

# Three-year canaloplasty outcomes for the treatment of open-angle glaucoma: European study results

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## Abstract

**Background** To report 3-year results investigating the safety and efficacy of canaloplasty, a procedure involving circumferential viscodilation of Schlemm's canal and tensioning of the inner canal wall to treat open-angle glaucoma.

**Methods** This was a prospective, multi-center, interventional study of 109 eyes of 109 adult, open-angle glaucoma patients undergoing canaloplasty or combined cataract-canaloplasty surgery. Qualifying preoperative intraocular pressures (IOP) were at least 16 mmHg with historical IOPs of at least 21 mmHg with or without medical therapy. A flexible microcatheter was used to viscodilate the full circumference of the canal and to place a trabecular tensioning suture. Primary outcome measures included IOP, glaucoma medication usage, and adverse events.

**Results** Eyes with canaloplasty showed a mean baseline IOP of  $23.0 \pm 4.3$  mmHg and mean glaucoma medication usage of  $1.9 \pm 0.7$  medications, which decreased to a mean IOP of  $15.1 \pm 3.1$  mmHg on  $0.9 \pm 0.9$  medications at 3 years postoperatively. Eyes with combined cataract-canaloplasty surgery showed a mean baseline IOP of  $24.3 \pm 6.0$  mmHg on  $1.5 \pm 1.2$  medications, which decreased to a mean IOP of  $13.8 \pm 3.2$  mmHg on  $0.5 \pm 0.7$  medications at 3 years. Intraocular pressure and medication use results for all study eyes were significantly decreased from baseline ( $p < 0.00001$ ) at all intervals. Late postoperative complications included cataracts (19.1%) and transient IOP elevation (1.8%).

**Conclusions** Canaloplasty demonstrated significant and sustained IOP reductions accompanied by an excellent short- and long-term safety profile in adult patients with open-angle glaucoma.

**Keywords** Canaloplasty · Microcatheter · Non-penetrating glaucoma surgery · Open-angle glaucoma · Schlemm's canal

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## Introduction

The surgical treatment of the natural aqueous outflow system for the management of open-angle glaucoma may minimize potentially severe complications associated with traditional filtering surgery by avoiding entry into the anterior chamber [1]. Elements common to such non-penetrating procedures such as deep sclerectomy with and without implant [2, 3], viscocanalostomy [4], and canaloplasty [5], involve the dissection of a superficial and deep scleral flap to create an intrascleral lake and a Descemet's window. In principle, aqueous can then bypass the presumably higher resistance of the trabecular meshwork by flowing through Descemet's window into the intrascleral

lake. In viscocanalostomy, aqueous within the lake may then re-enter the natural outflow system through adjacent surgically created ostia in Schlemm's canal. In contrast to deep sclerectomy, viscocanalostomy intends to route the aqueous through the canalicular outflow system without a subconjunctival bleb.

Canaloplasty extends the principles of non-penetrating glaucoma surgery by allowing surgeons to viscodilate Schlemm's canal along its entire length using a flexible microcatheter [5]. The placement of an intracanalicular tension suture within Schlemm's canal distends the full circumference of the trabecular meshwork inward to maintain an open canal. The two reconstructive steps in Schlemm's canal in combination with a water-tight surgical closure result in a non-bleb-dependent surgical treatment for glaucoma. Prior studies have reported on 1-, 2-, and 3-year results from prospective clinical trials of canaloplasty, which showed significant reductions in IOP and glaucoma medication usage in conjunction with an excellent safety profile [6–9]. The 3-year study results reported herein describe the long-term safety and efficacy of canaloplasty.

## Materials and methods

### Study design

This paper reports the 3-year results of a multicenter, prospective, single-arm study of canaloplasty at three clinical sites in Germany involving four surgeon investigators. This research was conducted in accordance with the principles set forth in the 1964 Declaration of Helsinki, ISO 14155–1, and the International Conference on Harmonization Good Clinical Practice. The protocol was approved for each study site by an Ethics Committee and all patients provided informed consent prior to their inclusion in the study. All enrollees underwent a complete baseline ophthalmic examination, which included the ocular history, ophthalmic and systemic medication usage, best-corrected visual acuity (BCVA), IOP by unmasked Goldmann applanation tonometry, slit-lamp examination, central corneal thickness, gonioscopy, and a fundus examination. Follow-up examinations were conducted at 1 day, 1 week, and 1, 3, 6, 12, 18, 24, 30, and 36 months.

