ORIGINAL ARTICLE

MicroPulse Transscleral Laser Therapy: A Retrospective Study of Dose Efficacy and Safety

Julia Nguyen[1], Orlando G González-Martínez[2], Albert S Khouri[3]

Received on: 22 January 2024; *Accepted on:* 15 September 2024; *Published on:* 29 October 2024

Abstract

Aim: To evaluate the efficacy and safety of MicroPulse transscleral laser therapy (MPTLT) for cyclophotocoagulation in the treatment of glaucoma with different doses of energy.

Materials and methods: A retrospective review was done of 136 eyes in 90 patients treated with MPTLT between 2018 and 2022. Intraocular pressures (IOP) at follow-ups were compared with a paired student *t*-test and treatment outcomes with a Chi-squared test. The cohort was stratified into subgroups to analyze the effect of total applied energy on outcomes. The variance between energy groups was analyzed with the Kruskal–Wallis test adjusted for multiple comparisons.

Results: A total of 136 eyes of 90 patients underwent MPTLT for mostly open angle (36.0%) and childhood glaucoma (30.1%). Applied energy range was between 37.5 and 195.6 J with a mean [standard deviation (SD)] of 100.7 (34.3) J. Applied energy of 125–200 J reduced IOP the most at 2 years with 90% of eyes within 6–21 mm Hg and 66% of eyes having IOP reduced at least 20% ($p < 0.001$) from baseline. However, at 2 years, energy 50–75 J achieved fewer eyes with two or more Snellen lines lost than energy 125–200 J and a lower proportion of eyes with at least one symptom ($p < 0.05$). No severe complications of hypotony, phthisis bulbi, or chronic inflammation were reported.

Conclusion: IOP reduction and safety outcome of MPTLT varied with applied energy. Doses should be adjusted to target the treatment goals for individual patients.

Clinical significance: MPTLT was found to be effective in lowering IOP in glaucoma. Using high levels of energy is associated with higher rates of complications.

Keywords: Cyclophotocoagulation, Glaucoma, MicroPulse, Transscleral laser therapy.

Journal of Current Glaucoma Practice (2024): 10.5005/jp-journals-10078-1450

Introduction

Glaucoma is characterized by elevated intraocular pressure (IOP), leading to permanent damage to the optic nerve and irreversible vision loss.[1] Glaucoma treatments aim to reduce IOP to preserve the optic nerve and prevent progressive visual field damage.[2] Medical therapy, laser surgery, microincisional, and traditional surgery are effective in lowering IOP. Transscleral laser therapy, in continuous and MicroPulse delivery modes, is a noninvasive therapy used in the management of elevated IOP in glaucoma.[3,4]

Transscleral photocoagulation uses photoenergy to induce multiple IOP-reducing changes including effects on the secretory ciliary body epithelium, suppressing aqueous humor production and lowering IOP, increased uveoscleral outflow through the increase in choroidal thickness and increased trabecular meshwork outflow by inducing changes by changing the configuration of the trabecular meshwork.[5–8] The current standard continuous wave cyclophotocoagulation (CWCPC) therapy is performed with a laser console Cyclo G6 and a G-Probe delivery device (IRIDEX, Mountain View, California). This platform uses a semiconductor diode infrared laser in a continuous wave mode of delivery to target the pigmented ciliary body epithelium, the primary site of aqueous humor production. While histological studies and experimental data demonstrated insignificant changes in the cellular structure of adjacent tissues in several studies,[9–11] there was clinical evidence of severe potential complications after CWCPC, and thus, it was mainly reserved for treatment of advanced glaucoma patients with poor vision or visual prognosis.[7,12–14]

MicroPulse transscleral laser therapy (MPTLT) uses the Cyclo G6 laser with a novel MicroPulse P3 delivery device, improves upon the selectivity and homogeneity of energy delivered across the treated area, and thus the overall safety profile of the therapy.[14] In the MicroPulse mode of delivery, the laser is repetitively cycled in both time and space. In the time dimension, the laser wave is cycled on (duty cycle) and off (rest cycle) repeatedly for the set duration of exposure. When longer rest cycles are interspersed in between to prevent thermal buildup, tissues can cool off before the next laser wave, thus avoiding a temperature rise and heat-induced damage.

[1–3]Department of Ophthalmology, Rutgers New Jersey Medical School, Newark, New Jersey, United States

Corresponding Author: Albert S Khouri, Department of Ophthalmology, Rutgers New Jersey Medical School, Newark, New Jersey, United States, Phone: +1 9739722065, e-mail: khourias@njms.rutgers.edu

How to cite this article: Nguyen J, González-Martínez OG, Khouri AS. MicroPulse Transscleral Laser Therapy: A Retrospective Study of Dose Efficacy and Safety. J Curr Glaucoma Pract 2024;18(3):121–129.

Source of support: Nil

Conflict of interest: None

In the space dimension, the MicroPulse P3 probe is designed to deliver energy in a multipass sweeping motion, effectively delivering multiple short exposures during the motion over treated tissue, in contrast to a single long static exposure delivered at selected treated spots as in CWCPC therapy.[13,15,16] While CWCPC is a destructive procedure, MPTLT conceptually induces inflammatory effects on the ciliary body to reduce IOP while sparing its tissue,[17–19] and thus significantly improves the therapy's safety profile. In recent studies, indication for MPTLT has been extended to earlier stages of glaucoma with good visual potential.[13,20–24]

However, standardizing MPTLT treatments to achieve optimal outcomes for patient selection was difficult because up to four different parameters can affect laser delivery. In addition to the rate of releasing laser energy (power in Watts) and exposure duration (time in seconds), surgeons can also select duty cycle (on time, when the laser is switched on) and decide on the velocity of probe passes over a treated area (sweeping rate).[7,14,25–27] Lacking a theoretical standard or a substantial evidence-based guideline, studies worldwide in the last decade have experimented with different sets of parameters, of which outcomes were difficult to compare.[22,23,28–42] Based on a small analysis, a group of researchers proposed an energy-response hypothesis in which three parameters—power, exposure time, and duty cycle—were reduced into a single reportable parameter (total energy) to facilitate comparison across studies.[7] This hypothesis neglected the effect of sweeping rates on outcomes. In another recent study, a guideline standardizing all four parameters was recommended.[25–27]

Without formal guidelines or long-term randomized controlled trials, evidence-based hypotheses need more clinical evidence for further confirmation or revision. This study provides clinical efficacy and safety data from MPTLT cases performed at our institution from 2018 to 2022. The extensive treatment cohort is diverse inpatient demographics, glaucoma types, stages, history of glaucoma-related surgeries, and treatment parameters. A comparative analysis considering prior published data on MPTLT dose response is conducted. Collectively, findings from this study and similar reports provide necessary clinical evidence to confirm or revise hypotheses and guidelines on optimal settings, thus assisting clinicians in practice.

