

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of ab externo canaloplasty for primary open-angle glaucoma

Primary open-angle glaucoma is a progressive condition that causes long-term increase of pressure in the eye. This damages the nerve that connects the eye to the brain (optic nerve) and may gradually lead to permanent loss of sight. This procedure involves inserting a tiny tube into the main drainage canal, to widen it. The tube is then removed and a stitch is placed in the canal to keep it open. The aim is to reduce pressure in the eye.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in August 2016.

Procedure name

- Ab externo canaloplasty for primary open-angle glaucoma

Specialist societies

- Royal College of Ophthalmologists.

Description

Indications and current treatment

Primary open-angle glaucoma is a chronic condition associated with elevated intraocular pressure. It leads to progressive damage to the optic nerve. Early stages are usually asymptomatic but as the condition progresses it causes visual impairment and, if untreated, blindness.

Treatment is usually eye drops containing drugs that either reduce the production of aqueous humor or increase its drainage. Surgical procedures such as trabeculectomy, drainage tubes, deep sclerectomy, viscocanalostomy, or laser trabeculoplasty may also be used.

What the procedure involves

Ab externo canaloplasty is a surgical technique that aims to reduce intraocular pressure, by improving drainage of aqueous fluid from the eye. It is done under local or general anaesthetic. A superficial hinged flap of sclera is made and a deeper flap excised, exposing the Schlemm's canal. An ultrasound imaging system is used to identify the canal and to visualise the surgical instruments when they are in the canal. A microcatheter with an illuminated tip is introduced into the canal and advanced around its entire circumference. As the catheter tip advances, viscoelastic fluid is injected into the canal to dilate it. When catheterisation of the entire canal is complete a suture is tied to the tip of the microcatheter and it is withdrawn, pulling the suture into the canal. The suture is cut, tied in a loop encircling the inner wall of the canal and tightened. This widens the canal. The superficial flap is sutured.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to ab externo canaloplasty for primary open-angle glaucoma. The following databases were searched, covering the period from their start to 16 August 2016: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with primary open-angle glaucoma.
Intervention/test	Ab externo canaloplasty.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on approximately 2,079 patients from 1 review¹, 2 randomised controlled trials^{2,3}, 3 retrospective comparative studies⁴⁻⁶, 1 case series⁷, 1 case report⁸ and 1 systematic review and meta-analysis⁹.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on ab externo canaloplasty for primary open-angle glaucoma

Study 1 Brandao L M (2013)

Details

Study type	Literature review on minimally invasive glaucoma surgery (including canaloplasty)
Country	15 studies included – countries not reported
Recruitment period	Literature review of 15 studies
Study population and number	n= 914 eyes (777 canaloplasty alone and 137 canaloplasty with phacoemulsification) from 15 studies
Age and sex	Not reported
Patient selection criteria	Not reported
Technique	Canaloplasty alone using the i-Track 250 A (iScience) microcatheter or combined with phacoemulsification.
Follow-up	9 to 36 months
Conflict of interest/source of funding	One of the authors had received a scholarship from the Swiss Government (ESKAS 2011.0167) and a grant from the Freiwillige Akademische Gesellschaft Basel. The other author had a proprietary interest in the Stegmann Canal Expander.

Analysis

Follow-up issues: Not reported.

Study design issues: This is a literature review and narrative synthesis of the current literature (as at 2013) – but the authors do not report their search strategy or how studies were included/excluded.

Study population issues: Not reported.

Other issues: There are probably overlaps between some of the studies included in the review.

Key efficacy and safety findings

Efficacy							Safety	
Number of patients analysed: 914 eyes (777 canaloplasty alone and 137 canaloplasty with phacoemulsification) from 15 studies							Intra- and post-operative complications	
IOP and number of medications							Complication	Frequency in %
Study	Number of eyes	Follow-up (months)	Mean IOP reduction (mmHg)	Mean IOP reduction (%)	Mean postop. IOP (mmHg)	Mean medications reduction (%)		
Canaloplasty alone								
Lewis (2007)	74	12	8.6±0.5	36	16.2±3.5	1.3 (68%)	Gross hyphaema	2 to 6
Lewis (2009)	84	24	6.9±0.1	29	16.3±3.7	1.4 (70%)	Descemet's detachment	2 to 6
Lewis (2011)	103	36	8.6±1.5	34	15.5±3.5	1.0±0.1	360° cannulation impossible	0 to 9
Peckar and Koerber (2011)	97	18	13.1±5.2	48	14.1±3.2	2.4 (76%)	False passage	3 to 12
Grieshaber (2010) a	90	15	28.6±7.2	36	16.2±4.9	–	IOP spike >30 mmHg	2 to 9
Grieshaber (2010) b	60	36	31.7±6.7	66	13.3±1.7	–	Cataract formation	0 to 8
Grieshaber (2011)	32	18	14.2±2.1	47	13.1±1.2	2.6	Suture cheese wiring	0 to 2
Koerber (2012)	15	18	12.0±0.1	45	14.5±2.6	1.7 (85%)	Flat anterior chamber	0 to 2
Matthaei (2011)	46	12	5.6±3.2	31	12.6±2.4	1.3 (43%)	Persistent hypotony	0 to 1
Bull (2011)	82	36	7.9±1.3	34	15.1±3.1	0.9 (53%)	Choroidal detachment	0
Fujita (2011)	11	12	8.4±1.8	36	15.0±4.1	1.6 (25%)	Bleb formation	0 to 4
Ayyala (2011)	33	12	7.4±1.5	32	13.8±4.9	2	Blebitis, endophthalmitis	0
Klink (2012)	20	9	10.6±4.2	33	13.3±9.9	2.6 (82%)		
Bruggemann (2013)	30	12	14.6±4.5	50	13.2±2.8	2.5 (100%)		
Canaloplasty combined with phacoemulsification								
Lewis (2007)	13	12	10.7±1.8	46	12.8±3.6	–		
Shingleton (2008)	54	12	10.7±1.7	44	13.7±4.4	1.3 (86%)		
Lewis (2011)	54	36	9.8±2.6	42	13.6±3.6	1.0±0.1		
Bull (2011)	16	36	10.5±2.8	43	13.8±3.2	1.0 (66%)		
Abbreviations used: IOP, intraocular pressure.								

Study 2 Matlach J (2015)

Details

Study type	Randomised controlled trial
Country	Germany
Recruitment period	2010 to 2012
Study population and number	n= 62 (30 canaloplasty versus 32 trabeculectomy) white patients with uncontrolled open-angle glaucoma
Age and sex	<ul style="list-style-type: none"> • Canaloplasty: Mean 67 years; 60% (18/30) male • Trabeculectomy: Mean 68 years; 34% (11/32) male
Patient selection criteria	<p><u>Inclusion criteria:</u> patients aged 18 years or older with medically uncontrolled primary or secondary (pseudoexfoliative and pigmentary) open-angle glaucoma.</p> <p><u>Exclusion criteria:</u> patients with previous penetrating or non-penetrating surgeries in the study eye, angle closure, normal tension, congenital or other secondary types or glaucoma (uveitic, neovascular or traumatic) and more than 1 laser trabeculoplasty or more than 1 cyclodestructive procedure was done in the study eye within at least 1 year before inclusion.</p>
Technique	<ul style="list-style-type: none"> • Canaloplasty: the iTrack 250A (iScience) microcatheter was used. After the surgery, all canaloplasty patients were treated by prednisolone acetate 1% eye drops with preservatives or dexamethasone dihydrogen phosphate 0.1% preservative-free eye drops, non-steroidal anti-inflammatory eye drops and antibiotic eye drops. If IOP increased after canaloplasty, Nd:YAG laser goniopuncture of the Descemet window was performed or anti-glaucomatous drugs were added if target IOP was not reached. • Trabeculectomy: mitomycin C was used as an antimetabolite in all trabeculectomy patients. After the procedure, all the trabeculectomy patients were treated by prednisolone acetate 1% eye drops with preservatives or dexamethasone dihydrogen phosphate 0.1% preservative-free eye drops, antibiotic eye drops and atropine 0.5% eye drops (with preservatives) or cyclopentolate hydrochloride 1% preservative-free eye drops. If treatment failed, topical glaucoma medications were added or second glaucoma surgeries were done.
Follow-up	2 years
Conflict of interest/source of funding	One of the authors received funding for consultancy (Pharm Allergan, European Glaucoma Advisory Board) and another author received travel grants for congress fees and accommodation (Novartis).

Analysis

Follow-up issues:

- Follow-up visits were scheduled at: days 1 and 7; 4 weeks; and 3, 6, 12 and 24 months after surgery.
- All patients completed the baseline visit and follow-up visits at day 1 and 7. 98% (61/62) completed the 4-week, 94% (58/62) the 3-month, 90% (56/62) the 6-month and 87% (54/62) the 12- and 24-month follow-up.
- The postoperative time-points were adjusted to the nearest possible time-point or post-operative data was acquired by ophthalmologists in private practice or clinics if patients had failed to attend a scheduled visit at the trial centre.

Study design issues:

- Single-centre study.
- Permuted block randomisation.
- Primary endpoint was complete (without medication) and qualified success (with or without medication) defined as an intraocular pressure (IOP) of 18 mmHg or less (definition 1) or IOP of 21 mmHg or less and IOP reduction of 20% or more (definition 2) 4 weeks after the procedure, IOP of 5 mmHg or more 4 weeks after the procedure, no vision loss, no further glaucoma surgery, and a completed follow-up until 2 years after the procedure.

Study population issues:

- Both groups were comparable for preoperative IOP, visual acuity, number of glaucoma medications, type of glaucoma, number of previous ocular surgeries, age and sex.
- There were 43% (13/30) of patients in the canaloplasty group and 59% (19/32) of patients in the trabeculectomy group with primary open-angle glaucoma (others had secondary open angle glaucoma).

Other issues: None reported.

Key efficacy and safety findings

Efficacy					Safety			
Number of patients analysed: 62 (30 canaloplasty versus 32 trabeculectomy)					Intraoperative complications			
Procedure Success					Canaloplasty:			
	Canaloplasty	Trabeculectomy	p value*		<ul style="list-style-type: none"> - microperforation of Descemet membrane: 7% (2/30) - anterior synechiae: 3% (1/30). It needed surgical peripheral iridotomy. 			
COMPLETE SUCCESS (without glaucoma medication)					Trabeculectomy: None reported.			
IOP ≤21 mmHg and ≥20% IOP reduction					Postoperative complications and surgical interventions			
					Canaloplasty	Trabeculectomy	p value*	
1 month	52% (15/29)	81% (26/32)	-		Early complications (≤90 days)			
3 months	62% (16/26)	84% (27/32)	-		Hypotony (IOP<5mmHg)	20% (6/30)	38% (12/32)	0.17
6 months	54% (13/24)	78% (25/32)	-		Shallow anterior chamber	0	6% (2/32)	0.49
1 year	61% (14/23)	77% (24/31)	-		Choroidal detachment	3% (1/30)	13% (4/32)	0.36
2 years	39% (9/23)	68% (21/31)	0.04		Elevated IOP (>25 mmHg)	30% (9/30)	25% (8/32)	0.78
IOP ≤18 mmHg					Conjunctival leak	10% (3/30)	9% (3/32)	1
1 month	55% (16/29)	91% (29/32)	-		Corneal erosion	3% (1/30)	44% (14/32)	<0.001
3 months	59% (16/26)	84% (27/32)	-		Hyphaema (>1mm layered blood)	23% (7/30)	3% (1/32)	0.02
6 months	58% (14/24)	78% (25/32)	-		Intracorneal haematoma after Descemet detachment	3% (1/30)	-	-
1 year	57% (13/23)	77% (24/31)	-		Secondary suture migration in anterior chamber	7% (2/30)**	-	-
2 years	39% (9/23)	74% (23/31)	0.01		Iris incarceration	-	3% (1/32)	-
QUALIFIED SUCCESS (with or without glaucoma medication)					Scarring of the filtering bleb	-	3% (1/32)	-
IOP ≤21 mmHg and ≥20% IOP reduction					Blebitis/ endophthalmitis	0	0	-
1 month	72% (21/29)	81% (26/32)	-		Early surgeries			
3 months	96% (25/26)	94% (30/32)	-		Laser suture lysis, eyes	-	75% (24/32)	-
6 months	83% (20/24)	91% (29/32)	-		5-FU bleb injections	-	91% (29/32)	-
1 year	100% (23/23)	97% (30/31)	-		Iris revision	-	3% (1/32)	-
2 years	83% (19/23)	90% (28/31)	0.40		Scleral flap revision (hypotony)	3% (1/30)	19% (6/32)	0.11
IOP ≤18 mmHg					Scleral flap revision (elevated IOP)	-	0	-
1 month	76% (22/29)	91% (29/32)	-		Bleb needling	-	3% (1/32)	-
3 months	89% (24/26)	97% (31/32)	-		Conjunctival suturing	7% (2/30)	3% (1/32)	0.61
6 months	96% (23/24)	97% (31/32)	-		Nd:YAG laser goniopuncture	13% (4/30)	-	-
1 year	96% (22/23)	100% (31/31)	-		Second surgeries	10% (3/30)***	0	-
2 years	83% (19/23)	97% (30/31)	0.01		Late complications (>90 days)			
IOP and medications					Elevated IOP (>25 mmHg)	3% (1/30)	3% (1/32)	1
	Canaloplasty		Trabeculectomy		Hypotony (IOP<5 mmHg)	0	19% (6/32)	0.03
	Mean IOP ± SD (mmHg)	Mean number of medications ± SD	Mean IOP ± SD (mmHg)	Mean number of medications ± SD				
Preoperative	23.7±5.1	2.6±1.6	22.2±5.3	3.3±1.0				
7 days	15.0±6.7	0.3±0.8	12.9±5.2	0				
1 month	15.7±5.1	0.7±1.2	12.1±5.1	0				
3 months	13.4±3.8	0.8±1.2	11.0±4.0	0.2±0.6				

*Log-rank test over the 2 years of follow-up

6 months	13.8±2.6	0.8±1.0	10.7±3.7	0.3±0.7
1 year	13.8±2.7	0.8±1.2	10.8±2.9	0.3±0.7
2 years	14.4±4.2	0.9±1.1	11.5±3.4	0.4±0.8

Both procedures statistically significantly reduced IOP during follow-up ($p < 0.001$, 1 to 24 months compared against baseline). There was no statistically significant difference between groups for IOP during follow-up ($p = 0.56$).

