NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of ab interno canaloplasty for open-angle glaucoma

Open-angle glaucoma is a progressive condition that causes increased pressure in the eye. This damages the nerve that connects the eye to the brain and may lead to permanent sight loss. This procedure involves making a small cut in the eye (ab interno) and inserting a tiny tube into the channel that drains fluid from the eye. The tube widens the drainage channel (canaloplasty), then gel is injected into it and the tube is removed. The gel keeps the channel wider for a few days then dissolves, leaving the channel permanently wider, allowing excess fluid to drain away. The aim is to reduce pressure in the eye.

Contents

Abbreviations

Word or phrase	Abbreviation
Intraocular pressure	IOP
Standard deviation	SD

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure 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 professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2022 and updated in August 2022.

Procedure name

- Ab interno canaloplasty for open-angle glaucoma

Professional societies

- Royal College of Ophthalmologists
- UK and Éire Glaucoma Society.

Description of the procedure

Indications and current treatment

Glaucoma is usually a chronic condition that is typically associated with raised IOP. The most common type of glaucoma in the UK is primary open-angle glaucoma. 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.

In the healthy eye, aqueous humor drains through the trabecular meshwork (into Schlemm's canal) and through the uveoscleral outflow pathway. In glaucoma,

this drainage becomes impaired either from resistance in the trabecular meshwork pathway (primary open-angle glaucoma) or from obstruction by the iris (primary closed-angle glaucoma).

Treatment usually involves eye drops containing medicines that either reduce the production of aqueous humor or increase its drainage. Surgical procedures such as trabeculectomy, deep sclerectomy, trabeculotomy, stenting, canaloplasty, or laser trabeculoplasty may be used.

What the procedure involves

Ab interno canaloplasty aims to reduce IOP by improving the drainage of aqueous fluid from the eye in people with open-angle glaucoma. It is done under local or general anaesthetic. Unlike traditional (ab externo) canaloplasty, which is done by cutting through the conjunctiva and sclera, ab interno canaloplasty uses an internal approach through a clear corneal or limbal incision. A microcatheter is introduced into the canal through a small opening in the trabecular meshwork and advanced around its entire circumference. As the catheter tip is withdrawn, viscoelastic fluid is injected into the canal to dilate it. The microcatheter is then removed. The viscoelastic fluid disperses down the collector channels of the eye within 2 to 3 days. The aim is to permanently dilate the canal to allow increased drainage of aqueous humor from the eye and thereby lower IOP. Some devices allow canaloplasty to be done simultaneously with trabeculotomy. Canaloplasty is often done concurrently with phacoemulsification (cataract surgery).

Efficacy summary

IOP reduction

In a before-and-after study of 60 eyes in 53 people, there was a statistically significant decrease in IOP from 20.7 mmHg before surgery to 13.6 mmHg at 12 months and 13.5 mmHg at 24 months after surgery (both $p<0.001$ compared with baseline). There was no statistically significant difference in the mean change in IOP between people who had canaloplasty alone and people who had canaloplasty and phacoemulsification (Gallardo, 2021). In a follow-up study of 44 eyes in 44 people, there was a statistically significant decrease in IOP from 20.5 mmHg before surgery to 13.3 mmHg at 36 months after surgery ($p<0.0001$ compared with baseline; Gallardo, 2022).

In a before-and-after study of 180 eyes in 130 people, results were presented as stratified by baseline IOP. In people with baseline IOP of 18 mmHg or more (n=111 eyes at baseline), there was a statistically significant decrease in IOP from 22.0 mmHg before surgery to 15.7 mmHg at 6 months and 17.2 mmHg at 12 months after surgery (both $p<0.0001$ compared with baseline). In people with

baseline IOP of less than 18 mmHg (n=69 eyes at baseline), there was little change in IOP from before to after surgery (statistical significance not reported) (Tracer, 2020).

In a before-and-after study of 89 eyes in 64 people, there was a statistically significant decrease in IOP from 24.5 mmHg before surgery to 16.5 mmHg at 12 months ($p<0.0005$) and 15.8 mmHg at 18 months ($p<0.0005$). There was no statistically significant difference in the mean change in IOP between people who had canaloplasty alone and people who had canaloplasty and phacoemulsification (Hughes, 2020).

In a before-and-after study of 106 eyes in 71 people, eyes were stratified by baseline IOP. In people with baseline IOP of 18 mmHg or more (n=72 eyes at baseline), there was a statistically significant decrease in mean IOP from 24.6 mmHg before surgery to 14.6 mmHg at 12 months after surgery ($p<0.001$). In people with baseline IOP of less than 18 mmHg (n=34 eyes at baseline), there was no statistically significant change in mean IOP from before surgery to 12 months after surgery (Ondrejka, 2019).

In a before-and-after study of 27 eyes in 21 people, there was a statistically significant decrease in mean IOP from 19.85 mmHg before surgery to 14.98 mmHg at 12 months, 15.58 mmHg at 24 months, 14.71 mmHg at 36 months and 14.56 mmHg at 48 months (all $p<0.001$ compared with baseline; Koerber, 2022).

In a before-and-after study of 80 eyes in 73 people, there was a statistically significant decrease in mean IOP from 22.5 mmHg before surgery to 15.0 mmHg at 12 months after surgery ($p<0.001$). There was no statistically significant difference in the mean change in IOP between people who had canaloplasty alone and people who had canaloplasty and phacoemulsification (Toneatto, 2022).

In a before-and-after study 71 eyes (total people not reported), there was a statistically significant decrease in mean IOP from 23.6 mmHg before surgery to 14.2 mmHg at 12 months after surgery ($p<0.001$) (Gillman, 2021).

Glaucoma medicine reduction

In the before-and-after study of 60 eyes in 53 people, there was a statistically significant decrease in the number of glaucoma medicines used per person from a mean of 2.8 before surgery to 1.1 at 12 months and 1.7 at 24 months after surgery (both $p<0.001$ compared with baseline). There was no statistically significant difference in the reduction in glaucoma medicine use between people who had canaloplasty alone and people who had canaloplasty and phacoemulsification (Gallardo, 2021). In the follow-up study of 44 eyes in 44 people, there was a statistically significant decrease in the mean number of

glaucoma medicines used per person from 2.8 before surgery to 1.3 at 36 months after surgery ($p<0.0001$ compared with baseline; Gallardo, 2022).

In the before-and-after study of 180 eyes in 130 people, results were presented as stratified by baseline IOP. In people with baseline IOP of 18 mmHg or more (n=111 eyes at baseline), there was no change in glaucoma medicine use per person from a mean of 0.9 before surgery to 1.0 at 12 months after surgery ($p=0.7$). In people with baseline IOP of less than 18 mmHg (n=69 eyes at baseline), there was a statistically significant decrease in the mean glaucoma medicine use per person from 1.1 at baseline to 0.6 at 12 months follow up ($p<0.05$) (Tracer, 2020).

In the before-and-after study of 89 eyes in 64 people, there was a statistically significant decrease in the number of glaucoma medicines used from a mean of 2.5 before surgery to 1.8 at 12 months ($p<0.0005$) and 1.7 at 18 months ($p<0.05$). There was no statistically significant difference in the reduction in glaucoma medicine use between people who had canaloplasty alone and people who had canaloplasty and phacoemulsification (Hughes, 2020).

In the before-and-after study of 106 eyes in 71 people, eyes were stratified by baseline IOP. In people with baseline IOP of 18 mmHg or more (n=72 eyes at baseline), there was a statistically significant decrease in mean glaucoma medicine use from 2.1 before surgery to 0.2 at 12 months ($p<0.001$). In people with baseline IOP of less than 18 mmHg (n=34 eyes at baseline), there was a statistically significant decrease in mean glaucoma medicine use from 1.8 before surgery to 0.2 at 12 months after surgery ($p<0.001$) (Ondrejka, 2019).

In the before-and-after study of 27 eyes in 21 people, there was a statistically significant decrease in mean glaucoma medicine use from 1.93 before surgery to 0.30 at 12 months, 0.40 at 24 months, 0.80 at 36 months and 0.89 at 48 months after surgery (all $p<0.05$ compared with baseline; Koerber, 2022).

In the before-and-after study of 80 eyes in 73 people, there was a statistically significant decrease in mean glaucoma medicine use from 3.2 before surgery to 1.9 at 12 months after surgery ($p<0.001$). There was no statistically significant difference in the reduction in glaucoma medicine use between people who had canaloplasty alone and people who had canaloplasty and phacoemulsification (Toneatto, 2022).