### Patient selection

All patients were at least 18 years old at the time of enrollment, able to understand and provide informed consent, and were scheduled for glaucoma surgery or combined cataract and glaucoma surgery. Inclusion criteria for this study included a diagnosis of primary open-angle

glaucoma (POAG), pigmentary glaucoma, or exfoliative glaucoma, and a baseline and most recent IOP of 16 mmHg or higher and a historical IOP of 21 mmHg or higher. With many patients on maximally tolerated medical therapy, the protocol was designed to allow patients to withdraw from medications due to intolerance or poor compliance provided they had a historical IOP  $\geq 21$  mmHg. All patients had documented visual field loss, were in various stages of the disease, and met the individual criteria of each surgeon for the diagnosis of glaucoma and failure of prior medical or laser therapy. Exclusion criteria included neovascular disease, uveitis, peripheral anterior synechiae, angle recession, developmental or secondary glaucoma with the exception of pigmentary and exfoliative glaucoma, previous ocular surgeries that would interfere with complete circumferential catheterization of Schlemm's canal, and more than two laser trabeculoplasty procedures. Only one eye per patient was eligible.

All patient enrollment and examination case report forms were verified against the original medical records by study monitors. Data which received 100% source data verification included all baseline data including inclusion and exclusion criteria; key efficacy and safety variables such as IOP, number of glaucoma medications, secondary procedures, and adverse events, and all patients who had early termination from study participation.

### Treatment

Following a non-penetrating, two-flap dissection technique to expose Schlemm's canal and create an intrascleral lake and a Descemet's window, a flexible microcatheter (iTrack™ 250A, iScience Interventional Corporation, Menlo Park, CA, USA) was used to dilate the full circumference of the canal by injecting Healon GV (Abbott Medical Optics, Santa Ana, CA, USA) during catheterization. The microcatheter has a 200- $\mu$ m-diameter shaft with an atraumatic distal tip of approximately 250  $\mu$ m in diameter, a lumen through which the viscoelastic is delivered, and illumination near the tip so that the surgeon can guide the microcatheter by observing the beacon transsclerally. A Descemet's window was formed just prior to catheterization of the canal. Following circumferential catheterization, a 10–0 prolene suture (Ethicon Inc., Somerville, NJ, USA) was tied to the microcatheter tip and the device was withdrawn pulling the suture into the canal. The suture was cut from the microcatheter and then tied in a loop encircling the inner wall of Schlemm's canal. The suture loop was tightened to distend the trabecular meshwork inwards placing the tissues in tension and then locking knots were added. The superficial scleral flap was then sutured watertight with a minimum of five sutures to avoid bleb formation.

The post-surgical medication regimen consisted of non-steroidal anti-inflammatory drugs such as ketorolac tromethamine (Acular, Allergan Inc., Irvine, CA, USA) four times per day used for up to 4 weeks; prednisolone acetate (Pred Forte, Allergan Inc.) four times per day with tapering for up to 4 weeks, and an antibiotic such as gentamicin three times per day for a week or as needed. During the course of the study, surgeons were allowed to intervene with medical or interventional therapy as they deemed necessary.

#### Data analysis

The efficacy analysis was stratified according to the treatment received and the results of different groups of patients were evaluated. Group 1 included all patients with successful suture placement during canaloplasty alone and group 2 included all patients with successful suture implantation during canaloplasty combined with cataract surgery. The primary endpoints evaluated included mean IOP and mean number of glaucoma medications at each follow-up visit. Combination glaucoma medications were enumerated as individual medications in this study. The secondary endpoints included surgical and post-surgical complications and secondary interventions.

Baseline characteristics were compared between surgical groups using the Pearson Chi-square test for categorical variables such as gender, race, OD/OS eyes, previous surgery, and diagnosis and analysis of variance (ANOVA) for IOP, visual acuity (logMAR units), and number of glaucoma medications [10]. For each of the three groups, repeated-measures ANOVA using a mixed-model approach for longitudinal data was applied to assess changes from baseline in IOP, acuity, and medications with Bonferroni adjusted  $p$  values for assessing group differences [11]. When comparing groups 1 and 2, age, baseline IOP, and medications were included as covariates to control for possible confounding with the group-by-time interaction.  $F$  test for comparing slopes between groups from baseline through 36 months and differences in IOP, medications, and visual acuity was performed at specific time points. A compound symmetry covariance structure was used to handle the repeated measurements for the same patients at different time points. Two-tailed values of  $p \leq 0.05$  were considered statistically significant with adjustment for multiple comparisons as appropriate. The SPSS statistical package was used for analysis of the data (version 18.0, SPSS Inc./IBM, Chicago, IL, USA).

