NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma

Primary open-angle glaucoma is a progressive condition that causes long-term increase of pressure within 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 placing a tiny soft gel tube into the eye to create a new channel to allow excess fluid to drain out. The aim is to reduce pressure in the eye.

Contents

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 specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2017.

Procedure name

- Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma

Specialist societies

- Royal College of Ophthalmologists.

Description of the procedure

Indications and current treatment

Open-angle glaucoma is a chronic condition associated with increased intraocular pressure, which 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, inserting drainage tubes, deep sclerectomy, viscocanalostomy or laser trabeculoplasty may also be used.

What the procedure involves

Microinvasive insertion of a trans-scleral gelatin stent via the ab interno approach (placed surgically from the anterior chamber, outwards to the subconjunctival space) for treating open-angle glaucoma is a minimally invasive procedure. It involves implanting a gelatin stent, a collagen-derived drainage device, to reduce intraocular pressure. The collagen is derived from animal sources. The procedure creates an artificial bypass channel and drainage pathway from the anterior chamber into the non-dissected tissue of the subconjunctival space to improve drainage and outflow of aqueous humor.

This procedure can be done at the same time as phacoemulsification and intraocular lens insertion for treating cataracts.

Under local or topical anaesthesia, a small incision is made in the cornea, and the anterior chamber is filled with viscoelastic. A preloaded implant injector is then advanced through the same corneal incision and directed towards the scleral spur. The injector needle is directed through the sclera to emerge under the conjunctiva, approximately 2 mm to 3 mm behind the limbus. The soft and permanent gelatin stent is then injected, to traverse the anterior chamber, sclera and conjunctival space. After placement is checked (using a gonioscopy mirror) the viscoelastic is exchanged for a balanced salt solution and the injector is withdrawn. The corneal incision is usually self-sealing but is sometimes sutured. Subconjunctival injection of mitomycin-C may be done during the procedure.

Efficacy summary

Intraocular pressure control, with and without medication

A multicentre comparative case series of 293 patients (354 eyes) comparing ab-interno gelatin microstent implantation plus mitomycin-C (n=159 patients, 185 eyes) with trabecluectomy plus mitomycin-C (n=139 patients, 169 eyes) reported that mean intraocular pressure (IOP) reduction was similar at 30-month follow-up, with a median IOP of 13.0 mmHg[1].

In a multicentre case series of 65 patients with refractory glaucoma implanted with an ab-interno gelatin microstent plus mitomycin-C, mean IOP reduced from 25.1(±3.7) mmHg (95% confidence interval [CI] 24.2 to 26.0) at baseline to 15.9(±5.2) mmHg (95% CI 14.5 to 17.4) at 12-month follow-up. Mean IOP change from baseline was −9.1 mmHg (95% CI −10.7 to −7.5, n=52; observed data) at 12-month follow-up, excluding patients with missing data (n=4) and those requiring a glaucoma-related secondary surgical intervention (n=9). At 12 months, 75% of patients (46/61; observed data) reported IOP reduction from baseline of 20% or more on the same or fewer medications[2].

In a case series of 33 patients (41 eyes) with open angle glaucoma and cataract, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, mean IOP reduced significantly from 22.5(±3.7) mmHg at baseline to 13.1(±2.4) mmHg at 12-month follow-up ($p<0.01$). The percentage of mean IOP reduction was 42% at 12-month follow-up[3].

In a case series of 18 patients (30 eyes) with cataract and slight or moderate chronic open angle glaucoma, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, mean IOP reduced significantly from 21.2(±3.4) mmHg at baseline to 15.03(±2.47) at 12-month follow-up ($p<0.001$). The percentage of mean IOP reduction was 29% at 12-month follow-up[4].

In a case series of 10 patients (13 eyes) with primary open angle glaucoma, implanted with an ab-interno gelatin microstent with subconjunctival mitomycin-C in combination with phacoemulsification (n=10 eyes), mean IOP significantly

reduced from 16(±4) at baseline to 12(±3) at 12-month follow-up (p=0.01)[5]. The percentage of mean IOP reduction was 23% at 12 month follow-up.

Medication use

In the multicentre comparative case series of 293 patients, more patients in the trabeculectomy plus mitomycin-C group were using glaucoma medications compared to those who had gelatin microstent plus mitomycin-C at last follow-up (on an adjusted basis using the last observation carried forward [LOCF] method for eyes that underwent reoperation: 34% [95% CI 26.3 to 43.4] compared with 25% [95% CI 18 to 33.6])[1].

In the multicentre case series of 65 patients with refractory glaucoma, implanted with an ab-interno gelatin microstent plus mitomycin-C, the mean number of different classes of medication used reduced from 3.5(±1.0) at baseline to 1.7(±1.5) at 12-month follow-up[2].

In the case series of 33 patients (41 eyes) with open angle glaucoma and cataract, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, the mean number of different classes of medication used reduced from 2.5(±0.9) at baseline to 0.4(±0.8) at 12-month follow-up (p<0.05). No patient was using additional medications compared to baseline[3].

In the case series of 18 patients (30 eyes) with cataract and slight or moderate chronic open angle glaucoma, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, the mean number of different classes of medication used reduced from 3.07(±0.69) at baseline to 0.17(±0.65) at 12-month follow-up (p<0.001). The number of medications had decreased by 95% at 12-month follow-up, and only 3 patients needed anti-glaucoma treatment[4].

In the case series of 10 patients (13 eyes) with primary open angle glaucoma, implanted with an ab-interno gelatin microstent plus subconjunctival mitomycin-C, the mean number of medication classes significantly reduced from 1.9(±1) at baseline to 0.3(±0.49) at 12-month follow-up (p=0.003)[5].

Success rate

In the multicentre comparative case series of 293 patients (354 eyes), comparing ab-interno gelatin microstent implantation plus mitomycin-C (n=159 patients, 185 eyes) with trabeculectomy plus mitomycin-C (n=139 patients, 169 eyes), there was no difference in risk of failure (as hazard ratios [HR]) between the 2 procedures. For the threshold of 6 to 17 mmHg, the adjusted HR of failure of the gelatin microstent relative to trabeculectomy was 1.20 (95% CI 0.73 to 1.96) for complete success and 1.34 (95% CI 0.64 to 2.81) for qualified success. The time to 25% failure was 10.7 months (95% CI 6.8 to 16.6 months) and 10.2 months (95% CI 5.3 to 15.7 months) for complete success, and 30.3 months (95% CI

18.7 to ∞months) and 33.3 months (95% CI 23.6 to 46.2 months) for qualified success[1].

In the multicentre case series of 65 patients with refractory glaucoma, implanted with an ab-interno gelatin microstent plus mitomycin-C, a Kaplan–Meier analysis of time to failure indicated a 75% probability of success at 12 months. Failures were due to glaucoma-related secondary surgical intervention in 9 eyes (with device explant in 6, without device explant in 2 and device explant alone in 1), or IOP reduction of less than 20% on the same or fewer number of medications at 12 months in 6 patients[2].

In the case series of 33 patients (41 eyes) with open angle glaucoma and cataract, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, complete success (defined as postoperative IOP of more than 6 mmHg and less than 18 mmHg without glaucoma medications) was achieved in 80% (33/41) of eyes at 12-month follow-up. Qualified success (defined as IOP of more than 6 mmHg and less than 17 mmHg with glaucoma medications) was achieved in 98% (40/41) of eyes[3].

