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 and updated in June 2017.

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 1 June 2017: 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 2,000 patients who had canaloplasty from 1 review[1], 2 randomised controlled trials[2,3], 3 retrospective comparative studies[4-6], 1 case series[7], 1 case report[8] and 1 systematic review and meta-analysis[9].

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

Number of patients analysed: **914 eyes (777 canaloplasty alone and 137 canaloplasty with phacoemulsification) from 15 studies**

IOP and number of medications

Study	Number of eyes	Follow-up (months)	Mean IOP reduction (mmHg)	Mean IOP reduction (%)	Mean postop. IOP (mmHg)	Mean medication reduction (%)
Canaloplasty alone						
Lewis (2007)	74	12	8.6±0.5	36	16.2±3.5	1.3 (68%)
Lewis (2009)	84	24	6.9±0.1	29	16.3±3.7	1.4 (70%)
Lewis (2011)	103	36	8.6±1.5	34	15.5±3.5	1.0±-0.1
Peckar and Koerber (2011)	97	18	13.1±5.2	48	14.1±3.2	2.4 (76%)
Grieshaber (2010) a	90	15	28.6±7.2	36	16.2±4.9	–
Grieshaber (2010) b	60	36	31.7±6.7	66	13.3±1.7	–
Grieshaber (2011)	32	18	14.2±2.1	47	13.1±1.2	2.6
Koerber (2012)	15	18	12.0±0.1	45	14.5±2.6	1.7 (85%)
Matthaei (2011)	46	12	5.6±3.2	31	12.6±2.4	1.3 (43%)
Bull (2011)	82	36	7.9±1.3	34	15.1±3.1	0.9 (53 %)
Fujita (2011)	11	12	8.4±1.8	36	15.0±4.1	1.6 (25%)
Ayyala (2011)	33	12	7.4±1.5	32	13.8±4.9	2
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%)

Safety

Intra- and post-operative complications

Complication	Frequency in %
Gross hyphaema	2 to 6
Descemet's detachment	2 to 6
360º cannulation impossible	0 to 9
False passage	3 to 12
IOP spike >30 mmHg	2 to 9
Cataract formation	0 to 8
Suture cheese wiring	0 to 2
Flat anterior chamber	0 to 2
Persistent hypotony	0 to1
Choroidal detachment	0
Bleb formation	0 to 4
Blebitis, endophtalmitis	0

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	• Canaloplasty: Mean 67 years; 60% (18/30) male • Trabeculectomy: Mean 68 years; 34% (11/32) male
Patient selection criteria	Inclusion criteria: patients aged 18 years or older with medically uncontrolled primary or secondary (pseudoexfoliative and pigmentary) open-angle glaucoma. Exclusion criteria: 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.
Technique	• 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 antiglaucoma 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

Number of patients analysed: **62 (30 canaloplasty versus 32 trabeculectomy**

Procedure Success

	Canaloplasty	Trabeculectomy	p value*
COMPLETE SUCCESS (without glaucoma medication)			
IOP ≤21 mmHg and ≥20% IOP reduction			
1 month	52% (15/29)	81% (26/32)	–
3 months	62% (16/26)	84% (27/32)	–
6 months	54% (13/24)	78% (25/32)	–
1 year	61% (14/23)	77% (24/31)	–
2 years	39% (9/23)	68% (21/31)	0.04
IOP ≤18 mmHg			
1 month	55% (16/29)	91% (29/32)	–
3 months	59% (16/26)	84% (27/32)	–
6 months	58% (14/24)	78% (25/32)	–
1 year	57% (13/23)	77% (24/31)	–
2 years	39% (9/23)	74% (23/31)	0.01
QUALIFIED SUCCESS (with or without glaucoma medication)			
IOP ≤21 mmHg and ≥20% IOP reduction			
1 month	72% (21/29)	81% (26/32)	–
3 months	96% (25/26)	94% (30/32)	–
6 months	83% (20/24)	91% (29/32)	–
1 year	100% (23/23)	97% (30/31)	–
2 years	83% (19/23)	90% (28/31)	0.40
IOP ≤18 mmHg			
1 month	76% (22/29)	91% (29/32)	–
3 months	89% (24/26)	97% (31/32)	–
6 months	96% (23/24)	97% (31/32)	–
1 year	96% (22/23)	100% (31/31)	–
2 years	83% (19/23)	97% (30/31)	0.01

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

IOP and medications

	Canaloplasty		Trabeculectomy	
	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

Safety

Intraoperative complications

Canaloplasty:

- **microperforation of Descemet membrane**: 7% (2/30)
- **anterior synechiae**: 3% (1/30). It needed surgical peripheral iridotomy.

