REVIEW

Outcomes of Micropulse Laser Trabeculoplasty Compared to Selective Laser Trabeculoplasty: A Systematic Review and Meta-Analysis

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Purpose: To perform a meta-analysis and systematic review to compare the efficacy and complications of micropulse laser trabeculoplasty (MLT) and selective laser trabeculoplasty (SLT) in adult patients with open-angle glaucoma (OAG) and ocular hypertension (OHT).

Methods: We performed a systematic review utilizing PubMed, Embase, and Scopus, on April 8, 2024. Meta-analyses were performed for the mean change in intraocular pressure (IOP) at one-month, six-month, and one-year follow-up visits, rate of IOP spikes (>5 mmHg increase from the pre-procedure baseline IOP), rate of treatment failure (<20% or <3 mmHg reduction in IOP or requiring additional medications or procedures), and mean change in number of medications.

Results: Six studies, with a total of 593 eyes, were included: 283 underwent MLT, while 310 underwent SLT. A statistically significant difference in the efficacy of MLT versus SLT at one-month and six-month follow-ups was present, with SLT reducing IOP by 0.83 mmHg (95% CI: 0.20, 1.47; P = 0.01) more and 0.55 mmHg (95% CI: 0.02, 1.08; P = 0.04) more than MLT, respectively. At the one-year follow-up, there was no significant disparity in IOP reduction between SLT and MLT (WMD = 0.16; 95% CI: -0.40, 0.71; P = 0.58). There was a significantly lower rate of IOP spikes in the MLT treatment group (RR = 0.37; 95% CI: 0.16, 0.89; P = 0.03). There was no statistically significant difference in the rate of treatment failures (RR = 1.05; 95% CI: 0.68, 1.62; P = 0.84) or number of topical medications reduced (WMD = 0.06; 95% CI: -0.13, 0.26; P = 0.53).

Conclusion: While SLT may offer greater short-term reductions in IOP, it may be associated with more postoperative IOP spikes when compared to MLT. At one-year follow-up, there were no significant differences in IOP reduction or failure rates between the MLT and SLT groups.

Keywords: trabeculoplasty, micropulse, SLT, selective laser trabeculoplasty, glaucoma

Introduction

Glaucoma is a leading cause of irreversible vision loss globally, with the primary goal of intervention being to reduce intraocular pressure (IOP).¹ The most common methods to achieve IOP reduction include topical medication drops and laser trabeculoplasty (LTP).² In the 1970s, the first laser treatment introduced for open-angle glaucoma (OAG) and ocular hypertension (OHT) was argon laser trabeculoplasty (ALT). ALT involved inducing thermal damage to the trabecular meshwork (TM) to enhance the drainage of aqueous humor, thereby reducing IOP.³ In the 1990s, selective laser trabeculoplasty (SLT) was introduced, which preferentially targeted pigmented TM cells, thereby sparing adjacent tissues from thermal damage as in the case of ALT.^{4,5} Laser trabeculoplasty is increasingly being accepted as the standard of

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care for the initial management of OAG and OHT, with the Laser in Glaucoma and Ocular Hypertension (LiGHT) trial demonstrating that initial SLT, rather than medication therapy, has better long-term outcomes.⁶ More recently, a new method of LTP, micropulse laser trabeculoplasty (MLT), has emerged.^{7,8}

Initially reported in 2005, MLT induces neither thermal nor cellular damage, as in the cases with ALT and SLT.^{7,8} It achieves this by fractionating a continuous laser beam into shorter pulses, allowing for the pigmented cells to cool during the interpulse periods, thereby preventing cellular and morphologic alterations to the TM.⁸ Studies comparing outcomes of MLT and SLT have shown that MLT can produce fewer IOP spikes and less pain than SLT.^{9–13} Studies have also reported on the efficacy of MLT at lowering IOP and reducing the number of drops compared to SLT, with conflicting results.^{9–11,13–16} While there are multiple studies on the topic, there is currently a lack of higher-level evidence directly comparing the efficacy and complications of MLT with those of SLT.¹⁷ To the best of our knowledge, no prior meta-analysis has pooled data from studies that directly compared MLT and SLT in patients with OAG and OHT, in order to compare their reductions in IOP and topical medications, IOP spikes, and failure rates.