In the before-and-after study 71 eyes (total people not reported), there was a statistically significant decrease in mean glaucoma medicine use from 2.9 before surgery to 0.6 at 12 months after surgery ($p<0.001$) (Gillman, 2021).

Surgical success

In the before-and-after study of 80 eyes in 73 people, eyes that reached a target IOP on no medicines were considered 'complete successes' and eyes that reached a target IOP on no more medicines than baseline were considered 'qualified successes'. At a target IOP of 16 mmHg or less and a 25% or more reduction in IOP, 10.3% of eyes were complete successes and a further 43.6% of eyes were qualified successes at 12 months. At a target IOP of 18 mmHg or less and a 25% or more reduction in IOP, 11.5% of eyes were complete successes and a further 50.0% of eyes were qualified successes at 12 months (Toneatto, 2022).

In the before-and-after study 71 eyes (total people not reported), eyes that had a 20% or more reduction in IOP with no medicine were considered 'complete successes'. 'Qualified successes' were those who had a 20% or more reduction in IOP with no more medicine use than baseline. Failures were those that did not meet the criteria for success, or those that needed additional glaucoma surgery or had loss of light perception. Complete success was achieved in 46% of eyes, with a further 19% achieving qualified success. Failure was seen in 35% of eyes, all due to uncontrolled IOP, 36.8% (7 eyes) of which needed further filtering surgery (Gillman, 2021).

Need for further surgery

In the before-and-after study of 89 eyes in 64 people, 6 people needed filtering surgery for glaucoma after canaloplasty. These people had higher baseline IOP and medicine use than the cohort mean (Hughes, 2020).

In the before-and-after study of 80 eyes in 73 people, 12 eyes needed further surgery after canaloplasty. This included 9 trabeculectomies and 3 deep sclerectomies (Toneatto, 2022).

In the before-and-after study of 71 eyes, 7 eyes needed further filtering glaucoma surgery after canaloplasty (Gillman, 2021).

Safety summary

Loss of visual acuity

In the before-and-after study of 60 eyes in 53 people, visual acuity was improved at 24-month follow up in all eyes, with 19 people (42.2%) gaining 2 or more lines of Snellen corrected distance visual acuity. Statistically significant improvements in visual acuity were only seen in the people who had both canaloplasty and phacoemulsification (Gallardo, 2021).

In the before-and-after study of 80 eyes in 73 people, there was no statistically significant change in visual acuity seen in people who had canaloplasty alone (p=0.31). In people who had canaloplasty and phacoemulsification, there was a statistically significant change in visual acuity in from 6.8/10 (SD 2.1) before surgery to 9.1/10 (SD 2.6) at 12 months after surgery (p<0.001).

In the before-and-after study of 27 eyes in 21 people, there was a statistically significant improvement in overall visual acuity between baseline and the last postoperative visit (p<0.001). Also, all eyes except 1 showed no change or improvement in visual field. One eye showed visual field (Koerber, 2022).

Raised IOP

In the before-and-after study and its follow up, complications of the entire cohort of 81 eyes having ab interno canaloplasty were reported. In this cohort, there were 3 cases of IOP spikes of 10 mmHg or more. Each occurred within 1 week after surgery (Gallardo, 2021; Gallardo, 2022).

In the before-and-after study of 180 eyes in 130 people, 2 people had IOP spikes of 10 mmHg or more above baseline. These were transient and resolved (Tracer, 2020).

In the before-and-after study of 80 eyes in 73 people, 1 person had an IOP spike of more than 10 mmHg above baseline more than 30 days postoperatively (Toneatto, 2022).

In the before-and-after study of 71 eyes, 12 people had IOP spikes over 30 mmHg. These were in the first month after surgery (Gillman, 2021).

Hypotony

In the before-and-after study of 80 eyes in 73 people, 4 people mild hypotony (Toneatto, 2022).

Bleeding and hyphaema

Note, Hughes (2020), Toneatto (2022), and Gillman (2021) did not consider mild or microhyphaema to be an adverse event of this procedure.

In the before-and-after study and its follow up, complications of the entire cohort of 81 eyes who had ab interno canaloplasty were reported. In this cohort, 13 eyes had hyphaema, including microhyphaema (10 eyes) and layered hyphaema (3 eyes) (Gallardo, 2021; Gallardo, 2022).

The before-and-after study of 180 eyes in 130 people reported 3 cases of hyphaema (Tracer, 2020).

The before-and-after study of 106 eyes in 71 people reported 14 cases of hyphaema (Ondrejka, 2019).

The before-and-after study of 80 eyes in 73 people reported 2 cases of moderate or severe hyphaema (Toneatto, 2022).

The before-and-after study of 71 eyes reported 1 case of a self-resolving corneal endothelial blood stain (Gillman, 2021).

Device malfunction

The before-and-after study of 106 eyes in 71 people reported 1 case of the VISCO360 device malfunctioning. The catheter detached from the handle and cannula and had to be retrieved with vitrectomy forceps. The person had no adverse sequalae. Note that this device is a precursor of the OMNI device and is no longer commercially available (Ondrejka, 2019).

Fibrin complications

The before-and-after study of 106 eyes in 71 people reported 1 case of fibrin in pupillary plane (Ondrejka, 2019).

The before-and-after study of 71 eyes reported 1 case of a fibrin plug (Gillman, 2021).

Other complications

Single cases of the following complications were reported:

- the before-and-after study of 180 eyes in 130 people (Tracer, 2020):
    - mild anterior chamber inflammation
- the before-and-after study of 71 eyes (Gillman, 2021):
    - intraocular lens subluxation.
    - iris atrophy.
    - pupillary block
- the before-and-after study of 27 eyes in 21 people (Koerber, 2022):
    - limited descemetolysis near the limbus.

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events that they have heard about) and

about theoretical adverse events (events that they think might possibly occur, even if they have never happened).

For this procedure, professional experts listed the following anecdotal adverse events: cyclodialysis, retinal detachment, Descement's detachment, formation of peripheral anterior synechiae, and transient refractive change. They considered that the following were theoretical adverse events: catheter entering a collector channel, subretinal space, or macular area.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to ab interno canaloplasty for open-angle glaucoma. The following databases were searched, covering the period from their start to 20 June 2022: 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 the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria 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.

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	People with open-angle glaucoma.
Intervention/test	Ab interno 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 613 eyes from approximately 450 people from 7 before-and-after studies reported in 8 publications.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on ab interno canaloplasty for open-angle glaucoma

Study 1 Gallardo MJ (2021) and Gallardo MJ (2022)

Note, Gallardo (2021) presents the 24-month outcomes for 53 people (60 eyes). Gallardo (2022) presents the 36-month outcomes for 44 people (44 eyes). All baseline characteristics are extracted from Gallardo (2021).

Study details

Study type	Single centre, retrospective, before-and-after study
Country	US
Recruitment period	2014 to 2016
Study population and number	n=53 people, 60 eyes (24 months) Adults with primary open-angle glaucoma.
Age and sex	Mean 73.6 years; 60% female
Patient selection criteria	Inclusion criteria: adults (18 or older) with a diagnosis of mild-moderate, or severe primary open-angle glaucoma. Exclusion criteria: any sign of angle disease; had had laser trabeculoplasty within 6 months of surgery or other angle-based micro-invasive procedure; had neovascular disease, uveitis, peripheral anterior synechiae, or developmental or other forms of secondary glaucoma, such as steroid-induced glaucoma.
Technique	Ab interno canaloplasty using the iTrack device. In 29 eyes, canaloplasty was done concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced 360 degrees, then withdrawn whilst depositing high-molecular-weight hyaluronic acid-based ophthalmic viscoelastic. Glaucoma treatments were stopped 1 day after surgery and only restarted if pressure rose above target.
Follow up	36 months
Conflict of interest/source of funding	Conflict of interest: The author is an investigator, consultant, and speaker for Nova Eye Medical, the manufacturer of iTrack, and for Sight Sciences, the manufacturer of the OMNI and VISCO360 devices. Source of funding: Not reported.

