NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of repetitive short-pulse transscleral cyclophotocoagulation for glaucoma

Glaucoma is a progressive condition that causes increased pressure in the eye. This damages the optic nerve, which connects the eye to the brain, and can lead to permanent sight loss. In this procedure, some of the cells in the eye that produce fluid are destroyed using repeated short pulses of laser energy (transscleral cyclophotocoagulation). The aim is to reduce fluid, and so pressure, in the eye. This may slow or stop damage to sight.

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

Date prepared

This overview was prepared in June 2020 and updated in October 2020.

Procedure name

- Repetitive short-pulse transscleral cyclophotocoagulation for glaucoma

Professional societies

- Royal College of Ophthalmologists (RCOphth)
- UK and Éire Glaucoma Society (UKEGS).

Description of the procedure

Indications and current treatment

Glaucoma is usually a chronic condition associated with raised intraocular pressure. The most common type of glaucoma in the UK is primary (or chronic) 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.

NICE's guideline on glaucoma describes its diagnosis and management. Treatment is usually eye drops containing drugs that either reduce aqueous humor production or increase its drainage. Surgical procedures such as trabeculectomy, drainage tubes, deep sclerectomy, viscocanalostomy, laser trabeculoplasty and cyclodiode laser treatment may also be used.

What the procedure involves

Repetitive short-pulse transscleral CPC (commonly known as micropulse transscleral CPC), uses a laser to target the same tissue as conventional

cyclodiode treatment but it is delivered in pulses lasting microseconds. This allows the tissue to cool between pulses, with the aim of reducing collateral damage.

The procedure is normally done under local or general anaesthesia and usually takes 10 to 20 minutes. A probe is applied to the surface of the eye with firm pressure and moved in a continuous sliding motion over the upper or lower limbus of the eye, or both. To prevent ciliary neurovascular injury, the 3 and 9 o'clock positions are avoided. The device is set to deliver repetitive short-pulse (micropulse) laser energy with specified 'on' and 'off' times. Lower laser settings are used for patients with higher pigments to avoid overtreatment and inflammation. The laser treatment usually lasts between 100 seconds and 360 seconds per session. After the procedure, patients may need to wear an eye patch over the treated eye for about 24 hours and may be prescribed topical corticosteroids and antibiotics.

Efficacy summary

Intraocular pressure reduction

In a randomised controlled trial (RCT) of 48 patients who had micropulse transscleral CPC (MPCPC) or continuous wave transscleral cyclophotocoagulation CPC (CWCPC) for refractory glaucoma, at 18-month follow up, the median intraocular pressure (IOP) was reduced by 45% in both groups from a baseline of 36.5 mmHg for MPCPC and 35.0 mmHg for CWCPC (no statistically significant difference between groups, p=0.7).[1]

In a non-randomised comparative study of 36 children (45 eyes) who had MPCPC or CWCPC, the mean reduction in IOP at 6-month follow up was 42% for the MPCPC group from a baseline of 28.3 mmHg and 35% for the CWCPC group from a baseline of 27.5 mmHg (no statistically significant difference between groups, p=0.3).[2]

In a case series of 161 patients (197 eyes) with uncontrolled glaucoma, at a median 12-month follow up, the mean reduction in IOP after MPCPC was 27% (from 21.5 mmHg preoperative IOP to 15.8 mmHg at final follow up, p<0.001).[3]

In a case series of 116 patients with refractory glaucoma, at a median 6.3-month follow up, the mean reduction in IOP was 31% (from baseline IOP of 22.2 mmHg, p<0.01). The IOP was statistically significantly lower in patients who had at least 1 previous traditional surgery, compared with those who did not have previous surgery (mean IOP 14.0 mmHg compared with 17.8 mmHg, p<0.001). The mean IOP was also statistically significantly lower in patients who had shorter (less than

180 seconds) laser treatment than in those who had longer treatment (more than 180 seconds; 14.8 mmHg compared with 15.6 mmHg, p=0.03).[4]

In a case series of 95 patients who had MPCPC for glaucoma, at 12-month follow up, the reduction in mean IOP was 30% from baseline (25.1 mmHg) (p=0.004).[5]

In a case series of 69 patients (75 eyes) with uncontrolled glaucoma, at 15-month follow up, the mean IOP reduction after MPCPC was 35% from baseline (26.0 mmHg, p<0.001).[6]

In a case series of 79 patients, at the last follow up (median 7.8 months), the mean IOP reduction was 51% from baseline (31.9 mmHg, statistically significance not indicated).[7]

In a case series of 29 children (36 eyes) who had MPCPC for glaucoma, at 15-month follow up, the reduction in IOP was 41% from baseline (33.8 mmHg) (p<0.001).[8]

In a case series of 84 patients with various types of uncontrolled glaucoma, at 12-month follow up, the reduction in IOP after MPCPC was 60%.[9]

In a case series of 214 patients (342 eyes) with glaucoma or ocular hypertension, the mean IOP reduction was 24% from baseline (19.8 mmHg) at 12 months (p<0.001). The mean IOP reduction at 12 months was 31% when baseline IOP was more than 21 mmHg and 20% when it was 21 mmHg or less (71% of overall cohort, p<0.0001). The mean IOP reduction at 12 months also varied according to the laser power: it was 32% with a laser power of 2500 mW or more and 18% with a laser power of less than 2500 mW (p<0.02).[11]

In a case series of 136 patients (141 eyes) with moderate to advanced glaucoma, the mean IOP reduction was 29% from baseline (23.5 mmHg) at 24 months (p<0.0001).[12]

In a case series of 143 patients (167 eyes) with different types of glaucoma, at 12-month follow up, the mean IOP reduction was 32% from baseline (14.8 mmHg ± 4.3, n=74 eyes, p<0.0001). At the last follow up, the mean IOP reduction was 17% from baseline (18.3 ± 6.8, p=0.0027). [16]

In a case series of 110 patients (143 eyes) with different types of glaucoma, at 12-month follow up, the median IOP reduction was 30% (IQR 18.5% to 43%) from baseline (16 mmHg, n=90 eyes). 78% (70/90) of eyes had an IOP of less than 20 mmHg at 12 months. [17]

Success rate

In the RCT of 48 patients, at 1-year follow up, the success rate (defined as IOP 6 to 12 mmHg and at least 30% reduction with or without medications) was 75% for MPCPC group and 29% for the CWCPC group ($p<0.01$). However, at 18-month follow up, there was no statistically significant difference in success rate between the 2 groups (52% compared with 30%, $p=0.13$). The cumulative probability of success using Kaplan-Meier survival analysis was 62% for MPCPC and 28% for CWCPC after 18-month follow up ($p=0.03$).[1]

In the non-randomised comparative study of 36 children (45 eyes), the success rate (defined as IOP less than 21 mmHg in addition to at least 20% reduction in IOP or reduction in number of medication used) was higher in MPCPC group (71%) compared with 46% in the CWCPC group, but the difference was not statistically significant ($p=0.1$).[2]

In the case series of 161 patients (197 eyes), in the 12-month follow-up period, the reported total success rate (defined as IOP more than 6 or less than 18 mmHg or 20% reduction, no other glaucoma procedures and no significant change in visual acuity) was 71% (139/197). In the subgroup analysis, the total success rate for patients with primary open-angle glaucoma was 73% (136/172), for patients who had had previous glaucoma surgery was 80% (58/73) and for patients with multiple concurrent procedures was 88% (22/25).[3]

The case series of 95 patients reported that the success rate with 1 MPCPC treatment was 76.8%.[5]

The case series of 69 patients (75 eyes) reported a success rate of 66% at 15-month follow up.[6]

The case series of 79 patients reported a success rate of 67% at the final follow up (mean follow up of 7.8 months).[7]

The case series of 29 children (36 eyes) reported a success rate of 61% at 15-month follow up.[8]

In the case series of 214 patients (342 eyes), the endpoint of a 20% or more mean IOP reduction from baseline occurred in 68% of the study cohort (n=82) at 12 months.[11]

In the case series of 136 patients (141 eyes), the success rates (defined as an IOP reduction of more than 20% compared with baseline or a decrease in the number of IOP lowering medications with stable target IOP) were 72% (102/141) at 12 months, 82% (74/90) at 18 months and 80% (40/50)at 24 months.[12]

In the case series of 143 patients (167 eyes), the success rate was 37% (61/167 eyes). In case of repeat MPCPC, the success rate increased to 58%. The

probabilities of survival by Kaplan Meier analysis was 82%, 71%, and 57% at 3, 6, and 12 months after the procedure, respectively.[16]

In the case series of 110 patients (143 eyes), the treatment success rates (defined as a pressure reduction of 5 mmHg or stopping at least 1 drug) were 91% (118/130) at 3 months and at 6 months (109/120), and 86% (77/90) at 12 months. The treatment failure rates (defined as the necessity of micropulse retreatment, conducting incisional surgery or increasing medication) were 13% (18/143) at 3 months, 17% (24/143) at 6 months and 8% (11/143) at 12 months. Overall, 29% (42/143) of eyes [corrected by the analyst] had at least 1 treatment failure during the study, and 25% (36/143) had another micropulse intervention.[17]

Reduction in IOP-lowering medication use

In the RCT of 48 patients, there was no difference in the number of IOP-lowering medications used after the surgery in the 2 treatment groups (p=0.88). The median number of medications fell from 2 to 1 (p<0.01) in MPCPC group and 2 to 1 in CWCPC group (p values not reported) after 18 months.[1]

In the non-randomised comparative study of 36 children (45 eyes), there was no statistically significant difference in the number of medications used between the MPCPC and CWCPC groups at 6-month follow up (p=0.3). The mean number of medications reduced to 2.3 at 6 months from 2.5 at baseline in the MPCPC group.[2]

In the case series of 161 patients (197 eyes), there was a reduction in median number of glaucoma medications used after the surgery from 3 in the preoperative to 2 in the postoperative period (p<0.001).[3]

The case series of 116 patients also reported a reduction in the mean number of glaucoma medications from 3.2 preoperatively to 2.5 postoperatively (p<0.01).[4]

In the case series of 95 patients, the mean number of topical medications used reduced statistically significantly from 3.0 at baseline to 1.4 at 12-month follow up (p=0.03).[5]

In the case series of 69 patients (75 eyes), the mean number of topical medications used after surgery reduced statistically significantly up to 12 month (p<0.05) and that of acetazolamide oral tablets decreased statistically significantly up to 15 months (p<0.05). The percentage of eyes needing oral acetazolamide tablets also decreased from 57% (43/75) at baseline to 28% (13/47) at 15-month follow up.[6]

In the case series of 29 children (36 eyes), the mean number of glaucoma medications reduced from 2.65 in the preoperative period to 1.7 at 15-month follow up ($p<0.001$).[8]

In the case series of 84 patients, the mean number of glaucoma medications decreased from 3.3 at baseline to 2.3 at 12-month follow up.[9]

In the case series of 214 patients (342 eyes), the number of topical glaucoma medications at baseline had not changed 12 months after the intervention (1.6). The rate of patients on topical glaucoma medications also remained stable from 78% at baseline to 79% at 12 months. Of the 25 patients initially having oral glaucoma medication, 72% (18) stopped after 12 months.[11]

In the case series of 136 patients (141 eyes), the number (mean±SD) of antiglaucoma medications used statistically significantly decreased from 3.3±1.4 at baseline to 2.2±1.5 at 24 months ($p<0.0001$, n=50 eyes at 24 months).[12]

In the case series of 143 patients (167 eyes), the mean number of antiglaucoma medications statistically significantly decreased from 3.6 ±1.4 at baseline to 2.8 ±1.4 at 6 months and 3.1±1.4 at final follow up ($p<0.0001$). [16]

In the case series of 110 patients (143 eyes), the proportions of eyes that stopped using at least 1 topical or oral medication were 78% (101/130) at 3 months, 75% (90/120) at 6 months and 74% (67/90) at 12 months ($p=0.0001$). The rates of acetazolamide use decreased from 29% (41/143) of eyes at baseline to 17% (24/143) at 3 months, 14% (20/143) at 6 months and 10% (14/143) at 12 months. 11% (10/90) of eyes [corrected by analyst] achieved a target IOP without the use of drugs at 12 months.[17]

Safety summary

Hypotony

Hypotony was reported in 1 patient in the non-randomised comparative study of 36 patients (45 eyes), which was resolved with conservative management.[2]

Hypotony was reported in 2% (n=2) in the case series of 116 patients.[4]

Hypotony was reported in 12% of patients (n=11) in the case series of 95 patients. Ten of them had mild hypotony (IOP 5 to 10 mmHg). All hypotony events in this study were transient, lasting less than a month.[5]

Hypotony was reported in 9% of patients (7/79) in the case series of 79 patients, including 6 patients with early hypotony (IOP less than 5 mmHg within the first postoperative month).[7]

Persistent hypotony (IOP 5 mmHg or less at 2 consecutive follow ups) was reported in 6% of patients (n=5) in the case series of 84 patients.[9]

Hypotony was reported in 4 surgeries out of 375 after 1 month in the case series of 214 patients.[11]

A persistent hypotony with an IOP of 3 mmHg was reported in 1 patient 5 months after the second procedure in the case series of 136 patients. In the same study, hypotony maculopathy was also reported in 1 patient less than 3 months after the procedure, but this complication was reversible.[12]

Anterior chamber inflammation

Prolonged anterior chamber (AC) inflammation was reported in 1 patient in the RCT of 48 patients.[1]

Prolonged AC inflammation was reported in 1 patient in the case series of 116 patients. Postoperative inflammation was reported in 47% (91/197) of eyes in the case series of 161 patients (197 eyes), which were treated with prednisolone 1% drops.[3]

Postoperative inflammation with mild to moderate AC reaction was reported in 23% of eyes in the case series of 69 patients (75 eyes).[6]

Prolonged AC inflammation was reported in 27% of patients (21/79) in the case series of 79 patients.[7]

The case series of 84 patients reported that 86% (63/73) of patients had postoperative AC inflammation at 1-week follow up and 46% (28/61) of patients had postoperative inflammation at 3-month follow up.[9]

