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Outflow Facility Effects of 3 Schlemm's Canal Microinvasive Glaucoma Surgery Devices

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Purpose: To study the effect of 3 Schlemm's canal (SC) microinvasive glaucoma surgery (MIGS) devices on outflow facility.

Design: Paired comparisons, randomized design, baseline-controlled study.

Participants: Thirty-six pairs of dissected anterior segments from donated human eye bank eyes without glaucoma were studied. A baseline measurement was collected from each eye to serve as its control.

Methods: Using a constant pressure perfusion method, outflow facility was measured in paired eyes from human donors. Measurements were made at perfusion pressures of 10 mmHg, 20 mmHg, 30 mmHg, and 40 mmHg. Outflow facility was measured before (baseline control) and after the implantation of an SC glaucoma drainage device or sham procedure. Three sets of experiments were carried out comparing 1 and 2 iStent Trabecular Micro-Bypass Stents and 2 iStent Inject implants with the Hydrus Microstent.

Main Outcome Measures: Change in outflow facility from baseline or contralateral eye.

Results: After Hydrus placement, the outflow facility increased from 0.23±0.03 μl/minute per millimeter of mercury at baseline to 0.38±0.03 μl/minute per millimeter of mercury ($P < 0.001$). The percent increase in outflow facility was 79±21% for the Hydrus and 11±16% for the 2 iStent Inject devices, a difference that was significant ($P = 0.018$). Outflow facility with 1 iStent (0.38±0.07 μl/minute per millimeter of mercury) was greater than baseline (0.28±0.03 μl/minute per millimeter of mercury; $P = 0.031$). The 1 iStent showed a greater increase in outflow facility from baseline (0.10±0.04 μl/minute per millimeter of mercury) compared with the sham procedure (−0.08±0.05 μl/minute per millimeter of mercury; $P = 0.042$). No other significant differences were found.

Conclusions: The longer the MIGS device, and thus the more SC that it dilates, the greater the outflow facility. *Ophthalmology Glaucoma 2020;3:114-121 © 2019 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Glaucoma, a leading cause of blindness worldwide,[1] is treated by lowering intraocular pressure (IOP).[2,3] Typically, medical therapy is used as the first line of treatment, followed by more invasive steps such as glaucoma filtration surgery.[4–6] Recently, several microinvasive glaucoma surgery (MIGS) techniques have been developed and are being used earlier in the treatment paradigm. These MIGS techniques share several common traits, including an ab interno approach that is minimally traumatic to the target area, a safety profile that avoids serious complications allowing for rapid recovery, and an IOP-lowering efficacy that justifies the intervention.[7–9]

Outflow MIGS devices are a subset of MIGS techniques that improve drainage of aqueous humor through Schlemm's canal (SC). Outflow MIGS devices reduce the resistance to outflow at the level of the trabecular meshwork (TM) by creating a bypass or removing the TM altogether. As soon as the TM is bypassed, aqueous humor can flow into collector channels, aqueous veins, and episcleral veins with less resistance. Growing scientific evidence supports the importance of bypassing the TM and dilating SC to reduce IOP.[10]

Multiple scientific studies have been published on the effect of several different outflow MIGS implants on outflow facility. The most common laboratory approach to test these implants is to isolate the conventional outflow pathway including the TM, SC, and aqueous humor outflow network that is contained within the anterior segment of a human eye. This approach provides a unique opportunity to directly compare the differences in outflow facility effects among the implants. These studies include the Hydrus Microstent[11,12] (Ivantis, Inc, Irvine, CA), first-generation iStent Trabecular Micro-Bypass (Glaukos Corp, San Clemente, CA),[13] and second-generation iStent Inject[14] (Glaukos Corp). The current study adds to the literature by comparing all 3 implants and a sham procedure within a single laboratory.

Methods

Test Articles

The first implant evaluated in the study was the Hydrus Microstent, which is a nitinol (nickel-titanium) scaffold approximately 8 mm in length with an inlet of 260 μm in diameter, designed to keep the SC dilated and maintain an opening in the TM. The second implant evaluated was the iStent Trabecular Micro-Bypass Stent, which is an L-shaped titanium stent with a 0.25-mm × 120-μm (bore diameter)