Trabeculectomy: None reported.

Postoperative complications and surgical interventions

	Canaloplasty	Trabeculectomy	p value*
Early complications (≤90 days)			
Hypotony (IOP<5mmHg)	20% (6/30)	38% (12/32)	0.17
Shallow anterior chamber	0	6% (2/32)	0.49
Choroidal detachment	3% (1/30)	13% (4/32)	0.36
Elevated IOP (>25 mmHg)	30% (9/30)	25% (8/32)	0.78
Conjunctival leak	10% (3/30)	9% (3/32)	1
Corneal erosion	3% (1/30)	44% (14/32)	<0.001
Hyphaema (>1mm layered blood)	23% (7/30)	3% (1/32)	0.02
Intracorneal haematoma after Descemet detachment	3% (1/30)	–	–
Secondary suture migration in anterior chamber	7% (2/30)**	–	–
Iris incarceration	–	3% (1/32)	–
Scarring of the filtering bleb	–	3% (1/32)	–
Blebitis/ endophtalmitis	0	0	–
Early surgeries			
Laser suture lysis, eyes	–	75% (24/32)	–
5-FU bleb injections	–	91% (29/32)	–
Iris revision	–	3% (1/32)	–
Scleral flap revision (hypotony)	3% (1/30)	19% (6/32)	0.11
Scleral flap revision (elevated IOP)	–	0	–
Bleb needling	–	3% (1/32)	–
Conjunctival suturing	7% (2/30)	3% (1/32)	0.61
Nd:YAG laser goniopuncture	13% (4/30)	–	–
Second surgeries	10% (3/30)***	0	–
Late complications (>90 days)			
Elevated IOP (>25 mmHg)	3% (1/30)	3% (1/32)	1
Hypotony (IOP<5 mmHg)	0	19% (6/32)	0.03

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 with 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 trabeculoplasty.

Scarring of the filtering bleb	–	25% (8/32)	
Blebitis/ endophtalmitis	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.

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

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 antiglaucoma 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 goniopuncture 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

Number of patients analysed: **59 (29 phaco-canaloplasty versus 30 phaco-non-penetrating deep sclerectomy)**

IOP

Time	PC group			PDS group			p
	Mean (SD)	Median	Range	Mean (SD)	Median	Range	
Pre-op	19.0±6.9	18	10 to 41	19.1±5.8	18	12 to 36	0.829
1 day	12.6±5.9	14	3 to 27	12.9±5.6	12	5 to 28	0.927
7 days	15.3±7.5	14	5 to 35	11.4±4.4	11.5	5 to 21	0.056
1 month	11.4±4.1	11	4 to 21	12.3±4.3	12	4 to 23	0.526
3 months	11.4±3.2	11	6 to 18	12.7±4.0	11	6 to 22	0.353
6 months	13.2±3.4	12	8 to 23	13.9±2.8	13.5	10 to 21	0.210
1 year	12.6±2.7	13	7 to 18	14.3±3.5	13	9 to 24	0.107

IOP reduction 1 year after the procedure

PC group: 33% (p<0.05)
PDS group: 28% (p<0.05)

Medications

Time	PC group			PDS group			p
	Mean (SD)	Median	Range	Mean (SD)	Median	Range	
Pre-op	2.64±0.68	3	2 to 4	2.89±0.94	3	1 to 4	0.326
1 day	0	0	–	0	0	–	–
7 days	0.18±0.94	0	0 to 5	0	0	–	0.823
1 month	0.04±0.19	0	0 to 1	0	0	–	0.823
3 months	0.04±0.19	0	0 to 1	0.07±0.37	0	0 to 2	1.000
6 months	0.22±0.58	0	0 to 2	0.24±0.69	0	0 to 3	0.967
1 year	0.27±0.67	0	0 to 3	0.55±0.94	0	0 to 4	0.304

Statistically significant reduction within groups (p<0.05) but no statistically significant difference between groups.

At the end of the follow-up period, IOP≤18 mmHg without antiglaucoma medication was achieved in 76% of PC patients and in 63% of PDS patients (p=0.005).

