

## Micropulse Trabeculoplasty in Open Angle Glaucoma

### Abstract

**Background:** We report the effect of micropulse laser trabeculoplasty (MLT) in the intraocular pressure (IOP) of patients with uncontrolled open-angle glaucoma (OAG). **Materials and Methods:** In this retrospective review, 30 eyes with OAG were treated with a single session of MLT at the Vista Clinic in Lima Perú. We used a 532 nm frequency doubled Nd: YAG laser to 360° of the trabecular meshwork with a power of 1000 mW, 15% of the duty cycle, and 300 ms of exposure. The IOP was measured at baseline and at 1 day, 1 week, 3 months, and 6 months post-treatment and were followed up for one last control. **Results:** The mean baseline IOP was 15.6 mmHg and in the last control was 12.8 mmHg, mean follow-up time of 19 months ( $\pm 10$  standard deviation [SD]). The mean reduction of IOP in the 1<sup>st</sup> day was 1.6 mmHg ( $\pm 2.6$  SD) and 1.2 mmHg ( $\pm 3.3$  SD) in the last follow-up. The mean percentage of IOP reduction was 17.9% and 7 eyes (40%) had IOP reduction  $>20\%$ . No statistical significant difference in relation to demographic characteristics of the patients. The greatest reduction was achieved in the 1<sup>st</sup> day with a median of 2.00 ( $P < 0.001$ ). A tendency to achieve a higher reduction of IOP in patients with higher baseline IOP was found but was not statistically significant. No adverse reactions occurred. **Conclusions:** MLT slightly reduced the IOP in a few patients with uncontrolled OAG for a very short time and may not be suitable for these patients.

**Keywords:** Diode laser, micropulse, open angle glaucoma, subthreshold, trabeculoplasty

### Introduction

The second leading cause of blindness worldwide and the leading cause of irreversible blindness is glaucoma, accounting for 8% of all blindness, affecting an estimated 3.12 million blind people in the world.<sup>[1]</sup> The World Health Organization estimated that 12.3% of blindness was caused by glaucoma in 2002.<sup>[2]</sup> and there will be 79.6 million people with glaucoma by 2020.<sup>[3]</sup> The prevalence of OAG in Hispanics was 1.97%.<sup>[4]</sup> and in Perú was 2%.<sup>[5]</sup>

The main aim of the treatment is to lower the intraocular pressure (IOP) to stop the retinal nerve fiber layer damage and visual field loss. Topical antiglaucoma medications are used before surgery since the latter is related to complications, despite its effectiveness in reducing IOP. The use of laser in the trabeculum was initially described by Wise and Witter in 1979 with the argon laser trabeculoplasty (ALT);<sup>[6]</sup> in 1995 Latina and Park began to use the

selective laser trabeculoplasty (SLT);<sup>[7,8]</sup> since then, they became widely used for the treatment of OAG, and demonstrated to have similar efficacy to reduce the IOP compared to topical medications, avoiding the side effects of these.<sup>[9]</sup> Several studies demonstrated the same efficacy between these two procedures. However, SLT has the advantage that it does not leave a scar on the trabeculum and is repeatable.<sup>[8,10-14]</sup>

More recently, micropulse laser trabeculoplasty (MLT) was introduced, and its efficacy for lowering the IOP was compared with ALT,<sup>[15]</sup> despite the few data reported, it showed promising results.<sup>[16-18]</sup> This technology uses a duty cycle algorithm that delivers subthreshold treatment to ocular tissues without scar formation, making it safe to apply the laser even directly over the fovea and its widely used for the treatment of several retinal maculopathies.<sup>[19-21]</sup> It minimizes time in which laser-induced heat can spread to adjacent tissues resulting in the absence of collateral damage with an

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induced biological response to the trabecular meshwork that decrease the IOP<sup>[22-25]</sup> and like SLT does not damage the trabeculum. Its efficiency is still on debate. We report on the pressure lowering effect of MLT in patients with uncontrolled OAG.

## Materials and Methods

### Study design

It is a brief case report and we retrospectively reviewed the medical records of patients who undergone MLT at the Vista Clinic, Lima, Perú. Thirty-two MLT patients were treated between August and December 2014.

### Eligibility and exclusion criteria

The study complied with the Declaration of Helsinki. The Ethics Committee of San Marcos University approved the study and written informed consent was obtained from patients before the procedure.

