22. Igarashi N, Honjo M, Yamagishi R, et al. Crosstalk between transforming growth factor β-2 and Autotaxin in trabecular meshwork and different subtypes of glaucoma. *J Biomed Sci*. 2021;28(1). doi:10.1186/s12929-021-00745-3

23. Ozcan AA, Ozdemir N, Canataroglu A. The aqueous levels of TGF-β2 in patients with glaucoma. *Int Ophthalmol*. 2004;25(1). doi:10.1023/B:INTE.0000018524.48581.79

24. Greenfield DS. Glaucoma associated with elevated episcleral venous pressure. *J Glaucoma*. 2000;9(2). doi:10.1097/00061198-200004000-00012

25. Rosenquist R, Epstein D, Melamed S, Johnson M, Grant WM. Outflow resistance of enucleated human eyes at two different perfusion pressures and different extents of trabeculotomy. *Curr Eye Res*. 1989;8(12). doi:10.3109/02713688909013902

26. Grieshaber MC, Pienaar A, Olivier J, Stegmann R. Clinical evaluation of the aqueous outflow system in primary open-angle glaucoma for canaloplasty. *Invest Ophthalmol Vis Sci*. 2010;51(3). doi:10.1167/iovs.09-4327

27. Battista SA, Lu Z, Hofmann S, Freddo T, Overby DR, Gong H. Reduction of the available area for aqueous humor outflow and increase in meshwork herniations into collector channels following acute IOP elevation in bovine eyes. *Invest Ophthalmol Vis Sci*. 2008;49(12). doi:10.1167/iovs.08-1707

28. Yu Z, Wu M, Tao Y, et al. Efficacy analysis of microinvasive glaucoma surgery alone or in combination with phacoemulsification in patients with normal tension glaucoma: a systematic review and meta-analysis. *BMC Ophthalmol*. 2025;25(1):283. doi:10.1186/s12886-025-04104-w

29. Okamoto Y, Akagi T, Kameda T, et al. Prediction of trabecular meshwork-targeted micro-invasive glaucoma surgery outcomes using anterior segment OCT angiography. *Sci Rep*. 2021;11(1). doi:10.1038/s41598-021-97290-8

30. Tojo N, Hayashi A. The outcomes of trabectome surgery in patients with low, middle, and high preoperative intraocular pressure. *Clinical Ophthalmology*. 2020;14. doi:10.2147/OPTH.S285883

31. Tojo N, Hayashi A. The outcomes of trabectome surgery in patients with low, middle, and high preoperative intraocular pressure. *Clinical Ophthalmology*. 2020;14. doi:10.2147/OPTH.S285883

32. Garway-Heath DF, Crabb DP, Bunce C, et al. Latanoprost for open-angle glaucoma (UKGTS): A randomised, multicentre, placebo-controlled trial. *The Lancet*. 2015;385(9975). doi:10.1016/S0140-6736(14)62111-5

33. Chihara E. Assessment of True Intraocular Pressure: The Gap Between Theory and Practical Data. *Surv Ophthalmol*. 2008;53(3). doi:10.1016/j.survophthal.2008.02.005

34. Garcia-Feijoo J, Martinez-de-la-Casa JM, Morales-Fernandez L, et al. New technologies for measuring intraocular pressure. In: *Progress in Brain Research*. Vol 221. 2015. doi:10.1016/bs.pbr.2015.06.003

35. Heijl A. Automatic perimetry in glaucoma visual field screening - A clinical Study. *Albrecht von Graefes Archiv für Klinische und Experimentelle Ophthalmologie*. 1976;200(1). doi:10.1007/BF00411430

36. Heijl A, Alm A, Bengtsson B, et al. The Glaucoma Guidelines of the Swedish Ophthalmological Society. *Acta Ophthalmol Suppl (Oxf)*. 2012;(251). doi:10.1111/j.1755-3768.2012.02415.x

37. Sobottka Ventura AC, Wälti R, Böhnke M. Corneal thickness and endothelial density before and after cataract surgery. *British Journal of Ophthalmology*. 2001;85(1). doi:10.1136/bjo.85.1.18

38. Hodapp E, Richard K. Parrish, Douglas R. Anderson. Clinical decisions in glaucoma. In: Mosby Incorporated; 1993:52-61.

39. Jampel HD. Target pressure in glaucoma therapy. *J Glaucoma*. 1997;6(2).

40. Jóhannesson G, Stille U, Taube AB, et al. Guidelines for the management of open-angle glaucoma. *Acta Ophthalmol*. 2024;102(2). doi:10.1111/aos.16599

41. McKean-Cowdin R, Wang Y, Wu J, Azen SP, Varma R. Impact of Visual Field Loss on Health-Related Quality of Life in Glaucoma. The Los Angeles Latino Eye Study. *Ophthalmology*. 2008;115(6). doi:10.1016/j.ophtha.2007.08.037

42. 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. doi:10.1016/j.ajo.2021.03.007

43. Bengtsson B, Heijl A, Aspberg J, Jóhannesson G, Andersson-Geimer S, Lindén C. The Glaucoma Intensive Treatment Study (GITS): A Randomized Controlled Trial Comparing Intensive and Standard Treatment on 5 Years Visual Field Development. *Am J Ophthalmol*. 2024;266:274-288. doi:10.1016/j.ajo.2024.06.017