In the case series of 18 patients (30 eyes) with cataract and slight or moderate chronic open angle glaucoma, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, success rate at 12-month follow-up was 90% (27/30). Of the remaining 3 patients, 2 needed medication to maintain IOP of less than 18 mmHg and the other patient with encapsulated bleb needed 3 medications to maintain IOP of less than 21 mmHg[4].

In the case series of 10 patients (13 eyes) with primary open angle glaucoma, implanted with an ab-interno gelatin microstent plus subconjunctival mitomycin-C, complete success (defined as IOP reduction of more than 20% from baseline to 1 year without any glaucoma medications) was achieved in 42% of patients and qualified success (defined as IOP reduction of more than 20% at 1 year with medications) was achieved in 66% of patients (assessed by Kaplan–Meier survival curve analysis)[5].

Visual acuity

In the multicentre comparative case series of 293 patients, the median best corrected visual acuity (BCVA) at last follow-up or before reoperation was 0.2 LogMar for gelatin stent plus mitomycin-C eyes and 0.3 for trabeculectomy plus mitomycin-C eyes (p=0.24)[1].

In the case series of 33 patients (41 eyes) with open angle glaucoma and cataract, implanted with an ab-interno gelatin microstent in combination with phacoemulsification, no patient had visual loss compared with preoperative visual acuity[3].

In the case series of 18 patients (30 eyes) with cataract and slight or moderate chronic open angle glaucoma, implanted with an ab-interno gelatin microstent in

combination with phacoemulsification, BCVA (LogMAR) changed from 0.37(±0.2) at baseline to 0.72(±0.15) at 12-month follow-up ($p<0.001$)[4].

In the case series of 10 patients (13 eyes) with primary open angle glaucoma, implanted with an ab-interno gelatin microstent plus subconjunctival mitomycin-C, BCVA (LogMAR) changed from 0.33(±0.34) at baseline to 0.13(±0.11) at 12-month follow-up[5]. None of the eyes lost 1 or 2 or more lines of visual acuity. Visual field and Heidelberg Retina Tomograph (HRT) results at 12 months were stable when compared to preoperative values.

Safety summary

Microstent problems

Exposure

Partial microstent exposure was reported in a case report of 1 patient 15 days after stent implantation. This was close to an area of scarred conjunctiva (previous superior bleb) from a previous failed trabeculectomy. The authors report that this was because of an extremely weak and thin conjunctiva and also because of the nasal location. The conjunctiva over the exposed area was removed and replaced by an amniotic membrane and a conjunctival autograft. Six months after surgery the stent was well-covered, IOP was well-controlled without medication and complete visual acuity regained[7].

Microstent exposure or extrusion as a result of repositioning requiring surgical intervention and microstent migration were reported in 1 patient each during 12-month follow-up in the case series of 65 patients[2]. Microstent extrusion (managed by repositioning of the implant in the subconjunctival space and applying conjunctival sutures) was seen in 1 eye (with a glaucoma procedure 20 years ago) in the case series of 10 patients[5]. Microstent obstruction or migration was reported in 1 patient in the case series of 33 patients and the device was explanted[3].

Removal and repositioning

Microstent removal and replacement using 2 or more injectors because of incorrect location of implant was reported in 14% (9/65) of patients the case series of 65 patients[2]. Microstent repositioning due to incorrect location of implant was reported in 12% (5/41) of eyes in the case series of 33 patients[3].

Microstent relocation was performed because of short subconjunctival pathway (under 2 mm) by means of sclera approach with blunt tweezers in 20% (6/30) of eyes in the case series of 18 patients. Microstent was extracted and re-implanted (due to long intra-chamber pathway) in 1 eye in the same study[4].

Implantation failure

Implantation failures (device extrusion to the subchoroidal space when trying to reposition in 1 patient, and subconjunctival hemorrhage in 1 patient) were reported in 2 eyes in the case series of 18 patients[4].

Increase in IOP

IOP increase of more than 10 mmHg from baseline was reported in 22% (14/65) of patients in the case series of 65 patients with refractory glaucoma[2]. The mean time to occurrence was 116.4 days.

Loss of best corrected visual acuity (BCVA)

Non-persistent loss of BCVA (of more than 2 lines from baseline) was reported in 15% (10/65) of patients within 30 days and 11% (7/65) of patients after 30-day follow-up in the case series of 65 patients with refractory glaucoma. Persistent loss was reported in 6% (4/65) of patients in the same study. 81% of these resolved spontaneously[2].

Bleb complications

Hypertrophic bleb with mechanical ectropion a few weeks after surgery was reported in a case report of 1 patient who had subconjunctival stent implantation for primary open-angle glaucoma. Topical medical treatment was first given but the condition persisted. Surgical emptying of the bleb was done to drain it, after blockage of the ab interno stent with viscoelastic and bleb sealing with tissue adhesive. Immediate symptom improvement and bleb reduction were seen. Intraocular pressure reduced without any medication. No complications were reported[8].

Bleb encapsulation 5 months after surgery was reported in 1 eye in the case series of 18 patients. This needed topical hypotensive medical treatment for controlling IOP less than 21 mmHg at 12-month follow-up.

Bleb needling

Bled needling without sight-threatening complications was reported in 32% (21/65) patients in the case series of 65 patients with refractory glaucoma during 12 months of follow-up[2]. Bleb fibrosis requiring needling after implantation was reported in 1 patient in the case series of 33 patients[3]. Bleb needling using slit lamp was reported in 31% (4/13) of eyes postoperatively in the case series of 10 patients[5].

Internal ostium obstruction

A small blood clot with mild hyphema, leading to internal ostium obstruction compromising bleb function (causing high IOP of 22 mmHg) was reported in a case report of 1 patient who had stent implantation. After 2 weeks of medical treatment with no clinical improvement an ab-interno revision was done and the

occluding clot was removed. 1 week after surgery there was IOP control (12 mmHg), a patent internal ostium, and an open diffuse filtering bleb. Three months after surgery, the IOP was well controlled using bimatoprost (13 mmHg)[6].

Choroidal detachment and hypotony

Transient hypotony (IOP less than 6 mmHg) needing no surgical intervention was reported in 25% (16/65) of patients in the case series of 65 patients with refractory glaucoma[2]. Transient peripheral choroidal detachment with hypotony (on day 1, resolved spontaneously within 1 week) was reported in 1 patient in the case series of 33 patients[3]. Choroidal detachment and hypotony that persisted for less than 1 month (treated conservatively using systemic steroids and atropine eye drops) was reported in 2 eyes in the case series of 10 patients[5].

Wound problems

Wound leak/dehiscence was reported in 9% (6/65) of patients and it was repaired in 8% (5/65) of patients in the case series of 65 patients[2].

Bleeding

Subconjunctival bleeding was reported intraoperatively in 37% (15/41) of eyes and transient anterior chamber bleeding in 24% (10/41) of eyes in the case series of 33 patients. Further details were not reported[3].

Subconjunctival bleeding during mitomycin injection was reported in 37% (11/30) eyes in the case series of 18 patients (30 eyes)[4]. Slight intracameral hemorrhage (resolved with mechanical irritation-aspiration) in 87% (26/30) of eyes and hemorrhage at scleral exit point (with no consequences) in 90% (27/30) of eyes were reported in the same study.

Secondary surgical interventions

Secondary surgical interventions (glaucoma procedures or device explant) were done in 14% (9/65) of patients in the case series of 65 patients[2]. Secondary surgical re-intervention (trabeculectomy after 1 month for stent failure due to device obstruction or migration) was reported in 1 patient in the case series of 33 patients[3]. Further surgical re-intervention (trabeculectomy) because of IOP inadequately controlled by topical medications was performed in 2 eyes in the case series of 10 patients[5].