Surgical success at 1 year

- **Complete success**
  PC group: 79%
  PDS group: 77%, p=0.708
- **Qualified success**
  PC group: 86%
  PDS group: 84%, p=0.691

Safety

Postoperative complications

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

*All cases of hyphaema resolved spontaneously within 2 weeks and no intervention was needed.

** It resolved spontaneously.

Postoperative interventions

PC group: none was needed.
PDS group: 59% of patients (5-fluorouracil injection, 59%; suture lysis, 48%; needling, 28%).

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	Inclusion criteria: 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. Exclusion criteria: 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

Number of patients analysed: **417 eyes (180 conventional canaloplasty versus 237 canaloplasty with suprachoroidal drainage)**

IOP

	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).

Safety

Operative and postoperative complications and secondary surgical intervention

Complication	Canaloplasty	Canaloplasty with suprachoroidal drainage
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
Endophtalmitis	0	0

All differences between both groups were not statistically significant.

Abbreviations used: IOP, intraocular pressure.

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

Number of patients analysed: **327 (175 canaloplasty versus 152 trabeculectomy)**

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.

Safety

Not reported.

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	• Canaloplasty with phacoemulsification using the iTrack 250 (iScience) device. • Trabeculectomy with mitomycin C with phacoemulsification. 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.
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's canal stenting; based on intent-to treat, these remained in the phacocanaloplasty group.

Other issues: Not reported.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **77 (36 phacocanaloplasty versus 41 phacotrabeculectomy)**

IOP (mean ± SD; mmHg)

	Canaloplasty	Trabeculectomy	p
Before surgery	19.5±5.7	23.6±13.8	0.09
1 year	14.1±4.4	11.8±5.4	0.07

Statistically significant reduction in IOP from baseline in both groups (p<0.001).

Visual acuity (mean±SD; LogMAR Units)

	Canaloplasty	Trabeculectomy	p (Student t test)
Before surgery	0.41±0.27	0.51±0.48	0.27
1 day	0.78±0.69	0.60±0.59	0.20
1 week	0.48±0.38	0.50±0.55	0.85
1 month	0.30±0.22	0.43±0.47	0.13
3 months	0.25±0.17	0.33±0.39	0.25
6 months	0.26±0.34	0.32±0.46	0.54
9 months	0.22±0.22	0.39±0.60	0.12
1 year	0.21±0.20	0.40±0.70	0.10

Statistically significant improvement in visual acuity from baseline in both groups (p<0.001).

Glaucoma medications (median [interquartile range])

	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 to1)	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

Safety

Complications and reoperations

	Canaloplasty	Trabeculectomy
Serious complications		
Choroidal effusion	1/36	1/41
Suprachoroidal haemorrhage	0	1/41
CRAO	1/36	0
Hypotony maculopathy	0	2/41
Minor complications		
Descemet detachment at 1 day	1/36	0
Hyphaema at 1 day	28% (10/36)	0
Major reoperations		
Ahmed glaucoma valve	1/36	1/41
EX-PRESS shunt	1/36	0
Minor reoperations		
Bleb needling with MMC	0	5/41
Scleral flap needling	5/36	0
Choroidal effusion	0	1/41
Bleb suturing at slit lamp	0	1/41

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 ≤ 21mmHg, ≤18mmHg, and ≤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

Number of patients analysed: **214 eyes from 185 patients**

Pre- and postoperative IOP (mmHg)

	n eyes	Mean±SD	95% CI	p value*
Preop	214	29.4 ± 7.9	18.0 to 52.1	–
1 day	214	13.3 ± 6.1	3.0 to 28.0	<0.0001
1 week	214	17.3 ± 6.8	4.2 to 31.1	<0.0001
1 month	214	18.1 ± 7.4	6.4 to 35.1	<0.0001
3 months	207	17.1 ± 4.7	8.0 to 27.0	<0.0001
6 months	194	17.3 ± 4.8	9.3 to 26.2	<0.0001
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**.**

Success rate

	≤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

Safety

Early complications

Complication	% eyes
Hyphaema	22% (47/214)
Aqueous leakage from the conjunctival flap	<1% (2/214)
Hypotony <5mmHg	10% (21/214)
Transient IOP spike >10 mmHg	6% (12/214)
Descemet membrane detachment	5% (11/214)
Suture cheese-wiring through trabecular meshwork	<1% (2/214)
Conjunctival bleb clinically detectable	1% (3/214)

Postoperative interventions

- **YAG laser goniopuncture:** 12% (26/214); after 2-12 months.
- **Trabeculectomy:** 8% (17/214); after 3-58 months.