Analysis

Follow up issues: Although not explicitly described in the publication, Gallardo (2021) and Gallardo (2022) capture a highly similar population as a 2018 study by the same author (as summarised in the appendix). In the 2018 study, the 12-month outcomes of 75 eyes in 68 people are described. Gallardo (2021) describes the

24-month outcomes of 60 eyes in 53 people, implying 15 eyes were lost to follow up. Gallardo (2022) describes the 36-month outcomes of 44 eyes in 44 people, implying a further 16 eyes were lost to follow up.

Study design issues: This single centre, before-and-after study reported the 36-month outcomes of people who had ab interno canaloplasty for primary open-angle glaucoma. Cases were identified retrospectively from an analysis of patient records. Primary outcomes included mean IOP and mean number of glaucoma medicines at 12, 24, and 36 months. Safety outcomes included complications and loss of visual acuity.

Gallardo (2021): A repeated-measures ANOVA test was used to compare mean IOP and number of medicines between groups over time followed by a post hoc Tukey's test for multiple comparisons across the visits.

Gallardo (2022): Paired t-tests were used to compare mean IOP and number of medicines between groups over time. The intergroup comparisons between the frequency of categorical changes in IOPs and numbers of medications between 2 time points were analysed with a Pearson chi-square test.

$p<0.05$ was considered statistically significant.

Study population issues: The study cohort consisted of people from Hispanic (74%), black (6%), or white (21%) ethnicity, and the glaucoma stages of mild (38%), moderate (17%) and severe (38%).

Key efficacy findings

IOP reduction

Number of people analysed: 53 people, 60 eyes
Follow up at time of assessment: 24 months

- There was a statistically significant decrease in IOP from 20.7 mmHg (SD 4.9 mmHg) before surgery to 13.6 mmHg (SD 1.9 mmHg) at 12 months and 13.5 mmHg (SD 2.6 mmHg) at 24 months after surgery (both $p<0.001$ compared with baseline).
    - In 29 eyes that had canaloplasty plus phacoemulsification, there was a statistically significant decrease in IOP from 19.8 mmHg (SD 3.9 mmHg) before surgery to 13.0 mmHg (SD not reported) at 12 months and 13.2 mmHg (SD 2.1 mmHg) at 24 months after surgery (both $p<0.001$ compared with baseline).
    - In 31 eyes that had with alone, there was a statistically significant decrease in IOP from 21.6 mmHg (SD 5.7 mmHg) before surgery to 14.1 mmHg (SD not reported) at 12 months and 13.8 mmHg (SD 3.1 mmHg) at 24 months after surgery (both $p<0.001$ compared with baseline).
    - There was no statistically significant difference in the IOP reduction between people who had canaloplasty alone and those who had canaloplasty and phacoemulsification.
    - There were similar decreases in IOP for people with mild/moderate glaucoma and for people with severe glaucoma.

Number of people analysed: 44 people, 44 eyes
Follow up at time of assessment: 36 months

- There was a statistically significant decrease in IOP from 20.5 mmHg (SD 5.1 mmHg) before surgery to 13.3 mmHg (SD 2.1 mmHg) at 12 months, 13.1 mmHg (SD 2.4 mmHg) at 24 months, and 13.3 mmHg (SD 2.1 mmHg) at 36 months after surgery (all $p<0.0001$ compared with baseline).

  - There was no separate statistical analysis presented for IOP reductions in people who had canaloplasty alone and people who had canaloplasty and phacoemulsification, though both decreased.
  - The mean percentage reductions in IOPs for both groups together were 33.9% at 12 months, 33.3% at 24 months, and 32.5% at 36 months.
  - The canaloplasty and phacoemulsification and canaloplasty alone groups showed comparable results of 35.8%, 37.0%, and 31.3%, and 32.1%, 29.7%, and 33.6% at 12, 24, and 36 months, respectively.

Glaucoma medicine reduction

Number of people analysed: 53 people, 60 eyes
Follow up at time of assessment: 24 months

- There was a statistically significant decrease in the mean number of glaucoma medicines used per person from 2.8 (SD 0.9) before surgery to 1.1 (SD 1.1) at 12 months and 1.7 (SD 1.3) at 24 months after surgery (both $p<0.001$ compared with baseline).
  - In 29 eyes that had canaloplasty plus phacoemulsification, there was a statistically significant decrease in the mean number of glaucoma medicines used per person from 2.5 (SD 1.1) before surgery to 0.8 (SD 0.9) at 12 months and 1.3 (SD 1.2) at 24 months after surgery (both $p<0.001$ compared with baseline).
  - In 31 eyes that had canaloplasty alone, there was a statistically significant decrease in the mean number of glaucoma medicines used per person from 3.0 (SD 0.7) before surgery to 1.4 (SD 1.2) at 12 months and 2.1 (SD 1.3) at 24 months after surgery (both $p<0.001$ compared with baseline).
  - There was no statistically significant difference in the reduction in glaucoma medicine use between people who had canaloplasty alone and those who had canaloplasty and phacoemulsification.
  - There were similar decreases in medicine use for people with mild/moderate glaucoma and for people with severe glaucoma.

Number of people analysed: 44 people, 44 eyes
Follow up at time of assessment: 36 months

- There was a statistically significant decrease in the mean number of glaucoma medicines used per person from 2.8 (SD 0.9) before surgery to 1.1 (SD 1.1) at 12 months, 1.0 (SD 1.1) at 24 months, and 1.3 (SD 1.3) at 36 months after surgery (all $p<0.0001$ compared with baseline).
  - There was no separate statistical analysis presented for glaucoma medicine use in people who had canaloplasty alone and people who had canaloplasty and phacoemulsification, though both decreased.
  - The percentages of eyes needing no medicine were 2.3% at baseline, 39.5% at 12 months, 43.6% at 24 months, and 34.1% at 36 months.

Key safety findings

Complications

Number of people analysed: 81 eyes (taken from Gallardo [2022] where complications were reported for all eyes that had ab interno canaloplasty)
Follow up at time of assessment: up to 36 months

- Hyphaema, including microhyphaema (10 eyes), layered hyphaema (3 eyes)
- IOP spike of ≥10 mmHg, n=3.
    - Each occurred within 1 week after surgery.

Visual acuity

Number of people analysed: 53 people, 60 eyes
Follow up at time of assessment: 24 months

- Visual acuity was improved at 24-month follow up in all eyes, with 19 people (42.2%) gaining 2 or more lines of Snellen corrected distance visual acuity.
- In 29 eyes that had canaloplasty plus phacoemulsification, there was a statistically significant improvement in the proportion of people with 20/40 vision from 34.5% before surgery to 80.8% at 24 months after surgery (p=0.0042).
- In 31 eyes that had canaloplasty alone, there was no statistically significant change in the proportion of people with 20/40 vision from 64.5% before surgery to 70.0% at 24 months after surgery (p=0.4716).
- Of the baseline 72 eyes, 1 eye in the canaloplasty plus phacoemulsification group and 3 eyes in the iT canaloplasty alone group lost 2 or more lines (Snellen) of vision acuity. However, those losses were attributed to ocular surface disease and not progression of the visual field defect.

Study 2 Tracer N (2020)

Study details

Study type	Single centre, before-and-after study
Country	US
Recruitment period	2015 to 2017
Study population and number	n=130 people, 180 eyes Adults with mild to moderate open-angle glaucoma.
Age and sex	Mean 70 years; 52% female
Patient selection criteria	Inclusion criteria: diagnosis of mild to moderate open-angle glaucoma (most were primary open-angle glaucoma). Exclusion criteria: advanced glaucoma, prior penetrating glaucoma surgery.
Technique	Ab interno canaloplasty using the VISCO360 device. In all eyes, canaloplasty was concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced 180 degrees, then withdrawn whilst depositing viscoelastic. This was repeated for the second 180 degrees. Glaucoma medicines were continued until the day of surgery and tapered postoperatively as warranted by IOP.
Follow up	12 months
Conflict of interest/source of funding	Conflict of interest: 1 author is an employee of Sight Sciences, the manufacturer of the VISCO360 and OMNI devices. One author reports personal fees from Sight Sciences. Source of funding: Not reported.

Analysis

Follow up issues: Of the 180 eyes that were treated, 122 had data available at 6 months, and 95 had data available at 12 months.

Study design issues: This single centre, before-and-after study reported the 12-month outcomes of ab interno canaloplasty for people with open-angle glaucoma. Cases were identified retrospectively from an analysis of patient records. As per the study design, patients were stratified by baseline IOP. In those with baseline IOP ≥18 mmHg, the primary endpoint was reduction in pressure. In those with baseline IOP <18 mmHg, the primary endpoint was medicine reduction (with maintenance of IOP).

