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Original Article

Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study

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Abstract

Background: The aim of this study was to compare the efficacy and safety of micropulse and continuous wave diode transscleral cyclophotocoagulation in refractory glaucoma.

Design: Randomized, comparative, exploratory study in a tertiary hospital setting.

Participants: Patients with refractory, end-stage glaucoma.

Methods: Forty-eight patients were randomized to either treatment. The intraocular pressure, visual acuity, number of medicines and repeat treatment were monitored for 18 months. Complications that include visual acuity decline, prolonged anterior chamber inflammation, phthisis bulbi, scleral thinning and ocular pain were noted.

Main Outcome Measure: Intraocular pressure between 6 and 21 mmHg and at least a 30% reduction with or without anti-glaucoma medications after 18 months.

Results: A successful primary outcome was achieved in 75% of patients who underwent micropulse cyclophotocoagulation and 29% of patients who received continuous wave cyclophotocoagulation after 12 months ($P < 0.01$). At 18 months, successful outcome was 52% and 30% ($P = 0.13$), respectively. The mean intraocular pressure was reduced by 45% in both groups ($P = 0.70$) from a baseline of 36.5 mmHg and 35.0 mmHg ($P = 0.50$) after 17.5 ± 1.6 months (range 16–19) follow up. No significant difference in retreatment rates or number of intraocular pressure lowering medications was noted. The ocular complication rate was higher in continuous wave treated eyes ($P = 0.01$).

Conclusion: Diode transscleral cyclophotocoagulation in both micropulse and continuous modes was effective in lowering intraocular pressure. The micropulse mode provided a more consistent and predictable effect in lowering intraocular pressure with minimal ocular complications.

Key words: ciliary body, glaucoma, laser surgery.

Introduction

Cyclophotocoagulation (CPC) is a form of cycloablation using laser to treat glaucoma. It involves ciliary body destruction by targeting the ciliary epithelium and stroma, resulting in a reduction in

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aqueous secretion and hence intraocular pressure (IOP). Contact transscleral CPC (TSCPC) using the continuous wave (CW) diode laser is the common mode of delivery. It is effective for all forms of glaucoma[1–5] but is often used as a treatment of last resort because of the perceived risk of morbidity from hypotony, visual deterioration and phthisis bulbi coupled with the unpredictability of effect and the frequent requirement for repeat treatments.

Our group described the use of micropulse CPC (MPCPC)[6,7] in a preliminary study as an alternative, and reported an IOP reduction that was sustained over 12–18 months without significant ocular morbidity.[8] The micropulse mode of laser delivery, which has also been successfully used for retinal laser photocoagulation,[9–11] administers a series of repetitive, short pulses of laser energy separated by rest periods, and is unlike conventional continuous wave CPC (CWCPC), which delivers continuous high intensity energy to the ciliary body. MPCPC is applied using a customized probe that is used to apply the laser in a continuous painting fashion, rather than individual burns, and to *pars plana* rather than the *pars plicata*. In our proof of concept case series, no sight-threatening complications were observed in the MPCPC group.[8]

This randomized, exploratory, comparison study was conducted to compare the safety and efficacy of MPCPC and CWCPC in terms of IOP reduction and frequency of complications.

Methods

Study design

This was a randomized, prospective exploratory study of 48 patients who were followed for 18 months. Approval was obtained from the Institutional Review Board of the National University Hospital of Singapore and the study was conducted in accordance with the principles of Declaration of Helsinki. Informed consent was obtained from all study participants.

Eligibility criteria

Patients attending one glaucoma subspecialty clinic between January 2007 and December 2008, aged 21 years old and above, with refractory glaucoma defined as IOP > 21 mmHg unresponsive to maximal tolerated medical therapy with or without previous surgical intervention, who were poor candidates for a filtration procedure and who had best corrected visual acuity (VA) of 6/60 or worse were eligible. Patients with ocular infection, inflammation or eye surgery in the study eye in the 2 months prior to enrolment were excluded.