## Results

#### Demographics

All intent-to-treat eyes consisted of 109 eyes of 109 patients at baseline with 96 eyes (88.1%) completing the 3-year

visit. Of the remaining 13 subjects, five (4.6%) were lost to follow-up, four (3.7%) underwent additional glaucoma surgery, three (2.8%) withdrew from the study for personal reasons, and one (0.9%) was terminated as the subject was later found not to have met the inclusion criteria.

Table 1 shows the demographics for the study group. The successful placement of a tensioning suture into Schlemm's canal was achieved in 98 eyes (89.9%). No significant adverse events occurred due to failure to fully catheterize the canal. Ninety-three eyes (85.3%) had canaloplasty only with or without tensioning suture placement and 16 eyes (14.7%) with visually significant cataracts underwent canaloplasty combined with cataract extraction (phacocanaloplasty), all with successful suture placement.

#### Change in intraocular pressure and glaucoma medication usage

Table 2 and Fig. 1 show the efficacy results for group 1 (canaloplasty with successful suture placement) and group 2 (phacocanaloplasty with successful suture placement). Three years postoperatively, group 1, consisting of eyes receiving canaloplasty alone with successful suture implantation, attained a 34.3% reduction in IOP. At baseline, two of 82 eyes (2.4%) were not on medical therapy and 14 eyes (17.1%) were on three or more medications in comparison to 31 of 74 eyes (41.9%) taking no medical therapy and three eyes (4.1%) on three or more medications at 3 years. IOP and medication use were significantly decreased from baseline ( $p < 0.00001$ ) at all time points.

For the 11 eyes that had canaloplasty only, without suture placement, the mean baseline IOP was  $24.4 \pm 5.5$  mmHg on  $1.9 \pm 1.2$  medications, decreasing to a mean IOP of  $15.6 \pm 3.6$  mmHg on  $1.2 \pm 0.7$  medications ( $n=9$ ), representing a 36.1% reduction in IOP at 3 years. The mean IOP at 36 months was lower in group 1, which had successful suture placement. Although the IOP for these 11 eyes was significantly decreased from baseline ( $p < 0.01$ ) at all time points, the sample size of this group was too small for meaningful statistical comparison to group 1.

Further analysis of group 1 (canaloplasty only with suture placement) included evaluating the effects of inadvertent intraoperative perforations of Descemet's window or the inner wall of Schlemm's canal and of postoperative neodymium:YAG (Nd:YAG) goniopuncture. Of the seven of 82 (8.5%) eyes that had intraoperative perforations, the mean baseline IOP was  $23.6 \pm 4.5$  mmHg on  $2.0 \pm 0.0$  glaucoma medications decreasing to  $14.0 \pm 1.4$  mmHg on  $0.8 \pm 0.8$  medications at 36 months, similar to outcomes of other eyes in group 1. None of these seven eyes had an IOP less than 10 mmHg at any interval. These

**Table 1** Study group demographics of all intent-to-treat eyes

Parameter	Value
Enrollees/eyes, <i>n</i>	109
Age in years	
Mean±SD	67.3±9.9
Range	41.1–86.9
Sex, <i>n</i> (%)	
Female	55 (50.5)
Male	54 (49.5)
Race, <i>n</i> (%)	
White	108 (99.1)
Black	1 (0.9)
Glaucoma diagnosis, <i>n</i> (%)	
Primary open-angle	101 (92.7)
Pseudoexfoliative	6 (5.5)
Mixed mechanism	1 (0.9)
Pigmentary dispersion	1 (0.9)
Previous ocular surgery, <i>n</i> (%)	
Cataract	20 (18.3)
Viscocanalostomy	12 (11.0)
Laser peripheral iridotomy	5 (4.6)
Laser trabeculoplasty	4 (3.7)
Nd:YAG capsulotomy	1 (0.9)
Cyclophotocoagulation	1 (0.9)
Successful placement of intracanalicular suture, <i>n</i> (%)	98 (89.9)
Combined cataract procedure (phacocanaloplasty), <i>n</i> (%)	16 (14.7)

*n* sample size; *POAG* primary open-angle glaucoma; *Nd:YAG* neodymium YAG

perforations occurred throughout the duration of the study and were not apparently related to a learning curve effect or to differences between surgeons. Of the seven of 82 (8.5%) eyes that had postoperative goniopuncture, the mean baseline IOP was 23.6±2.0 mmHg on 2.1±0.7 glaucoma medications, decreasing to 18.2±2.5 mmHg on 1.5±0.5

medications at 36 months, which was higher than outcomes of other eyes in group 1.

