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Treatment Outcomes Using the PAUL Glaucoma Implant to Control Intraocular Pressure in Eyes with Refractory Glaucoma

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Purpose: To investigate efficacy 1 year after implantation of a novel glaucoma tube shunt, the PAUL Glaucoma Implant (PGI; Advanced Ophthalmic Innovations, Singapore, Republic of Singapore), in the treatment of eyes with refractory glaucoma.

Design: Clinical trial.

Participants: Glaucoma patients who are recalcitrant to maximum tolerated medical therapy and require tube shunt surgery.

Methods: Interventional cohort study involving consecutive PGIs implanted at 6 international centers between December 1, 2017, and December 1, 2018. All the participants were followed up for 1 year after surgery.

Main Outcome Measures: The primary outcome measure was failure, defined prospectively as intraocular pressure (IOP) of more than 21 mmHg or less than 20% reduction from the preoperative baseline on 2 consecutive visits, 3 months or more after surgery; persistent late hypotony, defined as IOP of less than 6 mmHg on 2 consecutive visits after 3 months; additional glaucoma surgery; loss of light perception vision; or removal of the implant for any reason.

Results: Of 82 patients enrolled, 74 (74 eyes) completed 12 months of follow-up. The mean age ± standard deviation at enrollment was 62.3±14.7 years, 73.0% were men, and 36.5% had secondary glaucoma. One year after surgery, 4 patients (5.4%) fulfilled the surgical criteria for failure, 68.9% (51/74 eyes) were deemed complete successes, and 93.2% (69/74 eyes) were considered qualified successes. Compared with the medicated preoperative IOP (23.1±8.2 mmHg), the postoperative IOPs at 6 and 12 months were 13.8±4.0 mmHg and 13.2±3.3 mmHg, respectively ($P < 0.001$). The mean number of IOP-lowering drugs used before surgery and after 12 months of follow-up were 3.3±0.9 and 0.3±0.6, respectively ($P < 0.001$). Significant postoperative complications included self-limiting shallow anterior chamber (n = 11; 14.9%), hypotony requiring intervention (n = 7; 9.5%), tube shunt occlusion (n = 5; 6.8%), tube exposure (n = 3; 4.1%), and endophthalmitis with resultant loss of vision (n = 1; 1.4%).

Conclusions: The PGI demonstrated comparable efficacy with other currently available implants, with almost three quarters of the enrolled patients with refractory glaucoma achieving complete surgical success after 1 year of follow-up. *Ophthalmology Glaucoma 2020;3:350-359 Crown Copyright © 2020 Published by Elsevier Inc. on behalf of the American Academy of Ophthalmology*

Supplemental material available at www.ophthalmologyglaucoma.org.

Intraocular pressure (IOP) reduction is the only proven method of retarding or arresting the progress of glaucoma, the leading cause of irreversible blindness globally. Tube shunt implantation often is the most effective treatment in the control of IOP in those with certain secondary glaucomas and those whose previous filtration surgery has failed.[1–4] A survey of American Glaucoma Society members performed initially in 2008 and subsequently repeated in 2016 demonstrated an increase in the use of tube shunts as the primary incisional procedure for glaucoma. This was also consistent with Medicare fee-for-service paid claims data between 1994 and 2012.[5] This increased usage has been limited by long-term concerns over the unpredictability of early IOP control, chronic corneal endothelial cell damage, and the long-term risk of exposure of the tube portion on the external ocular surface.

The PAUL Glaucoma Implant (PGI; Advanced Ophthalmic Innovations, Singapore, Republic of Singapore) is a novel shunt manufactured from medical-grade silicone that differentiates itself from others currently available in that both the external tube diameter of 467 μm and the internal diameter of 127 μm are smaller, and thereby occupy less space in the anterior chamber angle while also preserving a large surface area end plate for aqueous absorption (342 mm^2). The purpose of this study was to report the safety and efficacy 1 year after surgery in a single-armed

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multicenter interventional study of patients implanted with the PGI.

Methods

This was a noncomparative, single-arm interventional study in which consecutively enrolled patients underwent implantation with a PGI between December 1, 2017, and December 1, 2018, at 6 tertiary ophthalmology centers (see Appendix 1, available at www.ophthalmologyglaucoma.org). All patients were followed up for a minimum of 12 months after surgery. The study was approved by the institutional review boards before initiating recruitment at the following sites: the National University Hospital (Singapore, Republic of Singapore), Chulalongkorn University and Hospital (Bangkok, Thailand), and the Chinese University of Hong Kong (Hong Kong, China). Written informed consent was obtained from all patients except at the National University Hospital, Singapore, where an informed consent waiver was approved. The study was registered as a prospective audit by the audit committees of Moorfields Eye Hospital (London, United Kingdom), St. Thomas' Hospital (London, United Kingdom), and the International Specialist Eye Centre (Kuala Lumpur, Malaysia). All research adhered to the tenets of the Declaration of Helsinki. This study has been registered at ClinicalTrials.gov (identifier, NCT04297930).

Patients between 21 and 80 years of age with glaucoma recalcitrant to maximum tolerated medical therapy were included in this study. As such, primary glaucoma with or without previous failed trabeculectomy, glaucoma tube shunt, or other intraocular surgery were included. In addition, patients with secondary glaucomas that are unlikely to be controlled with trabeculectomy, for example, neovascular, certain uveitics, traumatic, aphakic, or iridocorneal endothelial syndrome-associated glaucoma were eligible. For patients in whom both eyes were eligible, only the first eye to be implanted was enrolled. Patients were excluded if they lacked light perception vision, were unwilling or unable to give informed consent, or were expected to be unavailable for follow-up visits.