The postoperative number of medications was statistically significantly reduced during follow-up ($p < 0.001$). The mean number of needed medications was statistically significantly lower in the trabeculectomy group after surgery ($p = 0.01$, 1 to 24 months compared to baseline).

Mean IOP reduction at 2 years (mmHg):

Canaloplasty: 9.3 ± 5.7

Trabeculectomy: 10.8 ± 6.9 mmHg ($p = 0.47$)

Visual acuity (logMAR)

	Canaloplasty	Trabeculectomy	p
Preoperative (median)	0.22 (0.08 to 0.40)	0.10 (0.00 to 0.28)	0.13
2 years (mean±SD)	0.20±0.26	0.30±0.56	

Visual acuity was not statistically significantly different from baseline in both groups during follow-up ($p = 0.08$, 1-24 months).

Regression analysis revealed no statistically significant difference in postoperative IOP, medication or complete and qualified success at 2 years for different glaucoma types (primary versus secondary open-glaucoma) or previous trabeculectomy.

Abbreviations used: 5-FU, 5-fluorouracil; IOP, intraocular pressure; MAR, minimum angle of resolution; Nd:YAG, neodymium: yttrium aluminium garnet; SD, standard deviation.

Scarring of the filtering bleb	–	25% (8/32)	
Blebitis/ endophthalmitis	3% (1/30)	0	0.48
Late surgeries			
Scleral flap revision (hypotony)	0	3% (1/32)	1
Second surgery: laser cyclophotocoagulation	3% (1/30)	0	0.48

*Fisher exact test, chi-square test, as appropriate.

**In 1 canaloplasty patient with suture displacement and penetration into the anterior chamber, suture had to be removed by paracentesis.

*** 2 laser cyclophotocoagulation, 1 trabeculectomy.

Study 3 Rekas M (2015)

Details

Study type	Randomised controlled trial
Country	Poland
Recruitment period	Not reported
Study population and number	n= 59 (29 phaco-canaloplasty versus 30 phaco-non-penetrating deep sclerectomy) patients with open-angle glaucoma and cataract
Age and sex	Phaco-canaloplasty: Mean 75 years; Phaco-deep sclerectomy: Mean 73 years 56% (33/59) male
Patient selection criteria	Inclusion criteria: coexisting glaucoma and cataract (NC1 and NC2) classified according to the LOCS III scale. Glaucoma types: primary open-angle glaucoma, pseudo-exfoliation glaucoma and pigmentary glaucoma with unsatisfactory intraocular pressure control despite maximally tolerated topical and systemic medication. Well documented progression of the visual field, daily fluctuations in pressure, non-compliance in anti-glaucoma therapy, or allergy to topical medications. Exclusion criteria: unwillingness to participate, any previous surgical procedure within the eye, closed or narrow angle glaucoma, poorly controlled diabetes mellitus with diabetic retinopathy, advanced macular degeneration and active inflammatory disease.
Technique	All procedures were done under retrobulbar anaesthesia (2% xylocaine and 0.5% bupivacaine) by 1 surgeon. For the phaco-canaloplasty, the iTrack 250A (iScience) microcatheter was used. For phaco-deep sclerectomy, the HealaFlow gel (Anteis Ophthalmology) was used. When goniotomy was needed, it was done with an Nd: YAG laser. Bleb fibrosis was treated with 5-fluorouracil subconjunctival injections and needling, if needed. On the day of surgery, glaucoma drugs were stopped. When surgery was unsuccessful, medications were started again in accordance with the guidelines of the European Glaucoma Society. All patients were treated with a topical steroid and antibiotic combination for 4 weeks after surgery.
Follow-up	Mean 13 months
Conflict of interest/source of funding	None.

Analysis

Follow-up issues:

- Examinations were conducted before surgery, on days 1 and 7, and 1, 3, 6 and 12 months after surgery.

Study design issues:

- Enrolment into groups was done by a random sorting algorithm with an allocation ratio set to 1.0 on the day of surgery.
- Complete (without medication) and qualified success (with or without medication) was defined as an intraocular pressure (IOP) of 18 mmHg or less. Corrected distance visual acuity, intraocular pressure and number of medications were evaluated.

Study population issues:

- Both groups were comparable for type of glaucoma, level of cataract, follow-up, age and sex.
- There were 83% (24/29) of patients in the phaco-canaloplasty group and 93% (28/30) of patients in the phaco-deep sclerectomy group with primary open-angle glaucoma. The remaining patients had pseudoexfoliation glaucoma.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy								Safety																																																																											
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IOP								<table border="1"> <thead> <tr> <th>Complications</th> <th>PC group</th> <th>PDS group</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>Intraoperative Trabeculo Descemet's membrane rupture</td> <td>3% (1/29)</td> <td>3% (1/30)</td> <td>0.981</td> </tr> <tr> <td colspan="4">Postoperative</td> </tr> <tr> <td>Hyphaema* Blood level in AC</td> <td>59% (17/29)</td> <td>–</td> <td>–</td> </tr> <tr> <td>Erythrocytes in AC (microhyphaema)</td> <td>34% (10/29)</td> <td>–</td> <td>–</td> </tr> <tr> <td>Descemet membrane detachment**</td> <td>3% (1/29)</td> <td>–</td> <td>0.313</td> </tr> <tr> <td>Anterior chamber cells</td> <td>7% (2/29)</td> <td>3% (1/30)</td> <td>0.554</td> </tr> <tr> <td>Hypotony Until 7 days</td> <td>28% (8/29)</td> <td>30% (9/30)</td> <td>0.879</td> </tr> <tr> <td>Until 30 days</td> <td>17% (5/29)</td> <td>10% (3/30)</td> <td>0.477</td> </tr> <tr> <td>Until 180 days</td> <td>–</td> <td>–</td> <td>–</td> </tr> <tr> <td>Choroidal detachment</td> <td>7% (2/29)</td> <td>–</td> <td>0.157</td> </tr> <tr> <td>Bleb fibrosis</td> <td>–</td> <td>27% (8/30)</td> <td>0.034</td> </tr> <tr> <td>Iris incarceration</td> <td>3% (1/29)</td> <td>3% (1/30)</td> <td>0.981</td> </tr> </tbody> </table>				Complications	PC group	PDS group	p	Intraoperative Trabeculo Descemet's membrane rupture	3% (1/29)	3% (1/30)	0.981	Postoperative				Hyphaema* Blood level in AC	59% (17/29)	–	–	Erythrocytes in AC (microhyphaema)	34% (10/29)	–	–	Descemet membrane detachment**	3% (1/29)	–	0.313	Anterior chamber cells	7% (2/29)	3% (1/30)	0.554	Hypotony Until 7 days	28% (8/29)	30% (9/30)	0.879	Until 30 days	17% (5/29)	10% (3/30)	0.477	Until 180 days	–	–	–	Choroidal detachment	7% (2/29)	–	0.157	Bleb fibrosis	–	27% (8/30)	0.034	Iris incarceration	3% (1/29)	3% (1/30)	0.981																				
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Corrected distance visual acuity (logMAR)							
Time	PC group			PDS group			p
	Mean (SD)	Median	Range	Mean (SD)	Median	Range	
Pre-op	0.74±0.70	0.69	0 to 2.53	0.57±0.45	0.51	0 to 1.61	0.507
1 day	2.14±2.24	0.91	0 to 6.21	0.55±0.40	0.46	0.11 to 1.61	0.001
7 days	0.71±1.23	0.46	0 to 6.21	0.46±0.48	0.46	0 to 1.83	0.631
1 month	0.29±0.35	0.22	0 to 1.61	0.39±0.26	0.34	0 to 1.13	0.081
3 months	0.10±0.17	0	0 to 0.46	0.14±0.20	0	0 to 0.69	0.758
6 months	0.13±0.21	0	0 to 0.69	0.11±0.19	0	0 to 0.69	0.878
1 year	0.11±0.17	0	0 to 0.46	0.11±0.16	0	0 to 0.46	0.779

Statistically significant improvement within groups (p<0.05).

Abbreviations used: AC, anterior chamber; IOP, intraocular pressure; MAR, minimum angle of resolution; PC, phaco-canaloplasty; PDS, phaco-deep sclerectomy; SD, standard deviation.

Study 4 Seuthe A-M (2016)

Details

Study type	Retrospective comparative study
Country	Germany
Recruitment period	2011 to 2014
Study population and number	n= 417 eyes (180 conventional canaloplasty versus 237 canaloplasty with suprachoroidal drainage) Patients with open-angle glaucoma or secondary forms of glaucoma.
Age and sex	Mean 67 years; sex not reported
Patient selection criteria	<u>Inclusion criteria</u> : patients with open-angle glaucoma or secondary forms of glaucoma such as pseudoexfoliation, pigmentary dispersion, or uveitic glaucoma. Patients with progression of visual field loss under current maximal topical treatment, allergic to topical medication or with repeated IOP measurements above target IOP range who had to be surgically treated. <u>Exclusion criteria</u> : no available IOP data after 3 months, eyes that had had cyclodestructive interventions in the past. Patients undergoing cataract surgery with canaloplasty and patients who had additional glaucoma surgery following canaloplasty or canaloplasty with suprachoroidal drainage. .
Technique	Canaloplasty with or without suprachoroidal drainage. After the procedure, patients received topical low-dose steroids for 3 days and a 2-week regimen.
Follow-up	1 year
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Control visits were done 3 and 12 months after surgery.

Study design issues:

- 4 experienced surgeons did the 2 procedures.
- Primary endpoint was reduction of IOP after 1 year and number of IOP-lowering medications.

Study population issues:

- There were 86% (155/180) of patients in each group with primary open-angle glaucoma.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy								Safety		
Number of patients analysed: 417 eyes (180 conventional canaloplasty versus 237 canaloplasty with suprachoroidal drainage)								Operative and postoperative complications and secondary surgical intervention		
IOP								Complication	Canaloplasty	Canaloplasty with suprachoroidal drainage
	Canaloplasty			Canaloplasty with suprachoroidal drainage			p value			
	n	Median IOP value (mmHg)	Reduction	n	Median IOP value (mmHg)	Reduction				
Baseline	180	20.8±3.6	–	237	20.9±3.5	–	0.785			
3 months	165	14.3±3.0	31%	223	13.4±2.9	36%	0.003			
1 year	152	14.0±2.6	33%	174	13.1±2.5	37%	0.003			
Statistically significant IOP reduction within groups in both groups at 3 months and 1 year ($p < 0.0001$).										
IOP-lowering medication										
	Canaloplasty		Canaloplasty with suprachoroidal drainage		p value					
	n	Mean number of medications	n	Mean number of medications	–					
Baseline	180	3.4±0.9	237	3.5±0.9	0.360					
3 months	165	0.4±0.8	223	0.5±1.0	0.255					
1 year	152	0.8±0.9	174	0.7±1.0	0.186					
Free of medication 1 year	45%	–	57%	–	0.038					
Significant reduction within groups (p value not given).										
Abbreviations used: IOP, intraocular pressure.										
								Hyphaema	34% (61/180)	34% (80/237)
								Anterior chamber irrigation	1% (1/180)	2% (4/237)
								Need for 360-degree trabeculectomy	16% (28/180)	16% (38/237)
								Need for additional IOP-lowering procedures following 360-degree trabeculectomy	2% (4/180)	3% (6/237)
								Postoperative conservatively uncontrollable IOP	8% (15/180)	6% (14/237)
								Transient hypotony	6% (11/180)	5% (13/237)
								Choroidal detachment	0	0
								Bleb formation	0	0
								Detachment Descemet membrane	0	0
								Endophthalmitis	0	0
								All differences between both groups were not statistically significant.		