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 Zhang B (2017)

Details

Study type	**Systematic review and meta-analysis**
Country	Paper from China
Recruitment period	Literature search from inception to February 2017
Study population and number	n= **1,498 eyes (at baseline) from patients** with open-angle glaucoma, from 28 studies
Age and sex	Canaloplasty standalone group: mean 63 years, sex not reported Phacocanaloplasty subgroups: mean 71 years, sex not reported
Patient selection criteria	Participants diagnosed with glaucoma regardless of age, sex, or race, studies limited in patients with another failed antiglaucoma surgery were excluded; interventions, included but not limited to canaloplasty, with or without phacoemulsification; research types, both prospective and retrospective studies, excluding case reports and reviews; outcomes: included but not limited to IOP, follow-up of at least 6 months; for literatures with overlapping data, only the one with the largest sample and then the longest follow-up was included.
Technique	Canaloplasty or trabeculectomy.
Follow-up	**1 year**
Conflict of interest/source of funding	This study was funded by the National Major Scientific Equipment program. The authors declared that they had no conflict of interest.

Analysis
Follow-up issues: Not reported.
Study design issues:

- This research was done according to a predetermined protocol based on the Cochrane Handbook for Systematic Reviews of Interventions.
- The primary outcomes were the changes in IOP and the number of antiglaucoma medications. The secondary outcomes were the complete and qualified successful rates and the incidence of adverse events.
- The meta-analysis was conducted with the software Review Manager V5.2 (Cochrane Collaboration).
- The changes in IOP and in antiglaucoma medications after canaloplasty were meta-analysed in 3 subgroups, canaloplasty standalone, canaloplasty with phacoemulsification and canaloplasty mixed (the former 2 subgroups mixed in the original papers).
- The mean between-group difference of reductions in IOP and antiglaucoma medications and the odds ratios of the success rates and the incidence of complications were analysed between canaloplasty and trabeculectomy in 2 subgroups, standalone canaloplasty versus standalone trabeculectomy and phacocanaloplasty versus phacotrabeculectomy.
- The random effects model was applied in most cases as heterogeneity was considered present in the enrolled studies for clinical and study differences.
- No unpublished data were included in this review.

Study population issues:

- There were 6 studies included in the meta-analysis outcomes between canaloplasty and trabeculectomy. The Matlach (2015) RCT and the Schoenberg (2015) retrospective comparative study are 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 Matlach (2013) retrospective comparative study was included in Appendix A. The Thederan (2014) study is a German retrospective comparative study which is not available in English language
- 78% of eyes were diagnosed with primary open-angle glaucoma.
- The average baseline IOP was 25.1±8.5mmHg with 3.04±1.18 antiglaucoma medications in canaloplasty standalone subgroup, and the mean baseline IOP was 20.7±6.4mm Hg with 2.23±1.14 antiglaucoma medications in the phacocanaloplasty subgroup.

Other issues: 18 of the 28 eligible studies were retrospective studies.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **1,498 eyes from 28 studies (at baseline)**

IOP reduction

Subgroup	Follow-up	Mean IOP reduction (95% CI), mmHg
All subgroups	6 months	10.69 (8.96 to 12.43)
	1 year	9.94 (8.42 to 11.45)
Standalone canaloplasty	6 months	12.01 (9.77 to 14.24)
	1 year	11.38 (9.43 to 13.34)
Phacocanaloplasty	6 months	8.32 (5.36 to 11.27)
	1 year	8.14 (4.83 to 11.46)

Comparison of canaloplasty with trabeculectomy

IOP reduction was statistically significantly lower with canaloplasty than with trabeculectomy.
Mean difference between groups: -3.61 (95% CI –5.53 to -1.69) mmHg 1 year after the procedure.

Antiglaucoma medication reduction

Subgroup	Follow-up	Mean antiglaucoma medication reduction (95% CI)
All subgroups	6 months	2.03 (1.69 to 2.37)
	1 year	2.11 (1.80 to 2.42)
Standalone canaloplasty	6 months	2.01 (1.51, 2.50)
	1 year	2.16 (1.79, 2.53)
Phacocanaloplasty	6 months	2.03 (1.36, 2.70)
	1 year	2.04 (1.15, 2.92)

Comparison of canaloplasty with trabeculectomy

No significant difference was found in the reduction of antiglaucoma medication between canaloplasty and trabeculectomy.