Materials and Methods

This retrospective study includes patients who received MPTLT procedures for glaucoma management at a tertiary care academic center from 2018 to 2022. The Rutgers University Institutional Review Board approved the study, and it was conducted in accordance with the tenets of the Declaration of Helsinki. A waiver of informed consent was granted because of its retrospective nature. Inclusion criteria included patients with moderate to end-stage glaucoma, uncontrolled on maximally tolerated medical management, and poor candidacy for or patient objection to incisional surgery. Adult and childhood glaucoma patients (age 0–90 years old) were included. Patients with and without a history of glaucoma surgeries were included. Records of presurgery and follow-up office visits at 3, 6, 9, 12, and 24 months were searched and included. Retreatment was determined clinically by attending surgeons as needed, and the last operation was included in the result. Eyes lost to follow-up before at least 3 months of follow-up or with incomplete baseline records or records of laser settings were excluded.

Pre- and postoperative data collected from office visit records included measured IOP, best corrected visual acuity (BCVA), topical and systemic antiglaucoma medications, clinical symptoms, and patient complaints. Applanation tonometry results from three measurements were averaged to obtain the reported IOP value. For pediatric patients, measurements were performed under general anesthesia. For BCVA, the decimal equivalence of Snellen fractions was used for ranking. Counting finger (CF), hand motion (HM), light perception (LP), and no light perception (NLP) measure visual function for poor acuity and were ranked below decimal values in order. Clinical symptoms and patient complaints were extracted from examination records. Pain assessment was based on patient interviews on a 0–10 scale. The use of medications that combined more than one active ingredient was counted by each ingredient (e.g., timolol–brimonidine was counted as two medications because of its two active ingredients).

Two surgeons performed all the procedures included in this study. The attending surgeons determined patient selection and parameter settings for MicroPulse procedures based on the individual patient glaucoma diagnosis and severity. MPTLT was performed using a Cyclo-G6 console coupled with an MP3 probe. Power levels from 2000 to 2500 mW at 31.3% duty cycle (0.5 ms on-time interleaved with 1.1 ms rest time) setting was used. A multipass slow sweep in painting fashion of approximately 10 seconds per pass was applied to each quadrant, sparing the 3 and 9 o'clock meridian, where ciliary arteries and nerves are located, to avoid the development of postoperative mydriasis. Power settings varied from 1400 to 2500 mW, with the most common exposure duration of 100–250 seconds for adequate energy within 37–195 J, generally distributed around the 100.7 J central (Fig. 1A). Five energy groups with cutoff values of 50, 75, 100, and 125 J were stratified (Fig. 1B).

The primary outcome was IOP reduction. The cohort was dichotomized using the cutoff IOP reduction of 30, 20%, or IOP range of 6–21 mm Hg. Absolute mean IOP, IOP reduction from baseline, and proportion within a controlled range of (6–21 mm Hg) were computed and compared at each follow-up. Successful outcomes were defined as IOP reduced by at least 20% and within 6–21 mm Hg. Eyes that failed to respond were retreated within 24 months by the same surgeon at the same or higher dose of laser energy. Secondary outcomes included central vision deterioration, reduction in antiglaucoma medication use, and complications.

Distributions of IOP from pre to postsurgery or between follow-ups were compared with a paired student *t*-test. Distributions of treatment outcomes were compared with the Chi-squared test. The cohort was stratified into subgroups to analyze the effect of applied energy on the outcome. To generate the most balanced grouping and avoid regrouping bias, a histogram and standard curve fit of the energy profile were constructed and visually guided the selection of the cutoff values. The Kruskal–Wallis test was used for the analysis of variance between energy groups. Bonferroni correction for multiple comparisons was applied *post hoc*. Nonparametric bivariate analysis was used to detect dependency of treatment effects and energy levels. All statistical analysis was performed in SAS Enterprise Guide 8.3. Statistical significance was set at p-value <0.05 before adjustment.

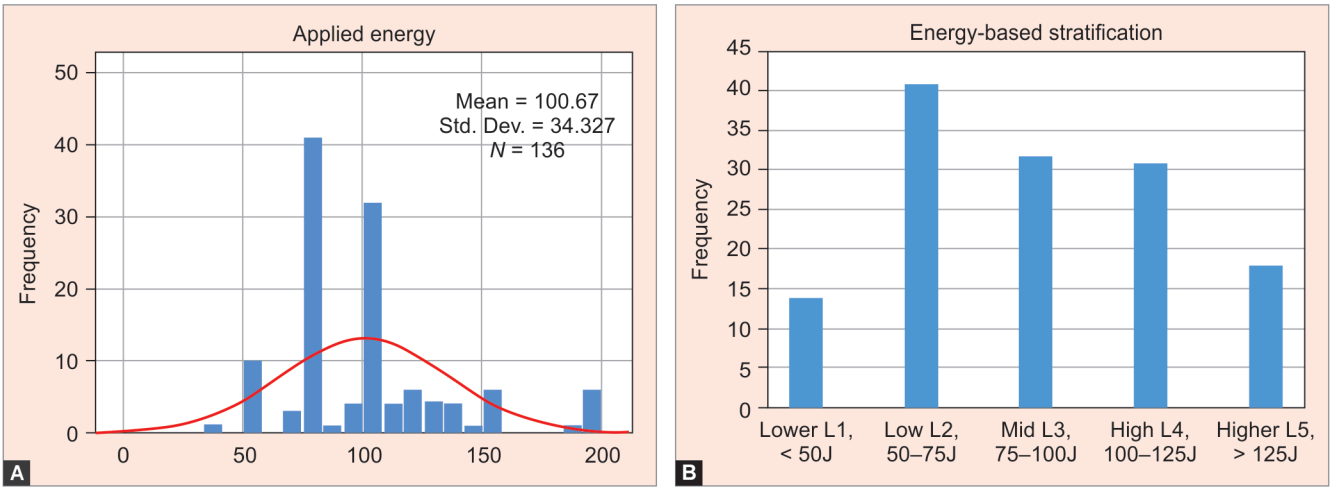
Results

Patient Characteristics

The study cohort includes 90 patients, 136 eyes, who underwent MPTLT procedures between 2018 and 2022 in our clinic. The median [interquartile range (IQR)] age was 55 (11–71) years. There were more black patients (39.7%) than white (14.7%). Males comprised 61.1%. The most common types of glaucoma treated were primary open-angle (49 eyes, 36.0%), childhood (41 eyes, 30.1%), and neovascular (21 eyes, 15.4%). Twenty-seven eyes (19.9% of the cohort) required at least one retreatment within 24 months. Eighty-eight eyes (64.7%) received laser unilaterally, including 43 right and 45 left, while 48 eyes (35.3%) were operated bilaterally. Seventeen patients (12.5%) had a family history of glaucoma. Forty-eight eyes (35.3%) had a history of a prior surgery with 24 tube shunt implants, 11 goniotomies, and 4 cataract removals (Table 1).