Other events

In the case series of 65 patients with refractory glaucoma, anterior chamber fill, bleb leak without revision, Dellen, fixed dilated pupil, corneal oedema, macular oedema, macular puckering, and shallow anterior chamber with peripheral iridocorneal touch were reported in 1 patient each during 12 months of follow-up.

Choroidal effusion extending posterior to equator was reported in 2 patients in the same study[2].

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: loss of implant in eye, and over-drainage of implant leading to large bleb, hypotony and failure of the procedure. They considered that the following were theoretical adverse events: stent blockage, stent extrusion, bleeding, wrong placement, damage to implant, cataract earlier in patients with a phakic lens, avascular blebs caused by the anti-metabolite mitomycin-C and long-term failure of the procedure.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma. The following databases were searched, covering the period from their start to 18.07.2017: 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 later in this document 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	Microinvasive subconjunctival insertion of a trans-scleral gelatin stent.
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 335 eyes (286 patients) from 1 retrospective comparative case series[1], 4 case series [2-5] and 3 case reports[6-8].

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 at the end of this document.

Table 2 Summary of key efficacy and safety findings on microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma

Study 1 Schlenker MB 2017

Details

Study type	**Comparative case series**
Country	Canada, Germany, Austria, Belgium (4 centres)
Recruitment period	2011-2015
Study population and number	n=**293 patients (354 eyes) with uncontrolled glaucoma and no prior incisional surgery** **185 eyes (159 patients) with ab-interno gelatin stent implantation plus mitomycin C versus 169 eyes (139 patients) with trabeculectomy plus mitomycin C** Glaucoma type: primary open angle glaucoma 202, pseudoexfoliative 80, pigment dispersion 20, primary angle closure 4, combined mechanism 20, normal tension 8, juvenile open angle 12, and other 8. Previous procedures: laser peripheral iridotomy 33, cataract surgery 119, laser trabeculoplasty 147
Age and sex	Median age 66.4 years; 50% (176/354) male
Patient selection criteria	Inclusion criteria: patients between 30 and 90 years of age with primary open angle glaucoma, pseudoexfoilation, pigment dispersion, normal tension, angle recession, combined mechanism, history of angle closure, or juvenile glaucoma, above target IOP on maximum medical therapy were included. Exclusion criteria: patients with prior incisional filtering glaucoma surgery, fibrous or epithelial down growth, previous corneal graft or retinal surgery or those who had less than 1 month of follow-up.
Technique	XEN 45 Gel Stent (Allergan plc) implantation as a standalone procedure with mitomycin C Following mitomycin C treatment the stent was implanted using an ab interno approach in 185 eyes. Trabeculectomy with mitomycin C (169 eyes) Following mitomycin C treatment, a fornix based conjunctival flap was dissected and a partial thickness scleral flap was fashioned. A temporal paracentesis was made and the anterior chamber was entered under the scleral flap. A sclerotomy was created and a peripheral iridectomy was performed if needed. The scleral flap was closed with sutures and the conjunctiva was reapposed with nylon. The presence of a bleb was confirmed. Postoperative topical regimen (antibiotics for 1 to 4 weeks and steroids for 6-8 weeks) was same for both interventions.
Follow-up	**30 months**
Conflict of interest/source of funding	Some of the authors are consultants for Allergan and some received honorarium from the company. Allergan had no role in the conduct, design or analysis of the study.

Analysis

Study design issues: large retrospective, multicentre cohort study in 4 academic ophthalmology centers. Cases were identified by billing codes and manual chart review. Baseline characteristics and follow-up data were collected through chart review and correspondence with eye professionals. Primary outcome measure was hazard ratio (HR) of failure, with failure defined as 2 consecutive intraocular pressure (IOP) readings of <6 mmHg with vision loss or >17 mmHg without glaucoma medications (complete success) at least 1 month after surgery despite in-clinic interventions (including needling), undergoing reoperation or loss of light perception vision. Secondary outcome measures included IOP thresholds of 6 to 14 mmHg and 6 to 21 mmHg and same thresholds allowing for medications (qualified success), interventions, complications, and reoperations.

Study population issues: Baseline characteristics were similar between the 2 groups, except more men (56% vs. 43%), younger patients (average, by 3 years), better preoperative visual acuity (22% vs. 32% with 0.4 logarithm of the minimum angle of resolution vision or worse), and more trabeculoplasty (52% vs. 30%) among microstent eyes. Half of the surgeries were done in Canada and the rest in other countries.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **185 eyes with gelatin stent versus 165 eyes with trabeculectomy**

Relative hazard ratio of failure between the 2 procedures

For the threshold of 6 to 17mmHg, The adjusted HR of failure of the gelatin stent relative to trabeculectomy was 1.20 (95% confidence interval [CI], 0.73–1.96) for complete success and 1.34 (95% CI, 0.64–2.81) for qualified success. The time to 25% failure was 10.7 months (95% CI, 6.8–16.6 months) and 10.2 months (95% CI, 5.3–15.7 months) for complete success and 30.3 months (95% CI, 18.7–∞ months) and 33.3 months (95% CI, 23.6–46.2 months) for qualified success.

Medication use, IOP and BCVA outcomes

At last follow-up, more patients in the trabeculectomy group were receiving glaucoma medications compared to the group of patients who received gelatin stent (on an adjusted basis using LOCF method for eyes that underwent reoperation: 34.3% [95%CI 26.3%-43.4%] versus 25% [95%CI 18%-33.6%]).

IOP reduction was similar in the gelatin stent and trabeculectomy groups at the last follow up - median IOP was 13.0 mmHg. The median BCVA at last follow-up or before reoperation was 0.2 LogMar for gelatin stent eyes and 0.3 for trabeculectomy eyes (p=0.24).

Characteristics associated with failure

Overall, white ethnicity was associated with decreased risk of failure (adjusted HR, 0.49; 95% CI, 0.25–0.96), and diabetes was associated with increased risk of failure (adjusted HR, 4.21; 95% CI, 2.10–8.45).

Safety

Postoperative complications

	Gelatin stent (n=185)	**Trabeculectomy (n=169)**
Leak/dehiscence	3	12
Hyphema	2	2
Vitreous hemorrhage	2	1
Choroidal/choroidal folds	1	2
Hypotony maculopathy	2	1
Uveitis	2	1
Corneal decompensation	0	1
Macular edema	0	3
Iris incarceration		2
Blocked stent	1	-
Exposed stent	1	-
Microstent-iris touch	2	-
Shallow anterior chamber	-	2
Dellen	2	0
Serious complications (anytime)		
Malignant glaucoma	4	2
Belbitis	0	1
Total	**22**	**30**
Postoperative interventions		
Needling	43.2% (80/185)	30.8% (52/169)
Laser suture lysis	-	49.7% (84/169)
Anterior chamber reformation	22	13
Bleb repair/conjunctival suturing	2	10
Iris sweep/synechiolysis	3	4
YAG to implant/ostomy	3	2
MMC injection	2	0
Microstent reposition	2	-
Iridoplasty	2	0
Bleb cautery	1	0
Total	**117**	**165**
Reoperations*	10.3% (19/185)	5.9% (9/169)
Other laser surgeries	6.9% (13/185)	10.7% (18/169)

*P=0.11. The most common operation done was repeat gelatin stent insertion, followed by a Baerveldt tube shunt.

