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# MicroPulse Laser Trabeculoplasty for the Treatment of Open-Angle Glaucoma

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**Abstract:** The aim of the study was to investigate the safety and efficacy of using MLT in the treatment of open-angle glaucoma (OAG).

This prospective cohort included subjects  $\geq 18$  years of age with OAG, defined as the open angle on gonioscopy with glaucomatous optic neuropathy evident from optical coherence tomography. Subjects with IOP  $< 21$  mm Hg were classified as normal tension glaucoma and those with IOP  $\geq 21$  mm Hg were classified as primary open-angle glaucoma. Those with angle closure, secondary glaucoma, prior laser trabeculoplasty, use of systemic IOP-lowering medications, corneal pathologies, follow-up  $< 6$  months, recent intraocular surgery, or only 1 functional eye were excluded. A single session of unilateral MLT treatment was delivered using a 577 nm diode laser to 360° of the trabecular meshwork to reduce IOP or medication load. Medications were titrated up or down at 1 month after laser to achieve a 25% IOP reduction from presentation or an IOP  $< 18$  mm Hg, whichever was lower. The following were compared using the Repeated Measures ANOVA with Bonferroni's Multiple Comparison Test: IOP (on presentation, pre-MLT, day 1, 1 week, 1 month, 3 months, and 6 months after MLT) and the number of medications (pre-MLT, 3 months, and 6 months after MLT). After 6 months, responders with initial success to MLT (IOP reduction  $\geq 20\%$  at 1 month) received treatment in the fellow eye.

In 48 subjects with OAG, the mean number of MLT shots applied was  $120.5 \pm 2.0$  shots using a mean energy of 1000 mW per shot. Only 7.5% had a mild, self-limiting anterior uveitis postlaser with no change in the Snellen visual acuity at 6 months ( $P > 0.5$ ). The IOP and number of medications were significantly reduced at all time intervals following MLT compared to the pre-MLT level ( $P < 0.0001$ ). At 6 months, the IOP was reduced by 19.5% in addition to a 21.4% reduction in medication compared to pretreatment levels. The MLT success rate was 72.9%. During the first 6 months only 2.1% required a repeated laser trabeculoplasty.

MLT was effective in reducing IOP and medications in OAG with minimal postlaser inflammation and low failure rate at 6 months following laser.

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**Abbreviations:** ALT = argon laser trabeculoplasty, IOP = intraocular pressure, MLT = MicroPulse laser trabeculoplasty, NTG = normal tension glaucoma, OAG = open-angle glaucoma, OCT = Optical coherence tomography, POAG = primary open-angle glaucoma, RNFL = retinal nerve fiber layer, SLT = selective laser trabeculoplasty.

## INTRODUCTION

The main aim of treatment in primary open-angle closure glaucoma (POAG) is to lower the intraocular pressure (IOP) to decelerate visual field and retinal nerve fiber layer deteriorations. Topical antiglaucoma medications are commonly used as first-line treatment before surgery to reduce the exposure to surgical complications.<sup>1</sup> In the past, argon laser trabeculoplasty (ALT) and later, selective laser trabeculoplasty (SLT) have been demonstrated to have a similar IOP-lowering efficacy as medications but without their side effects such as ocular irritation, allergies, redness, dryness, or inconvenience; laser trabeculoplasty has also been demonstrated to potentially reduce IOP-related fluctuations on 24-h recordings.<sup>2-8</sup>