A fibrinous AC reaction was reported in 1 patient less than 3 months after the procedure in the case series of 136 patients.[12]

A fibrinous AC reaction was reported in 3% (5/167) of eyes after the procedure in a case series of 143 patients (167 eyes). [16]

Visual acuity decline

In the RCT of 48 patients, visual acuity decline was reported in 1 patient, who had worse visual acuity score after the MPCPC than the baseline.[1]

Postoperative decline in visual acuity was reported in 8% (9/116) of patients in the case series of 116 patients. Eight of these patients had a reduction of 2 lines or more in best corrected visual acuity (BCVA) and 1 of the patients had a reduction from light perception to no light perception.[4]

A 2-line (logMAR) reduction in corrected distance visual acuity (CDVA) was reported in 14% (8/75) of eyes treated MPCPC at 3-month follow up in the case series of 69 patients (75 eyes). The mean CDVA in logMAR scale deteriorated statistically significantly up to 1 month (from 0.86 at baseline to 0.95 at 1 month, $p<0.05$), and then improved. But the scores were statistically not significant compared with baseline.[6]

Loss of more than 2-lines of BCVA for more than 3 months was reported in 17% (13/79) of patients in the case series of 79 patients.[7]

The case series of 84 patients reported that 26% of patients lost 2 lines of vision or more at 3-month follow up.[9]

Visual acuity loss was reported in 16% (61/375) of surgeries after 1 month in the case series of 214 patients.[11]

A decline in CDVA from 0.27 LogMAR at baseline to 0.30 LogMAR at 24 months was reported in 65% (24/37) eyes with a baseline CDVA of more than 1.3 LogMAR in the case series of 136 patients.[12]

A decrease of 1 or more Snellen lines was reported in 42% (68/163) of eyes in the case series of 143 patients (167 eyes). There was a decrease in visual acuity of 3 or more Snellen lines in 15% (24/163) of eyes. In the same study, 1% (2/167) of eyes lost light perception after MPCPC. There was also 1 eye that developed severe anterior segment inflammation, hyphaema, corneal oedema, and intumescent cataract, leading to severe, permanent reduction in visual acuity. [16]

Phthisis bulbi

The case series of 79 patients reported that 3% (2/79) of patients developed phthisis after the procedure.[7]

Vitreous or suprachoroidal or choroidal or subconjunctival haemorrhage

A vitreous haemorrhage was reported in 1 patient after 1 month in the case series of 214 patients.[11]

A suprachoroidal haemorrhage was reported in 1 patient 2 months after the procedure in a single case report.[13]

A choroidal and a vitreous haemorrhage were reported in 1 patient 1 day after the procedure in a single case report.[14]

A subconjunctival haemorrhage was reported during the procedure in 1 patient who was on anticoagulants in a case series of 110 patients (143 eyes). [17]

Hyphaema

Hyphaema was reported in 6% (6/95) patients after MPCPC in the case series of 95 patients.[5]

Hyphaema was reported in 4% (3/84) of patients in the case series of 84 patients.[9]

Cystoid macular oedema

Postoperative cystoid macular oedema was reported in 2% (4/197) of eyes in the case series of 161 patients (197 eyes), which was successfully managed with prednisolone drops.[3]

Cystoid macular oedema was reported in 1 patient in the case series of 116 patients.[4]

Macular oedema was reported in 5% (4/79) of patients in the case series of 79 patients.[7]

Cystoid macular oedema was reported in 2% (4/167) of eyes after the procedure in the case series of 143 patients (167 eyes). In the same study, cystoid macular oedema that was persistent at last follow up was reported in 1 eye. [16]

Choroidal effusion

Choroidal effusion was reported in 1 patient after the MPCPC in the case series of 116 patients.[4]

Choroidal effusion was reported in 3% (3/95) of patients in the case series of 95 patients.[5]

The case series of 84 patients reported that 1 patient developed choroidals, which resolved before 3-month follow up.[9]

Pain

Perioperative pain was reported in 63% (123/197) of eyes in the case series of 161 patients (197 eyes). The same study reported 45% (86/197) of eyes were painful during the immediate postoperative period.[3]

Severe neurotrophic keratitis

Severe neurotrophic keratitis was reported in 2 patients in a case report. Both patients, who had significant predisposing factors for decreased corneal sensation, developed neurotrophic keratitis 1 month after MPCPC for glaucoma. One patient had treatment with a bandage and contact lens and the other patient had tarsorrhaphy. Both patients developed recurrence of the epithelial defects needing repeat management.[10]

Severe superficial punctate keratitis was reported in 7% (11/167) of eyes after the procedure in the case series of 143 patients (167 eyes). In the same study, superficial punctate keratitis that was persistent at last follow up was reported in 2% (4/167) of eyes. [16]

Other complications

Scleral thinning was reported in 1 patient in the RCT of 48 patients.[1]

Corneal abrasion was reported in 1 patient after the MPCPC in the case series of 116 patients.[4]

Corneal oedema was reported in 3% (2/79) of patients in the case series of 79 patients.[7]

Worsening of pre-existing corneal oedema was reported in 1 eye after the procedure in the case series of 143 patients (167 eyes).[16]

Postoperative posterior synechiae was reported in 1 patient in the case series of 95 patients.[5]

Persistent mydriasis was reported in 3% (3/95) of patients in the case series of 95 patients.[5] Persistent mydriasis was reported in 7% (11/167) of eyes in the case series of 143 patients (167 eyes). [16]

Symptomatic mydriasis was reported in 2% (6/375) of surgeries after 1 month in the case series of 214 patients.[11] Mydriasis was reported in 11% (18/167) of eyes after the procedure in the case series of 143 patients (167 eyes). [16]

Slight or moderate mydriasis with a 2-line visual acuity reduction was reported in 2 patients after the procedure in the case series of 110 patients (143 eyes). The patients recovered within 30 days. [17]

Keratopathy was reported in 11% (10/95) of patients in the case series of 95 patients.[5]

Iritis was reported in 2% (6/375) of surgeries after 1 month in the case series of 214 patients.[11]

Recurrent iritis was reported in 1 eye after the procedure in the case series of 143 patients (167 eyes). In the same study, persistent iritis was reported in 1% (2/167) of eyes.[16]

Cataract was reported in 2% (7/375) of surgeries after 1 month in the case series of 214 patients.[11]

Intraocular pressure spike was reported in 9% (34/375) of surgeries after 1 month in the case series of 214 patients.[11]

Rejection of corneal graft was reported in 1 patient less than 3 months after the procedure in the case series of 136 patients.[12]

Acute corneal subepithelial hydrops was reported in 1 patient during the procedure in a single case report. [15]

Conjunctival laceration was reported in 1 eye during the procedure in the case series of 143 patients (167 eyes).[16]

Decreased accommodation that was persistent at the last follow up was reported in 2% (3/167) of eyes in the case series of 143 patients (167 eyes).[16]

Severe chemosis with subconjunctival haemorrhage was reported in 1 eye during the procedure in the case series of 143 patients (167 eyes).[16]

Abduction restriction was reported in 1 eye during the procedure in the case series of 143 patients (167 eyes).[16]

Vitreous in AC was reported in 1 eye during the procedure in the case series of 143 patients (167 eyes).[16]

Worsening of pre-existing dry eyes was reported in 1 eye during the procedure in the case series of 143 patients (167 eyes).[16]

Pupillary abnormalities were reported in 4 patients in a case series of 349 patients. [18]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts 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, professional experts listed the following anecdotal adverse event: pupil irregularity.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to repetitive short-pulse transscleral cyclophotocoagulation for glaucoma. The following databases were searched, covering the period from their start to 19 October 2020: 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 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 glaucoma
Intervention/test	Repetitive short-pulse transscleral cyclophotocoagulation
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 1,674 patients (about 1,923 eyes) from 1 randomised controlled study, 1 non-randomised comparative study, 1 retrospective cohort study, 11 case series and 4 case reports[1-18].

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

Table 2 Summary of key efficacy and safety findings on repetitive short-pulse transscleral cyclophotocoagulation for glaucoma

Study 1 Aquino M (2015)

Details

Study type	**Randomised controlled trial**
Country	Singapore
Recruitment period	2007 to 2008
Study population and number	**n=48 (24 MPCPC versus 24 CWCPC)** Patients with refractory, end-stage glaucoma
Age and sex	MPCPC: mean 63.5 years; 71% (17/24) male CWCPC: mean 66.0 years; 58% (14/24) male
Patient selection criteria	Inclusion criteria: Age ≥21 years, patients with refractory glaucoma (defined as IOP >21 mmHg unresponsive to maximal tolerated medical therapy, with or without previous surgical intervention), patients for whom filtration procedure may not be suitable, patients who had best corrected visual acuity (VA) of 6/60 or worse. Exclusion criteria: ocular infection, inflammation or eye surgery in the study eye in the 2 months before enrolment.
Technique	MPCPC: Standard micropulse diode laser cyclophotocoagulation treatment using a ball lens tip, customised contact tip (Iris Medical Instruments) emitting 810 nanometre infrared radiation from diode source. CWCPC: Using the G-Probe (Iris Medical Instruments), the laser was delivered 1.2 mm from the limbus. The laser settings used were 1.5 to 2 W, 2 s exposure time per burn, 20 to 28 burns per eye delivering 60 to 112 J per treatment. The power was decreased when audible pops were heard, and laser energy delivery was adjusted based on the eye's response. After the procedure, topical prednisolone acetate 1% was prescribed 3 times a day for 10 to 14 days in both treatment groups.
Follow up	**Mean 17.5 months**
Conflict of interest/source of funding	No stated conflict of interest. No stated funding sources.

Analysis

Follow-up issues: After 1 laser treatment, patients were followed up at 1 day, 1 week, 1 month, 3 months, 6 months, 12 months and 18 months. 1 patient in MPCPC and 1 in CWCPC group were lost to follow up after 12 months.

Study design issues: A randomised, exploratory, single-centre study. Patients were enrolled from a glaucoma clinic. One eye was enrolled for each eligible patient. If both eyes met eligibility criteria, the eye with the higher IOP was randomised. Randomisation was done with a code obtained from sequentially numbered, opaque sealed envelopes. Laser treatment was done by a single surgeon who was not masked. Patients were masked for the type of laser intervention.

The primary outcome measure of success was IOP between 6 and 21 mmHg with at least a 30%reduction in IOP at the final follow up with or without medications. IOP was measured using Goldmann applanation tonometry. The secondary outcome measures of success were the number of repeat treatments, number of IOP lowering medications at 18 months, and the frequency of complications. Second treatment was offered if IOP reduction from baseline after 1 month was less than 30%. Third treatments were given when necessary according to the same criteria as second treatments. Statistical

analyses were done using R. Difference between MPCPC and CWCPC were assessed using Wilcoxon Rank-Sum test, Chi-square test, Mantel-Haenszel and Ansari-Bradley test as appropriate.

Study population issues: In the MPCPC group, 21% of patients had POAG, 21% had primary angle-closure glaucoma (PACG), 29% had Neovascular glaucoma (NVG) and 29% had other types of glaucoma such as silicone oil, aphakic and traumatic. In the CWCPC group, 25% had POAG, 4% had PACG, 50% had NVG and 21% had other types. More patients with NVG were randomised to CWCPC group (50% versus 29% MPCPC). Baseline demographics (age and sex) were not significantly different between the 2 groups.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **48 (24 versus 24)**

Intraocular Pressure (IOP), Median (25th, 75th percentile)

Follow up	MPCPC (n=24)	CWCPC(n=24)	adjusted *p**
Baseline	36.5 (29.5,56.5)	35.0 (29.5,46.5)	0.5
1 day	21.5 (16.8,34.5)	27.0 (21.8,39.0)	0.21
1 week	16.5 (14.0,27.0)	21.0 (12.8,31.2)	0.80
1 month	22.5 (15.0,34.0)	22.0 (14.0,34.5)	0.85
3 months	20.0 (14.8,26.5)	20.5 (11.5,34.5)	0.98
6 months	20.0 (16.0,24.0)	18.5 (11.5,28.5)	0.98
12 months	18.0 (15.5,20.2)	20.0 (7.5,28.5)	0.63
18 months	20.0 (16.0,23.5)	19.0 (8.0,30.0)	0.70

*adjusted for NVG via robust linear regression

The median IOP was reduced by 45% in both groups from the baseline measurements at 18-month follow up (p=0.70).

Success rate (IOP between 6-21 mmHg with at least 30% reduction in IOP)

Follow up	MPCPC	CWCPC	*p*
1 year	75% (18/24)	29% (7/24)	<0.01
18 months	52% (12/23)	30% (7/23)	0.13

The cumulative probability of success using Kaplan-Meier survival analysis was 62% for MPCPC and 28% for CWCPC after 18 months follow up (p=0.03).

Number of treatments

Number of treatments	MPCPC % (n)	CWCPC % (n)	p*
1	53% (12)	44% (10)	0.46
2	30% (7)	30% (7)	
3	17% (4)	26% (6)	

*Cochran-Armitage trend test

There is no difference in the number of treatment sessions needed in each group (p=0.36).

Safety

Complications

Ocular complications	MPCPC % (n)	CWCPC %(n)	*p*
Prolonged AC inflammation	4% (1)	30% (7)	
Phthisis bulbi	0 % (0)	1 (4%)	
Scleral thinning	4% (1)	17% (4)	
VA decline	4% (1)	9% (2)	
Overall ocular complication rate	13 % (3/23)	61% (14/23)	0.01

Prolonged hypotony (IOP ≤ 5mmHg for at least 6 months)

Prolonged hypotony was seen in 5 eyes in CWCPC group but not in MPCPC group. 4/5 CWCPC eyes had NVG and 1 had silicone oil-induced glaucoma.