Paired t-tests were used to evaluate differences between baseline and 12-month outcomes. $p<0.05$ was considered statistically significant. There was no adjustment for multiple comparisons.

Study population issues: Six eyes were from people who self-reported that they were Caucasian, 45 from people who were Black, 120 from people who were Hispanic, and 9 listed as 'other'.

Key efficacy findings

IOP reduction

Number of people analysed: 180 eyes at baseline; 122 eyes at 6 months; 95 eyes at 12 months
Follow up at time of assessment: 12 months

- In people with baseline IOP of ≥18 mmHg (n=111 eyes at baseline; number at follow up not reported), there was a statistically significant decrease in IOP from 22.0 mmHg (SD 5.5 mmHg) before surgery to 15.7 mmHg (SD 4.3 mmHg) at 6 months and 17.2 mmHg (SD 5.1 mmHg) at 12 months after surgery (both $p<0.0001$ compared with baseline). The increase in IOP between 6 months and 12 months was not quite statistically significant ($p=0.058$).
- In people with baseline IOP of <18 mmHg (n=69 eyes at baseline; number at follow up not reported), there was little change in IOP from 14.3 mmHg (SD 2.3 mmHg) at baseline to 15.0 mmHg (SD 3.3 mmHg) at 6 months and 15.4 mmHg (SD 4.1 mmHg) at 12 months follow up (statistical significance not reported).

Glaucoma medicine reduction

Number of people analysed: 180 eyes at baseline; 122 eyes at 6 months; 95 eyes at 12 months
Follow up at time of assessment: 12 months

- In people with baseline IOP of ≥18 mmHg (n=111 eyes at baseline; number at follow up not reported), there was no change in the mean glaucoma medicine use per person from 0.9 (SD 0.9) before surgery to 1.0 (SD 0.9) at 12 months after surgery ($p=0.7$).
- In people with baseline IOP of <18 mmHg (n=69 eyes at baseline; number at follow up not reported), there was a statistically significant decrease in the mean glaucoma medicine use per person from 1.1 (SD 0.9) at baseline to 0.6 (SD 0.6) at 12 months follow up ($p<0.05$).

Key safety findings

Number of people analysed: 180 eyes at baseline; 122 eyes at 6 months; 95 eyes at 12 months
Follow up at time of assessment: 12 months

- Hyphaema. n=3 eyes
- IOP spikes ≥10 mmHg above baseline IOP, n=2 eyes
- Mild anterior chamber inflammation, n=1 eye.

Study 3 Hughes T (2020)

Study details

Study type	Single centre, before-and-after study
Country	US
Recruitment period	2018 to 2019
Study population and number	n=64 people, 89 eyes Adults with mild to moderate open-angle glaucoma.
Age and sex	Mean 72.1 years; 64% male
Patient selection criteria	Inclusion criteria: Adults with mild to moderate open-angle glaucoma. Exclusion criteria: pseudoexfoliative glaucoma, pigmentary glaucoma, glaucoma associated with ocular trauma, glaucoma associated with ocular inflammation, previous incisional glaucoma surgery, and eyes with less than 90 degrees of viscodilation.
Technique	Ab interno canaloplasty using the OMNI or VISCO360 device. In 72 eyes, canaloplasty was concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced 180 degrees, then withdrawn whilst depositing viscoelastic. This was repeated for the second 180 degrees. The anterior chamber was irrigated, pressurised to physiological pressure, and injected with an antibiotic/corticosteroid. Glaucoma medicines were continued after surgery and tapered postoperatively as warranted by IOP.
Follow up	18 months
Conflict of interest/source of funding	Conflict of interest: Both authors report research grants from Sight Sciences, the manufacturer of the OMNI and VISCO360 devices, for this research. Source of funding: See above.

Analysis

Follow up issues: Of the 89 eyes assessed preoperatively, 61 had 6 month follow up data, 42 had 12 month, and 22 had 18 month.

Study design issues: This single centre, before-and-after study assessed the 18-month outcomes of ab interno canaloplasty for open-angle glaucoma. Cases were identified retrospectively from an analysis of patient records. Eyes with less than 90 degrees of viscodilation were excluded, potentially excluding people in whom the procedure was attempted but not completed. The efficacy and safety outcomes of these eyes were not reported. The primary outcomes were the difference in IOP and glaucoma medicine use from before to after surgery.

Paired t-tests were used to evaluate the differences between baseline and each postoperative timepoint for IOP and medicine use. $p<0.05$ was considered statistically significant. There was no adjustment for multiple comparisons.

Key efficacy findings

IOP reduction

Number of people analysed: 89 eyes at baseline, 42 at 12 months, 22 at 18 months
Follow up at time of assessment: 18 months

- There was a statistically significant decrease in IOP from 24.5 mmHg (SD 8.3 mmHg) before surgery to 16.5 mmHg (SD 3.4 mmHg) at 12 months ($p<0.0005$) and 15.8 mmHg (SD 2.5 mmHg) at 18 months ($p<0.0005$).
    - There was no statistically significant difference in the mean change in IOP between people who had ab interno canaloplasty combined with phacoemulsification and for those people who had ab interno canaloplasty only.

Glaucoma medicine reduction

Number of people analysed: 89 eyes at baseline, 42 at 12 months, 18 at 18 months
Follow up at time of assessment: 18 months

- There was a statistically significant decrease in the mean number of glaucoma medicines used from 2.5 (SD 1.3) before surgery to 1.8 (SD 1.4) at 12 months ($p<0.0005$) and 1.7 (SD 1.5) at 18 months ($p<0.05$).
    - There was no statistically significant difference in the change in glaucoma medicine use between people who had ab interno canaloplasty combined with phacoemulsification and for those people who had ab interno canaloplasty only.

Need for further surgery

Number of people analysed: 89 eyes at baseline, 42 at 12 months, 18 at 18 months
Follow up at time of assessment: 18 months

- Need for future glaucoma filtering surgery, n=6
    - These people had higher baseline IOP and medicine use than the cohort mean.

Key safety findings

Number of people analysed: 89 eyes at baseline, 42 at 12 months, 22 at 18 months
Follow up at time of assessment: 18 months

Mild intraoperative bleeding at the surgery site with subsequent microhyphaema not considered an adverse event for this surgery. There were no clinically significant hyphaemas.

Study 4 Ondrejka S (2019)

Study details

Study type	Single centre, before-and-after study
Country	Germany
Recruitment period	2015 to 2018
Study population and number	n=71 people, 106 eyes Adults with mild to moderate open-angle glaucoma.
Age and sex	Mean 75.0 years; 63% female
Patient selection criteria	Inclusion criteria: people who had insufficiently controlled IOP on current medicine (Group 1; baseline IOP ≥18 mmHg) or, if adequately controlled, in need of reduced medicine burden (Group 2; baseline IOP <18 mmHg). Exclusion criteria: glaucoma other than primary open-angle glaucoma, prior glaucoma surgery, terminal stage of open-angle glaucoma, or central retinal vein occlusion.
Technique	Ab interno canaloplasty using the VISCO360 device. In 94 eyes, canaloplasty was concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced 180 degrees, then withdrawn whilst depositing viscoelastic. This was repeated for the second 180 degrees. The anterior chamber was then irrigated and aspirated. Glaucoma medicines were continued until the day of surgery and were then discontinued.
Follow up	12 months
Conflict of interest/source of funding	Conflict of interest: The authors declared no conflict of interest. Source of funding: Sight Sciences, the manufacturer of the VISCO360 device, provided financial assistance to support writing, editorial, and statistical analysis.

Analysis

Follow up issues: 105 eyes had data available for analysis at 12 months (SD 3 months) follow up.

Study design issues: This single centre, before-and-after study assessed the outcomes of ab interno canaloplasty in people with open-angle glaucoma. Cases were identified retrospectively from an analysis of patient records. As per the study design, patients were stratified by baseline IOP into Group 1 (baseline IOP ≥18 mmHg) and Group 2 (baseline IOP <18 mmHg). The primary outcome measure for Group 1 was change in mean IOP and mean number of glaucoma medicines at 12 months. The primary outcome for Group 2 was change in the mean number of glaucoma medicines at 12 months.

