Journal of Glaucoma Publish Ahead of Print
DOI:10.1097/IJG.0000000000002062

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Energy Dose-Response in Selective Laser Trabeculoplasty: A Review

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Peng T Khaw is supported by NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology.
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PRÉCIS

A literature review of SLT energy dose response found no definitive relationship between IOP reduction with respect to total or pulse energy, race, pigmentation, or application pattern.

Disclosure: The authors declare no conflict of interest.

ABSTRACT

Purpose: Selective laser trabeculoplasty (SLT) is a safe and effective treatment for lowering intraocular pressure (IOP). While evidence is mounting for the advantage of its use as a first-line treatment for IOP reduction, the SLT procedures in use vary widely. The purpose of this literature review was to investigate if there were any relationships between SLT energy and efficacy for lowering IOP in the published literature.

Methods: A literature review was undertaken that included studies in which energy levels required for successful SLT treatment were investigated: in general, with respect to angle pigmentation, race or ethnicity, and treatment arc extent.

Results: There was no indication that higher (or lower) energy used in the treatment leads to greater (or less) IOP reduction. Similar results were obtained regarding level of trabecular meshwork (TM) pigmentation. Race was not found to be associated with altered dose response in SLT. There were indications that treating the full 360 degrees, as opposed to smaller arcs, could be beneficial for more IOP reduction**.** IOP reduction from SLT was found to be similar to that provided by topical medications.

Conclusions: The optimal energy level of SLT needed for IOP reduction has not yet been definitively established, with all reported pulse energies resulting in similar IOP reduction. Furthermore, similar lack of conclusive findings exists regarding optimal SLT energy dosage for use in different races and degrees of TM pigmentation. This parameter, as well as each of the above-mentioned factors, requires further research.

Key Words: Selective laser trabeculoplasty, Energy dose-response, Glaucoma, Trabecular meshwork pigmentation, Ethnicity

INTRODUCTION

Glaucoma is a heterogenous group of diseases, characterized by progressive optic nerve head (ONH) damage, which is often accompanied by elevated intraocular pressure (IOP), leading to losses in visual field and resulting visual impairment. Glaucoma is the most common cause of irreversible blindness worldwide. High IOP is its only treatable risk factor.[1–3] Glaucoma treatment has therefore been focused on IOP reduction, which traditionally is performed by application of topical agents, followed by laser therapy and, finally, if needed, by incisional surgery.[4] While both the efficacy and the safety of modern-day topical agents for IOP reduction have been verified in clinical trials, widespread patient non-adherence reduces the effectiveness of such treatments[5–8] and leads to visual field loss.[9]

Selective laser trabeculoplasty (SLT), introduced by Latina et al. in 1995,[10] is a subclass of laser treatments for IOP reduction that offers a safe and effective alternative to first-line treatments for glaucoma.[11–13] SLT functions by causing a variety of trabecular meshwork (TM) changes, including cytokine release, cellular division and replenishment, changes in intercellular connections, macrophage recruitment and induction of matrix metalloproteases and changes in extracellular matrix turnover.[14,15] One of the fundamental tenets of selective photothermolysis, introduced by Anderson and Parrish, is that exact laser focus should be unnecessary.[16]

SLT is typically performed with a Q-switched frequency-doubled Nd:YAG laser with a spot size of 400 µm, wavelength of 532 nm and pulse duration of 3 ns.[10] Nowadays SLT is most commonly performed by starting at 0.8 mJ per treatment spot and titrating the energy to 0.1 mJ below the threshold energy that produces champagne-sized cavitation bubbles.[17] This regimen of energy delivery for IOP reduction was defined following observations of optimal energy absorption by

trabecular meshwork (TM) cells cultured *in vitro*.[10] While the regimen is widely accepted, there is nevertheless significant clinical variability in how SLT is performed. Owing to the lack of standardization, SLT can be performed, for example, by delivering 25, 50 or 100 laser pulses covering 90, 180 or 360 degrees of the TM, respectively, at energy levels just below or sufficient for champagne bubble formation. Poor understanding of the tissue effects of laser treatments for IOP reduction[18] is an important potential contributor to the lack of international standards, and largely accounts for the widely accepted regimen still used, albeit outdated, for SLT treatments.

In this review we present the currently available evidence for optimal SLT energy-dose delivery for IOP reduction in general, and specifically with regard to the level of TM pigmentation, race and ethnicity, and pattern of application.

Before continuing with this review it is noted that most SLT studies have been performed using the unproven dogma that the energy dosing for lowering IOP occurs around the champagne bubble level,[19] and thus making it extremely difficult to find an energy dose response as pulse energy is adjusted for each laser shot. However, some studies have purposefully used sub-champagne bubble energy with the same IOP lowering results.[20,21,22] As the mechanism of action and bubble formation is believed to be based on thermal absorption of melanin, highly pigmented eyes should lead to lower SLT pulse energies, which is not necessarily the case,[23] and in other studies pigmentation has not been shown to be a reliable predictor of SLT success.[24–26] Thus, this review will disregard the champagne bubble energy level as a clinically significant dosing method.

METHODS

A review of the medical literature was conducted, mainly using PubMed and Google Scholar. Search terms included, but were not limited to, "selective laser trabeculoplasty", "laser trabeculoplasty", "energy dose response", "IOP reduction", "glaucoma", "race", "ethnicity", "trabecular meshwork pigmentation", "pattern", "topical treatment", "efficacy". Search terms were used alone or in combination. Some of the included articles were accessed through cross-referencing.

The review included prospective, cross-sectional, and retrospective articles which discussed the IOP lowering effect of SLT, not only in relation to energy levels used, patterns of illumination, TM pigmentation and race/ethnicity, but also in comparison with topical treatment. In addition, we included articles that stratified their study populations according to energy levels, patterns of illumination, races or ethnicities and degree of TM pigmentation.

The review excluded articles published in languages other than English, articles which were presented as abstracts only, articles without an abstract, review articles, articles that included fewer than ten study subjects, and articles solely discussing argon laser trabeculoplasty and/or topical treatment.

All articles were assessed by two investigators (M.A. and Z.S.), and where there was any disagreement, this was resolved by review using other investigators (M.B., G.G., L.J.K., P.T.K.). In total, 44 articles were analyzed, and were divided into the following subsections – SLT dose-response, SLT dose-response and race/ethnicity, SLT dose-response and TM pigmentation, and SLT dose-response and pattern of illumination. Although not directly related to energy dosing, Appendix 1, Supplemental Digital Content 1, http://links.lww.com/IJG/A627 is included

describing the effect(s) of SLT dose-response compared to topical treatment effect(s) which were noted during the review process.

RESULTS

SLT Dose-Response

Table 1 provides a summary of 17 studies that performed SLT, including their energy, pattern settings, and some other variables. Currently, pre-treatment IOP is the only accepted positive predictive factor for the extent of IOP lowering following SLT.[27–29] Although the total amount of energy delivered to the TM during SLT has also been described as a predictor for success, very few studies have examined high versus low-energy SLT, or tried to define the optimal energy for IOP reduction**.** Thus, for example, in a prospective cohort of 49 Chinese patients with open-angle glaucoma (OAG), Lee et al. reported the optimal energy for maximal IOP reduction. When total energy level (mJ) was plotted as a function of percentage of IOP reduction, two intervals gave the greatest reduction (>25%) – 81.0-82.7 mJ and 214.6-234.9 mJ. The former interval, however, was excluded from further analysis owing to its close proximity to the boundaries of the analysis curve. Furthermore, the patients in this study were only followed up for 1 month.[30] Whilst such a short time-frame might be sufficient to define the immediate or short-term outcomes of a particular SLT treatment, this would not be adequate for deriving long-term conclusions associated with optimal energy settings. In a prospective case series of primary open-angle glaucoma (POAG), ocular hypertension (OHT) and suspected glaucoma patients (N=74), Tang et al. found no significant differences in success rates, after 12 months of follow-up, between low and standard energy settings for SLT. The energy range per treatment spot was defined as 0.6−1.0 mJ for the standard (control) group, and 0.3−0.5 mJ for the low-energy group. However, the mean energy per spot and the

total energy were not reported.[22] In a retrospective cohort of 220 patients with OHT, OAG or normal tension glaucoma (NTG), Mao et al. attempted to develop a prediction rule for successful SLT treatment. Whereas higher pre-SLT IOP was also identified here as an important predictor for SLT success, this was not the case for the total energy dose delivered during the treatment.[29] In a prospective case series of 52 patients with POAG, Zhang et al. compared success rates of SLT between traditional energy and subthreshold energy settings (the latter defined as two-thirds of that of traditional energy), and found no significant differences in success rates between the two study groups at any time point during the 12 months of follow-up.[21]