More recently, MicroPulse laser technology used a duty-cycle algorithm that delivers subthreshold treatment to ocular tissues without scar formation, making it safe to apply the laser directly over the fovea for the treatment of macular edema in diabetic retinopathy, retinal vein occlusion, and central serous chorioretinopathy.<sup>9-11</sup> MicroPulse technology can also be used for the treatment of open-angle glaucoma (OAG) via a laser trabeculoplasty procedure that delivers laser energy at low-irradiance, 300- $\mu$ s pulses to the pigmented cells in the trabecular meshwork. The permeability of the trabecular meshwork is increased after the laser due to the release of inflammatory cytokines and the IOP is reduced. Due to the MicroPulse subthreshold treatment technology and the longer laser wavelength (532 or 577 nm), MicroPulse Laser Trabeculoplasty (MLT) is superior to ALT because there is no collateral damage.<sup>10,12</sup> Whereas both SLT and MLT do not cause trabecular meshwork scarring, MLT has theoretical advantages over SLT by not destroying the pigmented trabecular meshwork cells. Preliminary small-scale studies have found comparable results in terms of IOP reduction between MLT and SLT.<sup>13</sup>

The aim of this study was to prospectively investigate the safety and efficacy of using MLT in the treatment of OAG.

## Patients and Methods

This study adhered to the tenets of the Declaration of Helsinki. Informed patient consent and approval by the Institutional Review Board of The Hospital Authority of Hong Kong were obtained prior to study commencement. The authors

declare no financial or conflicting interests. No research funding was received for this study. Provision of the MicroPulse laser machine was lent by Iridex Corporation.

This was a prospective cohort study conducted at Cartias Medical Centre in Hong Kong Special Administrative Region from 2014 to 2015. Subjects were consecutively recruited from a Specialist Outpatient Ophthalmology Clinic. The inclusion criteria included those  $\geq 18$  years of age with OAG on anti-glaucoma medications, defined as the open angle on gonioscopy (Shaffer grading  $> 1$  in  $270^\circ$ ) in the presence of progressive retinal nerve fiber layer thinning on Optical Coherence Tomography (OCT). It is known that structural loss precedes functional loss in glaucoma and that 50% of ganglion cell loss is required prior to the onset of visual field defects.<sup>14,15</sup> The OCT can detect preperimetric disease and it is a repeatable tool that has a high degree of diagnostic sensitivity and specificity in the diagnosis and monitoring of glaucoma.<sup>16,17-19</sup> Those with a Goldmann applanation measured IOP  $< 21$  mm Hg on all documented clinical visits were classified as having normal tension glaucoma (NTG) and those with an IOP  $\geq 21$  mm Hg of any documented visit were classified as POAG. Subjects were given the option of a unilateral MLT treatment in 1 eye first, with the aim of reducing IOP and/or the number of medications as well as a unilateral therapeutic trial to evaluate their individual response to laser trabeculoplasty prior to treatment in the fellow eye.<sup>20</sup> Shuffling and drawing of cards with a premarked “right eye” or “left eye” was used to randomize the treatment eye whereas the fellow eye was kept on the same medication. The treatment eye was made known to the subject who signed an informed consented prior to laser. After 6 months, subjects who were successful responders to the initial MLT treatment ( $\geq 20\%$  IOP reduction) were given the option to receive laser trabeculoplasty in the fellow eye. Cases were excluded if they had angle closure, secondary glaucoma, received prior laser trabeculoplasty, taking any systemic medications that may affect IOP (such as oral acetazolamide), corneal pathologies or scars, follow-up  $< 6$  months, any intraocular surgery within the first 6 months of MLT, or in those with only 1 functional eye.

Baseline measurements including the presenting IOP (prior to the start of antiglaucoma medication), the pre-MLT IOP (with medication), and the number of medications used pre-MLT were recorded. Fixed combination medications were counted as 2 types of antiglaucoma medication.

Prior to treatment, an individual post-MLT target IOP was calculated for each subject as either a 25% IOP reduction from the presenting IOP as per the Early Manifest Glaucoma Trial<sup>21</sup> or an IOP  $\leq 18$  mm Hg as per the Advanced Glaucoma Intervention Study,<sup>22</sup> whichever was lower. This target serves as a clinical reference for the addition or subtraction of antiglaucoma medications after MLT in hope to maintain an IOP that minimizes disease progression. The definition of MLT success on the other hand is defined as an IOP reduction of  $\geq 20\%$  after MLT while on the same number of antiglaucoma medications (prior to medication titration).