Endpoint

This study defined success as having IOP within the 6–21 mm Hg range and reducing it by at least 20%. The overall success rate was 52.4% at 1 year and 54.8% at 2 years. When considering individual energy groups, success rate varied at 1 year from 33% (lowest in L1 group) to 61% (highest in L2 group), and at 2 years from 41 (lowest in L2 group) to 80% (highest in L5 group). There were no significant differences in success rates between groups after adjustment ($p > 0.01$).



Figs 1A and B: (A) Effective energy normally distributed at 100.67 J center, range (37.56–195.63 J); (B) Cohort was stratified into five groups L1–L5 based on cutoff energy of 50, 75, 100, and 125 J

Table 1: Patient characteristics

Characteristics	*N*	*%*	*Characteristics*	*N*	*%*
Patients	90		Glaucoma (eyes)		
Eyes	136		Primary open angle	49	36.0
Age (years)			Congenital	41	30.1
Median (IQR)	55 (11–71)		Neovascular	21	15.4
Gender (patients)			Uveitic	10	7.4
Female	53	39	Juvenile	8	5.9
Male	83	61	Secondary	5	3.7
Race (patients)			Traumatic	2	1.5
Black	54	39.7	S/P (eyes)	48	35.3
Other	59	45.6	Tube shunt	24	17.6
White	20	14.7	Goniotomy	11	8.1
Laterality (eyes)			Cataract removal	4	2.9
OD	43	31.6	Iridotomy	3	2.2
OS	45	33.1	Retina surgery	3	2.2
OU	48	35.3	Corneal transplant	3	2.2
Family Hx (eyes)	17	12.5	Reoperation (eyes)	27	19.9

OD, oculus dexter; OS, oculus sinister; OU, oculus uterque

Intraocular Pressure Response

Overall means and 95% confidence intervals of IOP at baseline, 1, 3, 6, 12, and 24 months were calculated to be 28.93 (27.26–30.58), 20.39 (18.39–22.40), 23.49 (21.09–25.90), 22.88 (2068–25.09), 21.11 (19.40–22.82), and 19.57 (17.59–21.56) mm Hg, respectively (Table 2). Significant pre- to postsurgery reduction in IOP was detected ($p \leq 0.003$), but there was no significant change between subsequent follow-ups. Overall, IOP reduced by 27.0 and 32.4% at 1- and 2-year follow-up, respectively.

When considering different levels of delivered energy, mean IOP was similarly reduced to 19.1–22.5 mm Hg among all five groups, representing 37.5% baseline reduction in the L1 group (the largest reduction) to 13.9% in the L5 group (the smallest reduction) at 1 year. At 2 years, mean IOP was reduced to 15.4 mm Hg, 39.3% (the lowest reduction) in the L5 group, and to 22.6 mm Hg, 35.8% (the highest reduction) in the L1 group. The linear smoothed approximation of the IOP in each energy group revealed the steepest declination in group L2, similar lower rates in groups L1 and L5, and the mildest rates in groups L3 and L4. Negative slopes (IOP declination) were observed in all groups up to 2 years follow-up (Fig. 2).

The follow-up cohorts were dichotomized using an IOP range of 6–21 mm Hg as the threshold. 57.3 and 66.2% of the treated eyes achieved IOP within 6–21 mm Hg at 1 and 2 years, respectively. Evidence of significant pre to postoperative proportions increase was detected ($p < 0.001$), but there were no substantial changes between follow-ups after 3 months.

When considering individual energy groups, at 1 year, L2, L3, and L5 achieved similar 53–55% of the cohort with IOP within the controlled range ($p > 0.30$), while L1 and L4 achieved significantly lower (40.0%) or higher (72.0%) proportions with controlled IOP, respectively. At 2 years, L1–L4 completed similar 60–68% of cohorts with controlled-IOP ($p > 0.20$). The linear smoothed approximation of the progression in each energy group revealed similar positive rates (increasing proportion of controlled IOP at each follow-up) in all groups up to 2 years follow-up. It is noted that the mean preoperative IOP in the L1 group was >35 mm Hg, significantly higher, and in the L5 group was < 26 mm Hg, significantly lower than other groups.

The cohort was dichotomized using a 30% IOP reduction as the cutoff value. 48.8% of the cohort at 1 year and 53.2% at 2 years achieved at least 30% IOP reduction ($p > 0.08$). Regarding individual energy groups, L2 had higher proportions of 30% + IOP reduction

Table 2: IOP progression by energy level. Significant reduction detected pre- to postsurgery

	Baseline		*Follow-up 1 month*		*Follow-up 3 months*		*Follow-up 6 months*		*Follow-up 1 year*		*Follow-up 2 years*	
Energy levels	*Eyes*	*IOP (mm Hg) mean (SD)*	*Eyes*	*IOP (mm Hg) mean (SD)*	*Eyes*	*IOP (mm Hg) mean (SD)*	*Eyes*	*IOP (mm Hg) mean (SD)*	*Eyes*	*IOP (mm Hg) mean (SD)*	*Eyes*	*IOP (mm Hg) mean (SD)*
L1, <50 J	13	35.21 (12.82)	11	16.72 (10.89)	10	26.49 (12.22)	6	26.83 (14.96)	10	22.00 (7.11)	5	22.60 (8.22)
L2, 50–75 J	31	30.38 (10.21)	31	20.46 (13.48)	26	25.51 (13.25)	20	22.33 (12.25)	30	21.23 (8.98)	27	17.91 (9.43)
L3, 75–100 J	32	28.44 (7.30)	22	20.22 (8.49)	15	20.91 (9.45)	20	23.11 (8.60)	18	22.54 (9.78)	16	20.43 (7.20)
L4, 100–125 J	27	27.17 (8.85)	23	22.32 (8.54)	19	23.79 (8.32)	26	23.80 (9.83)	24	19.10 (5.62)	18	21.61 (8.42)
L5, >125 J	18	25.37 (5.50)	15	20.23 (6.03)	13	19.73 (10.18)	14	19.92 (8.60)	13	21.85 (10.57)	5	15.40 (3.57)
		Mean (95% CI)		Mean (95% CI)		Mean (95% CI)		Mean (95% CI)		Mean (95% CI)		Mean (95% CI)
Overall	121	28.93 (27.26–30.58)	102	20.39 (18.39–22.40)	83	23.49 (21.09–25.90)	86	22.88 (2068–25.09)	95	21.11 (19.40–22.82)	71	19.57 (17.59–21.56)
p-value		Ref		<0.001		0.003		<0.001		<0.001		<0.001

