Title: Micropulse Laser Trabeculoplasty (MLT) Versus Selective Laser Trabeculoplasty (SLT) for Treatment of Open Angle Glaucoma

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Study Protocol and Statistical Analysis Plan with Results

A total of 69 patients with uncontrolled open-angle glaucoma were recruited at the George Washington University by two glaucoma attending professors. Research protocol approval was obtained from the institutional review board of George Washington University (Washington, DC, USA) under IRB #041, 310 and registered on ClinicalTrials.gov with identifier NCT01956942. Written informed consent was received from all patients, and the protocol followed the Declaration of Helsinki.

This study included all laser trabeculoplasty candidates with open-angle glaucoma on maximally tolerated medical therapy with the need for additional IOP lowering. Patients with end-stage, neovascular, uveitic, or angle closure glaucoma were excluded. In all, 38 patients were randomized to MLT and 31 patients to SLT via a random number generator protocol approved for up to 100 patients. All patients had only one eye included in the study. Patients were allocated to each group without any stratification based on prior characteristics via sealed numbers in a set sequence. Recruitment was concluded after a power analysis revealed an 80% power at a 0.05 α level detecting an average 2.99 mmHg or 16.19% decrease from baseline between the SLT and MLT groups. This level was determined based on prior studies defining a $3 mmHg or $20.0% decrease in IOP as a significant difference from baseline.11 Patients, physicians, and researchers were not blinded to the different laser treatments. Each of the two physicians performed both the laser treatments and all subsequent follow-ups for a particular patient.

The MLT group underwent 360° treatment with the IQ 577 nm™ yellow laser (Iridex Corporation, Mountain View, CA, USA) with laser applied to the pigmented trabecular meshwork in a confluent manner. The laser settings for MLT were 1,000 mW, 300 ms duration, 300 µm spot size, and a 15% duty cycle. The SLT group received 360° treatment with the 532 nm Q-switched, frequency-doubled Nd:YAG Selecta II™ (Lumenis Inc, San Jose, CA, USA). The energy for SLT was titrated, between ~0.6 and ~2.0 mJ, based on trabecular meshwork pigmentation to achieve a noticeable gas bubble response, utilizing a 400 µm spot size and a 3 ns duration.

All patients were treated with one drop of apraclonidine prior to the treatment. Patients were discharged with topical diclofenac 0.1% to use as needed for discomfort. At week 1, patients completed a standardized survey querying discomfort experienced both during and after the procedure and use of the topical diclofenac.

Patients' IOP was measured at predefined intervals of 1 hour and 1-, 6-, 6–12-, 12–24-, 24–36-, and 36–52-week intervals based on a fixed follow-up of 1 and 6 weeks and a tendency to follow these patients every 3–4 months thereafter. Pretreatment IOP values were calculated as the average of up to three preceding visits to reduce fluctuations. Only the preceding visits without the addition of a drop or a laser were included to avoid confounding influences. If patients were examined multiple times within an interval, IOP values were averaged for statistical analysis. Patients' responses were excluded from the analysis if they underwent any interventions that may affect their IOP, including the addition of a topical antihypertensive drop, cataract surgery, cyclophotocoagulation, incisional glaucoma surgery, or further laser trabeculoplasty. However, their data were still included for the intervals up to the time of these interventions. Comparison between groups was calculated with Student's *t*-test for continuous data and a two-tailed Fisher's exact test for categorical data.

Results

There was no statistically significant difference in demographic characteristics between groups, as seen in Table 1. The MLT patients had a higher average starting IOP (18.26 mmHg) than the SLT group (16.85 mmHg), approaching significance (*P*=0.08). Both groups had very similar 1 hour posttreatment IOP, 15.15 mmHg in the MLT group and 15.65 mmHg in the SLT group. An IOP spike was defined as an elevation of .5 mmHg from the pretreatment mean. Incidence of post-procedure spikes were 5.3% and 12.9% in the MLT and SLT groups, respectively, but this difference was not statistically significant (*P*=0.4). No group experienced any anterior chamber inflammation upon examination at the 1 week follow-up time point.

Follow-up data at the 1-, 1–6-, 6–12-, 12–24-, 24–36-, and 36–52-week intervals were tabulated as absolute IOP decreases from pretreatment levels (Figure 1) and percentage IOP decreases from baseline (Figure 2). These data demonstrated that both MLT and SLT provided comparable decreases in IOP from baseline as both an absolute measurement and a percentage decrease at all intervals up 52 weeks (*P*.0.05). In addition, the confidence intervals at each time period were, 3 mmHg when viewed as an absolute decrease in IOP and, 20.0% when viewed as a percentage decrease from baseline IOP, except one outlier interval (week 24–36 in Figure 1). A Kaplan–Meier curve is demonstrated in Figure 3. As expected, the larger proportion of failures in the MLT group produced a lower curve, with more of the MLT failures occurring in the early period. However, the survival curve steps in both groups were similar at later intervals, leading to a log-rank *P*-value of 0.31.

The data from the standardized pain survey (scale of 0= none to 10= severe) revealed that the MLT patients experienced a mean 1.34/10 during treatment and 0.89/10 during the 1 week posttreatment period, while the SLT patients noted 2.83/10 during treatment and 2.81/10 during the 1 week posttreatment period. The MLT patients on average experienced less pain both during and after the treatment (*P*=0.005).

Prior authors defined a successful laser trabeculoplasty as $3 mmHg IOP decrease or $20.0% IOP decrease from baseline.6,8 Using these criteria, 29.6% of the MLT and 36.0% of the SLT patients experienced a 20.0% IOP decrease from baseline during the 24–52-week interval (*P*=0.77). Similarly, 37.0% of the MLT patients and 36.0% of the SLT patients experienced a $3 mmHg IOP reduction from baseline at the 24–52-week interval (*P*=1.0).

Patients in each group were also assessed to determine the proportion that required further intervention for their glaucoma during the 52-week follow-up period, indicating a failure of the laser therapy. In the MLT group, a total of 23.7% of patients failed and required further treatment for their glaucoma. A topical antiglaucoma agent was added in 15.8% of the MLT patients, incisional glaucoma surgery was performed in 2.6% of the MLT patients, and transscleral cyclophotocoagulation was performed in 5.3% of the MLT patients. In the SLT group, 12.9% of the patients failed, with all the failures due to the addition of another topical antiglaucoma medication. Although there were a greater number of failures in the MLT group (23.7%) compared to the SLT group (12.9%), the analysis did not meet significance in each individual category or when considered in sum (*P*=0.22). No patient in either group experienced any complications, other than a transient rise in IOP.