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First-in-Human Safety Study of Femtosecond Laser Image-Guided Trabeculotomy for Glaucoma Treatment

24-month Outcomes

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Purpose: Pilot study to evaluate adverse events and intraocular pressure (IOP)-lowering of a novel, noninvasive glaucoma procedure, femtosecond laser, image-guided, high-precision trabeculotomy (FLIGHT).

Design: Prospective, nonrandomized, single-center, interventional, single-arm clinical trial.

Participants: Eighteen eyes from 12 patients with open-angle glaucoma.

Methods: Eighteen eyes from 12 patients underwent FLIGHT, creating a single channel measuring 500-μm wide by 200-μm high through the trabecular meshwork and into Schlemm's canal. Adverse events, IOP, and other parameters were evaluated out to 24 months.

Main Outcome Measures: Outcomes were the rates and types of adverse events and the rate of post-procedure best-corrected visual acuity loss ($\geq$ 2 lines) compared with baseline. Efficacy outcomes were reduction in mean intraocular pressure (IOP) with respect to baseline and the percentage of eyes with a $\geq$ 20% reduction in IOP.

Results: Eighteen eyes from 12 patients were enrolled in the study; 11 patients (17 eyes) returned at 24 months. There were no serious adverse events related to the laser treatment. Well-defined channels were clearly visible at 24 months by gonioscopy and anterior segment OCT, with no evidence of closure. At 24 months, the mean IOP was reduced by 34.6% from 22.3 $\pm$ 5.5 to 14.5 $\pm$ 2.6 mmHg ($P < 5e\text{-}5$), with an average of 2.0 $\pm$ 1.2 hypotensive medications compared with 2.2 $\pm$ 1.1 at baseline ($P = 0.22$). Fourteen out of the 17 study eyes (82.3%) achieved a $\geq$ 20% reduction in IOP at 24 months when compared with baseline.

Conclusion: The FLIGHT system demonstrated a favorable safety profile in this initial pilot study, with no device-related serious adverse events. The channels appeared patent at 24 months, indicating medium-term durability.

Financial Disclosure(s): Proprietary or commercial disclosure may be found after the references.

Supplemental material available at www.ophthalmologyscience.org.

Lowering intraocular pressure (IOP), and thus reducing visual field progression, is the only proven glaucoma treatment today. The current glaucoma management paradigm can be thought of as 3-tiered and typically begins noninvasively with medicated eye drops and/or selective laser trabeculoplasty, advances to minimally invasive glaucoma surgeries (MIGSs) and minimally invasive bleb surgery, before resorting to invasive, traditional filtration surgery.[1] Minimally invasive glaucoma surgeries have assumed an increasingly prominent role in glaucoma management over the last decade, due in part to their favorable safety profile when compared with filtering surgeries.[2] In general, most MIGS target the conventional outflow pathway via the trabecular meshwork (TM) and Schlemm's canal and, to a lesser degree, the suprachoroidal/supraciliary space or subconjunctival space.[3] Minimally invasive glaucoma surgeries that target the conventional outflow pathway typically connect the anterior chamber and Schlemm's canal either by an implant (iStent inject; Hydrus), canaloplasty (OMNI; iTrack), or removal of a portion of the TM and inner wall of Schlemm's canal (Trabectome, Kahook Dual Blade, and excimer laser trabeculostomy [ELT]).[2,4–7] Minimally invasive glaucoma surgeries that target the suprachoroidal, supraciliary, or subconjunctival spaces do so via implants connecting the anterior chamber to the respective anatomic site of effluence (iStent SUPRA, XEN Gel Stent, SOLX gold shunt, STARflo implant, and MINIject).[8,9] Regardless of the specific MIGS modality, all

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approaches aim to bypass the resistance to the aqueous humor outflow, whether by the removal of tissue or by the addition of an implant. Furthermore, all MIGSs procedures are invasive to a degree, by definition, and require opening of the eye. In this respect, there currently exists an unmet medical need for a noninvasive glaucoma procedure with a favorable safety profile that bypasses the aqueous humor outflow resistance found in the TM, juxtacanalicular tissue, and inner wall of Schlemm's canal without the need to open the eye.