Study 5 Klink T (2015)

Details

Study type	Cross-sectional retrospective comparative study
Country	Germany
Recruitment period	2008 to 2010
Study population and number	n= 327 (175 canaloplasty versus 152 trabeculectomy) patients with primary open-angle glaucoma
Age and sex	Canaloplasty: mean 70 years; trabeculectomy: mean 67 years 47% (153/327) male
Patient selection criteria	Consecutive patients with primary open-angle glaucoma undergoing canaloplasty or trabeculectomy with mitomycin C.
Technique	Canaloplasty with or without phacoemulsification. Trabeculectomy with mitomycin C with or without phacoemulsification.
Follow-up	2 years
Conflict of interest/source of funding	None

Analysis

Follow-up issues: The questionnaire was sent to 423 patients (212 canaloplasty and 211 trabeculectomy) 2 years after surgery. The return rate was 76% (327/423).

Study design issues:

- The following outcomes were assessed: influence of surgery on daily activities, postoperative complaints, subjective outcomes of surgery, rate of revision surgeries, patients' postoperative mood, and the influence of postoperative care on quality of life.
- The following questionnaires were used: Glaucoma Symptom Scale, Visual Activities Questionnaire, Impact of Vision Impairment, National Eye Institute–Visual Functioning Questionnaire, National Eye Institute–Visual Functioning Questionnaire–25 items, Glaucoma Health Perception Index, Glaucoma Quality of Life–15 items, Activities of Daily Vision Scale, and Visual Function Questionnaire–14 items. Additionally, surgery-specific questions developed by expert consensus were included.
- The questionnaire included 21 items.
- The procedures were done by 1 of 3 surgeons.

Study population issues:

- Phacocanaloplasty was done in 36% (63/113) of canaloplasty patients and phacotrabeculectomy was done in 20% (31/121) of trabeculectomy patients.
- Patient characteristics were not compared between the 2 groups before surgery.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy					Safety
Number of patients analysed: 327 (175 canaloplasty versus 152 trabeculectomy)					Not reported.
Quality of life outcomes					
Item description	Canaloplasty		Trabeculectomy		p value*
	n**	Mean±SD	n**	Mean±SD	
Change in visual acuity ^a	110	3.29±0.82	112	2.83±0.94	0.001
Reading newspapers ^a	108	4.27±1.08	118	3.65±1.15	<0.001
Watching television ^a	109	4.37±0.92	117	3.79±1.11	<0.001
Seeing at night ^a	108	4.31±0.98	119	3.82±1.10	<0.001
Driving ^a	94	4.28±1.06	96	3.56±1.20	<0.001
Glare ^a	110	4.02±1.09	120	3.36±1.31	<0.001
Pain ^a	112	4.33±0.84	118	3.86±1.15	<0.001
Foreign body sensation ^a	176	4.08±1.08	152	3.78±1.18	0.016
Tearing ^a	176	4.28±0.85	152	4.04±1.05	0.024
Redness ^a	171	3.85±0.98	150	3.47±1.21	0.003
Dry eye ^a	170	4.09±0.95	151	3.44±1.20	<0.001
Fulfillment of expectations not to use drops anymore ^a	113	4.09±1.36	116	4.00±1.43	0.6
Stress caused by surgery ^a	175	4.18±0.86	149	3.59±1.12	<0.001
Stress caused by follow-ups/treatments ^a	176	4.36±0.80	151	3.40±1.20	<0.001
Difference in number of eye drops before/after surgery ^c	113	2.76±0.51	118	2.73±0.56	0.7
Difference in number of follow-ups before/after surgery ^c	174	4.36±0.80	151	3.40±1.20	0.2
Revision surgeries ^d	176	0.12±0.43	150	0.67±1.14	<0.001
Postoperative mood ^b	176	2.30±0.83	151	1.96±0.87	0.009
Satisfaction with results of surgery ^e	175	8.09±2.71	152	7.46±2.61	0.034
Restriction of social contacts ^a	110	4.54±0.99	115	4.57±0.90	0.8
Loss of independence ^a	112	4.45±0.88	121	4.45±0.88	0.9
*Student's t-test, Pearson's chi-square test as appropriate.					
**Number of answers					
^a Items scored on a five-level scale: 5 = not at all, 4 = slightly, 3 = partially, 2 = predominantly, 1 = extremely, 0 = not rated. Higher score indicates a better quality of life for this activity.					
^b Patients could select 2 terms from a list of words associated with a negative meaning (for example, frustrated, helpless), a neutral meaning (for example, uncertain), or a positive meaning (for example, happy, carefree). Higher score equals better quality of life.					
^c Items scored on a 3-level scale: 1 = more, 2 = equal, or 3 = less.					
^d Number of revision surgeries after the initial procedure (zero, once, twice, three times, four times or more than four times. Lower score equals less revision surgeries.					
^e This item had 10 levels, from 0 = totally discontent up to 10 = totally content.					
Abbreviations used: SD, standard deviation.					

Study 6 Schoenberg E D (2015)

Details

Study type	Retrospective comparative case series
Country	US
Recruitment period	2007 to 2011
Study population and number	n= 77 (36 phacocanaloplasty versus 41 phacotrabeculectomy) eyes from 77 patients with moderate to advanced open-angle glaucoma
Age and sex	Phacocanaloplasty: mean 67 years, 67% (24/36) male; Phacotrabeculectomy: mean 70 years, 24% (10/41) male.
Patient selection criteria	Patients with moderate to advanced open-angle glaucoma.
Technique	<ul style="list-style-type: none"> • Canaloplasty with phacoemulsification using the iTrack 250 (iScience) device. • Trabeculectomy with mitomycin C with phacoemulsification. <p>All patients received the same postoperative steroid and antibiotic drop regimen of prednisolone acetate 1% and moxifloxacin 4 times daily for 1 month followed by a taper of the prednisolone over 2 months.</p>
Follow-up	1 year minimum
Conflict of interest/source of funding	One of the authors was a paid statistics consultant for iScience Interventional; the company had no direct involvement in this study. The remaining authors declared no conflicts of interest. This study was supported in part by the Tulane Glaucoma Research Fund.

Analysis

Follow-up issues: Only eyes with a minimum of 12-month follow-up after the combined cataract-glaucoma procedure were included in the study.

Study design issues:

- The decision to do phacocanaloplasty or phacotrabeculectomy was based on the prior approval of phacocanaloplasty by the insurance companies.
- If surgery was done on both eyes, only the chronologically first eye was included.
- Primary endpoints were IOP failure (IOP >18 mmHg with or without glaucoma medications or IOP <4 mmHg at the 12-month examination), visual failure (decrease in vision by >0.20 logarithmic units of the minimum angle of resolution [logMAR] compared with the preoperative visual acuity), and operative failure (need for surgery to manage a complication or failure of the original combined cataract and glaucoma surgery), any one of which was sufficient for the surgery to be considered an overall failure. Bleb revision or needling, with or without mitomycin C injection, was not considered a failure.
- The procedures were done by a single surgeon.

Study population issues:

- All patients in both groups had primary open-angle glaucoma except for 2 patients in the phacocanaloplasty group who had pseudoexfoliation glaucoma.
- There was a statistically significant difference between the 2 groups for the sex baseline characteristics of the patients ($p < 0.01$).
- In the phacocanaloplasty group, there were 53% (19/36) white and 47% (17/36) African American. In the phacotrabeculectomy group, there were 51% (21/41) white, 42% (17/41) African American, 5% (2/41) Hispanic and 2% (1/41) Asian.
- Three phacocanaloplasty eyes did not undergo Schlemm canal stenting; based on intent-to treat, these remained in the phacocanaloplasty group.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy				Safety		
Number of patients analysed: 77 (36 phacocanaloplasty versus 41 phacotrabeculectomy)				Complications and reoperations		
IOP (mean ± SD; mmHg)				Serious complications		
	Canaloplasty	Trabeculectomy	p		Canaloplasty	Trabeculectomy
Before surgery	19.5±5.7	23.6±13.8	0.09	Choroidal effusion	1/36	1/41
1 year	14.1±4.4	11.8±5.4	0.07	Suprachoroidal haemorrhage	0	1/41
Statistically significant reduction in IOP from baseline in both groups (p<0.001).				CRAO	1/36	0
Visual acuity (mean±SD; LogMAR Units)				Hypotony maculopathy	0	2/41
	Canaloplasty	Trabeculectomy	p (Student t test)	Minor complications		
Before surgery	0.41±0.27	0.51±0.48	0.27	Descemet detachment at 1 day	1/36	0
1 day	0.78±0.69	0.60±0.59	0.20	Hyphaema at 1 day	28% (10/36)	0
1 week	0.48±0.38	0.50±0.55	0.85	Major reoperations		
1 month	0.30±0.22	0.43±0.47	0.13	Ahmed glaucoma valve	1/36	1/41
3 months	0.25±0.17	0.33±0.39	0.25	EX-PRESS shunt	1/36	0
6 months	0.26±0.34	0.32±0.46	0.54	Minor reoperations		
9 months	0.22±0.22	0.39±0.60	0.12	Bleb needling with MMC	0	5/41
1 year	0.21±0.20	0.40±0.70	0.10	Scleral flap needling	5/36	0
Statistically significant improvement in visual acuity from baseline in both groups (p<0.001).				Choroidal effusion	0	1/41
Glaucoma medications (median [interquartile range])				Bleb suturing at slit lamp	0	1/41
	Canaloplasty	Trabeculectomy	p (Mann-Whitney U Test)			
Before surgery	3 (2 to 4)	3 (2 to 3)	0.25			
1 day	0 (0 to 0)	0 (0 to 0)	0.85			
1 week	0 (0 to 0)	0 (0 to 0)	0.57			
1 month	0 (0 to 1)	0 (0 to 0)	0.17			
3 months	0 (0 to 1)	0 (0 to 0)	0.25			
6 months	0 (0 to 1)	0 (0 to 1)	0.78			
9 months	0 (0 to 1)	0 (0 to 1)	0.90			
1 year	0 (0 to 1)	0 (0 to 1)	0.61			
Statistically significant reduction in number of medications from baseline in both groups (p<0.001).						
Failure rates						
	Canaloplasty	Trabeculectomy	p			
Overall failure	22% (8/36)	20% (9/41)	0.79			
Vision failure	0%	5% (2/41)	0.50			
Operative failure	6% (2/36)	5% (2/41)	1.00			
IOP failure	17% (6/36)	12% (5/41)	0.75			
Abbreviations used: CRAO, central retinal artery occlusion; IOP, intraocular pressure; logMAR, logarithmic units of the minimum angle of resolution; MMC, mitomycin C; SD, standard deviation.						

Study 7 Brusini P (2014)

Details

Study type	Case series
Country	Italy
Recruitment period	Not reported
Study population and number	n= 256 eyes from 224 patients with open-angle glaucoma
Age and sex	Mean 64 years; sex not reported
Patient selection criteria	Patients with open-angle glaucoma under maximum tolerated medical therapy.
Technique	Canaloplasty was done under local or general anaesthesia. All patients underwent postoperative local medical treatment with levofloxacin drops 4 times daily for 1 week and dexamethasone drops 4 times daily for 7 days followed by diclofenac drops 4 times daily for 1 month.
Follow-up	Mean 20 months (maximum 5 years)
Conflict of interest/source of funding	None.

Analysis

Follow-up issues: The full procedure could not be done in 42 eyes (16%), either due to a large perforation of trabeculodescemet membrane with iris prolapse (2 eyes) or to the impossibility of cannulating the full 360° of Schlemm's canal (40 eyes) due to anatomical obstacles or other intraoperative complications, such as the misdirection of the microcatheter in the anterior chamber.

Study design issues:

- The patients were recruited from 1 single centre.
- The definition of “complete” success was based on 3 different criteria: postoperative IOP \leq 21mmHg, \leq 18mmHg, and \leq 16mmHg without any medical treatment. When the same IOP levels were obtained with medical treatment, the success was defined as “qualified.”

Study population issues: The types of open-angle glaucoma were: primary open-angle glaucoma, 74% (189/256); pseudoexfoliation glaucoma, 21% (53/256); juvenile glaucoma, 4% (10/256) and pigmentary glaucoma, 2% (4/256).

Other issues: Not reported.