The inclusion criteria included those with more than 40 years of age that had uncontrolled OAG (including pseudoexfoliation and pigmentary glaucoma as long as angles were open) that was defined as a persistently high IOP (or failing to achieve target IOP) or progression of visual field/retinal nerve fiber layer loss that were with medical therapy (application of one or a combination of two to four topical medications with/without oral hypotensive medical treatment) or had previous glaucoma surgery. Exclusion criteria included failure to obtain consent, patients with poor access to the angle on gonioscopy (two or more quadrants with iridotrabecular contact), patients who received prior laser trabeculoplasty, laser iridotomy, concomitant infection or inflammation, and infirmity sufficient to prevent the adequate application of the laser.

We analyze the pressure lowering effect and safety of the procedure and compared to various criteria such as age, sex, baseline IOP, and previous surgery on the outcome. Complications such as hypotony, loss of vision, IOP spikes, and anterior uveitis were also evaluated.

### Subjects, follow-up and measure the outcome

The procedure was explained to the patients, and written consent was obtained. Patients were evaluated at baseline, day 1, week 1, month 1, month 3, 6 months, and one last follow-up. At each visit, anterior segment examination, best-corrected visual acuity, and IOP measurements were performed. The IOP was measured using the Goldmann applanation tonometry (AT900, Haag-Streit, König, Switzerland). MLT success was defined as an IOP reduction of >20% after the procedure.

### Laser technique

The procedure was done with a frequency doubled Nd: YAG laser (Supra 532 Laser System; Quantel Medical, Clermont-Ferrand, France). The micropulse laser settings

were as follows: 300 µm spot size of diameter, 1000 mW of power, and 300 ms of duration with a 15% of duty cycle.

All MLT procedures were performed by a single surgeon. After a drop of topical anesthetic (proximetacaine 0.5%), the patient was seated at the slit lamp and a laser antireflective coated Goldmann three-mirror lens (Ocular Instruments, Bellevue, WA, USA) was placed on the eye to be treated. The laser was focused on the anterior trabecular meshwork, and confluent applications were administered over 360°. Since no visible laser-induced tissue change endpoint is produced at the trabecular meshwork, we relied on the surgeon's skill, resulting in a variable number of confluent and overlapping spots. The total number of laser applications delivered to each eye was recorded after each treatment. Immediately, after the treatment, diclofenac 0.1% eye drops were administered and continued three times daily for 5 days. The patients were maintained on their pretreatment drug regimen because most of the patients had advanced optic nerve damage. Patients received a single MLT treatment, and no retreatment was done. In patients with previous surgery, the procedure was done sparing the tube shunt or the trabeculectomy area.

### Statistics

Central tendency and dispersion values were determined for quantitative variables, as well as absolute and relative frequencies for categorical variables. The post-treatment values were compared with the baseline values using the Wilcoxon signed-rank test with significance corresponding to a  $P < 0.05$ . The Spearman correlation coefficient was used to assess the relationship between baseline IOP and the percent reduction on the last follow-up. Data were collected in a retrospective fashion from chart reviews and were analyzed using Stata® version 14 (StataCorp. 2015, Stata Statistical Software: Release 14. StataCorp LP, College Station, Texas, US).

### Results

The baseline demographic characteristics are listed in Table 1. In all, 30 eyes were evaluated. The mean age of the patients was 70 years, with a female: male ratio of 3:1. The average pretreatment cup-disc ratio was 0.85, 86.7% of the patients were on medications, 8 (26.7%) patients has previous glaucoma surgery and 76.7% of patients were phakic. From the eyes that had previous glaucoma surgery, only 4 (50%) were off medications. The mean follow-up period was 19 months (standard deviation [SD] ±10) with a maximum follow-up of 36 months [Table 1].