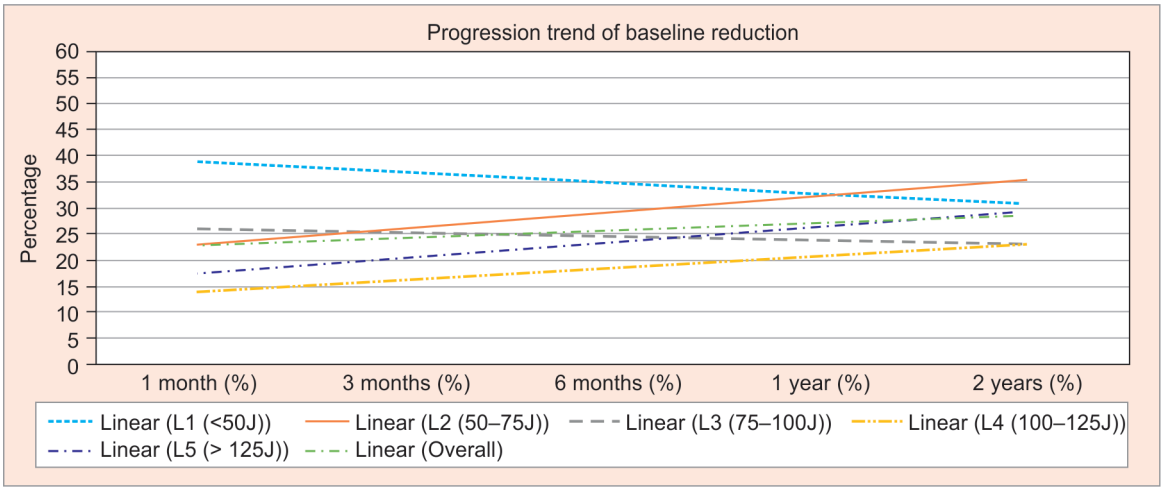


Fig. 2: Baseline reduction varies ± 10% between 1 and 24 months in all groups, with the highest decrease in L2. Overall reduction of 27% in 1 year and 32% in 2 years

at 1 year, 60.9%, and 2 years, 63.6% than other groups, but the difference was not statistically significant.

The cohort was again dichotomized using 20% IOP reduction as the cutoff value. Overall, at 1 year, 64.3%, and at 2 years, 66.1% of the cohort achieved at least 20% IOP reduction. Follow-up to follow-up, there were no statistical differences ($p > 0.20$). When considering individual energy groups, the proportions with 20% + IOP reduction increased to between 55 (in L1 and L5 groups) and 70% (in L2 and L4 groups) at 12 months.

Best Corrected Visual Acuity Progression

About 69.2 and 67.5% of the cohort did not experience BCVA changes at 1 and 2 years, respectively, while 15.4% at 1 year and 9.1% at 2 years gained one or more lines (in good vision eyes) or one or more visual function ranks (in poor vision eyes). Severe loss of two or more lines of vision or visual function ranks were reported for 6 and 12% at 1 and 2 years, respectively (Fig. 3).

When considering individual energy groups, higher energy groups L4 and L5 had the largest proportions of eyes with VA decreased by one or more lines. In comparison, lower energy groups L1 and L2 had the smallest proportions. The differences, however, were not significant after adjusting for multiple comparisons. Approximately, one-third of each group observed changes in BCVA of one or more lines at each follow-up.

Use of Antiglaucoma Medicine

At 1 and 2 years of follow-up, overall mean medication use per eye decreased to 3.09 and 2.75 per eye, respectively, from a preoperative baseline of 3.85 per eye. Medication use declined in all energy groups but remained high in the highest energy group, L5 (down to 4.6 at 24 months from 4.9 preoperative). No statistically significant difference between groups was detected.

Complications and Patient Complaints

No severe complications such as phthisis bulbi, loss of light perception, persistent hypotony, chronic inflammation, persistent mydriasis, or choroidal/retinal detachment were reported. Patient complaints were based on patient-generated statements as documented in the medical record. Most common complaints reported up to 2 years after surgery included redness (6.5%), blurred vision (5.7%), IOP spike (3.1%), followed by tearing (2.5%), headache (1.4%), and flashes (1.2%) (Fig. 4). Overall, 77.6% of the treated eyes reported no complaint within 2 years postoperatively. The mean number of complaints per eye reduced to 0.24 at 1 year and 0.26 at 2 years from 0.32 at 1 month, $p = 0.37$ and $p = 0.45$, respectively. When considering individual groups of energy, higher energy groups L4 and L5 had significantly higher rates of complaints than the lower energy groups L1 and L2 ($p < 0.01$).

Pain-free Eyes

The number of pain-free eyes increased from 74.3% preoperatively to 78.8% ($p = 0.045$) at 1 year and 94.8% ($p < 0.001$) at 2 years. At 1 year, severe pain was only reported for 1 out of 104 treated eyes (Table 3). No severe pain among treated eyes was reported at 2 years. When considering individual energy groups, higher energy groups L4 and L5 reported the smallest proportions of pain-free eyes, while low energy groups L1 and L2 reported the largest

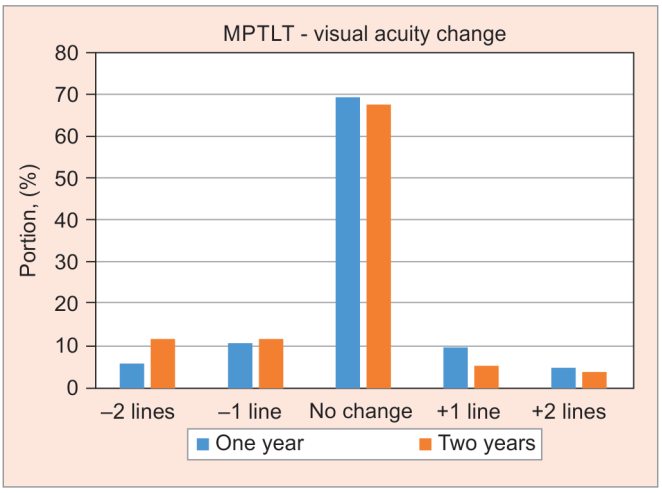


Fig. 3: Visual acuity changes at 1 and 2 years postoperatively. 6 and 12% loss of two or more lines in 1 and 2 years, respectively. 15% at 1 year and 9% at 2 years had VA improved by one or more lines. More than half did not experience VA change