Number of glaucoma medicines

Number of medicines	MPCPC % (n)	CWCPC % (n)	p*
0	22% (5)	35% (8)	0.76
1	48% (11)	22% (5)	
2	26% (6)	30% (7)	
3	4% (1)	13% (3)	

*Cochran-Armitage trend test

There is no difference in the number of medicines used in the 2 treatment groups (p=0.88). The median number of medications were reduced from 2 to 1 (p<0.01) in MPCPC group and 2 to 1 in CWCPC group (p values not reported) after 18 months

Visual acuity score

VA	MPCPC % (n)	CWCPC % (n)	p*
Better or equal	96% (22)	91% (21)	1.0
Worse	4% (1)	9% (2)	

Ocular pain
Moderate to severe ocular pain:

	MWCPC	CWCPC
Preoperative	1	1
Perioperative	1	4
Postoperative (1 week)	0	1

Abbreviations used: MPCPC, micropulse (transscleral) cyclophotocoagulation; CWCPC, continuous wave (transscleral) cyclophotocoagulation; NVG, neovascular glaucoma; VA, visual acuity; AC, anterior chamber.

Study 2 Abdelrahman A (2018)

Details

Study type	**Non-randomised comparative study**
Country	Egypt
Recruitment period	2016 to 2017
Study population and number	n=**36 patients (13 MPCPC versus 23 CW-PCP), 45 eyes (17 MPCPC versus 28 CW-PCP)** Children with refractory glaucoma
Age and sex	MPCPC: mean 67.8 months; 65% (11/17) male CWCPC: mean 61.3 months; 50% (14/28) male
Patient selection criteria	Not reported.
Technique	MPCPC: Cyclo G6 laser (Iridex) was used with a setting of 2000 mW of 810 nanometre infrared diode laser. The duty cycle was 31.3% with 0.5 milliseconds of 'on time' and 1.1 milliseconds of 'off time'. The treatment time ranged from 100 to 120 seconds. CWCPC: The IRIDEX G-probe was used with a power of 1500 mW and duration of 1500 milliseconds. The power and duration of the laser was increased until a popping sound was heard. Approximately 15 shots were delivered in the superior quadrants and 15 in the inferior quadrants, avoiding the 3 and 9 o'clock positions. All laser procedures were done under general anaesthesia. Postoperatively, both groups had topical prednisolone 1%, cycloplegic eye drops and systemic NSAIDs. Patients were kept on their antiglaucoma medications, which were adjusted as per reduction in IOP.
Follow up	**6 months**
Conflict of interest/source of funding	The authors declared no conflict of interest.

Analysis

Follow-up issues: Patients were followed up at 1 week, 2 weeks, 1 month, 3 months and 6 months after laser treatment.

Study design issues: A prospective, single-centre, non-randomised comparative study. Patients were children below 12 years of age with uncontrolled glaucoma. The primary outcome measure was the rate of complications. Hypotony was defined as IOP<5mmHg. Secondary outcome measures were the IOP, number of glaucoma medications and the rate of success.

- Complete success was defined as an IOP of 5 to 21 mmHg at last follow up, with no other signs of glaucoma progression.
- Qualified success was defined as an IOP <21 mmHg on medications in addition to at least 20% reduction in IOP and/or reduction in the number of medications used.
- Failure was considered if these criteria were not achieved, or if a subsequent glaucoma procedure or cyclophotocoagulation was needed to control the IOP, or if a devastating complication happened.

IOP was measured by Perkins tonometer. SPSS was used for statistical analysis. IOP comparisons between the 2 groups were analysed using the independent t test, success rates by Fisher's exact test and survival analysis of surgical success was analysed using Kaplan-Meier survival plots, with the Mantel-Cox test.

Study population issues: 15 eyes (88%) of the MPCPC group had previous CWCPC, compared with 14 eyes (50%) in the CWCPC group (p=0.01). Most patients had very poor vision; therefore, visual field testing was not done. Type of glaucoma included PCG 64% (n=11) in MPCPC versus 53% (n=15) in CWCPC; aphakia/pseudophakia 18 % (n=3) versus 32% (n=9); aniridia 12% (n=2) versus 4% (n=1); Peter's anomaly 6% (n=1) versus 0; microspherophakia 0 versus 7%

(n=2); Sturge Weber syndrome 0 versus 4% (n=1). MPCPC group had a slightly higher mean cup-to-disc ratio compared with CWCPC group (0.9 versus 0.7, p=0.02)

Key efficacy and safety findings

Efficacy

Number of eyes analysed: **45 (17 versus 28)**

Intraocular Pressure (IOP)

Follow up	MPCPC mean (SD)	CWCPC mean (SD)	p
Preop	28.3 (8.2)	27.5 (6.1)	0.7
2 weeks	12.1 (4.7)	15.9 (6.8)	**0.05**
1 month	16.8 (7.3)	17.7 (8.0)	0.7
3 months	15.5 (3.7)	19.4 (8.4)	**0.05**
6 months	16.4 (4.6)	17.9 (5.6)	0.3

The IOP reduction in MPCPC group was 42.0%, compared with 34.9% in the CWCPC group at 6 months (p=0.3).

Note: The paper reported different values for these percentages and did not report how they were calculated. We recalculated the percentage based on the preoperative and 6-month values from the above table.

The mean IOP was lower in the MPCPC group compared with CWCPC group at all follow ups, however, only statistically significant at 2 weeks and 3 months follow up (p=0.05).

Success rate at 6 months follow up

	MPCPC(n=17)	CWCPC(n=28)
Complete success	6% (1)	18% (5)
Qualified success*	71% (12)	46% (13)
Failure	29% (5)	54% (15)

*Qualified success includes complete success cases

The difference in success and failure rates between the 2 groups were not significant (p=0.1).

Mean survival time (Kaplan-Meier survival analysis)

MPCPC = 4.7 months (CI, 3.7-5.7 months)
CWCPC = 3.4 months (95% CI, 2.5-4.39months), p=0.09

Safety

Complications

Although the CWCPC group tended to have more serious complications, the difference in the rate of complications between the 2 groups was not significant (p=0.3).

Hypotony

MPCPC = 1 eye (resolved with conservative management)

CW-PCP = 3 eyes (2 spontaneously resolved, 1 developed phthisis bulbi)

Number of glaucoma medications

Follow up	MPCPC mean (SD)	CWCPC mean (SD)	p
Preop	2.5 (0.6)	2.3(0.9)	0.5
2 weeks	2.2(0.9)	1.3(1.4)	**0.02**
1 month	1.7(0.8)	1.25(1.2)	0.2
3 months	2.0(1.0)	1.4(1.1)	0.3
6 months	2.3(0.9)	1.7(1.3)	0.3

The number of medications were lower in the CWCPC group; however, the difference was statistically significant only at 2 weeks follow up.

Study 3 Yelenskiy A (2018)

Details

Study type	**Case series**
Country	USA
Recruitment period	2015 to 2017
Study population and number	n=**161 patients/ 197 eyes** Patients with uncontrolled glaucoma
Age and sex	Mean 73 years; 55% male.
Patient selection criteria	Patients who had MPCPC with P3 probe for the treatment of any type and stage of glaucoma were included retrospectively.
Technique	A transscleral diode laser (Iridex Cyclo G6 laser system) with a P3 probe was used for the procedure. The laser settings were standardised at: power 2000 mW, micropulse 'ON' time 0.5 milliseconds, 'OFF' time 1.1 milliseconds, duty cycle at 31.3%. The laser was delivered over 90 and 120 seconds to each arc. Prednisolone eye drops 1% and cycloplegic eye drops were used postoperatively. The eye was not patched.
Follow up	**Median 12 months (range 3 to 25 months)**
Conflict of interest/source of funding	The authors declared no conflict of interest. The study is supported by Tulane Glaucoma Research Fund.

Analysis

Follow-up issues: Patients were followed up postoperatively at 1 day, 1 week, 1 month, 3 months, 6 months and every 3 months thereafter.

Study design issues: A retrospective, longitudinal, multicentre study. The patient data were collected retrospectively from 5 different clinical sites. The outcome measures were IOP, visual acuity (logMAR), need for repeat micropulse, need for incisional glaucoma surgery, number of topical medications used, surgical success rates and complications. Total success was defined as: IOP >6 or <18 mmHG or 20% reduction, without the need for repeat MPCPC or other glaucoma procedures, and did not lose 3 or more lines in VA. Statistical analysis using logistic regression and Kaplan-Meier analysis was done with STATA. Repeated measures analysis of variance, paired t test and Wilcoxon signed-rank test were used as appropriate.

Study population issues: 88% (n= 141) of patients had POAG, 5% (n=8) had NVG, 2.5 %(n=4) had uveitic glaucoma, 2.5 %(n=4) had chronic angle closure glaucoma, 2%(n=3) had penetrating keratoplasty glaucoma and 1 patient had iridocorneal endothelial syndrome. 55% (n=89) had previous laser treatments, which included either selective trabeculoplasty or argon laser trabeculoplasty.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **161 patients (197 eyes)** **Mean Intraocular pressure (IOP) at final follow up** Preoperative = 21.5 mmHg (SD, 9 mmHg) Postoperative = 15.8 mmHg (SD, 6 mmHg) Mean IOP reduction = 27%, p<0.001 **Median number of glaucoma medications** Preoperative = 3 (IQR, 1-4) Postoperative = 2 (IQR, 1-3), p<0.001 **Visual acuity (Median logMAR)** preoperative = 0.4 (IQR, 0.2-1.0) Postoperative = 0.3 (IQR, 0.2-1.0), p=0.65 **Success rate** Total success rate = 71% (139/197) IOP success rate (IOP ≥6 and ≤18) = 85% **Subgroup analysis** Total success rate POAG patients = 73% (136/172) Patients with previous glaucoma surgery = 80% (58/73) Patients with multiple concurrent procedures = 88% (22/25) However, after adjusting for preoperative IOP, there was no significant difference in total success rate for those patients with multiple concurrent surgeries and those without (p=0.12). **Free from repeat MPCPC (Kaplan-Meier analysis)** At 3 months = 97% At 12 months = 90% (95% CI, 86% - 94%).	**Complications** **Cystoid macular oedema (CMO)** 2% (4/197) eyes with CMO were reported. These were successfully managed with postoperative prednisolone eye drops. **Postoperative inflammation** 47% (91/197) of eyes had postoperative inflammation, which was treated with prednisolone 1 % eye drops. **Pain** 63% (n=123) of patients reported pain during the procedure and 45% (n=86%) reported pain during the immediate postoperative period.
Abbreviations used: IQR, interquartile range.	

Study 4 Garcia G (2019)

Details

Study type	**Case series**
Country	USA
Recruitment period	2016 to 2018
Study population and number	n=**116** Patients with refractory glaucoma
Age and sex	Mean 65.8 years; 47% (55/116) male
Patient selection criteria	Inclusion criteria: patients with refractory glaucoma defined as: glaucoma that remained uncontrolled despite previous IOP lowering surgery, laser treatment, maximum tolerated medical treatment, or a combination thereof; patients who had MPCPC with at least 3 months of follow up after surgery. For participants who had had treatment for both eyes, only 1 eye was selected randomly for the study.
Technique	MPCPC procedure using Iridex Cyclo G6 laser with P3 probe and standard parameters (power 2000 mW, duty cycle 31.3%, 0.5 milliseconds 'ON' and 1.1 milliseconds 'OFF'). The duration of laser delivery was at the discretion of the treating surgeon. Mean treatment time was 212.9 seconds. After surgery, all eyes had topical prednisolone and ketorolac drops. All glaucoma medications were continued until 1-week visit, then adjusted accordingly.
Follow up	**6.3 months (range, 3 to 12 months)**
Conflict of interest/source of funding	Equipment support from Iridex. No other conflict of interest was reported.

Analysis

Follow-up issues: Patients were followed-up postoperatively at 1 day, 1 month, 3 months, 6 months, 9 months, and 12 months. The number of patients at the follow-up time points were 116 (100%) at 3 months, 77 (66.4%) at 6 months, 37 (30.8%) at 9 months, 20 (16.7%) at 12 months.

Study design issues: A retrospective, single centre study. Charts of 116 cases who had MPCPC procedure by 4 surgeons were reviewed. IOP was measured using Goldmann applanation tonometer. The statistical analysis was done using R software. Paired-sample t test was used to evaluated differences between preoperative and postoperative IOPs. Kaplan-Meier method was used to estimate the cumulative probability of success. Success was defined as IOP between 6 and 21 mmHg with or without topical anti-hypertensives, no additional medications, 20% or more IOP reduction from baseline for 2 consecutive follow ups after 3 months after surgery, no subsequent glaucoma surgery, and no loss of light perception vision or vision-threatening severe complications.

Study population issues: 56.9% (n=66) had POAG, 6%(n=7) had chronic angle closure, 5.2% (n=6) had congenital, 4.3% (n=5) had juvenile open-angle, 5.2% (n=6) had pseudoexfoliation, 6.9% (n=8) had low tension and 11.2% (n=18) and other types of glaucoma. 90.5% of the patients had prior glaucoma surgery, which include trabeculectomy (26.7%), tube shunt surgery (49.1%), trabectome (11.2%), Ex-PRESS miniature glaucoma shunt (4.3%), endocyclophotocoagulation (7.8%), contact transscleral cyclophotocoagulation using continuous wave diode laser (TSCPC) (2.6%), selective laser trabeculoplasty (7.8%), laser peripheral iridotomy (7.8%), goniotomy (3.4%) and other procedures. 68.1% of patients had prior cataract surgery.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **116**

Intraocular pressure (IOP)

Follow up	N	Mean IOP (mmHg) (SD)	*p*
Baseline	116	22.2 (7.9)	
1 day	116	15.3 (6.9)	<0.01
1 month	116	16.0 (6.6)	
3 months	116	15.8 (6.9)	
6 months	77	16.1 (7.0)	
9 months	37	14.9 (5.3)	
12 months	20	17.0 (4.2)	

Mean intraocular pressure (IOP) at final follow up (median 6.3 months)

Baseline = 22.2 mmHg (SD, 7.9 mmHg)

Postoperative= 15.3 mmHg (SD,6.6 mmHg), p<0.01

Mean percentage reduction in IOP = 31.1%

Mean number of glaucoma medications at final follow up

Baseline = 3.2 (SD, 1.6)

Postoperative = 2.5 (SD, 1.3), p<0.01

Visual acuity (mean logMAR) at final follow up

Baseline = 0.84 (SD, 0.78)

Postoperative = 0.86 (SD, 0.81), p=0.294

Success rate (Kaplan-Meier analysis)

Follow up	N	Cumulative probability of success
3 months	116	93.1%
6 months	77	74.3%
9 months	37	67.5%
12 months	20	59.6%

Mean final IOP based on treatment duration*

Treatment duration <180 seconds = 14.8 mmHg (SD, 6.4)

Treatment duration >180 seconds = 15.6 mmHg (SD, 5.5), p= 0.03*

*after adjusting for number of medications at time for surgery, number of previous surgeries and type of glaucoma.