Materials and Methods

Design

A systematic literature review was conducted utilizing the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Cochrane Handbook of Systematic Reviews of Interventions.^{18,19} We prospectively registered the study protocol in the international prospective register of systematic reviews (PROSPERO, CRD42024535238). This study only used previously published and publicly available data, so institutional review board approval was not required.

Search Strategy

A search was performed using the Pubmed, Scopus, and Embase databases, on April 8, 2024, for all articles to that date. Variations of the following terms were used in the search strategy: "trabeculoplasty", "micropulse", "glaucoma", and "MLT." <u>Supplemental eTable 1</u> contains the detailed search strategy.

Article Selection

Articles were screened independently by authors DZ and PPS in two different phases: (1) screening of titles and abstracts and (2) screening of full texts. During first phase, articles were retained if they reported the outcomes of MLT and SLT in either the title or the abstract. If the focus of the article was ambiguous from just the title and abstract, the study was included for additional review in full-text screening.

During this second phase, specific inclusion and exclusion criteria were independently utilized by the authors to screen full-text articles. These criteria were: (1) the study compared outcomes of MLT and SLT in adult OAG or OHT patients; (2) the article reported on outcomes or complications including change in IOP, change in number of topical medications, rate of IOP spikes, and failure rates (3) the published language was English; (4) the study was a clinical trial, cohort study, or case-control study. The study was excluded if it: was a case report, review, meta-analysis, or conference abstract, contained non-human subjects, or was a duplicate.

Quality Assessment

Authors DZ and PPS utilized the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool and the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) tool for nonrandomized comparative studies and randomized comparative studies, respectively, to determine the risk of bias.^{20,21} There are seven independent domains in the ROBINS-I risk of bias tool with each carrying anywhere from low-high risk that is assessed using set preset questions. The results of these questions together provide an overall assessment of risk. There are five domains in the RoB 2 tool, and similar to ROBINS-I, each domain carries anywhere from low-high risk, followed by an overall risk assessment. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework was utilized to perform quality assessment.²²

Data Extraction

Data from six studies was extracted by two authors (DZ, PS), with disagreements being solved through discussion. The following data were extracted: first author's name, publication year, nation in which the study was conducted, sample size, duration of follow-up, MLT parameters, IOP change in MLT and SLT treatment groups, failure rates, IOP spike rates, and change in the number of topical medications. Failure was defined as a <20% or <3 mmHg reduction in IOP or requiring additional medications or procedures for IOP control.²³ An IOP spike was defined as a >5 mmHg increase from the pre-intervention baseline IOP. PlotDigitizer was utilized to deduce data along with measures of variance if studies only reported outcomes in a graphical format (https://plotdigitizer.com/). For articles that solely reported pre- and post-treatment IOPs and corresponding standard deviations (SD), a mean difference was computed, and the SD was estimated as per the Cochrane Handbook.^{24,25}

Statistical Analysis

The RevMan 5.4.1 software was utilized to perform meta-analyses of weighted mean differences (WMD) to compare change in IOP and number of topical medications between MLT and SLT.²⁶ The six-week follow-up visit was used in one study which did not report data at one-month.⁹ For studies that compared the failure rates of MLT and SLT or the proportion of eyes with IOP spikes, a meta-analysis of risk ratios (RR) was performed. Due to expected heterogeneity from the differences in study protocols, follow-up durations, and differences in patient populations, random-effects models were utilized. Forest plots were used to visually represent the summary effect measure and confidence intervals (CI). Cochran's Q and Higgins' I^2 were used to assess for heterogeneity. Cochran's Q P of less than 0.1 and I^2 greater than 40% were used as thresholds of significant heterogeneity. All statistical tests were conducted using a two-tailed approach, and a P-value of less than 0.05 was deemed statistically significant.