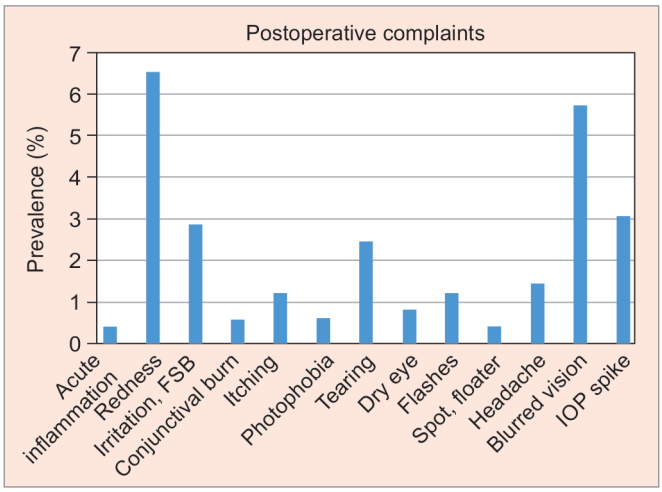
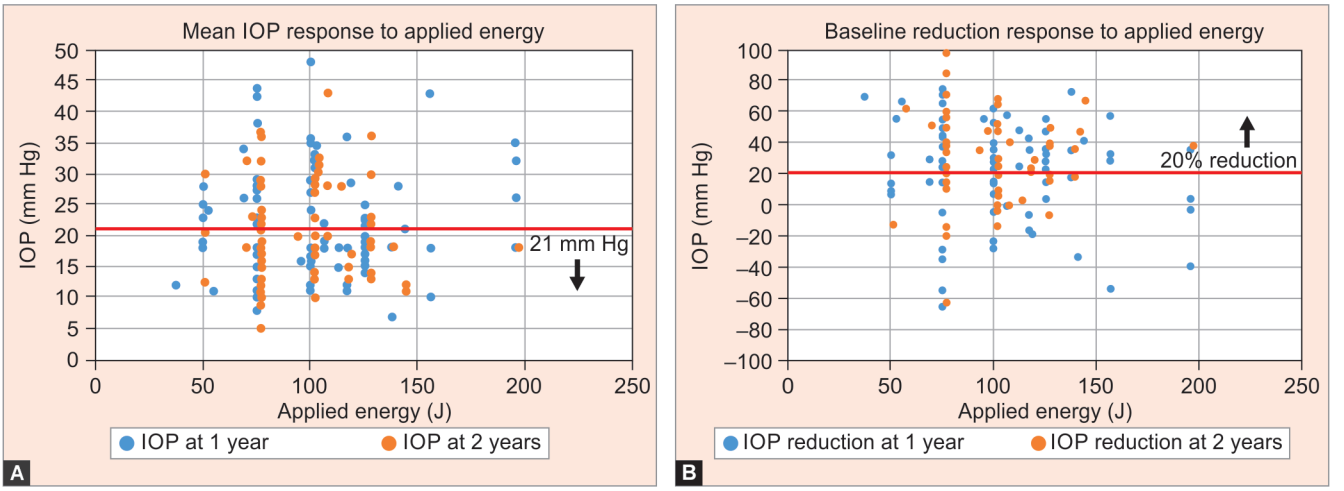


Fig. 4: Patient complaints were reported within 2 years postoperatively. Redness and blurred vision were the chief complaints

Table 3: Complaints of eye pain at pre- and postsurgery visits up to 24 months on the patient interview-based scale

Eye pain	*None*	*Mild*	*Moderate*	*Severe*	*Total eyes*	*Pain-free (%)*	*p-value*
Presurgery (eyes)	101	25	8	2	136	74.3	Ref
1 month (eyes)	81	23	4	2	110	73.6	0.618
3 months (eyes)	83	9	1	0	95	87.4	0.024
6 months (eyes)	79	14	7	2	104	76.0	0.172
1 year (eyes)	82	15	5	1	104	78.8	0.045
2 years (eyes)	73	5	0	0	77	94.8	<0.001

Significant pain-free proportions were reported at 94.8 and 78.8% at 12 and 24 months, respectively



Figs 5A and B: IOP response to applied energy. No significant associations were observed

proportions at each follow-up. At 3, 6, and 12 months, 80–96% of L1, L2, and L3 groups were pain-free compared with 53–75% in L4 and L5 groups ($p < 0.01$).

Intraocular pressure effects, IOP mean, and baseline reduction at 12 and 24 months were plotted against treated energy in Figure 5. Nonparametric bivariate analysis revealed poor association at 12 and 24 months ($p > 0.40$).

Discussion

MicroPulse transscleral laser therapy emerged over the last decade as an effective and safe modality for glaucoma management.[7,13,14,20,25–27] In everyday practice, however, optimal integration of MPTLT into treatment paradigms continues to evolve as clinicians gain a better understanding of laser energy parameters and patient selection from increasing clinical evidence added by recent studies of MPTLT. Until a formal guideline for parameter selection is confirmed by a multicenter, long-term, randomized controlled trial, evidence of differential outcomes from independent studies can augment efficacy and safety hypotheses in practice. This study contributes novel clinical outcomes from glaucoma treatment with MPTLT using a broad spectrum of delivery time and energy settings.

To facilitate the analysis of laser response, we characterized our cohort based on the adequate energy delivered and stratified it into energy groups. Energy characterization was first introduced by Johnstone et al.,[43] using the equation energy (J) = power (W) × exposure (second) × duty cycle. An energy distribution histogram guided the stratification to avoid grouping bias.

Criteria of success varied in literature. Some studies,[15,16,35,38] including this study, defined success as achieving IOP within the 6–21 mm Hg range and reduction of at least 20%, while others[23–29,34,40] used an "or" condition (IOP within 6–21 mm Hg or reducing by 20%). Yet other studies required a 30% IOP reduction, 6–18 mm Hg range, reduction in medication use, no loss of light perception, or no additional interventions as exit conditions. Therefore, comparing success outcomes across studies should weigh in this considerable variation.

The IOP reduction effect was observed in all groups, and no significant association was detected after adjusting for multiple comparisons ($p > 0.01$). Higher energy groups were not associated with faster or more IOP reduction (Fig. 2). It is noted that the size of IOP response varied widely in the literature from over 50%[15,32,33,41,42] to <25%[35,44,45] due to contributing confounders in heterogeneous cohorts. Smaller IOP reduction effect has been reported to be associated with lower preoperative IOP,[36,44,46,47] or diagnoses of pediatric, neovascular, and uveitic glaucoma,[13,16,33–35,40] which comprised 62% of our cohort. The cohorts treated by Yelenskiy et al.[23] and Keilani et al.[28] with approximately 56 J had slightly lower preoperative IOP of 22 and 28.4 mm Hg, respectively, compared with the cohort treated with comparable L2 level in this study with preoperative IOP of 30.4 mm Hg. The studies reported slightly lower IOP reductions of 27 and 28.2% in 1 year compared with 30.1% reported in this study. On the other hand, Aquino et al.[16] and Tan et al.[34] reported higher IOP reduction at 1 year of 45 and 40%, respectively, from higher preoperative IOP of 36.5 and 39.3 mm Hg, using similar effective energy. The L2 cohort in this study had a success rate of 40.7% compared with 52% in Aquino's study (using "and" success criterion) and 71–83% in the other studies (using "or" success criterion) (Table 4). All these cohorts had a similar mixture of 40–50% primary open-angle glaucoma (POAG) and 10–20% neovascular glaucoma (NVG). The outcomes suggest that IOP response to this range of treatment energy may be consistent and predictable when adjusted for patient selection.

