

A Novel 8-mm Schlemm's Canal Scaffold Reduces Outflow Resistance in a Human Anterior Segment Perfusion Model

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PURPOSE. To study the effect on outflow facility and outflow resistance of a nitinol microstent implanted into Schlemm's canal.

METHODS. Using a constant pressure perfusion method, outflow facility and outflow resistance were measured in 26 pairs of dissected anterior segments from donated human eyes. Measurements were made at perfusion pressures of 10, 20, 30 and 40 mm Hg. The Hydrus Microstent was placed in Schlemm's canal of one eye and the contralateral eye underwent a sham procedure. Outflow facility and outflow resistance were measured again after the microstent implantation or sham procedure.

RESULTS. The Hydrus Microstent significantly increased outflow facility from 0.33 ± 0.17 $\mu\text{L}/\text{min}/\text{mm Hg}$ to 0.52 ± 0.19 $\mu\text{L}/\text{min}/\text{mm Hg}$ ($P < 0.001$). Outflow resistance was significantly reduced from 4.38 ± 3.03 mm Hg/ $\mu\text{L}/\text{min}$ at baseline to 2.34 ± 1.04 mm Hg/ $\mu\text{L}/\text{min}$ ($P < 0.001$) with the microstent. There was a linear correlation between outflow resistance at baseline and decrease in outflow resistance with the microstent ($R^2 = 0.89$, $P < 0.0001$).

CONCLUSIONS. The increase in outflow facility and decrease in resistance supports the potential use of the Hydrus Microstent as a surgical option to reduce intraocular pressure (IOP). The IOP-lowering effect may be higher in eyes with higher outflow resistance (and IOP) as compared with eyes with lower outflow resistance (and IOP). (*Invest Ophthalmol Vis Sci*. 2013;54:1698-1704) DOI:10.1167/iovs.12-11373

Lowering of intraocular pressure (IOP) is a critical component of glaucoma management. As a disease process, IOP elevation in open-angle glaucoma has been shown to be consequent to an increase in outflow resistance and a compromise of the pressure-dependent and pressure-independent outflow pathways of the eye.¹⁻⁶ The increased resistance in the pressure-dependent pathway has been localized to structures inner to Schlemm's canal (SC).^{3,7} Surgically, outflow

can be enhanced and IOP lowered by trabeculectomy or glaucoma drainage devices.⁸ Trabeculectomy and traditional glaucoma drainage devices bypass the normal drainage pathways through SC by creating alternate drainage channels. Angle surgical procedures attempt to improve the flow through SC or into the suprachoroidal space.⁹⁻¹² Procedures like trabeculotomy, by external or internal approach, and placement of implants into SC, bypass this site of most resistance in an attempt to restore "physiological" flow through the normal drainage pathways.^{7,13-19}

The current study evaluated a novel SC microstent (Hydrus Microstent; Ivantis, Inc., Irvine, CA) in human anterior segments (Fig. 1). The microstent is composed of nitinol (nickel-titanium alloy) and has a flexible nonluminal open structure to improve flow of aqueous humor into SC and gain access to collector channels within SC. The microstent is designed to increase outflow facility by bypassing the trabecular meshwork (TM), with an inlet to provide support to the opening in the TM and dilating SC, with an intracanalicular scaffold. The scaffold is designed to increase circumferential flow in a region spanning 8 mm or approximately one quadrant of SC. The scaffold has a crescent-shaped profile to minimize contact with the back wall of SC. The inlet creates a maximum SC dilation of 241 μm or approximately four to five times the natural cross-sectional area of SC (Fig. 2). The microstent comes preloaded in a delivery system designed for ab-interno implantation under gonioscopic visualization. The cannula tip is designed to facilitate the entry through the TM into SC where the microstent can be precisely advanced and released from the delivery system. The 8-mm microstent evaluated in this study is a modification of an earlier design that was 15 mm in length and had a larger, nearly circular profile (Fig. 3). The study design and protocol were similar to a prior report addressing the effects on outflow facility of the longer 15-mm version of the microstent.²⁰

Studies of aqueous humor dynamics in a clinical setting are the most useful evidence needed to support any claims of long-term improvement in outflow facility achieved by these implants. However, because many of the angle surgical procedures are combined with cataract surgery, postprocedure changes in aqueous humor dynamics are difficult to interpret.^{21,22} Moreover, any incisional surgical procedure has the potential of altering the aqueous humor dynamics because of the local release of inflammatory mediators and postoperative use of steroids, which further confounds the assessment of aqueous humor dynamics, at least in the early postoperative period. In a more controlled environment, laboratory experiments of donated anterior segments can provide useful information on changes in outflow facility by angle surgical procedures or devices. These well-controlled experiments avoid confounding factors, such as changes in episcleral venous pressure, uveoscleral outflow, aqueous production, inflammatory responses, and drug interactions. This experimental approach was chosen to evaluate the effects of an 8-mm Hydrus

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FIGURE 1. The 8-mm Hydrus Microstent consists of a scaffold to dilate SC and an inlet (*left*) into the anterior chamber to bypass the trabecular meshwork.