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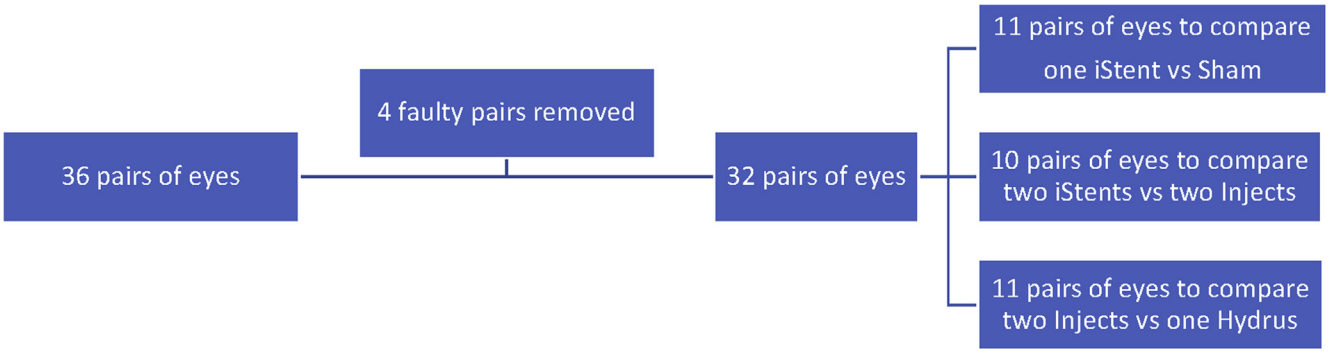

Figure 1. Diagram showing experimental design of study eyes and procedures.

snorkel and a 1-mm rail that fits into SC. The third implant evaluated was the iStent Inject, which is a cylindrical titanium stent with a central lumen of 80 µm and side lumens of 50 µm. Three sets of experiments were carried out, as summarized in Figure 1.

Tissue Preparation

This study used enucleated human donor eyes. Before the study began, the project was evaluated by The Center for Clinical Research and Technology at Case Western Reserve University and determined not to be a human subjects research study under Federal regulation 45 CFR46 or 21 CFR 56. Therefore, institutional review board approval and informed consent were not needed. The study was performed in compliance with the principles of the Declaration of Helsinki. Thirty-six pairs of globes were obtained from Eversight, Minnesota Eye Bank, and Saving Sight. Four of the pairs were rejected because of postmortem age or leaks in the tissue or the system. The remaining globes were wrapped in saline-wetted gauze, packed in moist containers cooled in crushed ice, and received within 48 hours of death. The average time from death of the donor until the start of the experiment was 45.7±12.7 hours. The eligible donors' lenses were phakic, and the donors had no known ocular disease history or had undergone prior ocular surgery. The mean donor age was 67.1±9.9 years. Demographic information is summarized Table 1. The eyes were dissected along the coronal equator, and the anterior segments were prepared as described previously.[11,12,15]

Perfusion System

The outflow facility measurement apparatus contained fluid columns filled with distilled water. The columns were connected via tubing to the tissue chamber holding the anterior segment. The tubing was filled with 5.5 mM D-glucose in Dulbecco's phosphate-buffered saline. Perfusion pressures were controlled by setting the fluid in the columns to heights corresponding to 10 mmHg, 20 mmHg, 30 mmHg, and 40 mmHg. During the perfusion time, the anterior segments were submerged partially in perfusion fluid maintained at 34° C by a temperature-controlled water bath. Pressure transducers, PowerLab 8/30 receiver (ADInstruments, Bella Vista, Australia), and LabChart 7 software (ADInstruments Pty Ltd, Richardson, TX) recorded perfusion pressures during the study.

Calculation of Outflow Facility

Outflow facility (C) values were calculated at each perfusion pressure as the ratio of flow (F) to IOP: $C = \frac{F}{IOP}$. Individual C values at each IOP were averaged.[11] If the calculated outflow facility was more than 1.0 µl/minute per millimeter of mercury, either before or after the sham procedure or stent insertion, this was a statistical outlier and taken as evidence of a leak. Based on the Goldmann equation, a change in outflow facility (C) is expected to show a linear relationship to IOP change.

Implant Study Design

Anterior segments were perfused sequentially at pressures of 40 mmHg, 30 mmHg, 20 mmHg, 10 mmHg, 20 mmHg, 30 mmHg, 40 mmHg, and 10 mmHg. Before implantation of the MIGS devices, baseline outflow facilities for each anterior segment were calculated at each perfused pressure.

