

IRIDEX Clinical Application Review

Application: **MicroPulse™ Diode Laser Trabeculoplasty (MDLT)**

Products: IRIS Medical® Infrared (810 nm) Laser Photocoagulators
Slit Lamp Adapter

Clinical Series: MicroPulse Diode Laser Trabeculoplasty versus Argon Laser Trabeculoplasty in the Treatment of Open Angle Glaucoma

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Purpose: To compare the short term intraocular pressure lowering ability of MDLT to that of argon laser trabeculoplasty (ALT) in patients with primary open angle glaucoma (POAG).

Methods: Twenty-one eyes of twenty-one patients with POAG were randomized to treatment with MDLT or ALT. All patients had a pre-operative IOP of 21 mm Hg or greater. Intraocular pressure (IOP) was also measured at 1 hour, 1 week, 1 month, and 3 months post-operatively. Anterior cell and flare reactions, pre-operative angle pigment, adverse reactions, and visual acuity were also recorded.

Results: Mean preoperative IOP was 24.6 mm Hg in the MDLT group and 24.3 mm Hg in the ALT group. At 1 week the mean MDLT IOP was 21.5 mm Hg and 22.4 mm Hg for ALT. At 1 month the mean IOP was 20.6 mm Hg and 20.5 mm Hg respectively. At 3 months the IOP was 20.1 and 19.7 respectively. There was no significant difference between the groups at any one visit. After three months both groups showed a statistically significant drop from baseline ($p < 0.05$).

Conclusions: The IOP lowering effects of MDLT were statistically significant. The IOP lowering effects of ALT were also significant in this group of patients. There was no statistically significant difference in pressure lowering between these groups.

<u>Laser Parameters</u>	<u>MDLT</u>	<u>ALT</u>
Spot Size Diameter (µm)	300	50
Power (Watts)	2	0.4 – 0.7
Irradiance (W/cm ²)	2,831	20,380 – 35,670
Duration (ms)	200*	100
Duty Cycle (%)	15	100 (continuous-wave)
Applications (#)	66 over nasal 180°	100 over 360°

*Time/application: 200 ms delivering a train of 100 micropulses (300 µs ON + 1700 µs OFF = 2 ms x 100 = 200 ms) for a cumulative: ON-time (300 µs x 100) = 30 ms; OFF-time (1700 µs x 100) = 170 ms



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Photothermal Laser Trabeculoplasty

Laser trabeculoplasty (LT) was first described in 1974 by Worthen and Whickham.¹ Following the publication of Wise and Witter's pilot study in 1979,² photothermal LT with either argon lasers (ALT) or diode lasers (DLT) became a commonly performed procedure for the treatment of primary open-angle glaucoma (POAG), exfoliation syndrome glaucoma, pigmentary glaucoma and normal-tension glaucoma.

The effectiveness and the role of LT in various phases of the management of open angle glaucoma (OAG) have been defined by landmark multicenter National Eye Institute (NEI)-sponsored trials: the Glaucoma Laser Trial (GLT);³ the Advanced Glaucoma Intervention Study (AGIS);⁴ the Collaborative Initial Glaucoma Treatment Study (CIGTS);⁵⁻⁶ and the Early Manifest Glaucoma Trial (EMGT).⁷⁻⁸

In 1996, on the basis of the evidence from the Glaucoma Laser Trial Follow-up Study (GLTFS),³ the NEI reported that ALT is at least as efficacious as medications as first-line therapy in newly diagnosed POAG; however, LT was not generally adopted as the primary treatment of choice and was mainly used as an adjunct therapy reserved for cases of uncontrolled IOP with maximum tolerated medications. Only in few selected cases, LT was used as an initial treatment (older patients, patients unable to use beta-adrenergic antagonists or poorly compliant with medications) or as an alternative to miotics and/or carbonic anhydrase inhibitors to reduce patients' discomfort and side effects.

The introduction of new pharmaceutical agents further shifted the use of LT, which, although proved superior than medications-first in a randomized trial in the UK⁹ and considered by some a cost-effective initial treatment of choice for chronic OAG,¹⁰⁻¹¹ gradually became a relatively underused therapy, probably due to:

- new advances in medical therapy
- fading long-term efficacy (decreasing effects in 50% of patients after 5 years)
- lower effectiveness in younger patients (LT works best in patients over 60 years of age)
- limited ability to retreat
- undesirable side effects and collateral damage, mostly caused by the laser protocols used for ALT and DLT, such as
 - post-op inflammatory response
 - acute and in few cases chronic IOP elevation
 - peripheral anterior synechiae (PAS)
 - scarring of the TM

In essence, LT, as administered with current ALT and DLT protocols, is a proven and cost-effective glaucoma therapy, whose usage however is limited by the concerns over iatrogenic acute and chronic photothermal damage.