Microstent (Ivantis, Inc.) implanted within the SC of human anterior segments on the outflow facility and outflow resistance measured using a constant pressure perfusion technique.

METHODS

Tissue Preparation

Freshly enucleated pairs of human donor eyes deemed unsuitable for transplantation were obtained from the Minnesota Lions' Eye Bank. Eyes without a history of any prior surgical procedures were requested. Eyes were shipped in a humid container on ice to maintain tissue quality. On receipt, the medical history was reviewed and the age of the donor and time since death and enucleation were recorded. The average time from donor death to enucleation was 5.0 ± 2.3 hours and that from death to the start of experiments was 44.0 ± 12.9 hours. Average donor age at death was 67 ± 14 years and 8 of 26 total donors were females. Whole globes were examined for noticeable trauma to the anterior sclera during the enucleation process. The superior and inferior poles of the globe were determined by identifying the position of extraocular muscle insertions. Using a marking pen, the nasal meridian was marked on the corneal epithelial side just central to the limbus. The globes were dissected at the equator. The uveal tissue was separated at its attachment close to the scleral spur with caution to prevent any trauma to the angle structures. Any remaining tags of uveal tissue were teased off the sclera using nontoothed forceps. Four of 52 eyes were found to be pseudophakic during dissection despite the history indicating otherwise. This was noted on the case report form and the pseudophakic eyes were processed in the same manner as the phakic eyes. The anterior

segment specimen thus obtained was mounted on the perfusion chamber, which was filled with freshly prepared phosphate-buffered solution with 5.5 mM glucose (GPBS). Absence of any air bubbles in the system was confirmed at the time of tissue mounting on the perfusion chamber. The chamber immediately surrounding the anterior segment specimen was filled with GPBS up to the level of the limbus. A moist gauze tissue was placed on the cornea to prevent drying during the experiment. The perfusion chamber was placed in a water bath preheated and maintained at 34°C throughout the experiments.

Perfusion System

The apparatus for outflow facility measurement was composed of two sets of four fluid columns filled with PBS to a level equivalent to 10, 20, 30, and 40 mm Hg. The columns were connected to a three-way stopcock connected to the pressure transducer and the perfusion chamber. The pressure transducer was connected to the signal amplifier to record the digital output in Powerlab software (AD Instruments, Colorado Springs, CO). The pressure decay curve of the perfused anterior segment at each individual pressure was recorded. The apparatus was tested for accuracy and potential leaks at all pressures before the start of each experiment. The anterior chamber was perfused for 10 minutes each at 40, 30, 20, 10, 20, 30, and 40 mm Hg in that order. The constant pressure perfusion technique calculates the rate of flow of fluid from the loss of fluid from the water columns. The fluid lost from the water columns is indirectly calculated as a function of change of recorded IOP from the water column. From the available IOP and rate of flow, the outflow facility (C) was calculated as described previously.²⁰ If the calculated C was higher than an arbitrary cutoff of greater than $1.0 \mu\text{L}/\text{min}/\text{mm Hg}$, either before or after the sham procedure or microstent insertion, this was taken as evidence of a leak. If after remounting the anterior segment the C value remained above the cutoff, the eye was not used in further experiments or analyses (Fig. 4). Based on the Goldmann equation, a change in outflow resistance ($R = 1/C$) is expected to have a linear relationship to IOP change. Thus R, as well as C, was calculated and changes therein evaluated.



FIGURE 2. Cross section of the Hydrus Microstent in Schlemm's canal of a donor eye. The canal is dilated and the trabecular meshwork is stretched but visibly intact.

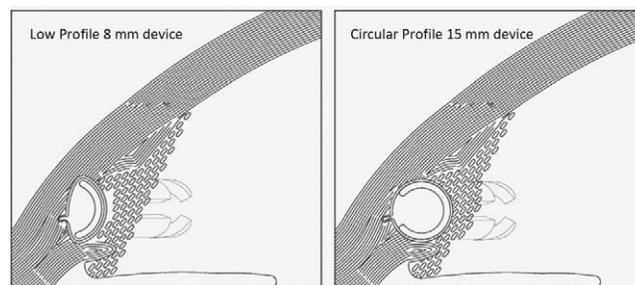


FIGURE 3. Pictorial representation (not to scale) of the cross section of the Hydrus Microstent in Schlemm's canal demonstrates the difference between a crescent-shaped low-profile 8-mm (used in this study) and a nearly circular profile 15-mm microstent evaluated in a previous study.²⁰