44. Bengtsson B, Lindén C, Heijl A, Andersson-Geimer S, Aspberg J, Jóhannesson G. The glaucoma intensive treatment Study: interim results from an ongoing longitudinal randomized clinical trial. *Acta Ophthalmol*. 2022;100(2). doi:10.1111/aos.14978

45. Nagar M, Luhishi E, Shah N. Intraocular pressure control and fluctuation: The effect of treatment with selective laser trabeculoplasty. *British Journal of Ophthalmology*. 2009;93(4). doi:10.1136/bjo.2008.148510

46. Katz LJ, Steinmann WC, Kabir A, Molineaux J, Wizov SS, Marcellino G. Selective laser trabeculoplasty versus medical therapy as initial treatment of glaucoma: A prospective, randomized trial. *J Glaucoma*. 2012;21(7). doi:10.1097/IJG.0b013e318218287f

47. Lai JSM, Chua JKH, Tham CCY, Lam DSC. Five-year follow up of selective laser trabeculoplasty in Chinese eyes. *Clin Exp Ophthalmol*. 2004;32(4). doi:10.1111/j.1442-9071.2004.00839.x

48. Kramer TR, Noecker RJ. Comparison of the morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. *Ophthalmology*. 2001;108(4). doi:10.1016/S0161-6420(00)00660-6

49. Nagar M, Ogunyomade A, O'Brart DPS, Howes F, Marshall J. A randomised, prospective Study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma. *British Journal of Ophthalmology*. 2005;89(11). doi:10.1136/bjo.2004.052795

50. Rasmuson E, Bengtsson B, Lindén C, et al. Long-term follow-up of laser trabeculoplasty in multi-treated glaucoma patients. *Acta Ophthalmol*. 2024;102(2). doi:10.1111/aos.15718

51. Ishida K. Update on results and complications of cyclophotocoagulation. *Curr Opin Ophthalmol*. 2013;24(2). doi:10.1097/ICU.0b013e32835d9335

52. Rasmuson E, Lindén C, Lundberg B, Jóhannesson G. Efficacy and safety of transscleral cyclophotocoagulation in Swedish glaucoma patients. *Acta Ophthalmol*. 2019;97(8). doi:10.1111/aos.14125

53. Zahid S, Musch DC, Niziol LM, Lichter PR. Risk of endophthalmitis and other long-term complications of trabeculectomy in the collaborative initial glaucoma treatment Study (CIGTS). *Am J Ophthalmol*. 2013;155(4). doi:10.1016/j.ajo.2012.10.017

54. Gedde SJ, Vinod K, Prum BE. Results from the Primary Tube Versus Trabeculectomy Study and translation to clinical practice. *Curr Opin Ophthalmol*. 2023;34(2). doi:10.1097/ICU.0000000000000928

55. Myers JS, Lamrani R, Hallaj S, Lee D, Wong J. 10-Year Clinical Outcomes of Tube Shunt Surgery at a Tertiary Care Center. *Am J Ophthalmol*. 2023;253. doi:10.1016/j.ajo.2023.04.001

56. Gedde SJ, Feuer WJ, Lim KS, et al. Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 5 Years of Follow-up. *Ophthalmology*. 2022;129(12). doi:10.1016/j.ophtha.2022.07.003

57. Christakis PG, Kalenak JW, Tsai JC, et al. The Ahmed Versus Baerveldt Study: Five-Year Treatment Outcomes. In: *Ophthalmology*. Vol 123. 2016. doi:10.1016/j.ophtha.2016.06.035

58. Khawaja AP, Abegão Pinto L, Stalmans I, et al. Additional Guidance on the Use of the PRESERFLO™ MicroShunt in the Treatment of Glaucoma: Insights from a Second Delphi Consensus Panel. *Ophthalmol Ther*. 2024;13(6):1569-1588. doi:10.1007/s40123-024-00902-5

59. Saeed E, Zalewska R, Konopińska J. Early Complications and Results of Preserflo MicroShunt in the Management of Uncontrolled Open-Angle Glaucoma: A Case Series. *Int J Environ Res Public Health*. 2022;19(14):8679. doi:10.3390/ijerph19148679

60. Galimi ME, Weller JM, Kruse FE, Laemmer R. Risk factors for ocular hypotony after XEN Gel Stent implantation. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2023;261(3). doi:10.1007/s00417-022-05831-2

61. Barkan O. A New Operation for Chronic Glaucoma. *Am J Ophthalmol*. 1936;19(11):951-966. doi:10.1016/S0002-9394(36)93838-2

62. SMITH R. A new technique for opening the canal of Schlemm. Preliminary report. *Br J Ophthalmol*. 1960;44. doi:10.1136/bjo.44.6.370

63. Luntz MH, Livingston DG. Trabeculotomy ab externo and trabeculectomy in congenital and adult-onset glaucoma. *Am J Ophthalmol*. 1977;83(2). doi:10.1016/0002-9394(77)90612-2