Group 2, consisting of eyes having canaloplasty with successful suture placement combined with phacoemulsification, showed a 43.2% reduction in IOP at 3 years. At baseline, 3 of 16 eyes (18.8%) were on no medical therapy and three eyes were on three or more medications in comparison to eight of 13 eyes (61.5%) on no medical therapy and no eyes on three more medications at 3 years. IOP and medication use results were significantly decreased from baseline ( $p<0.00001$  and  $p<0.006$ , respectively) at all time points. Postoperative IOP was lower in group 2 (phacocanaloplasty) than group 1 (canaloplasty alone) at all time points, but this difference was not statistically significant ( $p=0.22$  at 3 years).

Visual acuity results

Snellen best-corrected visual acuities were converted to logarithm of the minimal angle of resolution (logMAR) equivalents for the purpose of data analysis. At 3 years, eyes in group 1 (canaloplasty alone), which had a mean baseline LogMAR of 0.22±0.25 and a LogMAR of 0.20±0.26 at 3 years, demonstrated no significant change from baseline values ( $p=0.70$ ).

Success results

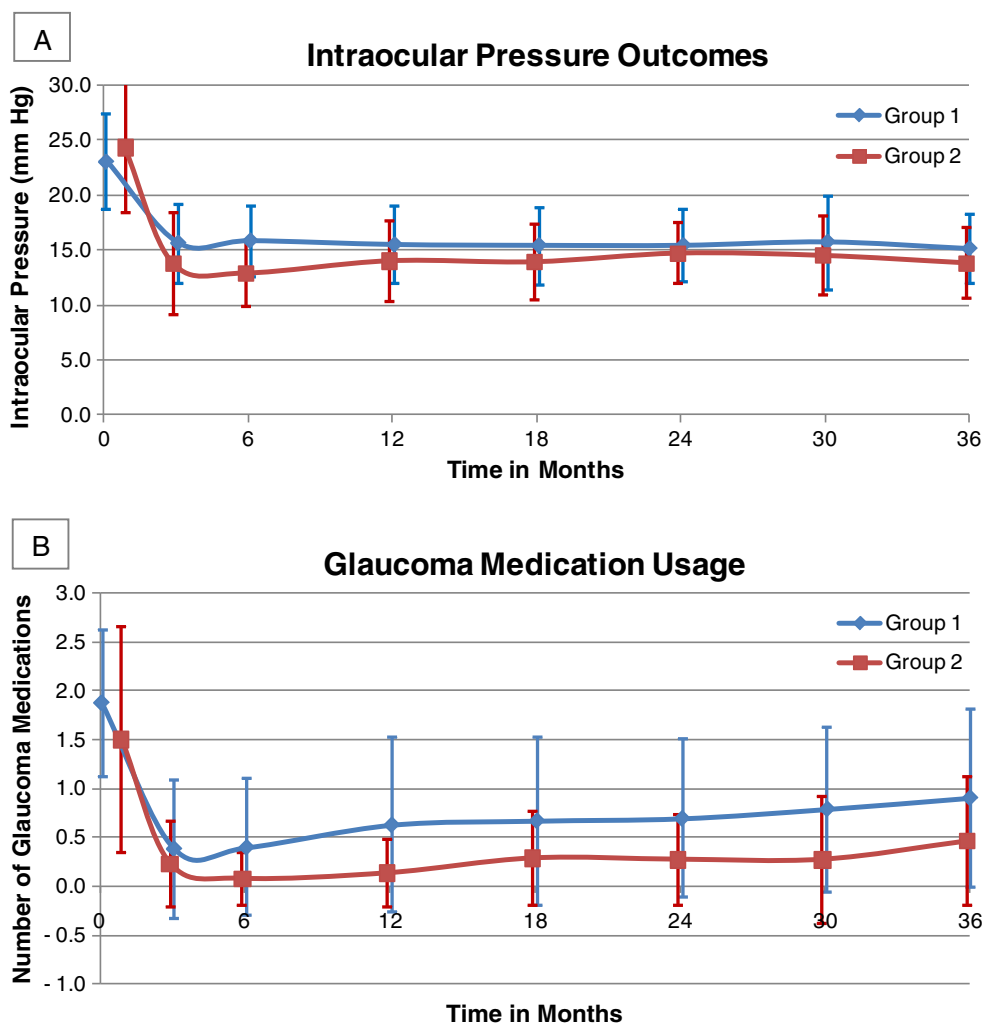
The success results for this study are presented in Table 3 and stratify the absolute IOP readings by the percentage of eyes with values of at least 21, 18, or 15 mmHg for group 1 (canaloplasty alone with suture placement) and group 2 (phacocanaloplasty with suture placement). A complete success is defined as reaching the specified IOP without glaucoma medication and a qualified success is defined as including the use of one or two medications. At 3 years, 36.5% of group 1 eyes attained an IOP of ≤18 mmHg with no medications and 82.4% achieved a qualified success. In