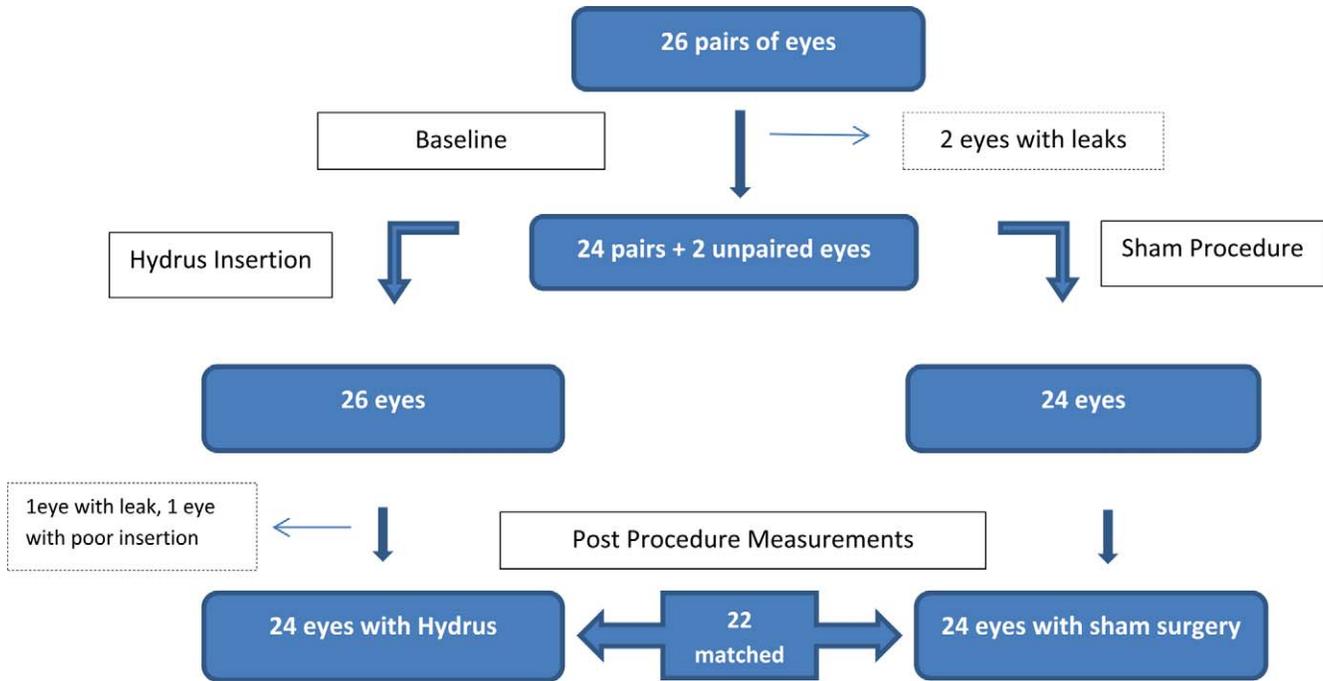


FIGURE 4. Summary of study procedures.

Implant Study Design

Once baseline C and R were determined, the anterior segment specimens were removed from the chamber mount, and placed in a GPBS-moistened petri dish under a dissecting microscope. The Hydrus Microstent (Ivantis, Inc.) was inserted into SC in one eye randomly selected from each pair. Approximately 1 mm of the inlet of the microstent remained in the anterior chamber. All control eyes underwent a sham procedure, in which the trabecular meshwork was punctured and manipulated using the cannula tip and core of the delivery system but without actual placement of a microstent. All microstents were inserted in the nasal quadrant previously marked on the cornea, corresponding to the preferred surgical placement in a patient. The insertion was subjectively graded on a scale of 1 to 3, with 1 being insertion with one to two punctures of TM, 2 being insertion with three to five punctures, and 3 being insertion failure after five punctures of the meshwork or improper placement. At the end of the experiment, the tissues were reexamined to ensure that no microstent had any noticeable shift in position during the experiments.

Sample Size and Statistical Methods

With a baseline outflow facility of 0.2 $\mu\text{L}/\text{min}/\text{mm Hg}$ and an SD of 0.1 $\mu\text{L}/\text{min}/\text{mm Hg}$, a sample size of 22 is required to detect a difference of 0.1 $\mu\text{L}/\text{min}/\text{mm Hg}$ with an alpha of 0.05 and a power of 0.90. Normal distribution of data was tested using Kolmogorov-Smirnov test. Group means were compared using paired and unpaired *t*-tests. Linear correlations were studied by evaluating the scatter plots and calculating the correlation coefficients. The effect of microstent insertion, perfusion pressure, and the interaction between the two parameters with respect to the outflow facility and resistance changes was evaluated using two-way ANOVA with Bonferroni post hoc test.