Abbreviations used: BCVA, best corrected visual acuity; CI, confidence interval; HR, hazard ratio; LOCF, last observation carried forward; IOP, intraocular pressure.

Study 2 Grover DS 2017

Details

Study type	**Case series**
Country	USA (12 centres)
Recruitment period	Not reported
Study population and number	n=**65 patients (65 eyes) with refractory glaucoma** glaucoma type: primary open angle glaucoma n=57 eyes, pseudoexfoliative n=6 eyes, pigmentary n=1, mixed mechanism n=1 previous procedures: prior cataract surgery in 45, prior glaucoma procedure in 55
Age and sex	Mean age 70 years; 46% (30/65) male
Patient selection criteria	Inclusion criteria: patients ≥45 years of age and had refractory glaucoma, who failed prior filtering/cilioablative procedure or had uncontrolled intraocular pressure (IOP) on maximum tolerated medical therapy, with medicated IOP ≥20, presence of an area of healthy, free and mobile conjunctiva in the target quadrant; trabecular meshwork visible by gonioscopy (with Shaffer angle grade ≥3 in the target quadrant); best-corrected visual acuity (BCVA) of light perception or better; and ≤35 mmHg and visual field mean deviation ≤−3 dB. Exclusion criteria: angle closure glaucoma, neovascular glaucoma, previous glaucoma shunt/valve, prior history of uveitis or endophthalmitis, prior ocular surgery (rather than glaucoma surgery sparing 2 clock hours of healthy conjunctiva in the supero-nasal quadrant), prior conjunctival surgery, scarring, inflammation or infection, corneal surgery, opacities, or disease, central corneal thickness 490µm, iris neovascularisation, aphakia, previous complicated phacoemulsification surgery, anterior chamber (AC) IOL, presence of intraocular silicone oil, vitreous in AC, diabetic retinopathy, retinal vein occlusion, proliferative retinopathy, choroidal neovascularisation, BCVA <20/200 in fellow eye, impaired episcleral venous drainage, allergy to drugs or any device components and fellow eye implanted with study device.
Technique	XEN 45 Gel Stent (Allergan plc) implantation as a standalone procedure. Following mitomycin C treatment the stent was implanted using an ab interno approach in 65 eyes. After implantation the incision was closed using sutures and viscoelastic was irrigated and aspirated as needed. Testing was done to check for leakage of aqueous humor. Needling is performed if there is evidence or risk of bleb failure to remove tissue adhesions between the sclera and conjunctiva. Anticoagulation therapy and IOP lowering medications discontinued prior to surgery and resumed postoperatively.
Follow-up	**12 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: follow-up visits were conducted at day 1, 1 week, and 1, 3, 6, 8, 10 and 12 months postoperatively. 83.1% (54/65) completed the 12 months follow-up and 11 patients were not included in the analysis (due to stent explantation in 7, death in 2, and loss of follow-up in 2).

Study design issues: Single-arm multicentre clinical study. The protocol developed under an FDA investigational device exemption (IDE G130175) was approved by review boards. Sample size was determined in accordance with the FDA guidance document titled “Aqueous Shunts – 510k Submissions”. Primary outcomes were % of patients achieving ≥20% IOP reduction from baseline on the same or fewer medications and mean IOP change from baseline at month 12, procedure-related complications and ocular adverse events (AEs). Only 52 patients were included in the performance analysis.

Study population issues: 84% patients had a failed prior glaucoma procedure, 57% needed >4 IOP lowering medications. More than 50% patients had prior cataract surgeries. If both eyes qualified for treatment, the eye with worse BCVA and visual field defect was selected for study. Fellow eyes received medical treatment.

Key efficacy and safety findings

Efficacy

Number of patients analysed: 65 (**65 eyes)**

Implantation outcomes

	% (n=65)
Successful implantation with 1 injector to implant	86.2 (56/65)
Intraoperative stent removal and replacement using 2 or more injectors	13.8 (9/65)

IOP and medications use

	Preoperative (mean±SD) (n=65)	**12 months (n=52 eyes included in analysis)**
IOP change mm Hg*	25.1±3.7 (95% CI 24.2, 26.0)	15.9±5.2 (95% CI 14.5, 17.4)
Number of Medication classes	3.5±1.0	1.7±1.5

Mean IOP change from baseline (mmHg)*

Mean IOP change from baseline was −9.1 mmHg (95% CI: −10.7, −7.5) (n=52; observed data) at 12 months, excluding patients with missing data (n=4) and those requiring a glaucoma-related secondary surgical intervention (n=9)[1].

≥20% IOP lowering from baseline on the same or fewer medications

At 12 months, 75.4% (46/61; observed data) reported ≥20% IOP lowering from baseline on the same or fewer medications and a mean diurnal IOP reduction from baseline was -6.4±1.1 mm Hg (95% CI: -8.7, -4.2). Stratification by demographic or baseline characteristics such as age, gender, ethnicity, IOP, or medication count had no statistically significant effect on outcomes.

Probability of failure (Kaplan Meier analysis)

A Kaplan Meier analysis of time to failure indicated a 75% probability of success at 12 months.

Failures were due to glaucoma related secondary surgical intervention in 9 (6 with device explant, without device explant in 2 and device explant alone in 1), or IOP reduction<20% on the same number of medications or fewer at 12 months in 6 patients.

Safety

Adverse events during 12 months follow-up

	% (n)
Bleb needling	32.3 (21/65)
Loss of BCVA from baseline>2 lines (81% self-resolved)	
<30 days non persistent loss	15.4 (10/65)
>30 days non persistent loss	10.8 (7/65)
Persistent loss	6.2 (4/65)
Transient hypotony (IOP<6mm Hg)	24.6 (16/65)
IOP increase>10mm Hg from baseline*	21.5 (14/65)
Anterior chamber tap procedure	9.2 (6/65)
Wound leak/dehiscence	9.2 (6/65)
Wound repair	7.7 (5/65)
Hyphema>2mm in height	4.6 (3/65)
Nd YAG capsulotomy	4.6 (3/65)
Choroidal effusion extending posterior to equator	3.1 (2/65)
Anterior chamber fill	1
Bleb leak without revision	1
Corneal edema grade 3 or 4	1
Dellen	1
Fixed dilated pupil	1
Macular edema	1
Macular puckering	1
Shallow anterior chamber with peripheral iridocorneal touch	1
stent exposure or extrusion requiring surgical intervention	1
Stent migration	1
Stent repositioning leading to exposure	1
Secondary surgical intervention	14 (9/65)
Glaucoma procedure with explant	9.2 (6/65)
Glaucoma procedure (tube)	1
Glaucoma procedure (cytophotocoagulation)	1
Explant	1
Events 30 days after surgery	
Anterior chamber cells	1
Blepharitis	1
Chalazion	1
Dysesthetic bleb	1
Hyperemia	1

*treated with medications or needling; or a combination of medications, needling and anterior chamber tap.

Abbreviations used: CI, confidence interval; IOP, intraocular pressure; POAG, primary open angle glaucoma; SD, standard deviation.