Enrolment and randomization

One eye was enrolled for each eligible subject. If both eyes met the eligibility criteria, the eye with the higher IOP was randomized to either the MPCPC or CWCPC treatment groups. After informed consent, a randomization code was obtained from one of the sequentially numbered, opaque sealed envelopes. A total of 48 patients were included. In the post-hoc analysis, there was an estimated power of 0.97 to discriminate between the two treatments in the proportions achieving the primary outcome (75% using MPCPC *vs.* 29% using CWCPC), which was defined as IOP between 6 and 21 mmHg and at least a 30% reduction with or without anti-glaucoma medications after 12 months.

Laser treatment was performed by a single surgeon (AMT). It was not possible to mask the surgeon performing the laser procedure because different probes were used for MPCPC and CWCPC, but subjects were masked regarding the type of laser intervention received.

Laser intervention

Adequate topical and periocular anesthesia (peribulbar or retrobulbar or sub-Tenon's administration of 3 mL combination of 0.5% bupivacaine and 2% lignocaine) were given prior to either procedure.

MPCPC[8]

A ball lens tip, customized contact probe (Iris Medical Instruments, Mountain View, CA, USA) emitting 810 nm infrared radiation from a diode source, set on micropulse mode was applied perpendicular to the limbus with the edge of the probe directly on the limbus at all times. The probe houses a quartz fiberoptic cable, 600 μm in diameter, with its hemispheric tip protruding 0.7 mm from the hand piece. The probe is designed to permit accurate positioning of the fiberoptic tip at 3 mm posterior to the limbus.[8] Laser settings of 2 Watts (W) applied for a 100 s treatment time, consisting of micropulses during which the laser was ON for 0.5 millisecond (ms) and OFF for 1.1 ms, and delivering 62.6 Joules (J) in total. The probe was applied with firm pressure and moved in a continuous sliding motion (painting) in the superior and inferior quadrants avoiding the 3 and 9 o'clock meridians.

CWCPC

The G probe (Iris Medical Instruments) was placed axially with its footplate at the edge of the limbus so that the probe tip delivers laser 1.2 mm from the

limbus. The laser settings used were 1.5–2 W, 2 s exposure time per burn, 20–28 burns per eye delivering 60–112 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 laser procedure, patients in both treatment groups were prescribed topical prednisolone acetate 1% three times daily for 10–14 days and extended as necessary including oral non-steroidal anti-inflammatory drug for 2 days as required.

Study measurements and follow up

The following baseline data were collected prior to treatment: age, sex, race, glaucoma diagnosis, ocular history (previous surgery and laser therapy), best-corrected Snellen VA, glaucoma medications, slit-lamp examination findings of the anterior and posterior segment and the severity of eye pain measured using the verbal analogue scale adopted from the earlier series.[8] IOP was measured using Goldmann applanation tonometry (GAT) by an ophthalmologist masked to the treatment group. The IOP value was read off the scale and recorded by a study coordinator. The IOP was measured twice, and the mean calculated.

After laser treatment, patients were seen at 1 day, 1 week, 1 month, 3 months, 6 months, 12 months and 18 months. At each visit, best-corrected Snellen VA, IOP by GAT and slit-lamp biomicroscopy were recorded. The number of glaucoma medicines was noted. Ocular pain by verbal analogue scale[8] was graded as mild (pain tolerable and not requiring the use of analgesia), moderate (pain tolerable with regular use of analgesia) and severe (pain intolerable despite regular dose of analgesia). Complications resulting from laser treatment were recorded including a two-line reduction in best-corrected VA from baseline or reduction in VA to no light perception (NLP), prolonged anterior chamber (AC) inflammation (1 + grade or higher of the number of cells and flare in a 1 mm × 1 mm slit-lamp beam based on the Standardization of Uveitis Nomenclature Working Group's consensus on grading inflammation) persisting for more than 2 weeks with topical steroid eye drops, scleral thinning (uvea visible on slit lamp biomicroscopy) and phthisis bulbi.

Outcome measures

The primary outcome measure of success was IOP between 6 and 21 mmHg and at least a 30% reduction in IOP at the final follow up with or without IOP lowering medications.

The secondary outcome measures of success included the number of repeat treatments, number of IOP lowering medications at 18 months and the frequency of complications associated with the laser therapy. A less than 30% reduction in IOP from baseline after 1 month on two consecutive visits separated by an interval of 1 week was the basis for second treatment. Retreatments were performed at least 6–8 weeks after the first treatment within the 18-month follow-up period. Third treatments were carried out when necessary according to the same criteria as second treatments.