Primary Outcomes

The primary outcome measure was failure, defined prospectively as IOP of more than 21 mmHg or less than 20% reduction from the preoperative baseline on 2 consecutive visits, 3 months or more after surgery; persistent late hypotony, defined as IOP less than 6 mmHg on 2 consecutive visits after 3 months; additional glaucoma surgery; loss of light perception vision; or removal of the implant for any reason.[6] Complete success was defined as unmedicated IOP of 21 mmHg or less and more than 5 mmHg and reduced by 20% or more from baseline at the 6- and 12-month visits. Qualified success was defined similarly and included eyes receiving medical treatment to lower the IOP. We also analyzed success based on alternative upper IOP limits of 18 and 15 mmHg. Office procedures based at the slit lamp, such as needling, removal of intraluminal stents, laser suture lysis, laser iridoplasty, and injection of viscoelastic gel into the anterior chamber were not considered glaucoma reoperations but were documented as postoperative interventions.

Secondary Outcomes

Secondary outcomes included the number of ocular hypotensive drugs and the number of surgical complications. A serious complication was defined as any that resulted in a 2-line reduction in Snellen acuity, a return to the operating room to manage, or both.[6] The Snellen visual acuity reduction was assessed at the 1-year visit, or if that visit was missed, at the 6-month visit.

Postoperative Examination

The schedule of examinations and visits is detailed in Table 1. Before surgery, baseline measurements were obtained, and planned postoperative follow-up appointments were scheduled for 1 day, 1 week, 1 month, 3 months, 6 months, and 12 months after surgery. All data were captured in a standardized data collection form.

Snellen Visual Acuity. Snellen visual acuity was measured before pupil dilation, tonometry, and gonioscopy. After proper instruction, the left eye was occluded and testing commenced with the right eye. Progressively smaller lines were presented to the patient until he or she made 2 or more errors in a line. The patient was encouraged to fix eccentrically if this improved the visual acuity, but care was taken to ensure that the fellow eye remained covered. The Snellen acuity was recorded as the smallest line in which the patient missed 1 or fewer optotypes. If the patient's visual acuity was so poor that he or she could not read the 20/400 line, the ability to count fingers was assessed. After testing of the right eye, the procedure was repeated for the left eye.

Refraction. Subjective refraction was performed by a trained optometrist before formal measurement of Snellen visual acuity testing at the baseline, 6-month, and 12-month visits.

Slit-Lamp Biomicroscopy. Anterior segment examination was performed using slit-lamp biomicroscopy to document preoperative features of relevance and at all scheduled visits to evaluate findings during the study that may be attributable to the disease or surgery. Slit-lamp biomicroscopy was performed in a standard fashion starting with the anterior and followed by the posterior segment.

Tonometry. Intraocular pressure was measured using Goldmann applanation tonometry, except when prevented by corneal pathologic features such as irregular astigmatism, scarring, or edema. In these cases, the Tono-Pen (XL Mentor, Reichert Ophthalmic Instruments, Buffalo, NY) was used. The IOP was measured before pupillary dilation. Intraocular pressure measurements were obtained until 2 successive readings differed by less than 1 mmHg. The last 2 successive measurements were taken as the final IOP.

Gonioscopy. Gonioscopy was performed with the patient sitting at the slit-lamp in a dim room using either a 4-mirror gonioprism or Goldmann-type gonioprism. A preoperative examination of the anterior chamber angle was performed to identify neovascularization, peripheral anterior synechiae, and the presence of silicone oil in the angle and to identify an appropriate implantation site for the tube.

Dilated Fundus Examination. After pupil dilation, the optic nerve, posterior pole, and retinal periphery were examined using slit-lamp biomicroscopy with an appropriate condensing lens with or without indirect ophthalmoscopy to evaluate the peripheral retina. At all postoperative scheduled visits, the posterior segment was examined to detect choroidal effusions, hemorrhage, or hypotony maculopathy.

Study Device

The PGI, a non-valved aqueous shunt constructed from medical implantable-grade silicone, is the tube shunt that was investigated in this study (Fig 1). Table 2 illustrates the PGI's dimensions in comparison with other comparable commonly implanted shunts, the Baerveldt Glaucoma Implant (BGI; Johnson & Johnson Vision, Santa Ana, CA) and the Ahmed Glaucoma Valve (AGV; New World Medical, Rancho Cucamonga, CA). The PGI end plate has a breadth (wingspan) of 21.9 mm and width (from front to back edge) of 16.1 mm with an end plate surface area of 342.1 mm^2 (Fig 1). The end plate surface area is considerably

Table 1. Schedule of Study Visits

	Baseline	1 Day	1 Week	1 Month	3 Months	6 Months	12 Months
Snellen visual acuity	X	X	X	X	X	X	X
Refraction	X					X	X
Slit-lamp examination	X	X	X	X	X	X	X
Goldman applanation tonometry	X	X	X	X	X	X	X
Indentation gonioscopy	X						X
Dilated fundus examination	X			X	X	X	X
Informed consent	X						

larger than that of the AGV, but slightly smaller than that of the BGI. However, compared with the BGI, the PGI has a shorter wingspan, so less of the plate is tucked under the recti, but with a larger anteroposterior depth, so that the plate extends further back. The internal diameter of the PGI tube is 0.127 mm, that is, less than half of the internal diameter of the AGV and BGI with an external diameter of 0.467 mm, again significantly smaller than that of the AGV or BGI. The smaller tube caliber offers the following theoretical advantages: less corneal endothelial damage, because the smaller tube will be in contact with a lower area of endothelium at the entry site, and potentially a lower erosion rate because the extraocular portion traversing the sclera under conjunctiva will be smaller than other shunts. The lower caliber still offers no significant flow resistance, but is easier to occlude surgically using a 6-0 or 7-0 polypropylene intraluminal stent than the 3-0 required to occlude a BGI (Fig 1).