After the baseline outflow facility measurement was completed, the anterior segment was removed from the tissue chamber and

Table 1. Demographic Information

Study	No. of Eyes	Age (yrs), Mean ± Standard Deviation	Ethnicity	Gender (No.)		Cause of Death	Postmortem Time (hrs), Mean±Standard Deviation
				Male	*Female*		
One iStent vs. sham	11	70.3±4.5	10 white, 1 Hispanic	7	4	Acute hypoxic respiratory failure, adenocarcinoma, cardiac arrest, lung cancer, myocardial infarction, sepsis	43.8±5.3
Two iStents vs. 2 iStent Injects	10	62.5±14.6	7 white, 2 black	2	7	Autoimmune encephalitis, cardiac arrest, CVA, Duchenne muscular dystrophy, leiomyosarcoma, myocardial infarction, pneumonia, sepsis	45.6±6.1
Two iStent Injects vs. Hydrus Microstent	11	67.1±8.4	7 white, 2 black	5	6	CVA, GI bleed, myocardial infarction, pneumonia, renal failure, sepsis	42.1±9.1
Total	32	66.8±10.0	26 white, 3 black, 2 Hispanic	14	17	Most common: myocardial infarction, cardiac arrest, pneumonia, sepsis	43.6±7.1

CVA = cerebrovascular accident; GI = gastrointestinal.

placed cornea side down on a specially designed mount. The TM of the inferonasal quadrant was viewed directly under the dissecting microscope. The anterior segment was kept moist during the device insertion or sham process. Choice of procedure was randomized. Using the injector, the Hydrus device was advanced approximately 3 clock hours into SC, with 1 to 2 mm of the proximal end protruding into the anterior chamber. One to 2 iStents were inserted into SC depending on the study.[16,17] If 2 iStents were used, they were placed at least 2 clock hours apart.[17] The study investigators were trained on how to insert the devices by an experienced board-certified glaucoma specialist before the study began. The iStent Inject device was inserted using the spring-loaded applicator to puncture the TM and position the head and side flow outlets in the SC, leaving the flange in the anterior chamber. All attempts were made to place each implant in the inferonasal region. The proper placement of all implants was verified under high-magnification light microscopy, as shown in Figure 2.

In total, 32 pairs of eyes were used in the study for a total of 64 samples. The eyes were assigned randomly to 3 different study groups, as shown in Figure 1. In the first study group, 11 pairs of eyes were used to measure changes in outflow facility after implanting 1 iStent versus a sham procedure consisting of a 1-mm incision made with a 25-gauge needle through the TM into SC in the inferonasal quadrant. In the second study group, 10 pairs of eyes were used to evaluate outflow facility change for 2 iStent implants versus 2 iStent Inject implants. In the third study group, 11 pairs of eyes were used to compare 2 iStent Inject implants versus 1 Hydrus Microstent.

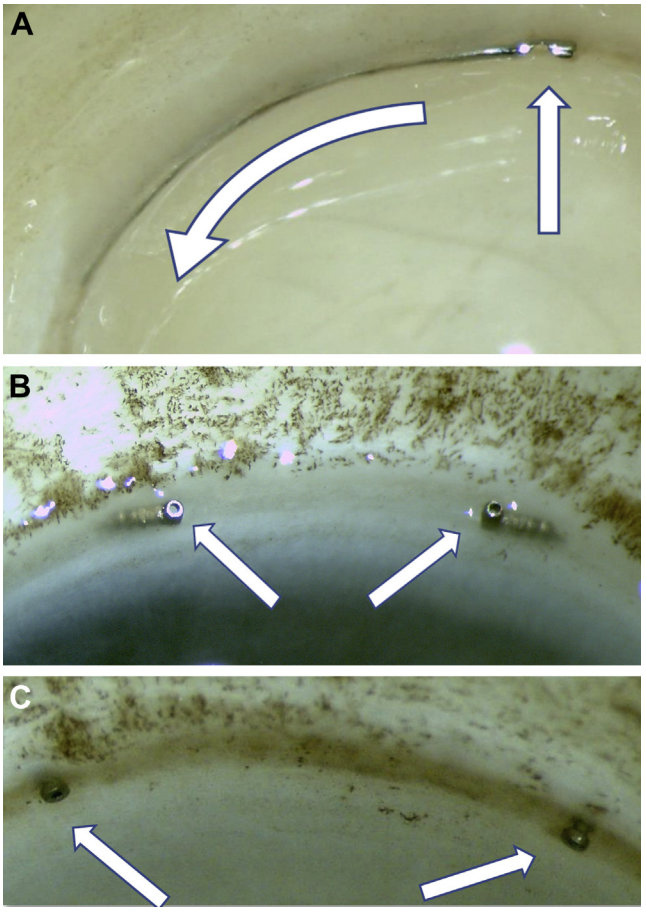

Figure 2. Photographs showing placement of 3 Schlemm's canal drainage devices. **A**, Curved arrow shows a Hydrus Microstent scaffold within Schlemm's canal and the straight arrow indicates the inlet of the Hydrus Microstent in the anterior chamber. **B**, Two iStents (arrows) with rails within the Schlemm's canal and snorkels open to the anterior chamber. **C**, Two iStent Injects (arrows) positioned in the trabecular meshwork with the head within Schlemm's canal and the flange exposed to the anterior chamber.