Publication Bias

RevMan 5.4.1 software was utilized to create a Begg's funnel plot for each meta-analysis. However, regression tests for funnel plot asymmetry were not carried out in this meta-analysis, as it included only six studies. According to the Cochrane Handbook, these tests lack sufficient power when the number of studies is fewer than ten.²⁴

Results

Search Results

A PRISMA chart for this analysis can be found in Figure 1.²⁷ The complete search string (Supplemental eTable 1) resulted in 310 studies that were exported into Covidence, and one additional reference was identified through hand-searching of bibliographies. After 88 duplicates were removed, 223 studies remained. Following the title and abstract screening phase, 15 studies were left. In final step involving screening of full-texts, nine studies were further excluded (Supplemental eTable 2), resulting in a final total of six studies that remained.

Study Characteristics

Our final analysis included six studies, with the year of publication ranging from 2017–2023. Overall, 593 eyes were included: 283 underwent MLT and 310 underwent SLT. The studies were carried out in these nations: United States (4), Mexico (1), and Brazil (1). Four studies were retrospective, one was a nonrandomized prospective study, and one was an RCT. Studies included patients with OHT and several forms of OAG, including primary open angle (POAG), pseudoexfoliative (PXG), and pigmentary (PG). Two studies used MLT with a wavelength 577nm, while four studies used a wavelength of 532nm. In regard to other MLT parameters, all studies had a spot size of 300µm, duration of 300ms, 15% duty cycle, and lasered 360° of the angle. For SLT parameters, four studies performed 360° SLT, one performed 180° SLT, and one performed >180° SLT. The energy used for SLT ranged from 0.3mJ to 2.0mJ with five studies titrating to the level of visible bubble formation and one study titrating to the level just below visible bubbles. Table 1 provides detailed characteristics of all included studies. <u>Supplemental eTable 3</u> shows the parameters for SLT that were used in each study.

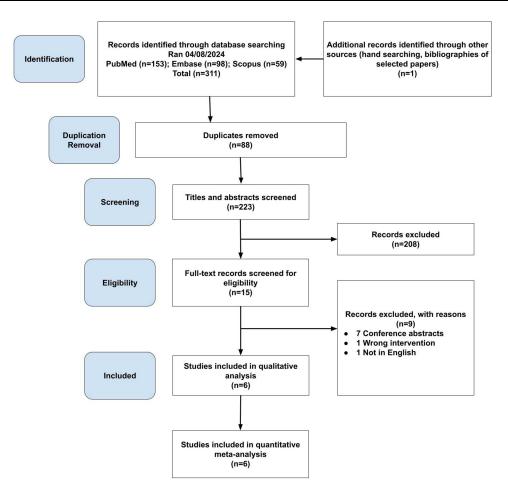


Figure I PRISMA flowchart for this meta-analysis. Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Quality Assessment

Five of the six studies were non-randomized, whereas one was a RCT. Three of the non-randomized studies were determined to have a "moderate" risk of bias. De León et al and Robin et al were both assessed a moderate risk of bias due to missing data.^{12,16} The former study lost over 40% of the patients in the MLT group and nearly 20% of the patients in the SLT group by three-month follow up, and the study excluded all such patients from the analysis completely. The latter study lost 30% of the eyes in the SLT group by merely one-week follow up. Hirabayashi et al was determined to have a moderate confounding bias risk due to a significant difference in the number of shots between the MLT and SLT groups (mean 130.2 versus 84.6 shots, respectively).¹⁰ Additionally, in all five included nonrandomized studies, the measurement of outcomes presented a moderate risk of bias. This was due to outcome assessors being aware of the interventions received by participants, a common issue in non-RCTs. Finally, there were "some concerns" of intervention deviations in Abramowitz et al, because although randomization was performed, neither the participant nor the examiners were blinded during the study period.¹⁰ The criteria and subdomains for each study are shown in <u>Supplemental eTable 4</u> and <u>Supplemental eTable 5</u>. Using the GRADE guidelines, the overall quality of evidence was determined to be very low, as shown in Supplemental eTable 6.