Key efficacy and safety findings

Efficacy					Safety	
Number of patients analysed: 214 eyes from 185 patients					Early complications	
Pre- and postoperative IOP (mmHg)					Complication	% eyes
	n eyes	Mean±SD	95% CI	p value*	Hyphaema	22% (47/214)
Preop	214	29.4 ± 7.9	18.0 to 52.1	–	Aqueous leakage from the conjunctival flap	<1% (2/214)
1 day	214	13.3 ± 6.1	3.0 to 28.0	<0.0001	Hypotony <5mmHg	10% (21/214)
1 week	214	17.3 ± 6.8	4.2 to 31.1	<0.0001	Transient IOP spike >10 mmHg	6% (12/214)
1 month	214	18.1 ± 7.4	6.4 to 35.1	<0.0001	Descemet membrane detachment	5% (11/214)
3 months	207	17.1 ± 4.7	8.0 to 27.0	<0.0001	Suture cheese-wiring through trabecular meshwork	<1% (2/214)
6 months	194	17.3 ± 4.8	9.3 to 26.2	<0.0001	Conjunctival bleb clinically detectable	1% (3/214)
1 year	144	16.8 ± 4.2	10.0 to 25.1	<0.0001		
18 months	129	16.7 ± 4.0	10.0 to 23.4	<0.0001		
2 years	80	17.1 ± 4.7	8.9 to 28.1	<0.0001		
30 months	69	16.4 ± 4.7	10.4 to 25.2	<0.0001		
3 years	29	17.3 ± 3.9	8.3 to 27.7	<0.0001		
42 months	19	16.9 ± 3.1	10.0 to 22.0	<0.0001		
* Paired t-test in comparison with the preoperative values.					Postoperative interventions	
Success rate					<ul style="list-style-type: none"> • YAG laser goniopuncture: 12% (26/214); after 2-12 months. • Trabeculectomy: 8% (17/214); after 3-58 months. 	
	≤21 mmHg		≤18 mmHg		≤16 mmHg	
	QS	CS	QS	CS	QS	CS
1 year	89% (128/144)	54% (75/144)	75% (108/144)	44% (64/144)	47% (68/144)	34% (49/144)
2 years	89% (71/80)	46% (37/80)	74% (59/80)	38% (30/80)	46% (37/80)	31% (25/80)
3 years	86% (25/29)	45% (13/29)	59% (17/29)	31% (9/29)	38% (11/29)	24% (7/29)
IOP-lowering medication						
	Mean number of medications±SD					
Before canaloplasty	3.3 ± 0.9					
1 year	0.7 ± 1.2					
2 years	1.1 ± 1.3					
3 years	1.3 ± 1.5					
Abbreviations used: CI, confidence interval; CS, complete success; IOP, intraocular pressure; QS, qualified success; SD, standard deviation.						

Study 8 Li G-Y (2016)

Details

Study type	Case report
Country	China
Recruitment period	Not reported
Study population and number	n= 1 patient with primary open-angle glaucoma
Age and sex	31 years, male.
Patient selection criteria	Primary open-angle glaucoma
Technique	Canaloplasty using the iTrack 250A device.
Follow-up	3 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Not reported.

Study design issues: Not reported

Study population issues: Not reported

Other issues: Not reported.

Key efficacy and safety findings

Safety
Canaloplasty drastically lowered IOP in the right eye from 40 to 7 mmHg. Ocular decompression retinopathy was revealed 1 day after surgery by fundus examination. The patient was treated with tobramycin and dexamethasone. 3 months after canaloplasty, IOP remained in control at 16 mmHg and all retinal haemorrhages had completely resolved.
Abbreviations used: IOP, intraocular pressure.

Study 9 Lin Z-J (2016)

Details

Study type	Systematic review and meta-analysis
Country	Paper from China; studies included were from US (1) and Germany (3).
Recruitment period	Literature search from inception to December 2015
Study population and number	n= 215 eyes (100 canaloplasty versus 115 trabeculectomy) from patients with open-angle glaucoma
Age and sex	Canaloplasty: mean age ranging from 67 years to 73 years; sex not reported Trabeculectomy: mean age ranging from 65 years to 72 years; sex not reported
Patient selection criteria	“Relevant controlled clinical trials” with patients undergoing canaloplasty compared to trabeculectomy for OAG were included.
Technique	Canaloplasty or trabeculectomy.
Follow-up	1 year
Conflict of interest/source of funding	None.

Analysis

Follow-up issues: Not reported.

Study design issues:

- The meta-analysis was undertaken according to the Preferred reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement.
- There was no language restriction applied to the literature search.
- Two review authors extracted data independently from eligible articles and the differences were resolved by discussion. They subjectively scored each selected article using a system previously reported by Downs and Black, which could evaluate RCTs and non-randomised studies. If the quality score was over 50%, the quality of the study was considered adequate.
- The outcomes measures reported were IOP reduction, postoperative success rate, anti-glaucoma medications and the incidence of adverse events.
- All statistical analyses were completed using Revman 5.3.
- Publication bias was not assessed due to the limited number of included studies in the meta-analysis.

Study population issues:

- The Matlach (2015) RCT is also reported in Table 2. The Bruggemann (2013) and the Ayyala (2011) retrospective comparative studies are also reported in the Brandao (2013) review which is included in Table 2. The Thederan (2014) study is a German retrospective comparative study which is not available in English language.
- The types of glaucoma were: OAG in the Ayyala (2011) study; POAG, PEXG and NTG in Bruggemann (2013); POAG, PEXG and PG in Matlach (2015) and POAG, PEXG, NTG and PG in Thederan (2014).

Other issues: Not reported.

Key efficacy and safety findings

Efficacy	Safety						
<p>Number of patients analysed: 215 eyes (100 canaloplasty versus 115 trabeculectomy) from 4 studies</p> <p>IOP reduction WMD: -2.33 (95% CI -4.00 to -0.66); no significant heterogeneity ($X^2=2.37$; $p=0.50$, $I^2=0$) Both of the procedures statistically significantly reduced postoperative IOP. IOP reduction for trabeculectomy was statistically significantly greater.</p> <p>Complete success (maximum postoperative IOP of 18 mmHg without medications) OR: 0.58 (95%CI 0.26 to 1.31); ($X^2=2.73$; $p=0.26$, $I^2=27\%$)</p> <p>Qualified success (maximum IOP of 18 mmHg with or without medications) OR: 0.50 (95%CI 0.10 to 2.44); ($X^2=0.28$; $p=0.60$, $I^2=0$) There was no statistically significant difference between groups for complete and qualified success rates.</p> <p>Anti-glaucoma medications reduction WMD: -0.54 (95% CI -1.18 to 0.09); statistically significant heterogeneity between studies ($X^2=7.86$; $p=0.02$, $I^2=75\%$) There was no statistically significant difference between groups for anti-glaucoma medications reduction.</p> <p>The sensitivity analyses suggested that each study did not significantly influence the estimation of IOP reduction.</p>	Comparison of postoperative complications at 12 months						
	Complication	Number of studies	OR (95% CI)	Test for heterogeneity			Overall effect
				X^2	p	I^2	p
	Hyphaema	3	8.80 (2.25 to 34.51)	0.47	0.79	0%	0.002
	Descemet detachment	3	4.49 (0.72 to 27.82)	0.18	0.92	0%	0.11
	Choroidal effusions	4	0.12 (0.03 to 0.48)	1.04	0.79	0%	0.002
	Hypotony (IOP<5 mmHg)	2	0.36 (0.13 to 0.99)	0.26	0.61	0%	0.05
	Shallow anterior chamber	2	0.32 (0.05 to 2.14)	0.17	0.68	0%	0.24
Abbreviations used: CI, confidence interval; IOP, intraocular pressure; NTG, normal tension glaucoma; OAG, open-angle glaucoma; OR, odds ratio; PEXG, pseudoexfoliate glaucoma; PG, pigmentary glaucoma; POAG, primary open-angle glaucoma; WMD, weighted mean difference.							

Efficacy

Procedure success

In an RCT of 62 patients comparing canaloplasty (n=30) with trabeculectomy (n=32) in patients with uncontrolled open-angle glaucoma, the rates of complete success (measured without glaucoma medication) were statistically significantly lower in the canaloplasty group after 2 years: 39% (9/23) versus 68% (21/31) when defined as IOP \leq 21 mmHg and \geq 20% IOP reduction (p=0.04) and 39% (9/23) versus 74% (23/31) when defined as IOP \leq 18 mmHg (p=0.01). In the same study, the rates of qualified success (measured with or without glaucoma medication) were not statistically significantly different between groups when defined as IOP \leq 21 mmHg and \geq 20% IOP reduction: 83% (19/23) versus 90% (28/31) but they were statistically significantly lower in the canaloplasty group when defined as IOP \leq 18 mmHg (83% [19/23] versus 97% [30/31], p=0.01).²

In an RCT of 59 patients comparing phaco-canaloplasty (n=29) with phaco-non-penetrating deep sclerectomy (n=30) in patients with open-angle glaucoma and cataract, complete and qualified success rates defined as an IOP of 18 mmHg or less at 1 year were not statistically significantly different between groups: 79% versus 77% for the complete success rate and 86% versus 84% for the qualified success rate.³

In a retrospective comparative study of 77 patients with moderate to advanced open-angle glaucoma treated by phacocanaloplasty (n=36) or phacotrabeulectomy (n=41), there was no statistically significant difference in overall failure between groups (22% [8/36] versus 20% [9/41], p=0.79).⁶

In a case series of 224 who had canaloplasty, the complete success rates (IOP \leq 18 mmHg without medication) at 1-, 2- and 3-year follow-up were 44% (64/144), 38% (30/80) and 31% (9/29) and the qualified success rates (IOP \leq 18 mmHg with medication) were 75% (108/44), 74% (59/80) and 59% (17/29).⁷

In a systematic review and meta-analysis of 215 eyes, comparing 100 eyes treated by canaloplasty against 115 eyes treated by trabeculectomy, there was no statistically significant difference between groups for complete and qualified success rates at 1-year follow-up; odds ratio (OR) 0.58 (95% confidence interval [CI] 0.26 to 1.31) and 0.50 (95%CI 0.10 to 2.44) respectively.⁹

Intraocular pressure (IOP)

In a review of 914 eyes treated by canaloplasty alone (n=777 eyes) or canaloplasty combined with phacoemulsification (n=137 eyes), the mean IOP reduction (after a maximum of 36 months follow-up) ranged from 29% to 66% in patients who had canaloplasty only and from 42% to 46% in patients who had canaloplasty with phacoemulsification.¹

In the RCT of 62 patients comparing canaloplasty (n=30) with trabeculectomy (n=32) in patients with uncontrolled open-angle glaucoma, there was a statistically significant reduced IOP during 1- to 24-month follow-up compared against baseline in both groups ($p<0.001$). The mean IOP \pm standard deviation (SD) statistically significantly decreased from 23.7 \pm 5.1 mmHg before the procedure to 14.4 \pm 4.2 mmHg at 2-year follow-up in the canaloplasty group and from 22.2 \pm 5.3 mmHg to 11.5 \pm 3.4 mmHg in the trabeculectomy group (no statistically significant difference between groups during follow-up, $p=0.56$).²

In the RCT of 59 patients comparing phaco-canaloplasty (n=29) with phaco-non-penetrating deep sclerectomy (n=30), there was a statistically significant IOP reduction within both groups of 33% and 28% respectively 1 year after surgery ($p<0.05$, no statistically significant difference between groups).³

In a retrospective comparative study of 417 eyes comparing conventional canaloplasty (n=180) against canaloplasty with suprachoroidal drainage (n=237) in patients with open-angle glaucoma or secondary forms of glaucoma, there was a statistically significant IOP reduction within both groups of 33% and 37% respectively 1 year after surgery ($p<0.0001$; statistically significant difference between groups, $p=0.003$).⁴

In the retrospective comparative study of 77 patients treated by phacocanaloplasty (n=36) or phacotrabeulectomy (n=41), the mean IOP \pm SD statistically significantly decreased from 19.5 \pm 5.7 mmHg before the procedure to 14.1 \pm 4.4 mmHg at 1-year follow-up in the phacocanaloplasty group and from 23.6 \pm 13.8 mmHg to 11.8 \pm 5.4 mmHg in the phacotrabeulectomy group ($p<0.001$ within groups; no statistically significant difference between groups, $p=0.07$).⁶

In the case series of 224 patients, there was a statistically significant decrease in mean IOP \pm SD at 1-year, 2-year and 42-month follow-up from 29.4 (\pm 7.9) mmHg before surgery to 16.8 (\pm 4.2) mmHg, 17.1 (\pm 4.7) mmHg and 16.9 (\pm 3.1) mmHg respectively ($p<0.0001$).⁷

In the systematic review and meta-analysis of 215 eyes, the mean IOP reduction was statistically significantly lower in the canaloplasty group at 1-year follow-up (weighted mean difference [WMD]: -2.33, 95% CI -4.00 to -0.66).⁹

Medication use

In the review of 914 eyes, mean medications reduction (after a maximum of 36-months follow-up) ranged from 25% to 100% in patients who had canaloplasty only and from 66% to 86% in patients who had canaloplasty with phacoemulsification.¹

In the RCT of 62 patients comparing canaloplasty (n=30) with trabeculectomy (n=32), there was a statistically significant decrease in the number of medications used during 1- to 24-month follow-up compared against baseline in both groups ($p<0.001$). The mean number of medications \pm SD statistically significantly

decreased from 2.6 ± 1.6 before the procedure to 0.9 ± 1.1 at 2-year follow-up in the canaloplasty group and from 3.3 ± 1.0 to 0.4 ± 0.8 in the trabeculectomy group (mean number of medications needed was statistically significantly higher in the canaloplasty group during follow-up compared to baseline, $p=0.01$).²

In the RCT of 59 patients comparing phaco-canaloplasty ($n=29$) with phaco-non-penetrating deep sclerectomy ($n=30$), there was a statistically significant decrease in the mean (\pm SD) number of medications used in both groups, from $2.64 (\pm 0.68)$ before surgery to $0.27 (\pm 0.67)$ at 1 year in the phaco-canaloplasty group and from $2.89 (\pm 0.94)$ to $0.55 (\pm 0.94)$ in the phaco-non-penetrating deep sclerectomy group ($p < 0.05$ for the difference within groups, no statistically significant difference between groups).³