Safety

Complications

Total ocular complications rate = 12.9 % (15/161)

Complications	% (n)
Hypotony	1.7 % (2/116)
Prolonged AC inflammation	<1 % (1/116)
Choroidal effusions	<1 % (1/116)
Corneal abrasion	<1 % (1/116)
Cystoid macular oedema	<1 % (1/116)
Decline in VA	7.8 % (9/116)

8 of the VA decline patients had a reduction of 2 lines or more in best corrected visual acuity (BCVA) and 1 of the patients had a reduction from light perception to no light perception

Retreatment

19.0 % (22/161) of patients had subsequent glaucoma surgery.

Mean IOP based on age

	Age <45 (n=47) (SD)	Age>45 (n=69) (SD)	*p*
Baseline	20.4 (±6.9)	25.0(±7.4)	<0.001
3 months	15.4 (±7.0)	16.1 (±7.9)	0.384
6 months	15.7 (±7.1)	16.4 (±6.4)	0.510

Mean IOP based on prior traditional glaucoma surgery

	Prior traditional surgery (n=79) (SD)	**No prior traditional surgery (n=37) (SD)**	***p***
Baseline	21.5 (±7.6)	23.6(±8.4)	0.319
Final follow up	14.0(±5.8)	17.8(±7.2)	<0.001

Traditional surgery was defined as at least 1 trabeculectomy, tube shunt surgery, miniature glaucoma shunt surgery or combination.

Abbreviations used: VA, visual acuity; AC, anterior chamber; TSCPC, transscleral cyclophotocoagulation; SD, standard deviation.

Study 5 Nguyen A (2019)

Details

Study type	**Case series**
Country	USA
Recruitment period	Not reported
Study population and number	n=**95** Patients with glaucoma
Age and sex	Mean 69.2 years; 40% (38/95) male
Patient selection criteria	95 consecutive patients with glaucoma who had MPCPC by a single surgeon were reviewed retrospectively. Patients were included only if they had at least 12 months follow up.
Technique	Patients had treatment with a Micropulse P3 device (Iridex) at 2.0 to 2.5 W with a duration of 90 seconds per hemisphere at a 31.3% duty cycle. Power was increased to 3.0 W if retreatment was indicated. Patients were given retreatment if they did not achieve a 20% reduction in IOP. Topical corticosteroids were given postoperatively.
Follow up	**12 months**
Conflict of interest/source of funding	One of the authors is a consultant of Iridex. The authors received no financial support for the study.

Analysis

Follow-up issues: Patients were followed up at 1 week, 1 month, 3 months, 6 months, and 12 months postoperatively.

Study design issues: A retrospective, single-centre study on 95 consecutive glaucoma patients who had MPCPC procedure done by a single surgeon. The primary outcome measure was IOP at various follow-up time points. Treatment success was defined as IOP-lowering of at least 20% of the baseline value at all time points. Qualified success was defined as achieving 20% reduction with eventual retreatment. Secondary outcome measures were number of IOP-lowering medications used and postoperative complications. Hypotony was defined as IOP <5mmHg, and mild hypotony as IOP between 5 and 10 mmHg. Student t test was used to compare with the baseline and follow-up measures.

Study population issues: 53.7% (n=51) had POAG, 25.3% (n=24) had pseudoexfoliation glaucoma, 15.8 % (n=15) had chronic angle-closure glaucoma, and 5.3% (n=5) had congenital/juvenile glaucoma. Average preoperative IOP was 25.1 mmHg.

Other issues: Visual acuity was not measured. There were no patients with neovascular glaucoma in this study.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **95**

Intraocular pressure (IOP)

Follow up	Mean IOP, mmHg (SD)	*p*
Baseline	25.1 (5.3)	
1 week	15.1 (7.4)	0.002
1 month	14.1 (5.6)	0.001
3 months	16.2 (4.5)	0.003
6 months	16.1 (4.4)	0.001
12 months	17.5 (5.1)	0.004

Compared with baseline, the average IOP at 12 months was reduced by 30.3%.

Number of topical medications

Follow up	Mean number of medications (SD)	*p*
Baseline	3.0 (1.1)	
1 week	1.2 (1.1)	0.001
1 month	0.9 (0.9)	0.001
3 months	1.3 (1.0)	0.01
6 months	1.5 (0.8)	0.01
12 months	1.4 (1.0)	0.03

Success rate

With 1 MPCPC treatment = 76.8 % (73/95)

Qualified success after retreatments= 100%

Safety

Complications

Hypotony

Any hypotony = 11.6% (11/95)

Hypotony with IOP <5mmHg = 1.1 % (1/95)

Mild hypotony (IOP 5-10 mmHg) = 10.5% (10/95)

All hypotony events were transient, lasting <1 month.

Other complications

Posterior synechiae	1.1% (1/95)
Hyphaema	6.3 % (6/95)
Persistent mydriasis	3.2% (3/95)
Choroidal effusion	3.2% (3/95)
Keratopathy	10.5% (10/95)

Abbreviations used: SD, standard deviation; POAG, primary open-angle glaucoma.

Study 6 Zaarour K (2019)

Details

Study type	**Case series**
Country	Lebanon
Recruitment period	2016 to 2018
Study population and number	**n= 69 patients/75 eyes** Patients with uncontrolled glaucoma
Age and sex	Mean 55.1 years; 53.6% (37/69) male
Patient selection criteria	Inclusion criteria: patients who had uncontrolled IOP >21 mmHg despite maximally tolerated topical and systemic antiglaucoma medications, and previous surgical therapy, if any. Exclusion criteria: Patients having any intraocular surgery within 2 months of enrolment, any signs of ocular infection or inflammation, non-compliant with treatment, unable to keep their follow up appointments, extended scleral thinning for >1 clock hour.
Technique	MPCPC was done with Cyclo G6 laser system with MP3 probe (Iridex), using standardised protocol with fixed parameters (power of 2000 mW, duty cycle of 31.3%, 0.5 milliseconds 'On' and 1.1 milliseconds 'Off', duration 180 seconds). Postoperatively, the eye was patched for 24 hours, and topical tobramycin 0.3% combined with dexamethasone 0.1%, ketorolac 0.45% and preservative-free lubricating eye drops were prescribed.
Follow up	**Mean 13.2 months (range 1 to 15 months)**
Conflict of interest/source of funding	The authors declared no conflict of interest.

Analysis

Follow-up issues: Patients were followed up postoperatively at 1 day, 1 week, 1 month, 3 months, 6 months, 9 months, 12 months and 15 months. The numbers reaching follow-up time points were 75 eyes (100%) at 1 month, 96% (n=72 eyes) at 3 months, 70 (93.3%) at 6 months, 65 (86.5%) at 9 months, 60 (80.0%) at 12 months, and 47 (62.7%) at 15 months follow up.

Study design issues: A prospective, noncomparative, single-centre interventional case series. The procedures were done by 1 of 2 surgeons in the centre using a standardised protocol with fixed parameters. Outcome measures were corrected distance visual acuity (CDVA), IOP, number of antiglaucoma medications, and complications. Success was defined as IOP between 6 and 21 mmHg or an IOP reduction of >20% from baseline, achieved with or without medications. Hypotony was defined as IOP <6 mmHg on 2 consecutive visits. A two-line (log MAR) reduction in CDVA from baseline or loss of light perception were also considered as complications. SPSS program was used for statistical analysis. Pre and postoperative data were compared using a dependent t test.

Study population issues: Patients' age range from 7 to 90 years (mean 55.51 years). 34.7 % (n=26) of eyes had POAG, 13.3% (n=10) of eyes had secondary glaucoma, 9.4% (n=7) of eyes had glaucoma after penetrating keratoplasty, 8.0 % (n=6) of eyes had chronic angle-closure, 6.7% (n=5) had congenital glaucoma, 5.3% (n=4) had NVG and 22.7% (n=17) had other types of glaucoma. 56% (n=42) of eyes had had previous glaucoma surgery, with Ahmed glaucoma valve implantation (26.7%, n=20) and trabeculectomy (18.7%, n=14) being the most common.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **69 patients/75 eyes**

Intraocular Pressure (IOP)

Follow up	Mean IOP, mmHg (SD)	% reduction from baseline	*p*
Baseline	26.0(7.9)	-	-
1 day	21.1 (6.9)	15.9%	<0.05
1 week	13.8 (5.6)	44.0%	<0.001
1 month	18.0 (7.7)	25.5%	<0.001
3 months	18.4 (7.1)	23.9%	<0.001
6 months	16.7 (6.2)	29.3%	<0.001
9 months	15.1 (4.1)	36.5%	<0.001
12 months	15.7 (5.3)	31.8%	<0.001
15 months	14.8 (5.5)	35.4%	<0.001

Number of antiglaucoma medications used

Follow up	Topical Mean (SD)	Acetazolamide tablets Mean (SD)
Baseline	3.53 (0.68)	0.72(0.73)
1 day	0	0
1 week	3.38(0.96)	0.38 (0.64)
1 month	3.24 (1.01)	0.29 (0.48)
3 months	3.25 (1.07)	0.27 (0.48)
6 months	3.11 (1.13)	0.27 (0.50)
9 months	3.16 (1.11)	0.26 (0.57)
12 months	3.08 (1.09)	0.23 (0.57)
15 months	3.03 (1.31) *	0.15 (0.29)

p <0.05 (significant) for all except * which was not significant

Percentage of eyes needing oral acetazolamide tablets

Baseline - 57.3% (43/75)
1 week - 34.7% (26/75)
1 month - 26.7% (20/75)
3 months - 27.8% (20/72)
6 months - 30.0% (21/70)
9 months - 30.8% (20/65)
12 months - 30.0% (18/60)
15 months - 27.7% (13/47)

Success rate

1 day - 65.3%
1 week - 92.0%
1 month - 76.0%
3 months - 80.6%

Safety

Complications

Postoperative inflammation = 23% of eyes

It was mild to moderate AC reaction, which resolved with postoperative topical corticosteroids.

Decline in CDVA

CDVA in LogMAR:

Baseline (SD)	0.86 (0.66)	
Day 1	0.90 (0.68)	<0.05
1 week	0.95 (0.65)	<0.05
1 month	0.95 (0.62)	<0.05
3 months	0.86 (0.6)	NS
6 months	0.87 (0.62)	NS
9 months	0.89 (0.62)	NS
12 months	0.85 (0.61)	NS
15 months	0.75 (0.58)	NS

A small and significant decrease in CDVA up to 1 month was seen.

A total of 8 eyes (14.0%) lost ≥ 2 logMAR lines at the 3-month follow up visit.

6 months - 81.4% 9 months - 78.5% 12 months - 73.3% 15 months - 66.0%	
Abbreviations used: CDVA, corrected distance visual acuity; AC, anterior chamber; NS, not significant; SD, standard deviation; POAG, Primary open-angle glaucoma; NVG, neovascular glaucoma.	

Study 7 Williams A (2018)

Details

Study type	**Case series**
Country	USA
Recruitment period	2014 to 2016
Study population and number	n=**79** Patients with refractory glaucoma
Age and sex	Mean 70.2 years; 39% (31/79) male
Patient selection criteria	Inclusion criteria: Patients who had MPCPC procedure and had at least 3 months of follow up. The criteria for the procedure was at the discretion of the treating surgeon, but generally had already failed or not a candidate for incisional glaucoma surgery. Exclusion criteria: Age ≤20 years, previous intraocular surgery or ocular laser treatment within 2 months of enrolment,
Technique	MPCPC was done using Cyclo G6 laser with standard parameters (power of 2000 mW, duty cycle of 31.3%, 0.5 milliseconds 'On' and 1.1 milliseconds 'Off', duration 120 to 360 seconds (mean=300 seconds)). The laser was delivered in a 'stop-and-go' pattern (held in 1 place for 10 seconds before being moved to the adjacent section of perilimbal conjunctiva). 3 o'clock and 9 o'clock positions were avoided. Postoperatively, patients had a tapering course of prednisolone 1% eye drops.
Follow up	**Mean 7.8 months (range, 3 to 25 months)**
Conflict of interest/source of funding	The authors declared no conflict of interest. An unrestricted grant was provided by Iridex Laser Systems for statistical analysis.

Analysis

Follow-up issues: Outcomes were assessed at 3 months, 6 months and last available follow up.

Study design issues: A retrospective, single-centre study. 79 consecutive patients who had MPCPC (by 1 surgeon) at an eye hospital in the US were recruited. Primary outcome was treatment success, which was defined as IOP between 6 and 21 mmHg or a 20% reduction from baseline without an increase in glaucoma medications. Qualified success was defined as achieving success with the aid of additional antiglaucoma medications. Secondary outcomes were hypotony and other postoperative complications. SAS software was used for statistical analysis. Linear effects models were used to predict the effect of time on IOP, BCVA and number of medications. A survival analysis was used for treatment success.

Study population issues: 50.6% of patients (n=40) had POAG, 22.8% (n=18) had chronic angle closure, 11.4% (n=9) had pseudoexfoliation, 3.8% (n=3 had uveitic, 7.6% (n=6) had neovascular and 3.8% (n=3) had pigmentary glaucoma. Ten eyes (12.6%) had a 2nd MPCPC and 1 eye had a 3rd treatment.