64. Tanihara H, Negi A, Akimoto M, et al. Surgical Effects of Trabeculotomy Ab Externo on Adult Eyes with Primary Open Angle Glaucoma and Pseudoexfoliation Syndrome. *Archives of Ophthalmology*. 1993;111(12). doi:10.1001/archopht.1993.01090120075025

65. Linnér E. Microsurgical trabeculectomy “ab externo” in glaucoma. *Trans Ophthalmol Soc U K*. 1970;89.

66. Barry M, Alahmadi MW, Alahmadi M, AlMuzaini A, AlMohammadi M. The Safety of the Kahook Dual Blade in the Surgical Treatment of Glaucoma. *Cureus*. Published online 2020. doi:10.7759/cureus.6682

67. Shalaby WS, Jia J, Katz LJ, Lee D. iStent inject: comprehensive review. *J Cataract Refract Surg*. 2021;47(3). doi:10.1097/j.jcrs.0000000000000325

68. Dick HB, Mackert MJ, Ahmed IIK, et al. Two-Year Performance and Safety Results of the MINIject Supraciliary Implant in Patients With Primary Open-Angle Glaucoma: Meta-Analysis of the STAR-I, II, III Trials. *Am J Ophthalmol*. 2024;260. doi:10.1016/j.ajo.2023.12.006

69. Falkenberry S, Singh IP, Crane CJ, et al. Excisional goniotomy vs trabecular microbypass stent implantation: a prospective randomized clinical trial in eyes with mild to moderate open-angle glaucoma. *J Cataract Refract Surg*. 2020;46(8). doi:10.1097/j.jcrs.0000000000000229

70. Barkander A, Economou MA, Jóhannesson G. Outcomes of iStent Inject Versus Kahook Dual Blade Surgery in Glaucoma Patients Undergoing Cataract Surgery. *J Glaucoma*. 2023;32(10). doi:10.1097/IJG.0000000000002243

71. Arnljots TS, Economou MA. Kahook dual blade goniotomy vs istent inject: Long-term results in patients with open-angle glaucoma. *Clinical Ophthalmology*. 2021;15. doi:10.2147/OPTH.S284687

72. Guedes J, Amaral DC, de Oliveira Caneca K, et al. Kahook Dual Blade Goniotomy Versus iStent Implantation Combined With Phacoemulsification: A Systematic Review and Meta-Analysis. *J Glaucoma*. 2025;34(3):232-247. doi:10.1097/IJG.0000000000002522

73. Ferguson TJ, Swan RJ, Bleeker A, et al. Trabecular microbypass stent implantation in pseudoexfoliative glaucoma: Long-term results. *J Cataract Refract Surg*. 2020;46(9). doi:10.1097/j.jcrs.0000000000000243

74. Ferguson TJ, Swan R, Ibach M, Schweitzer J, Sudhagoni R, Berdahl JP. Trabecular microbypass stent implantation with cataract extraction in pseudoexfoliation glaucoma. In: *Journal of Cataract and Refractive Surgery*. Vol 43. 2017. doi:10.1016/j.jcrs.2017.02.029

75. Koylu MT, Yilmaz AC, Gurdal F, et al. Kahook dual blade goniotomy combined with phacoemulsification in eyes with primary open angle glaucoma and pseudoexfoliation glaucoma: comparative Study. *BMC Ophthalmol*. 2025;25(1):184. doi:10.1186/s12886-025-04026-7

76. Sieck EG, Epstein RS, Kennedy JB, et al. Outcomes of Kahook Dual Blade Goniotomy with and without Phacoemulsification Cataract Extraction. *Ophthalmol Glaucoma*. 2018;1(1). doi:10.1016/j.ogla.2018.06.006

77. Lu Y, Hua Y, Wang B, et al. Impact of Elevated Intraocular Pressure on Lamina Cribrosa Oxygenation: A Combined Experimental–Computational Study on Monkeys. *Ophthalmology Science*. 2025;5(3):100725. doi:10.1016/j.xops.2025.100725

78. Lamoureux EL, Fenwick E, Pesudovs K, Tan D. The impact of cataract surgery on quality of life. *Curr Opin Ophthalmol*. 2011;22(1). doi:10.1097/ICU.0b013e3283414284

79. Slabaugh MA, Bojikian KD, Moore DB, Chen PP. The effect of phacoemulsification on intraocular pressure in medically

controlled open-angle glaucoma patients. *Am J Ophthalmol*. 2014;157(1). doi:10.1016/j.ajo.2013.08.023

80. Carolan JA, Liu L, Alexeeff SE, Amsden LB, Shorstein NH, Herrinton LJ. Intraocular Pressure Reduction after Phacoemulsification: A Matched Cohort Study. *Ophthalmol Glaucoma*. 2021;4(3). doi:10.1016/j.ogla.2020.10.002

81. Damji KF, Konstas AGP, Liebmann JM, et al. Intraocular pressure following phacoemulsification in patients with and without exfoliation syndrome: A 2 year prospective Study. *British Journal of Ophthalmology*. 2006;90(8). doi:10.1136/bjo.2006.091447

82. Melancia D, Pinto LA, Marques-Neves C. Cataract surgery and intraocular pressure. *Ophthalmic Res*. 2015;53(3). doi:10.1159/000377635