There were two studies that reported on positive associations between total SLT energy dosage and IOP reduction. Habib et al. retrospectively followed 75 patients with OAG. The study population was divided into 3 groups: low energy (<85 mJ), medium energy (85—105 mJ) and high energy (>105 mJ). Analysis showed that higher energy was associated with greater IOP reduction for up to 36 months post-treatment. Whilst there was no significant difference in IOP reduction between the high and medium energy groups, IOP reductions in the low-energy group were significantly lower. The difference was most notable for up to 24 months of follow-up, after which it decreased significantly. Importantly, Habib et al. reported that patients in the high-energy group had higher baseline IOP levels,[31] which might present an important bias in this study, since, as previously mentioned, baseline IOP is a known predictor of successful SLT treatment. In a retrospective study, Elahi et al. carried out post-SLT follow up of 126 patients with POAG or OHT. Whilst no association was found between higher energy and greater IOP reduction, these authors reported that higher energy was associated with longer duration of qualified success (defined as either >20% reduction in IOP or any reduction in IOP-lowering

medications). As both studies by Habib[23] et al. and Elahi et al.,[25] were retrospective, IOP reduction may have been influenced by factors other than treatment energy that determine IOP response. No such association was found for complete success (defined as >20% reduction in IOP),[32] which is more frequently used as a criterion for a successful SLT treatment.[33]

In general, the reported energy settings of the different studies summarized in Table 1 varied significantly. Furthermore, most of those studies reported only partial data associated with energy settings. The energy range per treatment spot across the different studies ranged between 0.3 and 1.5 mJ, the mean energy per spot between 0.6 and 1.0 mJ, and the mean total energy between 32.5 and 167.1 mJ. Results also varied between the studies: for example, Xu et al. reported a 73.3% success rate at 6 months of follow-up and a 55.2% success rate at 2 years of follow-up, for a mean total energy of 32.5 mJ.[34] In contrast, Hong et al.[35] and Khouri et al.[36] reported similar success rates using much higher total energy levels (88.1 and 104.0 mJ, respectively).

Variations in energy settings, sample sizes, follow-up periods and definitions of success pose a challenge when comparing between different studies, and hence in attempting to reach objective conclusions with respect to optimal energy settings for SLT. However, it seems that higher energy is not clearly associated either with greater reduction in IOP or with higher success rates.

SLT Dose-Response and TM Pigmentation

A small subset of studies reported on the association between successful SLT treatment and level of TM pigmentation (Table 2). During SLT, energy is delivered to the TM, leading—at least in part—to IOP reduction by various mechanisms, which are only partially understood.[18] As melanin containing granules in the TM highly absorb the 532nm SLT light, it was expected that the IOP-lowering effect of SLT is

proportional to the level of pigmentation, as is known to be the case with argon laser trabeculoplasty (ALT).[37,38] In some studies, the choice of energy level was indeed based on the level of TM pigmentation.[39,40] This could be partially explained by the fact that SLT, when performed in heavily pigmented eyes, could lead to severe IOP spikes in patients with pigmentary glaucoma or pseudo-exfoliative glaucoma. For such patients, lower energy settings were recommended.[41] In such cases, even if energy levels are not explicitly adjusted for pigmentation differences, if the same clinical end-point is used, then less power will be required to achieve bubble formation for more pigmented angles.

The energy levels used across the studies summarized in Table 2 ranged between 0.6 and 1.4 mJ per treatment spot. The mean energy per spot was reported only by Ayala et al. (0.88 mJ),[42] and the mean total energy over these six studies ranged between 43.87 and 64.9 mJ.

Ayala et al. retrospectively followed 120 patients with OAG or OHT for 24 months after SLT. Failure was defined as a change in topical treatment or repeat SLT or incisional surgery, and the primary outcome measure was time to failure**.** While the laser energy level in that study showed a slight positive correlation with time to failure, no association was found between TM pigmentation and time to failure.[42] Mcllraith et al. found no differences in the IOP-lowering effect of SLT on the basis of TM pigmentation.[43] In a prospective study of 89 OAG patients, Hodge et al. reported that the level of TM pigmentation was not a predictor for success, as the total energy delivered to the TM was similar in the success and the non-success groups (44.95 and 43.87 mJ, respectively).[28] Hirabayashi et al. retrospectively followed 198 patients with POAG, NTG, or secondary open angle glaucoma (SOAG) for 6 months after SLT. Success was defined as ≥20% reduction in IOP or reduction in any medication,

and the success rate was 38.5%. While the mean total energy was listed as 64.2 mJ, the authors state, without elaborating, that the energy varied depending on the level of TM pigmentation. Furthermore, some patients had 180 degrees of their TM treated, while others had 360 degrees**.** TM pigmentation was thus not a predictor for successful SLT treatment.[39]

In a retrospective case series of 667 patients with OAG or primary angle closure glaucoma (PACG), Kuley et al. attempted to define predictors for successful SLT treatment. Both baseline IOP and greater angle pigmentation were found to be associated with success upon univariate analysis, whereas total energy was not. In multivariate analysis the association between TM pigmentation and success lost its statistical significance, and baseline IOP remained as the sole significant predictor for success.[40] In another study (not included in Table 2), Martow et al. prospectively examined the influence of pre-SLT antiglaucoma medications on the success of the procedure. Here too, TM pigmentation was not found to be associated with success.[27] The only study in this category that reported some association between TM pigmentation and successful SLT was conducted by Chen et al. In that study, the energy was set at 0.9 mJ per treatment spot, and IOP reduction over 90 and 180 degrees of SLT was compared. TM pigmentation was found to be associated with IOP reduction only at 7 months of follow-up (but not at 1 or 4 months). Nevertheless, no difference in IOP reduction was found between the study groups.[37]

Currently, there is no strong scientific evidence suggesting that greater angle pigmentation is associated with better SLT efficacy, thus requiring less energy to achieve the same effect as with standard energy, or alternatively, requiring more energy to achieve a better effect on IOP reduction. Further research is required in that area. In particular, prospective studies with adequate sample sizes need to be

conducted, and their study populations should be stratified by levels of energy and by levels of TM pigmentation. Associations between energy levels and TM pigmentation should be derived through multivariate regression models, adjusting for potential confounders such as baseline IOP and other risk factors for glaucoma.

SLT Dose Response and Race/Ethnicity

Our review also examined the efficacy of SLT in specific races/ethnicities (Table 3). Ethnicity has previously been described as an important factor in susceptibility to glaucoma, with a higher prevalence of POAG demonstrated in patients of African or Hispanic descent. There are also reports that in patients of African descent, glaucoma tends to be more severe and less responsive to topical and surgical treatment.[44–46] Investigators at Moorfields Eye Hospital in London suggested that primary SLT could be more efficacious in Caucasians, whilst the Glaucoma Laser Treatment Study (GLT) suggested that primary ALT could be more efficacious in patients of African-American descent.[4,47] In light of the above information, it is not unreasonable to assume that owing to various physiological, genetic and environmental factors, patients of different ethnicities could potentially require different energy settings in order to achieve maximal SLT effect.