The ViaLase Laser System (ViaLase Inc) is a novel, image-guided femtosecond laser designed to noninvasively create a channel connecting the anterior chamber to the Schlemm's canal with micron precision, thus bypassing aqueous humor outflow resistance, via a procedure called femtosecond laser, image-guided, high-precision trabeculotomy (FLIGHT). A custom engineered optical scanning system enables the delivery of tightly focused femtosecond laser pulses through the cornea and into the iridocorneal angle, thus permitting precise photodisruption of the TM. The safety profile of the photodistruptive femtosecond laser mechanism underpinning this technology is well documented in ophthalmology and has been utilized to great effect in the cornea, lens capsule, and crystalline lens.[10–14] More recently, FLIGHT has been demonstrated to reduce IOP in perfused human cadaver eyes with little to no collateral damage to the surrounding tissues, as evaluated by transmission electron microscopy and second-harmonic generation imaging.[15,16] The primary purpose of this pilot study was to evaluate the safety of FLIGHT with the ViaLase Laser System and, secondarily, to investigate the effect on IOP. This report describes the 24-month outcomes of the first-in-human study of FLIGHT.

Methods

This is a prospective, single-center study designed to evaluate the adverse event profile of FLIGHT. Efficacy data were also recorded. The study was conducted at the Semmelweis University in Budapest, Hungary; Semmelweis University Institutional Review Board approval was obtained, and the study was performed in compliance with the tenets of the Declaration of Helsinki. All participants were recruited in Hungary between August and October 2020 and provided informed written consent to participate before enrollment. The study was in compliance with Health Insurance Portability and Accountability Act and was registered on ClinicalTrials.gov (identifier: NCT04949802). Before enrollment, subjects underwent a comprehensive ophthalmic screening examination comprising ocular history, slit lamp/gonioscopy, best-corrected visual acuity (BCVA), visual field, and IOP measurement to determine the eligibility for the study. Intraocular pressure measurements were performed by a 2-operator system with a masked reader and were taken between the hours 8:00AM and 11:00AM at screening and baseline visits. Two measurements were taken at each IOP timepoint. The mean was recorded unless the 2 measurements differed by $>$ 2 mmHg, in which case a third measurement was taken and the median was recorded. The patient inclusion criteria were as follows: Patients were aged at least 35 years and diagnosed with open-angle glaucoma (primary or secondary), with open anterior chamber angles (Shaffer grade $\geq$ 3), and with a medicated IOP (1–4 hypotensive medications) between 12 mmHg and 26 mmHg or an unmedicated IOP of 22 to 38 mmHg. Patients either had uncontrolled IOP with maximum tolerable medications or did not tolerate medications well. Notable exclusion criteria were previous glaucoma surgeries, including selective laser trabeculoplasty and implants, and any corneal conditions that could inhibit TM visualization. Participants with other types of glaucoma, such as neovascular glaucoma, uveitic glaucoma, and angle closure glaucoma, were also excluded from the study. Participants maintained their pretreatment medication regimen up to the 12-month follow-up, after which management was left to the treating physician, and there was no preset target IOP.

Intervention

The FLIGHT system is intended to create a channel through the TM into the Schlemm's canal. The system, shown in Figure 1, consists of several major components: a chassis containing the laser engine and electronics, a graphical user interface and touchscreen, the optical delivery head, a handheld gonio camera (not pictured), and a proprietary lens that couples the patient to the laser system (coupling lens). The specialized, scanning, optical delivery system is designed to deliver tightly focused femtosecond laser pulses through the cornea and into the iridocorneal angle, thus creating micron-sized photodisruption sites within the target tissue. A channel is created from the anterior chamber, through the TM, and into Schlemm's canal by contiguously scanning microphotodisruption spots through a predefined target volume using a computer-controlled scanner system. During treatment, a single channel 500 μm in width and 200-μm high is created through the TM, thus treating just 5° of the angle.

The following is a brief description of the procedure (Video clip, available at www.ophthalmologyscience.org). Pilocarpine (2%) drops were applied to the study eye 1 hour before treatment. Acetazolamide (250 mg) was given orally 2 hours before treatment out of an abundance of caution to prevent IOP spikes, considering that these were the first in-human FLIGHT procedures. Just before treatment, the patient was laid down, and topical anesthetic drops were applied. A bead of gonio gel (GenTeal Tears Gel, Alcon Laboratories) was applied to the surface of the cornea before placement of the proprietary handheld gonio camera onto the eye. The handheld gonio camera displays real-time, high-resolution video of the iridocorneal angle and was used to inspect the angle and select the location for treatment. Next, the coupling lens, shown in Figure 1, was placed onto the study eye and secured via vacuum suction using a suction ring attached to the coupling lens. The laser delivery system was then docked into the coupling lens cone via a motorized x-y-z–axis gantry and joystick. Once contact was established between the coupling lens and laser system, the 2 were secured via a second vacuum suction button on the touchscreen, thus connecting the patient to the laser system.