Results

The results from each of the study groups are shown in Table 2 and Figures 3, 4, 5, and 6.

One iStent Device versus Sham Study

The first study compared 1 iStent implant versus sham surgery. No significant difference was found between change in outflow facility from baseline between the 2 groups ($P = 0.073$). The single iStent significantly increased outflow facility by 0.10±0.04 µl/minute per mmHg when compared with baseline ($P = 0.031$). This change equated to a 31.5±11.3% increase from baseline. The sham surgery did not affect outflow facility significantly ($P = 0.187$). A significant difference was found between the change in outflow facility when comparing the iStent with sham surgery ($P = 0.042$; Fig 3).

Two iStent Devices versus 2 iStent Inject Devices Study

The second study compared 2 iStent implants versus 2 iStent Inject implants. No significant difference was found in change in outflow facility from baseline between the 2 groups ($P = 0.577$). Two iStent-implanted eyes were excluded because of leaks. The group that received 2 iStent implants showed increased outflow facility by 47.0±23.3% (n = 8) from baseline, but this did not reach significance ($P = 0.092$). The 2 iStent Inject implants increased outflow facility by 10.4±21.8% (n = 10) from baseline and did not reach significance ($P = 0.536$). No significant difference was found in the change of outflow facility between the iStent and the iStent Inject groups (Fig 4).

Two iStent Inject Devices versus 1 Hydrus Device Study

The third study compared 2 iStent Inject implants versus a single Hydrus Microstent. No significant difference was found in change in outflow facility from baseline between the 2 groups ($P = 0.43$). The iStent Inject implants increased outflow facility by 10.5±16.1% from baseline, but this was not significant ($P = 0.52$). The Hydrus device significantly increased outflow facility by 79.3±21.2% from baseline ($P < 0.001$). The mean outflow facility of the eyes implanted with Hydrus device were 0.13 µl/minute per millimeter of mercury more than those implanted with the iStent Inject device ($P = 0.017$). In addition, eyes implanted with the Hydrus device showed a greater change in outflow facility ($P < 0.001$) and significantly higher percent change in outflow facility ($P = 0.018$) when compared with eyes implanted with the iStent Inject device (Fig 5).

Table 2. Outflow Facility (Microliters per Minute per Millimeter of Mercury)

	Study 1 (n = 11)*			Study 2 (n = 10)†			Study 3 (n = 11)‡		
	First Eye, 1 iStent	*Paired Eye, Sham*	P Value§	*First Eye, 2 iStents*	*Paired Eye, 2 iStent Injects*	P Value§	*First Eye, 2 iStent Injects*	*Paired Eye, Hydrus Microstent*	P Value§
Before‖	0.28±0.03	0.44±0.09	0.073	0.22±0.04	0.26±0.06	0.58	0.28±0.04	0.23±0.03	0.43
After¶	0.38±0.07	0.36±0.07	0.851	0.31±0.05	0.31±0.09	1.00	0.25±0.03	0.38±0.03	**0.017**
Change#	0.10±0.04	−0.08±0.05	**0.042**	0.08±0.04	0.04±0.07	0.62	−0.02±0.03	0.14±0.02	**<0.001**
% Change	32±11%	−8±10%	0.096	47±23%	10±22%	0.27	11±16%	79±21%	**0.018**
Range**	−38% to 74%	−53% to 29%		−5% to 190%	−65% to 127%		−47% to 119%	9%−275%	
P value††	**0.031**	0.187		0.092	0.536		0.520	**<0.001**	

Values are mean±standard error of the mean unless otherwise indicated. Boldface indicates statistical significance.
*One iStent vs. a sham procedure, n = 11 pairs of eyes.
†Two iStents vs. 2 iStent Inject implants, n = 10 pairs of eyes.
‡Two iStent Inject implants vs. 1 Hydrus Microstent, n = 11 pairs of eyes.
§Comparing treatments, paired *t* test.
‖Mean at baseline.
¶Mean after microinvasive glaucoma surgery device placement.
#Mean change from baseline.
**Range of percent changes from baseline.
††Comparing before versus after, paired *t* test.

