Developments in laser trabeculoplasty

Susanna Tsang,[1] Jason Cheng,[2] Jacky WY Lee[1]

[1]Department of Ophthalmology, Caritas Medical Centre, Kowloon, Hong Kong
[2]Department of Ophthalmology and Visual Sciences, Khoo Teck Puat Hospital, Yishun, Singapore

Correspondence to
Dr Jacky WY Lee, Department of Ophthalmology, Caritas Medical Centre, 111 Wing Hong Street, Kowloon, Hong Kong; jackywylee@gmail.com

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ABSTRACT

Laser trabeculoplasty has an increasing important role in the management of glaucoma as more emphasis is placed on minimally invasive therapies. In recent years, the following laser trabeculoplasty technologies have been introduced: micropulse laser trabeculoplasty, titanium-sapphire laser trabeculoplasty and pattern scanning trabeculoplasty. These lasers help to reduce the intraocular pressure (IOP) and the burden of glaucoma medical therapy. Literature findings regarding the safety and efficacy of these newer forms of laser trabeculoplasty in the treatment of open-angle glaucoma is summarised. These relatively newer procedures appear to have similar efficacy when compared with the former selective laser trabeculoplasty or argon laser trabeculoplasty. In addition, they potentially offer a more favourable safety profile with fewer complications, including postlaser inflammation and IOP spikes. Further large-scale studies are necessary to evaluate the long-term benefits of these newer forms of laser trabeculoplasty. Their initial promising results offer patients with glaucoma additional treatment alternatives.

INTRODUCTION

The clinical management of glaucoma is evolving with advances in medical, laser and surgical technologies. Laser trabeculoplasty has a significant role in the management of glaucoma in reducing intraocular pressure (IOP). Argon laser trabeculoplasty (ALT) has historically been the preferred laser procedure in eyes with open-angle glaucoma after it was first introduced in the 1970s.[1 2] A large multicentre prospective clinical trial demonstrated its safety and efficacy.[3] There has been a shift from ALT to the newer selective laser trabeculoplasty (SLT) when studies demonstrated that there is no difference between 360° SLT and 180° ALT in terms of IOP-lowering effect.[4 5] SLT produces less postlaser anterior chamber inflammation, and leaves the trabecular meshwork intact with minimal damage to the endothelial cells.[6] This is in contrast to ALT, which may result in scarring of the trabecular meshwork and peripheral anterior synechiae formation.[7]

There has been much research demonstrating equivalent efficacy of SLT in comparison with medical therapy.[8–11] Medication adherence is a major challenge for many patients with open angle glaucoma, and laser trabeculoplasty gives a more consistent IOP control in these patients.[12–14] SLT has also been performed as a primary therapy for primary open-angle glaucoma (POAG) and ocular hypertension prior to the use of medications.[15] Annual repeated SLT may be a safe and effective maintenance therapy after an initial successful SLT has begun to fade, although there is still limited evidence in the literature at the moment on SLT repeatability.[16 17] SLT has the potential to reduce antiglaucoma medication use, improving convenience, comfort and appearance, which may potentially improve patients' quality of life.[18] In recent years, various studies have been performed to investigate the safety and efficacy of SLT in different glaucoma subtypes and to establish how to maximise its potential by investigating optimal energies, predictive factors for success, IOP correlations in bilateral treatments and influences on other glaucoma progression risk factors like IOP fluctuation.[19–27]

With the introduction of minimally invasive glaucoma surgery, there have been suggestions that it may signify the gradual decline of trabeculoplasty use. While there is an overlap of target patient population, trabeculoplasty has the advantage of being less invasive, is an extraocular procedure, does not need to be combined with lens extraction and is much less costly. Trabeculoplasty still has an important role to play in the treatment paradigm, and new research advancements will continue to improve outcomes and safety.

Several new generations of laser trabeculoplasty have been introduced into clinical practice to lower IOP and reduce medications, including micropulse laser trabeculoplasty (MLT), titanium-sapphire laser trabeculoplasty (TSLT) and pattern scanning trabeculoplasty (PLT). The aim of this review is to summarise the finding from the literature regarding the safety and efficacy of these newer forms of laser trabeculoplasty.