Next, the investigator identified the predetermined treatment location on the TM using the live gonioscopic video of the system and positioned the aiming lasers onto that location via the graphical user interface on the touchscreen. The aiming lasers were overlapped onto the TM by rotating a focusing knob on the system, thus coarsely adjusting the depth of the femtosecond laser focal point. The system gonioscopic view and aiming beams focused on the TM are shown in Figure 2. The depth of the surface of the TM was determined with micron precision using OCT, and the depth of the femtosecond laser focal point was finely adjusted relative to the location of the TM surface. Once aiming of the laser was complete, the user initiated the preprogrammed laser treatment using a footswitch. After the laser treatment, suction was released between the eye and the laser before removing the patient, thus completing the procedure.

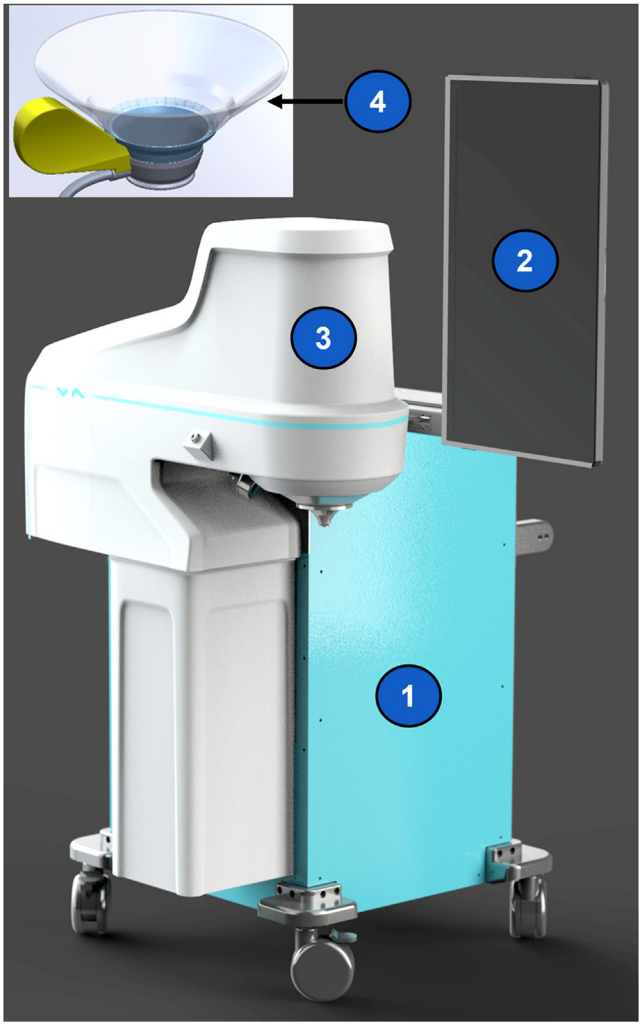

Figure 1. ViaLase Laser System. 1, System chassis. 2, Touchscreen. 3, Optical delivery head. 4, Proprietary coupling lens.

Postoperative Measures

Dexamethasone drops were prescribed for the week after treatment (3 times daily). Preoperative IOP-lowering medications were continued throughout the postoperative period up to the 12 months follow-up, after which medications were removed at the discretion of the physician. Follow-up visits were conducted at 1 day, 1 week, 1 month, 3 months, 6 months, 12 months, 18 months, and 24 months. Intraocular pressure measurement using Goldmann applanation tonometry and slit lamp examinations were performed

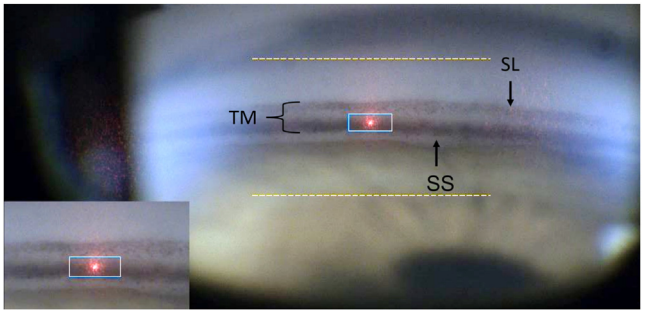

Figure 2. This is a view of the irido-corneal angle through the on board gonio-camera. The trabecular meshwork (TM), scleral spur (SS, and Schwalbe's line (SL) are clearly visible. The blue box is the laser treatment area and measures 500-µm wide by 200-µm high. The position of the blue box is adjusted by simply dragging it to the desired location on the TM via the touchscreen. The red aiming beams in the center of the blue box are overlapped into a single spot, indicating the femtosecond laser is properly focused onto the TM.

at every visit. Best-corrected visual acuity, gonioscopy, and dilated fundus examination with cup-to-disc ratio were performed at predefined follow-up time points per the protocol. The visual field was measured at baseline and at 24 months. Intraocular pressure was measured by an experienced operator between the hours 8:00AM and 11:00AM on follow-up visits. The handheld gonio camera as well as anterior segment OCT (AS-OCT) were used to confirm the creation of the channel.