RESULTS

The experiments were successfully completed and data analyzed from 24 eyes in the control group and 24 eyes in the microstent insertion group (Fig. 4). Twenty-two of these were matched pairs. Twenty-five of 26 eyes with microstent

insertion had an insertion rating of 1. In one pair, an unsuccessful insertion rating of 3 occurred in one eye. This eye was used as a control (sham procedure) eye and the microstent was inserted with a rating of 1 in the contralateral eye. Another pair had unsuccessful insertion ratings of 3 in both eyes from an 89-year-old male. The first eye was excluded while the contralateral eye was used as a control (sham procedure) eye and was included in the analysis. An additional eye with microstent insertion rating of 1 had postinsertion outflow facility greater than 1 $\mu\text{L}/\text{min}/\text{mm Hg}$ at all perfusion pressures. Per protocol, this was taken as presumptive evidence of a leak and the eye was not included in the final analysis. After the experiment, none of the microstents exhibited any noticeable shift of position.

There was no significant difference in the outflow facility at baseline between the two groups ($P = 0.27$, Table 1). The change in C from the sham surgical procedure in control eyes was not statistically significant ($P = 0.82$). The eyes with the microstent showed a statistically significant ($P < 0.001$)

TABLE 1. Outflow Facility and Resistance at Baseline and after the Sham Procedure or Microstent Insertion in 48 Eyes from 26 Subjects

	Intervention		P Value
	Sham, n = 24, Mean \pm SD	Microstent, n = 24, Mean \pm SD	
Outflow facility, $\mu\text{L}/\text{min}/\text{mm Hg}$			
Before	0.39 \pm 0.21	0.33 \pm 0.17	0.27
After	0.38 \pm 0.19	0.52 \pm 0.19	0.014
P value	0.82	<0.001	
Outflow resistance, mm Hg/ $\mu\text{L}/\text{min}$			
Before	4.30 \pm 3.64	4.38 \pm 3.03	0.94
After	3.47 \pm 1.68	2.34 \pm 1.04	0.007
P value	0.31	<0.001	

Experiments were successfully completed in 24 eyes in each group (see Fig. 4 for details). *P* values obtained using *t*-test.

TABLE 2. Outflow Facility and Resistance at Baseline and after Sham Procedure or Microstent Insertion in 22 Matched Pairs of Eyes Where All Experiments Were Successfully Completed

	Intervention		P Value
	Sham, n = 22, Mean ± SD	Microstent, n = 22, Mean ± SD	
Outflow facility, $\mu\text{L}/\text{min}/\text{mm Hg}$			
Before	0.40 ± 0.22	0.33 ± 0.17	0.12
After	0.39 ± 0.19	0.52 ± 0.19	0.023
P value	0.69	<0.001	
Outflow resistance, mm Hg/ $\mu\text{L}/\text{min}$			
Before	4.33 ± 3.75	4.42 ± 3.15	0.85
After	3.49 ± 1.76	2.37 ± 1.06	0.008
P value	0.15	0.003	

P values are obtained using paired t-test.

increase in outflow facility from $0.33 \pm 0.17 \mu\text{L}/\text{min}/\text{mm Hg}$ to $0.52 \pm 0.19 \mu\text{L}/\text{min}/\text{mm Hg}$. When the data were analyzed for changes in outflow resistance, the results were similar, with no significant changes observed in the sham surgery group ($P = 0.31$). The eyes with the microstent showed a significant ($P < 0.001$) decrease in outflow resistance from $4.38 \pm 3.03 \text{ mm Hg}/\mu\text{L}/\text{min}$ to $2.34 \pm 1.04 \text{ mm Hg}/\mu\text{L}/\text{min}$. These results were unchanged (Table 2) when the data were analyzed for the 22 matched pairs of eyes (Fig. 4).

Increase in outflow facility (Fig. 5A) and decrease in resistance (Fig. 5B) were observed at all levels of perfusion pressure from 10 to 40 mm Hg. In a two-way model analyzing the perfusion IOP and microstent implantation as separate variables, the P value for the microstent effect for both the increase in outflow facility and decrease in outflow resistance was less than 0.0001 (two-way ANOVA). The microstent's effects on outflow facility ($P = 0.86$, two-way ANOVA) or resistance ($P = 0.88$, two-way ANOVA) were not affected by the perfusion pressure. The decrease in outflow resistance was linearly correlated with the baseline outflow resistance ($r = 0.94$, $R^2 = 0.89$, $P < 0.0001$, Fig. 6). The higher the outflow resistance at baseline, the greater was the decrease in resistance with the placement of the microstent.