Mean difference between groups 1 year after the procedure: −0.37 (95% CI –0.83 to 0.08)

Success rates

No statistically significant difference in the complete or qualified success rates was found between canaloplasty and trabeculectomy.

Sensitivity Analysis

- The difference between before and after removing all retrospective studies in IOP reduction was 14% at 6 months and 17% at 12 months; the corresponding difference in antiglaucoma medication reduction was 5% at 6 months and 5% at 12 months.
- The difference between before and after removing the small weight studies in IOP reduction was −3% at 6 months and −9% at 12 months; the corresponding change in antiglaucoma medication reduction was 4% at 6 months and 0% at 12 months.
- A publication bias might exist with missing studies on the left hand side of the funnel plots of IOP reduction at 6 months and 12 months.

Safety

Incidence of complications of canaloplasty

Complication	Incidence% (events/pooled eyes)
Hyphaema (blood layer > 1 mm)	24.9 (304/1221)
Hypotony < 5mmHg	8.6 (94/1091)
Descemet membrane detachment	3.1 (37/1185)
Detectable conjunctival bleb	1.9 (17/899)

Comparison of canaloplasty with trabeculectomy

Hyphaema was statistically significantly more reported after canaloplasty with an OR of 9.24 (95% CI 3.09 to 27.60).

Descemet membrane detachment was only observed with canaloplasty with a reported incidence of 3%.

The suprachoroidal haemorrhage and bleb needling were only reported after trabeculectomy with incidences of 2.3% and 10.9%, respectively.

Hypotony and choroidal effusion or detachment were statistically significantly less frequent with canaloplasty than with trabeculectomy: OR 0.32 (95% CI 0.13 to 0.80) and 0.25 (95% CI 0.06 to 0.97) respectively.

No significant difference was found in the incidence of conjunctiva leakage (OR 0.72, 95% CI 0.16 to 3.14).

Abbreviations used: CI, confidence interval; IOP, intraocular pressure; OR, odds ratio.

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 ≤21 mmHg and ≥20% IOP reduction (p=0.04) and 39% (9/23) versus 74% (23/31) when defined as IOP ≤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 ≤21 mmHg and ≥20% IOP reduction: 83% (19/23) versus 90% (28/31) but they were statistically significantly lower in the canaloplasty group when defined as IOP ≤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 phacotrabeculectomy (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 patients who had canaloplasty, the complete success rates (IOP ≤18 mmHg without medication) at 1-, 2- and 3-year follow-up were 44% (64/144), 38% (30/80) and 31% (9/29) respectively, and the qualified success rates (IOP ≤18 mmHg with medication) were 75% (108/44), 74% (59/80) and 59% (17/29) respectively. [7]

In a systematic review and meta-analysis of 1,498 eyes, comparing canaloplasty with trabeculectomy, there was no statistically significant difference between groups for complete and qualified success rates after the procedure.[9]

Intraocular pressure (IOP)

In a review of 914 eyes treated by canaloplasty alone (n=777 eyes) or with phacoemulsification (n=137 eyes), the mean IOP reduction (after a maximum of 36 months' follow-up) ranged from 29% to 66% with canaloplasty alone and from 42% to 46% with canaloplasty plus 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 ±standard deviation (SD) statistically significantly decreased from 23.7±5.1 mmHg before the procedure to 14.4±4.2 mmHg at 2-year follow-up in the canaloplasty group and from 22.2±5.3 mmHg to 11.5±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 phacotrabeculectomy (n=41), the mean IOP±SD statistically significantly decreased from 19.5±5.7 mmHg before the procedure to 14.1±4.4 mmHg at 1-year follow-up in the phacocanaloplasty group and from 23.6±13.8 mmHg to 11.8±5.4 mmHg in the phacotrabeculectomy 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±SD from 29.4±7.9 mmHg before surgery to 16.8±4.2 mmHg at 1 year, 17.1±4.7 mmHg at 2 years and 16.9±3.1 mmHg at 42 months; p<0.0001). [7]

In the systematic review and meta-analysis of 1,498 eyes, the mean IOP reduction was 9.94 mmHg (95% confidence interval [CI] 8.42 to 11.45) and was statistically significantly lower in the canaloplasty group (mean difference between groups −3.61, 95% CI −5.53 to −1.69 mmHg) at 1-year follow-up. [9]