Surgical Procedure

The study protocol specified that: (1) shunts should be implanted in the quadrant that is deemed most suitable by the surgeon; (2) the conjunctiva and Tenon's capsule should be dissected adequately for insertion of the implant; (3) the PGI end plate should be positioned under the respective recti muscles depending on the quadrant of placement; (4) the end plate should be sutured to sclera at a measured distance 9 to 10 mm posterior to the limbus; (5) the

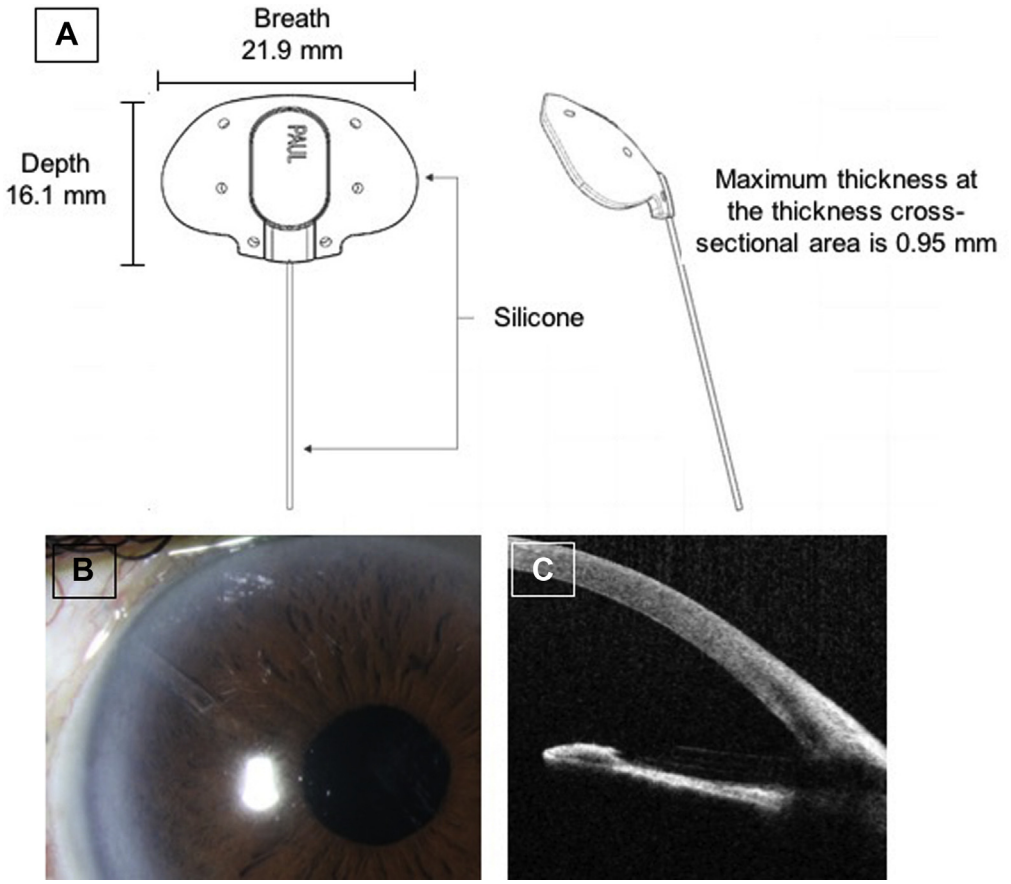

Figure 1. **A**, Diagram showing the novel PAUL Glaucoma Implant (Advanced Ophthalmic Innovations, Singapore, Republic of Singapore). **B**, Clinical photograph showing the implant inside the anterior chamber. **C**, Anterior segment OCT image showing the implant resting just above the iris plane.

Table 2. Comparison of the Physical Characteristics of the PAUL Glaucoma Implant with the Ahmed Glaucoma Valve (Model FP7) and Baerveldt Glaucoma Implant (Model 101-350)

Characteristic	Ahmed Glaucoma Valve	Baerveldt Glaucoma Implant	PAUL Glaucoma Implant
Plate surface area (mm^2)	184	350	342
Plate thickness (mm)	1.0	0.9	0.95
Plate breadth (mm)	13	32	21.9
Plate width (mm)	16	15	16.1
Fenestration holes, no.	3	4	6
Reservoir depth (mm)	0.5	Nil	0.4
Tube size (mm)			
Outer diameter	0.64	0.64	0.467
Internal diameter	0.3	0.3	0.127

anterior chamber entry should be made with either a 25- or 27-gauge needle at the limbus parallel to the iris plane; (6) the tube should be trimmed, bevel up, to extend several millimeters into the anterior chamber; (7) the tube should be inserted through the needle track and positioned in the anterior chamber away from the corneal endothelium and just above the iris; (8) the limbal portion of the tube should be covered with a donor patch of sclera, cornea, pericardium, or fascia lata, based on tissue availability and surgeon preference; and (9) the conjunctiva should be sutured closed.

Other parts of the procedure were left to the surgeon's discretion, including the use of viscoelastic at the conclusion of the surgery, the use of ligation sutures, a so-called ripcord technique for tube occlusion, and the use of mitomycin C (MMC) for wound modulation. After surgery, all eyes required the use of antibiotics eye drops for a short period and steroid eye drops tapering over 3 months after surgery. Participating surgeons were permitted to change or extend the postoperative eye drop regimen based on clinical findings and recovery.