**Table 2** Outcome results

Exam	Group 1 (Canaloplasty alone)			Group 2 (Phacocanaloplasty eyes)		
	<i>n</i>	Mean IOP in mmHg±SD	Mean medications±SD	<i>n</i>	Mean IOP in mmHg±SD	Mean medications±SD
Baseline	82	23.0±4.3	1.9±0.7	16	24.3±6.0	1.5±1.2
3 months	70	15.6±3.6	0.4±0.7	13	13.7±4.7	0.2±0.4
6 months	65	15.8±3.2	0.4±0.7	13	12.8±3.0	0.1±0.3
12 months	73	15.5±3.5	0.6±0.9	15	14.0±3.7	0.1±0.4
18 months	67	15.4±3.5	0.7±0.9	8	13.9±3.5	0.3±0.5
24 months	70	15.4±3.3	0.7±0.8	12	14.7±2.8	0.3±0.5
30 months	67	15.7±4.3	0.8±0.8	11	14.5±3.6	0.3±0.6
36 months	74	15.1±3.1	0.9±0.9	13	13.8±3.2	0.5±0.7

*n* sample size; IOP intraocular pressure; *SD* standard deviation

**Fig. 1** Graph comparing efficacy outcomes of group 1 (canaloplasty alone with successful suture placement) and group 2 (combined cataract-canaloplasty eyes with successful suture placement). **a** The top graph presents the intraocular pressure results through 36 months. **b** The bottom graph shows the glaucoma medication usage through 36 months. The bars represent 1 standard deviation



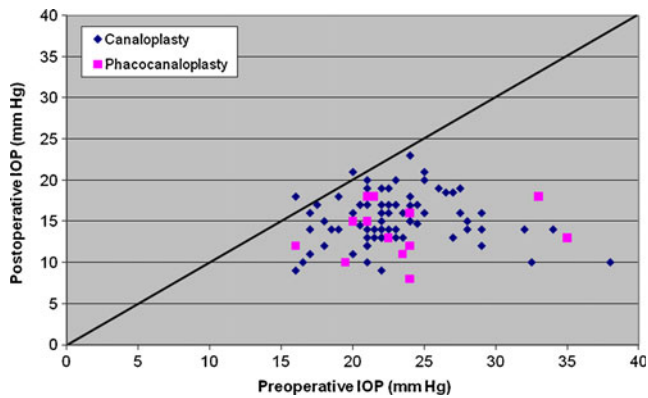
group 2, 61.5% of eyes achieved an IOP of  $\leq 18$  mmHg with no medications and 100.0% achieved a qualified success. Postoperative interventions and patient attrition would make these percentage figures in actual clinical practice less than stated. In Fig. 2, specific IOP results at 3 years postoperatively as compared to baseline for each eye are presented graphically in a scatter plot for groups

1 and 2. Figure 3 shows Kaplan–Meier survival plots for cumulative failure rates of groups 1 and 2 using failure criteria of an IOP  $>18$  mmHg on two consecutive visits. The Chi-square approximations for logrank and Wilcoxon tests comparing the failure proportions of groups 1 and 2 did not demonstrate a significant difference in cumulative failure rate ( $p < 0.27$ ).