Medication use

In the review of 914 eyes, mean medication use reduction (after a maximum of 36 months' follow-up) ranged from 25% to 100% with canaloplasty alone and from 66% to 86% with canaloplasty plus 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 ±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 with 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 (±SD) number of medications used in both groups, from 2.64 ±0.68 before surgery to 0.27±0.67 at 1 year in the phaco-canaloplasty group and from 2.89±0.94 to 0.55±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 ±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 1,498 eyes, the mean reduction in antiglaucoma medication use was 2.11 (95% CI 1.80 to 2.42) 1 year after canaloplasty, and there was no statistically significant difference in medication reduction between groups (mean difference −0.37, 95% CI −0.83 to 0.08).[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 discontented, to 10 totally contented) was statistically significantly higher in the canaloplasty group (8.09±2.71) compared with the trabeculectomy group (7.46±2.61, $p=0.034$). In the same study, there were statistically significantly fewer revision surgeries reported in the canaloplasty group (mean number of revision surgeries per patient 0.12±0.43) compared with the trabeculectomy group (0.67±1.14, $p<0.001$). Also, patients were statistically significantly more likely to have a positive mood after canaloplasty (2.30±0.83) compared with trabeculectomy (1.96±0.87, $p=0.009$), stress caused by surgery or follow-ups and treatments was statistically significantly lower with canaloplasty (4.18±0.86 and 4.36±0.80 respectively) compared with trabeculectomy (3.59±1.12 and 3.40±1.20 respectively; $p<0.001$), 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 phacotrabeculectomy. [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 by canaloplasty 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

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 statistically significantly more frequent in the canaloplasty group than in the trabeculectomy group at 1-year follow-up, in a systematic review and meta-analysis of 1,498 eyes (OR 9.24, 95% CI 3.09 to 27.60). The incidence of hyphaema in the canaloplasty group was 25% (304/1221). [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 membrane detachment was only seen in the canaloplasty group, with an incidence of 3% (37/1185) at 1-year follow-up in the systematic review and meta-analysis of 1,498 eyes.[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 statistically significantly less frequent after canaloplasty than after trabeculectomy at 1-year follow-up, in the systematic review and meta-analysis of 1,498 eyes (OR 0.32, 95% CI 0.13 to 0.80). The incidence of hypotony in the canaloplasty group was 9% (94/1091). [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 phacotrabeculectomy (n=41). [6]

Choroidal effusion or detachment was statistically significantly less frequent in the canaloplasty group than in the trabeculectomy group, in the systematic review and meta-analysis of 1,498 eyes within 1 year of the procedure (OR 0.25, 95% CI 0.06 to 0.97).[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]

Conjunctival leak incidence was not statistically significantly different between the canaloplasty group and the trabeculectomy group within 1-year follow-up, in the systematic review and meta-analysis of 1,498 eyes (OR 0.72, 95% CI 0.16 to 3.14).[9]

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]

Detectable conjunctival bleb was reported in 2% (17/899) of patients after canaloplasty, in the systematic review and meta-analysis of 1,498 eyes. [9]

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 2016[10]. 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 2016[11]. 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

- Trabeculotomy 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 was unable to gather patient commentary for this procedure.

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]

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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. Acta Opthalmologica 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. Journal of Glaucoma 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. Ophthalmology 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. Journal of Glaucoma 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. Klinische Monatsblatter fur Augenheilkunde 231(4), 348-50	Case report n=2 FU= 9 months	Circumferential cannulation and viscodilation of the Schlemm's 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.

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. Journal of Glaucoma 22(7), 577-83	Retrospective comparative study n=30 eyes (15 canaloplasty versus 15 trabeculectomy) FU=1 year	Canaloplasty and trabeculectomy were both effective in lowering IOP. However, less follow-up visits and significantly fewer complications and interventions were favourable for canaloplasty.	Larger studies or studies with longer follow-up are already included in table 2.
Brusini Paolo, Caramello Guido, Benedetti Stefano, and Tosoni Claudia (2016) Canaloplasty in Open-angle Glaucoma: Mid-term Results From a Multicenter Study. Journal of Glaucoma 25(5), 403-7	Prospective case series n=178 (198 eyes) FU=3 to 42 months	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.	Larger studies or studies with longer follow-up are already included in table 2.
Brusini P, and Tosoni C (2014) Canaloplasty after failed trabeculectomy: a possible option. Journal of Glaucoma 23(1), 33-4	Case series n=6 FU=6-28 months	Canaloplasty can be considered as a possible surgical option in eyes with failed trabeculectomy showing undamaged Schlemm's canal from previous filtrating surgery.	Larger studies or studies with longer follow-up are already included in table 2.
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. Graefes Archive for Clinical & Experimental Ophthalmology 249(10), 1537-45	Prospective case series n=109 FU=3 years	Canaloplasty demonstrated significant and sustained IOP reductions accompanied by an excellent short- and long-term safety profile in adult patients with open-angle glaucoma.	Study already included in the Brandao (2013) review.
Cagini Carlo, Peruzzi Claudia, Fiore Tito, Spadea Leopoldo, Lippera Myrta, and Lippera Stefano (2016) Canaloplasty: Current Value in the Management of Glaucoma. Journal of ophthalmology 2016, 7080475	Review	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.	The results of the studies included in the review were not synthesised.