83. Vahedian Z, Salmanroghani R, Fakhraie G, et al. Pseudoexfoliation syndrome: Effect of phacoemulsification on intraocular pressure and its diurnal variation. *J Curr Ophthalmol*. 2015;27(1-2). doi:10.1016/j.joco.2015.09.006

84. Cimetta DJ, Cimetta AC. Intraocular pressure changes after clear corneal phacoemulsification in nonglaucomatous pseudoexfoliation syndrome. *Eur J Ophthalmol*. 2008;18(1). doi:10.1177/112067210801800113

85. Benekos K, Katsanos A, Laspas P, Vagiakis I, Haidich AB, Konstas AG. Intraocular Pressure Reduction Following Phacoemulsification in Patients with Exfoliation: A Systematic Review and Meta-Analysis. *J Clin Med*. 2024;13(22):6774. doi:10.3390/jcm13226774

86. Kristianslund O, Østern AE, Räen M, Sandvik GF, Drolsum L. Does cataract surgery reduce the long-term risk of glaucoma in eyes with pseudoexfoliation syndrome? *Acta Ophthalmol*. 2016;94(3). doi:10.1111/aos.12945

87. Gaasterland DE, Blackwell B, Ederer F, et al. The advanced glaucoma intervention Study, 8: Risk of cataract formation

after trabeculectomy. *Archives of Ophthalmology*. 2001;119(12). doi:10.1001/archopht.119.12.1771

88. Siriwardena D, Kotecha A, Minassian D, Dart JKG, Khaw PT. Anterior chamber flare after trabeculectomy and after phacoemulsification. *British Journal of Ophthalmology*. 2000;84(9). doi:10.1136/bjo.84.9.1056

89. Husain R, Liang S, Foster PJ, et al. Cataract surgery after trabeculectomy: The effect on trabeculectomy function. *Archives of Ophthalmology*. 2012;130(2). doi:10.1001/archophthalmol.2011.329

90. Snježana S. Cataract Surgery in Eyes with Pseudoexfoliation (PEX) Syndrome. *J Clin Exp Ophthalmol*. 2013;04(02). doi:10.4172/2155-9570-s1-009

91. Drolsum L, Ringvold A, Nicolaissen B. Cataract and glaucoma surgery in pseudoexfoliation syndrome: A review. *Acta Ophthalmol Scand*. 2007;85(8). doi:10.1111/j.1600-0420.2007.00903.x

92. Capitena Young CE, Seibold LK, SooHoo JR, Kahook MY. Microinvasive Glaucoma Surgeries and When to Use Them. *Adv Ophthalmol Optom*. 2019;4. doi:10.1016/j.yaoo.2019.04.018

93. Zhang X, Vadoothker S, Munir WM, Saeedi O. Ocular surface disease and glaucoma medications: A clinical approach. *Eye Contact Lens*. 2019;45(1). doi:10.1097/ICL.0000000000000544

94. Schwartz GF, Quigley HA. Adherence and Persistence with Glaucoma Therapy. *Surv Ophthalmol*. 2008;53(6 SUPPL.). doi:10.1016/j.survophthal.2008.08.002

95. Broadway DC, Grierson I, O'brien C, Hitchings RA. Adverse Effects of Topical Antiglaucoma Medication: II. The Outcome of Filtration Surgery. *Archives of Ophthalmology*. 1994;112(11). doi:10.1001/archopht.1994.01090230060021

96. Boimer C, Birt CM. Preservative exposure and surgical outcomes in glaucoma patients: The PESO Study. *J Glaucoma*. 2013;22(9). doi:10.1097/IJG.0b013e31825af67d

97. Sheheitli H, Tirpack AR, Parrish RK. Which patients would most likely to benefit: MIGs or MeGs, which one is it? *Asia-Pacific Journal of Ophthalmology*. 2019;8(6). doi:10.1097/APO.0000000000000260

98. Sieck EG, Epstein RS, Kennedy JB, et al. Outcomes of Kahook Dual Blade Goniotomy with and without Phacoemulsification Cataract Extraction. *Ophthalmol Glaucoma*. 2018;1(1). doi:10.1016/j.ogla.2018.06.006

99. Dorairaj S, Radcliffe NM, Grover DS, Brubaker JW, Williamson BK. A Review of Excisional Goniotomy Performed with the Kahook Dual Blade for Glaucoma Management. *J Curr Glaucoma Pract*. 2022;16(1):59-64. doi:10.5005/jp-journals-10078-1352

100. Hirabayashi MT, King JT, An JA. Outcome of phacoemulsification combined with excisional goniotomy using the Kahook Dual Blade in severe glaucoma patients at 6 months. *Clinical Ophthalmology*. 2019;13. doi:10.2147/OPTH.S196105

101. Bravetti GE, Gillmann K, Salinas L, et al. Surgical outcomes of excisional goniotomy using the kahook dual blade in severe and refractory glaucoma: 12-month results. *Eye*. Published online August 9, 2022. doi:10.1038/s41433-022-02196-y