To evaluate whether the changes in outflow facility and resistance were affected by the postmortem time to the start of experiment, the following correlations were evaluated. Pearson's coefficient was used to assess the correlation between postmortem time (to the start of the experiments) and outflow facility at baseline in all eyes (Fig. 7) or change in outflow facility with microstent placement (Fig. 8). The linear correlation of postmortem time and baseline outflow facility was not statistically significant ($r = 0.03$, $R^2 = 0.00$, $P = 0.84$). Similarly, no statistically significant correlation was found between postmortem time and the increase in outflow facility observed with microstent insertion ($r = 0.26$, $R^2 = 0.07$, $P = 0.20$). The results were unchanged with a similar analysis of outflow resistance. The results also were unchanged (data not

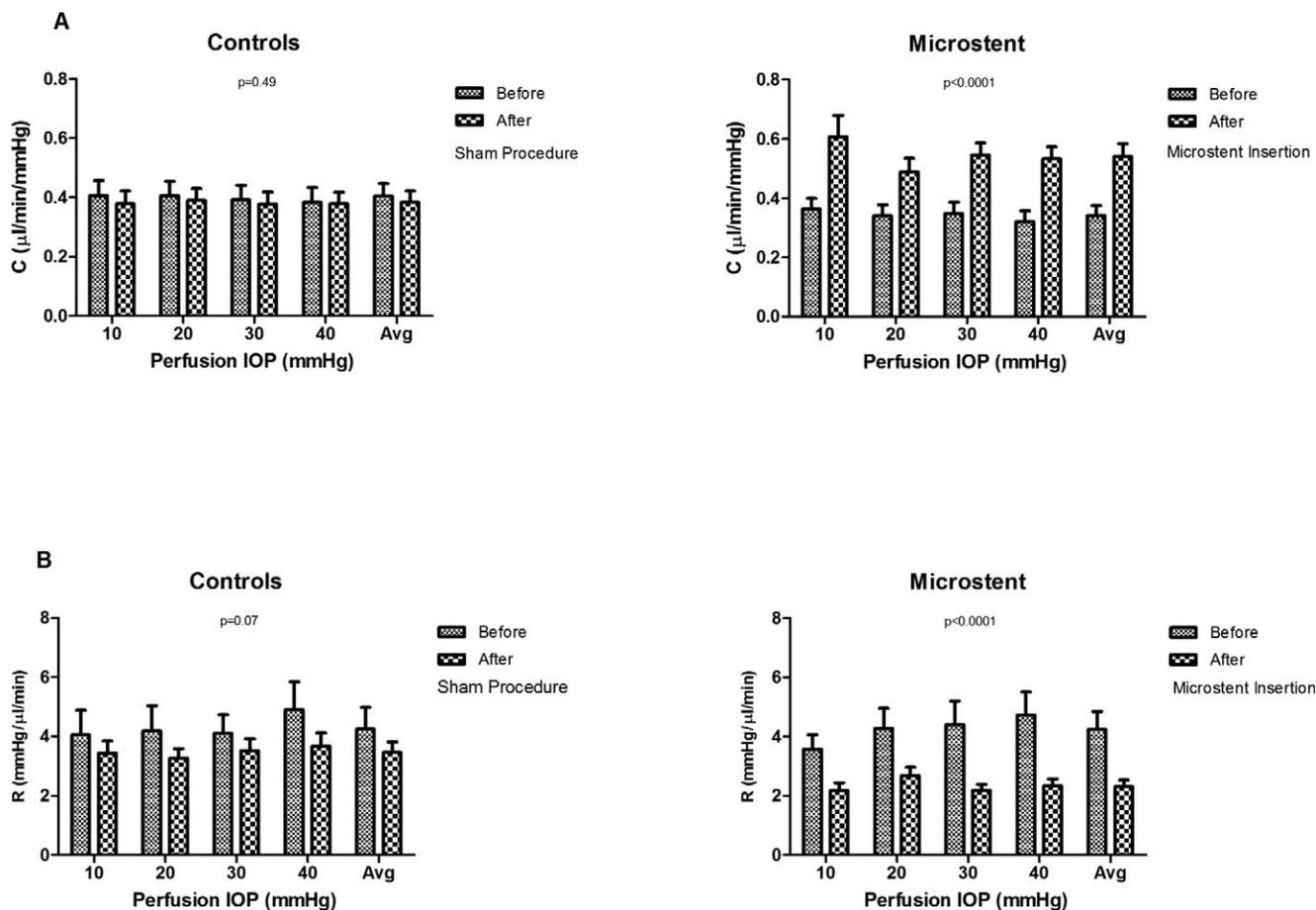


FIGURE 5. (A) Outflow facility and (B) outflow resistance at different levels of perfusion pressure in the microstent and control (sham surgery) eyes. Indicated P values are for the effect of surgical intervention (sham or microstent) using two-way ANOVA. The interaction of perfusion IOP and surgical intervention was not statistically significant ($P > 0.05$) in either group in (A) or (B).