Paired t-tests with post hoc Tukey adjustment to account for multiple comparisons was done to compare IOP and the number of glaucoma medicines with baseline. $p<0.05$ was considered statistically significant.

Key efficacy findings

IOP reduction

Number of people analysed: 72 eyes (Group 1: baseline IOP ≥18 mmHg), 34 eyes (Group 2: baseline IOP <18 mmHg)
Follow up at time of assessment: 12 months (plus or minus 3 months)

- Group 1: There was a statistically significant decrease in mean IOP from 24.6 mmHg (SD 7.1 mmHg) before surgery to 14.6 mmHg (SD 2.8 mmHg) at 12 months after surgery ($p<0.001$).
- Group 2: There was no statistically significant change in mean IOP from before surgery to 12 months after surgery.

Glaucoma medicine reduction

Number of people analysed: 72 eyes (Group 1: baseline IOP ≥18 mmHg), 34 eyes (Group 2: baseline IOP <18 mmHg)
Follow up at time of assessment: 12 months (plus or minus 3 months)

- Group 1: There was a statistically significant decrease in mean glaucoma medicine use from 2.1 (SD 1.0) before surgery to 0.2 (SD 0.6) at 12 months after surgery ($p<0.001$).
- Group 2: There was a statistically significant decrease in mean glaucoma medicine use from 1.8 (SD 0.9) before surgery to 0.2 (SD 0.6) at 12 months after surgery ($p<0.001$).

Key safety findings

Number of people analysed: 106 eyes (105 at 12 months)
Follow up at time of assessment: 12 months

- VISCO360 device deficiency, n=1
    - Catheter detached from the handle and cannula and had to be retrieved with vitrectomy forceps.
    - The patient had no adverse sequalae.
    - Note that this device is a precursor of the OMNI device and is no longer commercially available.
- Hyphaema, n=14
    - All resolved within 7 days without the need for further intervention.
- Fibrin in pupillary plane, n=1

Study 5 Koerber N (2022)

Study details

Study type	Single centre, before-and-after study
Country	Germany
Recruitment period	2014 to 2016
Study population and number	n=21 people, 27 eyes Adults with uncontrolled or controlled open-angle glaucoma.
Age and sex	Mean 77.3 years; 52% female
Patient selection criteria	Inclusion criteria: all patients aged 18 years or older with a diagnosis of either uncontrolled or controlled open-angle glaucoma were eligible for inclusion. Controlled IOP was defined as an IOP equal to or less than 18mmHg. Cases of pseudoexfoliative glaucoma due to progression despite treatment were also eligible for inclusion. Exclusion criteria: secondary forms of glaucoma such as those with neovascular disease, uveitis, peripheral anterior synechiae, angle closure, narrow-angle glaucoma, or traumatic glaucoma were excluded.
Technique	Ab interno canaloplasty using the iTrack device. In 23 eyes, canaloplasty was done concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced through Schlemm's canal, then withdrawn whilst depositing viscoelastic. The anterior chamber was then irrigated and aspirated.
Follow up	48 months
Conflict of interest/source of funding	Conflict of interest: The authors declared no conflict of interest, however, 1 author is the principal investigator in a study of the iTrack device. Source of funding: Not reported.

Analysis

Follow up issues: Outcomes were assessed at 12, 24, 36, and 48 months. Nine eyes were lost to follow up for the 48-month visit.

Study design issues: This single centre, before-and-after study assessed the outcomes of ab interno canaloplasty in people with open-angle glaucoma. Cases were identified retrospectively from an analysis of patient records. The primary outcome measure for was change in mean IOP and mean number of glaucoma medicines at 12 months.

Comparative analysis between visits was done using repeated measures ANOVA test followed by a post hoc Tukey test for multiple comparisons and nonparametric Friedman test followed by Wilcoxon signed-rank test for multiple comparisons. $p<0.05$ was considered statistically significant.

Key efficacy findings

IOP reduction

Number of people analysed: 27 eyes in 21 people
Follow up at time of assessment: 48 months

- There was a statistically significant decrease in mean IOP from 19.85 mmHg (SD 5.2 mmHg) before surgery to 14.98 mmHg (SD 2.6 mmHg) at 12 months, 15.58 mmHg (SD 3.3 mmHg) at 24 months, 14.71 mmHg (SD 3.8 mmHg) at 36 months, and 14.56 mmHg (SD 3.0 mmHg) at 48 months (all $p<0.001$ compared with baseline).
- There was no statistically significant change in IOP between each postoperative visit ($p=0.35$).
- The proportion of eyes with at least a 25% reduction in IOP was:
    - 12 months: 46.2%
    - 24 months: 40.0%
    - 36 months: 57.1%
    - 48 months: 50.0%
- The proportion of eyes with IOP of ≤17 mmHg was:
    - 12 months: 80.8%
    - 24 months: 80.0%
    - 36 months: 71.4%
    - 48 months: 77.8%
- The proportion of eyes with IOP of ≤15 mmHg was:
    - 12 months: 53.8%
    - 24 months: 48.0%
    - 36 months: 57.1%
    - 48 months: 66.7%

Glaucoma medicine reduction

Number of people analysed: 27 eyes in 21 people
Follow up at time of assessment: 48 months

- There was a statistically significant decrease in mean glaucoma medicine use from 1.93 (SD 1.00) before surgery to 0.30 (SD 0.54) at 12 months, 0.40 (SD 0.64) at 24 months, 0.80 (SD 0.83) at 36 months, and 0.89 (SD 0.83) at 48 months after surgery (all $p<0.05$ compared with baseline).
    - There was no statistically significant difference in medicine use between 12 and 24 months.
    - There was a statistically significant increase in medicine use between 12 and 36 months ($p=0.03$) and 12 and 48 months ($p=0.048$).

Key safety findings

Complications

Number of people analysed: 27 eyes in 21 people
Follow up at time of assessment: 48 months

- No significant complications were noted.
- Limited descemetolysis near the limbus, n=1

Visual outcomes

Number of people analysed: 27 eyes in 21 people
Follow up at time of assessment: 48 months

- All eyes except 1 showed no change or improvement in visual field. One eye demonstrated a deterioration of the visual field.
- There was a statistically significant improvement in visual acuity between baseline and the last postoperative visit ($p<0.001$).

Study 6 Toneatto G (2022)

Study details

Study type	Double-centre, before-and-after study
Country	Italy
Recruitment period	2017 to 2020
Study population and number	n=73 people, 80 eyes Adults with mild to moderate open-angle glaucoma.
Age and sex	Mean 74.5 years; 59% female
Patient selection criteria	Inclusion criteria: people who had primary open angle glaucoma, pigmentary glaucoma, and pseudoexfoliative glaucoma. Exclusion criteria: not reported.
Technique	Ab interno canaloplasty using the OMNI device. In 30 eyes, canaloplasty was concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced 180 degrees, then withdrawn whilst depositing viscoelastic. This was repeated for the second 180 degrees. The anterior chamber was then irrigated and aspirated.
Follow up	12 months
Conflict of interest/source of funding	Conflict of interest: The authors declared that they had no conflict of interest. Source of funding: The authors declared that external funding was not received.

Analysis

Follow up issues: Of the 80 eyes at baseline, 66 completed the 12 months follow up.

Study design issues: This double-centre, before-and-after study assessed the outcomes of ab interno canaloplasty in people with open-angle glaucoma. Cases were identified retrospectively from an analysis of patient records. This study allowed people with pseudoexfoliative glaucoma or pigmentary dispersion glaucoma, and those who had previous glaucoma surgery. The primary outcome measures were IOP reduction and reduction in the mean number of glaucoma medicines at 12 months. Surgical success rates were also calculated. Complete successes were those who reached an IOP target no glaucoma medicine. Qualified successes were those reached an IOP target with no more glaucoma medicine use than baseline.

The mean levels of IOP at different follow-up times were compared with baseline by a paired sample t-test. The decrease of glaucoma medicine use in each group was analysed by a non-parametric Wilcoxon matched-pairs signed rank test. There was no adjustment for multiple comparisons.

Study population issues: Diagnoses included primary open-angle glaucoma (63.8%), pseudoexfoliative glaucoma (33.7%), and pigmentary dispersion glaucoma (2.5%). Previous glaucoma surgeries included laser trabeculoplasty (18.8%), deep sclerectomy (12.5%), and trabeculectomy (3.8%).