102. ElMallah MK, Seibold LK, Kahook MY, Williamson BK, Singh IP, Dorairaj SK. 12-month retrospective comparison of Kahook Dual Blade excisional goniotomy with Istent trabecular bypass device implantation in glaucomatous eyes at the time of cataract surgery. *Adv Ther*. 2019;36(9). doi:10.1007/s12325-019-01025-1

103. Dorairaj SK, Seibold LK, Radcliffe NM, et al. 12-month outcomes of goniotomy performed using the Kahook Dual

Blade combined with cataract surgery in eyes with medically treated glaucoma. *Adv Ther*. 2018;35(9). doi:10.1007/s12325-018-0755-4

104. Wellik SR, Dale EA. A review of the iStent® trabecular micro-bypass stent: Safety and efficacy. *Clinical Ophthalmology*. 2015;9. doi:10.2147/OPTH.S57217

105. Kahale F, Chanbour W, El Zein L, Brenner J, You JY, Melki S. Phacoemulsification with and without iStent: A Systematic Review and Meta-Analysis of Comparative Studies. *Ophthalmic Res*. 2023;66(1). doi:10.1159/000531077

106. Clement C, Howes F, Ioannidis A, et al. Multicenter Effectiveness and Disease Stability Through 3 Years After iStentTrabecular Micro-Bypass with Phacoemulsification in Glaucoma and Ocular Hypertension. *Clinical Ophthalmology*. 2022;16. doi:10.2147/OPTH.S373290

107. Alqudah A, Mansberger SL, Gardiner SK, Demirel S. Vision-related quality of life in glaucoma suspect or early glaucoma patients. *J Glaucoma*. 2016;25(8). doi:10.1097/IJG.0000000000000445

108. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Archives of Ophthalmology*. 2001;119(7). doi:10.1001/archopht.119.7.1050

109. Jones L, Garway-Heath DF, Azuara-Blanco A, et al. Are Patient Self-Reported Outcome Measures Sensitive Enough to Be Used as End Points in Clinical Trials?: Evidence from the United Kingdom Glaucoma Treatment Study. *Ophthalmology*. 2019;126(5). doi:10.1016/j.ophtha.2018.09.034

110. 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. doi:10.1016/j.ajo.2021.03.007

111. Skalicky SE, Martin KR, Fenwick E, Crowston JG, Goldberg I, McCluskey P. Cataract and quality of life in patients with glaucoma. *Clin Exp Ophthalmol*. 2015;43(4). doi:10.1111/ceo.12454

112. Wakil SM, Birnbaum F, Vu DM, McBurney-Lin S, ElMallah MK, Tseng H. Efficacy and safety of a single-use dual blade goniotomy: 18-month results. *J Cataract Refract Surg*. 2020;46(10). doi:10.1097/j.jcrs.0000000000000263

113. Boopathiraj N, Wagner I, Lentz P, et al. 36-Month Outcomes of Standalone Kahook Dual Blade Goniotomy Compared with Ab-Interno Closed Conjunctiva Xen Gel Stent Implantation. *Clinical Ophthalmology*. 2024;Volume 18:2593-2603. doi:10.2147/OPTH.S473303

114. Elmallah MK, Berdahl JP, Williamson BK, et al. Twelve-month outcomes of stand-alone excisional goniotomy in mild to severe glaucoma. *Clinical Ophthalmology*. 2020;14. doi:10.2147/OPTH.S256423

115. Duong RT, Pittner AC, Roa TM, Dirghangi AJ, Netland PA. Stand-Alone Xen Gel Microstent Implantation Compared With Kahook Dual Blade Goniotomy. *J Glaucoma*. 2022;31(11). doi:10.1097/IJG.0000000000002120

116. Chen YY, Chen YY, Chen YY, et al. Use of iStent as a Standalone Operation in Patients with Open-Angle Glaucoma. *J Ophthalmol*. 2020;2020. doi:10.1155/2020/8754730

117. 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). doi:10.1097/IJG.0000000000001805

118. Lee D, King J, Thomsen S, Hirabayashi M, An J. Comparison of surgical outcomes between excisional goniotomy using the kahook dual blade and istent trabecular micro-bypass stent in combination with phacoemulsification. *Clinical Ophthalmology*. 2019;13. doi:10.2147/OPTH.S224109

119. Deneri S, Merté RL, Eter N, Brücher VC. Comparison of the iStent Inject® versus the iStent Inject® W—Both in Combination with Cataract Surgery—In Open-Angle Glaucoma. *J Clin Med*. 2023;12(23). doi:10.3390/jcm12237259

120. Morita S, Sakanishi Y, Riyu I, Watanabe S, Ebihara N. Comparative evaluation of iStent versus iStent inject W combined with phacoemulsification in open angle glaucoma. *PLoS One*. 2024;19(2 February). doi:10.1371/journal.pone.0297514

121. Samuelson TW, Sarkisian SR, 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). doi:10.1016/j.ophtha.2019.03.006

122. Falkenberry S, Singh IP, Crane CJ, et al. Excisional goniotomy vs trabecular microbypass stent implantation: a prospective randomized clinical trial in eyes with mild to moderate open-angle glaucoma. *J Cataract Refract Surg*. 2020;46(8). doi:10.1097/j.jcrs.0000000000000229