In the retrospective comparative study of 417 eyes comparing conventional canaloplasty ($n=180$) against canaloplasty with suprachoroidal drainage ($n=237$), there was a statistically significant decrease in the mean number of glaucoma medications used within both groups from 3.4 ± 0.9 before surgery to 0.8 ± 0.9 at 1 year in the canaloplasty group and from 3.5 ± 0.9 to 0.7 ± 1.0 in the canaloplasty with suprachoroidal drainage group (p value for the difference within groups not reported; no statistically significant difference between groups, $p=0.186$ at 1 year). In the same study, the rate of eyes free of medication at 1 year was statistically significantly lower in the canaloplasty-only group (45% versus 57%, $p=0.038$).⁴

In the retrospective comparative study of 77 patients treated by phacocanaloplasty ($n=36$) or phacotrabeculectomy ($n=41$), there was a statistically significant decrease in the median number of glaucoma medications used from 3 before surgery to 0 at 1 year within both groups ($p < 0.001$ for the difference within groups; no statistically significant difference between groups, $p=0.61$).⁶

In the case series of 224 patients, the mean number of medications \pm SD decreased from 3.3 ± 0.9 before surgery to 0.7 ± 1.2 at 1-year, 1.1 ± 1.3 at 2-year and 1.3 ± 1.5 at 3-year follow-up (p value not reported).⁷

In the systematic review and meta-analysis of 215 eyes there was no statistically significant difference between groups for reduction in anti-glaucoma medications at 1 year (weighted mean difference -0.54 , 95% CI -1.18 to 0.09).⁹

Visual acuity

In the RCT of 62 patients comparing canaloplasty ($n=30$) with trabeculectomy ($n=32$), visual acuity was not statistically significantly different from baseline in both groups during 1- to 24-month follow-up ($p=0.08$) (there were non-significant changes in visual acuity (logMAR) from 0.22 before surgery to 0.20 at 2-year follow-up in the canaloplasty group and from 0.10 to 0.30 in the trabeculectomy group).²

In the RCT of 59 patients comparing phaco-canaloplasty (n=29) with phaco-non-penetrating deep sclerectomy (n=30), there was a statistically significant improvement in the mean±SD corrected distance visual acuity in both groups from 0.74±0.70 logMAR before surgery to 0.11±0.17 logMAR at 1 year in the phaco-canaloplasty group and from 0.57±0.45 logMAR to 0.11±0.16 logMAR in the phaco-non-penetrating deep sclerectomy group (p<0.05 for the difference within groups, no statistically significant difference between groups).³

In the retrospective comparative study of 77 patients treated by phacocanaloplasty (n=36) or phacotrabeculectomy (n=41), there was a statistically significant improvement in the mean±SD visual acuity (LogMAR) from 0.41±0.27 before surgery to 0.21±0.20 at 1 year within the phacocanaloplasty group and from 0.51±0.48 to 0.40±0.70 within the phacotrabeculectomy group (p<0.001 for the difference within groups; no statistically significant difference between groups, p=0.10).⁶

Quality of life

In a retrospective comparative study of 327 patients who had canaloplasty (n=175) or trabeculectomy (n=152), which collected self-reported questionnaire data 2 years after surgery, the mean score (±SD) for satisfaction with results of surgery (ranging from 0, totally discontent, to 10 totally content) was statistically significantly higher in the canaloplasty group (8.09±2.71 compared with 7.46±2.61, p=0.034). There were statistically significantly fewer revision surgeries reported in the canaloplasty group (mean number of revision surgeries per patient ±SD 0.12±0.43 compared with 0.67±1.14, p<0.001), patients were statistically significantly more positive after canaloplasty (2.30±0.83 compared with 1.96±0.87, p=0.009), stress caused by surgery and follow-up or treatments was statistically significantly lower in the canaloplasty group (4.18±0.86 compared with 3.59±1.12, p<0.001 and 4.36±0.80 compared with 3.40±1.20, p<0.001 respectively), and nonvisual and visual ocular symptoms were statistically significantly lower in the canaloplasty group (p<0.05). For the following items, there were no statistically significant difference between groups: fulfilment of expectations not to use drops anymore, difference in number of eye drops and in number of follow-up before/after surgery, restriction of social contacts and loss of independence.⁵

Secondary surgical interventions

Secondary surgeries within 90 days of the procedure (2 laser cyclophotocoagulation and 1 trabeculectomy) were reported in 10% (3/30) of patients treated by canaloplasty and in none of the patients treated by trabeculectomy in the RCT of 62 patients; another laser cyclophotocoagulation was reported in 1 patient treated by canaloplasty after 90 days of the procedure.²

Secondary surgery were reported in none of the patients treated by phacocanaloplasty and in 59% of patients treated by phaco-non-penetrating deep sclerectomy in the RCT of 59 patients within a mean 13-month follow-up. ³

Anterior chamber irrigation was reported in less than 1% (1/180) of patients treated by canaloplasty alone and in 2% (4/237) of patients treated by canaloplasty with suprachoroidal drainage in a retrospective comparative study of 417 eyes (p value not statistically significant). In the same study, need for 360-degree trabeculectomy was reported in 16% (28/180) and 16% (38/237) of patients respectively and need for additional IOP-lowering procedures following 360-degree trabeculectomy was reported in 2% (4/180) and 3% (6/237) of patients respectively. ⁴

Ahmed glaucoma valve was reported in 1 patient in each group, EX-PRESS shunt in 1 patient in the phacocanaloplasty group only and scleral flap needling in 14% (5/36) of patients in the phacocanaloplasty group only in the retrospective comparative study of 77 patients treated by phacocanaloplasty or phacotrabeulectomy. ⁶

YAG laser goniopuncture was reported in 12% (26/214) of eyes after 2 to 12 months and trabeculectomy was reported in 8% (17/214) after 3 to 58 months in the case series of 224 patients. ⁷

Safety

Elevation of intraocular pressure (IOP)

IOP of more than 30 mmHg after the procedure was reported in 2% to 9% of eyes in a review of 914 eyes treated by canaloplasty alone (n=777 eyes) or canaloplasty combined with phacoemulsification (n=137 eyes) at a maximum of 36 months follow-up. ¹

Elevated IOP of more than 25 mmHg was reported in 30% (9/30) of patients treated by canaloplasty and in 25% (8/32) of patients treated by trabeculectomy within 90 days of the procedure in an RCT of 62 patients (p=0.78). After 90 days of the procedure, elevated IOP was also reported in 1 patient in each group (p=1). ²

Postoperative conservatively uncontrollable IOP was reported in 8% (15/180) of patients treated by canaloplasty alone and in 6% (14/237) of patients treated by canaloplasty with suprachoroidal drainage in a retrospective comparative study of 417 eyes (p value not statistically significant). ⁴

Transient IOP spike of more than 10 mmHg was reported as an 'early complication' (time not specified) in 6% (12/214) of eyes in a case series of 224 patients treated by canaloplasty. ⁷

Hyphaema

IP overview: Ab externo canaloplasty for primary open-angle glaucoma

Gross hyphaema was reported in 2% to 6% of eyes in the review of 914 eyes treated by canaloplasty alone (n=777 eyes) or canaloplasty combined with phacoemulsification (n=137 eyes).¹

Hyphaema (greater than 1-mm layered blood) was reported in 23% (7/30) of patients treated by canaloplasty and in 1 patient treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients (p=0.02).²

Hyphaema was reported in 93% (27/29) of patients (59% had blood in the anterior chamber and 34% had erythrocytes in the anterior chamber [microhyphaema]) treated by phacocanaloplasty and in none of the patients treated by phaco-non-penetrating deep sclerectomy in an RCT of 59 patients; all cases resolved within 2 weeks without treatment.³

Hyphaema was reported in 34% (61/180) of patients treated by canaloplasty alone and in 34% (80/237) of patients treated by canaloplasty with suprachoroidal drainage in a retrospective comparative study of 417 eyes (p value not statistically significant).⁴

Hyphaema was reported in 28% (10/36) of patients in the phacocanaloplasty group and in none of the patients in the trabeculectomy group in the retrospective comparative study of 77 patients 1 day after the procedure.⁶

Hyphaema was reported in 22% (47/214) of eyes in the case series of 224 patients, within 90 days of the procedure.⁷

Hyphaema was reported statistically significantly more frequently in the canaloplasty group (n=100) than in the trabeculectomy group (n=115) at 1-year follow-up, in a systematic review and meta-analysis comparing of 215 eyes (OR 8.80, 95% CI 2.25 to 34.51).⁹

Descemet's membrane complications

Descemet's membrane detachment

Descemet's membrane detachment was reported in 2% to 6% of eyes in the review of 914 eyes at a maximum of 36 months follow-up.¹

Descemet's membrane detachment causing an intracorneal haematoma was reported in 1 patient treated by canaloplasty and in none of the patients treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients.²

Descemet's membrane detachment was reported in 1 patient out of 29 treated by phacocanaloplasty and in none of the patients treated by phaco-non-penetrating deep sclerectomy within 13-month follow-up in the RCT of 59 patients (p=0.313); it resolved without treatment.³

Descemet's membrane detachment was reported in 1 out of 36 patients in the phacocanaloplasty group and in none of the patients in the trabeculectomy group in the retrospective comparative study of 77 patients, 1 day after the procedure. ⁶

Descemet's membrane detachment was reported in 5% (11/214) of eyes in the case series of 224 patients, within 90 days of the procedure. ⁷

Descemet's membrane detachment was reported in 10% (10/105) of eyes in a retrospective case series of 92 patients; 3/10 were non-haemorrhagic and 7/10 were haemorrhagic. The non-haemorrhagic Descemet membrane detachment eyes resolved completely within 2 weeks without intervention. One eye with haemorrhagic Descemet membrane detachment was treated with 15% sulphur hexafluoride intracameral injection after 2 weeks. The patient developed a dense corneal stain that resolved after 30 months. Another eye with haemorrhagic Descemet membrane detachment underwent YAG laser membranotomy after 2 weeks, which regained corneal transparency 1 month after treatment. The remaining 5 eyes with haemorrhagic Descemet membrane detachment underwent immediate surgical drainage and regained corneal transparency 1 day after the procedure. ⁸

Descemet's membrane detachment reporting was not statistically significantly different between groups in the systematic review and meta-analysis of 215 eyes (OR 4.49, 95% CI 0.72 to 27.82).⁹

Perforation of Descemet's membrane

Microperforation of Descemet's membrane during the procedure was reported in 7% (2/30) of patients treated by canaloplasty in the RCT of 62 patients comparing canaloplasty (n=30) with trabeculectomy (n=32). ²

Descemet's membrane rupture

Trabeculo Descemet's membrane rupture was reported in 1 patient in each group during the procedure in the RCT of 59 patients treated by phaco-canaloplasty (n=29) or phaco-non-penetrating deep sclerectomy (n=30, p=0.981). ³

Hypotony/anterior chamber collapse

Flat anterior chamber was reported in 0% to 2% of eyes in the review of 914 eyes, and persistent hypotony was reported in 0% to 1% of eyes. ¹

Hypotony (IOP of less than 5 mmHg) was reported in 20% (6/30) of patients treated by canaloplasty and in 38% (12/32) of patients treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients (p=0.17). ²

Hypotony within 7 days of the procedure was reported in 28% (8/29) of patients treated by phacocanaloplasty and in 30% (9/30) of patients treated by phaco-non-penetrating deep sclerectomy in the RCT of 59 patients (p=0.879); rates

decreased to 17% (5/29) and 10% (3/30) respectively after 1 week and up to 30 days after the procedure ($p=0.477$). After 30 days and up to 180 days, no hypotony was reported in either group. ³

Transient hypotony was reported in 6% (11/180) of patients treated by canaloplasty alone and in 5% (13/237) of patients treated by canaloplasty with suprachoroidal drainage in a retrospective comparative study of 417 eyes (p value not statistically significant). ⁴

Hypotony of less than 5 mmHg was reported in 10% (21/214) of eyes in the case series of 224 patients, within 90 days of the procedure. ⁷

Hypotony was reported statistically significantly less frequently in the canaloplasty group in the systematic review and meta-analysis of 215 eyes (OR 0.36, 95% CI 0.13 to 0.99). ⁹

Shallow anterior chamber reporting was not statistically significantly different between groups in the systematic review and meta-analysis of 215 eyes (OR 0.32, 95% CI 0.05 to 2.14). ⁹

Central retinal artery occlusion

Central retinal artery occlusion was reported in 1 out of 36 patients in the phaco-canaloplasty group and in none of the patients in the trabeculectomy group in the retrospective comparative study of 77 patients. ⁶

Ocular decompression retinopathy

Ocular decompression retinopathy was reported in a single case report 1 day after canaloplasty. It was treated with tobramycin and dexamethasone. Three months after canaloplasty, IOP remained in control at 16 mmHg and all retinal haemorrhages had completely resolved. ⁸