An average of 120 burns was applied per session. The mean pre-laser IOP was 15.6 mmHg (SD ±3.5) and the post-laser IOP at 1 day, 1 week, 1 month, 3 months, 6 months, and in the last follow-up, was 14.0, 14.7, 14.9, 15.2, 14.4, and 12.8 mmHg, respectively [Figure 1]. The average absolute reduction of IOP at the 1<sup>st</sup> day, 3 months, and in the last follow-up was 1.60, 1.1, and

**Table 1: Baseline demographic characteristics (n=30)**

Characteristics	Results
Age (years), mean±SD	70.20±10.5
Cup/disc ratio, mean±SD	0.85±0.12
Follow up (months), mean±SD	19.00±10
Sex, n (%)	
Female	22 (73.3)
Male	8 (26.7)
Previous glaucoma surgery, n (%)	
None	22 (73.3)
Trabeculectomy	6 (20.0)
Drainage device	2 (6.7)
Number of glaucoma medication, n (%)	
0	4 (13.3)
1 drop	8 (26.7)
2 drops	8 (26.7)
3 drops	6 (20.0)
4 drops	4 (13.3)
Lens status, n (%)	
Phakic	23 (76.7)
Pseudophakic	7 (23.3)

SD: Standard deviation

1.2 mmHg, respectively [Table 2]. Post-laser immediate drop (at the 1<sup>st</sup> day) has a median of 2.00 mmHg and was statistically significant (CI - 3.00–0, *P* = 0.0012) [Table 3]. At 1<sup>st</sup> day, the IOP was reduced by 10.3% and in the last follow-up was 17.9%. Table 4 shows the distribution of the percentage of eyes with IOP reduction ≥20%, and <20% through the entire follow-up. 30% (*n* = 9) of the eyes had an IOP reduction ≥20% at the 1<sup>st</sup> day and 7 (41%) in the last control [Figure 2]. Some patients were lost in the follow-up. In addition, there was a trend toward greater IOP reduction with higher baseline IOP, but this was not statistically significant due to the small sample and design of the study [Figure 3].

The patients were maintained on their pretreatment drug regimen, and no changes were applied in their medications. The treatment was uneventful in 100% of patients with no thermal pain and no uncomfortable laser flashes, none of the patients had a significant inflammatory reaction that was documented during the follow-up. There were no pressure spikes. At the last follow-up, no patient had peripheral anterior synechiae. Visual acuity was unchanged in all eyes. There was no statistically significant difference in IOP reduction between groups (age, cup-to-disc ratio, phakic state, number of medications, and previous glaucoma surgery).

**Discussion**

The idea behind the pulsed laser delivery system is to minimize thermal energy and therefore, its resultant physiological damage to ocular tissue. Similar technology has been adapted to other subspecialties of ophthalmology,

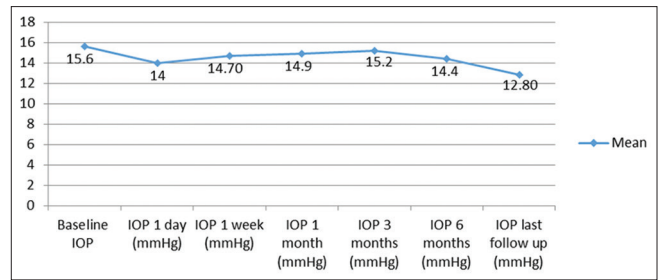


Figure 1: Mean intraocular pressure at various time points up to the last follow up

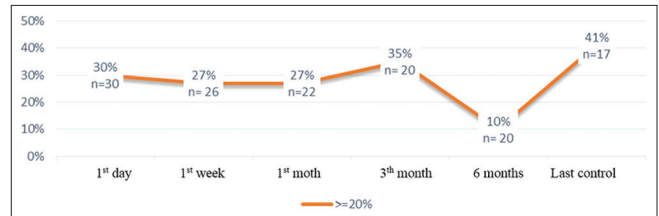


Figure 2: Percentage of eyes with intraocular pressure reduction >20% from baseline

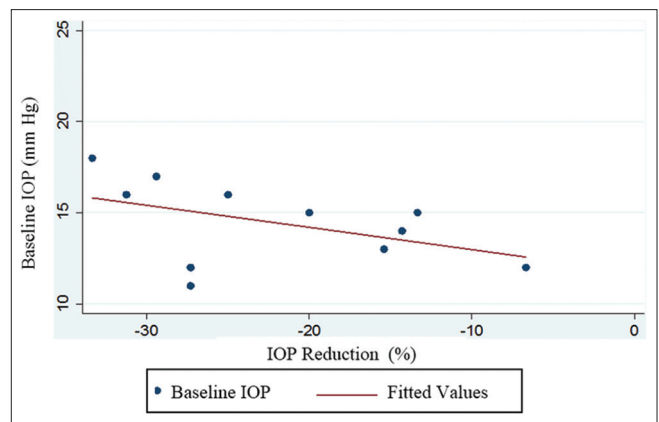


Figure 3: Baseline intraocular pressure and percentage of reduction

including retinal diseases<sup>[21]</sup> and phacoemulsification for cataract surgery.