123. Salimi A, Watt H, Harasymowycz P. Three-Year Outcomes of Second-generation Trabecular Micro-bypass Stents (iStent inject) with Phacoemulsification in Various Glaucoma Subtypes and Severities. *J Glaucoma*. 2021;30(3). doi:10.1097/IJG.0000000000001716

124. Ferguson T, Swan R, Ibach M, Schweitzer J, Sudhagoni R, Berdahl JP. Evaluation of a Trabecular Microbypass Stent with Cataract Extraction in Severe Primary Open-angle

Glaucoma. *J Glaucoma*. 2018;27(1):71-76. doi:10.1097/IJG.0000000000000825

125. Chansangpetch S, Ittarat M, Yang S, et al. Comparison of 1 year effectiveness of trabecular microbypass stent implantation (iStent) among mild, moderate, and severe primary open angle glaucoma. *Invest Ophthalmol Vis Sci*. 2019;60(9).

126. Singh IP, Jnr SS, Hornbeak D, Katz LJ, Samuelson T. 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. *Clinical Ophthalmology*. 2021;15. doi:10.2147/OPTH.S316270

127. Hengerer FH, Auffarth GU, Conrad-Hengerer I. 7-Year Efficacy and Safety of iStent inject Trabecular Micro-Bypass in Combined and Standalone Usage. *Adv Ther*. 2024;41(4). doi:10.1007/s12325-024-02788-y

128. Omoto T, Sugiura A, Fujishiro T, et al. Twelve-month surgical outcome and prognostic factors of stand-alone ab interno trabeculotomy in Japanese patients with open-angle glaucoma. *PLoS One*. 2021;16(1). doi:10.1371/journal.pone.0245015

129. Shingleton BJ, Neo YN, Cvintal V, Shaikh AM, Liberman P, O'Donoghue MW. Outcome of phacoemulsification and intraocular lens implantion in eyes with pseudoexfoliation and weak zonules. *Acta Ophthalmol*. 2017;95(2). doi:10.1111/aos.13110

130. Ong AY, Shalchi Z. Outcomes of cataract surgery in pseudoexfoliation syndrome in England: 10-year retrospective cohort Study. *J Cataract Refract Surg*. 2021;47(2). doi:10.1097/j.jcrs.0000000000000397

131. Klamann MKJ, Gonnermann J, Maier AKB, Bertelmann E, Joussen AM, Torun N. Influence of Selective Laser Trabeculoplasty (SLT) on combined clear cornea

phacoemulsification and Trabectome outcomes. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2014;252(4). doi:10.1007/s00417-014-2569-7

132. Maier AKB, Arani P, Pahlitzsch M, et al. Influence of Selective Laser Trabeculoplasty (SLT) on the iStent inject® outcomes. *BMC Ophthalmol*. 2020;20(1). doi:10.1186/s12886-020-01723-3

133. Phillips SS, Patnaik JL, Capitena Young CE, et al. Selective Laser Trabeculoplasty and Outcomes of Subsequent Phacoemulsification Combined with Kahook Dual Blade Goniotomy. *Ophthalmol Ther*. 2022;11(5). doi:10.1007/s40123-022-00554-3

134. King J, Lee D, Thomsen S, Hirabayashi MT, An J. Relationship between selective laser trabeculoplasty and excisional goniotomy outcomes in glaucomatous eyes. *Canadian Journal of Ophthalmology*. 2022;57(2). doi:10.1016/j.jcjo.2021.02.040

135. Mitchell W, Yang SA, Ondeck C, et al. Effectiveness of Angle-Based Minimally Invasive Glaucoma Surgery after Laser Trabeculoplasty. *Ophthalmol Glaucoma*. 2024;7(4):335-344. doi:10.1016/j.ogla.2024.03.003

136. Clement CI, Nguyen V, Howes F, et al. Longitudinal outcomes of iStent inject with cataract surgery compared with cataract surgery alone: real-world data from the Fight Glaucoma Blindness registry. *J Cataract Refract Surg*. 2025;51(2):113-118. doi:10.1097/j.jcrs.0000000000001567

137. Radwan L, El Jalbout JD, Trad K, et al. Outcomes of Phacoemulsification With or Without Kahook Dual Blade Goniotomy for Glaucoma Patients With Cataract. *J Glaucoma*. 2024;33(10):769-779. doi:10.1097/IJG.0000000000002429

138. DeVience EX, DeVience SJ, Villarreal G, et al. Needle goniotomy decreases early intraocular pressure spike compared with phacoemulsification alone. *AJO*

International. 2024;1(1):100004. doi:10.1016/j.ajoint.2024.100004

139. Zebardast N, Zheng C, Jampel HD. Effect of a Schlemm's Canal Microstent on Early Postoperative Intraocular Pressure after Cataract Surgery: An Analysis of the HORIZON Randomized Controlled Trial. In: *Ophthalmology*. Vol 127. 2020. doi:10.1016/j.ophtha.2020.01.025

140. Kalogeropoulos D, Vartsakis G, Moustafa GA, et al. Choroidal vascularity index in pseudoexfoliation syndrome: a review of the literature. *Spektrum der Augenheilkunde*. 2023;37(5). doi:10.1007/s00717-022-00529-6