IOP Differences at One Month

Figure 2a shows the mean reduction in IOP at one month following treatment with MLT and SLT, along with the corresponding forest plot. Four studies with 345 eyes were analyzed. Compared to MLT, SLT reduced the IOP

Table I Summary of Included Studies

Source	Year	Country	Design	Types of Glaucoma	Number of eyes	Wave- length* (nm)	Spot Size* (µm)	Spot Duration* (ms)	Duty Cycle* (%)	Degrees*	Follow-up (months)
Abramowitz et al ⁹	2018	USA	RCT	OAG ^a	69	577	300	300	15	360	12
De León et al ¹⁶	2017	Mexico	NRCT	POAG, PG, PXG, OHT	67	577	300	300	15	360	3
Hirabayashi et al ¹⁰	2019	USA	RCS	OAG	100	532	300	300	15	360	6
Pimentel et al ¹¹	2023	Brazil	RCS	POAG	98	532	300	300	15	360	12
Robin et al ¹²	2023	USA	RCS	OAG ^b	131	532	300	300	15	360	12
Sun et al ¹³	2021	USA	RCS	OAG	128	532	300	300	15	360	24

Notes: *Reported parameters for micropulse laser trabeculoplasty ^aExcluded end-stage, neovascular, uveitic, and angle-closure glaucoma. ^bExcluded uveitic, angle-closure, and neovascular glaucoma. ^cExcluded mixed-mechanism, uveitic, neovascular, juvenile open-angle, congenital, and angle-closure glaucoma.

Abbreviations: USA, United States of America; RCT, randomized controlled trial; NRCT, non-randomized controlled trial; RCS, retrospective cohort study; OAG, open-angle glaucoma; POAG, primary open-angle glaucoma; OHT, ocular hypertension; PXG, pseudoexfoliative glaucoma; PG, pigmentary glaucoma.

			MLT			SLT			Mean Difference		Mean Difference	
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
	Abramowitz 2018	-2.43	1.29	38	-3.11	1.39	31	50.7%	0.68 [0.04, 1.32]			
	De Leon 2017	-3.5	3.88	29	-4.74	3.51	38	11.2%	1.24 [-0.56, 3.04]			
	Pimentel 2023	-5	2.8	46	-5.4	2.2	52	28.9%	0.40 [-0.61, 1.41]			
a)	Sun 2021	-0.1	4.58	38	-2.65	6.04	73	9.2%	2.55 [0.54, 4.56]			
	Total (95% CI)			151			104	100.0%	0.83 [0.20, 1.47]			
		0.10.0	1.12		6 D (D	0.0			0.85 [0.20, 1.47]			1
	Heterogeneity: $Tau^2 =$,		,	f = 3 (P)	= 0.2	8); I ² =	22%		-4	-2 0 2	4
	Test for overall effect:	Z = 2.5	6 (P =	0.01)							Favours MLT Favours SLT	
			MLT			SLT			Mean Difference		Mean Difference	
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
	Abramowitz 2018	-2.52	1.17	38	-3.11	1.45	31	71.3%	0.59 [-0.04, 1.22]		⊢ ∎−	
	Hirabayashi 2019	-2.1	4.1	50	-1.8	6.6	50	6.1%	-0.30 [-2.45, 1.85]			
	Pimentel 2023	-6.4	2.6	39	-6.6	3.8	48	15.6%	0.20 [-1.15, 1.55]			
b)	Sun 2021	-0.64	4.56	35	-2.33	6	75	6.9%	1.69 [-0.34, 3.72]			
	Total (95% CI)			162			204	100.0%	0.55 [0.02, 1.08]			
		0 00. 0	· L:2		5 J /D	0.5			0.33 [0.02, 1.08]	Υ		
Heterogeneity: Tau ² = 0.00; Chi ² = 2.08, df = 3 (P = 0.56); I ² = 0% Test for overall effect; Z = 2.02 (P = 0.04)					0%		-4	-2 0 2	4			
	Test for overall effect.	2 = 2.0	2 (F =	0.04)							Favours MLT Favours SLT	
			MLT			SLT			Mean Difference		Mean Difference	
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
	Abramowitz 2018	-2.56	1.29	38	-2.57	1.45	31	72.0%	0.01 [-0.64, 0.66]			
	Pimentel 2023	-5.8	2.6	37	-6	3.3	45	18.9%	0.20 [-1.08, 1.48]			
C)	Sun 2021	-1.29	4.48	43	-2.53	6	85	9.0%	1.24 [-0.61, 3.09]			-1
	Total (95% CI)			118			161	100.0%	0.16 [-0.40, 0.71]			
		0.00.0	1.:2 1		2 (5	0.4			0.16 [-0.40, 0.71]	1		
	Heterogeneity: $Tau^2 =$ Test for overall effect:	,		,	= 2 (P)	= 0.4	/); I ² =	0%		-4	-2 0 2	4
	rest for overall effect:	z = 0.5	5 (P =	0.58)							Favours MLT Favours SLT	