Key efficacy findings

IOP reduction

Number of people analysed: 73 people, 80 eyes at baseline, 66 eyes at 12 months
Follow up at time of assessment: 12 months

- There was a statistically significant decrease in mean IOP from 22.5 mmHg (SD 5.3 mmHg) before surgery to 15.0 mmHg (SD 3.6 mmHg) at 12 months after surgery ($p<0.001$).
    - In people who had canaloplasty alone, there was a statistically significant reduction in mean IOP from 23.0 mmHg (SD 5.7 mmHg) before surgery to 15.6 mmHg (SD 3.6 mmHg) at 12 months after surgery ($p<0.001$).
    - In people who had canaloplasty and cataract surgery, there was a statistically significant reduction in mean IOP from 21.5 mmHg (SD 4.7 mmHg) before surgery to 14.1 mmHg (SD 3.3 mmHg) at 12 months after surgery ($p<0.001$).
    - The difference in mean IOP decrease between groups was not statistically significant.

Glaucoma medicine reduction

Number of people analysed: 73 people, 80 eyes at baseline, 66 eyes at 12 months
Follow up at time of assessment: 12 months

- There was a statistically significant decrease in mean glaucoma medicine use from 3.2 (SD 1.0) before surgery to 1.9 (SD 1.4) at 12 months after surgery ($p<0.001$).
    - In people who had canaloplasty alone, there was a statistically significant reduction in mean glaucoma medicine use from 3.0 (SD 1.1) before surgery to 2.0 (SD 1.4) at 12 months after surgery ($p<0.001$).
    - In people who had canaloplasty alone, there was a statistically significant reduction in mean glaucoma medicine use from 3.4 (SD 0.8) before surgery to 1.9 (SD 1.4) at 12 months after surgery ($p<0.001$).
    - The difference in mean glaucoma medicine use decrease between groups was not statistically significant.

Surgical success

Number of people analysed: 73 people, 80 eyes at baseline, 66 eyes at 12 months
Follow up at time of assessment: 12 months

- Target IOP 16 mmHg or less and 25% or more reduction in IOP:
    - At 12 months, 10.3% of eyes were complete successes.
    - A further 43.6% of eyes were qualified successes.
- Target IOP 18 mmHg or less and 25% or more reduction in IOP:
    - At 12 months, 11.5% of eyes were complete successes.
    - A further 50.0% of eyes were qualified successes.

Need for further surgery

Number of people analysed: 73 people, 80 eyes at baseline, 66 eyes at 12 months
Follow up at time of assessment: 12 months

- Further surgery, n=12
    - Trabeculectomy, n=9
    - Deep sclerectomy, n=3

Key safety findings

Complications

Number of people analysed: 73 people, 80 eyes at baseline, 66 eyes at 12 months
Follow up at time of assessment: 12 months

Mild or microhyphaema were not considered adverse events for this surgery.

- Moderate or severe hyphaema, n=2
    - Both cases needed a wash of the anterior chamber. Both recovered within 10 days.
- Mild hypotony, n=4
- IOP spike of 10 mmHg or more above baseline, n=1

Visual acuity

Number of people analysed: 73 people, 80 eyes at baseline, 66 eyes at 12 months
Follow up at time of assessment: 12 months

- No statistically significant change in visual acuity was seen in people who had canaloplasty alone ($p=0.31$)
- There was a statistically significant change in visual acuity in people who had canaloplasty and phacoemulsification from 6.8/10 (SD 2.1) before surgery to 9.1/10 (SD 2.6) at 12 months after surgery ($p<0.001$).

Study 7 Gillman K (2021)

Study details

Study type	Single centre, before-and-after study
Country	Switzerland
Recruitment period	2015 to 2019
Study population and number	n=71 eyes, total people not reported Adults with mild to moderate open-angle glaucoma.
Age and sex	Mean 73.1 years; 52% female
Patient selection criteria	Inclusion criteria: uncontrolled mild-to-moderate open-angle glaucoma with concomitant clinically significant cataract. Exclusion criteria: not reported.
Technique	Ab interno canaloplasty using the iTrack device. In all eyes, canaloplasty was concurrently with phacoemulsification. The microcatheter was inserted via a clear corneal incision and goniotomy into Schlemm's canal. The microcatheter was advanced 360 degrees, then withdrawn whilst depositing viscoelastic. Postoperatively, glaucoma medicine was initially withheld, then reinstated as needed to maintain IOP below 15 mmHg.
Follow up	12 months
Conflict of interest/source of funding	Conflict of interest: The authors declared that they had no conflict of interest. Source of funding: The authors declared that external funding was not received.

Analysis

Follow up issues: Of the 71 eyes identified that had ab interno canaloplasty during the study period, 54 eyes in 41 people had 12 month follow up data.

Study design issues: This single centre, before-and-after study assessed the outcomes of ab interno canaloplasty for open-angle glaucoma in combination with phacoemulsification. Cases were identified retrospectively from an analysis of patient records. Cases without 12 month follow up were excluded unless they were considered failures due to reoperation or severe complications. The primary outcome measure was IOP reduction. Surgical success rates were also calculated. Complete successes were those who had a 20% or more reduction in IOP with no medicine. Qualified successes were those who had a 20% or more reduction

in IOP with no more medicine use than baseline. Failures were those who did not meet the criteria for success, or those who had additional glaucoma surgery or loss of light perception.

The cumulative probability of success was assessed using Kaplan-Meier survival curves. The tests were 2-tailed. $p<0.05$ was considered statistically significant. There was no adjustment for multiple comparisons.

Study population issues: All included people were Caucasian. Diagnoses included primary open-angle glaucoma (66.7%), pseudoexfoliative glaucoma (18.5%), and pigmentary glaucoma (14.8%). A total of 4 eyes had previous glaucoma surgery.

Key efficacy findings

IOP reduction

Number of people analysed: 41 people, 54 eyes
Follow up at time of assessment: 12 months

- There was a statistically significant decrease in mean IOP from 23.6 mmHg (SD 7.4 mmHg) before surgery to 14.2 mmHg (SD 2.9 mmHg) at 12 months after surgery ($p<0.001$).

Glaucoma medicine reduction

Number of people analysed: 41 people, 54 eyes
Follow up at time of assessment: 12 months

- There was a statistically significant decrease in mean glaucoma medicine use from 2.9 (SD 1.0) before surgery to 0.6 (SD 1.1) at 12 months after surgery ($p<0.001$).

Surgical success

Number of people analysed: 41 people, 54 eyes
Follow up at time of assessment: 12 months

- Complete success was achieved in 46% of eyes, with a further 19% achieving qualified success.
- Failure was seen in 35% of eyes, all due to uncontrolled IOP, 36.8% of which needed further filtering surgery.

Need for further surgery

Number of people analysed: 41 people, 54 eyes
Follow up at time of assessment: 12 months

- Additional glaucoma surgery, n=7

Key safety findings

Number of people analysed: 41 people, 54 eyes

Follow up at time of assessment: 12 months

Self-resolving hyphaema was not considered an adverse event.

- Complications up to 30 days after surgery:
  - IOP spikes over 30 mmHg, n=12
  - Self-resolving endothelial blood stain, n=1
  - Iris atrophy, n=1
  - Pupillary block, n=1
  - Fibrin plug, n=1
- Complications from 1 month after surgery onwards:
  - IOL subluxation, n=1

Validity and generalisability of the studies

- The studies were similar regarding patient characteristics. However, there were differences in the types of glaucoma permitted – some studies permitted pigmentary or pseudoexfoliative glaucoma as well as primary open-angle glaucoma.

- The surgical technique was highly consistent across studies. Minor differences were seen in the degrees of cannulation (180 degrees twice, or 360 degrees) and in the postoperative care.

- All of the studies included at least some people who had canaloplasty combined with phacoemulsification. Phacoemulsification can often lower IOP by a small amount. However, each of the studies that included people who had canaloplasty alone and people who had canaloplasty plus phacoemulsification reported that there were no statistically significant differences in the amount of IOP reduction between the 2 groups.

- CE marked devices were used in all studies.

- Cases were identified retrospectively from patient records. This can lead to selection bias – though this was mitigated by some studies by selection of consecutive patients. Furthermore, outcome data was typically collected as part of normal follow up – this may have been a reason for the high attrition reported by several studies.