**Table 3** Success results at 12, 24, and 36 months for group 1 (canaloplasty only) and group 2 (phacocanaloplasty)

	Group 1			Group 2		
	12 months	24 months	36 months	12 months	24 months	36 months
Unqualified success						
$\leq 21$ mmHg	58.9%	47.8%	40.5%	86.7%	72.7%	61.5%
$\leq 18$ mmHg	50.7%	42.0%	36.5%	86.7%	63.6%	61.5%
$\leq 15$ mmHg	37.0%	24.6%	21.6%	73.3%	45.5%	30.8%
Qualified success						
$\leq 21$ mmHg	95.9%	97.1%	98.6%	93.3%	100.0%	100.0%
$\leq 18$ mmHg	76.7%	81.4%	82.4%	93.3%	91.7%	100.0%
$\leq 15$ mmHg	52.1%	51.4%	56.8%	73.3%	66.7%	69.2%

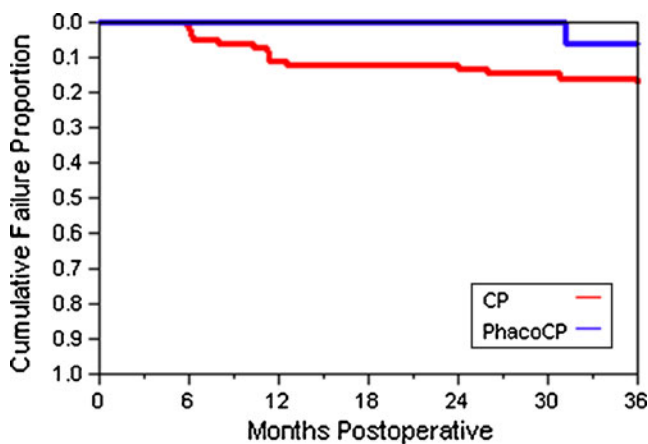




**Fig. 2** Scatter plot of preoperative IOP after 36 months for group 1 (canaloplasty only with successful suture placement) and group 2 (phacocanaloplasty or combined cataract-canaloplasty with successful suture placement). Each point represents one eye showing the preoperative IOP value on the *x*-axis and the 36-month postoperative IOP on the *y*-axis. Points falling below the oblique line (which represents no change) are lower than the preoperative readings

### Surgical and post-surgical complications

Table 4 shows all ocular-related surgical and postoperative complications reported regardless of severity. Most complications occurred intraoperatively or in the early postoperative phase ( $\leq 90$  days postoperatively). During the early postoperative period, hyphema was observed in six of 109 eyes (5.5%), all resolving by the 1-week visit with the exception of one eye (0.9%), which resolved by 1 month. Microhyphema, defined as circulating red blood cells without layered blood in the anterior chamber, was observed in 14 eyes (12.8%). Six eyes (5.5%) had IOP elevation  $\geq 30$  mmHg. The IOP rises were transient and resolved by the next scheduled follow-up visit with the exception of one case (0.9%), which received cyclopho-



**Fig. 3** Kaplan-Meier plot of the cumulative probability of failure for group 1 (CP or canaloplasty only with successful suture placement) and group 2 (PhacoCP or combined cataract-canaloplasty eyes with successful suture placement). Failure was defined as an IOP  $> 18$  mmHg on two consecutive visits

coagulation. Descemet's membrane detachments without involvement of the visual axis occurred in four eyes (3.7%), all resolving by the next scheduled visit with the exception of one eye which resolved by 6 months postoperatively. There were no instances of hypotony defined as IOP  $\leq 5$  mmHg with shallow or flat anterior chambers.

During the late-postoperative period ( $> 90$  days postoperatively), two of 109 eyes (1.8%) experienced an IOP elevation  $\geq 30$  mmHg. One instance of elevated IOP was successfully managed with glaucoma medical therapy. The other eye underwent cyclophotocoagulation at 27 months after experiencing an IOP elevation when medical therapy was inadvertently not administered during hospitalization for non-study related reasons. No eyes were reported to have blebs at 3 years.

### Postoperative interventions

Table 5 includes all postoperative interventions, defined as any procedure or process undertaken following surgery with the goal of enhancing the success of the surgical outcome [12]. The most commonly performed procedures included cataract extraction (19.1% of phakic eyes) followed by Nd:YAG goniotomy (8.3%), Nd:YAG capsulotomy (7.3%), and conjunctival suture replacement (7.3%). Five of the 17 patients receiving cataract extraction during the 3-year postoperative period were identified as having significant pre-existing cataracts prior to canaloplasty. The surgeons in these cases chose to perform cataract surgery at some point following canaloplasty. Patients who received additional glaucoma surgery including trabeculectomy, cyclophotocoagulation, and repeat canaloplasty were excluded from further analysis following these reoperations.