Statistical analysis

All statistical analyses were performed using R version 2.14.2 (R Development Core Team, R Foundation for Statistical Computing, Vienna, Austria) with statistical significance set at $P < 0.05$. Due to the small sample size, median (25th percentile, 75th percentile) was calculated to describe continuous variables, and frequency distribution and percentage were used for categorical data. Demographic analysis used Wilcoxon rank-sum test for age and chi-square test for gender. Fisher's exact test evaluated equivalence of glaucoma types in each group. Differences between MPCPC and CWCPC were assessed by using Wilcoxon Rank-Sum test, Chi-square test (or Fisher's exact test), Mantel-Haenszel and Ansari-Bradley test as appropriate. The differences in the proportion of the primary outcome measures from baseline between the two treatment groups were assessed using Chi-square test. Longitudinal IOP was summarized as median (25th percentile, 75th percentile). Robust linear regression was performed to compare IOP between MPCPC and CWCPC adjusting for neovascular glaucoma (NVG). For ordinal variables, the Cochran–Armitage test was performed for trend. Parameters tested included number of treatment, number of medicines and degree of eye pain.

Results

Twenty-four eyes received MPCPC and 24 received CWCPC. The two groups did not differ significantly in age and gender (Table 1). The distribution of glaucoma diagnoses in each group is summarized in Table 1. Forty-six out of 48 patients attended the 18-month follow-up visit (mean follow up 17.5 ± 1.6 months, range 16–19 months). One patient in MPCPC and one in CWCPC group were lost to follow up after 12 months.

The baseline IOP was similar in the two treatment groups (36.5 mmHg MPCPC *vs*. 35.0 mmHg CWCPC; $P = 0.50$). There was a significant difference in numbers of patients achieving the primary outcome at 1 year (18 out of 24 or 75% of MPCPC eyes *vs*. 7 out of 24 eyes or 29% CWCPC eyes, $P < 0.01$). However, there was no significant difference at 18

Table 1. Characteristics of patients under MPCPC and CWCPC

	MPCPC (n = 24)	CWCPC (n = 24)	P value*
Age, years	63.50 (54.75,74)	66 (55, 72.75)	0.79
Gender			0.37
Male	17 (71%)	14 (58%)	
Female	7 (29%)	10 (42%)	
Types of glaucoma			0.24
POAG	5 (21%)	6 (25%)	
PACG	5 (21%)	1 (4%)	
NVG	7 (29%)	12 (50%)	
Others: Silicone oil, Aphakic Traumatic	7 (29%)	5 (21%)	

*P value based on Wilcoxon rank-sum test or Chi-square test (or Fisher's exact test) as appropriate. Data represented as median (25th percentile, 75th percentile) or number (percentage) as appropriate. POAG, primary open angle glaucoma; PACG, primary angle closure glaucoma; NVG, neovascular glaucoma.

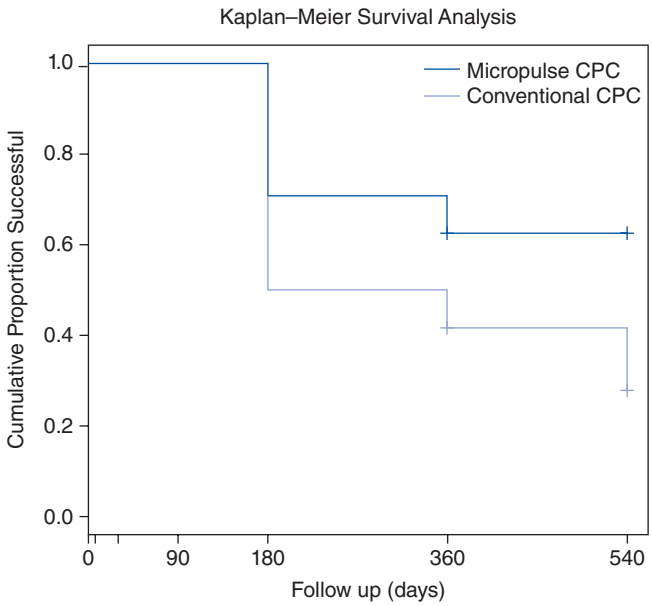

Figure 1. Kaplan–Meier survival analysis using cumulative probability of success based on primary intraocular pressure criteria of 6–21 mmHg and ≥30% reduction from baseline (P = 0.03 Log-rank or Mantel-Haenszel test).