Statistical Analysis

Safety was assessed by the number and percentage of eyes with adverse events identified by patients or investigators. The nature, severity, and relationship to the device/procedure were also recorded. Safety was assessed per eye (n = 18). Pressure outcome measures were reduction in IOP at 24 months compared with baseline as well the percentage of patients achieving a reduction in IOP $\geq$ 20 percent on the same or fewer medications at 24 months. To address intercorrelation between fellow eyes in the 6 patients treated bilaterally, 1 eye was randomly selected, using statistical software (MATLAB), for analysis from each patient. Adverse events were summarized using frequency tables and percentages. Descriptive statistics were used to describe continuous variables, such as IOP. A paired *t* test was used to calculate the significance between baseline and 24-month data (n = 12). The sample size for this study was not calculated using a power analysis beforehand because this was a pilot study with IOP effects being secondary.

Results

Eighteen eyes from 12 patients were enrolled in the study and treated with FLIGHT. Eleven out of 12 patients completed the 24-month follow-up (n = 17 eyes). The mean age of participants was 72.2 ± 9.7 years, with 91.7% of the patients being female and 100% of patients being White. All patients were diagnosed with open-angle glaucoma. Baseline characteristics are summarized in Table 1. There were no serious, laser-related, adverse events at any time point up to 24 months and no reports of hyphema, IOP spikes, corneal edema, hypotony, or peripheral anterior synechiae at any time point. There were anticipated adverse events such as blood reflux and conjunctival hemorrhage. Eleven of 18 eyes (61.1%) had blood reflux in the 2 hours after the creation of the drainage channel. Blood reflux was characterized by blood exiting the Schlemm's canal through the FLIGHT channel and into the anterior chamber, providing a confirmation of channel patency. These events were visible only under gonioscopy, and all cases were resolved by postoperative day 1. There were also instances of transient conjunctival hemorrhage in 3 eyes (n = 3 of 18; 16.7%), which were related to the coupling lens suction ring.

At 24 months, the visual field mean deviation for the cohort was −9.4 ± 7.8 decibels (dB), which was not significantly different compared with the −9.0 ± 7.3 dB mean deviation at baseline (P = 0.75). There were 2 cases (n = 2 of 17; 11.7%) of BCVA loss of $\geq$ 2 lines at 24 months, both of which also reported a visual field mean deviation progression > 2.5 dB. The first eye with BCVA loss had advanced glaucoma with a baseline visual acuity of 20/100 and visual field mean deviation of −19.6 dB. Immediately postoperatively, there was no change in vision or the visual field. At the 18-month visit, visual acuity had dropped to 20/2000, and the visual field had progressed to −21.3 dB. Advanced glaucoma was determined to be the cause of BCVA loss in this patient and not related to the laser treatment, despite a 46% reduction in IOP from baseline (26−14 mmHg). The second eye with BCVA loss at 24 months was in a patient with mild glaucoma whose visual field changed from −1.2 dB at baseline to −4.8 dB at 24 months. This patient had developed a cataract during the study, which was the cause of BCVA loss. Intraocular pressure in this eye was reduced from 24 mmHg at baseline to 16 mmHg at 24 months (33%). Additionally, moderate cystoid macular edema (n = 1 of 18; 5.6%) was diagnosed in 1 eye during a dilated fundus examination at the 3-month follow-up. Ocular history of the patient/eye included epiretinal membrane. The cystoid macular edema was treated with nepafenac and resolved by the 6-month examination. It was determined that this adverse event was not related to the laser treatment or the laser system but was rather a consequence of pre-existing moderate epiretinal membrane. The adverse events are summarized in Table 2.