### Laser Technique:

Prior to MLT, 2 drops of topical anesthesia (proparacaine hydrochloride 0.5%) were applied the treatment eye 5 min apart. All patients received a single session of MLT by a single surgeon (JWYL) using a Diode True-Yellow 577 nm Laser with MicroPulse technology (IQ 577<sup>TM</sup> Laser System, Iridex Corporation, 1212 Terra Bella Avenue, Mountain View, CA) with the following settings as detailed in Table 1.

**TABLE 1. MLT Laser Settings**

Laser Wavelength	577 nm
Contact lens	MLT lens
Spot size	300 $\mu$ m
Treatment duration	300 ms
Power	1000 mW
Duty cycle	15% duty, 85% rest
Degree of treatment	$360^\circ$ confluent applications (120 shots)
Location of treatment	Pigmented trabecular meshwork

MLT = MicroPulse laser trabeculoplasty.

The MLT lens is a laser goniolens with an integrated, visible, inner reference guide that allow the surgeon to deliver exactly 10 confluent laser shots per clock hour. The lens can then be rotated via a rotating indexing ring to facilitate treatment to the other clock hours.

Subjects were immediately sent home after the procedure and no post-MLT medications were required apart from the patient's preexisting antiglaucoma medications. Subjects were kept on the same number and type of antiglaucoma medications for the first month after MLT. After 1 month, antiglaucoma medications were titrated up if the IOP was above the individual target IOP and titrated down if the IOP was below the target. The protocol for antiglaucoma medication titration was as follows.

### Medication Step-Down

Pilocarpine, topical carbonic anhydrase inhibitors, B-blockers, alpha-adrenergic agonists, and then prostaglandin analogs.

### Medication Step-up

Prostaglandin analogs, adrenergic agonists, B-blockers, topical carbonic anhydrase inhibitors, and then pilocarpine.

When multiple medications were required, fixed combination medications were given to simplify the drug regimen.

The primary outcome measures included: the Goldmann applanation measured IOP and the number of medications at the following time intervals: pre-MLT and day 1, 1 week, 1 month, 3 months, and 6 months after MLT. IOP was measured once per visit, usually between 2 and 4 PM. The secondary outcome measures included: the success rate (IOP reduction  $\geq 20\%$  at 1 month from pre-MLT level), complications from MLT including the incidence of reactive uveitis, visual acuity before and after MLT, as well as the number of subjects requiring additional antiglaucoma lasers or surgery. A repeated laser trabeculoplasty was offered at any time point following MLT for subjects with an IOP  $> 21$  mm Hg on 2 clinical visits despite maximally tolerated topical medications. For those with IOP  $> 25$  mm Hg, a filtration surgery was offered.

### STATISTICS

Data was tested for normality using the D'Agostino & Pearson omnibus normality test and the.

Bartlett's test was used to test for sphericity.

The following were compared using the repeated measures ANOVA with Bonferroni's Multiple Comparison Test.

- (1) *Treatment eye IOP*: presentation, pre-MLT, day 1, 1 week, 1 month, 3 months, and 6 months after MLT.

**TABLE 2.** Patient Demographics

Baseline Characteristics	N = 53
Laterality:	
Right	70.8%
Left	29.2%
Gender:	
Male	70.8%
Female	29.2%
Type of glaucoma:	
Primary open angle glaucoma	81.6%
Normal tension glaucoma	16.7%
Phakic status:	
Phakic	70.8%
Pseudophakic	29.2%
Mean baseline visual field:	
Pattern standard deviation	6.3 ± 3.4 dB
Visual field index	61.2 ± 33.8%
Mean baseline OCT	
Average RNFL	59.2 ± 16.5 μm
Mean baseline VCDR	0.8 ± 0.13

OCT = optical coherence tomography, RNFL = retinal nerve fiber layer, VCDR = vertical cup-disc ratio.