Table 3 summarizes the energy range, between 0.4 and 1.5 mJ per treatment spot, across nine different studies. The mean energy per spot ranged between 0.73 and 1.0 mJ, and the mean total energy between 56.83 and 125.0 mJ. Shibata et al. reported the clinical results of SLT in 54 Japanese OAG patients. While both IOP reductions and success rates were greater in patients who had undergone 360 than 180 degrees SLT, total energy was not associated with IOP reduction.[48] Al-Busaidi et al. examined the short-term efficacy of SLT in OAG and OHT in Omani patients. The mean total energy was 64.03 mJ, which is significantly lower than that reported by Shibata et al.,

while the success rates were significantly higher (51.5% at 5 weeks and 72.7% at 12 weeks versus 46% and 29% in the 360-degree SLT group, at 1 and 2 years, respectively).[48,49] Although the definitions of success in both studies were similar, differences in their follow-up periods may account for their different results, since in most studies the IOP-reducing effect of SLT is found to wane with time. Lai et al. reported a 32.1% reduction in IOP, after 5 years of follow-up, in 32 OAG and OHT Chinese patients who underwent SLT at a mean total energy of 73.6 mJ.[50] Miki et al. reported treatment outcomes and prognostic factors of SLT in Japanese OAG patients on maximal tolerable therapy. Whilst 85.8% of eyes showed >20% reduction in IOP during the 12-month follow-up period, energy dose was not associated with treatment failure.[51] In another post hoc analysis of eight years follow up, Realini showed that SLT alone with retreatments (without topical medications) was able to maintain acceptable IOP in more than 70% of the 265 eyes of 133 Afro-Caribbean participants in Saint Lucia and Dominica. The average total energy used in a 360 degree treatment with 103.3 spots on average was 82.5 and 87.0 mJ in the right and left eyes, respectively. Thus, SLT may be an effective long term treatment for Afro-Caribbean patients.[52]

It is difficult to carry out valid comparisons between different studies for the various reasons mentioned above, but 2 studies—one by Realini et al. and the other by Soboka et al.—show striking similarities. Both studies are prospective, with similar patterns of application, numbers of spots, sample sizes and follow-up periods. Realini et al. studied POAG patients of West African descent while Soboka et al. studied POAG, OHT and pseudo-exfoliative glaucoma patients from Ethiopia. The most important differences between the two studies were in the mean total energy and in the fact that SLT was performed in both eyes by Realini et al. and in one eye by

Soboka et al. After 12 months, Realini et al. reported IOP reductions of 34.1%−38.8% in the right eye and 36.0%−38.9% in the left eye, and a 77.7% success rate (defined as ≥10% IOP reduction: of those, 93% had >20% reduction). In comparison, Soboka et al. performed SLT at a slightly higher mean total energy, and at 12 months reported a 25.9% reduction in IOP and a 60% success rate (defined as >20% reduction in IOP).[53,54] One possible explanation for the significantly better results of Realini et al. could be that IOP-lowering treatment of one eye has been shown to produce an IOP-lowering effect on the contralateral eye.[55,56] The impressive efficacy of SLT reported in these two cited studies might provide a clue to the required SLT energy settings for optimal IOP reduction in glaucoma patients of African descent.

In an important study conducted by Goosen et al. of 84 patients, the efficacy of SLT in African (60/84), Indian (21/84) and Caucasian (3/84) glaucoma patients was compared. IOP reductions of 42.2% were obtained in African patients 27.7% in Indian patients. Approximately 90% of the African patients, compared to 50% of the Indians, had >20% reduction in IOP.[57] This highlights racial differences in SLT efficacy, suggesting that SLT could be more efficacious in African patients than in other races, with Caucasians and Indians (and potentially other races) requiring higher levels of energy to achieve the same effect. Clearly, however, conclusions cannot be drawn on the basis of a single comparative study with small ethnic sample size. Further research is required.

SLT Dose Response to Different Patterns of Application

The efficacies of SLT in different patterns of laser application were compared in eight studies (Table 4). In most cases of SLT the laser is applied to either 360 or 180 degrees of the TM, but in some cases only to 90 degrees. Correspondingly, the numbers of laser spots applied are, respectively, approximately 100, 50 or 25, though

some study protocols deviate from these regimens. Different regimens also differ, not only with respect to the energy levels delivered to the TM during SLT, but also to treatment efficacy, so that whilst 360-degree SLT usually has the highest energy level, it does not necessarily result in the best efficacy in IOP reduction. The energy per spot across the different studies depicted in Table 4 ranged between 0.5 and 1.6 mJ, the mean energy per spot ranged between 0.74 and 1.03 mJ, and the mean total energy between 45.7 and 125.0 mJ. Notably, most of those studies did not report mean energy per spot and/or mean total energy.

In a prospective randomized controlled trial, Nagar et al. compared the efficacies of SLT, as well as of topical antiglaucoma treatments, in OHT and OAG patients. In the SLT group, patients were subdivided according to the extent of the TM subjected to laser treatment (90-, 180- and 360-degree SLT). IOP reduction was highest with 360-degree SLT. Success rates were higher with SLT degrees of 360 or 180 than of 90, but did not differ significantly between 360- and 180-degree SLT. Energy settings were not reported, but Nagar et al. concluded that total energy level was not associated with treatment success.[58] Shibata et al. retrospectively compared the results of 180- and 360-degree SLT in 54 OAG patients. Similarly to the findings of Nagar et al., both IOP reduction and success rates were highest with 360-degree SLT, and total energy was not associated with IOP reduction.[48]

Ozen et al. compared the efficacies of 180- and 360-degree SLT in 26 POAG patients. Both groups showed impressive IOP reductions (33.0% and 37.1%, respectively) and success rates (73.1% and 76.9%, respectively), and their differences were not statistically significant.[59] Tufan et al., when similarly comparing the results of 180- and 360-degree SLT in their 40 POAG patients, reported that energy levels in the 360-degree group were significantly higher, however IOP reductions between the two

groups were not significantly different. Associations between energy level and IOP reduction were not examined in that study.[60] In contrast to Ozen et al. and Tufan et al., Tawfique et al. compared the results of 90-degree and 360-degree SLT in 67 patients with OAG or OHT. In that study IOP reductions were not examined, but treatment survival extents between the two groups were reported. No significant differences were found between the two treatments with respect to the distributions of treatment survival times. Once again, higher baseline IOP was the only predictor of treatment success (defined as longer survival time).[61]

In several studies, laser application regimens differed from the commonly accepted regimens described in the literature. George et al., for example**,** compared 180-degree SLT and overlapping treatment spots with 360-degree SLT and non-overlapping treatment spots, in 284 OAG patients. The rate of responders to the treatment was found to be approximately 20% higher in the non-overlapping SLT group,[62] suggesting that treatment success is not related to laser energy level. The rationale for this lies in the fact that between each pair of overlapping spots lies a small region of pigmented cells that necessarily receive more energy than the adjacent areas of each spot. Such a treatment protocol would therefore result in higher total energy than a treatment involving non-overlapping spots with similar spot numbers and similar mean energy per spot. Furthermore, in the study conducted by George et al., the mean energy per spot was higher in the non-overlapping 180-degree SLT group, and the total treatment energy in the two groups was similar.[62] Thus, it is possible that lower energy and more extensive lasering extent, could set in motion physiological processes which contribute more to IOP reduction than that provided by higher energy levels delivered to a smaller extent of the TM. Wong et al. examined the efficacy of 360-degree SLT at different spot numbers (120 spots versus 160 spots).

Whilst IOP reduction was greater with 160 spots, success rates between the two groups did not differ.[63] Pukl et al. examined the efficacy of 360-degree SLT in both study groups, using different times of irradiation per treatment spot (1 ns per spot versus the standard 3−5 ns per treatment spot). The numbers of spots, the mean energy per spot and the mean total energy were similar in the two groups. Unsurprisingly, during the 6 months of follow-up visits, no significant difference in IOP reduction were found between the two groups.[64]

The findings described in this section support those in previous sections, maintaining that there is no consistent evidence of higher total energy application is associated with more successful SLT treatment. More complete coverage of the TM, on the other hand, might be associated with successful treatment. The jury is still out, and the survival times of different treatment patterns might be similar, even if their extents of lasering differ. Further research is required in that field.