Comparison of All Studies

The percent increase in outflow facility relative to baseline among the implants was 79.3±21.2% for the Hydrus device (n = 11; $P < 0.001$), 31.5±11.3% for 1 iStent implant (n = 11; $P < 0.05$), 47.0±23.3% for 2 iStent implants (n = 8; $P < 0.001$), and 10.4±13.0% for the pooled iStent Inject implants (n = 21; $P = 0.807$). The data are summarized in Table 2 and Figure 6.

Discussion

Previous studies compared the Hydrus Microstent and iStent.[11,12] These studies were performed using the same perfusion methods and techniques as the current study. Therefore, it is possible to compile all data to obtain an even more robust comparison of the MIGS devices evaluated here. Including this study, 35 eyes receiving the Hydrus Microstent, 20 eyes receiving 2 iStent devices, and 21 eyes receiving 2 iStent Inject have been tested. Overall, the Hydrus Microstent increased outflow facility by 0.17±0.02 µl/minute per millimeter of mercury (75.1±11.7%; $P < 0.001$), 2 iStent implants increased outflow facility by 0.08±0.03 µl/minute per millimeter of mercury (39.3±11.3%; $P = 0.051$), and 2 iStent Inject implants increased outflow facility 0.01±0.04 µl/minute per millimeter of mercury, although this was not significant (10.4±13.0%; $P = 0.88$). When comparing implantation of the 2 iStents with implantation of the Hydrus Microstent, the Hydrus eyes showed higher outflow facility ($P = 0.007$), higher increase in outflow facility ($P = 0.008$), and higher percent increase in outflow facility ($P = 0.048$). When comparing implantation of the iStent Inject with implantation of the Hydrus Microstent, Hydrus eyes showed higher outflow facility ($P < 0.001$), higher increase in outflow facility ($P < 0.001$), and higher percent increase in outflow facility ($P < 0.001$).

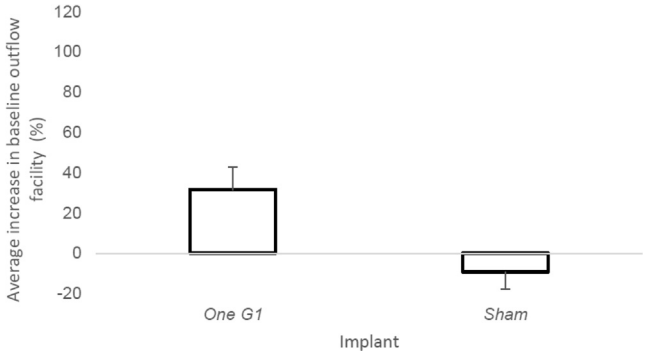

Figure 3. Graph showing the results of study 1, implantation of 1 iStent (G1) versus sham procedure. Eleven pairs of globes were tested, with 1 randomly assigned globe receiving 1 G1 and the paired eye undergoing a sham procedure. The percent change in outflow facility comparing the 2 procedures was significant ($P = 0.042$). The bars indicate percent change from baseline outflow facility (mean±standard error of the mean).

Statistically, no difference was found in outflow facility change between implantation of 2 iStent devices and 2 iStent Inject devices, probably because of the large standard errors with the iStent Inject implants. The range of outcomes for each device provides additional insight into the study results. In terms of change in outflow facility, sham treatment ranged from −53% to 29%. The Hydrus and 2 iStent groups showed consistent improvement in outflow facility compared with baseline. A single G1 iStent was less reliable in improving outflow than 2 G1 iStents. The iStent Inject showed the most variable outcome of all groups. Change in outflow facility from baseline ranged from −65% to a maximum of 127%. The highest value from the iStent Inject group (127%) is better than the highest value seen in the single G1 iStent group (74%) but lower than the highest value observed with the 2 G1 iStents group (190%).