### Discussion

The desire to improve incisional glaucoma procedures has been motivated by the need to achieve long-term intraocular pressure control in the safest possible manner. Canaloplasty obviates the need for a subconjunctival filtering bleb, which shunts aqueous to non-physiological routes. This non-filtering, bleb-free procedure restores the natural trabeculo-canalicular outflow system by circumferentially catheterizing, viscodilating, and suture tensioning the entire length of Schlemm's canal with the use of a flexible microcatheter. The 3-year results reported here reveal significant and sustained pressure lowering accompanied by a low incidence of late-postoperative complications.

Although it is difficult to compare results from studies with differing study designs and patient populations, canaloplasty

**Table 4** Ocular-related surgical and post-surgical complications of all intent-to-treat eyes

Surgical/early postoperative complications ( $\leq 90$ days post-op)	<i>n</i> (%)
Microhyphema: $< 1.0$ mm layered blood	14 (12.8%)
Hyphema: $\geq 1.0$ mm layered blood	6 (5.5%)
Elevated intraocular pressure	6 (5.5%)
Descemet's membrane detachment	4 (3.7%)
Hypotony: IOP $\leq 5$ mmHg with shallow anterior chamber	0
Flat/shallow anterior chamber	0
Late Postoperative Complications ( $> 90$ days post-op)	
Cataracts	17 of 89 (19.1%)
Elevated intraocular pressure	2 (1.8%)
Blebs at 36 months	0
Endophthalmitis	0
Choroidal effusion	0
Hypotony: IOP $\leq 5$ mmHg with shallow anterior chamber	0

*n* sample size; *mm* millimeter

efficacy results are comparable to the lowest IOPs achieved in non-penetrating glaucoma surgery including viscocanalostomy [13–15], deep sclerectomy with various implants [16, 17], and deep sclerectomy with adjunctive mitomycin C [18, 19]. There is some rationale to believe that the addition of circumferential viscodilation and the trabecular meshwork tensioning suture in canaloplasty may provide an additional IOP lowering effect compared to the creation of a scleral lake and a Descemet's window alone, as is often achieved with deep sclerectomy or viscocanalostomy. To our knowledge, the only study directly comparing canaloplasty to another non-penetrating procedure did indeed retrospectively reveal a significant difference in postoperative IOP and medication use at 3 years in favor of patients who received

canaloplasty as compared to patients who underwent viscocanalostomy [20]. In a study by Lewis et al. [8], which reported 3-year results of canaloplasty in an international, 15-site study, outcomes of eyes were highly comparable to outcomes reported for this study. For eyes having canaloplasty alone with suture placement, Lewis reported a mean IOP of  $23.5 \pm 4.5$  mmHg on  $1.9 \pm 0.8$  medications decreasing to  $15.5 \pm 3.5$  mmHg on  $0.9 \pm 0.9$  medications at 36 months. For phacocanaloplasty eyes with suture placement, the mean IOP was  $23.5 \pm 5.2$  mmHg on  $1.5 \pm 1.0$  medications decreasing to  $13.6 \pm 3.6$  mmHg on  $0.3 \pm 0.5$  medications at 36 months.

The frequency of acute and late postoperative complications was also low, and compares favorably to trabeculectomy. Early complications included a 12.8% incidence of microhyphema and a 5.5% incidence of hyphema. Following canaloplasty, it is not uncommon to observe a small amount of blood in the anterior chamber, which likely occurs when the IOP decreases to less than episcleral venous pressure. No eye in this study exhibited hypotony or flat/shallow anterior chambers. In comparison, the incidence of hyphema following trabeculectomy is reported in the range of 4–43% [18, 21–23] hypotony is reported in the range of 10–42% [20–22, 24] and flat/shallow anterior chambers are reported with an incidence of 13–43% [18, 21, 22].

Late complications following canaloplasty were infrequent, and only included elevated IOP (1.8% of eyes) and cataracts (19.1% of phakic eyes) potentially related to the procedure or due to age-related progression; 29.4% of the eyes with cataracts had significant pre-existing cataracts. For those eyes that did not have significant pre-existing cataracts, the mean length of time to postoperative cataract extraction was 23.5 months. Only 6.4% of eyes in this study experienced a 2 or more line loss of visual acuity, none of which was directly attributable to the canaloplasty procedure.