Table 3. Baseline Demographic and Ocular Characteristics of Enrolled Participants (n = 74)*

Demographic and Ocular Characteristics	Data
Age (yrs), mean ± SD	62.3±14.7
Gender, no. (%)	
Male	54 (73.0)
Female	20 (27.0)
Ethnicity, no. (%)	
Asian	48 (64.9)
White	14 (18.9)
Afro-Caribbean	12 (16.2)
Mean visual acuity (logMAR), mean ± SD	0.61±0.53
Mean intraocular pressure (mmHg), mean ± SD	23.15±8.17
Mean vertical cup-to-disc ratio, mean ± SD	0.79±0.14
Lens status, no. (%)	
Phakic	36 (48.6)
Pseudophakic	37 (50.0)
Aphakic	1 (1.4)
No. of classes of intraocular pressure-lowering medications, no. (%)	
1	3 (4.1)
2	10 (13.5)
3	22 (29.7)
4	36 (48.6)
>4	3 (4.1)
Mean ± SD	3.3±0.9
Diagnosis, no. (%)	
Primary open-angle glaucoma	35 (47.3)
Primary angle-closure glaucoma	12 (16.2)
Neovascular glaucoma	6 (8.1)
Uveitic glaucoma	6 (8.1)
Traumatic glaucoma	4 (5.4)
Others	11 (14.9)
Previous glaucoma procedures, no. (%)	24 (32.4)
Trabeculectomy	20 (27.0)
Glaucoma tube shunt	6 (8.1)
Minimally invasive glaucoma procedures*	2 (2.7)

logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.
*Both had a Cypass Micro-stent (Alcon Surgical, Fort Worth, TX [withdrawn from market]).

Statistical Analysis

All statistical analysis was performed using SPSS software version 25.0 (IBM Analytics, Chicago, IL). Continuous variables are reported as mean ± standard deviation and were compared using the paired *t* test. Categorical data were compared using the chi-square test. Snellen visual acuity measurements were converted to the logarithm of the minimum angle of resolution equivalents for analysis. For Kaplan-Meier survival analysis, the time to failure was defined as the time from implantation to reoperation for glaucoma, loss of light perception vision, or the first of 2 consecutive study visits after 3 months in which the patient showed persistent hypotony (i.e., IOP ≤6 mmHg) or inadequately reduced IOP (i.e., IOP >21 mmHg or reduced <20% from baseline). A *P* value of 0.05 or less was considered statistically significant.

Results

Of 82 patients enrolled, 6 did not complete 1 year of follow-up, 2 died in the first year, and 74 eyes of 74 patients completed the study and were analyzed. Table 3 details the demographics and ocular characteristics of the study participants. In our study, 47 participants (63.5%) had primary glaucomas and 27 participants (36.5%) had secondary glaucomas. Twenty-four eyes (32.4%) had undergone previous glaucoma surgeries in our study.

Intraoperative Procedures

Of the 74 eyes, 26 eyes (35.1%) underwent combined cataract and PGI surgery and 2 eyes (2.7%) underwent a different procedure at the same sitting (1 vitrectomy for vitreous in the anterior chamber and 1 removal of a BGI in a patient with a truncated tube that was no longer in the anterior chamber). Intraoperative MMC was applied to the equatorial subconjunctival space in the region of the

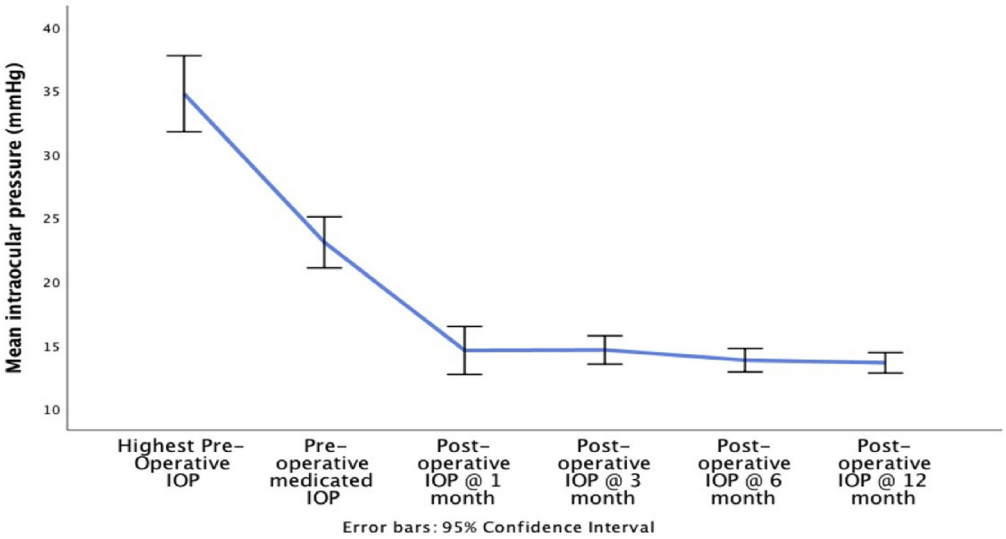

Figure 2. Line graph showing the intraocular pressure (IOP) trend before and after surgery up to 1 year, with both highest recorded preoperative and preoperative medicated IOPs. The error bars indicate 95% confidence limits.

plate in 11 eyes (14.9%), but no postoperative use of MMC occurred. In 7 eyes (9.5%), a ligating suture only was used to prevent hypotony; in 2 eyes (2.7%), both a ligating suture and an intraluminal stent were used; and in 11 eyes (14.9%), only an intraluminal stent was used.