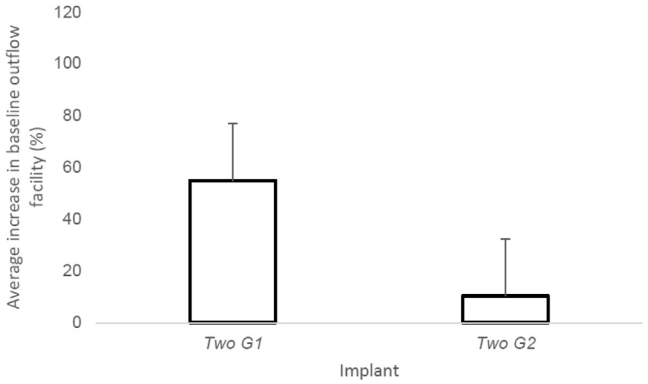

Figure 4. Graph showing the results of study 2, implantation of 2 iStents (G1) versus implantation of 2 iStent Injects (G2). Ten pairs of globes were tested, with 1 randomly assigned globe receiving 2 G1s (n = 8) and the fellow eye receiving 2 G2s (n = 10). The percent change in outflow facility from baseline was not significantly different within groups, nor when comparing groups. The bars indicate percent change from baseline outflow facility (mean ± standard error of the mean).

However, the lowest value from the iStent Inject group is similar to that for the sham group (−65% vs. −53%). These data suggest that the iStent Inject device is less predictable than either single or dual G1 iStent implantation.

Previously published studies have investigated multiple iStent and iStent Inject implants using an organ culture perfusion model in which eyes were perfused with culture media for days at a set flow rate of 2.5 µl/minute. The first study reported an outflow facility increase of 0.10 µl/minute per millimeter of mercury from a baseline of 0.12 µl/minute per millimeter of mercury to 0.22 µl/minute per millimeter of mercury with a single iStent (n = 9). No outflow facility data were reported on implantation of 2 iStents, although it was stated that no significant difference was seen.[13] The second study reported an outflow facility increase of 0.22 µl/minute per millimeter of mercury from a baseline of 0.16±0.05 µl/minute per millimeter of mercury to 0.38±0.23 µl/minute per millimeter of mercury with a single iStent Inject (n = 7). This study also reported an outflow facility increase of 0.63 µl/minute per millimeter of mercury from a baseline of 0.15±0.05 µl/minute per millimeter of mercury to 0.78±0.66 µl/minute per millimeter of mercury with 2 iStent Injects, although the number was extremely small (n = 2).[14] The third study, which used whole globes, reported only pressures, but an outflow facility increase of 0.05 µl/minute per millimeter of mercury from a baseline of 0.13 µl/minute per millimeter of mercury to 0.18 µl/minute per millimeter of mercury with a single iStent (n = 3) can be calculated using the Goldmann equation. This study also reported results with implantation of 2 iStents, which showed an increase of 0.10 µl/minute per millimeter of mercury from a baseline of 0.13 µl/minute per millimeter of mercury to 0.23 µl/minute per millimeter of mercury (n = 3).[18] Procedural differences between those study methods and methods reported in the current article make comparison of the results difficult. In addition, comparing results with different baseline values can be problematic. It has been shown that the resulting outflow resistance ($R = \frac{1}{C}$), and therefore the change in resistance, is dependent on the baseline outflow resistance. That is, higher baseline outflow resistance values correlate with larger changes in outflow resistance.[11] Because the baseline outflow resistance values in the previous studies were lower than those in the current study, the percent changes of outflow facility they showed could be exaggerated. Combine that factor with small numbers of eyes tested in those studies, and comparisons with the current study become unfeasible.

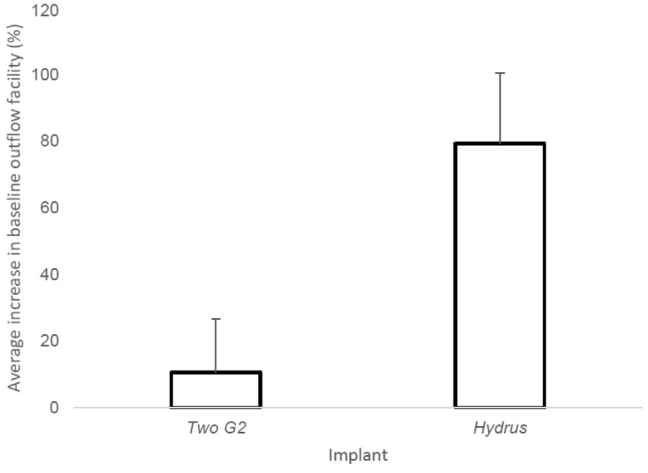

Figure 5. Graph showing the results of study 3, implantation of 2 iStent Injects (G2) versus implantation of 1 Hydrus Microstent. Eleven pairs of globes were tested, with 1 randomly assigned globe receiving 2 G2s and the fellow eye receiving 1 Hydrus Microstent. In the Hydrus Microstent globes, the percent changes in outflow facility from baseline ($P = 0.001$) and from the 2 G2s ($P = 0.018$) were significant. The bars indicate percent change from baseline outflow facility (mean ± standard error of the mean).