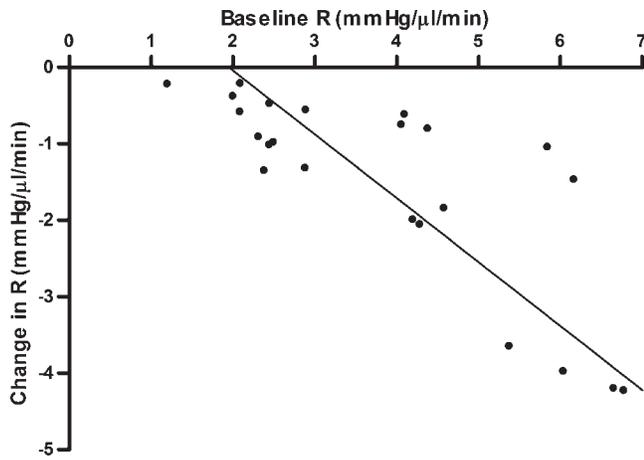


FIGURE 6. Scatter plot between baseline outflow resistance (R) and decrease in outflow resistance after Hydrus implantation. The correlation was statistically significant ($R^2 = 0.89$, $P < 0.0001$). The regression equation is $y = -0.84x + 1.63$. Data point (16.4, -13.2) is outside the range of the axis shown in the figure.

shown) when data analysis similar to that shown in Tables 1 and 2 were performed, including only eyes in which postmortem time to start of experiment was less than 48 hours (20 controls, 19 microstent, 17 matched pairs).

There was no significant correlation between the donor age at death and either the baseline outflow facility ($R^2 = 0.04$, $P = 0.19$) or the change in outflow facility observed in the microstent placement group ($R^2 = 0.05$, $P = 0.30$). The results were similar when outflow resistance was used instead of outflow facility in this analysis.

DISCUSSION

Of the several available microinvasive glaucoma surgeries that claim to improve the flow of aqueous humor through SC or uveoscleral pathways, experimental evidence to support the claim is fairly limited. At the time of this report, laboratory evidence for improvement in outflow resistance has been reported only for intracanalicular procedures.^{17,18} Such evidence is critical in validating the claimed mechanism of action

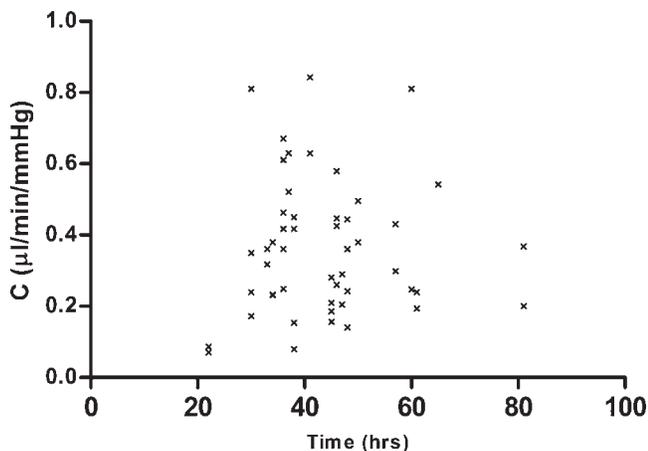


FIGURE 7. Scatter plot of baseline outflow facility in 50 eyes plotted against time elapsed from death of the donor to the start of the experiments. No systematic pattern is notable on the scatter plot. Linear correlation was not statistically significant ($r = 0.03$, $R^2 = 0.00$, $P = 0.84$).

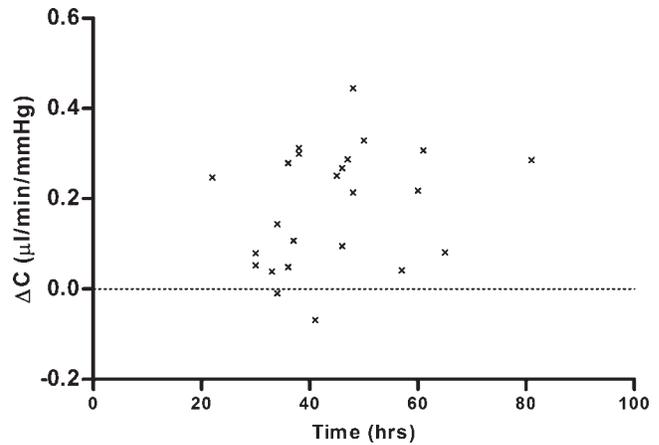


FIGURE 8. Scatter plot of change in outflow facility in 24 eyes plotted against time elapsed from death of the donor to the start of the experiments. No systematic pattern is notable on the scatter plot. Linear correlation was not statistically significant ($r = 0.26$, $R^2 = 0.07$, $P = 0.20$).

for procedures that improve outflow. In a research setting, a single variable (microstent versus sham) can be controlled while eliminating or keeping other variables constant. Thus, changes can be detected in a single parameter (outflow facility) that is claimed to be an intermediary in the IOP-lowering effect. The results of this study provide evidence that the Hydrus Microstent (Ivantis, Inc.), in the ex vivo setting, has the necessary effect on outflow resistance to be a candidate for IOP lowering in the surgical setting. Similar information can be very challenging to obtain in the clinical setting, especially when the microstent is typically combined with cataract surgery, in itself a potential IOP-lowering procedure.²² Future clinical studies will help elucidate how the biological healing response within the eye affects the IOP lowering of the Hydrus Microstent (Ivantis, Inc.) in vivo.