- (2) *Treatment eye medications:* pre-MLT, 3 months, and 6 months after MLT.
- (3) *Visual acuity:* pre-MLT, 1 month, and 6 months after MLT.

A post-hoc paired *t* test was performed to compare all pairs of the independent variable to determine the significance detailed in Table 2.

**RESULTS**

In 48 eyes of 48 subjects with OAG (POAG or NTG), all were of Chinese ethnicity with a Shaffer angle grading ≥ 3 in terms of angle openness and a Spaeth trabecular meshwork pigmentation grading ≥ 3. The patient demographics were summarized in Table 3.

The mean number of MLT shots applied was 120.5 ± 2.0 using a mean energy of 1000 mW per shot. There were no significant complications from the procedure and 7.5% had a mild, self-limiting anterior uveitis that occurred between 1 and 4 weeks postlaser. None of the eyes experience IOP spikes after MLT. The Snellen visual acuity was statistically similar before laser (0.5 ± 0.2) as well as at 1 month (0.5 ± 0.2) and 6 months after laser (0.5 ± 0.3) (all *P*'s > 0.5).

The data was tested and confirmed to be of a Gaussian distribution. Bartlett's test for sphericity demonstrated an approximate chi square of 108.9 and a significant of 0.000, confirming that the data is not an identity correlation matrix, allowing for repeated-measures ANOVA analysis. The IOP was significantly reduced at all time intervals following MLT compared to the pre-MLT level (Table 3, Figure 1, all *P*'s < 0.0001). The number of medications at 3 and 6 months after MLT were also significantly reduced compared to the pre-MLT level (Table 3, all *P*'s < 0.0001). At 6 months, the IOP was reduced by 19.5% in addition to a 21.4% reduction in medication use compared to pretreatment levels. Comparison of the mean IOP reductions between the POAG (22.6 ± 12.5%, range: 0–63.6%, 95% CI: 18.7–26.5%) and NTG (30.3 ± 9.2%, range: 18.8–44.4%, 95% CI: 20.7–40.0%) group did not show any statistical difference (*P* = 0.2).

At 1 month, 35/48 subjects had an IOP reduction ≥ 20%, representing a 72.9% MLT success rate, with a mean IOP reduction of 23.8% from pre-MLT levels among all treated subjects. During the first 6 months following MLT, only 1/48 subject (2.1%) required a repeated laser trabeculoplasty for an IOP of 22 mm Hg occurring at 6 months post-MLT (Figure 2). None of the subjects required any glaucoma filtration surgery following MLT.

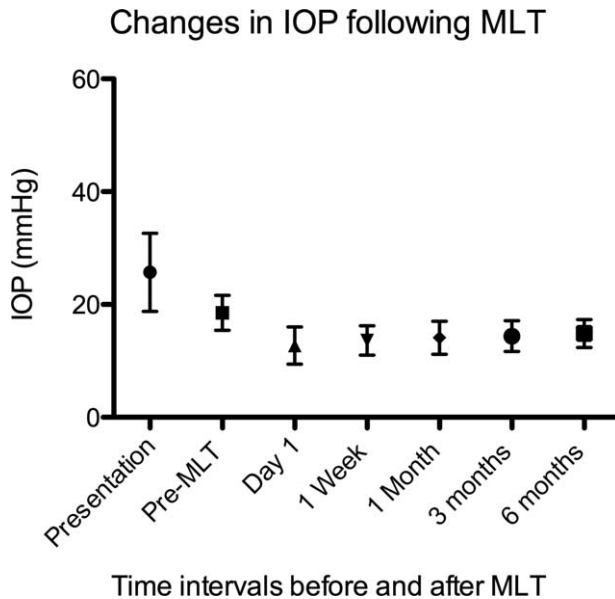
**DISCUSSION**

MLT differs from the former laser trabeculoplasty procedures, ALT and SLT, in that it uses a pulsed laser treatment (15% duty cycle) rather than a continuous laser wave (100% duty cycle). Histologically, ALT causes shrinkage with adjacent stretching and scarring of the trabecular meshwork. SLT selectively destructs the pigmented trabecular meshwork cells without causing collateral damage. MLT, on the other hand, does not result in any cellular destruction, scarring, or collateral damage.<sup>23</sup>