The MIGS devices in the current study increased *C* using TM bypass and SC dilation to improve outflow directly into SC. The resulting *C* was correlated positively to the size of the inlet bypass and length of SC dilation. The iStent inlet bypass was 1.5 times larger than iStent Inject. In addition, 1 iStent dilates up to 1 mm of SC compared with less than 0.25 mm of SC dilation seen with 1 iStent Inject device.[16] Subsequently, the data showed that 2 iStents improved outflow facility more than 2 iStent Injects with a difference of 36.6%, although this was not significant (n = 8; $P = 0.271$). When the TM inlet bypass of the Hydrus Microstent was 2 times larger than that of the iStent and 3 times larger than that of the iStent Inject, the SC dilation with the Hydrus Microstent was 8 times more than that of 1 iStent and approximately 32 times more than that of 1 iStent Inject. Overall, in the current study, the Hydrus Microstent increased *C* more than the smaller MIGS devices, with the smallest MIGS device affecting *C* the least.

Placing a 1-mm slit in the TM without implanting a stent, as was carried out in the sham procedure, has minimal effect on *C*. Placing a small bypass device such as the iStent Inject does increase *C* more than sham but not as much as the larger bypass MIGS devices, the iStent and Hydrus Microstent. The larger bypass lumen of the iStent increased *C*

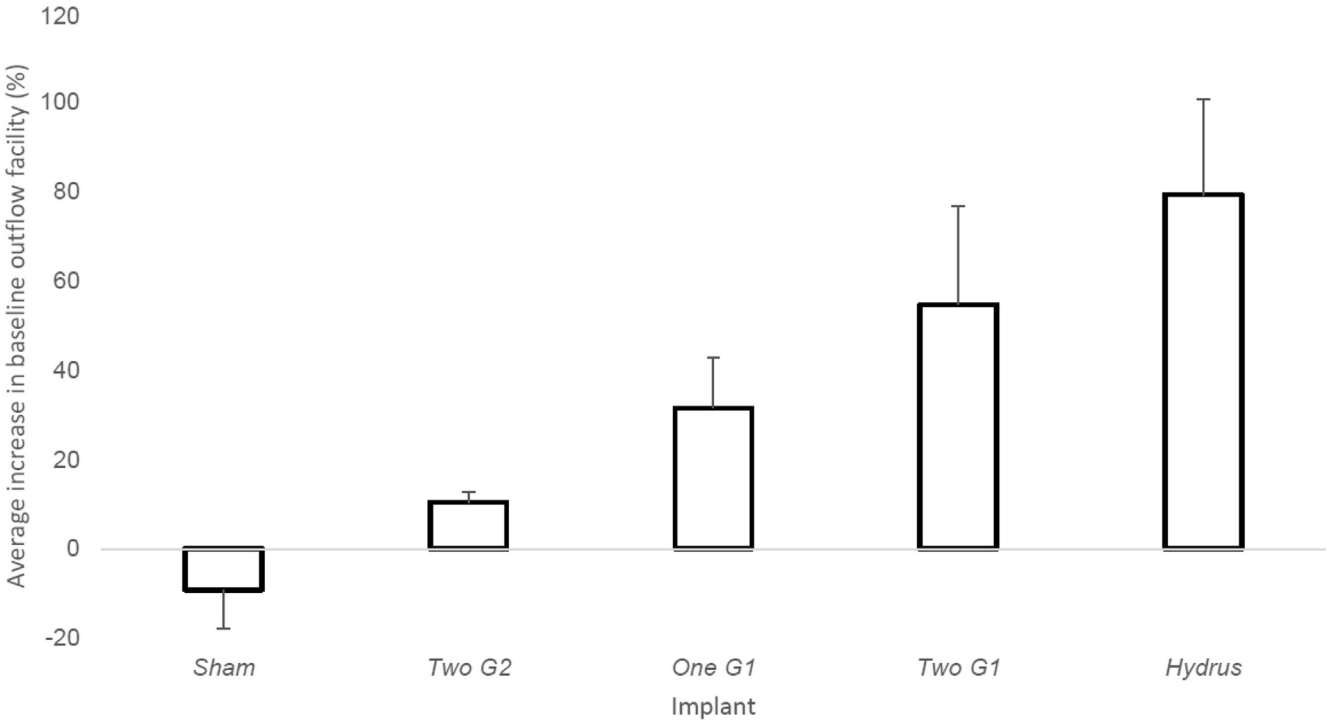

Figure 6. Graph showing percent change from baseline of all study results. Data collected from all experiments on each implant were averaged, and the results were compared. The bars show percent changes from baseline outflow facility (mean ± standard error of the mean) in globes treated with sham procedure (sham), implantation of 2 iStent Injects (G2), implantation of 1 iStent (G1), implantation of 2 G1s, and implantation of 1 Hydrus Microstent.