Other issues: Mean IOP and number of medications for each follow-up time point were reported in charts, but values were not provided.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 79

Intraocular pressure
Baseline IOP = 31.9 mmHg (SD±10.2 mmHg)
Mean IOP reduction from baseline at last follow up = 51%

Linear mixed effects models predicting the effect of time on IOP indicated that posttreatment IOP did not change significantly during the follow-up periods (p=0.85)

Treatment success rate
At 3 months follow up = 74.7 %
At 6 months follow up = 66.1 %
Last follow up (>6 months) = 66.7%

A further 11.1% of patients met the criteria for treatment success with the addition of medications (qualified success) at last follow up.</td><td>Complications

<table><tr><td>Hypotony</td><td>8.8 % (7/79)</td></tr><tr><td>Prolonged AC inflammation</td><td>26.6 % (21/79)</td></tr><tr><td>Loss of ≥2 lines of BCVA</td><td>16.5 % (13/79)</td></tr><tr><td>Macular oedema</td><td>5.1 % (4/79)</td></tr><tr><td>Corneal oedema</td><td>2.5% (2/79)</td></tr><tr><td>Phthisis</td><td>2.5% (2/79)</td></tr></table></td></tr>
<tr><td colspan="2">Abbreviations used: AC, anterior chamber; BCVA, best corrected visual acuity.</td></tr>
</table>

Study 8 Elhefney

Details

Study type	**Case series**
Country	Egypt
Recruitment period	2017
Study population and number	**n= 29 patients/ 36 eyes** Children with glaucoma
Age and sex	Median 24 months; 62% (18/29) male
Patient selection criteria	Inclusion criteria: diagnosis of childhood glaucoma; previous glaucoma surgery; uncontrolled IOP (defined as IOP>21 mmHg despite maximal tolerated antiglaucoma medications). Exclusion criteria: previous cyclodestructive procedure, significant scleral thinning (thinning of more than 1 clock hour)
Technique	Procedure done under general anaesthesia. The laser settings were: power of 1750-2000 mW for upper hemisphere and 2000 mW for the lower part, duty cycle 31.3% (0.5 ms duration, 1.1 ms interval), laser time 55-65 s per hemisphere. Postoperative, topical corticosteroids were prescribed as tapering dose.
Follow up	**Mean 15.08 months**
Conflict of interest/source of funding	The authors declared no potential conflict of interest. The study had no financial support.

Analysis

Follow-up issues: Follow up was scheduled in 1 day, 1 week, 1 month, 3 months, 6 months, 12 months and 15 months. 5 patients were lost to follow up at 15th month.

Study design issues: A prospective, single-centre, interventional study on patients younger than 16 years with recurrent childhood glaucoma. Qualified success was defined as IOP between 6 and 21 mmHg or reduction by ⩾20% with or without antiglaucoma medications. Failure was defined as IOP was higher 21 mmHg despite used of antiglaucoma medications, development of devastating complications or need for other glaucoma surgeries. SPSS was used for statistical analysis. Paired t-test was used to compare 2 parametric variables. Repeated measure analysis of variance (ANOVA) test was used to compare between more than 2 variables within the whole studied group. Kaplan-Meier survival curves were used to evaluate survival rate. One-way ANOVA test, log-rank (Mantel-Cox) test, Chi-square test were also used as appropriate.

Study population issues: 47.2% (n=17) of eyes had primary congenital glaucoma, 41.7 %(n=15) of eyes had aphakic glaucoma and 11.1% (n=4) had pseudophakic glaucoma. All patients had previous glaucoma surgeries. 12 eyes (33.3%0 had single session of MPCPC, 24 eyes (66.7%) had second session after 8 weeks from the initial treatment.

Other issues: The study reported 2 different figures for baseline mean (±SD) IOP. In the table, the baseline mean IOP was reported as 33.8±9.37 mmHg but in the abstract, it was reported as 37.5±11.3 mmHg. The lower value was used for this document.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 29 patients/36 eyes
Intraocular Pressure (IOP)
<table>
<tr><th>Follow up</th><th>Mean IOP, mmHg (SD)</th><th>p</th></tr>
<tr><td>Baseline</td><td>33.8 (9.37)</td><td></td></tr>
<tr><td>1 day</td><td>15.6 (7.6)</td><td rowspan="7"><0.001</td></tr>
<tr><td>1 week</td><td>17.6 (7.6)</td></tr>
<tr><td>1 month</td><td>20.0 (5.6)</td></tr>
<tr><td>3 months</td><td>21.2 (5.2)</td></tr>
<tr><td>6 months</td><td>20.8 (3.7)</td></tr>
<tr><td>12 months</td><td>20.9 (3.9)</td></tr>
<tr><td>15 months</td><td>20.0 (2.7)</td></tr>
</table>
The total IOP reduction at the 15th month follow up was 40.8%

Mean number of glaucoma medications
Preoperative = 2.65 ± 0.5
15th month follow up = 1.7 ± 0.6, p<0.001

Success rates
Qualified success at 15th month = 61 % (22/36)

Cumulative probability of success by Kaplan-Meier survival analysis
1 month = 69.4 %
3 months = 58.3%
6 months = 52.8%
12 months = 47.2%
15 months = 41.7%

The overall mean survival time was 8.7 months (SD,1.1 months).</td><td>Complications
The study reported that none of the eyes experienced any major ocular complications.</td></tr>
<tr><td colspan="2">Abbreviations used: SD, standard deviation;</td></tr>
</table>

Study 9 Emanuel M (2017)

Details

Study type	**Case series**
Country	USA
Recruitment period	Not reported
Study population and number	**n=84** Adults patients with various types of uncontrolled glaucoma
Age and sex	Mean 74 years; 43% (36/84) male
Patient selection criteria	All adult glaucoma patients who had MPCPC procedure were included in the study.
Technique	The laser settings were determined by the treatment physician without strict parameters. Some used a technique of fast-sweeping motion of about 10 seconds back-and-forth over 180 degrees and others used slow-sweeping motion about 1 minute over the same distance.
Follow up	**Mean 4.3 months**
Conflict of interest/source of funding	The authors declared no conflict of interest Funding information – not reported

Analysis

Follow-up issues: 88% (n=74) of patients completed 1 month follow up, 73% (n=61) completed 3 months, 46% (n=39) completed 6 months and 12% (n=10) completed 12 months follow up.

Study design issues: A retrospective, single centre study. Chart review was done for all patients who had MPCPC from a glaucoma centre. All eyes with any types of glaucoma, any past ocular histories and all available follow up were included in the study. 68% (n=57) had prior glaucoma surgeries.

Study population issues: 58% (n=49) had POAG, 7% (n=6) had chronic-angle closure, 10% (n=8) had pseudoexfoliation, 6%(n=5) had neovascular glaucoma and 19% (n=16) had other types of glaucoma.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 84

Intraocular Pressure (IOP)
<table>
<tr><th>Follow up</th><th>n</th><th>Mean IOP, mmHg (SD)</th><th>% reduction from baseline</th></tr>
<tr><td>Baseline</td><td>84</td><td>27.7 (10.3)</td><td>-</td></tr>
<tr><td>1 month</td><td>74</td><td>16.3 (9.5)</td><td>41.2%</td></tr>
<tr><td>3 months</td><td>61</td><td>14.6 (8.8)</td><td>47.3%</td></tr>
<tr><td>6 months</td><td>39</td><td>13.0 (6.9)</td><td>53.1%</td></tr>
<tr><td>12 months</td><td>10</td><td>11.1 (4.4)</td><td>59.9%</td></tr>
</table>
Mean number of antiglaucoma medications
Preoperative - 3.3 (±1.0)
1 month - 1.9 (±1.3)
3 months - 2.0 (±1.4)
6 months - 2.0 (±1.4)
12 months - 2.3 (±1.5)</td><td>Complications

Hypotony
6% (n=5) had persistent hypotony (≤5 mmHg at 2 consecutive follow ups).
5% (n=4) had single IOP reading of ≤ 5mmHg but resolved later.
2 patients had IOP ≤ 5mmHg but lost to follow up.

Postoperative AC Inflammation
1 week = 86% (63/73)
3-month = 46% (28/61)

Vision loss (lost 2 lines of vision or more)
1 week = 33.3% (n=25)
1-month= 35.1% (n=26)
3-month = 26.2% (n=16)

3 patients lost light perception vision post0operatively.

Other complications
- IOP spike (increase in IOP >25% from baseline within 1 month of laser) = 3.6 % (n=3)
- Hyphaema = 3.6 % (n=3)
- Choroidals = 1.2 % (n=1)
All hyphaemas and choroidals resolved before 3-month follow up.</td></tr>
<tr><td colspan="2">Abbreviations used: AC, anterior chamber; POAG, primary open-angle glaucoma</td></tr>
</table>

Study 10 Perez C (2019)

Details

Study type	**Case report**
Country	USA
Recruitment period	Not reported
Study population and number	**n=2** Patients with glaucoma
Age and sex	Both patients: 79 years; female
Patient selection criteria	N/A
Technique	The procedure was done under general anaesthesia. The Cyclo G6 micropulse prove (Iridex) was used. Laser settings were power of 2000 mW, and duty cycle of 31.3%. 180 degrees were treated over the limbus by moving the probe in a continuous painting fashion, over 80 seconds. Using the same procedure, the other hemisphere was treated to achieve 360 degrees of treatment. 3 and 9 o'clock positions were avoided. Postoperatively, prednisolone 1% was given 4 times a day as a tapering course.
Follow up	**7 months for case 1, 6 months for case 2**
Conflict of interest/source of funding	The authors reported no financial disclosures related to the topic. No funding was received for the study.

Severe neurotrophic keratitis

Two patients with significant predisposing factors for decreased corneal sensation developed neurotrophic keratitis 1 month after MPCPC. Both patients did not respond to initial treatment with topical antibiotics and preservative-free artificial tears. One patient had treatment with a bandage contact lens and the other patients needed tarsorrhaphy. Both patients developed a recurrence of the epithelial defects and were subsequently managed with repeated corneal treatments.

Study 11 Kaba Q (2020)

Details

Study type	**Retrospective cohort study**
Country	Canada
Recruitment period	2016 to 18
Study population and number	n=**214** patients (342 eyes) with ocular hypertension and all severities and types of glaucoma for a total of 399 procedures
Age and sex	Mean 67 years; 54% (116/214) male
Patient selection criteria	Consecutive eyes with glaucoma or ocular hypertension
Technique	Micropulse cyclophotocoagulation using the Iridex Cyclo G6 Glaucoma Laser System, Mountain View, CA. Micropulse cyclophotocoagulation laser settings were maintained at 80 seconds per hemisphere for a total of 160 seconds in each eye with a duty cycle of 31.3% (0.5 millisecond duration, 1.1 millisecond interval). Laser power ranged from 900 to 2800 mW. Patients were prescribed difluprednate 0.05% 4 times daily for the first week after laser treatment. At the discretion of the surgeon and with consideration of target IOP, medical therapy was reduced via a stepwise approach starting with oral glaucoma medication. Retreatment was considered if IOP reduction was over target. Retreatment was not considered if there was a lack of effectiveness or if significant adverse events occurred. The repeat procedure occurred at least 1 month from initial treatment.
Follow up	**12 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: The follow-up cohort included 94% (375/399) of the original procedures at 1 month, 60% (240/399) at 3 months, 37% (148/399) at 6 months, and 34% (134/399) at 12 months.

Study design issues: The main outcome measures were intraocular pressure, visual acuity, glaucoma medications and ocular adverse events.

Study population issues:

- The diagnoses were primary open-angle glaucoma (56% [223/399]), chronic angle-closure glaucoma (11% [43/399]), neovascular glaucoma (9% [36/399]), normal-tension glaucoma (7% [26/399]) and ocular hypertension (6% [22/399]).
- Most of the eyes had had prior glaucoma medical treatment (78% [310/399]) and glaucoma surgery (86% [344/399]).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **214 patients (342 eyes)**

Intraocular Pressure (IOP)

Follow up	n (surgeries)	Mean IOP±SD (mmHg)	% reduction from baseline
Baseline	399	19.8±7.4	-
1 month	375	15.3±6.0*	23%
3 months	240	15.8±6.6*	20%
6 months	148	15.7±5.7*	21%
12 months	134	15.1±6.3*	24%

***p <0.0001 for all**

The endpoint of 20% or more mean IOP reduction from baseline occurred in 68% of the study cohort (n=82) at 12 months.

Analysis based on IOP stratification:

31% mean IOP reduction at 12 months when baseline IOP was more than 21 mmHg and 20% when it was 21 mmHg or less (71% of overall cohort; p<0.0001).

Analysis based on laser power stratification

32% mean IOP reduction at 12 months with laser power of 2500 mW or more and 18% with laser power of less than 2500 mW (p<0.02).

Number of topical glaucoma medications

Follow up	n (surgeries)	Mean number of topical medications	p	% of patients on topical glaucoma medications
Baseline	399	1.6±1.1	-	78% (310)
1 month	375	1.4±1.1	0.01	71% (266)
3 months	240	1.5±1.1	0.27	78% (186)
6 months	148	1.6±1.1	0.79	80% (118)
12 months	134	1.6±1.1	0.91	79% (106)

Of the 25 patients initially having oral glaucoma medication, 60% (15) and 72% (18) ceased after 1 month and 12 months respectively.

Safety

Visual acuity

		Snellen Corrected Distance Visual Acuity Range (%)		
Follow up	n (surgeries)	20/40 or Better	20/50-20/80	20/100 or Worse
Baseline	399	52	16	32
1 month	375	52	16	32
3 months	240	52	19	29
6 months	148	48	20	32
12 months	134	58	11	31

Ocular Adverse Events at 1 month

Adverse Event	% eyes
Visual acuity loss	16% (61/375)
Intraocular pressure spike	9% (34/375)
Cataract	2% (7/375)
Iritis	2% (6/375)
Symptomatic mydriasis	2% (6/375)
Hypotony	<1% (4/375)
Vitreous haemorrhage	<1% (1/375)

Conversion to other glaucoma surgery

Eight patients needed additional glaucoma surgical intervention during the study period.

Re-treatment

One or more repeat procedures was administered to 14% of the cohort (n =57). Additional mean IOP reduction of 16% (p < 0.0001) was achieved with each re-treatment.