Intraocular Pressure Reduction

The baseline and follow-up IOPs are shown in Figure 2. Patients who underwent additional glaucoma surgery or had the implant removed during follow-up were censored from analysis after the time of reoperation. The mean highest preoperative IOP was 34.3±11.8 mmHg, and the mean medicated preoperative IOP was 23.1±8.2 mmHg (mean number of classes of medication, 3.3±0.9, with 23.0% requiring oral acetazolamide). Compared with either mean preoperative highest IOP or mean medicated preoperative IOP, the postoperative IOP at 1, 3, 6, and 12 months were significantly lower at 14.9±7.3 mmHg, 14.5±4.6 mmHg, 13.8±4.0 mmHg, and 13.2±3.3 mmHg, respectively ($P < 0.001$, paired t test). Compared with mean medicated preoperative IOP, a 42.9% reduction in IOP was observed at 1 year after surgery. Figure 3 shows the number of glaucoma medications in both groups at baseline and follow-up. In comparison with the preoperative level (3.3±0.9 medications), the number of medications was reduced to 0.4±0.7, 0.5±0.7, 0.4±0.6, and 0.3±0.6, respectively, at 1, 3, 6, and 12 months after surgery ($P < 0.001$, paired t test). Table 4 summarizes the postoperative outcomes of all the participants in our study.

Primary Treatment Outcomes

At 1 year, 4 patients (5.4%) fulfilled the surgical failure criteria. The reasons for failure were 1 patient (1.4%) whose IOP was less than 6 mmHg and required reoperation, 1 patient (1.4%) whose IOP was more than 21 mmHg and required reoperation, and 2 patients (2.8%) who required removal of the implant, 1 because of presumed exogenous endophthalmitis and the other because of recurrent conjunctival erosions over the plate. Figure 4 shows the Kaplan-Meier survival analysis over 1 year. Fifty-one eyes (68.9%), 45 eyes (60.8%), and 40 eyes (54.1%) were classified as complete successes at IOP cutoffs of 21 mmHg, 18 mmHg, and 15 mmHg, respectively. Sixty-nine eyes (93.2%), 63 eyes (85.1%), and 54 eyes (73.0%) were classified as qualified successes at IOP cutoffs of 21 mmHg, 18 mmHg, and 15 mmHg, respectively.

We performed additional analyses according to the history of previous glaucoma surgery. The rates of complete success for eyes with and without prior glaucoma surgery were 54.2% and 76.0%, respectively ($P = 0.028$). The rates of qualified success for eyes were 91.7% and 94%, respectively ($P = 0.21$). The failure rates therefore were 8.3% and 6%, respectively ($P = 0.47$).

Complications

Significant postoperative complications included self-limiting shallow anterior chamber (n = 11 [14.9%]), hypotony requiring intervention, largely slit-lamp viscoelastic injections (n = 7 [9.5%]), tube shunt occlusion (n = 5 [6.8%]), tube exposure (n = 3 [4.1%]), and endophthalmitis with resultant loss of vision (n = 1 [1.4%]). Of the 5 eyes with tube occlusion, 3 were the result of the iris occluding the tip of the tube inside the anterior chamber, and in all cases, argon laser iridoplasty successfully unblocked the tube. In 1 case, the tube was blocked by vitreous in an eye with aphakic glaucoma, which required anterior vitrectomy. In the last case of tube occlusion, the IOP was elevated for 10 days after the initial implantation procedure in an eye with uveitic glaucoma. Clinically, no vitreous or blood blocked the tube. The eye underwent anterior chamber washout and tube flushing with subsequent resolution of the pressure problem. Of the 11 eyes with self-limiting anterior chamber shallowing, 8 resolved within 2 weeks of surgery and 3 resolved within 4 weeks of surgery. Of the 7 eyes with hypotony requiring intervention, 6 required an intracameral injection of viscoelastic and 1 required reinsertion of the intraluminal stent suture. In addition, in 4 eyes, the conjunctiva eroded over the implant. Three tube exposures required repair, but 1 of these patients experienced a plate exposure that required implant removal.

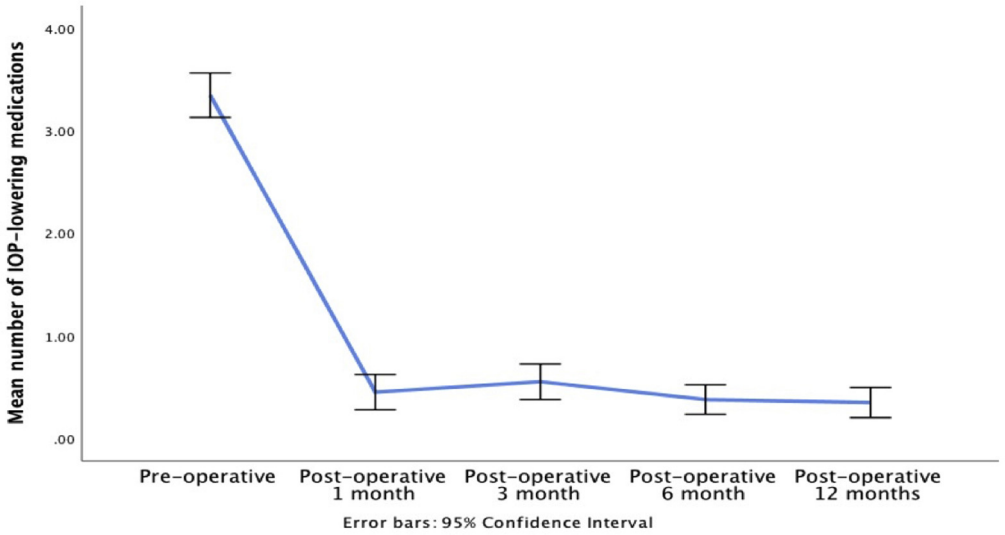

Figure 3. Line graph showing the number of intraocular pressure (IOP)-lowering medications used before and after surgery. The error bars indicate 95% confidence limits.