At baseline, the mean IOP was 22.3 ± 5.5 mmHg, and the number of medications was 2.2 ± 1.1. At 24 months, the mean IOP had been significantly reduced by 34.6% to 14.5 ± 2.6 mmHg (P < 5e-5), with 82.3% of eyes (14/17) achieving a $\geq$ 20% reduction in IOP compared with baseline while on the same or fewer medications. At 24 months, the mean number of medications was statistically unchanged (2.2 ± 1.1 at baseline to 2.0 ± 1.2 at baseline, P = 0.22). At

Table 1. Baseline Characteristics

Patient Characteristics	
Number of patients	12
White, no. (%)	12 (100)
Number of eyes	18
Age (yrs)	72.2 ± 9.7
Age range (yrs)	52−85
Male, no. (%)	1 (8.3)
Female, no. (%)	11 (91.7)
OD eyes, no. (%)	9 (50)
OS eyes, no. (%)	9 (50)
Baseline IOP, mmHg	22.3 ± 5.5
IOP range	18−38
Schaffer grade $\geq$ 3, no. (%)	18 (100)
OAG, no. (%)	18 (100)
Visual field mean deviation (dB), mean (SD)	−9.0 (7.3)
Glaucoma severity	
Mild, no. (%)	6 (33.3)
Moderate, no. (%)	5 (27.8)
Severe, no. (%)	7 (38.9)
Lens status, no. (%)	
Phakic	2 (11.1)
Pseudophakic	16 (88.9)
Number of medications, mean (SD)	2.1 ± 1.0
0, no. (%)	1 (5.6)
1, no. (%)	4 (22.2)
2, no. (%)	7 (38.9)
3, no. (%)	5 (27.8)
4, no. (%)	1 (5.6)

IOP = intraocular pressure; OAG = open-angle glaucoma; OD = right eye; OS = left eye; SD = standard deviation.

Table 2. Summary of Adverse Events

Adverse Events	Number (%)
Conjunctival hemorrhage	3 (16.7)
Blood reflux	11 (61.1)
VF MD progression ≥ 2.5 dB	2 (11.7)
Loss BCVA ≥ 2 lines	2 (11.7)
Cystoid macular edema	1 (5.5)
IOP spike > 10 mmHg	—
Hyphema	—
Hypotony	—
Peripheral anterior synechiae	—

BCVA = best-corrected visual acuity; IOP = intraocular pressure; MD = mean deviation;
VF = visual field.

24 months, 2 patients had a reduction of 1 medication, whereas 1 patient was medication free. Intraocular pressure and medications during follow-up are summarized in Table 3. Figure 3 displays IOP data over the 24 month follow-up period. At 3 months, 1 patient declined to come back for follow-up dates because of coronavirus disease 2019 (COVID-19) concerns. At 6 months, 2 more patients declined to return because of COVID-19 concerns. By 18 months, these patients returned to for follow-up. One patient declined to return for 18- and 24-month follow-up because of COVID-19 related concerns. No patients required secondary surgical intervention to reduce IOP during the study.

The FLIGHT channels were clearly visible with the handheld gonio camera and AS-OCT at the 24-month follow-up. Figure 4 shows handheld gonio camera images of the same channel at 1 day (Fig 1A), 18 months (Fig 1B), and 24 months (Fig 1C) postoperatively. In Figures 4B and 4C, the channel at 18 and 24 months has well-defined edges and corners. The residual pigment in the channel that was present at day 1 is not visible at later time points. Figure 5A is an AS-OCT b-scan showing a side view of the FLIGHT channel (arrow) at 1 day postoperatively (Casia OCT, TOMEY GmbH). Figures 5B and 5C are AS-OCT images of the same channel at 18 months and 24 months, respectively. The images in Figures 4 and 5 were acquired from the same eye.

Discussion

The primary objective of this study was to evaluate the safety of the FLIGHT procedure. Overall, there were no serious device-related adverse events, and the procedure was well tolerated by patients, with no reports of significant postoperative pain or visual effects. There were no cases of loss of vision as a direct result of the laser treatment. Upon completion of the procedure, all patients were able to exit the room unassisted without any postoperative restrictions. There were instances of minor blood reflux in 11 eyes immediately after surgery, which all resolved by postoperative day 1. The blood was only visible under gonioscopy and did not affect vision or constitute a hyphema. Blood reflux was expected because FLIGHT creates direct aqueous communication between the Schlemm's canal and anterior chamber, which can result in a small amount of blood reflux from the Schlemm's canal. During the treatment, because the IOP is maintained in the eye, the risk of bleeding during the procedure obscuring the treatment is less likely. The risk of developing hyphema is still unknown but should be evaluated in future studies. Indeed, treatments were all able to be performed uneventfully. There were also 3 cases of conjunctival hemorrhage out to 1 week, which were graded from trace to moderate. Some degree of conjunctival hemorrhage is anticipated for laser systems utilizing a patient interface secured with suction around the limbus. Reported rates of conjunctival hemorrhage for other femtosecond devices such as the LensX (Alcon), CATALYS (Johnson & Johnson), VICTUS femtosecond laser platform (Bausch & Lomb), and LensAR were 33% to 73%,[17,18] 33%,[18] 26%,[19] and 8.9 to 43.8,[17,20] respectively. The rate of conjunctival hemorrhage reported in this study (16.7%) is comparable with the previously reported clinical data from femtosecond devices utilizing patient interface suction.