Study 3 Gregorio AD 2017

Details

Study type	**Case series**
Country	Italy
Recruitment period	Not reported
Study population and number	n=**33 patients** (**41 eyes) with open angle glaucoma (OAG)** glaucoma type: primary open angle glaucoma (POAG) n=35 eyes, exfoliation n=6 eyes previous glaucoma procedures: n=1 eye (deep sclerectomy)
Age and sex	Mean age 74 years; 39.4% (13/33) male
Patient selection criteria	Inclusion criteria: patients older than 18 years with primary or secondary (pigmentary and pseudoexfoilation) open angle glaucoma with a baseline >18mmHg and <32 mmHg under maximal tolerated medical therapy and with cataract. Exclusion criteria: angle closure, congenital and neovascular glaucoma, prior history of uveitis or endophthalmitis, prior ocular surgery (rather than glaucoma surgery sparing 2 clock hours of healthy conjunctiva in the supero-nasal quadrant) and aphakia.
Technique	XEN 45 Gel Stent was implanted in combination with phacoemulsification (micro-incisional cataract surgery-MICS) in patients with POAG and cataract. Surgery was done under local or topical anesthesia. Mitomycin C at the concentration of 0.1mg/ml was injected in the subconjunctival, supero-temporal quadrant space to obtain a bubble that was rolled towards supero-nasal quadrant. MICS with 2.0mm incision and IOL implantation was performed. Then the XEN gel stent was implanted as described in procedure description section of the overview. All corneal incisions were hydro-sutured. All hypotensive medications were discontinued 1 day before surgery. Postoperative treatments included a combination of dexamethasone and tobramycin 4 times daily for 15 days and reduced dose after 3 weeks.
Follow-up	**12 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: follow-up visits were conducted at day 1, 1 week, and 1, 2, 3, 4, 6, 9 and 12 months postoperatively.

Study design issues: prospective nonrandomised study in a single centre. Study was designed and conducted according to the World Glaucoma Association Guidelines on design and reporting of glaucoma surgical trials. Preoperative and postoperative clinical examinations included visual acuity, Glodman Applanation Tonometry, split lamp examination, optical coherence tomography analysis, gonioscopy, corneal pachymetry, visual field and fundus oculi examination. Outcomes measured at each follow-up visit included IOP measurements, medication use and complications.

Complete success was defined as postoperative IOP > 6 mmHg and < 18 mmHg without glaucoma medications while qualified success was defined as IOP >6mmHg and <17mmHg with glaucoma medications. Failure was defined as vision loss of light perception or worse, need for additional glaucoma surgery, or <20% reduction of IOP from baseline at 1 year.

Study population issues: 15 patients had allergies to anti-hypertensive drugs.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **33 (41 eyes)**

IOP and medications use

	Preoperative (mean±SD)	**12 months**
IOP reduction mm Hg*	22.5±3.7	13.1±2.4 (p<0.01)
Number of Medication classes	2.5±0.9	0.4±0.8 (p<0.05)

*the percentage of mean IOP reduction was 41.82% at 12 months follow-up.

No patient was on additional medications compared to baseline.

Visual acuity

No patient had visual loss compared with preoperative visual acuity.

Qualified success rate at 12 months 97.5% (40/41)

Complete success rate at 12 months 80.4% (33/41 eyes)

Safety

Intraoperative complications

	% (n)
Subconjunctival bleeding	36.5% (15/41)
Transient anterior chamber bleeding	24.3 (10/41)
Stent repositioning due to incorrect location of implant	12.1 (5/41)

Postoperative complications

	% (n)
Transient peripheral choroidal detachment with hypotony (on day 1 resolved spontaneously within 1 week)	2.4 (1/41)
Secondary surgical re-intervention (additional trabeculectomy after 1 month for stent failure due to device obstruction/migration)	2.4 (1/41)
Bleb fibrosis requiring needling	2.4 (1/41)
Device obstruction/migration	2.4 (1/41)
Device explant	2.4 (1/41)

Abbreviations used: IOP, intraocular pressure.

Study 4 Perez-Torregrosa VT 2016

Details

Study type	**Case series**
Country	Spain
Recruitment period	Not reported
Study population and number	n=**18 patients (30 eyes) with cataract and slight or moderate chronic open angle glaucoma (COAG)**
Age and sex	Mean age 76 years; 28% (5/18) male
Patient selection criteria	Inclusion criteria: patients 18 and older, previous slight or moderate COAG diagnostic (determined by a mean deviation between 0 and −12 dB in the 24-2 Humphrey campimetry strategy); IOP under 30 mmHg with at least 2 medications to control intraocular pressure, associated cataracts diagnostic with BCVA not above 0.6, healthy and mobile conjunctival area in the superior nasal quadrant, Shaffer angle equal to or above 3 in gonioscopy. Exclusion criteria: any condition other than the above or associated pathology that could hinder follow-up or the surgical procedure.
Technique	Combined FACO-XEN surgery with temporal access and 2 single incisions for both techniques: XEN 45 implant surgery combined with phacoemulsification was performed within 15 minutes of administering subconjunctival mitomycin C. Surgery was performed through 2 temporal incisions, separated by 90 degrees, using the inferior to enter the XEN 45 and to implant it in the superior nasal region. All patients underwent standard phacoemulsification. Bilateral surgery was done In 12 patients and unilateral surgery in 6 patients with same technique by the same surgeon. Peribulbar anesthesia was applied. Postoperative care included antibiotic prophylaxis with 0.3% ciprofloxacin 4 times a day during 2 weeks, and anti-inflammatory therapy with 0.1% sodium diclofenac 4 times a day during 4 weeks, in association with 0.1% dexamethasone in decreasing dosage during 8 weeks.
Follow-up	**12 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: follow-up visits were conducted at day 1, 1 week, and 1, 3, 6, 9 and 12 months postoperatively.

Study design issues: prospective nonrandomised study in a single glaucoma centre. Preoperative and postoperative ophthalmic examinations included visual acuity, Glodman Applanation Tonometry, split lamp examination, optical coherence tomography analysis, gonioscopy, corneal pachymetry, visual field and fundus oculi examination. Outcomes measured at each follow-up visit included best corrected visual acuity, IOP measurements, medication use and complications. Success rate was defined as IOP reduction to ≤ 18 mmHg without medications.

Study population issues: 2 patients were excluded prior to analysis because of implantation failures. The baseline comprised a higher number of presurgery drugs and no presurgery cleansing period was carried out.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **18 (30 eyes)**

IOP and medications use

	Preoperative (mean±SD)	**6 months**	**12 months**
IOP reduction mm Hg*	21.2±3.4	14.63±1.81	15.03±2.47 (p<0.001)
Number of medication classes**	3.07±0.69	NR	0.17±0.65 (p<0.001)
BCVA (LogMar)	0.37±0.2	NR	0.72±0.15 (p<0.001)

*the percentage of mean IOP reduction was 61.65% on the first day, 37.26% at 1 month, 35.05% at 3 months, 31% at 6 months, 30.6% at 9 months, and 29.34% at 12 months follow-up.

**The number of medications decreased by 94.57%. At 12 months follow-up, 3 patients needed anti glaucoma treatment.

Success rate at 12 months was 90% (27/30)

Of the remaining 3 patients, 2 needed medication to maintain IOP<18mmHg and the other patient with encapsulated bleb needed 3 medications to maintain IOP <21mmHg.

Visual acuity

None of the patients exhibited diminished visual acuity when compared to pre-operative values.

Safety

Intraoperative complications

	% (n)
Subconjunctival bleeding (during mitomycin injection)	36.6 (11/30)
Device implantation	
Difficulties introducing device injector needle (resolved by rotating the head and relocating the blepharostat)	26.6 (8/30)
Slight intracameral hemorrhage (resolved with mechanical-irritation-aspiration)	86.6 (26/30)
Hemorrhage at scleral exit point (with no consequences)	90 (27/30)
Device relocation needed (due to short subconjunctival pathway-under 2mm) by sclera approach with blunt tweezers	20 (6/30)
Device extracted and re-implanted (due to long intra-chamber pathway)	3.3 (1/30)

Postoperative complications (n=20 patients)

	% (n)
Implantation failures (280 degree subconjunctival hemorrhage in 1 patient and device extrusion to the subchorodial space when trying to reposition in another patient)	2 eyes
Bleb encapsulation (at 5 months after surgery needed topical hypotensive medication to maintain IOP<21mmHg)	1 eye

None of the patients exhibited severe intra- or post-surgery complications.