Selective Laser Trabeculoplasty

To minimize the iatrogenic damage of LT, Latina introduced the concept of selective laser trabeculoplasty (SLT) in 1995. SLT uses a 532 nm Q-switched frequency-doubled Nd:YAG laser emitting short pulses to limit the destruction to the trabecular meshwork (TM) pigment-laden cells, in accordance with the principles of selective laser photothermolysis. Indeed SLT has demonstrated isolated destruction of pigmented TM cells without collateral damage to surrounding non-pigmented cells. SLT protocol uses pulse energy of 0.8-1.0 mJ delivered in a single 3ns pulse at a very high peak power ($\cong 0.3$ megawatts). Despite the relatively large 400 μ m spot, this peak power translates in a very high irradiance (265 megawatts/cm²) that produces micro-explosions (the champagne-like bubbles endpoint), which unfortunately cause acute anterior chamber (AC) reactions and post-op IOP spikes requiring post-op steroid therapy. IOP lowering was found equally effective as with ALT in a number of clinical



studies, and in March 2001, SLT received the PMA by the FDA.

Interestingly, the average percentage of IOP reduction reported by the great majority of studies with SLT, ALT, and DLT has been comparable and consistently within the 20-25% range, regardless of the LT technique/protocol used.

The efficacy and the success rate of LT appear to be more dependent on patients' factors (race, age, pigmentation, pre-op IOP, stage of glaucoma and fellow eye response to laser) than on the LT technique/protocol. Thus, the least possible damaging LT technique/protocol could have the best chance to gaining the acceptance by the ophthalmic community and to enhance LT's role and time of intervention in the sequence of glaucoma management.

Glaucoma is a 24 hours/day degenerative disease in which each single mm Hg counts: a successful, long-lasting or repeatable LT could constitute a cost-effective therapy with the added benefit of blunting diurnal IOP variations.¹²

Micropulse Diode Laser Trabeculoplasty (MDLT)

MDLT is a large-spot, low-irradiance minimum intensity photocoagulation™ (MIP) protocol for the reduction of IOP with a non-destructive laser/tissue interaction to minimize collateral cell damage. MDLT utilizes trains of short 810 nm laser pulses (100-300 µsec) to control and spatially confine the laser-induced thermal elevation in order to produce sublethal, photothermal cellular effects only around the TM pigmented cells.

MDLT is typically performed delivering 66 confluent 300 µm diameter invisible laser applications covering the whole height of the TM over 180°. Due to the combination of a) low absorption of the 810 nm laser wavelength by the TM, b) the relatively large 300 µm spot at low irradiance (2 W over 300 µm spot = 2,830 W/cm²), MDLT interacts with most pigmented cells in

the superficial and deep layers of the TM without producing visible effects, tissue blanching, or bubble formation. The treatment is invisible to the surgeon and uneventful for the patient with no thermal pain and no laser flashes (810 nm is invisible). The eye remains quiet with negligible or no flare, no visible post-op inflammation, no IOP spikes and no need for post-op steroids therapy.

In a randomized pilot study conducted at the University of Missouri Kansas City,¹³ MDLT and ALT showed an equal IOP lowering effect at 3 months. IOP reduction from baseline was statistically significant for both study's arms with no difference between arms. At 1-hour from treatment, cell and flare reaction at "trace-1+" level was found in 10/11 (91%) of the ALT eyes and in 2/10 (20%) of the MDLT eyes.

These early results seem to support the hypotheses that all forms of LT may share a same cellular mechanism of action. Unlike other modalities, MDLT interacts but does not destroy pigmented endothelial cells in the TM, and reaches the unknown thresholds of cytokines activation and MMP-3 upregulation without visible photothermal damage and inflammatory reactions.

The rationale for MDLT can be summarized as follows:

- DLT works. It has shown an IOP lowering effect equivalent to ALT,¹⁴ with less inflammatory reaction, less disruption of the blood-aqueous barrier, no postoperative pain, and no PAS.¹⁵
- MDLT is a lower dose DLT that uses low-irradiance micropulsing to allow better control and confinement of the photothermal effects¹⁶⁻¹⁷ to minimize the damage to the TM.
- Less TM damage with no scarring would theoretically minimize the risk for late IOP rise and offer the potential for retreatments and/or staged periodical enhancements.
- MDLT is painless and has no reported complications (eyes are quiet with negligible inflammation, no IOP spikes, no PAS).



- MDLT is easy to perform: the large 300 µm spot is less critical to aim and focus than the smaller spots used with ALT and DLT.
- MDLT, unlike SLT, does not require a dedicated expensive new laser.

MDLT is performed with the IRIS Medical SLx OcuLight 810 nm photocoagulator, a multipurpose

ophthalmic laser that is readily available to the glaucoma specialist performing DLT or transscleral cyclophotocoagulation with the G-Probe™ and that can be found in many ophthalmic departments where is routinely used for transpupillary, transscleral and intraocular treatments of several ocular disorders in the office or in the operating room.

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