DISCUSSION

While SLT is an effective IOP-lowering treatment for glaucoma, there is as yet no formal dose-response study that defines the laser parameters for achieving optimal IOP reduction by SLT in terms of the extent of IOP reduction, success rate and duration of effects. Such a study is essential to optimize the treatment to be used at earlier stages of disease progression. The results of such a trial may shed light on the poorly understood mechanisms of SLT effects. Alternatively, given the wide variety of SLT treatments reported, the dose-response paradigm may not be the optimal one for IOP reduction. In fact, another systematic review has shown various forms of SLT procedures, including low energy and various number of laser shots, to have the same pressure lowering effect.[65] It seems more likely that there may be a threshold energy level of response (yet to be determined), above which IOP is sufficiently

reduced. This threshold level would seem to be below all of the values reported in this literature review. A low energy SLT threshold effective dose is supported by the formulation of the COAST trial glaucoma study, as the authors of the study provided evidence for the rationale to use low-energy repeat SLT as primary therapy for mild to moderate POAG or high-risk OHT.[20]

The apparent lack of dose-response for SLT treatment may be due to the multiple modes of action of SLT with each process having a different activation energy.[66] The physical disruption caused by argon laser treatment does not seem to be necessary to reduce the intraocular pressure equally, supporting the hypothesis of non-disruptive levels of laser to create biological stimulation of the meshwork.[67]

Regarding factors that could potentially affect the required dose of energy for optimal IOP reduction, it seems that it would include either race or TM pigmentation. It also seems that while a more extensive coverage of TM lasering is beneficial for IOP reduction, this is not associated with the energy dose applied at each laser shot.

CONCLUSIONS

The optimal energy level needed for IOP reduction is not known as all reported single pulse energies as well as total energy applied to TM lead to similar IOP reduction in all reported ethnicities of patients and the extent of their TM pigmentation. Further specific research is required to determine the dose-response of SLT, if any exists. Until such a study is performed, it is advisable to use the accepted SLT energy dosing procedure, in spite of the rarity of the procedure's serious side effects.[20] (see Appendix, Supplemental Digital Content 1, http://links.lww.com/IJG/A627)

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Table 1. SLT dose response

Table 2. SLT dose response and TM pigmentation

Table 3. SLT dose response and race/ethnicity

Table 4. SLT dose response at different patterns of application

Table 5. SLT dose response vs. topical anti-glaucoma treatment

Table 1. SLT dose response											
Author	Methodology	Laser manufacturer	Sample size	Glaucoma type	Energy range (mJ)	Energy per spot in mJ (mean ± SD)	Pattern	Number of spots (mean ± SD)	Total energy in mJ (mean ± SD)	Follow-up (months)	Medications after SLT
Lee (2015)[30]	Prospective	Ellex, Adelaide, Australia	49	POAG, NTG	-	1.0 ± 0.06	360º	171.5 ± 41.2	167.1 ± 41.4	1	1 drop Alphagan P post laser. Dexamethasone 0.1%, and neomycin 0.5%, twice daily for 1 day
Tang (2011)[22]	Prospective	GE Healthcare, Munich, Germany	74	OHT, POAG	0.6-1.0 for control group and 0.3-0.5 for low-energy group	-	360º	100 (approximately), no SD reported	-	12	Diclofenac sodium 3 times daily for 3 days
Habib (2013)[31]	Retrospective	-	75	-	0.41-1.05	0.88 ± 0.14	360º	102 ± 15.2	93.73 ± 21.83	36	-
Mao (2018)[29]	Retrospective	-	158	-	-	-	180º	50 ± 5	-	6	1 drop brimonidine 0.2% and either prednisolone acetate 1% or ketorolac 0.5% post laser. Prednisolone acetate 1% or ketorolac 0.5% for 5 days

Xu (2019)[34]	Retrospective	Ellex, Adelaide, Australia	44	POAG	-	-	360°	105 ± 6	32.5 ± 2.5	24	-
Elahi (2020)[32]	Retrospective	Ellex, Adelaide, Australia	126	OHT, OAG	-	0.6 ± 0.2	-	94.4 ± 15.8	54.0 ± 16.9	24	1 drop of apraclonidine 1% post SLT. Ketorolac tromethamine 0.5% 1 drop daily for 4 days
Hong (2009)[35]	Retrospective	-	35	POAG, PE, pigmentary	-	-	360°	102.1 (no SD reported)	88.1 (no SD reported)	-	Bromfenac or diclofenac for 4-7 days post-SLT
Khouri (2014)[36]	Retrospective	-	25	OAG	-	0.94 ± 0.05	360°	111 ± 8	104 ± 8	24	None
Lee (2015)[73]	Prospective	Ellex, Adelaide, Australia	42	POAG, NTG	-	-	360°	-	163.8 ± 42.9 in the right eye and 158.3 ± 43.2 in the left eye	1	1 drop of Alphagan P post-SLT and a dexamethasone 0.1% and neomycin 0.5% combination eye drops twice daily for 1 day
Lee (2015)[74]	Prospective	Ellex, Adelaide, Australia	34	NTG	-	1.0 ± 0.08	360°	191.0 ± 27.3	-	24	1 drop of Alphagan P post-SLT and a dexamethasone 0.1% and neomycin 0.5% combination eye drops twice daily for 1 day
Liu (2020)[75]	Retrospective	Ellex, Adelaide,	79	POAG, OHT	0.8-1.2	-	180°	55 (no SD reported)	-	12	None

		Australia									
Melamed (2003)[76]	Prospective	Coherent, Inc, Santa Clara, California	31	POAG, PE, NTG, OHT, pigmentary	-	1.0 (no SD reported)	180°	approximately 50 (no SD reported)	-	18	1% prednisolone acetate only in eyes with increased inflammation after SLT
Solu (2020)[77]	Prospective	Ellex, Adelaide, Australia	15	POAG	0.4-1.2	0.6 (no SD reported)	180°	49 (no SD reported)	-	6	-
Raj (2018)[78]	Prospective	-	34	PACG	0.6-1.2	-	360°	At least 100 (no SD reported)	-	12	-
Schlote (2016)[79]	Retrospective	-	71	POAG, PE, OHT, pigmentary	0.6-1.0	-	180°	50-70 (no SD reported)	-	12	NSAIDs 4 times daily for 1 week
Wang (2020)[80]	Retrospective	Ellex, Adelaide, Australia	52	POAG, NTG, pigmentary	0.8-1.5	-	360°	70-85 (no SD reported)	-	-	Topical prednisolone 0.1% twice daily for 3 days
Zhang (2016)[21]	Prospective	Ellex, Adelaide, Australia	52	POAG	-	0.6 ± 0.1 in the conventional SLT group and 0.4 ± 0.1 in the subthreshold SLT group	360°	100 (no SD reported)	51.8 ± 5.7 in the conventional SLT group and 37.6 ± 3.3 in the subthreshold SLT group	12	None

Table 1. Continued

Number of glaucoma medications		IOP (mm Hg)			Adverse events	Definition of success	Main results
Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Reduction (mean ± SD)			
1.9 ± 1.1	-	17.1 ± 2.9	13.5 ± 2.8	-	None	IOP reduction ≥ 20% at 1 month post-SLT	There was a 20.2% ± 14.6% in IOP

							reduction and a 57.1% success rate
None	None	25.05 ± 2.24 in the low-energy group and 24.47 ± 1.85 in the control group	20.22 ± 1.83 in the low-energy group and 20.41 ± 1.98 in the control group at 12 months	-	Conjunctival hyperemia, mild anterior uveitis, in the low-energy group	IOP reduction ≥ 20%	There was no significant difference in IOP reduction and success rate between low-energy SLT group and control group
2.03 ± 1.01	2.0 ± 1.2	19.62 ± 3.69	16.11 ± 5.82 at 3 years	3.44 ± 6.58	-	-	Higher energy was associated with higher IOP reduction at 36 months
-	-	24 ± 4.7 in IOP reduction ≥20% group and 21 ± 4.4 in IOP reduction <20% group	-	-	-	≥20% reduction in IOP from baseline at 6 months after SLT	Neither high energy SLT (>41 mJ) nor low energy SLT (<41 mJ) was associated with higher IOP reduction in univariate analysis
1.5 ± 0.7	-	-	19.8 ± 3.9	16.5 ± 2.8 at 2 years	-	IOP≤21 mm Hg combined with an IOP decrease ≥20% without a change in glaucoma medications or IOP≤21 mm Hg combined with a reduction of medications	Success rate was 73.3% at 6 months and 55.2% at 2 years
1.5 ± 1.2	1.0 ± 1.2 at 2 years	18.6 ± 4.8	15.4 ± 3.2 at 2 years	-	IOP spikes, anterior chamber flare, hypertonia, corneal edema	Complete success if ≥20% IOP reduction was observed at a given time, and qualified success if any reduction of IOP was observed with either at least	There was 16.8% complete success and 24.4% qualified success at 2 years. Higher energy was associated with longer