Abbreviations used: BCVA, best corrected visual acuity; IOP, intraocular pressure; NR, not reported; SD, standard deviation.

Study 5 Galal A 2017

Details

Study type	**Case series**
Country	Germany
Recruitment period	Not reported
Study population and number	n=**10 patients (13 eyes) with primary open angle glaucoma (POAG).** 3 eyes were pseudophakic and 10 eyes had simultaneous cataract.
Age and sex	Mean age 73 years; 60% (6/10) male
Patient selection criteria	Inclusion criteria: patients with POAG with or without cataract already diagnosed and being followed up for at least 5 years or those eyes not reaching target intraocular pressure (IOP) with maximal pressure, medication intolerance or patients with lack of compliance. Exclusion criteria: previous trabeculectomy surgery, any possible allergic reaction with the material of the implant, controlled IOP by less than 3 different medications, single eyed patients, pseudoexfoilation, shallow anterior chamber and angle closure glaucoma.
Technique	3 pseudophakic eyes had XEN 45 implantation (using an ab interno approach) with subconjunctival mitomycin-C 0.001% and 10 eyes with simultaneous cataract underwent phacoemulsification and XEN implantation with subconjunctival mitomycin C. Surgery was done under general anesthesia by the same surgeon. All prostaglandin medications were discontinued for 1 week before surgery. Phacoemulsification surgery was done through a main incision at the steepest corneal axis and the paracentesis incisions were done one nasal and one temporal-inferior at 7o'clock position and 5'oclock position for the right and left eyes. Intraocular lens implanted using standard technique in phacoemulsification procedures.
Follow-up	**12 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: follow-up visits were conducted at day 1, 1 week, and 1, 3, 6 and 12 months postoperatively.

Study design issues: prospective study in a single centre. Primary open angle glaucoma was diagnosed by extensive ocular examination, and IOP measurement confirmed by Glodman Applanation Tonometry, visual field and HRT. Outcomes measured at each follow-up visit included visual acuity, IOP measurements, medication use and complications.

Complete success was defined as IOP reduction >20% from preoperative baseline at 1 year without any glaucoma medications while partial success was defined as IOP reduction of >20% at 1 year with medications. Failure was defined as vision loss of light perception or worse, need for additional glaucoma surgery, or <20% reduction of IOP from baseline at 1 year.

Other issues: Authors state that severe complications that might affect sight or mitomycin C related complications were not recorded.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **10 (13 eyes)**

IOP and medications use

	Preoperative (mean±SD)	**1 month (mean±SD)**	**6 months (mean±SD)**	**12 months**
IOP reduction mm Hg*	16±4	11±6 (p=0.026)	12±4 (p=0.01)	12±3 (p=0.01)
Number of Medication classes	1.9±1	NR	NR	0.3±0.49 (p=0.003)
BCVA (LogMar)	0.33±0.34	NR	NR	0.13±0.11

*the percentage of mean IOP reduction was 23% at 12 months follow-up.

Partial success rate at 12 months 66%

Complete success rate off medication 42%

Visual acuity

At 12 months none of the eyes have lost 1 or 2 or more lines of visual acuity. Visual field and HRT results at 12 months were stable when compared to preoperative values.

Safety

Complications

	% (n)
Bleb Needling	31% (4/13)
Choroidal detachment and hypotony for<1 month (responded to medical treatment)	2 eyes
Microstent extrusion (managed by repositioning and conjunctival sutures)*	1 eye
Secondary surgical re-intervention due to inadequately controlled IOP by medications (Trabeculectomy)	2 eyes

*20 years ago the patient had a non-specified glaucoma procedure.

Abbreviations used: BCVA, best corrected visual acuity; HRT, Heidelberg Retina Tomograph; IOP, intraocular pressure; NR, not reported; SD, standard deviation.

Study 6 Ferreira P 2017

Details

Study type	**Case report**
Country	Portugal
Recruitment period	Not reported
Study population and number	n=**1 patient with primary open angle glaucoma (POAG) in both eyes.**
Age and sex	age 64 years; male
Patient selection criteria	Patient with POAG in both eyes, visual field deterioration in the left eye despite medical treatment, IOP>17mmHg.
Technique	XEN gel stent (diameter not reported) implanted using an ab interno approach under peribulbar anesthesia and preceded with a subconjunctival injection of mitomycin C.
Follow-up	**Postoperative**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Safety
Number of patients analysed: **1**
Blood clot leading to internal ostium obstruction compromising bleb function following a hyphema
Following implantation, repositioning was needed because of failure and complication at first attempt.
Patient presented with a mild hyphema, a small blood clot over the internal ostium and a flat bleb causing high IOP (22mmHg). After 2 weeks of medical treatment with no clinical improvement surgical revision under peribulbar anaesthesia was done.
The occluding clot was removed through an ab-interno direct lens visualisation. 1 week after surgery the patient showed IOP control (12mmHg), a patent internal ostium, and an open diffuse filtering bleb. Three months after surgery, the IOP was well controlled under bimatoprost (13mmHg).
Abbreviations used: IOP, intraocular pressure.

Study 7 Fea A [2015]

Details

Study type	**Case report**
Country	Italy
Recruitment period	2014-15
Study population and number	**n=1 patient** with a long-term failed prior trabeculectomy and a badly scarred superior bleb with increased IOP and severe visual field damage.
Age and sex	51 year old male
Patient selection criteria	
Technique	Minimally invasive glaucoma surgery (with Xen Aquesys subconjunctival shunt implantation) performed. The diameter of the device not stated.
Follow-up	**6 months**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Safety
Number of patients analysed: **1** **Stent exposure** The stent was placed nasally and close to an area of scarred conjunctiva from the previous trabeculectomy (previous bleb); the IOP was well controlled but on day 15 the stent became partially exposed due to extremely thin and weak conjunctiva and the nasal location. **Treatment**: the conjunctiva over the stent exposed area was removed and the stent was patched by an amniotic membrane transplant and a conjunctival autograft. Six months after surgery the IOP is under control (lower than 14 mmHg) without medication and with complete visual recovery.
Abbreviations used: IOP, intraocular pressure.

Study 8 Fernandez-Garcia A [2015]

Details

Study type	**Case report**
Country	Spain
Recruitment period	2014-15
Study population and number	**n=1** patient with primary open-angle glaucoma in both eyes
Age and sex	69 year old; sex not reported
Patient selection criteria	
Technique	Minimally invasive glaucoma surgery (with ab interno Xen Aquesys subconjunctival shunt implantation) performed under topical anaesthesia. The diameter of the device not stated.
Follow-up	**4 months**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Safety
Number of patients analysed: **1** **Hypertrophic bleb** Patient presented with hypertrophic bleb and mechanical ectropion a few weeks after surgery. Topical medical treatment was given but the condition persisted. **Surgical treatment: bleb drainage, viscoelastic tamponade of stent and tissue adhesion** Under topical anaesthesia 'dry lake' procedure (surgical emptying of bleb) was done to drain the hypertrophic bleb following blockage of the ab interno stent with viscoelastic and bleb sealing with tissue adhesive. Immediate symptom improvement and bleb reduction were seen and IOP reduced without any medication. No complications were seen.
Abbreviations used: IOP, intraocular pressure.