MICROPULSE LASER TRABECULOPLASTY

MLT delivers energy in repetitive microsecond pulses followed by an intermittent rest period, thereby reducing the build-up of thermal energy.[28] It controls thermal elevation, and does not cause observable coagulative damage to the trabecular meshwork on scanning electron microscopy.[29] This differentiates from the conventional continuous wave lasers like ALT that causes mechanical damage and scarring to the trabecular meshwork.[30] The mechanism of newer forms of laser trabeculoplasty is to stimulate a cellular biochemical cascade via cytokine release to increase aqueous outflow while reducing tissue damage.[31 32]

Laser settings

Earlier research focused on using the 810 nm wavelength laser, but later studies have switched to using the 532 or 577 nm laser. Similar to other laser trabeculoplasties, MLT is performed under topical anaesthesia. Common settings for MLT are 300 μm spot size (smaller than the 400 μm SLT spot size), 300 ms duration, 1000 mW power and 15% duty cycle. The duty cycle is the percentage of time that the laser will be active during the treatment duration. Radcliffe recommended 100 shots over 360°, whereas Ahmed suggested confluent applications.[33 34] The laser energy is titrated down if the patient experiences pain during the procedure. There are no visible endpoints in MLT, no visible blanching or bubble formation over trabecular meshwork during the treatment process. As the postlaser inflammation is minimal to non-existent, no anti-inflammatory medications are required after MLT.

Efficacy

There have been several studies demonstrating the efficacy of MLT. In a phase II prospective interventional case series with the 810 nm MLT laser, a total of 20 patients were assessed. The authors used confluent subthreshold laser applications over the inferior 180° of the anterior trabecular meshwork with settings of 200 μm spot size, 2000 mW power, 200 ms duration with a 15% duty cycle and 70–84 laser spots. MLT was successful in 15 patients (75%) with a mean IOP reduction of around 20% at 12 months. Five patients (25%) failed, four in the first week and one at 6 months.[35]

Gossage *et al* reported a 2-year data after treatment using 532 nm MLT in 18 POAG eyes. Laser energies were set to 300 mW, increasing to 700 mW and then 1000 mW. Those treated with 1000 mW showed significantly better results with the amount of IOP reduction reaching 24% at 24 months.[36]

The preliminary data of a study comparing MLT with SLT showed that the two laser technologies were comparable. Twelve eyes had MLT and 14 eyes underwent SLT. Both groups had significantly lower IOP; MLT achieved a mean IOP reduction of 3.9 mm Hg, while the reduction in SLT was 2.6 mm Hg. MLT had a slightly greater decrease in the number of medications compared with SLT-treated eyes. The mean change in the number of medication was 0.6 versus 0.1 in the MLT and SLT group, respectively.[37] There have also been reports of successful MLT treatment after previous SLT.[38]

However, there is one published study that questions the efficacy of the MLT. A retrospective study of 40 patients found that only one patient (2.5%) had ≥20% reduction in IOP and only three patients (7.5%) had ≥3 mm Hg decrease in IOP after up to 19 months of follow-up. The average time for failure was around 3 months. This study population had a relatively lower pretreatment mean IOP of 21.8±4.9 mm Hg (range, 14–34 mm Hg) on a mean of 2.0±1.3 medications. Laser settings used were 300 μm spot size, 2000 mW power, 200 ms duration, 15% duty cycle and 60–66 laser spots over 180° of the trabecular meshwork. Their result suggested that 180° MLT is ineffective in managing patients with open-angle glaucoma.[39]

Safety

In a short-term prospective controlled pilot study comparing MLT with ALT in 21 eyes, patients were randomised to receive either MLT or ALT. MLT setting used was 300 μm spot size, 2000 mW energy, 200 ms duration, 15% duty cycle with 66 laser spots over the nasal 180° of the trabecular meshwork. Both groups achieved around a 20% reduction of IOP at 3 months with no significant difference between the groups. Intralaser pain and postlaser inflammation (cell or flare) were negligible and significantly lower in the MLT group.[40] Fea *et al* reported one patient with pigmentary glaucoma that had an IOP spike and anterior chamber flare after MLT treatment; the IOP normalised after 3 days with systemic drugs. MLT was well tolerated apart from a burning or heat sensation that was reported in four (20%) of the patients.[34] There are no reported late postlaser complications arising from MLT in the literature.