SLT and MLT differ in their theoretical mechanisms of actions. SLT targets intracellular melanin and activates macrophages,<sup>[26]</sup> and selectively damages pigmented cells in the trabecular meshwork, which may induce postoperative inflammation and IOP spikes. MLT thermally affects trabecular cells without destroying them by allowing a cooling period between pulses, thereby preventing tissue destruction. The goal of MLT is to stimulate a biological response with the trabecular meshwork while reducing tissue damage.<sup>[22,24,27]</sup>

MLT does not result in any cellular destruction, scarring, or collateral damage because it uses a pulsed wave (15% duty cycle) rather than a continuous laser wave (100% duty cycle) into the trabeculum.<sup>[24]</sup>

In our experience, the maximum IOP reduction was achieved at the 1<sup>st</sup> day and only half of the

**Table 2: Mean intraocular pressure with standard deviation and mean intraocular pressure reduction from baseline at various time points up to the last follow up**

Intraocular pressure data	Baseline (n=30)	1 day (n=30)	1 week (n=26)	1 month (n=22)	3 months (n=20)	6 months (n=20)	Last follow up (n=17)
Mean IOP (mmHg)±SD	15.6±3.5	14±3.2	14.7±3.5	14.9±4.9	15.2±5.3	14.4±3.2	12.8±2.6
Minimum–maximum	10–25	9–22	10–24	10–30	10–30	11–24	08–20
IQR	13–17	12–16	12–16	12–15	12–16	12–16	12–14
Mean IOP reduction (%)		10.2	5.7	4.4	2.5	7.7	17.9

IQR: Interquartile range, SD: Standard deviation, IOP: Intraocular pressure

**Table 3: Intraocular pressure reduction from baseline (median and interquartile range) at various time points up to the last follow up and P value**

IOP reduction (mmHg)	Median	IQR	P*
1 day	-2.00	-3 to 0	0.001
1 week	-1	-3 to 1	0.0997
1 months	-1	-3 to 0	0.0263
3 months	-2	-3 to 1	0.3191
6 months	0.5	-1.5 to 2	0.986
Last follow up	-2	-3 to 1	0.1106

\*Wilcoxon signed rank test. IQR: Interquartile range, IOP: Intraocular pressure

**Table 4: Distribution of the percentage of eyes with intraocular pressure reduction ≥20%, and <20% through the entire follow up**

Follow up	n	IOP reduction n (%)	
		≥20 mm Hg	<20 mm Hg
1 day	30	9 (30)	21 (70)
1 week	26	7 (27)	19 (73)
1 month	22	6 (27)	16 (73)
3 months	20	7 (35)	13 (65)
6 months	20	2 (10)	18 (90)
Last follow up	17	7 (41)	10 (59)

IOP: Intraocular pressure

patients (17 eyes) were followed until the end (19 months) with a mean IOP reduction of 17.9%; these findings are lower than those obtained in previous studies [Table 5], Ingvaldstad *et al.*<sup>[15]</sup> and Detry-Morel *et al.*,<sup>[23]</sup> reported IOP reductions of 18.3% and 12.2% respectively with an 810 nm diode laser in 3 months. Gossage<sup>[16]</sup> used a 532 nm diode laser and performed 3 dosages 300, 700, and 1000 mW, obtaining a drop of 18%, 21% and 30% of IOP, respectively, at 4 months; at 24 months, he achieved a 24% reduction; no more data was reported about the patients or the need for additional topical medication.

Fea *et al.*<sup>[17]</sup> performed MLT (810 nm diode laser system) with 2000 mW of power in a cohort of 20 patients; they achieve an IOP reduction of 21.3% at 12 months and ten of the 15 eyes (66.7%) had an IOP reduction >20% at the 1<sup>st</sup> day, through the end of the study almost half of the patients maintained this success in comparison with