141. Lee RK. The molecular pathophysiology of pseudoexfoliation glaucoma. *Curr Opin Ophthalmol*. 2008;19(2). doi:10.1097/ICU.0b013e3282f49cda

142. Küchle M, Nguyen NX, Hannappel E, Naumann GOH. The blood-aqueous barrier in eyes with pseudoexfoliation syndrome. *Ophthalmic Res*. 1995;27. doi:10.1159/000267859

143. Widder RA, Lappas A, Rennings C, Hild M, Roessler GF, Dietlein TS. Influence of oral anticoagulation on success rates and risk of bleeding events after iStent inject implantation combined with phacoemulsification. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2020;258(11). doi:10.1007/s00417-020-04894-3

144. Lidder AK, Vanner EA, Chang TC, Lum F, Rothman AL. Intraocular Pressure Spike Following Stand-Alone Phacoemulsification in the IRIS® Registry (Intelligent Research in Sight). *Ophthalmology*. 2024;131(7). doi:10.1016/j.ophtha.2024.01.022

145. DeVience EX, DeVience SJ, Villarreal G, et al. Needle goniotomy decreases early intraocular pressure spike compared with phacoemulsification alone. *AJO*

International. 2024;1(1):100004. doi:10.1016/j.ajoint.2024.100004

146. 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. doi:10.1016/j.ajo.2023.02.014

147. Dorairaj S, Balasubramani GK. Corneal endothelial cell changes after phacoemulsification combined with excisional goniotomy with the kahook dual blade or istent: A prospective fellow-eye comparison. *Clinical Ophthalmology*. 2020;14. doi:10.2147/OPTH.S263072

148. Fan Gaskin JC, Bigirimana D, Kong GYX, et al. Prospective, Randomized Controlled Trial of Cataract Surgery vs Combined Cataract Surgery With Insertion of iStent Inject. *Ophthalmol Glaucoma*. 2024;7(4):326-334. doi:10.1016/j.ogla.2024.02.004

149. Salinas L, Chaudhary A, Berdahl JP, et al. Goniotomy using the kahook dual blade in severe and refractory glaucoma: 6-month outcomes. *J Glaucoma*. 2018;27(10). doi:10.1097/IJG.0000000000001019

150. Berdahl JP, Gallardo MJ, ElMallah MK, et al. Six-month outcomes of Goniotomy performed with the Kahook Dual Blade as a stand-alone glaucoma procedure. *Adv Ther*. 2018;35(11). doi:10.1007/s12325-018-0803-0

151. Kramer TR, Noecker RJ. Comparison of the morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. *Ophthalmology*. 2001;108(4). doi:10.1016/S0161-6420(00)00660-6

152. Rudnicka AR, Mt.-Isa S, Owen CG, Cook DG, Ashby D. Variations in primary open-angle glaucoma prevalence by age, gender, and race: A Bayesian meta-analysis. *Invest Ophthalmol Vis Sci*. 2006;47(10). doi:10.1167/iovs.06-0299

153. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. *Ophthalmology*. 2014;121(11). doi:10.1016/j.ophtha.2014.05.013

154. Landers J, Martin K, Sarkies N, Bourne R, Watson P. A twenty-year follow-up Study of trabeculectomy: Risk factors and outcomes. *Ophthalmology*. 2012;119(4). doi:10.1016/j.ophtha.2011.09.043

155. Ayala M. Comparison of visual field progression in new-diagnosed primary open-angle and exfoliation glaucoma patients in Sweden. *BMC Ophthalmol*. 2020;20(1). doi:10.1186/s12886-020-01592-w

APPENDIX

Visual Function Questionnaire 25 (25 frågor om Din syn)

DEL 1 – ALLMÄN HÄLSA OCH SYN

1. Som helhet, skulle Du vilja säga att Din allmänna hälsa är:

(Sätt en ring runt en av siffrorna)

Utmärkt.....	1
Mycket bra.....	2
Bra.....	3
Varken bra eller dålig....	4
Dålig.....	5

2. I dagsläget, skulle Du vilja säga att Din syn när Du använder båda ögonen (med glasögon eller kontaktlinser på, om Du har sådana) är utmärkt, bra, varken bra eller dålig, dålig, mycket dålig, eller är Du helt blind?

(Sätt en ring runt en av siffrorna)

Utmärkt.....	1
Bra.....	2
Varken bra eller dålig.....	3
Dålig.....	4
Mycket dålig.....	5
Helt blind.....	6

3. Hur stor del av tiden bekymrar Du Dig över Din syn?

(Sätt en ring runt en av siffrorna)

Aldrig	1
Sällan	2
Ibland	3
Större delen av tiden	4
Hela tiden	5

4. Hur mycket smärta eller obehag har Du i och kring Dina ögon (t.ex. en brännande känsla, klåda, eller värk)?

(Sätt en ring runt en av siffrorna)

Ingen	1
Mild	2
Måttlig	3
Svår	4
Mycket svår	5

DEL 2 – SVÅRIGHETER MED AKTIVITETER

De närmast följande frågorna handlar om hur svårt Du har att utföra en viss aktivitet då Du bär Dina glasögon eller kontaktlinser, om Du brukar använda dem vid denna aktivitet.