months. Twelve MPCPC eyes (52%) achieved an IOP between 6 and 21 mmHg with at least 30% IOP reduction compared with 7 (30%) CWCPC eyes (P = 0.13). Kaplan–Meier survival analysis was used to compare the success rates between the two groups (Fig. 1). The cumulative probability of success was 62% for MPCPC and 28% for CWCPC after 18 months of follow up (P = 0.03).

Prolonged hypotony (IOP ≤ 5 mmHg for at least 6 months) was observed in five eyes of CWCPC group but not in the MPCPC group. Four out of five eyes had NVG and one had silicone oil-induced glaucoma. All these eyes received single treatment with laser energy ranging from 88 J to 106 J. Two of these eyes developed hypotony after 3 months, one eye after 6 months and two eyes after 12 months.

More patients with NVG were randomized to the CWCPC group (50% *vs.* 29% MPCPC). Robust linear regression analysis was used to adjust for the effect of NVG on the IOP outcome of CWCPC treated eyes. No significant difference was observed between the median IOPs after MPCPC and CWCPC from day 1 to 18 months (Table 2). The beta coefficient of IOP was 4.28 (standard deviation = 4.33; P = 0.33) after adjusting for NVG and baseline IOP. Therefore, the adjusted mean IOP at month 18 is 4.28 mmHg higher in the CWCPC than MPCPC group (NS).

We observed reduced IOP variance in the MPCPC group compared with the CWCPC group (Ansari-Bradley Test) for equality of variance of the residuals obtained from robust linear regression (P < 0.01) (Fig. 2). We acknowledge that we are comparing a highly controlled group (MPCPC) with an intention-to-treat type group and that differing energy levels might explain the difference in variability in the results. Therefore, a scatterplot was added to illustrate that the variability in outcome in the CWCPC group was not related to treatment energy. A scatterplot of percent IOP reduction to laser treatment energy delivered in CWCPC is shown in Figure 3. Robust linear regression was used to assess the relationship between IOP reduction and laser energy. Though a positive association was observed (Beta: 0.65, standard error: 0.48), it was not significant (P = 0.20). No association was found between CPC outcome and the number of prior glaucoma surgical procedures.

We observed more complications in the CWCPC than MPCPC group (P = 0.01) (Table 3). Prolonged AC inflammation and phthisis bulbi were seen more in CWCPC-treated eyes (Table 3A). We observed a reduction in vision from finger counting to light perception (LP) and LP to NLP in two subjects in the CWCPC group and one in the MPCPC group from hand motion (HM) to NLP (P = 1.0).

We observed no difference in the number of treatment sessions required in each group (P = 0.36) (Table 3B). After the 2nd treatment performed at a mean of 6.8 months (range 2–17) for the MPCPC group, the IOP remained uncontrolled in four (one primary open angle glaucoma [POAG], two primary angle closure glaucoma and one juvenile glaucoma) out of seven eyes at 25.5 mmHg (mean) (range 22–28) IOP. Six (two POAG, three NVG and one iridocorneal endothelial syndrome) out of seven CWCPC eyes with repeat treatment at 5.3 months (range 3–12) remained uncontrolled with a mean IOP of 35.3 mmHg (range 26–50). No significant difference in IOP was noted between the two groups after 2nd treatment

Table 2. Intraocular pressure in mmHg after MPCPC and CWCPC

	MPCPC (n = 24)	CWCPC (n = 24)	Adjusted P*	P** for NVG
Preoperation	36.5 (29.5, 56.5)	35.0 (29.5, 46.5)	0.50	0.75
1 Day	21.5 (16.8, 34.5)	27.0 (21.8, 39.0)	0.21	0.18
1 Week	16.5 (14.0, 27.0)	21.0 (12.8, 31.2)	0.80	0.61
1 Month	22.5 (15.0, 34.0)	22.0 (14.0, 34.5)	0.85	0.16
3 Month	20.0 (14.8, 26.5)	20.5 (11.5, 34.5)	0.98	0.43
6 Month	20.0 (16.0, 24.0)	18.5 (11.5, 28.5)	0.98	0.60
12 Month	18.0 (15.5, 20.2)	20.0 (7.5, 28.5)	0.63	0.45
18 Month	20.0 (16.0, 23.5)	19 (8.0, 30.0)	0.70	0.55

*P value adjusted for NVG via robust linear regression to compare between MPCPC and CWCPC. **P value for NVG in the robust linear regression. IOP represented as median (25th percentile, 75th percentile).