Figure 2 This forest plot displays the meta-analysis comparing the mean reduction in intraocular pressure (IOP) between micropulse laser trabeculoplasty (MLT) and selective laser trabeculoplasty (SLT) at three different time points: (a) I month, (b) 6 months, and (c) I year. Each study is represented by the first author's last name along with the mean difference (MD) and the 95% confidence interval (CI). The overall mean difference and 95% CI, calculated using random-effect estimations, are also depicted. The green squares indicate the effect sizes of the individual studies with their 95% confidence intervals, while the diamonds represent the pooled effect sizes with their 95% confidence intervals.

Abbreviation: IV, inverse variance; SD, standard deviation.

significantly more by 0.83 mmHg (WMD = 0.83; 95% CI: 0.20, 1.47; P = 0.01). Heterogeneity was not present ($I^2 = 22\%$; P = 0.28). The corresponding Begg's funnel plot can be found in <u>Supplemental eFigure 1</u>.

A subgroup analysis was performed at the one-month follow-up for studies that used 577nm MLT compared to those that used 532nm since differences in wavelength can affect tissue penetration and energy absorption.¹¹ In studies using 532nm MLT, the difference in IOP reduction between SLT and MLT was no longer statistically significant (WMD = 1.29; 95% CI: -0.78, 3.37; P = 0.22). The difference in IOP reduction between SLT and MLT remained significant in the studies that performed 577nm MLT (WMD = 0.74; 95% CI: 0.14, 1.34; P = 0.02). The forest plot for this subgroup analysis is shown in <u>Supplemental eFigure 2</u>.

IOP Differences at Six Months

Figure 2b displays the mean reduction in IOP at six months after treatment with MLT and SLT, along with the corresponding forest plot. Four studies with 366 eyes were analyzed. Compared to MLT, SLT reduced the IOP significantly more by 0.55 mmHg (WMD = 0.55; 95% CI: 0.02, 1.08; P = 0.04). Heterogeneity was not present ($I^2 = 0\%$; P = 0.56). The corresponding Begg's funnel plot can be found in <u>Supplemental eFigure 1</u>.

IOP Differences at One-Year

Figure 2c presents the mean reduction in IOP at one year following treatment with MLT and SLT, along with the corresponding forest plot. Three studies with 279 eyes were analyzed. Compared to MLT, SLT reduced the IOP more by 0.16 mmHg (WMD = 0.16; 95% CI: -0.40, 0.71; P = 0.58); however, the difference was not statistically significant. Heterogeneity was not present ($I^2 = 0\%; P = 0.47$). The corresponding Begg's funnel plot can be found in <u>Supplemental eFigure 1</u>.

Rate of IOP Spikes

Figure 3 illustrates the rate of IOP spikes, defined as an increase of more than 5 mmHg from the pre-procedure baseline IOP, along with the corresponding forest plot. Five studies with 526 eyes were analyzed. All the included studies in this meta-analysis except Hirabayashi et al stated that a topical alpha-2 agonist was administered prior to the procedure to reduce the risk of IOP spikes.¹⁰ There was a statistically significant lower rate of IOP spikes in the MLT treatment group compared to the SLT treatment group (RR = 0.37; 95% CI: 0.16, 0.89; P = 0.03). Heterogeneity was not present in the studies ($I^2 = 13\%$; P = 0.33). The corresponding Begg's funnel plot can be found in <u>Supplemental eFigure 1</u>.