- Several studies did not report adjustment for multiple comparisons. Testing many hypotheses without adjustment for multiple comparisons increases the likelihood of a type 1 error (false positive). However, the p-values obtained in most analyses were small enough to not be affected by adjustment for multiple comparisons.

- All studies had a before-and-after design. There were no randomised studies identified.

- Studies were conducted in the US, Germany, Italy, and Switzerland. There may exist differences in clinical practice between the UK and these countries that prevent generalisation of the findings to a UK context.

- The longest follow-up assessment was 4 years, and some studies showed an attenuation of treatment effect over time.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- High-intensity focused ultrasound for glaucoma (2019) NICE interventional procedures guidance 661.
- Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma (2018) NICE interventional procedure guidance 612.
- Ab externo canaloplasty for primary open-angle glaucoma (2017) NICE interventional procedure 591.
- Trabecular stent bypass microsurgery for open-angle glaucoma (2017) NICE interventional procedures guidance 575.
- Trabeculotomy ab interno for open angle glaucoma (2011) NICE interventional procedure guidance 397.

NICE guidelines

- Glaucoma: diagnosis and management (2017) NICE guideline NG81

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional 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 professional experts, 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.

Four professional expert questionnaires for ab interno canaloplasty for open-angle glaucoma were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 3 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the professional experts. One patient discussed a possible complication with postoperative eye drops, but appeared to not be directly related to canaloplasty.

Company engagement

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Most studies using the OMNI device were included in Appendix A. This is because the OMNI device is capable of ab interno canaloplasty and trabeculotomy and these studies used both techniques. This overview is focused on ab interno canaloplasty alone.

- The following randomised controlled trial was identified:

    - Multicenter Ab-interno Glaucoma Study Investigating Canaloplasty (MAGIC; NCT04769453). RCT of ab interno canaloplasty with iTrack vs. OMNI. Est. enrolment: 156 patients. As of November 2022, this study is suspended; private communication with the sponsor suggests that this trial will resume with recruitment in Europe. This study is sponsored by Nova Eye, the manufacturer of the iTrack device.

References

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2. Gallardo MJ. (2022) 36-Month Effectiveness of Ab-Interno Canaloplasty Standalone versus Combined with Cataract Surgery for the Treatment of Open-Angle Glaucoma. Ophthalmology Glaucoma.
3. Tracer N, Dickerson JE, and Radcliffe NM. (2020) Circumferential viscodilation ab interno combined with phacoemulsification for treatment of open-angle glaucoma: 12-month outcomes. Clinical Ophthalmology 14:1357-64.
4. Hughes T and Traynor M. (2020) Clinical results of ab interno canaloplasty in patients with open-angle glaucoma. Clinical Ophthalmology 14:3641-50.
5. Ondrejka S and Korber N. (2019) 360-degree ab-interno schlemm's canal viscodilation in primary open-angle glaucoma. Clinical Ophthalmology 13:1235-46.
6. Koerber N and Ondrejka S. (2022) Four-Year Efficacy and Safety of iTrack Ab-interno Canaloplasty as a Standalone Procedure and Combined with Cataract Surgery in Open-Angle Glaucoma. Klinische Monatsblätter für Augenheilkunde.
7. Toneatto G, Zeppieri M, Papa V, et al. (2022) 360° Ab-interno schlemm's canal viscodilation with OMNI viscosurgical systems for open-angle glaucoma-midterm results. Journal of Clinical Medicine 11(1).
8. Gillmann K, Aref A, Niegowski LJ, and Baumgartner JM. (2021) Combined ab interno viscocanaloplasty (ABiC) in open-angle glaucoma: 12-month outcomes. International Ophthalmology 41(10):3295-301.

Literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	20/06/2022	1946 to June 17, 2022
MEDLINE In-Process (Ovid)	20/06/2022	1946 to June 17, 2022
MEDLINE Epubs ahead of print (Ovid)	20/06/2022	1946 to June 17, 2022
EMBASE (Ovid)	20/06/2022	1974 to 2022 June 17
EMBASE Conference (Ovid)	20/06/2022	1974 to 2022 June 17
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	20/06/2022	Issue 6 of 12, June 2022
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	20/06/2022	Issue 5 of 12, May 2022

Trial sources searched

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

Websites searched

- 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)
- General internet search

MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

1 Glaucoma, Open-Angle/
2 ((Primary or second* or refract* or compensat*) adj4 open angle glaucoma*).tw.
3 (POAG or COAG).tw.
4 Ocular Hypertension/
5 Intraocular Pressure/
6 IOP.tw.

7	((Ocular* or intraocul* or eye) adj4 (hypertens* or pressure*)).tw.
8	(open adj4 angle* adj4 glaucoma*).tw.
9	Pseudo-exfoliative glaucoma.tw.
10	Pigment* glaucoma*.tw.
11	(simpl* adj4 glaucoma).tw.
12	or/1-11
13	ab interno.tw.
14	canaloplast*.tw.
15	ABiC.tw.
16	(circumferent* adj4 viscodilat*).tw.
17	or/13-16
18	12 and 17
19	iTrack.tw.
20	18 or 19
21	Animals/ not Humans/
22	20 not 21

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Brown RH, Tsegaw S, Dhamdhere K et al. (2020) Viscodilation of Schlemm canal and trabeculotomy combined with cataract surgery for reducing intraocular pressure in open-angle glaucoma. Journal of cataract and refractive surgery 46(4)	n=24 people, 41 eyes FU=4.1 months	This study found that OMNI combined with phacoemulsification reduced IOP. The magnitude of pressure lowering with OMNI was highly correlated with the preoperative IOP.	Combined use of canaloplasty and trabeculotomy.
Davids AM, Pahlitzsch M, Boeker A et al. (2019) Ab interno canaloplasty (ABiC)-12-month results of a new minimally invasive glaucoma surgery (MIGS). Graefe's archive for clinical and experimental ophthalmology 257(9): 1947-53	n=28 people, 36 eyes FU=12 months	Ab interno canaloplasty effectively lowered the IOP in primary open-angle glaucoma in the short-term follow up of 12 months. A reduction of glaucoma therapy was not achieved.	Studies with more people or longer follow up were included.
Docherty G, Waldner D, Schlenker M, et al. (2020) Ab interno canaloplasty in open-angle glaucoma patients combined with in vivo trypan blue. Aqueous	n=5 people FU=up to 18 months	The primary purpose of this paper is to describe canalogram patterns seen during ab interno canaloplasty with trypan blue. There were drops in IOP and medicine use in all patients who had	Studies with more people or longer follow up were included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Venography. Journal of glaucoma 29(12): e130-e134		treatment. There were no complications.	
Gallardo MJ, Dhamdhere K, and Dickerson JE. (2022) Canaloplasty and trabeculotomy ab interno combined with cataract surgery: 12-month outcomes in hispanic patients with open-angle glaucoma. Clinical Ophthalmology 16:905-8	n=39 FU=12 months	The present analysis indicates that the favourable safety and effectiveness for OMNI reported in the broader population is also seen in Hispanic patients.	Combined use of canaloplasty and trabeculotomy.
Gallardo MJ, Pyfer MF, Vold SD et al. (2022) Canaloplasty and trabeculotomy combined with phacoemulsification for glaucoma: 12-month results of the GEMINI study. Clinical Ophthalmology 16:1225-34	n=120 FU=12 months	Canaloplasty and trabeculotomy done with the OMNI surgical system at the time of phacoemulsification significantly reduces unmedicated mean diurnal IOP and medication use 12 months postoperatively, with an excellent safety profile. This procedure should be considered for eyes with mild-moderate OAG to reduce IOP, medication burden, or both.	Combined use of canaloplasty and trabeculotomy.
Gallardo MJ, Supnet RA, Ahmed IIK. (2018) Viscodilation of Schlemm's canal for the reduction of IOP via an ab-interno approach. Clinical Ophthalmology 12:2149-55	n=68 people, 75 eyes FU=12 months	Ab interno canaloplasty was effective at reducing IOP and medicine use in eyes with uncontrolled primary open-angle glaucoma with or without cataract surgery.	Overlap with Gallardo (2021), with shorter follow up.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Gallardo MJ, Supnet RA, and Ahmed IIK. (2018) Circumferential viscodilation of Schlemm's canal for open-angle glaucoma: Ab-interno vs ab-externo canaloplasty with tensioning suture. Clinical Ophthalmology 12:2493-2498	n=12, 12 eyes FU=12 months	This paired eye study found ab interno canaloplasty to have comparable IOP lowering and glaucoma medicine reduction to ab externo canaloplasty in open-angle glaucoma. This suggests ab interno canaloplasty may be a suitable method for improving aqueous outflow via the trabecular pathway. Further large-scale investigation is needed.	Studies with more people or longer follow up included.
Gallardo MJ, Sarkisian SR, Vold SD, et al. (2021) Canaloplasty and trabeculotomy combined with phacoemulsification in open-angle glaucoma: Interim results from the GEMINI study. Clinical Ophthalmology 15:481-489	n=137 people FU=6 months	Canaloplasty followed with trabeculotomy (done by the OMNI system) and done concomitantly with phacoemulsification has favourable intra and perioperative safety, significantly reduces IOP and glaucoma medicines through 6 months in eyes with mild-moderate open-angle glaucoma.	Combined use of canaloplasty and trabeculotomy.
Gillmann K and Mansouri K. (2020) Minimally Invasive glaucoma surgery: where is the evidence? Asia-Pacific journal of ophthalmology 9(3):203-14	n=4 studies	Systematic review and meta-analysis. Based on meta-analysis of 4 studies, ab interno canaloplasty reduced IOP by 36.2% and reduced glaucoma medicine use by 62.1%.	One of the studies included in the meta-analysis used ab externo canaloplasty. The other 3 studies are either described in the key evidence or appendix of this overview.
Grabska-Liberek I, Duda P, Rogowska M, et al. (2021) 12-month interim results of a prospective study of	n=15 people, 17 eyes	Viscodilation of Schlemm's canal and collector channels paired with ab interno trabeculotomy done with	Combined use of canaloplasty and trabeculotomy.