						a 20% difference from baseline or a reduction in IOP-lowering medications	duration of qualified success
-	-	20.1 (no SD reported) for the 1st SLT	16.2 (no SD reported), at 5-8 months	4.0 (no SD reported)	-	≥20% peak IOP reduction	54.5% eyes that reached >20% reduction after the 1st SLT
1.7 ± 0.9	1.5 ± 0.8 at 24 months	19.7 ± 2.3	17.3 ± 3.2 at 24 months	2.8 ± 3.4	-	-	There were 55% eyes with IOP reduction >20% from baseline
2.0 ± 1.1 in both eyes	-	17.3 ± 3.2 in the right eye and 16.9 ± 3.0 in the left eye	13.5 ± 3.0 in the right eye and 13.5 ± 2.6 in the left eye, at 1 month	-	-	IOP reduction of ≥ 20%	There was 20.9 ± 15.7% and 19.0 ± 14.0% success in IOP reduction in the right and left eyes, respectively. Both success and non-success in one eye were associated with success or nonsuccess in the other eye, respectively
1.5 ± 0.8	0.9 ± 0.9	16.2 ± 2.3	12.6 ± 2.7 at 24 months	-	-	IOP reduction >20% from pre-SLT, without medication	There was 22% reduction in IOP from pre-SLT levels and 41.1% reduction in number of medications at 24 months
-	-	27.05 ± 3.57 in young patients (age<40)	18.83 ± 3.12 in young patients (age<40), at 12 months	8.22 ± 3.11	IOP spikes, conjuctival hyperemia, anterior chamber flashing, epithelial punctate	≥ 20% in IOP with no change in pharmaceutical treatment or additional surgery needed at 1-	There was 30.4% IOP reduction and 71.4% success rate in young patients' eyes (vs.

					keratitis	year follow-up	25.2% and 56.5%, respectively, in elderly patients)
None	None	25.6 ± 2.5	17.9 ± 2.8 at 18 months	7.7 ± 3.5	Conjunctival redness and injection, mild anterior chamber flare, ocular pain, IOP spikes	IOP reduction of ≥ 20%	There was 30% reduction in IOP from baseline. 89% of eyes had a reduction of 5 mmHg
1.6 (no SD reported)	0.17 (no SD reported)	25.93 ± 3.17 without medications and 19.67 ± 2.63 with medications	18.80 ± 2.38 at 6 months	7.13±1.53 and 0.87 ± 1.55 (without vs. with medications)	-	IOP decrease of > 3 mmHg or IOP decrease of > 20%	There was 27.49% reduction in IOP at 6 months from baseline at the time of diagnosis. Success was achieved in all eyes (100% success rate). In 87% of eyes topical medications were discontinued
-	-	23.76 ± 1.92	16.96 ± 2.82 at 12 months	6.82 ± 3.49	None	-	20% or more reduction in IOP was achieved in 51.51% eyes at 6 months and 46.42% at 12 months, without any medications.
1.3 ± 0.8 in the early glaucoma group and 1.9 ± 1.0 in the advanced glaucoma group	1.3 ± 1.1 in the early glaucoma group and 1.9 ± 1.0 in the advanced glaucoma group, at 12	22.9 ± 4.4 in the early glaucoma group and 22.1 ± 4.1 in the advanced glaucoma group	18.2 ± 2.9 in the early glaucoma group and 14.8 ± 2.4 in the advanced glaucoma group, at 12 months	-	None	Early: IOP<21 mmHg and >20 % of the initial IOP, and eyes with discomfort from antiglaucoma medication but controlled IOP should achieve a	63% of eyes in the early glaucoma group had IOP reduction <21 mmHg/>20 % of the preoperative IOP and reduction in

	months					reduction in the number of medications ≥1 and an IOP <21 mmHg. Advanced: IOP reduction <18 mmHg and >30 % of the baseline IOP	medication. 50% of eyes in the advanced glaucoma group had IOP reduction <18 mmHg and >30 % reduction from baseline IOP
-	-	23 ± 4.6	18 ± 3.2 at 4 months	-	-	-	SLT resulted in a mean of 27% IOP reduction at 4-8 weeks follow up and 79% response rate. Mean time to failure was 22.2 months.
-	-	25.0 ± 2.5 in the conventional SLT group and 25.7 ± 1.9 in the subthreshold SLT group	20.0 ± 1.7 in the conventional SLT group and 20.3 ± 1.6 in the subthreshold SLT group, at 12 months	-	-	IOP reduction >20% from pre-SLT, without medication	There was no significant difference in IOP reduction between the traditional SLT and the subthreshold SLT group. Success rate was 71.4% in the traditional and 76.2% in the subthreshold SLT group

SLT: Selective laser trabeculoplasty; **POAG:** Primary open angle glaucoma; **NTG:** Normal tension glaucoma; **OHT:** Ocular hypertension; **PE:** Pseudo-exfoliation; **OAG:** Open angle glaucoma; **PACG:** Primary angle closure glaucoma; **IOP:** Intra-ocular pressure

Table 2. SLT dose response and TM pigmentation

Author	Methodology	Laser manufacturer	Sample size	Pigmentation	Glaucoma type	Energy range (mJ)	Energy per spot in mJ (mean ± SD)	Pattern	Number of spots (mean ± SD)	Total energy in mJ (mean ± SD)	Follow-up (months)	Medications after SLT
Ayala (2011)[42]	Retrospective	Ellex, Adelaide, Australia	120	0.77 ± 0.66	POAG, PE, pigmentary, OHT	06-1.0	0.88 ± 0.11	90º	26.9 ± 4.8	-	24	Apraclonidine instilled once
Kuley (2020)[40]	Retrospective	-	667	-	PACG, POAG, PE, pigmentary	-	-	360º	97.4 ± 9.4	64.9 ± 22.0	12	-
Mcllraith (2006)[81]	Prospective	-	100	-	OAG	-	-	180º	50 ± 5	-	12	1 drop of brimonidine 0.2% and either prednisolone acetate 1% or ketorolac 0.5% post-laser. Prednisolone acetate 1% or ketorolac 1% 4 times daily for 5 days
Hodge (2005)[28]	Prospective	-	89	2.5 ± 0.9	POAG, PE, pigmentary	0.8-1.4	-	180º	50 (no SD reported)	44.95 ± 10.73 in the success group and 43.87 ± 10.83 in the no success group	12	1 drop of 1% apraclonidine post laser, prednisolone acetate 1% four times a day for 5 days
Hirabayashi (2020	Retrospective	-	198	-	POAG, NTG,	0.6-1.4	-	180º and	-	64.2 ± 24.5	6	None

)[39]					SOAG			360º		in successful cases		
Chen (2004)[37]	Prospective	-	64	1* (no SD reported)	POAG, PE, pigmentary, OHT	-	0.9 (no SD reported)	90º and 180º	25 in the 90º group and 50 in the 180º group	-	7	1 drop of 1% Iopidine[apraclonidine]. Dexamethasone eye drops 3 times daily for 5 days

Table 2. Continued

Number of glaucoma medications		IOP (mm Hg)			Adverse events	Definition of success	Main results
Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Reduction (mean ± SD)			
-	-	24.7 ± 4.6	-	-	-	-	Higher TM pigmentation was not associated with longer time to failure of SLT treatment
-	-	19.6 ± 5.2	16.0 ± 4.5 at 12 months	7.8 ± 4.3 for eyes with successful treatment	-	IOP decrease of 20% or more from baseline at the 3-month, 6-month, and 12-month follow-up visits	19.8% eyes achieved success (IOP<18 mmHg and IOP reduction>20%). Greater angle pigment and higher IOP at baseline were associated with success on univariate analysis
None	None	26.0± 4.3 in the SLT group and 24.6± 3.7 in the control group	17.8 in the SLT group and 16.9 in the control group, at 12 months (no SD reported)	8.3 in the SLT group and 7.7 in the control group (no SD reported)	Minimal inflammatory reaction, flare	-	The average % reduction in IOP was 31.0% in the SLT group and 30.6% in the control group. There were no differences in IOP lowering with selective laser trabeculoplasty on the basis of angle pigmentation.
-	-	23.84 ± 4.88	16.6 ± 3.39 in the success group and 20.0 ±	-	-	IOP reduction of >20% at 1-year post-treatment follow up.	TM pigmentation was not a predictor of success. There was no significant difference between success and no