Rate of Treatment Failures

Figure 4 depicts the rate of treatment failures, defined as a decrease in IOP of less than 20% or less than 3 mmHg, or the need for additional medications or procedures for IOP control, along with the corresponding forest plot. Four studies with 359 eyes were analyzed. There was no statistically significant difference in the rate of treatment failures between MLT and SLT (RR = 1.05; 95% CI: 0.68, 1.62; P = 0.84). Heterogeneity was not present in the studies ($I^2 = 0\%$; P = 0.68). The corresponding Begg's funnel plot can be found in <u>Supplemental eFigure 1</u>

Reduction in Topical Medications

Figure 5 shows the mean reduction in topical medications at one year after treatment with MLT and SLT, along with the corresponding forest plot. Three studies with 310 eyes were analyzed. Two studies reported the average number of baseline medications in each group. In the Sun et al study, MLT and SLT patients were on an average of 1.8 and 2.0

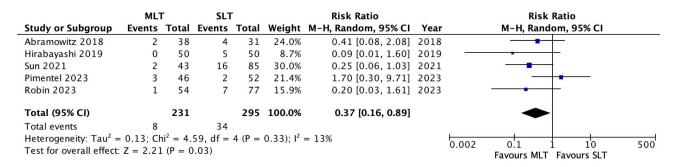


Figure 3 This forest plot illustrates the meta-analysis of the risk ratio (RR) comparing the incidence of IOP spikes (defined as an increase of more than 5 mmHg following laser treatment) between micropulse laser trabeculoplasty and selective laser trabeculoplasty. Each study is identified by the first author's last name and shows the odds ratio (OR) with the 95% confidence interval (CI). The combined effect and 95% CI, derived from random-effect estimations, are also shown. The blue squares reflect the effect sizes of individual studies with their 95% confidence intervals, and the diamonds represent the pooled effect sizes with their 95% confidence intervals. Abbreviation: MH, Mantel-Haenszel.

	ML	Г	SLT	Г		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Abramowitz 2018	9	38	4	31	11.6%	2.09 [0.58, 7.60]	
Hirabayashi 2019	28	50	30	50	30.4%	0.85 [0.38, 1.88]	
Pimentel 2023	19	46	20	52	29.3%	1.13 [0.50, 2.53]	
Robin 2023	23	48	22	44	28.7%	0.92 [0.41, 2.09]	
Total (95% CI)		182		177	100.0%	1.05 [0.68, 1.62]	-
Total events	79		76				
Heterogeneity: Tau ² =	= 0.00; Cł	$ni^2 = 1.$	51, df =	3 (P =	0.68); I ²	= 0%	0.1 0.2 0.5 1 2 5 10
Test for overall effect:							0.1 0.2 0.5 1 2 5 10 Favours MLT Favours SLT

Figure 4 This forest plot presents the meta-analysis of the risk ratio (RR) comparing failure rates between micropulse laser trabeculoplasty and selective laser trabeculoplasty. Failure is defined as a less than 20% or less than 3 mmHg reduction in IOP, or the need for additional medications or procedures to control IOP. Each study is shown with the first author's last name and the odds ratio (OR) with 95% confidence interval (CI). The combined effect and 95% CI, calculated using random-effect estimations, are also presented. The blue squares represent the effect sizes of individual studies with their 95% confidence intervals, and the diamonds depict the pooled effect sizes with their 95% confidence intervals.

Abbreviation: MH, Mantel-Haenszel.