Choroidal detachment

Choroidal detachment was reported in 3% (1/30) of patients treated by canaloplasty and in 13% (4/32) of patients treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients ($p=0.36$). ²

Choroidal detachment was reported in 7% (2/29) of patients who had phaco-canaloplasty and in none of the patients who had phaco-non-penetrating deep sclerectomy, in the RCT of 59 patients ($p=0.157$). ³

Choroidal effusion was reported in 1 patient in each group in the retrospective comparative study of 77 patients treated by phacocanaloplasty ($n=36$) or phacotrabeulectomy ($n=41$). ⁶

Choroidal effusion was reported statistically significantly less frequently in the canaloplasty group than in the trabeculectomy group, in the systematic review and meta-analysis of 215 eyes (OR 0.12, 95% CI 0.03 to 0.48).⁹

Cataract formation

Cataract formation was reported in 0% to 8% of eyes in the review of 914 eyes at a maximum of 36 months follow-up.¹

Synechiae

Anterior synechiae during the procedure was reported in 1 patient treated by canaloplasty in the RCT of 62 patients. It was treated by surgical peripheral iridotomy.²

Conjunctival leak

Conjunctival leak was reported in 10% (3/30) of patients treated by canaloplasty and in 9% (3/32) of patients treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients ($p=1$).²

Aqueous leakage from the conjunctival flap was reported in less than 1% (2/214) of eyes in the case series of 224 patients, within 90 days of the procedure.⁷

Corneal erosion

Corneal erosion was reported in 1 patient treated by canaloplasty and in 44% (14/32) of patients treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients ($p<0.001$).²

Bleb formation

Bleb formation was reported in 0% to 4% of eyes in the review of 914 eyes.¹

Conjunctival bleb that was clinically detectable was reported in 1% (3/214) of eyes in the case series of 224 patients, within 90 days of the procedure.⁷

Cells in the anterior chamber

Cells in the anterior chamber after the procedure were reported in 2 patients who had phaco-canaloplasty and in 1 patient who had phaco-non-penetrating deep sclerectomy, in the RCT of 59 patients ($p=0.554$).³

Iris incarceration

Iris incarceration was reported in 1 patient in each group in the RCT of 59 patients who had phaco-canaloplasty or phaco-non-penetrating deep sclerectomy ($p=0.981$).³

Suture complications

Suture cheese wiring was reported in 0% to 2% of eyes in the review of 914 eyes. ¹

Secondary suture migration in anterior chamber was reported in 7% (2/30) of patients treated by canaloplasty and in none of the patients treated by trabeculectomy within 90 days of the procedure in the RCT of 62 patients; in 1 patient, suture had to be removed by paracentesis. ²

Suture cheese-wiring through the trabecular meshwork was reported in less than 1% (2/214) of eyes in the case series of 224 patients, within 90 days of the procedure. ⁷

Validity and generalisability of the studies

- Some patients were treated with canaloplasty during cataract surgery, while others had the procedure done as a stand-alone treatment.
- In the studies included in table 2, the longest follow-up was 5 years.⁷
- One case report was included in table 2 because it reported a safety complications that was not reported in the other included studies (ocular decompression retinopathy). ⁸
- The review (study 1) included in table 2 is not a systematic review and does not include a meta-analysis. ¹
- Study 9 is a systematic review with a meta-analysis. ⁹

Existing assessments of this procedure

- A guideline on canaloplasty and viscocanalostomy was published by EmblemHealth in May 2016¹⁰. It stated: “Canaloplasty is considered medically necessary for the treatment of primary open-angle glaucoma to reduce IOP.”
- A guideline on viscocanalostomy and canaloplasty was published by Blue Cross and Blue Shield of Florida in January 2016¹¹. It stated: “Canaloplasty meets the definition of medical necessity as a method to reduce intraocular pressure in individuals with chronic primary open-angle glaucoma under the following conditions:

- Medical therapy has failed to adequately control intraocular pressure, AND
- The individual is not a candidate for any other intraocular pressure lowering procedure (e.g. trabeculectomy or glaucoma drainage implant) due to a high risk for complications.”

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Trabeculectomy ab interno for open angle glaucoma. NICE interventional procedure guidance 397 (2011). Available from <https://www.nice.org.uk/guidance/ipg397>
- Trabecular stent bypass microsurgery for open angle glaucoma. This guidance is currently under review and is expected to be updated in 2017. For more information, see <https://www.nice.org.uk/guidance/ipg396>

NICE guidelines

- Glaucoma: diagnosis and management. NICE guideline 85 (2009). Available from <https://www.nice.org.uk/guidance/cg85>

Specialist advisers’ opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for ab externo canaloplasty for primary open-angle glaucoma were submitted and can be found on the [NICE website](#).

Patient commentators’ opinions

NICE’s Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has

received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 1 company who manufactures a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Potential short-term impact of phacoemulsification alone on IOP makes evaluating the efficacy of the procedure difficult.
- In 4 of the studies included in table 2, there were patients with primary open-angle glaucoma as well as patients with other types of open-angle glaucoma^{3, 4, 6, 7}.
- Patients considered in the studies included in table 2 were either treated for uncontrolled glaucoma or for uncontrolled IOP while on maximum glaucoma medication (for the studies in which the criteria for inclusion were reported).
- Primary open-angle glaucoma is 3 to 4 times more common in people of African-Caribbean family origin in whom it tends to present earlier and is more severe. However, in the only study included in table 2 where ethnicity was reported, all patients were white.²

References

1. Brandao Livia M, and Grieshaber Matthias C (2013) Update on Minimally Invasive Glaucoma Surgery (MIGS) and New Implants. *Journal of ophthalmology* 705915
2. Matlach Juliane, Dhillon Christine, Hain Johannes, Schlunck Gunther, Grehn Franz, and Klink Thomas (2015) Trabeculectomy versus canaloplasty (TVC study) in the treatment of patients with open-angle glaucoma: a prospective randomized clinical trial. *Acta Ophthalmologica* 93(8), 753-61
3. Rekas M, Byszewska A, Petz K, Wierzbowska J, and Junemann A (2015) Canaloplasty versus non-penetrating deep sclerectomy - a prospective, randomised study of the safety and efficacy of combined cataract and glaucoma surgery; 12-month follow-up. *Graefes Archive for Clinical & Experimental Ophthalmology* 253(4), 591-9
4. Seuthe Anna-Maria, Ivanescu Ciprian, Leers Stephan, Boden Karl, Januschowski Kai, and Szurman Peter (2016) Modified canaloplasty with suprachoroidal drainage versus conventional canaloplasty-1-year results. *Graefes Archive for Clinical & Experimental Ophthalmology* 254(8), 1591-7
5. Klink Thomas, Sauer Johannes, Korber Norbert J, Grehn Franz, Much Martin M, Thederan Luisa, Matlach Juliane, and Salgado Josefina Parente (2015) Quality of life following glaucoma surgery: canaloplasty versus trabeculectomy. *Clinical Ophthalmology* 9, 7-16
6. Schoenberg E D, Chaudhry A L, Chod R, Zurakowski D, and Ayyala R S (2015) Comparison of Surgical Outcomes Between Phacocanaloplasty and Phacotrabeculectomy at 12 Months' Follow-up: A Longitudinal Cohort Study. *Journal of Glaucoma* 24(7), 543-9
7. Brusini P (2014) Canaloplasty in open-angle glaucoma surgery: a four-year follow-up. *TheScientificWorldJournal* 2014, 469609
8. Li G Y, Alantaree S, Wang J M, and Zhang H (2016) Ocular decompression retinopathy following canaloplasty for primary open angle glaucoma: A case report. *Medicine (United States)* 95 (9) (no pagination)(e2907)
9. Lin Z-J, Xu S, Huang S-Y et al. (2016) Comparison of canaloplasty and trabeculectomy for open angle glaucoma: a meta-analysis. *International Journal of Ophthalmology* 9(12):1814-1819.
10. EmblemHealth guideline on canaloplasty and viscocanalostomy. Published on 13 May 2016.
http://www.emblemhealth.com/~media/Files/PDF/ med_guidelines/MG_Canaloplasty_and_Viscocanalostomy.pdf
11. Blue Cross and Blue Shield of Florida guideline on viscocanalostomy and canaloplasty. Published on 10 January 2016.
<http://mcgs.bcbsfl.com/?doc=Viscocanalostomy%20and%20Canaloplasty>

Appendix A: Additional papers on ab externo canaloplasty for primary open-angle glaucoma

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Alobeidan Saleh A, and Almobarak Faisal A (2016) Incidence and management of haemorrhagic Descemet membrane detachment in canaloplasty and phacocanaloplasty. <i>Acta Ophthalmologica</i> 94(5), e298-304	Retrospective case series n=92 FU= 1 year	Haemorrhagic Descemet membrane detachment occurred in up to 7% in canaloplasty and phacocanaloplasty procedures, mostly during catheter withdrawal and the viscodilation step. Early recognition and management prevented further manipulation.	Larger studies or studies with longer follow-up are already included in table 2.
Arthur S N, Cantor L B, WuDunn D, Pattar G R, Catoira-Boyle Y, Morgan L S, and Hoop J S (2014) Efficacy, safety, and survival rates of IOP-lowering effect of phacoemulsification alone or combined with canaloplasty in glaucoma patients. <i>Journal of Glaucoma</i> 23(5), 316-20	Retrospective comparative study n=69 (32 phacocanaloplasty versus 37 phacoemulsification alone) FU=19 months	A combination of canaloplasty with phaco results in a decreased number of glaucoma medications and increased survival rate of IOP-lowering effect compared with phaco alone.	Larger studies or studies with longer follow-up are already included in table 2.
Ayyala R S, Chaudhry A L, Okogbaa C B, and Zurakowski D (2011) Comparison of surgical outcomes between canaloplasty and trabeculectomy at 12 months' follow-up. <i>Ophthalmology</i> 118(12), 2427-33	Retrospective comparative study n=79 (33 canaloplasty versus 46 trabeculectomy) FU=1 year	Canaloplasty and trabeculectomy both achieved significant reduction in IOP at 12 months.	Study already included in the Brandao (2013) review.
Barnebey H S (2013) Canaloplasty with intraoperative low dosage mitomycin C: a retrospective case series. <i>Journal of Glaucoma</i> 22(3), 201-4	Retrospective case series n=20 FU=1 year	The adjunctive use of MMC in canaloplasty is safe and effective.	Larger studies or studies with longer follow-up are already included in table 2.
Brandao L M, Orgul S, and Grieshaber M C (2014) Hemorrhagic descemet membrane detachment after classic canaloplasty. <i>Klinische Monatsblätter für Augenheilkunde</i> 231(4), 348-50	Case report n=2 FU= 9 months	Circumferential cannulation and viscodilation of the Schlemm canal increases the risk for DMD, which may be aggravated by blood reflux resulting from the tensioning suture and low postoperative IOP. Surgeons should be aware of this specific and potentially sight-threatening complication in classic canaloplasty. Immediate intervention is recommended for good visual prognosis.	Complication already reported in table 2.

<p>Bruggemann A, Despouy J T, Wegent A, and Muller M (2013) Intraindividual comparison of Canaloplasty versus trabeculectomy with mitomycin C in a single-surgeon series. <i>Journal of Glaucoma</i> 22(7), 577-83</p>	<p>Retrospective comparative study n=30 eyes (15 canaloplasty versus 15 trabeculectomy) FU=1 year</p>	<p>Canaloplasty and trabeculectomy were both effective in lowering IOP. However, less follow-up visits and significantly fewer complications and interventions were favorable for canaloplasty.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Brusini Paolo, Caramello Guido, Benedetti Stefano, and Tosoni Claudia (2016) Canaloplasty in Open-angle Glaucoma: Mid-term Results From a Multicenter Study. <i>Journal of Glaucoma</i> 25(5), 403-7</p>	<p>Prospective case series n=178 (198 eyes) FU=3 to 42 months</p>	<p>Canaloplasty is a quite difficult surgical technique; however, mid-term results are promising. Complications can sometimes occur, but are seldom serious. The main advantage of this promising bleb-less procedure is that physiological humor aqueous outflow is restored.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Brusini P, and Tosoni C (2014) Canaloplasty after failed trabeculectomy: a possible option. <i>Journal of Glaucoma</i> 23(1), 33-4</p>	<p>Case series n=6 FU=6-28 months</p>	<p>Canaloplasty can be considered as a possible surgical option in eyes with failed trabeculectomy showing undamaged Schlemm's canal from previous filtering surgery.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Bull H, von Wolff , K , Korber N, and Tetz M (2011) Three-year canaloplasty outcomes for the treatment of open-angle glaucoma: European study results. <i>Graefes Archive for Clinical & Experimental Ophthalmology</i> 249(10), 1537-45</p>	<p>Prospective case series n=109 FU=3 years</p>	<p>Canaloplasty demonstrated significant and sustained IOP reductions accompanied by an excellent short- and long-term safety profile in adult patients with open-angle glaucoma.</p>	<p>Study already included in the Brandao (2013) review.</p>
<p>Cagini Carlo, Peruzzi Claudia, Fiore Tito, Spadea Leopoldo, Lippera Myrta, and Lippera Stefano (2016) Canaloplasty: Current Value in the Management of Glaucoma. <i>Journal of ophthalmology</i> 2016, 7080475</p>	<p>Review</p>	<p>The main advantage of canaloplasty is that this technique avoids the major complications of fistulating surgery related to blebs and hypotony. Currently, canaloplasty is performed in glaucoma patients with early to moderate disease and combination with cataract surgery is a suitable option in patients with clinically significant lens opacities.</p>	<p>The results of the studies included in the review were not synthesised.</p>