**TABLE 3.** Changes in IOP and Number of Medications Following MLT

Intraocular Pressure:	mm Hg ± SD	Percentage Reduction from the Pre-MLT Level (%)	<i>P</i> Value
Presenting	25.7 ± 6.9	–	–
Pre-MLT	18.5 ± 3.0	–	–
Day 1 post-MLT	12.7 ± 3.2	–31.4	<0.0001
1 Week post-MLT	13.6 ± 2.6	–26.5	<0.0001
1 Month post-MLT	14.1 ± 2.9	–23.8	<0.0001
3 Months post-MLT	14.4 ± 2.7	–22.2	<0.0001
6 Months post-MLT	14.9 ± 2.5	–19.5	<0.0001
Medications:	Mean number of medications ± SD	Percentage reduction from the pre-MLT level (%)	<i>P</i> value
Pre-MLT	2.8 ± 1.7	–	–
3 Months post-MLT	2.3 ± 1.1	–17.9	<0.0001
6 Months post-MLT	2.2 ± 1.1	–21.4	<0.0001

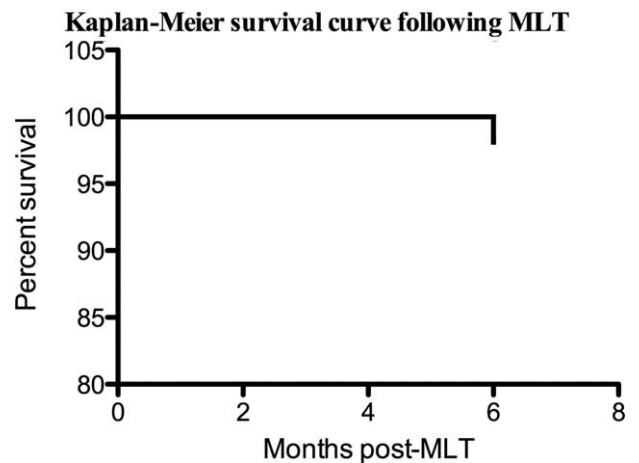
IOP = intraocular pressure, MLT = MicroPulse laser trabeculoplasty, SD = standard deviation.



**FIGURE 1.** Changes in IOP following MLT with standard deviation bars above and below the mean. IOP = intraocular pressure, MLT = MicroPulse laser trabeculoplasty.

In a randomized prospective trial by Detry-Morel et al, 26 POAG subjects were randomized to receive either MLT using a diode laser (810 nm) versus ALT. The MLT group had significantly less IOP reduction ( $12.2 \pm 11.9\%$ ) compared to the ALT group ( $21.8 \pm 11.1\%$ ), although MLT induced less anterior chamber inflammation and did not result in any pain during the procedure.<sup>13</sup> In the present study, we used a 577 nm wavelength MLT system and our mean IOP reduction following laser, prior to medication titration, was 24% and only 7.5% of our subjects had a mild self-limiting anterior chamber reaction. The number of medications required by our subjects at 6 months was  $2.2 \pm 1.1$ . In the study by Detry-Morel et al, the number of medications at 3 months was  $2.1 \pm 0.8$ .<sup>13</sup> We postulate that the greater IOP reduction in our study was attributed to the closer proximity of our MLT wavelength (577 nm) to that of SLT (532 nm), as the 810 nm MLT laser may not be targeting the pigmented trabecular meshwork cells adequately.