	MLT			SLT				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Hirabayashi 2019	-0.14	1.2	50	0	1	50	20.8%	-0.14 [-0.57, 0.29]	
Pimentel 2023	0.04	0.54	37	-0.03	0.61	45	62.8%	0.07 [-0.18, 0.32]	
Sun 2021	0.1	1.3	43	-0.2	1.39	85	16.4%	0.30 [-0.19, 0.79]	+
Total (95% CI)			130				100.0%	0.06 [-0.13, 0.26]	◆
Heterogeneity: Tau ² = Test for overall effect:		-2 -1 0 1 2 Favours MLT Favours SLT							

Figure 5 This forest plot shows the meta-analysis comparing the mean reduction in the use of topical medications between micropulse laser trabeculoplasty and selective laser trabeculoplasty. Each study is identified by the first author's last name along with the mean difference (MD) and 95% confidence interval (CI). The overall mean difference and 95% CI, derived from random-effect estimations, are also displayed. The green squares indicate the effect sizes of the individual studies with their 95% confidence intervals, while the diamonds represent the pooled effect sizes with their 95% confidence intervals. **Abbreviation**: IV, inverse variance; SD, standard deviation.

medications, respectively, and in the Pimentel et al study, MLT and SLT patients were on an average of 1.52 and 1.42 medications, respectively.^{11,13} There was no statistically significant difference in the number of medications SLT reduced compared to MLT (WMD = 0.06; 95% CI: -0.13, 0.26; P = 0.53). Heterogeneity was not present (I² = 0%; P = 0.42). The corresponding Begg's funnel plot can be found in <u>Supplemental eFigure 1</u>

Discussion

In this meta-analysis, we pooled data from six studies to compare various outcomes between MLT and SLT, including degree of IOP reduction, rates of IOP spikes, failure rates, and number of topical medications reduced. Patients treated with MLT were found to have significantly lower rates of IOP spikes compared to those treated with SLT. However, SLT-treated patients had significantly greater IOP reductions at one and six-months of follow-up. Interestingly, at the one-year time point, the reduction in IOP was no longer statistically significant. There was also no significant difference in failure rates or topical medication reduction between the two treatment groups.

As IOP spikes in patients with glaucoma can lead to further damage of the optic nerve, it is important to reduce the incidence of this complication after LTP.²⁸ In a prior review of the literature on postoperative IOP spikes, the authors recommended rigorous control of moderate IOP spikes in eyes that are at higher risk of damage associated with these spikes, such as patients with advanced glaucoma.^{28,29} In addition to treating IOP spikes with IOP lowering medications, when necessary, it is also important to investigate methods to reduce the rate of this complication following LTP. One method is to preoperatively treat with a topical alpha-2 agonist, which has been shown to prevent IOP increases after LTP through reduction of ciliary blood flow and aqueous formation.³⁰ All included studies in this meta-analysis, except Hirabayashi et al, explicitly stated they gave a drop of an alpha-2 agonist prior to the procedure to reduce the risk of IOP spikes.¹⁰

It has also been hypothesized that the cellular damage to the TM and the excessive early pigment dispersion can result in elevated levels of inflammation, which may contribute to SLT's complications.³¹ In this study, we found that there was a significantly lower risk of having an IOP spike following MLT compared to SLT. This is likely related to the fact that, compared to other forms of LTP, MLT is less likely to result in structural damage to the TM due to its ability to minimize the thermal spread and coagulative effects of the laser.³² However, the degree of IOP spike is also important to consider. Although every included study used a definition of >5 mmHg increase in IOP from baseline as their definition of an IOP spike, most studies did not specify the average IOP spike beyond this definition. However, in Robin et al, the authors mentioned that the average IOP spike increase in the SLT group was 7.57 mmHg compared to a 5 mmHg IOP spike in the MLT group.¹² Another factor to consider is that the majority of included studies used an SLT energy level that produced visible cavitation bubbles, as opposed to using a level just below bubble formation. The literature has not shown a significant energy dose-response benefit of increased energy on SLT efficacy and increased levels could contribute to increased rates of IOP spikes.³³ MLT, on the other hand, does not induce any visible tissue reaction which makes energy titration more difficult.³⁴ Therefore, it is possible that undertreatment of laser energy, relative to SLT, may explain the lower likelihood of adverse events. Although the findings in this meta-analysis suggest that MLT may offer an alternative to SLT with fewer post-laser complications, further research is necessary to determine if MLT

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still produces fewer IOP spikes compared to SLT when the target energy levels are titrated to be below a visible bubble response.