**Table 5** Postoperative Interventions for all intent-to-treat eyes

Surgical	Number (%)
Cataract surgery	17 of 89 (19.1%)
Trabeculectomy	1 (0.9%)
Canaloplasty	1 (0.9%)
Tube shunt	0
Laser	
Nd:YAG goniopuncture	9 (8.3%)
Nd:YAG capsulotomy	8 (7.3%)
Cyclophotocoagulation	3 (2.8%)
Peripheral laser iridotomy	1 (0.9%)
Iridoplasty	1 (0.9%)
Synechialysis	1 (0.9%)
Selective laser trabeculoplasty	0
Other procedures	
Conjunctival suture replacement	8 (7.3%)
Pars plana steroid injection (for central retinal vein occlusion)	1 (0.9%)

*Nd:YAG* neodymium-YAG

Subconjunctival bleb formation has often been classified as a postoperative complication in non-filtering glaucoma surgery [4, 25, 26]. In this canaloplasty study, no blebs were present at 3 years, and there were no reports of the postoperative complications related to blebs. No antimetabolites were used, as they have their own inherent risks. As canaloplasty is not dependent upon external filtration, immediate postoperative care does not necessitate bleb manipulations to enhance flow, such as massage, laser suture lysis, needling, and subconjunctival injections of anti-metabolites, which are often required after trabeculectomy [27].

Traditionally, safety concerns have often posed a barrier to earlier incisional glaucoma surgery, particularly in regards to the potential vision-threatening complications associated with trabeculectomy. However, the distal collector system may have a better chance of survival if intervention is undertaken earlier in the disease process, before the outflow system collapses or before chronic topical medical therapy negatively impacts the tissues [28, 29]. The excellent safety profile of canaloplasty or other non-penetrating surgery may make such procedures an earlier option in many instances, such as in younger patients where cataract formation is of concern, where medical therapy has proven insufficient, or the conjunctiva is not suitable for bleb formation. A non-filtering, bleb-independent procedure such as canaloplasty can also be offered to patients where complications cannot be tolerated, such as single-eyed patients, patients with high myopia, and patients with tubular visual fields [30].

The incidence of Descemet's membrane perforations, suggested as an indicator of an individual surgeon's experience in non-penetrating techniques [31], occurred in only 3.4% of eyes in this study and did not appear to be related to a learning curve effect as all surgeons were experienced in nonpenetrating glaucoma surgery. Should a macroperforation with iris prolapse occur, conversion to a fully penetrating procedure was not required. A canaloplasty was still performed with the addition of miocchol, a peripheral iridectomy, and any additional procedures needed to reverse or prevent a subsequent iris prolapse. Eyes with Descemet's membrane perforations had similar outcomes to eyes without perforations and did not display an increased incidence of hypotony, although the number of perforations was too small to meaningfully evaluate a statistically significant effect of perforation on IOP.

Failure to place a tensioning suture into Schlemm's canal was similarly unpredictable, occurring in approximately 10% of eyes, and was often related to the microcatheter tip consistently entering a particular collector channel ostium, preventing further advancement. Complete circumferential catheterization was often successful after encountering an initial obstacle by either

catheterizing in the opposite direction or by exerting pressure over the presumed collector channel ostia with a second instrument to prevent the microcatheter tip from deviating from its intended course. No significant adverse events occurred due to failure to fully catheterize the canal. Eyes without a tensioning suture were viscodilated to the fullest extent possible by catheterizing the canal from both ostia, and did not display a statistically significant difference in IOP compared to eyes with a tensioning suture, although the sample size was too small for meaningful comparison.

Combined cataract surgery with canaloplasty appears to be adjunctive. At 3 years postoperatively, the subset of eyes undergoing primary cataract surgery in conjunction with canaloplasty surgery demonstrated a lower IOP as compared to eyes undergoing canaloplasty alone. Removal of the crystalline lens could potentially improve outflow by further increasing trabecular meshwork tensioning in conjunction with canaloplasty. Other studies investigating non-penetrating glaucoma surgery in combination with phacoemulsification cataract surgery are supportive of this combined beneficial effect [32–36].

This multicenter, prospective clinical trial provides further evidence of the significant IOP lowering efficacy of canaloplasty, with continued control through a 3-year postoperative period. The risk profile of canaloplasty was favorable and consistent with the well-documented, lower risks associated with other non-penetrating procedures. Predictive factors for successful canaloplasty outcomes and reasons for later failure remain unclear and should be explored in future studies.

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