In a retrospective study involving 180° treatment of 40 POAG using an 810 nm diode MLT, the success rate (IOP reduction  $\geq 20\%$ ) was only 2.5% (1/40).<sup>24</sup> In our study, 73% of eyes that received 360° treatment achieved success with MLT. Our findings were consistent with Fea et al who reported using the 810 nm MLT that 75% of treated patients had an IOP reduction, with 60% of patients having  $>20\%$  IOP reductions.<sup>25</sup> The higher success rate in our study may be related to our use of the 577 nm MLT laser and our 360° treatment protocol. The correlation between the extents of angle treatment versus laser success has been well documented for SLT, with 360° treatment being most favorable followed by 180° then 90° treatment.<sup>26</sup> For SLT, delivering a higher total energy has been demonstrated to increase the amount of IOP reduction with no permanent changes to the cornea.<sup>27,28</sup> In MLT, no such evidence exists on the optimal number of laser shots but Ahmed et al reported that at 4 months postlaser, the greatest IOP reduction was achieved when using an energy of 1000 mW per shot as compared to 300 mW or 700 mW.<sup>29</sup> This formed the basis of our treatment



**FIGURE 2.** Kaplan-Meier survival curve following MLT, where mortality = need of a repeat laser trabeculoplasty for IOP  $> 21$  mm Hg at any time point following MLT. IOP = intraocular pressure, MLT = MicroPulse laser trabeculoplasty.

protocol in delivering a mean of 1000 mW per shot in each patient. Unlike in the former ALT and SLT where champagne bubble formation is visible on the trabecular meshwork during treatment, MLT does not result in any visible tissue reaction or endpoint during treatment making energy titration more difficult than the former technologies.

When compared to SLT, the amount of IOP reduction with MLT was comparable to that of SLT in a similar POAG population. In a randomized control trial comparing SLT versus topical antiglaucoma medication alone for a population of 41 Chinese POAG subjects, the SLT-treated subjects had a mean IOP reduction of 15% and medication reduction of 35% at 6 months compared to baseline, which in principle was comparable to our 6-month IOP reduction of 20% and medication reduction of 21%; in the present study, a 5% lower IOP was achieved at the expense of using 14% more medication but on the whole, subjects in both the SLT and MLT studies benefited from substantial IOP and medication reductions.<sup>30</sup> In terms of laser response, previous SLT studies reported a mean IOP reduction of 18% to 22% and a success rate of 47% to 62% at 1 month compared to pretreatment baseline prior to medication adjustment, depending on the type of glaucoma (POAG or NTG) and the pre-laser parameters such as IOP and the number of medications, which have been found to influence SLT success.<sup>31-34</sup> In the present MLT study, the mean percentage of IOP reduction (24%) and success rate (73%) at 1 month were slightly higher than that reported in previous SLT studies, for a similar OAG population, although a future head-to-head comparative study between SLT and MLT would be required to validate these preliminary observations.

No postlaser medications were required after MLT and only 7.5% of our subjects had a self-limiting anterior chamber reaction postlaser. At 6 months, only 1 subject (2.1%) required a repeated laser trabeculoplasty following MLT, which was comparable to the mean 1-year survival rate of 95% in a study involving 41 NTG subjects treated with SLT.<sup>35</sup>

The study had its limitations. It would have been ideal to treat naive eyes that did not use any antiglaucoma medications before as to prevent the confounding IOP-lowering effects of medications but the setting of the study also represents a more



realistic clinical scenario where laser trabeculoplasty is often offered to glaucoma patients with preexisting medication to further reduce IOP or medication use. Furthermore, this study was limited by a potential regression to the mean and the relatively short follow-up; future studies reporting the long-term results would provide a more in-depth understanding of this novel technology. The study population involves pigmented OAG subjects previously on medications; thus the results may not be generalizable to other populations.

To the best of our knowledge, this is one of the largest prospective trials involving MLT in the treatment of OAG, demonstrating that a single treatment was effective in reducing the IOP by 20% and medication use by 21% at 6 months with an initial laser success rate of >70%. The procedure was well tolerated, with the majority (>90%) of treated subjects having no postlaser anterior chamber reaction nor required any further glaucoma lasers or procedures at up to 6 months following MLT.

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