Severe vision loss of two or more lines or two or more visual function ranks was the most common long-term safety concern in CWCPC and could affect as high as 55% in some studies.[48,49] MPTLT studies, thus, often reported numbers or proportions of eyes with severe vision loss of two or more lines or visual functions at last follow-up (12-month average), from a low of 5%,[16,40] 15%,[45] and 19%,[36] to as high as 21%,[39] 25%,[22] and 26%.[32] These studies, however, reported no statistical significance in BCVA changes when converting to the logMAR scale. In comparison, in this study, we observed 6 and 12% of severe loss of two or more lines or visual function ranks at 1 and 2 years, respectively. More than half of the eyes did not experience BCVA changes, while up to 15% improved one or more lines (Fig. 3). The low BCVA impact outcome may be explained by the relatively lower energy used in this study and low severity and cyclodestruction naïve eyes. Medication use was reduced at all follow-ups and energy groups but did not reach statistical significance in our study. Most MPTLT studies reported none or very few severe complications such as bulbi, persistent hypotony, inflammation, or mydriasis and often attributed them to preoperative severity or other eye diseases.[16,23,28,29,32,34,41] In

Table 4: MPTLT studies

	Benhatchi et al.[29]	*Keilani* et al.*[28]	*Keilani** et al.*[28]	*Yelenskiy et al.*[23]	*Tan et al.*[34]	*Aquino **** et al.*[16]	*Elhefney*** et al.*[37]	*Sarrafpour et al.*[36]	*Varikuti et al.*[39]	*Souissi et al.*[46]	*Tekeli et al.*[38]
Effective energy (J)	50–75	50–75	50–75	50–75	50–75	50–75	75–100	75–100	100–125	100–125	100–125
No. of eyes	44	20	20	197	40	24	36	73	61	37	32
No. of sessions	>1	>1	>1	>1	2	>1	>1	1	1	>1	>1
Last follow-up (months)	12	12	12	12	18	18	15	12	12	12	12
Preop IOP (mm Hg)	32.8	28.4	27.0	22.0	39.3	36.5	37.5	25,5	25.7	28.7	31.3
IOP at follow-up (mm Hg)	18.8	20.4	15.8	15.8	24.6	20	20.0	13.8	15.4	18.5	18.5
IOP reduction (%)	45	28.2	41.5	27	40	45	37.1	46	40	35	40
Success rate (%)	66	83.5	65	71	80	52	61	76	75	35	75
VA decrease	Yes Not sig.	Yes Not sig.	Yes Not sig.	No >3 lines	No >2 lines	4%	Not reported	18.8% >2 lines	20.8% >2 lines	2 eyes NLP	12.5% >1 line
Severe complications	None	Hypotony inflammation mydriasis	Hypotony inflammation mydriasis	None	None	NLP	None	None	Hypotony edema	Hypotony inflammation	None
No meds Preoperative	3.4	3	3	3	2.1	2	2.6	3.1	3.5	4.7	2.9
No meds at last FU	3.0	2.1	2	2	1.3	1	1.7	2.5	2.7	3.6	2.3
Ocular pain preoperative	Not reported	Not reported	Not reported	Not reported	8 patients	32%	Not reported	Not reported	Not reported	Not reported	Not reported
Ocular pain at last FU	Not reported	Not reported	Not reported	None	None	None	Not reported	Not reported	Not reported	None	Not reported

*Used 50 J; **Used 62.5 J; ***Pediatric patients; ****Adult patients

this study, no severe complications were observed. To augment the safety profile, we reported 13 patient complaints from most common redness to least common photophobia or conjunctival burn (Fig. 4). Overall, up to 75% of the eyes were fuss-free within 2 years postoperatively. Ocular pain after 1-month post-MPTLT was rarely reported in the literature. Aquino et al.[16] said that 32% of the eyes, Tan et al.[34] with eight eyes, and Jammal et al.[40] with three eyes experienced moderate to severe pain at 12 months postoperatively (Table 4). In our treated cohort, six eyes with moderate or severe pain were reported at 1 year, but no incidents were reported at 2 years. The proportion of pain-free eyes reached statistical significance at 1 and 2 years (Table 3).

IOP effects—mean and baseline reduction—were plotted against treated energy in Figure 5, and formal bivariate analysis was performed to detect an association between treatment and outcomes. This study did not find a significant IOP response to energy; while visual acuity (VA) decreases, mild complications and eye pain were significantly associated with higher energy.

Weighing all effects equally, the 50–75 J level achieved the optimal balance between efficacy and safety in this study. At 1- and 2-year follow-ups, eyes treated with L2 energy level revealed equal or better IOP reduction effects, least BCVA impact, lowest medication use, lowest rate of complications per eye, and over 95% pain-free. This finding supports the VA-based protocol proposed by Sarrafpour et al.[36] The researchers suggested an optimal effective energy of approximately 62 J (2000 mW, 100 seconds at 31.3% DC) for eyes with good vision (above CF). This finding is also in accordance with hypotheses by de Crom et al.[22] and Preda et al.[47] that duration with treatment could be scaled with IOP (less energy needed for lower preoperative IOP). These findings underline the importance of patient selection and careful consideration of potential confounding effects when determining optimal treatment parameters.

This study offers novel clinical evidence of MPTLT efficacy and safety. The strength of this study is the heterogeneity of the dataset, inclusiveness of a large spectrum of energy levels studied, and comprehensive records of responses. Two surgeons at the same center performed a relatively large number of cases in 5 years, using from 37 to 195 J in treatments. Our study, however, also has limitations. The heterogeneous characteristics of glaucoma diagnoses with approximately one-third of POAG, NVG, and childhood glaucoma may affect the outcomes since glaucoma types have been known to respond differentially to MPTLT.[13,16,33–35,40] Some other patient characteristics that may have influenced the differential outcomes between energy levels are severity, preoperative IOP, preoperative VA, and history of filtering or cyclodestruction surgery. Future work on multivariate characterization of MPTLT vs treatment parameters, glaucoma types, severity, preoperative IOP and VA, laser surgical history, age, and race may help further elucidate the effect of parameter settings.

Conclusion

This study used different MPTLT parameters to treat a cohort of patients with glaucoma. Significant IOP reductions were observed post-MPTLT, but no definitive associations were detected between IOP reduction and treatment times or effective delivered energy. VA decreases, patient complaints and eye pain were significantly

associated with energy >100 J. On good VA eyes in this study, we observed more significant IOP effects and fewer patient complaints or impact on vision with 80–120 second exposure at 31.3% duty cycle and 2000 mW. Our finding supports the hypothesis that MPTLT is safe and effective for eyes with good vision. However, patient selection and careful weighing of potential contributing effects are necessary when determining optimal treatment parameters.