			5.78 in the no success group, at 12 months				success in terms of total energy applied
2.0 ± 1.3	2.0 ± 1.3 at 6 months	17.8 ± 4.4	15.2 ± 4.9 at 6 months	-	IOP spikes	≥20% IOP reduction or ≥1 medication reduction without an IOP lowering procedure	Success rate at 6 months was 38.5%. TM pigmentation was not a predictive factor for success
-	-	25.44 ± 1.41 in the 90º group and 26.06 ± 1.73 in the 180º group	18.43 ± 1.38 in the 90º group and 19.90 ± 1.59 in the 180º group, at 7 months	-	-	-	There was no difference in IOP reduction between the groups. TM pigmentation was associated with successful SLT only at 7 months (but not at 1 and 4 months)

* Median

r; **POAG:** Primary open angle glaucoma; **SOAG:** Secondary open angle glaucoma; **NTG:** Normal tension glaucoma; (
gle glaucoma; **PACG:** Primary angle closure glaucoma; **IOP:** Intra-ocular pressure; **SD:** Standard deviation; **TM:** Tra

Table 3. SLT dose response and race/ethnicity

Author	Methodology	Laser manufacturer	Sample size	Race/ethnicity	Glaucoma type	Energy range (mJ)	Energy per spot in mJ (mean ± SD)	Pattern	Number of spots (mean ± SD)	Total energy in mJ (mean ± SD)	Follow-up (months)	Medications after SLT
Shibata (2012)[48]	Retrospective	Lumenis, Inc Coherent Inc, Palo Alto, CA, USA	54	Japanese	POAG, PE	0.8 - 1.4	-	180º and 360º	75 ± 22 and 121 ± 19 in 180º and 360º, respectively	73 ± 29 and 125 ± 30 in 180º and 360º, respectively	36	Apraclonidine 1% once. Fluorometholone 0.1% eye drops 4 times/day for 7 days
Al-busaidi (2020)[49]	Retrospective	Ellex, Adelaide, Australia	36	Omani	OHT, OAG	0.4 - 0.9	-	360º	99.52 ± 10.31	64.03 ± 10.26	3	Apraclonidine 0.5% once
Lai (2004)[50]	Prospective	Coherent Inc., Palo Alto CA, USA	32	Chinese	POAG, OHT	-	1.0 ± 0.1	360º	Approximately 100 (no SD reported)	73.6 ± 16.4	60	One drop of 1% apraclonidine and 1% prednisolone acetate immediately post-laser. Prednisolone acetate 4 times daily for 7 days
Miki (2016)[51]	Retrospective	Ellex, Adelaide, Australia	78	Japanese	POAG, NTG, PE, SOAG	-	-	360º	-	71.7± 20.2	12	Steroid eye drops administered at the discretion of the physician
Ono (2020)[68]	Retrospective	-	65	Japanese	POAG, NTG, PE	0.7 - 1.0	-	360º	Approximately 100 (no SD	-	12	-

									reported)			
Realini (2013)[53]	Prospective	Lumenis	64	African	POAG	-	-	360º	104.5 ± 4.1 in the right eye and 104.7 ± 3.6 in the left eye	78.4 ± 14.8 in the right eye and 86.4 ± 15.8 in the left eye	12	None
Sobo ka (2020)[54]	Prospective	Lumenis Inc., Santa Clara, CA	61	Ethiopian	POAG, PE, OHT	0.4 - 1.5	0.79 ± 0.23	360º	100 (no SD reported)	89.82 ± 29.64	12	Daily topical NSAIDS for 1 week
Goosen (2017)[57]	Retrospective	Lumenis; Yokneam, Inc, Israel	82	African, Indian (21/84), white (3/84)	-	1.1 - 1.4	-	360º	120-140 (no SD reported)	-	12	Ketorolac eye drops 3 times daily for 28 days
Funarunart (2021)[82]	Retrospective	Optimis Fusion, Quantel Medical, Cournon d'Auvergne, France	96 eyes (exact number of patients wasn't reported)	Thai	POAG, NTG, OHT, PE, JOAG	0.5 - 1.0	0.73 ± 0.11	180º and 360º (depending on the surgeon's preference)	-	56.83 ± 19.77	24	-
Realini[52] (2021)	Retrospective	Lumenis Selecta II	265 eyes	Afro-Caribbean	OAG	-	-	360º	R: 103.3 ± 3.5 L: 103.1 ± 3.1	R: 82.5 ± 18.8 L: 87.0 ± 18.5	94	Medication free survival rate of repeat SLT over 94 months was 71.2% and 71.7% in right and left eye

Table 3. Continued

Number of glaucoma medications	IOP (mm Hg)	Adverse events	Definition of success	Main results

Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Reduction (mean ± SD)			
3.0 ± 1.0 and 2.8 ± 0.7 in 180º and 360º, respectively	-	19.5 ± 4.3 and 21.0 ± 4.1 in 180º and 360º, respectively	-	2.6 ± 4.0 and 5.6 ± 4.3 and in 180º and 360º at 6 months, respectively	IOP spikes	IOP reduction by ≥20% of pretreatment IOP without additional medications, laser or surgery	IOP reduction was significantly greater in the 360º group than in the 180º group. Response rate between groups was similar. Success rate was higher in the 360º group at 1 and 2 years than in the 180º group. Total energy was not associated with IOP reduction.
1 ± 0.4	-	25.77 ± 4.57	18.82 ± 4.68, at 3 months	6.95 (no SD reported)	IOP spikes, redness, pain/discomfort, corneal epitheliopathy	at least 20% IOP reduction from baseline without further medications or interventions	Success rate was 51.5% at 5 weeks and 72.7% at 12 weeks post laser
-	-	26.8 ± 5.6	-	8.6 ± 6.7 at 5 years	-	-	There was 32.1% reduction in IOP in the SLT group at 5 years. Eyes treated with SLT needed substantially fewer anti-glaucoma medications
3.4 ± 1.3	3.1 ± 1.1	23.9 ± 6.2	-	-	-	-	54.7% eyes had IOP equal to or greater than baseline at the last visit, and 85.8% eyes had <20% IOP reduction on 2 consecutive visits. Energy dose was not associated with failure.
2.6 ± 1.2 in the SLT group	2.38 (no SD reported) in the SLT group, at 12 months	18.8 ± 5.3 in the SLT group	-	-	IOP spikes	≥ 20% reduction in IOP from baseline without any additional medication during post-treatment periods	There was 21% reduction in IOP at 6 months and 18.5% reduction in IOP at 12 months in the SLT group.
-	None	21.4 ± 3.6 in the right eye and 21.1 ± 3.5 in the left eye	13.1 ± 3.3 in the right eye and 12.9 ± 3.1 in the left eye, at 12 months	8.9 ± 3.2 in the right eye and 8.9 ± 3.3 in the left eye	IOP spikes, photophobia	10% reduction in IOP from baseline after washout	IOP reduction ranged from 34.1% to 38.8% in the right eye and from 36.0% to 38.9% in the left eye. Success rate was 77.7% (≥10% reduction in IOP. Out of those, 93% had >20% IOP reduction)