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patients with mild to moderate open-angle glaucoma undergoing combined viscodilation of Schlemm's canal and collector channels and 360degree trabeculotomy as a standalone procedure or combined with cataract surgery. European Journal of Ophthalmology	FU=12 months	a single integrated instrument (OMNI), whether as standalone or combined with phacoemulsification, effectively lowers both IOP and the need for glaucoma medicines through 12 months of follow up.	
Habash AA, Aljindan M, Alrushoud M, et al. (2020) Combined gonioscopy-assisted transluminal trabeculotomy (GATT) with ab interno canaloplasty (ABiC) in conjunction with phacoemulsification: 12-month outcomes. Clinical Ophthalmology 14: 2491-96	n=19 people, 20 eyes FU=12 months	The 12-month results of this study suggest that combined GATT with ab interno canaloplasty in conjunction with phacoemulsification is a safe and effective alternative in decreasing the IOP and number of glaucoma medicines in people with primary open-angle glaucoma.	Combined use of canaloplasty and trabeculotomy.
Heersink M and Dovich JA. (2019) Ab interno canaloplasty combined with trabecular bypass stenting in eyes with primary open-angle glaucoma. Clinical Ophthalmology 13:1533-42	n=86 eyes FU=6 months	At 6 months, a greater proportion of people who had cataract extraction, trabecular meshwork bypass, and canaloplasty achieved an IOP reduction of 20% or more and an IOP of less than 18 mmHg on the same or fewer medicines than for people who had trabecular meshwork bypass and cataract extraction.	Combined use of canaloplasty and stenting.

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Hirsch L, Cotliar J, Vold S, et al. (2021) Canaloplasty and trabeculotomy ab interno with the OMNI system combined with cataract surgery in open-angle glaucoma: 12-month outcomes from the ROMEO study. Journal of cataract and refractive surgery 47(7):907-15	n=81 FU=12 months	The OMNI system provided effective IOP reduction, sustained IOP control, and meaningful medicine reduction for up to 12 months postoperative.	Combined use of canaloplasty and trabeculotomy.
Kazerounian S, Zimbelmann M, Lortscher M et al. (2021) Canaloplasty ab interno (AbiC) - 2-year-results of a novel minimally invasive glaucoma surgery (MIGS) technique. Klinische Monatsblatter fur Augenheilkunde 238(10):1113-9	n=23 people, 25 eyes FU=24 months	Ab interno canaloplasty done independently or combined with cataract surgery seems to be a safe and effective MIGS-technique with good long-term regulation of IOP and low risk profile.	Studies with more people included.
Klabe K and Kaymak H. (2021) Standalone trabeculotomy and viscodilation of Schlemm's canal and collector channels in open-angle glaucoma using the OMNI surgical system: 24-Month Outcomes. Clinical ophthalmology (Auckland, N.Z.) 15	n=27 FU=24 months	The OMNI surgical system provides clinically relevant and statistically significant reductions in both IOP and medications with an excellent safety profile and should be considered in phakic or pseudophakic eyes with mild-moderate OAG needing IOP or medication reduction, or both.	Combined use of canaloplasty and trabeculotomy.
Körber N. (2018) Ab interno canaloplasty for the treatment of glaucoma: a case	n=20 people, 20 eyes	Findings from this study indicate that ab interno canaloplasty is comparable to	Studies with more people or longer follow up included.

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series study. Spektrum der Augenheilkunde : Zeitschrift der Osterreichischen Ophthalmologischen Gesellschaft, OOG 32(6)	FU=12 months	conventional canaloplasty in lowering IOP and medicine dependency. Long-term follow up in a large cohort is needed to confirm the efficacy of this minimally invasive glaucoma procedure	
Porsia L and Nicoletti M. (2020) Combined viscodilation of schlemm's canal and collector channels and 360degree ab-interno trabeculotomy for congenital glaucoma associated with sturge-weber syndrome. International Medical Case Reports Journal 13:217-20	n=1 FU=10 months	Successful treatment of glaucoma in an infant. Through 10 months of follow-up, IOP was adequately controlled without the need for adjunctive medical therapy.	Studies with more people or longer follow up included.
Pyfer MF, Gallardo M, Campbell A, et al. (2021) Suppression of diurnal (9am-4pm) IOP fluctuations with minimally invasive glaucoma surgery: An analysis of data from the prospective, multicenter, single-arm GEMINI study. Clinical Ophthalmology 15:3931-8	n=128 people FU=12 months	This study shows that eyes with open-angle glaucoma can benefit from an overall decreased IOP and degree of IOP fluctuations for as long as 12 months after surgical treatment with canaloplasty and trabeculotomy.	Combined use of canaloplasty and trabeculotomy.
Riaz KM, Gill MS, Murphy DA et al. (2022) Surgical management of intraocular pressure with ab interno canaloplasty in	n=17 FU=12 months	ab interno canaloplasty is a clinically safe and effective treatment that can be done in postkeratoplasty patients to reduce IOP for at least	Studies with more people or longer follow up included.

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postkeratoplasty patients: 12-month results. Cornea		1 year without any significant complications.	
Villa KRM, Agudelo N, Rubio B, et al. (2019) Ab interno canaloplasty after failed trabeculectomy in uncontrolled open-angle glaucoma. Investigative Ophthalmology and Visual Science 60(9)	n=7 people, 9 eyes FU=6 months	In people with uncontrolled open-angle glaucoma after failed trabeculectomy ab interno canaloplasty appears to be a safe and effective procedure. At 6 months follow up reduction in IOP remain stable and reduction in glaucoma medicines was significantly reduced.	Conference abstract. Studies with more people or longer follow up included.
Vizzari G and Bordin P. (2018) Mid and long-term outcomes of viscodilation associated with trabeculotomy using the VISCO360 microinvasive device for the treatment of open angle glaucoma. Investigative Ophthalmology and Visual Science 59(9)	n=37 people, 55 eyes FU=12 months	Viscodilation and trabeculotomy achieved a high percentage of surgical success during the whole follow up time and was effective in preventing the most serious immediate complications of other most invasive surgeries.	Conference abstract. Combined use of canaloplasty and trabeculotomy.
Vold SD, Williamson, BK, Hirsch L, et al. (2021) Canaloplasty and trabeculotomy with the OMNI system in pseudophakic patients with open-angle glaucoma: the ROMEO study. Ophthalmology Glaucoma 4(2):173-81	n=48 FU=12 months	The sequential combination of canaloplasty followed by trabeculotomy done as stand-alone procedures using the OMNI system in pseudophakic patients with open-angle glaucoma provides effective IOP reduction or sustained IOP control and meaningful medicine reduction for up to 12 months postoperatively.	Combined use of canaloplasty and trabeculotomy.