more than the smaller iStent Inject, regardless of whether 1 or 2 stents were placed. These results suggest that a large patent bypass is critical to *C* increase. This could also be because of the 1 mm of SC dilation from the iStent, which may provide more access to collector channels than the iStent Inject. The Hydrus Microstent has the largest inlet bypass and dilates SC to a greater extent, which could help to explain the significant increase in *C*. It is postulated that the greater length of SC dilated provides greater access to collector channels and greater outflow potential. A mathematical model[19] shows that the TM bypass provides the most effect when placed relatively close to a collector channel. In cases where the TM bypass is farther from a collector channel, SC dilation helps to provide lower resistance for flow to that collector channel. Additionally, the larger the region of SC dilation, the less dependent the placement location of the TM bypass.[17]

Evidence supports that placement of these MIGS devices into SC is critical to their efficacy. First, the bypass must be patent. If the bypass does not cross the TM fully or is buried so deep that the opening is covered, the outflow through the stent can be compromised. Even with direct visualization of the TM and SC, as in the current study, confirmation of the exact placement at times can be difficult. In live patients, surgeons not only have to view the angle through a goniolens and fluid-filled eye, they also have to clear refluxed blood that can obscure the stent placement further. Although it is a critical consideration for all outflow MIGS devices, because of their extremely small size, iStent Inject implants pose a significant challenge in this regard. Conversely, the Hydrus Microstent is large enough that placement in SC is readily confirmed. Finally, the position of the stents relative to collector channels, as mentioned above, is also a practical challenge during the surgical placement of these devices. Advanced techniques used to target placement, not performed in this study, such as identifying pigmented areas of TM, inducing blood reflux into SC, or intraoperative assessment of the aqueous outflow network, can impact the results of these procedures positively.[20] Such intraoperative clues are more evident in a live patient than a cadaver eye. The Hydrus Microstent's size may offer an advantage in this regard as well, because its relatively long length provides access to more collector channels, obviating the need for such intraoperative clues.

Comparison of implantation of the Hydrus Microstent and 2 iStents in human clinical trials was published recently.[21] The study was a prospective, multicenter, randomized trial comparing implantation of the Hydrus Microstent and 2 iStents in standalone surgery. Eligible patients had mild to moderate open-angle glaucoma that was treated with 2 to 4 glaucoma medications. The mean numbers of medications before washout were 2.5 in the Hydrus Microstent group and 2.7 in the 2 iStents group. The baseline washed-out diurnal IOP was 27.5±4.4 mmHg in eyes randomized to the Hydrus Microstent (n = 75) and 27.3±4.2 mmHg in eyes randomized to 2 iStents (n = 77). Medications were reintroduced throughout follow-up as needed if IOP exceeded 19 mmHg. At 12 months, IOP was 17.3 and 18.1 mmHg in the Hydrus Microstent and 2 iStents groups (*P* = not significant). The number of

medications were reduced by 1.6±1.2 in the Hydrus Microstent group and 1.0±1.2 in the 2 iStents group. The between-group difference of −0.6 medications was significant ($P = 0.004$). Although comparing ex vivo perfusion testing and clinical trial results is difficult, the conclusions of the recent clinical trial are consistent with the conclusions of the current study. Larger increases in outflow facility translate to lower medication use in patients with the Hydrus Microstent compared with patients receiving 2 iStents.

Despite the numerous differences between the design of clinical trials and cadaver eye experiments, findings in the nonglaucomatous cadaver eyes of the current study as well as clinical trials of SC MIGS devices support the same idea, that is, that the longer the MIGS device and the more SC it dilates, the greater the outflow facility, the lower the IOP, and reduced the need for topical ocular hypotensive medications. Larger SC MIGS devices in the glaucoma armamentarium can provide a favorable choice for the glaucoma patient and clinician.

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Abbreviations and Acronyms:
C = outflow facility; **F** = aqueous flow; **IOP** = intraocular pressure; **MIGS** = microinvasive glaucoma surgery; **R** = resistance; **SC** = Schlemm's canal; **TM** = trabecular meshwork.

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