Freiberg F J, Parente Salgado, J , Grehn F, and Klink T (2012) Intracorneal hematoma after canaloplasty and clear cornea phacoemulsification: surgical management. European Journal of Ophthalmology 22(5), 823-5	Single case report FU=6 months	Case report of intracorneal haematoma after canaloplasty and clear cornea phacoemulsification. It was removed through a clear corneal tunnel. Six months postoperatively, BCVA was 20/25 in the right eye. The IOP with one medication was 17 mmHg.	Complication already reported in table 2.
Fujita Kazuya, Kitagawa Kiyotaka, Ueta Yoshiki, Nakamura Tomoko, Miyakoshi Akio, and Hayashi Atsushi (2011) Short-term results of canaloplasty surgery for primary open-angle glaucoma in Japanese patients. Case Reports in Ophthalmology 2(1), 65-8	Case series n=9 FU=1 year	Canaloplasty may be an alternative surgery for POAG patients to reduce IOP to a value of approximately 15 mm Hg.	Larger studies or studies with longer follow-up are already included in table 2.
Gandolfi Stefano A, Ungaro Nicola, Ghirardini Stella, Tardini Maria Grazia, and Mora Paolo (2016) Comparison of Surgical Outcomes between Canaloplasty and Schlemm's Canal Scaffold at 24 Months' Follow-Up. Journal of ophthalmology 2016, 3410469	Retrospective comparative study n=45 (24 canaloplasty versus 21 microstent) FU=2 years	Both CP and HM implant allowed significant IOP reductions, with comparable rate of clinical success and safety profile. A slightly (albeit not significant) better trend for a "complete" clinical success was observed in the CP group.	Larger studies or studies with longer follow-up are already included in table 2.
Grieshaber MC, Schoetzau A, Grieshaber HR, and Stegmann R (2017) Canaloplasty with Stegmann Canal Expander for primary open-angle glaucoma: two-year clinical results. Acta Ophthalmol. doi: 10.1111/aos.13372	Prospective case series n=42 FU=2 years	Canaloplasty with the Stegmann Canal Expander was a safe and effective procedure to reduce IOP in White patients with moderate to advanced POAG.	Larger studies or studies with longer follow-up are already included in table 2.
Grieshaber Matthias C, Grieshaber Hans R, and Stegmann Robert (2016) A New Expander for Schlemm Canal Surgery in Primary Open-angle Glaucoma- Interim Clinical Results. Journal of Glaucoma 25(8), 657-62	Prospective case series n=22 FU=1 year	Implantation of the Stegmann Canal Expander in canaloplasty lowered IOP significantly in POAG without complications related to the device in this 1-year observation period.	Larger studies or studies with longer follow-up are already included in table 2.

Grieshaber M C, Schoetzau A, Flammer J, and Orgul S (2013) Postoperative microhyphema as a positive prognostic indicator in canaloplasty. Acta Ophthalmologica 91(2), 151-6	Prospective case series n=51 FU=21 months	Microhyphema the first postoperative day seems to be a significant positive prognostic indicator in uneventful canaloplasty in regard to IOP reduction, possibly representing a restored and patent physiologic aqueous outflow system.	Larger studies or studies with longer follow-up are already included in table 2.
Grieshaber M C, Fraenkl S, Schoetzau A, Flammer J, and Orgul S (2011) Circumferential viscocanalostomy and suture canal distension (canaloplasty) for whites with open-angle glaucoma. Journal of Glaucoma 20(5), 298-302	Prospective case series n=32 FU >1 year	Canaloplasty seems to be a promising and effective surgical procedure in Whites with OAG. Postoperative IOP levels are in the low-to-mid-teens. The procedure can be regarded as safe, but has its own profile of complications.	Study already included in the Brandao (2013) review.
Grieshaber M C, Pienaar A, Olivier J, and Stegmann R (2010) Canaloplasty for primary open-angle glaucoma: long-term outcome. British Journal of Ophthalmology 94(11), 1478-82	Prospective case series n=60 FU=31 months	Canaloplasty produced a sustained long-term reduction of IOP in black Africans with POAG independent of preoperative IOP. As a bleb-independent procedure, canaloplasty may be a true alternative to classic filtering surgery, in particular in patients with enhanced wound healing and scar formation.	Study already included in the Brandao (2013) review.
Grieshaber M C, Pienaar A, Olivier J, and Stegmann R (2010) Clinical evaluation of the aqueous outflow system in primary open-angle glaucoma for canaloplasty. Investigative Ophthalmology & Visual Science 51(3), 1498-504	Case series n=28 FU=6 months	High mean IOP may be associated with poor blood reflux and filling of SC. A collapsed canal, probably secondary to high IOP, may be an underestimated sign in black African patients with POAG. The quality of blood reflux and episcleral venous egress may both be predictive of the level of IOP after surgery.	Larger studies or studies with longer follow-up are already included in table 2.
Grieshaber M C, Pienaar A, Olivier J, and Stegmann R (2010) Comparing two tensioning suture sizes for 360 degrees viscocanalostomy (canaloplasty): a randomised controlled trial. Eye 24(7), 1220-6	RCT n=90 (45 with 6-0 Prolene suture versus 45 with 10-0 Prolene suture) FU=15 months	IOP reduction was substantial in canaloplasty and slightly greater in combination with 10-0 Prolene than 6-0 Prolene sutures at an equally low complication rate. Younger age, but not the level of IOP at surgery, had a positive effect on the amount of IOP reduction, thus suggesting that an early surgical intervention to re-establish physiological outflow offers the best prognosis.	RCT comparing 2 tensioning suture sizes. It is included in the Brandao (2013) review.

<p>Hamid M, Thompson P, and Harasymowycz P (2015) Novel Treatment for Hemorrhagic Descemet Detachment After Canaloplasty. <i>Cornea</i> 34(12), 1611-2</p>	<p>Single case report FU=3 months</p>	<p>Hemorrhagic Descemet detachment is a rare and serious complication of canaloplasty. The use of pre-Descemet TPA dissolves the intracorneal blood clot and helps reattach Descemet membrane, allowing quick rehabilitation of patient's vision and preserving integrity of the cornea.</p>	<p>Complication already reported in table 2.</p>
<p>Ichihashi Tsunetomo, Suzuki Yasuyuki, Nagahara Miyuki, and Kawai Kenji (2015) A Case of Open-Angle Glaucoma Successfully Treated Using Canaloplasty. <i>Tokai Journal of Experimental & Clinical Medicine</i> 40(4), 157-60</p>	<p>Single case report FU=4 years</p>	<p>There were no complications either during or after the surgery. The IOP values at 2 weeks, 1 month, 6 months, 1 year, 2 years, 3 years, and 4 years were, 13, 14, 18, 12, 10, 12, and 8 mmHg, respectively. No deteriorations in visual field or reductions in visual acuity were detected during this follow-up. There were no long-term complications such as cataract formation or exposure of the suture. Spectral domain optical coherence tomography showed that the trabecular meshwork was inwardly distended because of the intracanalicular suture in the affected eye.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Jaramillo A, Foreman J, and Ayyala R S (2014) Descemet membrane detachment after canaloplasty: incidence and management. <i>Journal of Glaucoma</i> 23(6), 351-4</p>	<p>Case series n=115 patients (162 eyes) FU=1 year</p>	<p>DMD with or without intracorneal hemorrhage is not an infrequent complication of canaloplasty and can occasionally lead to corneal decompensation.</p>	<p>Complication already reported in table 2. Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Klink T, Panidou E, Kanzow-Terai B, Klink J, Schlunck G, and Grehn F J (2012) Are there filtering blebs after canaloplasty?. <i>Journal of Glaucoma</i> 21(2), 89-94</p>	<p>Case series n=20 FU=245 days</p>	<p>Filtering blebs occur rarely after canaloplasty. In canaloplasty, IOP reduction seems to be independent of subconjunctival aqueous drainage, thus, avoiding the problems of conjunctival scarring.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>

<p>Koerber N J (2012) Canaloplasty in one eye compared with viscocanalostomy in the contralateral eye in patients with bilateral open-angle glaucoma. Journal of Glaucoma 21(2), 129-34</p>	<p>Comparative case series n=15 (30 eyes, 15 canaloplasty in 1 eye versus 15 viscocanalostomy in contralateral eye) FU=18 months</p>	<p>Canaloplasty and viscocanalostomy were safe and effective in the surgical management of open-angle glaucoma. Canaloplasty procedures showed superior efficacy to viscocanalostomy in the reduction of IOP (P=0.02) and both procedures demonstrated excellent safety profiles.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Lewis R A, von Wolff , K , Tetz M, Koerber N, Kearney J R, Shingleton B J, and Samuelson T W (2011) Canaloplasty: Three-year results of circumferential viscodilation and tensioning of Schlemm canal using a microcatheter to treat open-angle glaucoma. Journal of Cataract & Refractive Surgery 37(4), 682-90</p>	<p>Case series n=157 eyes FU=3 years</p>	<p>Canaloplasty led to a significant and sustained IOP reduction in adult patients with open-angle glaucoma and had an excellent short- and long-term postoperative safety profile.</p>	<p>Study already included in the Brandao (2013) review.</p>
<p>Lewis R A, von Wolff , K , Tetz M, Koerber N, Kearney J R, Shingleton B J, and Samuelson T W (2009) Canaloplasty: circumferential viscodilation and tensioning of Schlemm canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults: two-year interim clinical study results. Journal of Cataract & Refractive Surgery 35(5), 814-24</p>	<p>Case series n=127 FU=2 years</p>	<p>Canaloplasty was safe and effective in reducing IOP in adult patients with OAG.</p>	<p>Study already included in the Brandao (2013) review.</p>
<p>Lewis RA, Von Wolff K, Tetz M et al. (2007) Canaloplasty: circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults. Journal of Cataract and Refractive Surgery 33: 1217–26.</p>	<p>Case series n=94 FU= 1 year</p>	<p>Circumferential viscodilation and tensioning of Schlemm's canal was a safe and effective surgical procedure to reduce IOP in adult patients with OAG.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2. This study was included in the previous overview.</p>

<p>Lopes-Cardoso I, Esteves F, Amorim M, Calvao-Santos G, Freitas M L, and Salgado-Borges J (2013) Circumferential viscocanalostomy with suture tensioning in Schlemm canal (canaloplasty)-one year experience. [Spanish]. Archivos de la Sociedad Espanola de Oftalmologia 88(6), 207-215</p>	<p>Case series n=35 FU=1 year</p>	<p>Ultrasound biomicroscopy assisted Canaloplasty, alone or combined, provided a sustained IOP reduction to medium-low levels, led to a decrease in the number of drugs and had a good safety profile, making this a good alternative to trabeculectomy.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Mansouri K, and Shaarawy T (2015) Update on Schlemm's canal based procedures. Middle East African journal of ophthalmology 22(1), 38-44</p>	<p>Review n=20 studies FU=9 to 36 months</p>	<p>Canaloplasty alone and combined with phacoemulsification has been shown to lower IOP by 40% in numerous studies/ The lack of comparative phacoemulsification alone group in the canaloplasty studies is a limitation of the available evidence. The safety profile is favourable, although comparative RCTs to trabeculectomy are lacking.</p>	<p>Another review is already included in Table 2. The reporting of the frequency of the safety complications is not exhaustive.</p>
<p>Mastropasqua L, Agnifili L, Salvatà M L, Ciancaglini M, Fasanella V, Nubile M, Mastropasqua R, Zeppieri M, and Brusini P (2012) In vivo analysis of conjunctiva in canaloplasty for glaucoma. British Journal of Ophthalmology 96(5), 634-9</p>	<p>Case series n=30 FU=12 weeks</p>	<p>Conjunctival microcysts were evident in all glaucomatous eyes prior to surgery, and tended to increase in density and surface area after successful canaloplasty. These findings indicated enhanced aqueous humor filtration across the sclera and conjunctiva after canaloplasty.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Matlach J, Freiberg F J, Leippi S, Grehn F, and Klink T (2013) Comparison of phacotrabeculectomy versus phacocanaloplasty in the treatment of patients with concomitant cataract and glaucoma. BMC Ophthalmology 13, 1</p>	<p>Retrospective comparative study n=39 eyes (19 phacocanaloplasty versus 20 phacotrabeculectomy) FU=1 year</p>	<p>Phacocanaloplasty offers a new alternative to phacotrabeculectomy for treatment of concomitant glaucoma and cataract, although phacotrabeculectomy yielded in better results in terms of IOP maintained without glaucoma medications.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>