Clinical Significance

MicroPluse transscleral laser therapy was found to be effective in lowering IOP in glaucoma. Using high levels of energy is associated with higher rates of complications.

Orcid

Julia Nguyen https://orcid.org/0000-0001-5130-1290
Orlando G González-Martínez https://orcid.org/0000-0003-1326-2782
Albert S Khouri https://orcid.org/0000-0002-0806-0898

References

1. What is glaucoma? Symptoms, causes, diagnosis, treatment. American Academy of Ophthalmology. 2022. https://www.aao.org/eye-health/diseases/what-is-glaucoma. Accessed on 12 Oct 2023.
2. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma. JAMA 2014;311(18):1901–1911. DOI: 10.1001/jama.2014.3192
3. Dastiridou AI, Katsanos A, Denis P, et al. Cyclodestructive procedures in glaucoma: a review of current and emerging options. Adv Ther 2018;35(12):2103–2127. DOI: 10.1007/s12325-018-0837-3
4. Glaucoma Laser Trial Research Group. The glaucoma laser trial (GLT) and glaucoma laser trial follow-up study: 7. results. Am J Ophthalmol 1995;120(6):718–731. DOI: 10.1016/S0002-9394(14)72725-4
5. Pantcheva MB, Kahook MY, Schuman JS, et al. Comparison of acute structural and histopathological changes of the porcine ciliary processes after endoscopic cyclophotocoagulation and transscleral cyclophotocoagulation. Clin Exp Ophthalmol 2007;35(3):270–274. DOI: 10.1111/j.1442-9071.2006.01415.x
6. Fong YYY, Wong BKT, Li FCH, et al. A retrospective study of transcleral cyclophotocoagulation using the slow coagulation technique for the treatment of refractory glaucoma. Semin Ophthalmol 2019;34(5):398–402. DOI: 10.1080/08820538.2019.1638946
7. Sanchez FG, Peirano-Bonomi JC, Grippo TM. Micropulse transscleral cyclophotocoagulation: a hypothesis for the ideal parameters. Med Hypothesis Discov Innov Ophthalmol 2018;7(3):94–100.
8. Liu GJ, Mizukawa A, Okisaka S. Mechanism of intraocular pressure decrease after contact transscleral continuous-wave Nd:YAG laser cyclophotocoagulation. Ophthalmic Res 1994;26(2):65–79. DOI: 10.1159/000267395
9. Maslin JS, Chen PP, Sinard J, et al. Histopathologic changes in cadaver eyes after MicroPulse and continuous wave transscleral cyclophotocoagulation. Can J Ophthalmol 2020;55(4):330–335. DOI: 10.1016/j.jcjo.2020.03.010
10. Pantcheva MB, Kahook MY, Schuman JS, et al. Comparison of acute structural and histopathological changes in human autopsy eyes after endoscopic cyclophotocoagulation and trans-scleral cyclophotocoagulation. Br J Ophthalmol 2007;91(2):248–252. DOI: 10.1136/bjo.2006.103580
11. Amoozgar B, Phan EN, Lin SC, et al. Update on ciliary body laser procedures. Curr Opin Ophthalmol 2017;28(2):181–186. DOI: 10.1097/ICU.0000000000000351
12. Michelessi M, Bicket AK, Lindsley K. Cyclodestructive procedures for non-refractory glaucoma. Cochrane Database Syst Rev 2018;2018(4):CD009313. DOI: 10.1002/14651858.CD009313.pub2
13. Souissi S, Le Mer Y, Metge F, et al. An update on continuous-wave cyclophotocoagulation (CW-CPC) and micropulse transscleral laser treatment (MP-TLT) for adult and paediatric refractory glaucoma. Acta Ophthalmol 2021;99(5):e621–e653. DOI: 10.1111/aos.14661
14. Sanchez FG, Peirano-Bonomi JC, Brossard Barbosa N, et al. Update on micropulse transscleral cyclophotocoagulation. J Glaucoma 2020;29(7):598–603. DOI: 10.1097/IJG.0000000000001539
15. Abdelrahman AM, El Sayed YM. Micropulse versus continuous wave transscleral cyclophotocoagulation in refractory pediatric glaucoma. J Glaucoma 2018;27(10):900–905. DOI: 10.1097/IJG.0000000000001053
16. Aquino MCD, Barton K, Tan AMW, et al. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. Clin Exp Ophthalmol 2015;43(1):40–46. DOI: 10.1111/ceo.12360
17. Selvam A, Ong J, Kumar RS, et al. Current systems and recent developments of subthreshold laser systems in glaucoma: a narrative review. Ann Eye Sci 2022;7:27–27. DOI: 10.21037/aes-21-69
18. Frizziero L, Calciati A, Midena G, et al. Subthreshold micropulse laser modulates retinal neuroinflammatory biomarkers in diabetic macular edema. J Clin Med 2021;10(14):3134. DOI: 10.3390/jcm10143134
19. Scholz P, Altay L, Fauser S. A review of subthreshold micropulse laser for treatment of macular disorders. Adv Ther 2017;34(7):1528–1555. DOI: 10.1007/s12325-017-0559-y
20. Radcliffe N, Vold S, Kammer JA, et al. Micropulse trans-scleral cyclophotocoagulation (mTSCPC) for the treatment of glaucoma using the micropulse P3 device. Presented at the American Glaucoma Society annual meeting; 2015.
21. Balendiran V, Landreneau J, An J. Micropulse transscleral laser therapy dosimetry utilizing the revised P3 delivery device: a randomized controlled trial. Ophthalmol Glaucoma 2023;6(3):283–290. DOI: 10.1016/j.ogla.2022.09.004
22. de Crom RMPC, Slangen CGMM, Kujovic-Aleksov S, et al. Micropulse trans-scleral cyclophotocoagulation in patients with glaucoma: 1- and 2-year treatment outcomes. J Glaucoma 2020;29(9):794–798. DOI: 10.1097/IJG.0000000000001552
23. Yelenskiy A, Gillette TB, Arosemena A, et al. Patient outcomes following micropulse transscleral cyclophotocoagulation: intermediate-term results. J Glaucoma 2018;27(10):920–925. DOI: 10.1097/IJG.0000000000001023
24. Fili S, Kontopoulou K, Vastardis I, et al. Transscleral cyclophotocoagulation with MicroPulse® laser versus Ahmed valve implantation in patients with advanced primary open-angle glaucoma. Int Ophthalmol 2021;41(4):1271–1282. DOI: 10.1007/s10792-020-01682-0
25. Grippo TM, Sanchez FG, Stauffer J, et al. MicroPulse® transscleral laser therapy—fluence may explain variability in clinical outcomes: a literature review and analysis. Clin Ophthalmol 2021;15:2411–2419. DOI: 10.2147/OPTH.S313875
26. Grippo TM, Töteberg-Harms M, Giovingo M, et al. Evidence-based consensus guidelines series for micropulse transscleral laser therapy—surgical technique, post-operative care, expected outcomes and retreatment/enhancements. Clin Ophthalmol. 2023;17:71–83. DOI: 10.2147/OPTH.S389198
27. Grippo TM, de Crom RMPC, Giovingo M, et al. Evidence-based consensus guidelines series for micropulse transscleral laser therapy: dosimetry and patient selection. Clin Ophthalmol 2022;16:1837–1846. DOI: 10.2147/OPTH.S365647
28. Keilani C, Benhatchi N, Bensmail D, et al. Comparative effectiveness and tolerance of subliminal subthreshold transscleral cyclophotocoagulation with a duty factor of 25% versus 31.3% for advanced glaucoma. J Glaucoma 2020;29(2):97–103. DOI: 10.1097/IJG.0000000000001409
29. Benhatchi N, Bensmail D, Lachkar Y. Benefits of subcyclo laser therapy guided by high-frequency ultrasound biomicroscopy in patients with refractory glaucoma. J Glaucoma 2019;28(6):535–539. DOI: 10.1097/IJG.0000000000001230