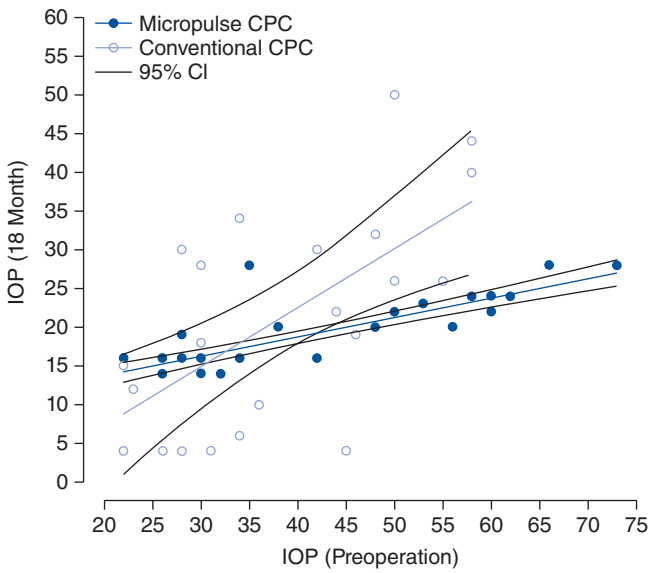

Figure 2. Intraocular pressure (IOP) measurements before and after treatment showing smaller IOP variation and close clustering of points in a straight line in micropulse CPC (MPCPC) compared with scattered, wide spread of IOP in conventional CPC (CWCPC) for patients who completed 18-month follow up. ($P < 0.01$, Ansari-Bradley test).

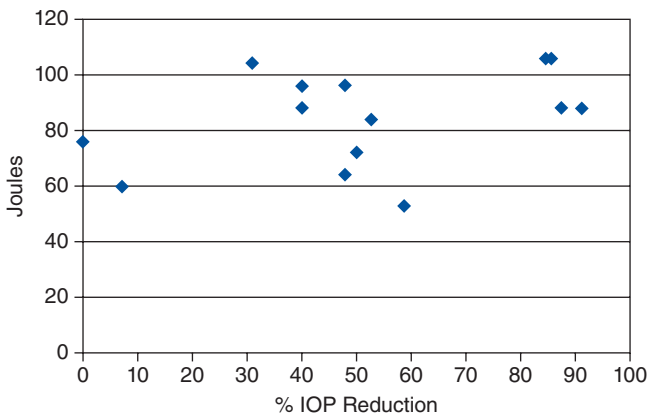

Figure 3. Continuous wave cyclophotocoagulation (CWCPC) scatterplot of percent (%) intraocular pressure (IOP) reduction with corresponding laser energy delivered during treatment.

($P = 0.11$). Four eyes with NVG in MPCPC group treated three times remained uncontrolled with a mean IOP of 24 (22–28) mmHg after 18 months and four (two POAG and two NVG) out of six CWCPC eyes were uncontrolled (mean 30.5 mmHg, range 22–40). There was no overall difference between the IOP of the two groups after three laser sessions ($P = 0.91$).

The number of IOP-lowering medications were reduced from two (1.75, 3.00) median (25th, 75th percentile) to one (1, 2) ($P < 0.01$; Wilcoxon signed-rank test) 18 months after MPCPC and two (1, 3) to one (0, 2) after CWCPC. We observed no difference in the number of medicines used in the two treatment groups ($P = 0.88$) (Table 3C). Eye pain scoring by verbal analogue scale[8] was analysed using Cochran–Armitage trend test (Table 3D). The first-week assessment after laser was regarded as equivalent to discomfort related to laser treatment rather than disease. During laser and immediately after laser, statistical analysis of the two treatment groups showed no difference.