In terms of efficacy between MLT and SLT, this meta-analysis found that at shorter follow-ups of one and six months, SLT lowered IOP slightly more in a statistically significant manner, however at one year, there was no significant difference in efficacy. The rates of treatment failures were comparable between MLT and SLT. Although the difference in IOP was statistically significant at one and six months, the difference was small, less than 1 mmHg at both time points, and this statistical significance was lost by one year. Therefore, it is important to raise the question if the difference is clinically significant. Moreover, since there are natural IOP fluctuations during the day, it is difficult to discern whether such a small difference in IOP is the effect of natural fluctuation or a treatment effect.^{35,36} Since the majority of the included studies were retrospective, it is unclear if an average of multiple IOP measurements was consistently taken or if just a single measurement was used. It has been reported that a single measure of IOP does not adequately estimate the average of multiple measurements.³⁷ Further, RCTs with more standardized protocols are necessary to determine if there is any clinically significant difference in the IOP-lowering effects of MLT compared to SLT.

An important factor to consider in the use of MLT is the lack of standardization, with significant variations between studies on the wavelength, spot size, power, and spot duration used, and the lack of a clear endpoint during application of the laser.⁸ Unlike in SLT where the target energy is either typically titrated to be at or just below visible cavitation bubble formation, MLT does not produce any visible reaction.^{31,33} Factors such as TM pigmentation and media opacity can impact the amount of energy delivered to the TM during LTP.³⁸ In the case of MLT where there is a lack of a visible endpoint during treatment, it can be difficult to titrate the level of energy needed to produce an effective response to treatment. Additional research is required to establish a standardized MLT protocol.

The wavelength of the laser used in MLT can influence the degree of tissue penetration and energy absorption. In this meta-analysis, two studies used 577nm MLT, while four studies used 532nm MLT.¹¹ Only the one-month follow-up for change in IOP meta-analysis had both studies that used 577nm MLT, so a subgroup analysis was performed and found that when stratified by wavelength, the difference in IOP between SLT and MLT was no longer statistically significant in the 532nm MLT subgroup. However, this result should be taken with caution due to the limited number of studies in each subgroup, and there was also significant heterogeneity in the 532nm MLT subgroup. There is currently a lack of a standardized MLT protocol, as seen by the studies in this meta-analysis, which poses a challenge to widespread use of the technology.⁸ Further research is needed to establish guidelines for MLT and assess if variations in wavelengths lead to significant differences in outcomes of the procedure.

While this meta-analysis provides valuable insights into outcomes of MLT compared to SLT, it is important to consider the limitations of this study. The majority of included studies were retrospective which inherently increases the risk of selection bias. There were also variations in whether patients were treatment naive to LTP between the included studies. Some included first time only SLT,^{12,13} whereas another included only those who did not have laser in the prior 6 months,¹¹ and the remainder did not specify. Although it has been reported that repeat SLT has similar efficacy as the initial treatment, it is something important to consider as a potential source of heterogeneity.³⁹ Additionally, two studies^{12,16} did not perform 360° SLT on some or all of their patients to match the 360° MLT performed. Since the two treatment groups in these studies received varying degrees of laser, this complicates the direct comparison between them because 360° SLT has been shown to be more effective than 180° SLT at reducing IOP.^{40–42} Another point to consider is that depending on the type of OAG, there can be differences in responsiveness to LTP.⁴³ However, due to a lack of stratification by the individual studies on MLT and SLT efficacy in various types of glaucoma, separate meta-analyses of subgroups could not be conducted.

Although the study has limitations, this meta-analysis offers valuable perspectives into the effectiveness and complications of MLT in comparison to SLT. Strengths of the study include a larger sample size to allow for greater power to detect differences between treatments. There were also multiple countries included with diverse patient populations, which can improve the generalizability of the findings. In light of reports that LTP is the preferred first-line treatment option for OAG and OHT, it is crucial to have further studies investigating MLT to determine the optimal laser parameters to achieve successful control of IOP while also minimizing unwanted complications.⁶

Data Sharing Statement

Data extracted from included studies and analysis are available from the authors upon reasonable request.

Disclosure

The authors report no conflicts of interest in this work.

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