A case of exogenous endophthalmitis occurred 3 months after implantation in an eye with primary open-angle glaucoma in which prior glaucoma filtering surgery had failed. A vitreous tap isolated pan-sensitive *Streptococcus mitis*. The PGI was removed, but vision eventually was reduced to no light perception. Two other eyes fulfilled the criteria of demonstrating serious complications. The first showed persistent hypotony and subsequent plate exposure requiring removal of the implant. The patient's preoperative vision was 6/12, dropping to counting fingers at 6 months and 12 months after initial surgery. The second such patient was the case of endophthalmitis mentioned above, in whom the preoperative vision was 6/24. Compared with the mean preoperative visual acuity (0.613±0.529), no statistically significant difference was found in postoperative visual acuity at 6 months (0.609±0.534; $P = 0.58$) and 12 months (0.608±0.535; $P = 0.74$).

Discussion

In this multicenter study involving 74 eyes implanted with the PGI, 4 eyes (5.4%), 51 eyes (68.9%), and 69 eyes (93.2%) fulfilled the criteria for failure, complete success, and qualified success, respectively. Compared with the mean medicated preoperative IOP (23.1±8.2 mmHg), a significant reduction in IOP was found at 12 months (13.2±3.3 mmHg). Similarly, a significant reduction was found in the number of glaucoma medications from before surgery (3.3±0.9) to 12 months after surgery (0.3±0.6). The complications that occurred were known to glaucoma tube shunt surgeries, including shallow anterior chamber, hypotony, tube shunt occlusion, tube exposure, and endophthalmitis.

The mainstay of treatment for most patients with glaucoma is still IOP-lowering medication and laser trabeculoplasty. Although the use of minimally invasive glaucoma surgery has become popular, many patients have advanced glaucoma or complex secondary glaucomas for which the above procedures are inappropriate. In these circumstances, trabeculectomy often is the procedure of choice. However, trabeculectomy is effective largely in carefully selected patients without significant failure risk factors. Tube shunts, however, have a much broader range of efficacy, working to some degree even in patients with the highest risk of failure. The Tube versus Trabeculectomy Study compared trabeculectomy with MMC with BGI implantation in eyes with a medium risk of failure with eyes with relatively advanced glaucoma and showed similar efficacy, prompting an increase in the popularity of tube shunt implantation.

Although both the Ahmed Baerveldt Comparison (ABC) and Ahmed versus Baerveldt (AVB) studies show superior efficacy of the BGI over the AGV at 5 years, the superior

Table 4. Postoperative Outcomes of Enrolled Participants (n = 74)

Outcome	Data (Mean ± Standard Deviation)
Mean visual acuity (logMAR)	
6 mos	0.609±0.534
12 mos	0.608±0.535
Mean intraocular pressure (mmHg)	
1 mo	14.9±7.3
3 mos	14.5±4.6
6 mos	13.8±4.0
12 mos	13.2±3.3
Mean no. of classes of intraocular pressure-lowering medications	
1 mo	0.4±0.7
3 mos	0.5±0.7
6 mos	0.4±0.6
12 mos	0.3±0.6

logMAR = logarithm of the minimum angle of resolution.

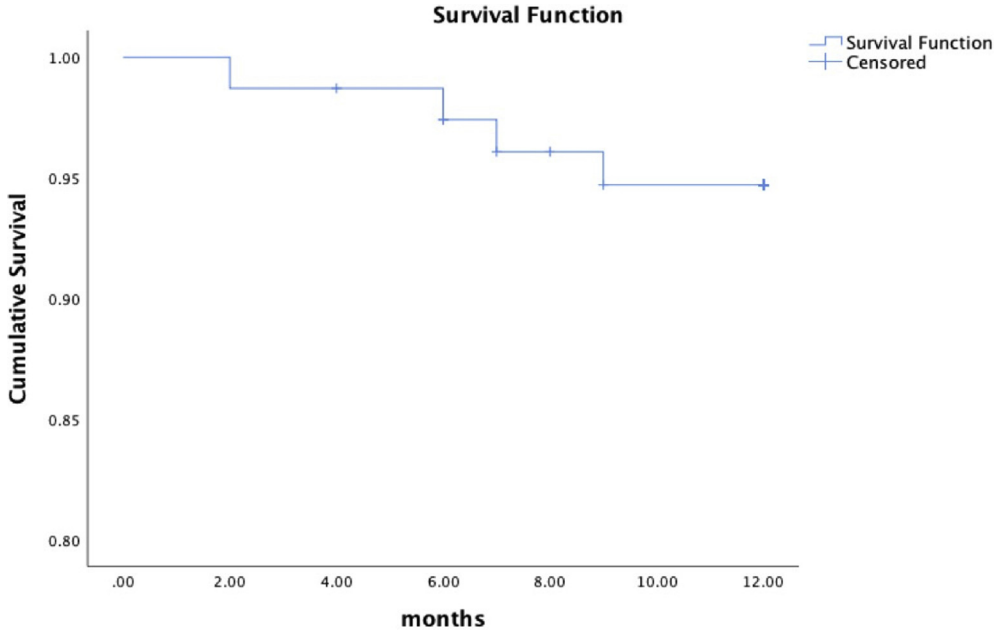

Figure 4. Kaplan-Meier survival curve for eyes implanted with the PAUL Glaucoma Implant (Advanced Ophthalmic Innovations, Singapore, Republic of Singapore) over 1 year of follow-up. The time to failure was defined as the time from implantation to reoperation for glaucoma, loss of light perception, or the first of 2 consecutive study visits after 3 months in which the patient showed persistent hypotony (i.e., IOP <5 mmHg) or inadequate IOP reduction (IOP >21 mmHg or reduced <20% from baseline).

success of the BGI comes at the expense of greater risk. It is likely that a simple improvement in design that could mitigate some of this risk, potentially without loss of efficacy, would be a smaller tube, as in the PGI. When currently available tubes were designed more than 20 years ago, the 0.3-mm internal caliber likely was the minimum that could be achieved without a significant increase in manufacturing costs.[7] This is no longer the case. Although the PGI has a smaller tube with less redundant flow capacity than the BGI, it is still large enough to provide only minimal resistance to aqueous outflow. This is advantageous for 2 reasons. First, a tube that is too small may occlude even more easily than the 5 tube occlusions that were documented in this study. Second, a tube with a small enough caliber to provide resistance would require a fixed length, thereby reducing considerably the surgical flexibility during implantation.