Discussion

In this exploratory study, MPCPC and CWCPC lowered IOP in eyes with refractory glaucoma with similar efficacy, and sustained over 18 months. Compared with CWCPC, MPCPC was associated with a lower incidence of vision-threatening complications. In addition, we observed a more predictable and consistent effect on IOP with MPCPC than that of CWCPC, as evidenced by reduced IOP variability after MPCPC. Treatment failures after 18 months were comparatively less in MPCPC eyes. It is of interest that there was a trend to lower adjusted IOP in the MPCPC than CWCPC group, in combination with lower complications, indicating that the lower complication rate is not experienced at the expense of IOP control.

Table 3. Secondary outcome measures of success

Outcome measure	MPCPC	CWCPC	*P*
A. Ocular Complication Rate 0.01†	*n* = 23	*n* = 23	
No	20 (88%)	9 (40%)	
Prolonged AC inflammation	1 (4%)	7 (30%)	
Phthisis bulbi	0 (0%)	1 (4%)	
Scleral thinning	1 (4%)	4 (17%)	
Visual Acuity (VA) decline	1 (4%)	2 (9%)	
Difference of VA between baseline and last follow-up	0 (0,0)	0 (0,0)	0.09‡
Visual Acuity Score			1.00§
Worse	1 (4%)	2 (9%)	
Better or equal	22 (96%)	21 (91%)	
B. Number of Treatment	*n* = 23	*n* = 23	0.46¶
1	12 (53%)	10 (44%)	
2	7 (30%)	7 (30%)	
3	4 (17%)	6 (26%)	
C. Number of medicine	*n* = 23	*n* = 23	0.76¶
0	5 (22%)	8 (35%)	
1	11 (48%)	5 (22%)	
2	6 (26%)	7 (30%)	
3	1 (4%)	3 (13%)	
D. Eye pain			
Before laser	*n* = 22	*n* = 22	0.80¶
No pain	15 (68%)	14 (64%)	
Mild	6 (27%)	7 (32%)	
Moderate	1 (5%)	1 (4%)	
Severe	0 (0%)	0 (0%)	
During laser	*n* = 22	*n* = 23	0.07¶
No pain	19 (86%)	15 (65%)	
Mild	2 (9%)	4 (17%)	
Moderate	1 (5%)	1 (5%)	
Severe	0 (0%)	3 (13%)	
After laser††	*n* = 22	*n* = 21	0.09¶
No pain	22 (100%)	18 (86%)	
Mild	0 (0%)	2 (9%)	
Moderate	0 (0%)	1 (5%)	
Severe	0 (0%)	0 (0%)	

Data represented as median (25th percentile, 75th percentile) or number (percentage) as appropriate. †Fisher's exact test; ‡Wilcoxon rank-sum test; §Chi-square test; ¶Cochran–Armitage trend test; ††1 week.

These findings are consistent with our earlier case series.[8] Tan *et al.* reported relative success (defined as IOP less than 21 mmHg or a 30% reduction of IOP from baseline, with or without anti-glaucoma medications) in 80% of the 40 eyes treated with MPCPC after 18 months without a single case of hypotony. In our present study, we observed 75% success at 12 months and 52% at 18 months for MPCPC without a case of hypotony. A 20–50% reduction in IOP was reported in earlier TSCPC studies.[12–14] In our comparative study, a 45% IOP reduction was achieved in both treatment arms at 18 months.

Our findings showed that 46% in MPCPC and 58% of eyes in CWCPC (Table 3) required multiple sessions of laser treatment, and the rates of re-treatment did not differ between MPCPC (mean 1.6) and CWCPC (mean 1.8). Vernon *et al.*[14] reported in a retrospective study that 59.6% of patients required multiple transscleral CW diode CPC sessions (mean 2.17) during a follow-up duration of 36–84 (mean 65.7) months.