Study 12 De Crom R (2020)

Details

Study type	**Prospective case series**
Country	The Netherlands (1 centre)
Recruitment period	2016 to 2018
Study population and number	n= **136** patients (141 eyes) with moderate to advanced glaucoma
Age and sex	Mean 67 years; 56% (79/136) male
Patient selection criteria	Inclusion criteria: patients with moderate to advanced uncontrolled despite maximal tolerated topical or systemic IOP lowering medication, or previous glaucoma surgery. Patients with maximal topical or systemic IOP lowering medication and a high risk for conventional glaucoma surgery or with stable (advanced) glaucoma. Patients with at least 12 months of follow up. Exclusion criteria: active neovascular glaucoma, active uveitis with secondary glaucoma or scleral thinning more than 1 clock hour.
Technique	Micropulse TSCPC (MicroPulse P3 probe, Iridex® cyclo G6 laser system, Mountain View, U.S.A.) at 2000mW with a duration of 80 seconds (when IOP <30mmHg) or 90 seconds (when IOP >30mHg) per hemisphere and at a 31.3% duty cycle. For retreatments, the same parameters were used with an increase of power to 2100mW (2nd treatment) or 2200mW (3rd treatment). Postoperative therapy included topical tobramycin 0.3% combined with dexamethasone 0.1% eye drops for 9 days and IOP lowering medications were withdrawn if appropriate.
Follow up	**24 months**
Conflict of interest/source of funding	The authors declared no conflict of interest.

Analysis

Follow-up issues: Patients were followed up at 1 day, 1 week and 1, 3, 6, 12, 18 and 24 months after the intervention.
Study design issues: IOP and the number of IOP lowering medication were recorded. Slit lamp examination was done to detect treatment complications. CVDA was done if patients reported visual complaints. Hypotony was defined as IOP lower than 6 mmHg measured at 2 or more consecutive follow-up visits.
Study population issues:

- The glaucoma subtypes treated were: 70% (99/141) primary glaucoma and 30% (42/141) secondary glaucoma.
- Prior glaucoma surgery was done in 42% of eyes (59/141).
- 47.5% (67/141) of eyes had pseudophakia, and 10% (14/141) had aphakia.
- Pretreatment CDVA was lower than 1.3 LogMar in 34 patients, between 1.3 and 0.3 LogMar in 47 patients and better than 0.3 LogMar in 60 patients.

Key efficacy **and safety findings**

Efficacy

Number of patients analysed: **136 (141 eyes)**

Intraocular Pressure (IOP)

Follow up	**n (eyes)**	**Mean IOP ± SD (mmHg)**	**% reduction from baseline**
Baseline	141	23.5 ± 9.4	-
1 day	134	17.1 ± 6.1*	-
1 week	137	13.1 ± 5.8*	-
1 month	139	15.9 ± 7.5*	-
3 months	136	16.2 ± 6.4*	-
6 months	139	16.6 ± 5.6*	-
12 months	141	16.8 ± 8.4*	28%
18 months	90	17.0 ± 7.8*	24%
24 months	50	16.8 ± 9.2*	29%

*Statistically significant p<0.0001 compared with preoperative values

Number of antiglaucoma medications

Follow up	**n (eyes)**	**Mean number of antiglaucoma medications ± SD**
Baseline	141	3.3 ± 1.4
1 day	134	3.3 ± 1.4
1 week	137	3.2 ± 1.5
1 month	139	2.9 ± 1.5*
3 months	136	2.7 ± 1.4*
6 months	139	2.6 ± 1.5*
12 months	141	2.6 ± 1.5*
18 months	90	2.5 ± 1.4*
24 months	50	2.2 ± 1.5*

*Statistically significant p<0.0001 compared with preoperative values

Treatment success (IOP reduction of >20% compared with baseline or a decrease in the number of IOP lowering medications with stable target IOP)

Follow up	Rate
12 months	72% (102/141)
18 months	82% (74/90)
24 months	80% (40/50)

Safety

Decline in CDVA (mean CDVA in LogMAR)

- Baseline versus 12 months (n=77/107 eyes with a baseline CDVA>1.3 LogMAR): from 0.35 to 0.46 LogMAR
- Baseline versus 24 months (n=24/37 eyes with a baseline CDVA>1.3 LogMAR): from 0.27 to 0.30 LogMAR

Complications

Early complications (< 3 months)

Complication rate	3.5% (5/141)
Fibrinous anterior chamber reaction	<1% (1/141)
Hypotony maculopathy	<1% (1/141)
Rejection of corneal graft	<1% (1/141)
Cystic Macular oedema	1% (2/141)

These complications were all reversible after treatment (prolonged use of topical corticosteroid treatment or reducing glaucoma medication).

1 patient developed a **persistent hypotony with an IOP of 3 mmHg** 5 months after the 2nd treatment. This patient had an ophthalmic history of congenital cataract, aphakia, vitrectomy with use of silicon oil after retinal detachment and neovascular glaucoma. No visual complaints and no signs of hypotony maculopathy were present.

Retreatment: 30% (42/141) of eyes needed 47 treatments.

Mean time between treatment and retreatment was 176±115 days.

In 55% (23/42) of eyes, treatment success was already achieved after the first treatment. Retreatment in this patient group was done to gain additional IOP lowering or further reduction of medication.

After retreatment(s), 64% (27/42) of eyes achieved treatment success. No success after retreatment could be reached in 36% (15/42) of eyes.

Conversion to other glaucoma surgery was necessary in 6 of 15 patients.

Study 13 Prager A (2020)

Details

Study type	**Case report**
Country	USA
Recruitment period	Not reported
Study population and number	**n=1 (2 eyes)** Patient with end-stage primary open angle glaucoma and multiple medical comorbidities including coronary artery disease and on anticoagulation treatment
Age and sex	77 years; male
Patient selection criteria	N/A
Technique	Micropulse cyclophotocoagulation using 810 nanometre infrared diode laser at 2000 mW with 31.3% duty cycle. The laser was applied for 90 seconds inferiorly and 90 seconds superiorly avoiding the 3 and 9 o'clock areas. The procedure was done twice in the right eye. Two months later, the left eye was treated with the same laser settings.
Follow up	**2 months**
Conflict of interest/source of funding	The authors reported no financial disclosures related to the topic. No funding was received for the study.

Suprachoroidal haemorrhage

Two weeks after the procedure in the left eye, the patient presented to the emergency department with 2 days of episodic, severe left eye pain. He had a visual acuity of count fingers at 2 feet and an IOP of 44 mmHg. The diagnostic was a suprachoroidal haemorrhage without evidence of retinal detachment. The patient had analgesics and atropine for pain management, prednisolone acetate drops for intraocular inflammation, and oral acetazolamide and topical IOP lowering medications to lower pressure. His condition was monitored with serial B-scans and the suprachoroidal haemorrhage decreased in size without surgical intervention. Two months after presentation, his visual acuity was back to count fingers at 2 feet and his IOP was undetectable.

Study 14 Aldaas K (2020)

Details

Study type	**Case report**
Country	USA
Recruitment period	Not reported
Study population and number	**n=1 (1 eye)** Patient with moderate to advanced primary open-angle glaucoma
Age and sex	82 years; female
Patient selection criteria	N/A
Technique	Micropulse cyclophotocoagulation using 2000 milliwatts x 120 seconds x 31.3% ON cycle for 75 Joules per hemilimbus in the right eye.
Follow up	**3 months**
Conflict of interest/source of funding	The authors had no conflicts of interest nor funding to disclose.

Choroidal and vitreous haemorrhage

One day after the intervention, the patient presented with blurry vision and pain in her right eye. Examination showed that she had a choroidal haemorrhage, 200 degrees of ciliary body swelling, and vitreous haemorrhage. The choroidal haemorrhage resolved with corticosteroids at 2 months, but a pars plana vitrectomy was needed for the vitreous haemorrhage at 3 months. Her visual acuity recovered to 20/70 1 month after vitrectomy with an IOP of 26mmHg.

Study 15 Chan P (2020)

Details

Study type	**Case report**
Country	China
Recruitment period	Not reported
Study population and number	**n=1 (1 eye)** Patient with neovascular glaucoma in the left eye
Age and sex	72 years; male
Patient selection criteria	N/A
Technique	Micropulse transscleral cyclophotocoagulation using 2000 milliwatts of 810 nanometre infrared diode laser radiation set on micropulse mode (Iris Medical Instruments) for 80 seconds for each superior and inferior hemisphere, sparing the 3 and 9 o'clock meridians.
Follow up	**2 months**
Conflict of interest/source of funding	The authors had no conflicts of interest nor funding to disclose.

Acute corneal subepithelial hydrops

The patient, who had primary angle closure glaucoma and had received bilateral laser iridotomy, presented with progressive left eye blurred vision (visual acuity of 20/40 right eye and 20/200 left eye). Examination showed a left eye central retinal venous occlusion. The IOP was 19 mmHg in the left eye and the patient was on maximally tolerated topical medications. Four weeks later, the left eye was complicated by neovascular glaucoma; the IOP was raised to 26 mmHg despite additional oral acetazolamide and remained elevated after panretinal photocoagulation and cataract extraction by phacoemulsification. The patient had micropulse transscleral cyclophotocoagulation (MPTSC) 8 days after the phacoemulsification. During the procedure, a sudden protrusion was formed on the corneal surface. On-table examination showed an intact corneal epithelium with a globular-shaped collection of fluid at the subepithelial layer – acute corneal subepithelial hydrops. The anterior chamber was formed and the globe was intact. After about 10 to 15 minutes, the swelling spontaneously ruptured and became a corneal epithelial defect. The defect healed on the tenth day after the event with conservative management. There was no irreversible corneal damage and the patient subsequently underwent a successful second MPTSC of the left eye because of poorly controlled IOP.

Study 16 Radhakrishnan S (2020)

Details

Study type	**Retrospective case series**
Country	USA (3 centres)
Recruitment period	2015 to 2016
Study population and number	n= **143** patients (167 eyes) with glaucoma
Age and sex	Mean 71 years; 47% (68/143) male 53% (76/143) of patient were Asian, and 29% (42/143) were Caucasian.
Patient selection criteria	Not reported
Technique	Patients were treated with the Iridex Cyclo G6 laser and the Micropulse P3® handpiece of the first generation design (IQ 810 Laser Systems; Iridex). Laser settings were 2000mW with a duty cycle of 31.3%. Patients received 2 to 4 180-degree treatments of 80 seconds duration each per treatment, depending on surgeon preference. The laser probe was applied circumferentially 1-2 mm posterior to the limbus with a continuous “painting” motion in the superior and inferior hemispheres, excluding the 3 o’clock and 9 o’clock positions and areas with filtering blebs and drainage devices. Several laser “passes” were conducted per treatment. Subconjunctival dexamethasone was given at the end of the procedure as well as topical steroid and cycloplegic. Post-operatively, prednisolone acetate 1% drops were used for 2 weeks. Decisions about additional IOP lowering treatment were based on the individual surgeon’s judgement. The total duration per treatment was 160 seconds in 23% (39/167), 240 seconds in 32% (53/167), and 320 seconds in 45% (75/167) of eyes.
Follow up	**12 months**
Conflict of interest/source of funding	The study received financial support from the Glaucoma Research Foundation, San Francisco, CA. The sponsor or funding organisation had no role in the design or conduct of this research. Three of the authors reported conflicts of interest.

Analysis

Follow-up issues:

Follow-up was recorded at 1 day, 1 week, 1 month, 3 months, 6 months, 9 months, and 12 months after MPCPC and thereafter at 6-month intervals until last follow-up. At each follow-up visit, IOP, number of medications, and complications were recorded.

Post-operative data was available for 93%, 80%, 63%, and 44% of eyes at 1, 3, 6, and 12 months, respectively.

Study design issues:

The procedure was considered a failure if any of the following occurred: additional IOP lowering intervention, severe complication, or less than 20% IOP reduction from baseline at the last follow-up (with or without medication).

The laser treatment protocol differed among the surgeons and could have been modified during the course of the study. Although the laser power, duty cycle and probe placement remained constant across surgeons, the total duration of treatment varied at the surgeon’s discretion, and the speed of the laser probe movement was not quantified or standardised.

Study population issues:

The types of glaucoma were primary open angle glaucoma (POAG) in 60% of patients (100/167), mixed mechanism glaucoma in 15% (25/167), primary angle closure glaucoma in 7% (12/167), exfoliation glaucoma in 5% (8/167), normal tension glaucoma in 4% (5/167), steroid-induced glaucoma in 2% (3/167), neovascular glaucoma in 1% (2/167), and other types in 5% (9/167) including pigment dispersion glaucoma, malignant glaucoma, Sturge Weber syndrome, congenital glaucoma, and glaucoma secondary to trauma.

60% (105/167) of eyes were pseudophakic and 38% (64/167) had prior glaucoma surgery including.

The mean number of procedures for patients with prior glaucoma surgery was 1.8±1.1 (range 1 to 6).

The indication for MPCPC was uncontrolled IOP in all except 2% (4/167) of eyes that had well-controlled IOP and underwent the procedure to reduce topical medications. Mean baseline IOP: 21.9 mmHg.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **143 (167 eyes)**

IOP

Follow-up	n (eyes)	Mean IOP (mmHg)	% reduction from baseline
Baseline	167	21.9 ± 8.4	-
1 day	166	16.4	-
1 week	158	13.6	-
1 month	155	15.9 ± 6.9	27%*
3 months	133	15.8 ± 5.4	28%*
6 months	106	16 ± 5.9	27%*
9 months	83	14.8	32%*
12 months	74	14.8 ± 4.3	32%*
Last follow-up	-	18.3 ± 6.8	17%**

*Statistically significant reduction in IOP compared with preoperative values (p<0.0001).

** Statistically significant reduction in IOP compared with preoperative values (p=0.0027).

At last follow-up, 41% (69/167) of eyes had IOP < 21 mm Hg and at least 20% IOP reduction from baseline, 33% (55/167) of eyes had IOP <18 mm Hg and at least 25% IOP reduction from baseline and 24% (40/167) had IOP < 15mm Hg and at least 30% IOP reduction from baseline.

Number of antiglaucoma medications

	Baseline	6 months	Final follow-up	p value at all time points
Mean number of medications	3.6 ±1.4	2.8 ±1.4	3.1±1.4	**<0.0001**

Treatment success at last follow-up: 36.5% (61/167) eyes

In case of repeat MPCPC, success rate increased to 58%.