In contrast, a tube smaller than the 0.64-mm external diameter of both the BGI and AGV offers the theoretical advantages of a lower cross-sectional profile on the outside of the sclera, resulting potentially in a lower risk of conjunctival erosion.[8,9] Second, the AGV and BGI tubes in the anterior chamber occupy almost the entirety of the 0.75-mm drainage angle. A smaller tube theoretically should reduce the risk of corneal endothelial contact and damage at the entry site, especially in eyes with smaller anterior segments or shallower anterior chambers.[10,11] Third, in eyes with lower scleral rigidity such as high myopia, congenital glaucoma, and collagen disorders, a larger tube diameter increases the risk of peritubular leakage and subsequent hypotony in the hands of those more surgically inexperienced, for example, trainees.[12] In contrast, the external caliber of the PGI is more than 30% smaller and the internal caliber is more than 50% smaller than either the BGI or AGV. An advantage of the smaller internal caliber also is that early postoperative hypotony can be prevented using a much smaller ripcord than the BGI (6-0 vs. 3-0), potentially resulting in less variability,

An additional feature, a well at the back of the PGI end plate (Fig 5), offers a potential enhancement to the conventional ripcord technique in which the surgeon occludes the tube with a stent suture to limit aqueous drainage. The posterior end of the PGI tube widens into a small well at its junction with the plate. When the tube is stented with a ripcord, the surgeon can visualize this well slowly filling with aqueous directly. The rate of aqueous drainage can be observed directly, and the length of the ripcord can be adjusted within the tube to vary the flow rate, potentially mitigating some of the early postoperative pressure variability. Intraocular pressure spikes can occur because of total occlusion of the tube, and late persistent postoperative hypotony may manifest after the intraluminal stent is removed.[2,13–15]

Compared with the AGV, several explanations may account for the higher published success rate of the BGI, including a bigger plate surface area, lower plate profile, smoother surface, and tapered curved edges.[16] In contrast, the AGV has a plate surface area that is roughly half that of the BGI, and this has been speculated to contribute to a higher risk of bleb encapsulation. In addition, the thick cross-sectional profile and rough surface of the AGV

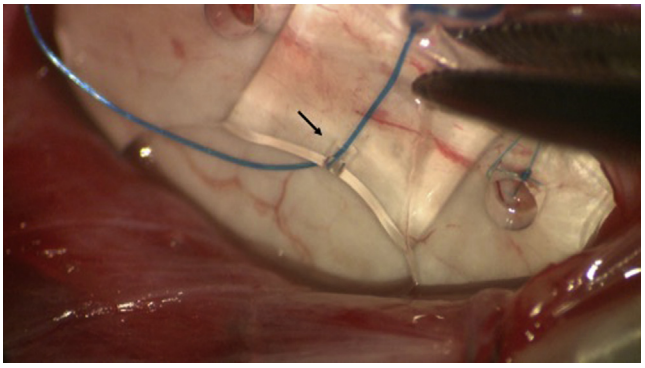

Figure 5. Intraoperative photograph showing the fluid well at the posterior aperture of the PAUL Glaucoma Implant (Advanced Ophthalmic Innovations, Singapore, Republic of Singapore) tube, half-filled with draining aqueous (black arrow). The speed at which this well fills when the tube is in the anterior chamber gives an estimate of the aqueous flow and informs the adjustment of any stenting ripcord suture used.

result in excessive and unnecessary stretching that stimulates fibroblastic activity responsible for the so-called hypertensive phase shortly after surgery.[17] However, the effective plate surface area of the BGI likely is limited to the parts not covered by the recti. In contrast, the PGI has a shorter wingspan, but a longer extension posteriorly, which theoretically increases the effective surface area with no obvious downside.

Although we have listed several theoretical benefits in the design of the PGI, this study was not designed or powered to test these individually, but rather, to report the overall safety and efficacy of this implant 1 year after surgery in a diverse group of patients with recalcitrant glaucoma, much as the Ahmed Baerveldt Comparison and Ahmed versus Baerveldt Studies reported. Hence, endothelial cell counts, the measurement of which was not easily available in all of the glaucoma clinics of the participating centers, were not acquired.

We did observe a significant IOP reduction 1 year after PGI implantation with a corresponding reduction in IOP-lowering medication. Although the conclusions we can draw in a single-arm noncomparative study are limited, it is interesting that the mean IOP 1 year after PGI surgery, at 13.2±3.3 mmHg, was comparable with that in the BGI group (13.2±6.8 mmHg) and lower than that in the AGV group (15.4±5.5 mmHg) at the same point in the Ahmed Baerveldt Comparison Study,[6] a finding that is perhaps not surprising because the PGI plate shares more characteristics in common with the BGI than the AGV. The final steady-state IOP of nonvalved implants is dependent almost exclusively on the extent of encapsulation around the plate,[18,19] which is influenced by plate size and height,[20] use of antimetabolites,[21,22] and underlying glaucoma diagnosis. In the case of a valved implant or a nonvalved implant in which the ripcord has not been removed, the final steady state will depend also on the additional serial resistance provided by the flow resistor. Considering that most eyes included in both the current study and the Ahmed Baerveldt Comparison Study had advanced refractory glaucoma, a low target IOP would be ideal for long-term visual preservation.[23] Interestingly, compared with both the BGI (1.5±1.4 medications) and the AGV (1.8±1.3 medications), the number of IOP-lowering medications in the eyes with a PGI was lower in this study at 0.3±0.6 medications after 1 year. The level of medication prescribed was influenced heavily by the behavior of individual participating surgeons, but the low medication level in combination with an IOP level comparable with that of the BGI group after 1 year in the ABC study is encouraging. Several potential reasons for this exist, not least of which may be a different profile of glaucoma diagnoses and severity compared with other studies.