MLT has advantages over SLT especially in patients at higher risk of postlaser pressure spikes, such as those with highly pigmented trabecular meshwork. MLT has shown encouraging results in these early studies in the treatment of open-angle glaucoma, and larger multicentre trials are currently underway. The hope is that MLT can prove to have equal efficacy, but an even safer profile compared with SLT.

TITANIUM-SAPPHIRE LASER TRABECULOPLASTY

TSLT is a subtype of laser trabeculoplasty with a 790 nm wavelength laser, emitting near-infrared energy in pulses ranging from 5 to 10 ms. This is thought to allow deeper penetration (about 200 μm) into the juxtacanalicular meshwork and the inner wall of Schlemm's canal. The laser is then selectively absorbed by pigmented phagocytic cells, preserving the trabecular meshwork tissue.[41]

Laser settings

The laser is focused at the pigmented trabecular meshwork and 50 non-overlapping shots are applied to 180° of the pigmented trabecular meshwork. The spot size is smaller than SLT or MLT at 200 μm. Treatment energy is started at 50 mJ, and can be titrated down to 30 mJ if necessary. The treatment endpoint is the formation of mini-bubbles or the visible burst of pigments from the trabecular meshwork.[41]

Efficacy

There are very limited published clinical studies reporting the efficacy of TSLT, and the device is also not widely available. A 15-month pilot study with 37 subjects comparing TSLT versus ALT was published in 2009. It demonstrated that TSLT-treated eyes had a mean IOP reduction of 8 mm Hg (32%), while the ALT group achieve a 6.5 mm Hg (25%) IOP reduction. There was no statistical difference between the two groups. The number of antiglaucoma medications was not significantly different between the two treatment arms, from 1.4±1.0 to 1.3 ±1.0 in the TSLT group and from 2.1±0.8 to 2.0±0.8 in the ALT group.[41]

Safety

IOP spikes occurred in one patient who underwent TSLT. There was no reported peripheral anterior synechiae formation in TSLT-treated eyes. No long-term complications have occurred in patients who received TSLT over a 2-year period.[41] Histological examination revealed some anatomical alterations in the trabecular meshwork at the laser exposure site by TSLT, but no thermal damage was noted. Therefore, it is postulated that TSLT is a repeatable procedure.[42]

As TSLT is still a relatively new technology, limited data exist in the literature describing its efficacy and safety. Larger scale randomised studies are warranted before its long-term safety in comparison with its predecessors can be determined.

PATTERN SCANNING TRABECULOPLASTY

PLT provides a computer-guided treatment method to apply a sequence of pattern laser spots onto the trabecular meshwork. Automatic rotation with calculated alignment of each pattern allows consecutive treatment of the entire trabecular meshwork without overlapping or excessive gaps in between.[43] It is a continuous wave light first introduced with a green wavelength of 532 nm and subsequently a 577 nm yellow laser is now available.

PLT is thought to achieve a cellular response with less tissue scarring and coagulative damage. Compared with ALT, PLT has much shorter pulse durations, therefore, reducing the thermal injury diffusion distance. The efficacy is maintained by applying approximately 10 times more spots for the same area of treated trabecular meshwork.[44]

Laser settings

The suggested laser settings are spot size of 100 μm, 5–10 ms duration and power is titrated until trabecular meshwork blanching is seen at 10 ms duration in the inferior segment of the eye where the highest laser penetration occurs. Tissue blanching is achieved within 10 ms at a power level below 1 W. Once the power is titrated, the duration is reduced to 5 ms, making the treatment endpoint invisible. A computer-guided pattern-scanning algorithm is then used. Each treatment pattern consists of two or three rows (24–66 spots) of arching spots that correspond to 22.5° of arc on the trabecular meshwork. After the completion of each segment, the aiming beam automatically rotates 22.5°. Eight adjacent treatment segments corresponds to 180° of the trabecular meshwork, and 16 treatment segments equates to 360°.[44]

Efficacy

In a prospective pilot study, 47 eyes in 25 patients were treated with 360° of a 532 nm PLT laser, in 16 treatment segments, the average IOP drop was from 21.9±4.1 to 15.5±2.7 mm Hg at 6 months of follow-up. However, 17 eyes were excluded because of either having a viral conjunctivitis or requiring additional antiglaucoma therapy for IOP lowering after the procedure. Twenty of the 30 eyes (67%) achieved an average IOP reduction of 24%.[44]