Despite proven efficacy, concerns remain regarding safety, especially the risk of visual reduction in sighted eyes, hypotony[15] in eyes with uveitis or after repeated treatments, transient hyphema and exudates in the AC,[16] severe visual loss,[17] necrotizing scleritis[18] and even phthisis bulbi.[19] As a result of the common perception that CPC is a therapeutic approach of last resort, most cases treated are very sick eyes with poor visual potential. Visual loss post-TSCPC may probably be related to the type of eye rather than to any specific treatment effect.[20] A prospective randomized study[20] of 92 patients with POAG treated with CWCPC demonstrated VA decline in 23% of eyes treated with laser as well as in 23% of fellow eyes treated only with medication.[3] In our study of poorly sighted eyes, VA decline was not different in CWCPC and MPCPC. The rate of hypotony seemed to be correlated with power settings[12,15,21,22] and certain type of glaucoma.[23] In our study, frequency of prolonged hypotony appeared to correlate with glaucoma etiology with four out of five cases of hypotony having NVG in the CWCPC-treated group. Two of these eyes that had hypotony suffered a corresponding decline in VA from HM to LP and LP to NPL. The absence of hypotony that we observed after MPCPC is similar to our earlier experience.[8]

Diode laser TSCPC is a well-accepted cycloablative procedure that targets pigmented epithelium and vascular core of ciliary body processes to suppress aqueous production. In a CW laser emission, the temperature rise for a specific application is controlled by adjusting power and duration of exposure to bring about coagulative tissue changes. Using the micropulse mode of laser delivery, finer control of photothermal effects is made possible by chopping the steady CW emission into a train of shorter laser pulses with adjustable width ("ON" time) and "interval" ("OFF" time). This, in theory, allows the adjacent non-pigmented tissues to cool during the off-cycle so they remain below their coagulation threshold.[8] It is hypothesized that MPCPC therefore results in less collateral tissue damage.

The mechanism of IOP lowering efficacy using MPCPC is unclear. Anatomically, MPCPC targets *pars plana* rather than *pars plicata*. It is hypothesized that inflammation in the ciliary body reduces aqueous formation and also possibly enhances uveoscleral aqueous outflow.[24] A non-lethal thermal insult possibly activates cellular biochemical cascade resulting to IOP lowering.[25]

The limitations of this exploratory study include: (i) the lack of standardized treatment protocol with equivalent laser energy as a result of insufficient data on the optimal treatment settings for cyclodiode laser,[26] (ii) proper stratification of glaucoma diagnoses to avoid bias and (iii) intrinsic endpoints used for CWCPC that resulted in a less predictable and less consistent effect on IOP.

In conclusion, the two techniques of diode laser delivery, MPCPC and CWCPC demonstrated efficient IOP reduction from baseline. The micropulse mode provided more consistent and more predictable effect in lowering IOP with minimal ocular complications. The results of this single-center randomized, exploratory study affirmed our earlier experience on MPCPC.