However, the PGI has its own issues with its postoperative safety profile, the most commonly observed one being self-limiting anterior chamber shallowing, most of which resolved within the first 2 weeks. The incidence of early postoperative shallow anterior chamber is attributed to the valveless PGI and surgical techniques used to prevent hypotony. In procedures in which a tube occlusion technique was not used, a combination of viscoelastic in the anterior chamber and viscoelastic patch graft over the posterior tube aperture at the end plate were used with the PGI to reduce the risk of early postoperative hypotony. Despite this, a considerable proportion of eyes still showed an early postoperative shallow anterior chamber. This could be attributed to factors that include manufacturing variability in the internal caliber of the tube and patient factors such as aqueous viscosity, lens status, ocular biomechanics, type of glaucoma, and patient behavior. Interestingly, for eyes with hypotony that require intervention, all except 1 required only intracameral viscoelastic injection for the hypotony to resolve. Only 1 eye with persistent chronic hypotony required a return to the operating room for reinsertion of an intraluminal stent suture (ripcord). In all of the above, no significant loss of vision was observed that would fulfill the criterion of a severe complication.[14] The successful reversal of hypotony by just 1 viscoelastic injection suggests that the small amount of resistance provided by the smaller PGI tube caliber may assist in preventing hypotony in comparison with larger tube diameters. In contrast, the smaller lumen of the PGI also may increase the risk of tube occlusion by iris, fibrin, blood, and viscoelastic. In our study, the most common cause of tube occlusion was iris, and this might be avoided by implanting the tube slightly further away from the iris plane. The smaller caliber of the PGI also facilitates implantation in the mid-anterior chamber angle, avoiding both the iris and corneal endothelium, which is much more difficult with a conventional 640-μm tube that occupies almost all of the 750-μm anterior chamber angle.

We acknowledge the limitations of the current study, which include its noncomparative nature. Although this was a treatment-to-target study, including visual field data would provide a much better indication of the efficacy of the PGI in treating different stages of glaucoma. The primary purpose, given limited resources, was to report outcomes and complications in a manner reported previously by large tube studies such as the Tube versus Trabeculectomy Study and the Ahmed Baerveldt Comparison Study.[24,25] Hence, we used the same primary and secondary outcome measures,

permitting some limited comparison with those studies. Other factors that limit generalizability include the predominance of Asian and male participants and the degree of license given to individual surgeons in the surgical technique, especially the tube occlusion technique; the variable use of MMC; and a relatively short follow-up period of 12 months.

In conclusion, the PGI is a novel tube shunt offering some potentially significant design advantages over others currently available. This study found comparable prospective safety and efficacy, in a relatively large sample size, as previously published studies of currently available implants 1 year after surgery in eyes with refractory glaucoma.

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Author Contributions:

Conception and design: Koh, Chew, Barton

Analysis and interpretation: Koh, Barton

Data collection: Koh, Triolo, Lim, Barton

Obtained funding: Barton, Chew

Overall responsibility: Koh, Chew, Triolo, Lim, Barton

Abbreviations and Acronyms:

AGV = Ahmed Glaucoma Valve; **BGI** = Baerveldt Glaucoma Implant; **IOP** = intraocular pressure; **MMC** = mitomycin C; **PGI** = PAUL Glaucoma Implant.

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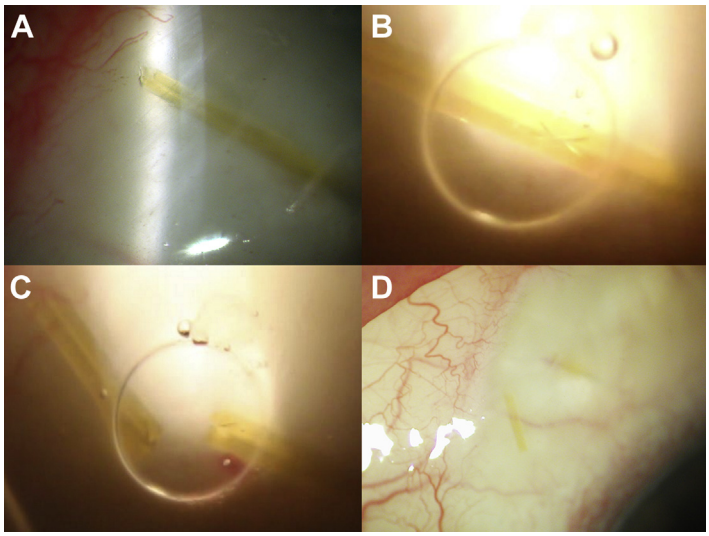
Pictures & Perspectives



YAG Laser Xen Stent Truncation

An 82-year-old anti-coagulated woman with an only-seeing eye had a Xen implantation with mitomycin-C (0.02%) 15-months previously, presented with threatened conjunctival extrusion (Fig **A**). Her intraocular pressure (IOP) was 9 mmHg. Due to avascularity of the overlying conjunctiva and risks of surgical intervention, a YAG laser was performed with a Blumenthal suture-lysis lens to truncate the stent. The first shot (1.6 mJ) fractured the material (Fig **B**). The second shot (1.8 mJ) truncated the implant at 1.7 mm from the scleral exit (Fig **C**). At 1 week, the IOP was 6 mmHg with the truncated stent lying freely and the end flush on the sclera (Fig **D**). (Magnified version of Fig **A**-**D** is available online at www.ophthalmologyglaucoma.org/).

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