other studies that only 35.7% of patients achieved such a reduction.<sup>[23]</sup> Others like Lee *et al.*<sup>[25]</sup> used a 577 nm diode laser system with an IOP reduction of 19.5% at 6 months; 35 (72.9%) patients achieved an IOP reduction of ≥20% at the 1<sup>st</sup> month. Unlike other studies, we only achieved an IOP reduction of ≥20% in 7 (35%) and 7 (41%) eyes at 3 months and at the last follow-up, respectively. In a retrospective case series carried out by Babalola<sup>[28]</sup> the average immediate drop (1 h) in IOP was 17.2% and was sustained through time with a mean follow-up of 5 months using an 810-nm diode laser, but no specific data were reported in this study. Abouhussein<sup>[29]</sup> used a 577-nm diode laser with a 15% duty cycle in 30 eyes with topical treatment, achieving a 12% reduction of IOP at the 1<sup>st</sup> day, 25% at 1 month and 21% at 6 months.

In addition, we found a trend toward greater IOP reduction with higher base line IOP but this was not statistically significant due to the small sample and design of the study; at least 29 patients would be needed in the last control to have a statistically significant result, considering a moderate lineal correlation ( $r = 0.5$ ), with a 95% of confidence level and 80% of power which means no loss to follow-up. This finding is correlated with several studies that evaluate the predictive factors for success with SLT.<sup>[30,31]</sup> Unlike other studies, we did not observe a significant inflammatory response.<sup>[17,23]</sup>

One major limitation of this study is the absence of a comparison group, to standard SLT or medical treatment, other several limitations were, a small number of patients, its retrospective nature, not all patients were examined at specific time intervals, there was a considerable loss of the number of patients through the follow-up. About 26.7% of the patients had a previous glaucoma surgery, and most of the patients were on topical medical treatment, and hence, there were many confounding effects.

Randomized clinical trials are needed to compare MLT with current IOP-lowering laser therapies, or antiglaucoma medications. The effect may not be long lasting in all cases, and some patients will not respond to the therapy. It is, however, repeatable because damage to the trabeculum is minimal.

Clearly, the IOP reduction after MLT is very low and his very short duration make this procedure not suitable for patients with uncontrolled OAG. We are still in the need of



**Table 5: Previous studies and comparison**

Authors	Study	Eyes	Laser wave length/ power/duty cycle	Maximum IOP reduction	Time at maximum IOP reduction	IOP reduction at last follow up	Last follow up	Percentage of patients achieving >20% reduction/follow up time
Valera <i>et al.</i> , 2017	RCS	30	532 nm/1000 mW/15%	10.2%	1 day	17.9%*	19 months	27%/1 month
Abouhussein, 2016 <sup>[29]</sup>	PCS	30	577 nm/1000 mW/15%	25%	1 month	21%	6 months	-
Chadha <i>et al.</i> , 2014 <sup>[18]</sup>	PCI	23 SLT	-	19% SLT	1 month	14.9% SLT	3 months	-
		25 MLT		16% MLT		16% MLT		
Gossage, 2014 <sup>[16]</sup>	PCS	18	532/1000 mW/15%	30%	4 months	24%	24 months	-
Babalola, 2015 <sup>[28]</sup>	RCS	30	810 nm/1000 mW/15%	17.2%	1 hour	-	5 months	-
Lee <i>et al.</i> , 2015 <sup>[25]</sup>	PCS	48	577 nm/1000 mW/15%	31%	1 day	19%	6 months	73%/1 month
Detry-Morel <i>et al.</i> , 2008 <sup>[23]</sup>	PCI	15 ALT	810 nm/2000 mW/15%	-	-	21% ALT	3 months	37%/3 months
		16 MLT				12% MLT		
Fea <i>et al.</i> , 2008 <sup>[17]</sup>	PCS	32	810 nm/2000 mW/15%	23.8%	1 month	21%	12 months	50%/1–12 months
Ingvoldstad <i>et al.</i> , 2005 <sup>[15]</sup>	PCI	21	-	-	-	18.9% ALT	3 months	-
						18.5% MLT		

\*Only half of the patients were evaluated at the last follow up, -: No data. PCS: Prospective case series, RCS: Retrospective case series, PCI: Prospective comparative interventional, IOP: Intraocular pressure, ALT: Argon laser trabeculoplasty, MLT: Micropulse laser trabeculoplasty, SLT: Selective laser trabeculoplasty

better and larger studies, identifying the ideal patient and customizing laser parameters for this procedure.

## Conclusions

MLT slightly reduced the IOP in a few patients with uncontrolled OAG for a very short time, making this procedure unsuitable for these patients.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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