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 Opthalmologica 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.

Hamid M, Thompson P, and Harasymowycz P (2015) Novel Treatment for Hemorrhagic Descemet Detachment After Canaloplasty. Cornea 34(12), 1611-2	Single case report FU=3 months	Haemorrhagic 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.	Complication already reported in table 2.
Ichihashi Tsunetomo, Suzuki Yasuyuki, Nagahara Miyuki, and Kawai Kenji (2015) A Case of Open-Angle Glaucoma Successfully Treated Using Canaloplasty. Tokai Journal of Experimental & Clinical Medicine 40(4), 157-60	Single case report FU=4 years	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.	Larger studies or studies with longer follow-up are already included in table 2.
Jaramillo A, Foreman J, and Ayyala R S (2014) Descemet membrane detachment after canaloplasty: incidence and management. Journal of Glaucoma 23(6), 351-4	Case series n=115 patients (162 eyes) FU=1 year	DMD with or without intracorneal haemorrhage is not an infrequent complication of canaloplasty and can occasionally lead to corneal decompensation.	Complication already reported in table 2. Larger studies or studies with longer follow-up are already included in table 2.
Klink T, Panidou E, Kanzow-Terai B, Klink J, Schlunck G, and Grehn F J (2012) Are there filtering blebs after canaloplasty?. Journal of Glaucoma 21(2), 89-94	Case series n=20 FU=245 days	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.	Larger studies or studies with longer follow-up are already included in table 2.
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	Comparative case series n=15 (30 eyes, 15 canaloplasty in 1 eye versus 15 viscocanalostomy in contralateral eye) FU=18 months	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.	Larger studies or studies with longer follow-up are already included in table 2.

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	Case series n=157 eyes FU=3 years	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.	Study already included in the Brandao (2013) review.
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	Case series n=127 FU=2 years	Canaloplasty was safe and effective in reducing IOP in adult patients with OAG.	Study already included in the Brandao (2013) review.
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.	Case series n=94 FU= 1 year	Circumferential viscodilation and tensioning of Schlemm's canal was a safe and effective surgical procedure to reduce IOP in adult patients with OAG.	Larger studies or studies with longer follow-up are already included in table 2.This study was included in the previous overview.
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.	Systematic review and meta-analysis n= 215 eyes (100 canaloplasty versus 115 trabeculectomy) FU=1 year	Trabeculectomy seems to be more effective in lowering IOP up to 12mo when comparing with canaloplasty. Canaloplasty does not seem to be inferior to trabeculectomy considering the postoperative success rate or the number of postoperative antiglaucoma medication. Meanwhile, it has an advantage of less bleb related complications.	This systematic review and meta-analysis has been replaced by a more recent one with a literature search done up until 3/02/2017

Liu H, Zhang H, Li Y et al. (2017) Safety and efficacy of canaloplasty versus trabeculectomy in treatment of glaucoma. Oncotarget	Systematic review and meta-analysis n=8 studies (canaloplasty versus trabeculectomy) Literature search up to December 2016	Both trabeculectomy and canaloplasty can significantly reduce the intraocular pressure in glaucoma patients at 12 months after operation, trabeculectomy leads a more marked IOP decrease than canaloplasty at the cost of a higher complication rate and more demanding for postoperative care.	Other systematic review and meta-analysis Zhang (2017) already included in Table 2 is more up-to-date.
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	Case series n=35 FU=1 year	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.	Larger studies or studies with longer follow-up are already included in table 2.
Mansouri K, and Shaarawy T (2015) Update on Schlemm's canal based procedures. Middle East African journal of ophthalmology 22(1), 38-44	Review n=20 studies FU=9 to 36 months	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.	Another review is already included in Table 2. The reporting of the frequency of the safety complications is not exhaustive.
Mastropasqua L, Agnifili L, Salvetat 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	Case series n=30 FU=12 weeks	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.	Larger studies or studies with longer follow-up are already included in table 2.