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References

1. Schlote T, Derse M, ZIerhut M. Trans-scleral diode laser cyclophotocoagulation for the treatment of refractory glaucoma secondary to inflammatory eye diseases. *Br J Ophthalmol* 2000; **84**: 999–1003.
2. Schlote T, Derse M, Rassman K *et al*. Efficacy and safety of contact trans-scleral diode laser cyclophotocoagulation for advanced glaucoma. *J Glaucoma* 2001; **10**: 294–301.
3. Egbert PR, Fladoyor S, Budenz DL *et al*. Diode laser trans-scleral cyclophotocoagulation as a primary surgical treatment for primary open angle glaucoma. *Arch Ophthalmol* 2001; **119**: 345–50.
4. Agarwal HC, Gupta V, Sihota R. Evaluation of contact versus non-contact diode laser cyclophotocoagulation for refractory glaucomas using similar energy settings. *Clin Experiment Ophthalmol* 2004; **32**: 33–8.
5. Leszczynski R, Gierek-Lapinska A, Forminska-Kapuscik M. Trans-scleral cyclophotocoagulation in the treatment of secondary glaucoma. *Med Sci Monit* 2004; **10**: CR542–8.
6. Ho CL, Wong EY, Chew PT. Effect of diode laser trans-scleral pars plana photocoagulation on intraocular pressure in glaucoma. *Clin Experiment Ophthalmol* 2002; **30**: 343–7.
7. Ho CL. Micropulse diode trans-scleral cyclophotocoagulation. *Asian J Ophthalmol* 2001; **3** (Suppl.): 3–4.
8. Tan AM, Aquino MCD, Chew PTK *et al*. Micropulse trans-scleral cyclophotocoagulation in the treatment of refractory glaucoma. *Clin Experiment Ophthalmol* 2010; **38**: 266–72.
9. Sivaprasad S, Sandhu R, Tandon A *et al*. Subthreshold micropulse diode laser photocoagulation for clinically significant diabetic macular oedema: a three-year follow up. *Clin Experiment Ophthalmol* 2007; **35**: 640–4.
10. Parodi MB, Spasse S, Iacono P *et al*. Subthreshold grid laser treatment of macular edema secondary to branch retinal vein occlusion with micropulse infrared (810 nanometer) diode laser. *Ophthalmology* 2006; **113**: 2237–42.
11. Desmettre TJ, Mordon SR, Buzawa DM, Mainster MA. Micropulse and continuous wave diode retinal photocoagulation: visible and subvisible lesion parameters. *Br J Ophthalmol* 2006; **90**: 709–12.
12. Spencer AF, Vernon SA. "Cyclodiode": results of a standard protocol. *Br J Ophthalmol* 1999; **83**: 311–6.
13. Hauber FA, Scherer WJ. Influence of total energy delivery on success rate after contact diode laser trans-scleral cyclophotocoagulation: a retrospective case review and meta-analysis. *J Glaucoma* 2002; **11**: 329–33.
14. Vernon SA, Koppens JM, Menon J *et al*. Diode laser cycloablation in adult glaucoma: long-term results of a standard protocol and review of current literature. *Clin Experiment Ophthalmol* 2006; **34**: 411–20.
15. Murphy CC, Burnett CAM, Spry PGD *et al*. A two centre study of the dose-response relation for trans-scleral diode laser cyclophotocoagulation in refractory glaucoma. *Br J Ophthalmol* 2003; **87**: 1252–7.
16. Chang SH, Chen YC, Li CY *et al*. Contact diode laser trans-scleral cyclo- photocoagulation for refractory glaucoma: comparison of two treatment protocols. *Can J Ophthalmol* 2004; **39**: 511–6.
17. Goldenberg-Cohen N, Bahar I, Ostashinski M *et al*. Cyclocryotherapy versus trans-scleral diode laser cyclophotocoagulation for uncontrolled intraocular pressure. *Ophthalmic Surg Lasers Imaging* 2005; **36**: 272–9.
18. Shen SY, Lai JS, Lam DS. Necrotizing scleritis following diode laser trans-scleral cyclophotcoagulation. *Ophthalmic Surg Lasers Imaging* 2004; **35**: 251–3.
19. Kramp K, Vick HP, Guthoff R. Trans-scleral diode laser contact cyclophotocoagulation in the treatment of different glaucomas as primary surgery. *Graefes Arch Clin Exp Ophthalmol* 2002; **240**: 698–703.
20. Wilensky JT, Kammer J. Long-term visual outcome of trans-scleral laser cyclotherapy in eyes with ambulatory vision. *Ophthalmology* 2004; **111**: 1389–92.
21. Bloom PA, Tsai JC, Hitchings RA *et al*. Cyclodiode trans-scleral diode laser cyclophotocoagulation in the treatment of advanced refractory glaucoma. *Ophthalmology* 1997; **104**: 1508–20.
22. Iliev ME, Gerber S. Long-term outcome of trans-scleral diode laser cyclophotocoagulation in refractory glaucoma. *Br J Ophthalmol* 2007; **91**: 1631–5.
23. Ramli N, Ho CL, Aung T. Risk factors for hypotony after trans-scleral diode cyclophotocoagulation. *J Glaucoma* 2012; **21**: 169–73.
24. Liu GJ, Mizukawa A, Okisaka S. Mechanism of intraocular pressure decrease after contact trans-scleral continuous wave Nd:YAG laser cyclophotocoagulation. *Ophthalmic Res* 1994; **26**: 65–79.
25. Fea AM, Bosone A, Rolle T *et al*. Micropulse diode laser trabeculoplasty (MDLT): a phase II clinical study with 12 months follow-up. *Clin Ophthalmol* 2008; **2**: 247–52.
26. Agrawal P, Dulku S, Nolan W, Sung V. The UK National Cyclodiode Laser Survey. *Eye* 2011; **25**: 168–73.