There are several factors that may have contributed to the overall lack of adverse events in this study and the overall safety of FLIGHT. First, FLIGHT does not require opening the eye and only treats about 5° of the angle, which reduces the potential for harm to the eye. Additionally, preoperative medications could have also played a role in minimizing adverse events. Systemic acetazolamide was given to the patients preoperatively out of an abundance of caution, given that this was a first-in-human study. Acetazolamide in conjunction with preoperative pilocarpine could have worked in tandem to reduce the potential for IOP spikes in the short term. Another factor potentially contributing to the favorable safety profile reported in this study is the lack of collateral damage to the surrounding tissue associated with femtosecond lasers in ophthalmology, already demonstrated in previous studies.[20,21] Previously, FLIGHT channels created in cadaver eyes were investigated using transmission electron microscopy as well as second-harmonic generation imaging.[16] The study showed no thermal collateral damage to tissues adjacent to the FLIGHT channel, as evidenced by collagen fibril integrity and absence of collagen denaturization. This was likely a contributing factor to the absence of a significant healing response or channel closure in the current study. For example, on gonioscopy and OCT images, FLIGHT channels had well-defined boundaries and were clearly visible at 24 months, indicating medium-term durability of the procedure and evidence of minimal inflammatory and wound healing response (Figs 4, 5). Additionally, as shown in Figure 4, the accumulation of pigments near the channel over time suggests increased outflow through the channel.

The efficacy of FLIGHT in lowering IOP was evaluated as a secondary outcome. At 24 months, the mean IOP was reduced by 34.6% to 14.5 ± 2.6 mmHg, and 9 out of the 11 patients who completed the study achieved an IOP reduction of ≥ 20%. The level of IOP reduction with FLIGHT in the current study (34.6%) has the potential to be comparable with numerous TM outflow procedures. Medication compliance was not assessed (medication numbers remained

Table 3. Intraocular Pressure and Medications during Follow-up

Patient Number	OS/OD	Medications	Number	IOP (mmHg) Baseline	1 Wk	1 Mo	3 Mos	6 Mos	12 Mos	18 Mos	24 Mos	Medications	Number
1	OS*	tafluprost, timolol, dorzolamide	3	20	16	14	12	10	14	15	13	no change	3
2	OD*	brinzolamide, timolol, latanoprost	3	26	14	14	16	10	10	14	14	latanoprost, brinzolamide	2
3	OS*	none	0	38	15	14			14			no change	0
4	OD*	latanoprost, timolol	2	20	16	15	16	16	20	16	16	no change	2
5	OD*	brinzolamide, brimonidine, tafluprost, timolol	4	24	14	19	18	19	18	18	16	no change	4
6	OS*	dorzolamide, timolol, latanoprost	3	22	20	18	20	16	16	18	14	no change	3
7	OD*	dorzolamide, timolol	2	20	15	14.5	14	13	14	16	16	no change	2
	OS	dorzolamide, timolol	2	20	16	15	18	13	14	18	16	no change	2
8	OD	dorzolamide, timolol, latanoprost	3	20	16	11	10			10	11	no change	3
	OS*	dorzolamide, timolol, latanoprost	3	18	10	12	10			10	10	no change	3
9	OD*	latanoprost	1	18	14	13	14	14	10		14	no change	1
	OS	latanoprost	1	19	14	15	15	12	10		16	no change	1
10	OD	dorzolamide, timolol	2	20	16	12	12	12	11	13	10	latanoprost	1
	OS*	dorzolamide, timolol	2	20	14	16	14	11	11	12	12	latanoprost	1
11	OD*	tafluprost	1	21	16	16	15	15	15	13	20	no change	1
	OS	tafluprost	1	21	18	16	15	12	15	15	20	no change	1
12	OD*	tafluprost, timolol	2	20	14	12	14	11	12	14	15	none	0
	OS	tafluprost, timolol	2	18	14	12	12	12	12	14	14	none	0
		Mean	2.2	22.3	14.8	14.8	14.8	13.5	14.0	14.6	14.5		2.0
		Standard deviation	1.1	5.5	2.3	2.2	2.7	3.0	3.2	2.5	2.6		1.2

IOP = intraocular pressure; OD = right eye; OS = left eye.
*Used for statistical analyses.