Validity and generalisability of the studies

- This procedure is done as a standalone one or in combination with cataract surgery in patients with primary open angle glaucoma.
- The gelatin microstent initially had 3 different lumen diameters: Xen 140, 63 and 45. The only size now recommended by the manufacturer and currently available in NHS clinical practice is Xen 45 (with a smaller lumen). The evidence on Xen 140 and 63 is not directly comparable to the recommended device and therefore has been included in this document.

Existing assessments of this procedure

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

Related NICE guidance

Interventional procedures

- Trabecular stent bypass microsurgery for open-angle glaucoma. NICE interventional procedure guidance 575 (2017). Available from http://www.nice.org.uk/guidance/IPG575
- Trabeculotomy ab interno for open-angle glaucoma. NICE interventional procedure guidance 397 (2011). Available from http://www.nice.org.uk/guidance/IPG397
- Canaloplasty for primary open-angle glaucoma. NICE interventional procedure guidance 260 (2008). Available from http://www.nice.org.uk/guidance/IPG260

NICE guidelines

- Glaucoma: diagnosis and management. NICE guideline 85 (2009). Available from http://www.nice.org.uk/guidance/CG85. This guidance is currently under review and is expected to be updated in November 2017. For more information, see https://www.nice.org.uk/guidance/indevelopment/gid-ng10017
- Glaucoma in adults. NICE quality standard 7 (2011). Available from https://www.nice.org.uk/guidance/qs7

Additional information considered by IPAC

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. Five Specialist Advisor Questionnaires for microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 7 questionnaires to 2 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 1 completed questionnaire.

The patient commentator's views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

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 was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- IPAC to consider whether to include 'ab-interno' to the title and amend as follows: Ab interno subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma.
- Ongoing studies:
  - NCT02006693: Post-market multicentre evaluation of the XEN implant in moderate primary open-angle glaucoma, n=200, location: Europe and Venezuela, completion date March 2017.

- NCT02036541: A prospective multicentre clinical trial designed to evaluate the safety and performance of the AqueSys XEN 45 glaucoma implant in refractory glaucoma with adjuvant mitomycin-C, n=60, location: USA, completion date September 2016.

References

1. Schlenker M, Gulamhusein H, Conrad-Hengerer I, Somers A, et al. Efficacy, safety, and risk factors for failure of standalone ab interno gelatin microstent implantation versus standalone trabeculectomy. Ophthalmology 2017 [epub before print]. http://www.sciencedirect.com/science/article/pii/S0161642017304645
2. Davinder S. Grover et al. Performance and Safety of a New Ab Interno Gelatin Stent in Refractory Glaucoma at 12 Months. 2017 American Journal of Ophthalmology. DOI: http://dx.doi.org/10.1016/j.ajo.2017.07.023
3. Perez-Torregrosa VT, Olate-Perez A, Cerda-Ibanez M, Gargallo-Benedicto A, et al. Combined phacoemulsification and XEN45 surgery from a temporal approach and 2 incisions. Arch Soc Esp Opthalm 2016;91(9):415-421.
4. De Gregorio A, Pedrotti E, Russo L, Morselli S. Minimally invasive combined glaucoma and cataract surgery: clinical results of the smallest ab interno gel stent. Int Ophthalmol 2017 [epub before print].
5. Galal A, Bilgic A, Eltanamly R, Osman A. XEN glaucoma implant with mitomycin C 1-year follow-up: results and complications. J Ophthalmology 2017 [epub before print].
6. Ferreira NP, Pinto LA and Marques-Neves C (2017). XEN Gel Stent Internal Ostium Occlusion: Ab-Interno Revision. Journal of Glaucoma (26) 4 e150-e152.
7. Fea A, Cannizzo PML, Consolandi G et al (2015). Managing Drawbacks in Unconventional Successful Glaucoma Surgery: A Case Report of Stent Exposure. Case reports in ophthalmological medicine pp 847439.
8. Fernandez-Garcia A, Romero C, and Garzon N (2015). "Dry Lake" technique for the treatment of hypertrophic bleb following XEN Gel Stent placement. Archivos de la Sociedad Espanola de Oftalmologia. Vol 90 (11) pp 536-8.

Additional relevant papers

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
Manasses DT and Au Leon (2016).The New Era of Glaucoma Micro-stent Surgery. Ophthalmology and therapy (5) 2 135-146.	Review	This review summarises the current published literature on these devices, including Sclemm's canal stents (iStent, Hydrus), Suprachoroidal stents (CyPass, iStent supra), and subconjunctival stents (Xen, Innfocus).	Review on devices used for minimally invasive glaucoma surgery.
Lewis RA (2014). Ab interno approach to the subconjunctival space using a collagen glaucoma stent. Journal of cataract and refractive surgery (40) 8 1301-6.	Review of the development of a new, soft, and permanent ab interno collagen implant (XEN gel stent) to optimize aqueous drainage to the subconjunctival space.	Preclinical and human eye testing shows that the implant does not seem to occlude inside the lumen and the implant material does not appear to cause tissue reaction in the eye. The ab interno placement of the stent offers an alternative for lowering IOP with a minimally invasive procedure, minimum conjunctival tissue disruption, restricted flow to avoid hypotony, and long-term safety.	Pre-clinical testing results only.
Brandao LM and Grieshaber MC (2013). Update on Minimally Invasive Glaucoma Surgery (MIGS) and New Implants. Journal of ophthalmology 705915.	Review on minimally invasive glaucoma surgery and new devices.	The clinical results of the latest techniques and devices are presented by their approach, ab interno (trabeculotomy, excimer laser trabeculotomy, trabecular microbypass, suprachoroidal shunt, and intracanalicular scaffold) and ab externo (canaloplasty, Stegmann Canal Expander, suprachoroidal Gold microshunt). Some of these procedures produce a limited IOP reduction compared to trabeculectomy. Currently, MIGS is performed in glaucoma patients with early to moderate disease and preferably in combination with cataract surgery.	Review of various approaches and devices.
Hohberger B, Welge-Luen UC and Lammer R (2016). ICE-Syndrome: A Case Report of Implantation of a Microbypass Xen Gel Stent After DMEK Transplantation. Journal of Glaucoma no pagination.	Case report N=1 patient with secondary glaucoma due to unilateral iridocorneal endothelial syndrome after descement membrane endothelial keratoplasty operation. Xen45 gel stent glaucoma surgery	A successful implantation of Xen45 gel stent. This may be a promising option for minimally invasive glaucoma surgery in difficult situations, as low adverse effects, good post-surgery visual acuity and sufficient regulation of intraocular pressure can be seen.	Larger studies with longer follow-up included in table 2.