The experimental data from this study can be used to estimate the magnitude of the potential IOP-lowering effect that can be expected by microstent insertion alone, at a given baseline IOP, without accounting for the subsequent healing response or postoperative events. Using Goldmann's equation, we can calculate the potential IOP change obtained by inserting the microstent into an eye with hypothetical values of parameters of aqueous humor dynamics. For example, an eye with an aqueous inflow rate of 2.5 $\mu\text{L}/\text{min}$, uveoscleral outflow of 1.0 $\mu\text{L}/\text{min}$ and episcleral venous pressure of 10 mm Hg, the amount of aqueous humor draining through the pressure-dependent pathways would be 1.5 $\mu\text{L}/\text{min}$. A post-insertion outflow resistance of 2.34 mm Hg/ $\mu\text{L}/\text{min}$ (as seen in this report) will translate into an IOP of approximately 13.5 mm Hg in such an eye. This is a drop of approximately 3 mm Hg from a calculated preinsertion resistance of 4.38 mm Hg/ $\mu\text{L}/\text{min}$ and IOP of 16.5 mm Hg. However, the reduction in outflow resistance was found to be related linearly to the baseline outflow resistance. This implies that eyes with higher outflow resistance can be expected to have greater reduction and thereby greater IOP lowering with the Hydrus Microstent (Ivantis, Inc.). The slope of the trend line was 0.84 (95% confidence interval [CI] 0.70-0.97). This indicates that the microstent implantation has the potential to provide an additional 0.84-mm Hg/ $\mu\text{L}/\text{min}$ decrease in outflow resistance for every 1.0 mm Hg/ $\mu\text{L}/\text{min}$ of baseline outflow resistance. Because changes in outflow resistance are directly proportional to the IOP, this also could be interpreted as an additional 0.84-mm Hg IOP lowering for an additional 1.0-mm Hg higher

baseline IOP. In the same example as above, an eye with an outflow resistance of 10 mm Hg/ μ L/min, and thereby an IOP of 25 mm Hg, can be expected to have a postinsertion IOP of approximately 15 mm Hg, or a 10-mm Hg IOP drop (calculated post microstent insertion resistance of 3.23 mm Hg/ μ L/min, using the regression equation shown in Fig. 6). This pattern is similar to the outcome of other studies of the effects of IOP-lowering interventions, in which greater IOP lowering correlated with higher baseline IOP.²³⁻²⁵

Outflow resistance has been reported to be higher at higher levels of IOP.²⁶⁻²⁸ One possible cause for increased resistance is collapse of the SC at higher pressures.^{27,28} A similar numeric trend of higher resistance at higher perfusion pressures was seen in our study data as well (Fig. 5B); however, the difference between groups did not reach statistical significance. The Hydrus Microstent (Ivantis, Inc.) may at least theoretically keep SC open at higher levels of IOP for a length of 8 mm, thereby maintaining access to collector channels and facilitating an equivalent improvement along all ranges of IOP studied. Whether or not the efficacy of a microstent less than 8 mm is affected by the level of IOP has not been studied. Our study shows that a mere puncture and manipulation of the trabecular meshwork is mechanically inadequate to significantly increase outflow facility. An intracanalicular scaffold was required to keep an open pathway through the trabecular meshwork and within several clock hours of SC to facilitate a lowering of the outflow resistance. Future studies directly comparing a microstent featuring a substantial intracanalicular segment (Hydrus Microstent; Ivantis, Inc.) with those devices without a significant intracanalicular (iStent; Glaukos Corp., Laguna Hills, CA) scaffold should better address this comparison and hypothesis.

It has been suggested that, in whole-globe perfusion experiments, trabecular cells may not be viable 36 hours after death.²⁹ A potential limitation of our study is that the mean postmortem time to the start of experiments was more than 36 hours; however, as the outcomes assessed in our study were purely mechanical and not biological, viability of trabecular meshwork cells is unlikely to affect the results. A sham-treated paired eye from the same subject was used as comparison to account for any systematic effect of time since death. Moreover, the analysis presented in the results section did not show any systematic effect of this factor on either the baseline outflow facility or outflow facility increases observed after the microstent implantation. Use of whole globes rather

than dissected anterior segments is an alternative approach available to study the effects of interventions on outflow pathways.²⁹ However, given the need to implant a microstent in the SC for these experiments, the whole-globe design was not feasible for this study without introducing the confounding effect of an additional incision in the anterior segment. The presence of uveal tissues and uveoscleral pathways in an intact globe during a surgical procedure presents circumstances that are a departure from those studied in these experiments and can potentially temper the applicability of the results to actual surgical implantation of the microstent in live human eyes.