1.29 ± 1.01	1.03 ± 0.70 at 12 months	24.3 ± 2.5	17.6 ± 3.4 at 12 months	6.7 ± 4.2	-	IOP lowering of > 20% from baseline without repeat treatment	There was a 25.9% reduction at 12 months with 60% success rate. There was a significant reduction in antiglaucoma medications.
-	-	27.7 in right eyes and 25.9 in left eyes (no SD reported)	13.6 at 12 months (no SD reported)	-	None	-	There was 49% reduction of IOP from pre-SLT baseline levels, at 12 months. There was 42.2% reduction of IOP in Blacks and 27.7% in Indians. Approximately 90% of black patients had>20% IOP reduction at 12 months
2.74 ± 1.09	2.16 ± 1.31 at 24 months	19.31 ± 3.59	14.79 ± 3.67 at 24 months	-	IOP spikes	Reduced IOP of 20% or decreased number of antiglaucoma drugs usage after SLT	59.4% met the definition of successful treatment at 3 months, where 33.3% of treated eyes had at least 20% IOP reduction and 30.2% needed fewer antiglaucoma drugs
R: 1.14 ± 0.55 L: 1.14 ± 0.54	0 – study exclusion	R: 21.2 ± 3.4 L: 21.2 ± 3.9	At eight years R: 15.7 ± 2.6 L: 14.7 ± 2.5	At eight years R: 6.1 ± 2.8 L: 7.4 ± 5.6	-	IOP controlled without medications	SLT treatments alone (no medications) were able to maintain IOP to 13-16mm Hg in more than 70% of the patients over 8 years

ive laser trabeculoplasty; **POAG:** Primary open angle glaucoma; **NTG:** Normal tension glaucoma; **OHT:** Ocular hypertension; **PE:** Pseudo-exfoliation; **OAG:** Open
OAG: Secondary open angle glaucoma; **JOAG:** Juvenile open angle glaucoma; **IOP:** Intra-ocular pressure.

Table 4. SLT dose response at different patterns of application

Author	Methodology	Laser manufacturer	Sample size	Glaucoma type	Energy range (mJ)	Energy per spot in mJ (mean ± SD)	Pattern	Number of spots (mean ± SD)	Total energy in mJ (mean ± SD)	Follow-up (months)	Medications after SLT
Nagar (2005)[58]	Prospective	Lumenis, Coherent, Inc, Palo Alto, CA, USA	167	OHT, OAG	-	-	90º, 180º and 360º	25-30 (90º), 48-53 (180º), 93-102 (360º), no SD reported	-	12	Dexamethasone 0.1% eye drops 4 times/day for 5 days or ketorolac eye drops 4 times/day for 5 days
Shibata (2012)[48]	Retrospective	Lumenis, Coherent, Inc, Palo Alto, CA, USA	54	POAG, PE	0.8-1.4	-	180º and 360º	75 ± 22 and 121 ± 19 in 180º and 360º, respectively	73 ± 29 and 125 ± 30 in 180º and 360º, respectively	36	Apraclonidine 1% once, fluorometholone 0.1% eye drops 4 times/day for 7 days
Ozen (2020)[59]	Prospective	Lightmed SeLecTor Deux	26	POAG	0.7-0.9	-	180º in group 1 and 360º in group 2	50 in group 1 and 100 in group 2 (no SD reported)	-	6	None
Tawfique (2019)[61]	Prospective	Ellex, Adelaide, Australia	67	POAG, PE, OHT, pigmentary	-	-	90º and 360º	25 in the 90º group and 100 in the 360º group	-	24	-
Tufan (2017)[60]	Prospective	Lumenis, Coherent, Inc., Palo Alto, CA, USA	40	POAG	-	-	180º and 360º	56.0 ± 6.5 in the 180º group and 97.5 ± 11.5 in the 360º group	65.6 ± 17.2 in the 180º group and 116.0 ± 31.7 in the 360º group	6	Apraclonidine 1% once post-laser
George (2008)[62]	Retrospective	Lumenis, Coherent Inc, Palo	284	POAG, PE	05-1.6 in the overlapping SLT	1.03 ± 0.17 in the overlapping	180º in the overlapping SLT	104 ± 18.67 in the overlapping	-	14	Diclofenac sodium 0.1% drops 4

		Alto, CA			group and 0.7-1.1 in the non-overlapping SLT group	SLT group and 0.89 ± 0.1 in the non-overlapping SLT group	group and 360º in the non-overlapping SLT group	SLT group and 105 ± 12.83 in the non-overlapping SLT group			times daily for 5 days
Wong (2018)[63]	Retrospective	Ellex, Adelaide, Australia	199	POAG, PACG, OHT, NTG, PE,	0.8-1.2	-	360º	119.39 ± 4.23 and 159.56 ± 3.56	-	12	Brimonidine tartrate 0.15%/ apraclonidine hydrochloride 0.5% post-laser for 4 days
Pukl (2016)[64]	Prospective	OptoSLT MDPSS, Optotek d.o.o, Slovenia	30	POAG, OHT, NTG	-	0.82 in the 1 ns group and 0.74 in the 3-5 ns group (no SD reported)	360º	64.9 in the 1 ns group and 61.8 in the 3–5 ns group (no SD reported)	53.0 in the 1 ns group and 45.7 in the 3-5 ns group (no SD reported)	6	Dexamethasone 1 mg/ml 3 times daily for 5 days, oral Acetazolamide 125 mg immediately post-laser, with an additional 125 mg given 6–8 h postoperatively

Table 4. Continued

Number of glaucoma medications		IOP (mm Hg)			Adverse events	Definition of success	Main results
Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Reduction (mean ± SD)			

-	-	29.3 (SD not reported)	17-25 in all groups, at 12 months (SD not reported)	-	Pain/discomfort, uveitis, IOP spikes	Both as a 20% or more reduction in IOP from baseline measurements and also as a 30% or greater IOP reduction from baseline with no additional antiglaucomatous interventions	Mean IOP was significantly lower with 360º SLT than 90º SLT and 180º SLT. Success rates were greater with 180˚ and 360˚ than with 90˚ SLT. With 360º SLT, 82% of eyes achieved a 20% IOP reduction and 59% a 30% reduction from baseline. Although success rates were better with 360º than with 180º SLT treatments, differences were not significant. There were no differences with regard to laser power settings or total laser energy delivered between eyes that responded, in terms of a 20% and a 30% IOP reduction, and those that did not respond with 180º and 360º SLT treatments.
3.0 ± 1.0 and 2.8 ± 0.7 in 180º and 360º, respectively	-	19.5 ± 4.3 and 21.0 ± 4.1 in 180º and 360º, respectively	-	2.6 ± 4.0 and 5.6 ± 4.3 and in 180º and 360º at 6 months, respectively	IOP spikes	IOP reduction by ≥20% of pretreatment IOP without additional medications, laser or surgery	IOP reduction was significantly greater in the 360º group than in the 180º group. Response rate between groups was similar. Success rate was higher in the 360º group at 1 and 2 years than in the 180º group. Total energy was not associated with IOP reduction.
2.2 ± 0.7 in group 1 and 2.25 ± 0.7 in group 2	-	27.4 ± 2.1 in group 1 and 27.7 ± 2.4 in group 2	18.3 ± 2.0 in group 1 and 17.4 ± 1.9 in group 2, at 6 months	-	-	Reduction of 20% or more in IOP at 6 months	There was 33.0% reduction in IOP in group 1 and 37.1% reduction in IOP in group 2. At 6 months, success rate was 73.1% in group 1 and 76.9% in group 2 (differences were not significant). No significant difference was determined between the two groups in terms of antiglaucoma drug numbers.