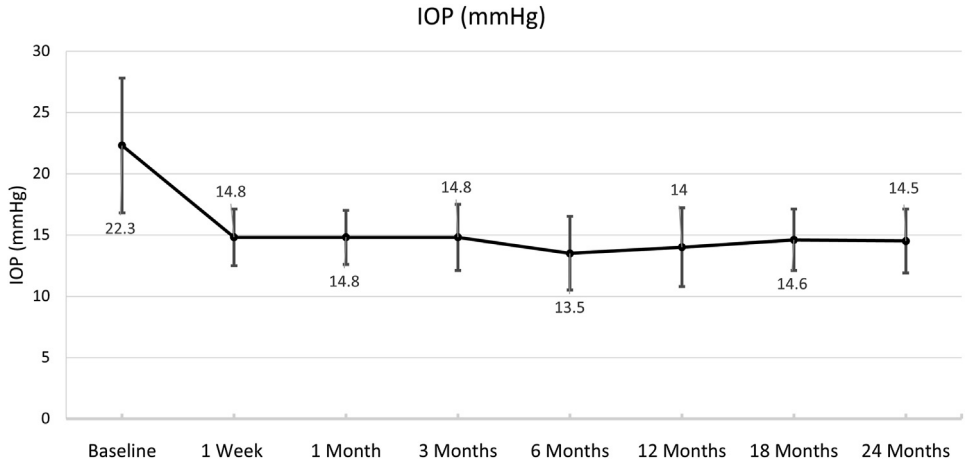

Figure 3. Intraocular pressure (IOP) over the course 24 months after treatment. Intraocular pressure at baseline was 22.3 ± 5.5 mmHg and reduced to 14.5 ± 2.6 mmHg at 24 months (a reduction of 34.6%).

unchanged), and it is possible that patients were more compliant after the procedure. More extensive studies are needed with medication washout to better assess the IOP reduction potential of this procedure. The Hydrus Microstent (Ivantis, Inc), iStent (Glaukos), Trabectome (NeoMedix), Kahook Dual Blade trabeculectomy (New World

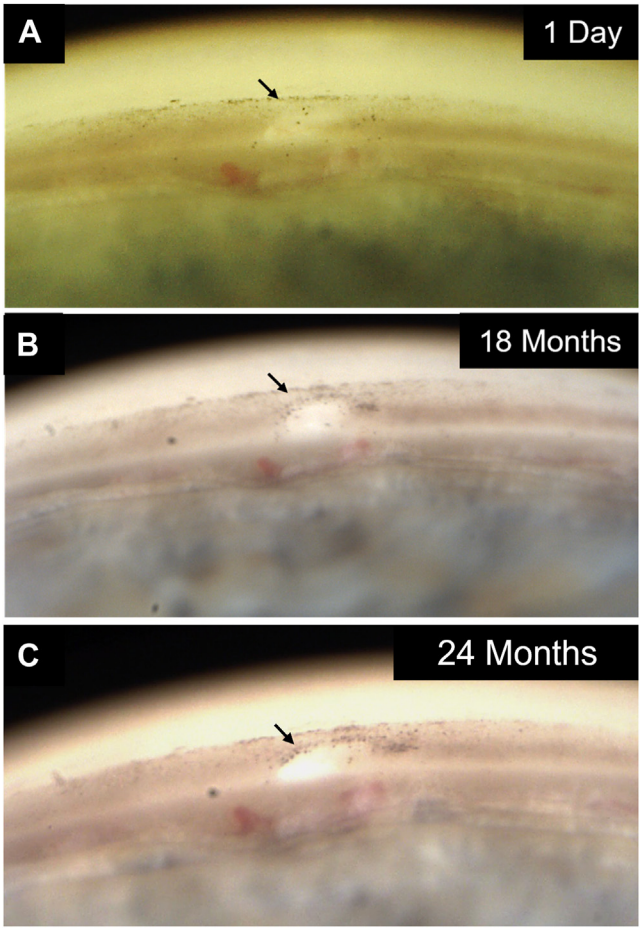

Figure 4. Proprietary handheld gonio-camera images showing the same femtosecond laser, image-guided, high-precision trabeculotomy channel at **A,** one day **B,** 18-months, and **C,** 24-months postoperatively. The black arrow indicates the upper left corner of the rectangular channel.