The current 8-mm version of the Hydrus Microstent (Ivantis, Inc.) is relatively shorter in length and lower in profile compared with the previous version, which was 15 mm long and nearly circular in profile (Fig. 3). The earlier design of the microstent has been shown to improve the outflow facility in a similar study design.²⁰ Camras et al.²⁰ reported an increase in outflow facility from 0.19 ± 0.02 to 0.39 ± 0.07 μ L/min/mm Hg (mean \pm SEM, $n = 9$) using the 15-mm version of the microstent. This is compared with an increase in outflow facility from 0.34 ± 0.17 μ L/min/mm Hg to 0.52 ± 0.19 μ L/min/mm Hg (mean \pm SD, $n = 24$) seen in this study. There is an obvious difference in the baselines encountered in the two studies, which significantly limits the direct comparison between the two designs. Standardized mean difference (between pre and post microstent insertion means) can be calculated using Hedge's unbiased g for the two studies. For outflow facility, the treatment effect size was $g = 1.23$ (95% CI 1.16-1.31) with the 15-mm microstent and $g = 0.98$ (95% CI 0.93-1.03) with the 8-mm microstent. For outflow resistance, the 15-mm microstent had an effect size of $g = 1.62$ (95% CI 0.63-2.60) compared with the 8-mm microstent, which had an effect size of $g = 0.89$ (95% CI 0.25-1.53). Even though the "effect size" is higher for outflow facility with the 15-mm microstent, this can be due to lower baseline outflow facility seen in the 15-mm microstent study. A very strong linear correlation seen between the baseline outflow resistance and change in outflow resistance with microstent implantation provides justification for extrapolating the associated trend lines for comparative purposes. A comparison between these trend lines is shown in Figure 9. The trend lines and data distribution show significant overlap without any significant difference in either the slope ($P = 0.43$) or the intercept ($P = 0.20$) of the two trend lines. This analysis, with its limitations, does suggest that there is likely no significant difference in the

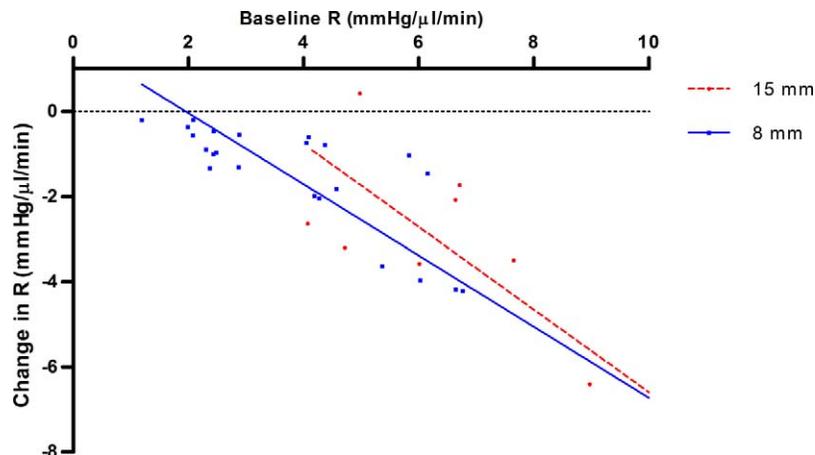


FIGURE 9. Comparison of linear regression of baseline outflow resistance and change in outflow resistance for the 8-mm and 15-mm versions of the Hydrus Microstent. For the 15-mm microstent, $R^2 = 0.75$ ($P = 0.003$) and the regression equation is $y = -0.97x + 3.11$. For the 8-mm microstent, $R^2 = 0.89$ ($P < 0.0001$) and the regression equation is $y = -0.84x + 1.63$. No significant differences were detected in the distribution of data points or the slope ($P = 0.43$) or the intercept ($P = 0.20$) of the two trend lines.

efficacy of the 8-mm microstent as compared with its prior 15-mm version. One possible explanation is that although the 15-mm microstent may in theory reach more collector channels, its more circular profile contacts significantly more of the back wall of SC, thereby potentially obstructing some of the collector channels. A future morphological study is needed to confirm or refute this possibility.

In summary, our study establishes the physiological basis for the use of Hydrus Microstent (Ivantis, Inc.) for lowering of IOP. Future clinical trials will determine whether the reductions in outflow resistance in the laboratory setting translate into sustained IOP lowering in the clinical setting.

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