Kerr NM, Wang J and Barton K (2017). Minimally invasive glaucoma surgery as primary stand-alone surgery for glaucoma. Clinical and Experimental Ophthalmology (45) 4 393-400.	Review	New studies have shown that primary ab interno trabeculectomy (Trabectome, NeoMedix Inc., Tustin, CA, USA), trabecular micro-bypass stent insertion (iStent and iStent Inject, Glaukos Corporation, Laguna Hills, CA, USA), canalicular scaffolding (Hydrus, Invantis Inc., Irvine CA, USA), the ab interno gel Implant (XEN, Allergan, Dublin, Ireland) or supraciliary stenting (CyPass Micro-Stent, Alcon, Fort Worth, TX, USA) may lower the lowering intraocular pressure and/or topical medication burden in phakic or pseudophakic patients with glaucoma. This effect seems to last at least 12 months but reliable cost-effectiveness and quality of life indicators have not yet been established by investigator-initiated randomized trials of sufficient size and duration.	Review
Nihr Hsric (2015). XEN Gel Stent for glaucoma treatment (Structured abstract). Health Technology Assessment Database 4.	Review of Xen gel stent (glaucoma drainage implant) in patients with primary open-angle glaucoma where previous treatments have failed.		Abstract only. Review

Nardi M, Posarelli C, Nasini F and Figus M (2017). Mini Drainage Devices for Anterior and Intermediate Filtration. Developments in Ophthalmology (59) 90-99.	Review	Mini glaucoma devices for external filtration may be implanted with an ab externo procedure (Ex-PRESS and InnFocus Microshunt) or with an ab interno procedure (XEN Gel stent). The Ex-PRESS is an FDA-approved mini glaucoma device that has been developed in order to simplify anterior guarded filtering procedures, making them faster, safer and easier. It is positioned under a scleral flap and it is introduced in the anterior chamber through a needle hole, avoiding the excision of the corneal-scleral button and the iridectomy. Like other anterior filtering guarded procedures, it may be associated with releasable sutures and with an everting suture (the safe Ex-PRESS procedure) in order to increase safety and efficacy. The InnFocus Microshunt is a new ab externo filtering device currently under investigation; it is very easy to implant and highly promising in terms of safety and efficacy. The XEN Gel stent is an ab interno implanted soft, collagen tube that makes a permanent bypass between the anterior chamber and the subconjunctival space. It is a smart, quick, effective and simple procedure that recently gained FDA approval.	Review
Richter GM. and Coleman AL (2016). Minimally invasive glaucoma surgery: current status and future prospects. Clinical ophthalmology (Auckland, N.Z.) (10) 189-206.	Review on current approaches for minimally invasive glaucoma surgery. Data on each surgical procedure are reviewed in this article, patient selection lessons learned to date are discussed, and expectations for the future are examined.	The current approaches include: increasing trabecular outflow (Trabectome, iStent, Hydrus stent, gonioscopy-assisted transluminal trabeculotomy, excimer laser trabeculotomy); suprachoroidal shunts (Cypass micro-stent); reducing aqueous production (endocyclophotocoagulation); and subconjunctival filtration (XEN gel stent).	No evidence on Xen gel implant.

Sheybani A, Reitsamer H and Ahmed IIK (2015). Fluid Dynamics of a Novel Micro-Fistula Implant for the Surgical Treatment of Glaucoma. Investigative ophthalmology & visual science (56) 8 4789-95.	Experimental study on Xen 45 gel stent for treatment of glaucoma.	The XEN 45 achieved a steady-state pressure calculated at 7.56 mm Hg at 2.5 muL/min. At the same flow rate, the Ex-Press device and Baerveldt tubing reached steady-state pressures of 0.09 and 0.01 mm Hg, respectively.	Experimental study on fluid dynamics.
Sheybani A, Lenzhofer M, Hohensinn M et al (2015). Phacoemulsification combined with a new ab interno gel stent to treat open-angle glaucoma: Pilot study. Journal of cataract and refractive surgery. Vol 41 (9) pp 1905-9.	Case series N=37 (37 eyes) patients with open-angle glaucoma (OAG). Implantation of 2 models of a gelatin stent (Xen140 and Xen63) was performed at the time of cataract surgery without mitomycin-C. Follow-up 12 months	The mean preoperative IOP was 22.4 mm Hg ± 4.2 (SD) on 2.5 ± 1.4 medication classes. Twelve months postoperatively, the mean IOP was reduced to 15.4 ± 3.0 mm Hg on 0.9 ± 1.0 medication classes (P < .0001). This resulted in a qualified success of 85.3% and a complete success rate off medications of 47.1%. There were no failures.	Device with larger lumen not used in clinical practice.
Sheybani A, Burkhard Dick H, Ahmed IIK (2016). Early Clinical Results of a Novel Ab Interno Gel Stent for the Surgical Treatment of Open-angle Glaucoma. J Glaucoma 25(7):e691-6.	Case series N=49 (49 eyes) with primary open angle glaucoma surgical implantation of the XEN140 implant follow-up 12 months	The average age was 64.3 (28.1 to 86.9) years old. Twenty-one eyes had prior failed trabeculectomy with mitomycin C surgery. IOP at 12 months decreased from a mean of 23.1 (±4.1) mm Hg to 14.7 (±3.7) mm Hg for a 36.4% reduction in IOP from baseline. The number of patients at 12 months who achieved an IOP≤18 mm Hg and ≥20% reduction in IOP was 40 (89%). The number of patients who achieved an IOP≤18 mm Hg and ≥20% reduction in IOP without antiglaucoma medications was 18 (40%).	Device with larger lumen not used in clinical practice.

Vinod K and Gedde SJ (2017). Clinical investigation of new glaucoma procedures. Current Opinion in Ophthalmology (28) 2 187-193.	Review of novel glaucoma procedures promoting aqueous outflow.	Newer glaucoma procedures targeting different aqueous outflow pathways have improved the safety profile of glaucoma surgery while preserving modest efficacy. Early studies of investigational subconjunctival filtering devices (XEN Gel Stent; AqueSys, Inc., Aliso Viejo, California, USA and InnFocus MicroShunt; InnFocus Inc., Miami, Florida, USA) offer promising evidence, but late complications are as yet unknown. Most can be combined with phacoemulsification, allowing for simultaneous treatment of comorbid cataract and glaucoma. Well-designed randomized clinical trials with extended follow-up remain necessary to evaluate the long-term efficacy and late complications of these novel procedures.	Review

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	18/07/2017	Issue 7 of 12, July 2017
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	18/07/2017	Issue 6 of 12, June 2017
HTA database (Cochrane Library)	18/07/2017	Issue 4 of 4, October 2016
MEDLINE (Ovid)	18/07/2017	1946 to July Week 1 2017
MEDLINE In-Process (Ovid)	18/07/2017	July 17, 2017
EMBASE (Ovid)	18/07/2017	1974 to 2017 Week 29
PubMed	18/07/2017	n/a
JournalTOCS	18/07/2017	n/a

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

1 Glaucoma, Open-Angle/ or Glaucoma/

2 glaucom*.tw.

3 POAG.tw.

4 Ocular Hypertension/

5 Intraocular Pressure/

6 ((ocular* or intraocul* or eye*) adj4 (hypertens* or tension or pressur*)).tw.

7 IOP.tw.

8 or/1-7

9 (Glaucom* adj4 filtrat* surger*).tw.

10 Glaucoma Drainage Implants/

11 ((aqeuous or glaucom*) adj4 (stent* or micro-stent* or tube* or device* or implan* or shunt*)).tw.

12 ((collagen or gelatin* or gel*) adj4 (stent* or micro-stent* or tube* or device* or implan* or shunt*)).tw.

13 (ab-interno or "ab interno").tw.

14 ((minimal* or micro*) adj4 glaucom*).tw.

15 MIGS.tw.

16 (space* or drain* or pathway* or channel* or bypass* or by-pass*).tw.

17 or/9-16

18 (subconjunctiv* or sub-conjunctiv*).tw.

19 8 and 17 and 18

20 ((xen adj4 (stent* or implant*)) or aquesys or microshunt* or micro-shunt*).tw.

21 19 or 20

22 animals/ not humans/

21 not 22

23 24 2017*.ed.
25 23 and 24