Moelle M C, Cursiefen C, Rejda R, Horn F K, and Junemann A G (2014) Time course of induced astigmatism after canaloplasty. Journal of Glaucoma 23(1), e53-9	Retrospective case series n=26 FU=6 months	The change of astigmatism after canaloplasty follows a clear time course with a maximum at 2 weeks reaching preoperative values at 6 months. The amount of surgically induced astigmatism might be helpful to predict outcome of canaloplasty in terms of IOP reduction.	Larger studies or studies with longer follow-up are already included in table 2.
Palmiero P M, Aktas Z, Lee O, Tello C, and Sbeity Z (2010) Bilateral Descemet membrane detachment after canaloplasty. Journal of Cataract & Refractive Surgery 36(3), 508-11	Single case report FU=3 months	Case report of a bilateral Descemet membrane detachment after canaloplasty. It resolved without treatment at 3 months.	Complication already reported in table 2.
Paulaviciute-Baikstiene Daiva, Vaiciuliene Renata, Jasinskas Vytautas, and Januleviciene Ingrida (2016) Evaluation of Outflow Structures In Vivo after the Phacocanaloplasty. Journal of ophthalmology 2016, 4519846	Case series n=9 (10 eyes) FU=1 year	The results showed statistically significant dilation of SC area and reduction of TM thickness after phacocanaloplasty in POAG patients. The degree of SC expansion was related to the IOP decrease.	Larger studies or studies with longer follow-up are already included in table 2.
Rekas Marek, Danielewska Monika E, Byszewska Anna, Petz Katarzyna, Wierzbowska Joanna, Wierzbowski Robert, and Iskander D Robert (2016) Assessing Efficacy of Canaloplasty Using Continuous 24-Hour Monitoring of Ocular Dimensional Changes. Investigative Ophthalmology & Visual Science 57(6), 2533-42	Case series n=10 FU=1 year	Canaloplasty alone or combined with cataract surgery is a successful surgical method of lowering IOP in glaucoma patients. Canaloplasty decreases 24-hour CSLA fluctuation pattern measured with CLS.	Larger studies or studies with longer follow-up are already included in table 2.
Rekas M, Petz K, Wierzbowska J, Byszewska A, and Junemann A (2014) Evacuating a pre-Descemet hematoma through a clear corneal incision during a canaloplasty procedure. Journal of Cataract & Refractive Surgery 40(12), 1953-7	Single case report FU=4 months	Case report of a technique to evacuate pre-Descemet haematoma through a clear corneal incision during canaloplasty. The CDVA was 20/20 at 3 weeks and remained stable over a 4-month follow-up. The IOP was 16 mm Hg without medication and was also stable.	Complication already reported in table 2.

Robert M C, and Harasymowycz P (2013) Hemorrhagic descemet detachment after combined canaloplasty and cataract surgery. Cornea 32(5), 712-3	Single case report FU=4 years	Hemorrhagic Descemet detachment is an uncommon complication after canaloplasty. Nd:YAG Descemet membranotomy is a successful means of clearing the hematoma and thus can prevent further complications, such as corneal blood staining.	Complication already reported in table 2.
Rossetti A, Koerber N, and Doro D (2013) Intracorneal blood removal six weeks after canaloplasty. Indian Journal of Ophthalmology 61(5), 232-4	Single case report FU=1 year	Case report of intracorneal blood removal 6 weeks after canaloplasty. After 2 months, visual acuity recovered to 20/50 and IOP was 16 mmHg without medication.	Complication already reported in table 2.
Rulli E, Biagioli E, Riva I, Gambirasio G, De Simone I, Floriani I, and Quaranta L (2013) Efficacy and safety of trabeculectomy vs nonpenetrating surgical procedures: a systematic review and meta-analysis. JAMA Ophthalmology 131(12), 1573-82	Systematic review and meta-analysis comparing trabeculectomy with nonpenetrating surgical procedures n=1 study for canaloplasty	Trabeculectomy seems to be the most effective surgical procedure for reducing IOP in patients with open-angle glaucoma. However, as expected, it was associated with a higher incidence of complications when compared with NPS.	There was only one study included in this review for canaloplasty (Ayyala 2011).
Shingleton B, Tetz M, and Korber N (2008) Circumferential viscodilation and tensioning of Schlemm canal (canaloplasty) with temporal clear corneal phacoemulsification cataract surgery for open-angle glaucoma and visually significant cataract: one-year results. Journal of Cataract & Refractive Surgery 34(3), 433-40	Prospective case series n=54 eyes FU=1 year	Circumferential viscodilation and tensioning of Schlemm canal combined with clear corneal phacoemulsification and posterior chamber IOL implantation was a safe and effective procedure to reduce IOP in adult patients with OAG.	Larger studies or studies with longer follow-up are already included in table 2.
Sluch I and Bailey A (2017) Hemorrhagic Descemet membrane detachment after canaloplasty. JAMA Ophthalmology.	Single case report FU=1 month	Case report of a haemorrhagic Descemet membrane detachment after canaloplasty.	Complication already reported in table 2.

<p>Szurman Peter, Januschowski Kai, Boden Karl Thomas, and Szurman Gesine Bettina (2016) A modified scleral dissection technique with suprachoroidal drainage for canaloplasty. Graefes Archive for Clinical & Experimental Ophthalmology 254(2), 351-4</p>	<p>Retrospective case series</p> <p>n=78 eyes</p> <p>FU=1 year</p>	<p>The modified dissection canaloplasty technique potentially improves the IOP-lowering effect due to the creation of additional suprachoroidal drainage and simplifies the most complicated step of the surgery, as the scleral spur and the Schlemm's canal can be located using suprachoroidal access.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2.</p>
<p>Tetz M, Koerber N, Shingleton B J, von Wolff , K , Bull H, Samuelson T W, and Lewis R A (2015) Phacoemulsification and intraocular lens implantation before, during, or after canaloplasty in eyes with open-angle glaucoma: 3-year results. Journal of Glaucoma 24(3), 187-94</p>	<p>Retrospective subset analysis of a prospective case series</p> <p>n=133 (82 canaloplasty alone versus 51phacocanaloplasty)</p> <p>FU=3 years</p>	<p>Clear corneal phacoemulsification performed before or in combination with canaloplasty is a safe and effective surgical procedure to reduce IOP in adult patients with open-angle glaucoma.</p>	<p>This is a subset analysis of the Lewis (2011) study which is included in the Brandao (2013) review.</p>
<p>Xin C, Chen X, Shi Y, Wang H, and Wang N (2016) Modified Canaloplasty: A New, Effective, and Safe Option for Glaucoma Patients With a Disrupted Schlemm Canal Wall. J Glaucoma</p>	<p>Prospective cohort study</p> <p>n=26 (17 without history of glaucoma surgery versus 9 with failed glaucoma surgery and disrupted Schlemm canal)</p> <p>FU=1 year</p>	<p>Modified canaloplasty is a feasible, safe, and potentially effective option for patients with POAG and regions of SC disruption resulting from previous glaucoma-filtering surgery.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2. No new safety</p>
<p>Xin C, Chen X, Shi Y, Li M, Wang H, and Wang N (2016) One-year interim comparison of canaloplasty in primary open-angle glaucoma following failed filtering surgery with primary canaloplasty. Br J Ophthalmol</p>	<p>Prospective comparative study.</p> <p>n=60 eyes (37 canaloplasty in patients with failed glaucoma filtration surgery [GFS] versus 23 without failed GFS)</p> <p>FU=18 months</p>	<p>Canaloplasty is an effective and safe option for primary open-angle glaucoma with failed GFS.</p>	<p>Larger studies or studies with longer follow-up are already included in table 2. No new safety complication reported.</p>

Appendix B: Related NICE guidance for ab externo canaloplasty for primary open-angle glaucoma

Guidance	Recommendations
Interventional procedures	<p>Canaloplasty for primary open-angle glaucoma. NICE interventional procedure guidance 260 (2008). [Current guidance]</p> <p>1.1 Current evidence on the safety and efficacy of canaloplasty for primary open-angle glaucoma is inadequate in both quality and quantity. Therefore, this procedure should only be used in the context of research or formal prospective data collection. Clinicians are encouraged to collaborate in the collection and publication of data.</p> <p>1.2 Further publication of safety and efficacy outcomes will be useful. The Institute may review the procedure upon publication of further evidence.</p> <p>Trabeculotomy ab interno for open angle glaucoma. NICE interventional procedure guidance 397 (2011).</p> <p>1.1 Current evidence on the safety and efficacy of trabeculotomy ab interno for open angle glaucoma is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.</p> <p>1.2 Patient selection should be carried out in units that specialise in glaucoma treatment that can offer a range of treatment options.</p> <p>11.3 NICE encourages the collection and publication of further data on long-term efficacy.</p> <p>Trabecular stent bypass microsurgery for open angle glaucoma. This guidance is currently under review and is expected to be updated in 2017.</p> <p><u>Draft recommendations</u></p> <p>1.1 Current evidence on the safety of trabecular stent bypass microsurgery for open-angle glaucoma raises no major safety concerns. Evidence on efficacy is adequate in quality and quantity. Therefore, this procedure may be used provided that standard arrangements are in place for clinical governance, consent and audit.</p>

	<p>1.2 Trabecular stent bypass microsurgery for open-angle glaucoma should only be done by clinicians with specific training in the procedure.</p> <p><u>Existing recommendations</u></p> <p>1.1 Current evidence on trabecular stent bypass microsurgery for open angle glaucoma raises no major safety concerns. There is evidence of efficacy in the short term but this is based on small numbers of patients. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.</p> <p>1.2 Clinicians wishing to undertake trabecular stent bypass microsurgery for open angle glaucoma should take the following actions.</p> <ul style="list-style-type: none"> • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/guidance/IPG396/publicinfo). • Audit and review clinical outcomes of all patients having trabecular stent bypass microsurgery for open angle glaucoma (see section 3.1). <p>1.3 Trabecular stent bypass microsurgery for open angle glaucoma should only be carried out by clinicians with specific training in the procedure.</p> <p>1.4 NICE encourages the publication of further evidence on long-term efficacy and any occurrence of device extrusion.</p>
NICE guidelines	<p>Glaucoma: diagnosis and management. NICE guideline 85 (2009).</p> <p>1.4.6 Check the person's adherence to their treatment and eye drop instillation technique in people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss despite pharmacological treatment.</p>

	<p>If adherence and eye drop instillation technique are satisfactory offer one of the following:</p> <ul style="list-style-type: none"> • alternative pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); more than one agent may be needed concurrently to achieve target IOP • laser trabeculoplasty • surgery with pharmacological augmentation (MMC or 5-FU1) as indicated <p>If the pharmacological treatment option is chosen, after trying two alternative pharmacological treatments consider offering surgery with pharmacological augmentation (MMC or 5-FU1) as indicated or laser trabeculoplasty.</p> <p>1.4.7 Offer surgery with pharmacological augmentation (MMC or 5-FU1) as indicated to people with COAG who are at risk of progressing to sight loss despite treatment. Offer them information on the risks and benefits associated with surgery.</p> <p>1.4.9 After surgery offer people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss one of the following:</p> <ul style="list-style-type: none"> • pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); more than one agent may be needed concurrently to achieve target IOP • further surgery • laser trabeculoplasty or cyclodiode laser treatment. <p>1.4.10 Offer people with COAG who prefer not to have surgery or who are not suitable for surgery:</p> <ul style="list-style-type: none"> • pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); more than one agent may be needed concurrently to achieve target IOP • laser trabeculoplasty or cyclodiode laser treatment.
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Appendix C: Literature search for ab externo canaloplasty for primary open-angle glaucoma

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	16/08/2016	
HTA database (Cochrane Library)	16/08/2016	
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	16/08/2016	
MEDLINE (Ovid)	16/08/2016	1946 to August Week 1 2016
MEDLINE In-Process (Ovid)	16/08/2016	August 15, 2016
EMBASE (Ovid)	16/08/2016	1974 to 2016 Week 33
PubMed	16/08/2016	n/a
BLIC	16/08/2016	n/a

Trial sources searched on 05/08/2016

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 05/08/2016

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

- 1 canaloplast*.tw.
- 2 (Phaco-viscocalanost* or Phacoviscocalanost*).tw.
- 3 (circumferential adj4 (viscodilat* or cannulat*).tw.
- 4 Viscocalanostomy.tw.

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- 5 (non-penetrat* or nonpenetrat*).tw.
- 6 (non-perforat* or nonperforat*).tw.
- 7 (schlemm* adj4 canal*).tw.
- 8 microcatheter*.tw.
- 9 itrack.tw.
- 10 or/1-9
- 11 Glaucoma, Open-Angle/ or Glaucoma/
- 12 (open adj4 angle adj4 glaucom*).tw.
- 13 glaucom*.tw.
- 14 Ocular Hypertension/
- 15 Intraocular Pressure/
- 16 ((ocular or intraocular or eye*) adj4 (tension or hypertens* or pressur*)).tw.
- 17 IOP.tw.
- 18 or/11-17
- 19 10 and 18
- 20 animals/ not humans/
- 21 19 not 20
- 22 limit 21 to ed=20071022-20160831