30. Sanchez FG, Lerner F, Sampaolesi J, et al. Efficacy and safety of micropulse® transscleral cyclophotocoagulation in glaucoma. Arch Soc Esp Oftalmol (Engl Ed) 2018;93(12):573–579. DOI: 10.1016/j.oftal.2018.08.003
31. Zaarour K, Abdelmassih Y, Arej N, et al. Outcomes of micropulse transscleral cyclophotocoagulation in uncontrolled glaucoma patients. J Glaucoma 2019;28(3):270–275. DOI: 10.1097/IJG.0000000000001174
32. Emanuel ME, Grover DS, Fellman RL, et al. Micropulse cyclophotocoagulation: initial results in refractory glaucoma. J Glaucoma 2017;26(8):726–729. DOI: 10.1097/IJG.0000000000000715
33. Williams AL, Moster MR, Rahmatnejad K, et al. Clinical efficacy and safety profile of micropulse transscleral cyclophotocoagulation in refractory glaucoma. J Glaucoma 2018;27(5):445–449. DOI: 10.1097/IJG.0000000000000934
34. Tan AM, Chockalingam M, Aquino MC, et al. Micropulse transscleral diode laser cyclophotocoagulation in the treatment of refractory glaucoma. Clin Exp Ophthalmol 2010;38(3):266–272. DOI: 10.1111/j.1442-9071.2010.02238.x
35. Lee JH, Shi Y, Amoozgar B, et al. Outcome of micropulse laser transscleral cyclophotocoagulation on pediatric versus adult glaucoma patients. J Glaucoma 2017;26(10):936–939. DOI: 10.1097/IJG.0000000000000757
36. Sarrafpour S, Saleh D, Ayoub S, et al. Micropulse transscleral cyclophotocoagulation: a look at long-term effectiveness and outcomes. Ophthalmol Glaucoma 2019;2(3):167–171. DOI: 10.1016/j.ogla.2019.02.002
37. Elhefney EM, Mokbel TH, Hagras SM, et al. Micropulsed diode laser cyclophotocoagulation in recurrent pediatric glaucoma. Eur J Ophthalmol 2020;30(5):1149–1155. DOI: 10.1177/1120672119858226
38. Tekeli O, Köse HC. Outcomes of micropulse transscleral cyclophotocoagulation in primary open-angle glaucoma, pseudoexfoliation glaucoma, and secondary glaucoma. Eur J Ophthalmol 2021;31(3):1113–1121. DOI: 10.1177/1120672120914231
39. Varikuti VNV, Shah P, Rai O, et al. Outcomes of micropulse transscleral cyclophotocoagulation in eyes with good central vision. J Glaucoma 2019;28(10):901–905. DOI: 10.1097/IJG.0000000000001339
40. Jammal AA, Costa DC, Vasconcellos JPC, et al. Prospective evaluation of micropulse transscleral diode cyclophotocoagulation in refractory glaucoma: 1 year results. Arq Bras Oftalmol 2019;82(5):381–388. DOI: 10.5935/0004-2749.20190076
41. Al Habash A, AlAhmadi AS. Outcome of MicroPulse® transscleral photocoagulation in different types of glaucoma. Clin Ophthalmol 2019;13:2353–2360. DOI: 10.2147/OPTH.S226554
42. Magacho L, Lima FE, Ávila MP. Double-session micropulse transscleral laser (CYCLO G6) for the treatment of glaucoma. Lasers Med Sci 2020;35(7):1469–1475. DOI: 10.1007/s10103-019-02922-1
43. Johnstone M, Wang R, Padilla S, et al. Transcleral laser induces aqueous outflow pathway motion and reorganization. 27th annual meeting of the American Glaucoma Society. 2017.
44. Kaba Q, Somani S, Tam E, et al. The effectiveness and safety of micropulse cyclophotocoagulation in the treatment of ocular hypertension and glaucoma. Ophthalmol Glaucoma 2020;3(3):181–189. DOI: 10.1016/j.ogla.2020.02.005
45. Radhakrishnan S, Wan J, Tran B, et al. Micropulse cyclophotocoagulation: a multicenter study of efficacy, safety, and factors associated with increased risk of complications. J Glaucoma 2020;29(12):1126–1131. DOI: 10.1097/IJG.0000000000001644
46. Souissi S, Baudouin C, Labbé A, et al. Micropulse transscleral cyclophotocoagulation using a standard protocol in patients with refractory glaucoma naive of cyclodestruction. Eur J Ophthalmol 2021;31(1):112–119. DOI: 10.1177/1120672119877586
47. Preda MA, Karancsi OL, Munteanu M, et al. Clinical outcomes of micropulse transscleral cyclophotocoagulation in refractory glaucoma-18 months follow-up. Lasers Med Sci 2020;35(7):1487–1491. DOI: 10.1007/s10103-019-02934-x
48. Vernon SA, Koppens JM, Menon GJ, et al. Diode laser cycloablation in adult glaucoma: long-term results of a standard protocol and review of current literature. Clin Exp Ophthalmol 2006;34(5):411–420. DOI: 10.1111/j.1442-9071.2006.01241.x
49. Rasmuson E, Lindén C, Lundberg B, et al. Efficacy and safety of transscleral cyclophotocoagulation in Swedish glaucoma patients. Acta Ophthalmol 2019;97(8):764–770. DOI: 10.1111/aos.14125Em consene cerunt volo beatum ut ut quassinum que nusam vellesti cum vel etum nos se et audae. Poressercias sunt dolorup tasperate voluptiberum quias excerior aut que verrum nem es elles dion ne