There are two published studies comparing ALT with PLT. In a retrospective German study, PLT demonstrated a reduction of mean IOP from 20.2±1.1 to 15.6±0.8 mm Hg ($p<0.001$) in 20 eyes of 20 patients at around 8 weeks of follow-up. There was no statistical difference in IOP reduction compared with ALT ($p=0.26$).[45] In a second study by Kim *et al*, PLT achieved a mean IOP reduction of 27.1%, from 24.1±4.2 to 17.6 ±2.6 mm Hg ($p=0.03$) at 6 months, and again there was no statistical difference to ALT.[46]

Safety

There were no pressure spikes or inflammation in eyes that received PLT according to Turati *et al*.[44] In a retrospective case series using the 577 nm PLT laser in 11 eyes of 9 patients, a 31% reduction in IOP during 6 months of follow-up was achieved. Preoperative and postoperative medication score (2.6 and 2.8, respectively) showed no significant difference. One eye had transient IOP elevation after PLT. There was no reported peripheral anterior synechiae formation or corneal endothelial damage.[47]

PLT appears to be an effective laser procedure for lowering IOP. With the initial promising results, a larger and controlled study with longer follow-up is required to affirm the efficacy and sustainability of the pressure-lowering effects in PLT.

CONCLUSION

Laser trabeculoplasty options for managing open-angle glaucoma have expanded in recent years. MLT, TSLT and PLT may be performed to provide IOP reduction and reduce the burden of glaucoma medical therapy for patients and healthcare systems. Comparison of these laser procedures are summarised in table 1. These new procedures appear to have similar efficacy when compared with the former SLT or ALT technologies. There is limited information in the literature on the role of these newer lasers as primary treatment in naive eyes versus adjuvant treatment in medically treated eyes. Further studies will be needed before we can critically analysis these differences with SLT or ALT. In addition, these newer lasers offer a more favourable safety profile with fewer complications namely postoperative inflammation and postlaser IOP spikes. A realistic expectation from laser treatment is roughly equal to one prostaglandin medication in the short-to-medium term, and it is not useful for secondary glaucomas, such as uveitic or neovascular

Table 1 Comparison of various laser trabeculoplasties

	SLT	MLT	TSLT	PLT
Wavelength	532 nm	532, 577 or 810 nm	790 nm	532 or 577 nm
Spot size	400 μm	200–300 μm	200 μm	100 μm
Pulse duration	3×10^{-9} s	$200–300\times10^{-3}$ s 15% duty cycle	$5–10\times10^{-3}$ s	$5–10\times10^{-3}$ s
Energy or power per pulse	0.6–1.2 mJ	1000–2000 mW	30–50 mJ	500–1000 mW
Mechanism	Selective destruction of pigmented trabecular meshwork cells without thermal or collateral damage	Thermal effects without trabecular meshwork damage in repetitive microsecond pulses followed by intermittent rest period	Near-infrared energy with deeper penetration into the juxtacanalicular meshwork and the inner wall of Schlemm's canal	Sequence of pattern laser spots on the trabecular meshwork without overlapping, much shorter pulse durations with more spots for the same area to reduce thermal injury diffusion distance
Recommended number of applications	50 or 100 confluent spots	60–100 spots or confluent spots	50 adjacent, non-overlapping laser spots	8 or 16 segments
Recommended extent of trabecular meshwork treatment	180° or 360° of trabecular meshwork	180° or 360° of trabecular meshwork	180° of trabecular meshwork	180° or 360° of trabecular meshwork
Expected endpoint	Small bubbles	No visible tissue reaction	Mini-bubble or burst of pigments	No visible tissue reaction after energy titration
Repeatable	Yes	Yes	Yes (theoretically)	Unknown
Common complications	IOP spikes and anterior uveitis	Burning or heat sensation. IOP spikes and anterior uveitis are uncommon	IOP spikes are possible	Transient IOP spikes are possible

IOP, intraocular pressure; MLT, micropulse laser trabeculoplasty; PLT, pattern scanning trabeculoplasty; SLT, selective laser trabeculoplasty; TSLT, titanium-sapphire laser trabeculoplasty.

glaucoma. Further large-scale studies are necessary to justify the benefits of these new laser treatment modalities and to determine if these challengers can replace SLT as the gold standard in laser trabeculoplasty.

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