If the IOP criterion was changed to at least 20% reduction or IOP 6-21 mm Hg, then the success rate increased from 36.5% to 48% (80/167).

The reasons for failure after MPCPC were additional IOP lowering intervention in 47% (79/167 eyes), IOP not reduced by at least 20% from baseline (but did not have additional intervention) in 14% (24/167 eyes) and severe complication in 1.8% (3/167 eyes).

The mean interval between MPCPC and additional IOP lowering intervention was 7.0 ± 5.4 months.

Safety

Visual acuity (n=163 eyes)

Mean change between baseline and last follow-up: -0.05 ± 0.36 LogMAR (range -1.7 to 1.15, p=0.0565)

Change in Snellen lines:
- No change from baseline to last follow up in 38% (62/163)
-An increase of 1 or more lines in 20% (33/163)
-A decrease of 1 or more lines in 42% (68/163).
-Two eyes lost light perception after MPCPC.
-In 15% (24/163) of eyes there was a decrease in visual acuity of 3 or more Snellen lines attributable to glaucoma progression in 25% (6/24), cataract progression in 17% (4/24), corneal oedema in 12.5% (3/24), and persistent mydriasis in 8% (2/24). There was one case (4%) each of severe anterior segment inflammation, severe superficial punctate keratitis, cystoid macular oedema, and inability to obtain visual acuity due to new-onset dementia. In 20% (5/24), the cause of decreased vision was not specified.

Complications

Complication	Number of eyes
None	73% (122/167)
Mydriasis	11% (18/167)
Severe superficial punctate keratitis	7% (11/167)
Fibrinous AC reaction	3% (5/167)
Cystoid macular oedema	2% (4/167)
Decreased accommodation	2% (3/167)
Loss of light perception	1% (2/167)
Persistent iritis (> 2 months post procedure)	1% (2/167)
Complication leading to severe, permanent reduction in VA[a]	<1% (1/167)

Probability of survival (Kaplan Meier analysis)

Follow-up	Probability of survival
3 months	82%
6 months	71%
12 months	57%

In a multivariable Cox proportional hazard model, female gender was associated with a 56% decrease in failure rate compared to males (p<0.0001) and a unit increase in baseline IOP corresponded with a 5.7% increase in failure rate (p<0.0001).

Other[b]	4% (7/167)
Persistent complication at last follow-up	11% (18/167)
Mydriasis	7% (11/167)
Superficial punctate keratitis	2% (4/167)
Decreased accommodation	2% (3/167)
Iritis	1% (2/167)
Cystoid macular oedema	<1% (1/167)

[a]One eye with baseline VA of 20/30 developed severe **anterior segment inflammation, hyphaema, corneal oedema, and intumescent cataract** following a 160s MPCPC treatment. After cataract surgery with anterior vitrectomy and a subsequent penetrating keratoplasty, the VA was 20/200 at last follow-up.

[b]One eye (0.6%) each with **intraoperative conjunctival laceration, severe chemosis with subconjunctival haemorrhage, abduction restriction, recurrent iritis, vitreous in AC, worsening of pre-existing corneal oedema and worsening of pre-existing dry eyes.**

Asian ethnicity (OR 13.5, p=0.0131) and phakic status (OR 3.1, p=0.0386) were associated with higher odds of developing mydriasis.

Abbreviations used: AC, anterior chamber; IOP, intraocular pressure; POAG, primary open-angle glaucoma; VA, visual acuity

Study 17 Logioco C (2020)

Details

Study type	**Retrospective case series**
Country	Argentina (single centre)
Recruitment period	2016 to 2018
Study population and number	n= **110** patients (143 eyes) with glaucoma
Age and sex	Mean 70 years; 54% (77/143) male
Patient selection criteria	Inclusion criteria: over 18 years of age, confirmation of glaucoma, failing to reach the therapeutic objective despite being treated with the highest tolerated medical treatment, intolerance to topical or oral medication of failing to exhibit IOP control with conventional surgeries. Exclusion criteria: patients who had previously had this procedure or found it impossible to attend the checkup visits.
Technique	The Cyclo G6 laser device (MP-TSCPC; IRIDEX IQ810 Laser Systems) was used with the P3 probe that emitted an infrared wavelength of 810 nanometre, preconfigured with an action cycle of 31.33%, 2.000 mW power and On cycles of 0.5 milliseconds and Off cycles of 1.1 milliseconds. 1 mg of lorazepam and 10 mg of sublingual ketorolac were administered before the procedure. Anaesthesia with sevofluoran and 2% topical viscous lidocaine was used. After the procedure, the patients had 1% prednisolone acetate every 4 hours during the first day and subsequently every 8 hours up to a maximum of 2 weeks. Hypotensive treatment was gradually withdrawn according to their evolution.
Follow up	**12 months**
Conflict of interest/source of funding	No conflict of interest was declared by the authors.

Analysis

Follow-up issues:
Study population issues:

- 71% (78/110) had an intervention in 1 eye. Overall, 82.5% of eyes had previous glaucoma surgery.
- The types of glaucoma were POAG in 17% (24/143) of eyes, primary angle closure in 11% (16/143), pseudoexfoliative in 17% (24/143), pigmentary in 2% (3/143), traumatic in 1% (2/143), neovascular in 9% (13/143), congenital in 7% (10/143), aphakic in 2% (3/143), juvenile in 1 eye and cortisonic in 2% (3/143).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **110 (143 eyes)**

IOP

Follow-up	**n (eyes** [corrected by the analyst]**)**	**Median IOP** (mmHg, IQR)	**% IOP reduction from baseline** (median of % and IQR)	**IOP < 20 mmHg % (n)**
Baseline	143	23 (19–30)	-	-
1 day	143	15 (12–18)	-	78% (111)
3 months	130	15 (13–18)	30.4% (19–40)	80% (104)
6 months	120	16 (14–18.5)	28% (15–40)	77% (93)
12 months	90	16 (14–18)	30% (18.5–43)	78% (70)

Antiglaucoma medications

	Baseline	**1 day**	**3 months**	**6 months**	**12 months**
One drug less* (% eyes)	-	-	78% (101/130)[a]	75% (90/120)[a]	74% (67/90)[a]
Acetazolamide use (% eyes)	29% (41/143)	-	17% (24/143)	14% (20/143)	10% (14/143)

*Discontinuation of one drug was defined as terminating the use of at least one topical or oral medication.

[a]p = 0.0001

11% (10/90) of eyes [corrected by analyst] achieved a target IOP without the use of drugs at 12 months.

Treatment success and failure

	Baseline	**1 day**	**3 months**	**6 months**	**12 months**
Success (%)**	-	-	91% (118/130)	91% (109/120)	86% (77/90)
Failure***	-	-	13% (18/143)	17% (24/143)	8% [corrected by analyst] (11/143)

**Success: pressure reduction of 5 mmHg or stopping at least one drug.

***Treatment failure was defined as the necessity of micropulse retreatment, conducting incisional surgery or increasing medication.

Overall, 29% (42/143) of eyes [corrected by the analyst] had at least 1 treatment failure during the study, and 25% (36/143) had another micropulse intervention.

Safety

Subconjunctival haemorrhage: 1/110 (patient was on anticoagulants)

Postoperative slight or moderate mydriasis with a 2-line visual acuity reduction that recovered within 30 days.

Abbreviations used: AC, anterior chamber; IOP, intraocular pressure; IQR, interquartile range; POAG, primary open-angle glaucoma; VA, visual acuity

Study 18 Dorairaj S (2020) - Conference abstract

Details

Study type	**Retrospective case series**
Country	USA (single centre)
Recruitment period	2016 to 2019
Study population and number	n= **349** patients with glaucoma
Age and sex	Mean 66 years; 25% male
Patient selection criteria	Not reported
Technique	All patients were treated with a laser power of 2000 mW and duty cycle of 31.33%. Treatment time was 80 seconds for each 180° hemisphere, totalling 160 seconds covering the entire 360 degrees. Patients with pupillary abnormalities had slit lamp photographs taken to document iris colour and anterior segment OCT was done in both light and dark conditions for qualitative assessment of pupillary diameter.
Follow up	**Not reported**
Conflict of interest/source of funding	Not reported

Pupillary abnormalities

Four patients presented with fixed and dilated pupils that did not react to light or accommodate after the procedure. All four patients had brown irises and myopia, 50% were phakic and 75% had severe glaucoma. Myopic females with brown iris had higher chances of having this complication. Pupil abnormalities resolved on their own in all patients within three months.

Validity and generalisability of the studies

- Most of the studies are retrospective case series with 6- to 12-month follow up. Only 1 RCT was identified which had 48 patients. The longest follow up was 24 months.
- The evidence includes studies from the USA, Canada, Egypt, Lebanon, The Netherlands and Singapore. Results from 1 country may not be generalisable to another.
- There are no studies that directly compare MPCPC with non-cyclophotocoagulation treatments for glaucoma.
- Studies are heterogenous in terms of types of glaucoma, enrolment criteria and prior surgical history. Outcome of MPCPC may differ depending on these factors.
- Most of the studies had patients with refractory or uncontrolled glaucoma.
- Although most studies used a standardised treatment technique and parameters, there were some variations in terms of power settings, duration of laser therapy, and application of the laser probe on the eye (slow-sweeping or fast sweeping).

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. NICE interventional procedures guidance 661 (2019). Available from https://www.nice.org.uk/guidance/ipg661

- Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma. NICE interventional procedures guidance 612 (2018). Available from http://www.nice.org.uk/guidance/IPG612

- Ab externo canaloplasty for primary open-angle glaucoma. NICE interventional procedures guidance 591 (2017). Available from http://www.nice.org.uk/guidance/IPG591

- Trabecular stent bypass microsurgery for open-angle glaucoma. NICE interventional procedures guidance 575 (2017). Available from http://www.nice.org.uk/guidance/IPG575

- Trabeculotomy ab interno for open angle glaucoma. NICE interventional procedures guidance 397 (2011). Available from http://www.nice.org.uk/guidance/IPG397

NICE guidelines

- Glaucoma: diagnosis and management. NICE guideline 81 (2017). Available from http://www.nice.org.uk/guidance/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. Two Professional expert questionnaires for repetitive short-pulse transscleral cyclophotocoagulation for glaucoma were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent questionnaires to 5 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 8 completed questionnaires.

Company engagement

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

Issues for consideration by IPAC

- The evidence includes studies with both children and adult patients.
- Various acronyms for the name of the procedure have been used in the literature (e.g. MPCPC, MPTSCPC, mTSCPC, MPCPC). This document use 'repetitive short-pulse' instead of 'micropulse' for the procedure name to avoid confusion with the trademarked name of the device.

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Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	19/10/2020	Issue 10 of 12, October 2020
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	19/10/2020	Issue 10 of 12, October 2020
MEDLINE (Ovid)	19/10/2020	1946 to October 19, 2020
MEDLINE In-Process (Ovid) & Medline ePub ahead (Ovid)	19/10/2020	1946 to October 19, 2020
EMBASE (Ovid)	19/10/2020	1974 to 2020 Week 24

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

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

1	exp Glaucoma/ (51270)
2	Intraocular Pressure/ (36535)
3	Ocular Hypertension/ (6325)
4	Ciliary Body/ (8100)
5	glaucom*.tw. (50754)
6	(POAG or PXF or COAG or IOP).tw. (17768)
7	((ocular* or intraocul* or eye*) adj4 (hypertens* or tension or pressur*)).tw. (33730)
8	(ciliar* adj4 (body or bodies)).tw. (5505)
9	or/1-8 (89771)
10	*Laser Coagulation/ (4479)
11	cyclophotocoagulation*.tw. (560)
12	(laser* adj4 (micropulse or short pulse*)).tw. (447)
13	(mTSCPC or MPTSCPC or Cyclo G6* or Micropulse P3*).tw. (3)
14	or/10-13 (5078)
15	9 and 14 (844)
16	animals/ not humans/ (4606946)
17	15 not 16 (767

Appendix

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
Al Habash A and AlAhmadi AS (2019) Outcome of micropulse® transscleral photocoagulation in different types of glaucoma. Clin Ophthalmol. 13:2353-2360.	Prospective case series n=68 Patients (71 eyes) FU=12 months (3 to 24 months)	µP-TSCPC showed good efficacy and safety profiles with minimal vision-threatening complications in treating a variety of glaucoma types.	Studies with more patients or longer follow up are included.
Awoyesuku E & Fiebai B (2019) Outcome of Micropulse Laser in Treatment of Open Angle Glaucoma in a Peripheral Hospital in Rivers State, Nigeria: Our Initial Experience. Journal of Advances in Medicine and Medical Research, 29(2),1-7.	Case series n=12 FU= 6 months	Micropulse Trans-scleral cyclophotocoagulation is a safe and effective way of managing glaucoma. It caused a mean drop in IOP of 10.46mmHg (38.20%) over 6 months in our study.	Studies with more patients or longer follow up are included.
Barac R, Vuzitas M, Balta F (2018) Choroidal thickness increase after micropulse transscleral cyclophotocoagulation. Rom J Ophthalmol. 2018;62(2):144–148.	Case series n=22 FU=6 months	The increase in choroidal thickness in all patients in whom we saw IOP reduction was a significant correlation that supported the mechanism of increased uveoscleral outflow obtained from LASER treatment.	Small case series describing OCT findings after MPCPC.
Chen MF, Kim CH, Coleman AL (2019) Cyclodestructive procedures for refractory glaucoma. Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD012223	Cochrane review	Only 1 RCT comparing MPCPC and CWCPC identified. In the study that compared micropulse with continuous-wave CPC, median IOP was reported to be similar between the 2 groups at all time points. At 18 months postintervention, the median number of IOP-lowering medications was reduced from 2 to one in both groups. One	The RCT is included in the table 2.

		participant in the micropulse and 2 in the continuous group exhibited worsened visual acuity. One case of prolonged inflammation was seen in the micropulse group (23 participants).	
Dhanireddy S, Yin HY, Dosakayala N et al (2020) Severe inflammation and hyphema after micropulse diode transscleral cyclophotocoagulation. J Glaucoma. 29(6):e50-e52. doi:10.1097/IJG.0000000000001508	Case reports n=2 FU= 4 and 2 months	In this case series, exuberant anterior segment inflammation and hyphaema occurred in 2 patients who had MP-TSCPC. The authors' goal is to raise awareness of severe anterior chamber inflammation and hyphaema as complications occurring after laser treatment with a reputation of minimal or no side-effect profile and to better understand this relatively new laser advancement in the treatment of glaucoma.	Complications already reported in the main extraction table.
Gavris MM, Olteanu I, Kantor E et al. (2017) Iridex MicroPulse P3: innovative cyclophotocoagulation. Rom J Ophthalmol, 61(2):107-111	Case series n=7 patients (7 eyes) Follow-up= 1 month	IRIDEX MP3 represents an innovation in cyclophotocoagulation. It is nondestructive, repeatable, non-invasive, with a high safety profile. A mean IOP decrease of 33.4% was registered at 1 month. Patient comfort and recovery are favorable. Long-term results will prove its efficacy in the future.	Studies with more patients or longer follow-up already included.
Jammal A, Costa D, Vasconcellos J, & Costa V (2019) Prospective evaluation of micropulse transscleral diode cyclophotocoagulation in refractory glaucoma: 1 year results. *Arquivos Brasileiros De Oftalmologia*, *82*(5)	Case series n=21 FU = 12 months	The mean IOP reduction was 44.72% ± 29.72% in the first week and 41.59% ± 18.93% at the end of follow up (p=0.006). The mean number of medications significantly dropped to 2.00 ± 1.7 at the 12-month visit (p=0.044).	Small case series.