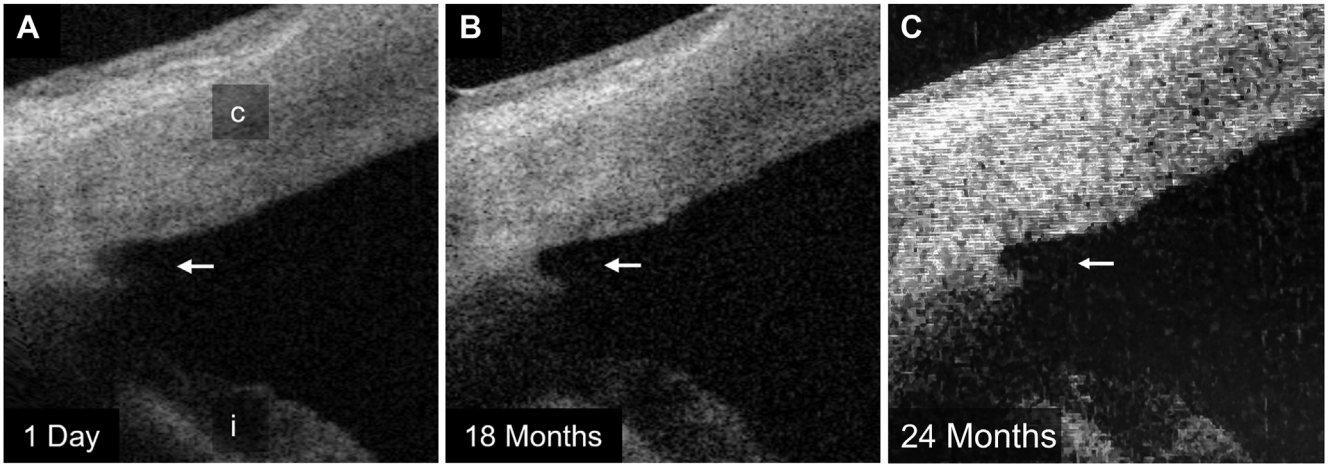

Figure 5. A, A side view b-scan of the iridocorneal angle and the femtosecond laser, image-guided, high-precision trabeculotomy (FLIGHT) channel at postoperative day 1, as indicated by the white arrow. The image was acquired with a commercially available anterior segment OCT. **B** and **C,** The same FLIGHT channel at 18- and 24-months postoperatively. c = cornea; i = iris.

Medical), and excimer laser trabeculoplasty all bypass the resistance to aqueous outflow in the TM and have reported IOP reductions between 30% and 40%, with medium-term durability.[22–28] Compared with the established Schlemm's canal-based procedures, FLIGHT does not require opening the eye; this may also contribute to the safety of the procedure. Although the tissue effects of the excimer laser used in ELT procedures and the femtosecond laser are substantially different, they are both referred to as "cold lasers," meaning that these lasers avoid heat transfer to adjacent tissues, thus minimizing the thermal collateral damages associated with other laser procedures. Thus, in both ELT and FLIGHT, cold lasers are used to create channels through the TM, thus bypassing resistance to aqueous outflow.[29] The important difference between the 2 is that ELT requires a corneal incision and physical contact between the excimer laser probe tip and the TM, whereas FLIGHT is totally noninvasive. Given an analogous principle of action between the 2 methods, it is interesting to note the ELT channel patency has been documented to 5 years and IOP reduction has been reported to the 8-year time point.[30,3132]

As with most MIGS and laser angle procedures, we studied this only in open angles (Shaffer grade $\geq$ 3). The ability to perform FLIGHT in narrow angles is unknown. Narrower angles could make the visualization of the TM more difficult and post−channel creation there would be an increased risk of iris incarceration. Further investigation in these eyes would be needed to assess these questions.

Although the data are preliminary and this is a pilot study, the initial safety profile of FLIGHT is favorable. The ability to noninvasively create a conduit between the Schlemm's canal and the anterior chamber, thus creating direct communication between the aqueous humor and the collector channels, is an advantage unique to FLIGHT technology. Clinical studies are under way to further evaluate safety and rigorously evaluate the efficacy of FLIGHT. Specifically, an appropriately powered, multicenter, randomized controlled study in a washed-out patient population of greater gender and racial diversity is necessary to understand the effects of femtosecond laser trabeculotomy.

Footnotes and Disclosures

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Abbreviations and Acronyms:
AS-OCT = anterior segment OCT; **BCVA** = best-corrected visual acuity; **COVID-19** = coronavirus disease 2019; **ELT** = excimer laser trabeculostomy; **FLIGHT** = femtosecond laser, image-guided, high-precision trabeculotomy; **IOP** = intraocular pressure; **MIGS** = minimally invasive glaucoma surgery; **TM** = trabecular meshwork.

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