-	-	24.9 ± 3.6 in the 90º group and 24.8 ± 4.2 in the 360º group	-	-	-	-	Distributions of survival times for the two treatment extents were not significantly different. The mean survival of the treatment effect was similar in the 90-degree and 360-degree SLT groups.
2.2 ± 0.4 in the 180º group and 2.4 ± 0.5 in the 360º group	-	17.3 ± 2.3 in the 180º group and 17.0 ± 2.9 in the 360º group	16.8 ± 2.4 in the 180º group and 17.6 ± 3.1 in the 360º group, at 6 months	-	Mild anterior chamber inflammation	-	There were no significant differences in IOP reductions between the groups
2.51 in the 180º overlapping SLT group and 2.48 in the 360º non-overlapping SLT group (no SD reported)	2.0 in the 360º non-overlapping SLT group at 14 months, no SD reported (change was not observed in the other groups)	18.44 in the 180º overlapping SLT group and 19.35 in the 360º non-overlapping SLT group, no SD reported	-	-	-	-	The percentage of responders was approximately 20% greater for non-overlapping SLT than for overlapping SLT (50% vs. 30%, respectively
1.11 ± 1.26 (120 spots), 0.55 ± 0.95 (160 spots)	-	18.81 ± 3.72 (120 spots), 19.21 ± 4.43 (160 spots)	-	2.88 ± 4.34 (120 spots) 4.11 ± 3.92 (160 spots) at 1 year	-	≥20% IOP reduction as defined by the World Glaucoma Association with no need for further SLT or trabeculectomy; or a decrease in glaucoma medications without an increase in IOP when compared to baseline	IOP reduction was greater in the 160-spot group in univariate analysis. There was no difference in success rates between the groups.
None	None	24.1 ± 3.72 in the 1 ns group and 24.3 ± 3.71 in the 3-5	18.28 ± 3.32 in the 1 ns group and 18.41 ± 3.53 in	5.8 in the 1 ns group and 5.9 in the 3-5 ns group	-	≥ 20% drop in IOP from baseline	There was no significant difference in mean IOP between groups at any follow-up visit. Success rate was 76% in the 1 ns

		ns group	the 3-5 ns group, at 6 months	(no SD reported)			group and 72% in the 3-5 ns group at 6 months

ive laser trabeculoplasty; **POAG:** Primary open angle glaucoma; **NTG:** Normal tension glaucoma; **OHT:** Ocular hypertension; **PE:** Pseudo-exfoliation; **OAG:** Open
ACG: Primary angle closure glaucoma; **IOP:** Intra-ocular pressure

Table 5. SLT dose response vs. topical anti-glaucoma treatment

Author	Methodology	Laser manufacturer	Sample size	Glaucoma type	Energy range (mJ)	Energy per spot in mJ (mean ± SD)	Pattern	Number of spots (mean ± SD)	Total energy in mJ (mean ± SD)	Follow-up (months)	Medications after SLT
Nagar (2005)[58]	Prospective	Lumenis, Coherent, Inc, Palo Alto, CA, USA	167	OHT, OAG	-	-	90º, 180º and 360º	25-30 (90º), 48-53 (180º), 93-102 (360º), no SD reported	-	12	Dexamethasone 0.1% eye drops 4 times/day for 5 days or ketorolac eye drops 4 times/day for 5 days
Nagar (2009)[69]	Prospective	Ellex, Adelaide, Australia	40	OHT, OAG	0.2-1.4	-	360º	100 ± 5	-	6	Ketorolac tromethamine 4 times/day for 5 days
Lai (2004)[50]	Prospective	Coherent, Palo Alto, CA, USA	32	POAG, OHT	-	1.0 ± 0.1	360º	Approximately 100 (no SD reported)	73.6 ± 16.4	60	One drop of 1% apraclonidine and 1% prednisolone acetate immediately post-laser. Prednisolone acetate was continued 4 times daily for 7 days
Narayanaswamy (2014)[71]	Prospective	-	100	PACG	-	-	360º	117.6 ± 25.6	90.2 ± 33.2	6	Prednisolone acetate 1% eyedrops 4 times daily for 1 week
Ono (2020)[68]	Retrospective	-	65	POAG, NTG, PE	0.7-1.0	-	360º	Approximately 100 (no SD reported)	-	12	-
Katz (2012)[70]	Prospective	-	69	POAG, PE,	0.2-1.2	-	360º	100 (no SD reported)	-	12	-

				OHT							
Gazzard (2019)[11]	Prospective	-	718	POAG, OHT	0.3-1.4	-	360º	100 (no SD reported)	-	36	-
De-Keyser (2017)[72]	Prospective	Lumenis, Dreieich, Germany	143	POAG, OHT	-	1.1 ± 0.3	360º	102.6 ± 9.2	-	18	Indomethacin/ Dexamethasone or no drops

Table 5. Continued

Number of glaucoma medications		IOP (mm Hg)			Adverse events	Definition of success	Main results
Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Pre SLT (mean ± SD)	Post SLT (mean ± SD)	Reduction (mean ± SD)			
-	-	29.3 (SD not reported)	17-25 in all groups, at 12 months (SD not reported)	-	Pain/discomfort, uveitis, IOP spikes	Both as a reduction in IOP of 20% or more from baseline measurements and as a reduction in IOP of 30% or more from baseline with no additional anti-glaucomatous interventions	Mean IOP was significantly lower in eyes receiving latanoprost than 90º SLT, 180º SLT and 360º SLT. Mean IOP was lower with 360˚SLT than 90˚ SLT. Differences in success rates with latanoprost and 360º were not significant.
-	-	26.1 ± 4.0 in the SLT group	-	6.2 ± 0.8 in the SLT group at 4-6 months	-	20% decrease in IOP	There was no significant difference between IOP reduction with SLT and with latanoprost
-	-	26.8 ± 5.6	-	8.6 ± 6.7 at 5 years	-	-	IOP reduction was similar between eyes treated with SLT and those with anti-glaucoma medications. Eyes treated with SLT needed substantially fewer anti-glaucoma medications

None	None	23.5 ± 2.5 in the SLT group and 22.4 ± 2.5 in the PGA group	19.5 ± 3.3 in the SLT group and 18.1 ± 2.4 in the PGA group, at 6 months	3.7 in the SLT group and 4.4 in the PGA group (no SD reported)	-	Complete success—patients with an IOP lower than 21 mm Hg and without any additional IOP-lowering medications at 6 months. Qualified success—those with IOP < 21 mm Hg and who required IOP-lowering medication.	There was a 16.9% reduction in IOP in the SLT group vs. 18.5% in the PGA group. After adjusting for baseline differences in IOP, the difference in effectiveness of IOP reduction between the 2 groups was not significant. There was 60% complete success in the SLT group vs. 84% in the PGA group.
2.0 ± 1.0 in the ripasudil group and 2.6 ± 1.2 in the SLT group	2.38 (no SD reported) in the SLT group, at 12 months	18.8 ± 5.3 in the SLT group	-	-	IOP spikes	≥ 20% reduction in IOP from baseline without any additional medication during post-treatment periods	There was a 21% reduction in IOP after 6 months and an 18.5% reduction in IOP after 12 months in the SLT group. The SLT group required significantly fewer medications at 1, 3 and 9 months than those who took ripasudil. There was no significant association between treatment success in the SLT group vs. the ripasudil group.
-	-	24.5 ± 2.2 in the SLT group	18.2 ± 2.8 in the SLT group, at 12 months	6.3 ± 2.7	-	-	IOP reduction from baseline was 26.4% for the SLT group and 27.8% in the medicated group. This difference is not significant
-	-	24.5 ± 5.2	18.2 ± 3.73 in OHT patients, 14.4 ± 3.07 in	-	Inflammation, IOP spikes	-	Target IOPi was achieved by 36 months in 95% of eyes in the SLT group and in 93.1% in the

			moderate OAG patients, at 36 months				eye drops group. By 36 months,. 78.2% eyes in the SLT group did not require any medications. There were no significant differences in IOP reduction between the 2 groups.
1.50 ± 0.85 in the SLT group and 1.41 ± 0.71 in the control group	0.44 ± 0.68 in the SLT group and 1.39 ± 0.68 in the control group at 6 months	13.97 ± 3.53 in the SLT group and 12.57 ± 3.50 in the control group with medications	11.85 ± 3.39 in the SLT group 10.59 ± 3.80 in the control group at 6 months	-	-	Reduction in medications while maintaining IOP, >20% IOP reduction, and >30% IOP reduction compared to baseline IOP before SLT treatment	Full replacement of the antiglaucoma medication by SLT treatment was achieved in 77% of the patients after 12 months, and in 74.1% after 18 months. Partial replacement was achieved in all other cases. No patient remained at the same number of medications after SLT. Mean IOP was 47.1% after 18 months. With >30% reduction employed as the criterion, SLT was a success in 86.2% of patients.

ive laser trabeculoplasty; **POAG:** Primary open angle glaucoma; **NTG:** Normal tension glaucoma; **OHT:** Ocular hypertension; **PE:** Pseudo-exfoliation; **OAG:** Open
ACG: Primary angle closure glaucoma; **IOP:** Intra-ocular pressure; **PGA:** Prostaglandin analogues.