		Complications included hypotony (4.8%), intraocular inflammation after 1 month (19%), and visual acuity loss (4.8%). MPCPC was safe and effective for reducing IOP in eyes with refractory and advanced glaucoma, with reduced need for glaucoma medications.	
Kuchar S, Moster MR, Reamer CB et al. (2016) Treatment outcomes of micropulse transscleral cyclophotocoagulation in advanced glaucoma. Lasers Med Sci;31(2):393–396.	Case series (retrospective) n= 19 Mean FU= 60.3 days	The novel MP-TSCPC laser had a high rate of surgical success after a short follow up period in patients with advanced glaucoma.	Studies with more patients or longer follow up are included
Lee JH, Vu V, Lazcano-Gomez G et al. (2020) Clinical outcomes of micropulse transscleral cyclophotocoagulation in patients with a history of keratoplasty. Journal of Ophthalmology 2020: 6147248	Retrospective case series n=28 patients/ 30 eyes Follow-up=1 year	• IOP was statistically significantly decreased from baseline at all follow-up points ($p < 0.001$). • There was no statistically significant change in the number of glaucoma drops, visual acuity, or central corneal thickness. • At 12 months, 21/30 eyes met the definition of success, and only 1 needed repeat penetrating keratoplasty due to graft rejection.	Studies with more patients or longer follow-up already included.
Lee JH, Shi Y, Amoozgar B, et al. (2017) Outcome of micropulse laser transscleral cyclophotocoagulation on pediatric versus adult glaucoma patients. J Glaucoma;26(10):936–939.	Case series (Retrospective) n= 36 (9 children versus 27 adults) FU= 12 months	Micropulse transscleral cyclophotocoagulation is a safe procedure for children and adult glaucoma patients. Its effect seems to be short lived in children and the rate of reoperation was high.	Studies with more patients or longer follow up are included.
Lutic I, Dragne C, Filip M, et al. (2018) Subcyclo laser procedure results in patients with glaucoma. *Rom J Ophthalmol* ;62(4):296–299.	Case series n= 50 FU= 6 months	For this period of follow up, we registered a mean IOP reduction of 37% from baseline and 18.47% average reduction of medications. No patient developed	Studies with more patients or longer follow up are included

		hypotony, all patients were pain free during and after the procedure and BCVA remained stable by the end of the follow up. SubCyclo laser procedure could determine a satisfactory decrease of the IOP with a low risk of complications.	
Ma A, Yu S, & Wong J (2019) Micropulse laser for the treatment of glaucoma: A literature review. *Survey Of Ophthalmology*, *64*(4), 486-497	Review	MP-TSCPC is suggested to be an efficacious and safe alternative to the traditional CW-TSCPC for adult patients with refractory glaucoma, lowering IOP and the number of ocular antihypertensive medications to a level comparable to CW-TSCPC. Severe complications such as hypotony and phthisis bulbi are less frequently seen in MP-TSCPC, but concerns remain over post-MP-TSCPC visual decline and anterior chamber inflammation.	Review
Magacho L, Lima FE, Ávila MP (2019) Double-session micropulse transscleral laser (CYCLO G6) for the treatment of glaucoma [published online ahead of print, 2019 Dec 4]. Lasers Med Sci. 10.1007/s10103-019-02922-1	Retrospective case series n=76 patients (89 eyes) FU= mean 17 months	MP3 laser in two consecutive 80-s sessions was shown to be safe and effective in the treatment of glaucoma. Primary eyes needed a lower number of MP3 laser procedures.	Studies with more patients or longer follow up are included.
Magacho L, Lima FE, Ávila MP (2020) Double-Session micropulse transscleral laser (CYCLO G6) as a primary surgical procedure for glaucoma. J Glaucoma 29(3):205-210	Retrospective comparative case series (no previous glaucoma surgery versus previous glaucoma surgery) n= 143 patients (185 eyes) FU=mean 11 months	Double-session MP3 therapy could be considered as a safe and effective procedure to treat glaucoma in eyes that have not had any previous glaucoma surgery. Primary eyes achieved a success-rate similar to those with refractory glaucoma with fewer MP3 procedures and	Studies with more patients or longer follow up are included.

		fewer glaucoma medications.	
Nutterova E, Pitrova S, Lestak J (2020) Our experience with micropulse cyclophotocoagulation in the therapy of glaucoma. Ceska a slovenska oftalmologie : casopis Ceske oftalmologicke spolecnosti a Slovenske oftalmologicke spolecnosti 76(1): 29-36	Retrospective case series n=47 patients (50 eyes) Follow-up=1 year	The values of intraocular pressure dropped by a minimum of 30% in 53.4% of eyes. The effect of therapy failed in 9 eyes (18%) where patients had a subsequent different therapeutic procedure.	Studies with more patients or longer follow-up already included.
Preda MA, Karancsi OL, Munteanu M et al (2020) Clinical outcomes of micropulse transscleral cyclophotocoagulation in refractory glaucoma-18 months follow-up [published online ahead of print, 2020 Jan 14]. Lasers Med Sci. doi:10.1007/s10103-019-02934-x	Case series n=97 patients (100 eyes) FU=18 months	No major postoperative complications were noted. Micropulse transscleral cyclophotocoagulation is a non-invasive, repeatable laser procedure that offers both good and stable results in lowering IOP and decreases the use of antiglaucoma medications for up to 18 months.	Studies with more patients or longer follow up are included.
Preda MA, Popa G, Karancsi OL et al. (2018) Effectiveness of subconjunctival bevacizumab associated with a laser-based procedure in the treatment of neovascular glaucoma. FARMACIA, 66(4):621-626.	Prospective comparative study n=6 (3 mTSCPC with bevacizumab vs mTSCPC alone) Follow-up=6 months	No significant difference was found between groups at baseline (p = 0.82) or final follow-up (p = 1) regarding the IOP reduction; neovascularisation regression was observed only in the combined therapy group (66.6%).	Studies with more patients or longer follow-up already included.
Sanchez FG, Lerner F, Sampaolesi J et al. (2018) Efficacy and Safety of Micropulse® Transscleral Cyclophotocoagulation in Glaucoma. Eficacia y seguridad de la ciclofotocoagulación transescleral con micropulsos en el tratamiento del glaucoma. Arch Soc Esp Oftalmol;93(12):573–579	Case series (retrospective) n=22 Mean FU= 7.9 months	In a heterogeneous population of glaucoma (mostly congenital and pseudoexfoliation types), a low success rate (27.3%) was obtained in the medium-term with a single session of Micropulse®.	Studies with more patients or longer follow up are included.
Sanchez FG, Peirano-Bonomi JC, Brossard Barbosa N et al. (2020) Update on micropulse transscleral cyclophotocoagulation [published online ahead of print, 2020 May 8]. J Glaucoma. doi:10.1097/IJG.0000000000001539	Review	This review article provides an update on the latest data available for this technique, including a discussion of the aspects in which there	Review

		is still limited data, such as the precise mechanism of action, the ideal laser parameters based on total energy levels, as well as an overview of other potentially relevant variables that may be playing an important role in outcomes.	
Sarrafpour S, Saleh D, Ayoub S & Radcliffe N (2019) Micropulse transscleral cyclophotocoagulation: a look at long-term effectiveness and outcomes. *Ophthalmology Glaucoma*, *2*(3), 167-171.	Case series (retrospective) n=62 FU= 1.8 years	At 1-year, average IOP was 13.8±7.0 (46% reduction) and average number of medications was 2.5±1.0 (19% reduction). This study provides evidence that mTS-CPC is a clinically useful procedure associated with good long-term medication burden reduction and IOP reduction that follows a dose-response pattern related to power used.	Studies with more patients or longer follow up are included.
Souissi S, Baudouin C, Labbé A & Hamard P (2019) Micropulse transscleral cyclophotocoagulation using a standard protocol in patients with refractory glaucoma naive of cyclodestruction [published online ahead of print. Eur J Ophthalmol;1120672119877586.	Case series (retrospective) n=37 FU= 9.7 months	Using a standardised procedure, micropulse transscleral diode laser cyclophotocoagulation allows a mild intraocular pressure decrease with a low rate of complications and thus achieves a relatively good profit risk benefit, mostly for moderately hypertensive refractory glaucoma.	Studies with more patients or longer follow up are included
Subramaniam K, Price M, Feng M et al. (2019) Micropulse transscleral cyclophotocoagulation in keratoplasty eyes. Cornea, 38(5), 542-545	Case series (retrospective) n=61 Median FU = 21 months	This study found that pulsed TSCPC was generally an effective non-invasive alternative to glaucoma filtration surgery in keratoplasty eyes; it reduced IOP by a mean of 35% at 12 months and was well-tolerated by most	Patients with keratoplasty eyes. Larger studies with glaucoma patients are included in table 2.

		people who had treatment.	
Tan A, Chockalingam, M, Aquino M et al. (2010) Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. Clinical & Experimental Ophthalmology	Case series n=40 Mean FU = 16.3 months	Micropulse TSCPC is a safe and effective method of lowering IOP in cases of refractory glaucoma and is comparable with conventional TSCPC	Larger, more recent studies are included.
Tekeli O, Köse HC (2020) Outcomes of micropulse transscleral cyclophotocoagulation in primary open-angle glaucoma, pseudoexfoliation glaucoma, and secondary glaucoma [published online ahead of print, 2020 Mar 31]. Eur J Ophthalmol. doi:10.1177/1120672120914231	Retrospective case series. n=96 FU=12 months	Micropulse transscleral cyclophotocoagulation is an equally effective method of lowering intraocular pressure in patients with primary open-angle glaucoma, pseudoexfoliation glaucoma, and other types of secondary glaucoma. The rate of reoperation was higher in refractory secondary glaucoma patients.	Studies with more patients or longer follow up are included
Toyos MM, Toyos R (2016) Clinical Outcomes of micropulsed transcleral cyclophotocoagulation in moderate to severe glaucoma. J of Clin Exp Ophthalmol 7: 620.	Case series (retrospective) n= 26	Micropulsed transscleral diode laser is a safe and effective alternative for glaucoma therapy for patients with open angle glaucoma. Patients can expect significant IOP lowering along with reduction in number of topical glaucoma medications needed for IOP control.	Small case series.
Varikuti V, Shah P, Rai O et al. (2019). Outcomes of micropulse transscleral cyclophotocoagulation in eyes with good central vision. *Journal Of Glaucoma*, *28*(10), 901-905.	Case series (retrospective) n=46 FU= 10.2 months	The significant reduction in IOP and glaucoma medication use, limited vision loss, less vision threatening complications, and multiple logistical advantages, shows MP-TSCPC as a safe and effective procedure to consider in patients with good baseline vision and can possibly offered as an alternative to incisional glaucoma surgeries.	Patients with good central vision. Studies with more patients or longer follow up are included.
Vig N, Ameen S, Bloom P et al. (2020) Micropulse transscleral cyclophotocoagulation: initial results	Retrospective case series	MP-TSCPC at a decreased duration is effective at reducing	Studies with more patients and

using a reduced energy protocol in refractory glaucoma. Graefes Arch Clin Exp Ophthalmol 258(5):1073-1079	n=29 FU=6 months	intraocular pressure in ethnically diverse glaucoma patients refractory to previous glaucoma laser or surgeries at 6-month follow up, with no significant complications. Further work is needed to confirm efficacy in the long term and to determine optimal settings.	longer follow up are included.
Wong K Y T, Aquino C, Macasaet A M et al. (2020) MP3 Plus: A modified micropulse transscleral cyclophototherapy technique for the treatment of refractory glaucoma. Journal of glaucoma 29(4): 264-270	Retrospective case series n=29 patients/ 32 eyes Follow-up= 1 year	Of the eyes presenting for follow-up, 52% (n=31), 37% (n=27), 36% (n=28), and 26% (n=27) achieved the primary outcome at 1, 3, 6, and 12 months, respectively. Baseline IOP was 33.7±11.6mmHg (n=32 eyes) and post-treatment IOP were 21.0±9.0mmHg at 1 month (n= 31; p<0.0001), 26.2±10.8mmHg at 3 months (n=25; p<0.0001), 23.2±9.4mmHg at 6 months (n=20; p<0.05), and 24.6±9.8mmHg at 12 months (n= 16; p<0.001). There was a reduction in glaucoma medications from 3.4 ±0.8 preoperatively to 2.8 ±1.2 (n=16; p< 0.05) at 12 months.	Studies with more patients or longer follow-up already included.