5. Hur stora svårigheter har Du med att läsa normal stil i en tidning? Skulle Du vilja säga att Du har:

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl eller är inte intresserad av att göra detta	6

6. Hur stora svårigheter har Du med att arbeta eller utöva hobbies som kräver att Du ser bra på nära håll, t.ex. att laga mat, sy, laga saker i huset, eller använda handverktyg? Skulle Du vilja säga:

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

7. På grund av Din syn, hur stora svårigheter har Du med att hitta någonting som står på en full hylla? Skulle Du vilja säga att Du har:

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

8. Hur stora svårigheter har Du med att läsa gatuskyltar eller namn på affärer?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

9. På grund av Din syn, hur stora svårigheter har Du med att gå ner för trappsteg, trappor eller trottoarkanter i svagt ljus eller på kvällen?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

10. På grund av Din syn, hur stora svårigheter har Du med att lägga märke till saker åt sidorna när Du går förbi?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

11. På grund av Din syn, hur stora svårigheter har Du med att se hur människor reagerar på saker som Du säger?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

12. På grund av Din syn, hur stora svårigheter har Du med att välja och matcha Dina kläder?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

13. På grund av Din syn, hur stora svårigheter har du när Du besöker andra människor i deras hem, på fester, eller på restaurang?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

14. På grund av Din syn, hur stora svårigheter har Du med att gå på bio, teater, eller idrottstävlingar?

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls	1
Små svårigheter	2
Måttliga svårigheter	3
Mycket stora svårigheter	4
Slutat göra detta på grund av synen	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta	6

15. Kör Du bil nuförtiden, åtminstone då och då?

(Sätt en ring runt en av siffrorna)

Ja.....	1	Gå till fråga 15c
Nej.....	2	

15a. OM NEJ: Har Du aldrig kört bil eller har Du slutat köra bil?

(Sätt en ring runt en av siffrorna)

Har aldrig kört.....	1	Gå till fråga 17
Har slutat.....	2	

15b. OM DU SLUTAT KÖRA BIL: Var det huvudsakligen på grund av Din syn, huvudsakligen av andra anledningar, eller på grund av både Din syn och andra anledningar?

(Sätt en ring runt en av siffrorna)

Huvudsakligen synen.....	1	Gå till fråga 17
Huvudsakligen av andra anledningar.....	2	Gå till fråga 17
Både synen och andra anledningar...	3	Gå till fråga 17

15c. OM DU FORTFARANDE KÖR BIL: Hur stora svårigheter har Du med att köra bil dagtid på kända ställen?

Skulle Du vilja säga att Du har:

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls.....	1
Små svårigheter.....	2
Måttliga svårigheter.....	3
Mycket stora svårigheter.....	4

16. Hur stora svårigheter har Du med att köra bil nattetid? Skulle Du vilja säga att Du har:

(Sätt en ring runt en av siffrorna)

Ingen svårighet alls.....	1
Små svårigheter.....	2
Måttliga svårigheter.....	3
Mycket stora svårigheter.....	4
Slutat göra detta på grund av synen.....	5
Slutat göra detta av andra skäl, eller är inte intresserad av att göra detta.....	6

DEL 3. REAKTIONER PÅ SYNPROBLEM

De närmast följande frågorna handlar om saker som Du kanske gör på grund av Din syn. För varje fråga, var snäll och ringa in en siffra för att visa om påståendet gäller Dig hela tiden, för det mesta, ibland, någon gång eller aldrig.

(Sätt en ring runt en av siffrorna på varje linje)

	LÄS KATEGORIER	Hela tiden	För det mesta	Ibland	Någon gång	Aldrig
17.	Får Du mindre gjort än Du skulle vilja på grund av Din syn?.....	1	2	3	4	5
18.	Är Du begränsad i hur länge Du kan arbeta eller utföra andra aktiviteter på grund av Din syn?.....	1	2	3	4	5
19.	Hur mycket hindrar Dig smärta eller obehag i och kring Dina ögon, t.ex. brännande känsla, klåda eller värk, från att göra vad Du skulle vilja göra? Skulle Du säga.....	1	2	3	4	5

För vart och ett av följande påstående, var snäll och ringa in den siffra som anger om påståendet är helt rätt, övervägande rätt, osäkert, övervägande fel eller helt fel.

(Sätt en ring runt en av siffrorna på varje linje)

		Helt rätt	Över-vägande rätt	Osäkert	Över-vägande fel	Helt fel
20.	Jag stannar hemma för det mesta på grund av min syn.....	1	2	3	4	5
21.	Jag känner mig frustrerad en stor del av tiden på grund av min syn.....	1	2	3	4	5
22.	Jag har mycket mindre kontroll över vad jag gör på grund av min syn....	1	2	3	4	5
23.	På grund av min syn är jag tvungen att lita för mycket på vad andra talar om för mig.....	1	2	3	4	5
24.	Jag behöver mycket hjälp från andra på grund av min syn.....	1	2	3	4	5
25.	Jag oroar mig för att göra saker som generar mig eller andra på grund av min syn.....	1	2	3	4	5