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	Retrospective comparative study n=39 eyes (19 phacocanaloplasty versus 20 phacotrabeculectomy) FU=1 year	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.	Larger studies or studies with longer follow-up are already included in table 2.
Moelle M C, Cursiefen C, Rejdak 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	Haemorrhagic descemet detachment is an uncommon complication after canaloplasty. Nd:YAG Descemet membranotomy is a successful means of clearing the haematoma 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).
Seuthe A M, Januschowski K, Mariacher S et al. (2017) The effect of canaloplasty with suprachoroidal drainage combined with cataract surgery - 1-year results. Acta Ophthalmologica.	Retrospective comparative case series n=328 eyes (193 canaloplasty with suprachoroidal drainage versus 135 phacocanaloplasty with suprachoroidal drainage) FU=1 year	Combining cataract surgery and suprachoroidal drainage achieves a higher IOP reduction, and patients postoperatively need less IOP-lowering medication than after suprachoroidal drainage alone.	The primary aim of this study was to investigate the value of conducting canaloplasty in combination with cataract surgery (phacocanaloplasty) or not.

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's 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.
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	Retrospective case series n=78 eyes FU=1 year	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.	Larger studies or studies with longer follow-up are already included in table 2.
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	Retrospective subset analysis of a prospective case series n=133 (82 canaloplasty alone versus 51phacocanaloplasty) FU=3 years	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.	This is a subset analysis of the Lewis (2011) study which is included in the Brandao (2013) review.
Wagdy F M (2017) Canaloplasty versus Viscocanalostomy in Primary Open Angle Glaucoma. Electronic Physician [Electronic Resource] 9, 3665-3671	Comparative study n=60 eyes (30 canaloplasty versus 30 viscocanalostomy) FU=6 months	Canaloplasty was more effective and safer than viscocanalostomy in management of uncontrolled primary open angle glaucoma with medication.	Larger studies or studies with longer follow-up are already included in table 2.

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 ,	Prospective cohort study n=26 (17 without history of glaucoma surgery versus 9 with failed glaucoma surgery and disrupted Schlemm's canal) FU=1 year	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.	Larger studies or studies with longer follow-up are already included in table 2. No new safety
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	Prospective comparative study. n=60 eyes (37 canaloplasty in patients with failed glaucoma filtration surgery [GFS] versus 23 without failed GFS) FU=18 months	Canaloplasty is an effective and safe option for primary open-angle glaucoma with failed GFS.	Larger studies or studies with longer follow-up are already included in table 2. No new safety complication reported.

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

Guidance	Recommendations
Interventional procedures	**Trabecular stent bypass microsurgery for open-angle glaucoma. NICE interventional procedure guidance 575 (2017).** 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.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. 1.2 Trabecular stent bypass microsurgery for open-angle glaucoma should only be done by clinicians with specific training in the procedure. **Trabeculotomy ab interno for open angle glaucoma. NICE interventional procedure guidance 397 (2011).** 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. 1.2 Patient selection should be carried out in units that specialise in glaucoma treatment that can offer a range of treatment options. 1.3 NICE encourages the collection and publication of further data on long-term efficacy.
NICE guidelines	**Glaucoma: diagnosis and management. NICE guideline 85 (2009).** 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.

	If adherence and eye drop instillation technique are satisfactory offer one of the following: • 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 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. 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. 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: • 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. 1.4.10 Offer people with COAG who prefer not to have surgery or who are not suitable for surgery: • 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.

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)	01/06/2017	Issue 6 of 12, June 2017
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	01/06/2017	Issue 5 of 12, May 2017
HTA database (Cochrane Library)	01/06/2017	Issue 4 of 4, October 2016
MEDLINE (Ovid)	01/06/2017	1946 to May Week 4 2017
MEDLINE In-Process (Ovid)	01/06/2017	May 31, 2017
EMBASE (Ovid)	01/06/2017	1974 to 2017 Week 22
PubMed	01/06/2017	n/a
JournalTOCS	01/06/2017	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-viscocanalost* or Phacoviscocanalost*).tw.

3 (circumferential adj4 (viscodilat* or cannulat*)).tw.

4 Viscocanalostomy.tw.

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 (201608* or 201609* or 20161* or 2017*).ed.

23 21 and 22