Energy Dose-Response in Selective Laser Trabeculoplasty: A Review

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Précis: A literature review of selective laser trabeculoplasty (SLT) energy dose-response found no definitive relationship between intraocular pressure (IOP) reduction with respect to total or pulse energy, race, pigmentation, or application pattern.

Purpose: SLT is a safe and effective treatment for lowering IOP. Although 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 whether 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 the level of trabecular meshwork 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 trabecular meshwork pigmentation. This parameter and each of the above-mentioned factors requires further research.

Key Words: selective laser trabeculoplasty, energy dose-response, glaucoma, trabecular meshwork pigmentation, ethnicity

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Glaucoma is a heterogenous group of diseases, characterized by progressive optic nerve head 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 the application of topical agents, followed by laser therapy and, finally, if needed, by incisional surgery.[4] Although both the efficacy and the safety of modern-day topical agents for IOP reduction have been verified in clinical trials, widespread patient nonadherence reduces the effectiveness of such treatments[5–8] and leads to visual field loss.[9]

Selective laser trabeculoplasty (SLT), introduced by Latina et al[10] in 1995, 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 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,[16] is that exact laser focus should be unnecessary.

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 after the observations of optimal energy absorption by TM cells cultured in vitro.[10] Although 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 subchampagne bubble energy with the same IOP-lowering results.[20–22] 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," and "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 the 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 10 study subjects, and articles solely discussing argon laser trabeculoplasty (ALT) and/or topical treatment.

All articles were assessed by 2 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., and P.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 is included describing the effect(s) of SLT dose-response compared with the 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, pretreatment IOP is the only accepted positive predictive factor for the extent of IOP lowering after SLT.[29,42,43] 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 and colleagues reported the optimal energy for maximal IOP reduction. When total energy level (mJ) was plotted as a function of percentage of IOP reduction, 2 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.[27] Although 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 and colleagues 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 and colleagues 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 2 study groups at any time point during the 12 months of follow-up.[21]

TABLE 1. SLT Dose-response

References	Methodology	Laser Manufacturer	Sample Size	Glaucoma Type	Energy Range (mJ)	Energy per Spot in mJ (Mean ± SD)	Pattern	No. Spots (Mean ± SD)	Total Energy in mJ (Mean ± SD)	Follow-up (mo)	Medications After SLT
Lee et al[27]	Prospective	Ellex, Adelaide, Australia	49	POAG, NTG	—	1.0 ± 0.06	360 degrees	171.5 ± 41.2	167.1 ± 41.4	1	1 drop Alphagan P postlaser. Dexamethasone 0.1%, and neomycin 0.5%, twice daily for 1 d
Tang et al[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	—	360 degrees	100 (approximately), no SD reported	—	12	Diclofenac sodium 3 times daily for 3 d
Habib et al[28]	Retrospective	—	75	—	0.41–1.05	0.88 ± 0.14	360 degrees	102 ± 15.2	93.73 ± 21.83	36	—
Mao et al[29]	Retrospective	—	158	—	—	—	180 degrees	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 d
Xu et al[30]	Retrospective	Ellex, Adelaide, Australia	44	POAG	—	—	360 degrees	105 ± 6	32.5 ± 2.5	24	—
Elahi et al[31]	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 d
Hong et al[32]	Retrospective	—	35	POAG, PE, pigmentary	—	—	360 degrees	102.1 (no SD reported)	88.1 (no SD reported)	—	Bromfenac or diclofenac for 4−7 d post-SLT
Khouri et al[33]	Retrospective	—	25	OAG	—	0.94 ± 0.05	360 degrees	111 ± 8	104 ± 8	24	None
Lee et al[34]	Prospective	Ellex, Adelaide, Australia	42	POAG, NTG	—	—	360 degrees	—	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 d
Lee et al[35]	Prospective	Ellex, Adelaide, Australia	34	NTG	—	1.0 ± 0.08	360 degrees	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 d
Liu et al[36]	Retrospective	Ellex, Adelaide, Australia	79	POAG, OHT	0.8–1.2	—	180 degrees	55 (no SD reported)	—	12	None
Melamed et al[37]	Prospective	Coherent, Inc, Santa Clara, CA	31	POAG, PE, NTG, OHT, pigmentary	—	1.0 (no SD reported)	180 degrees	approximately 50 (no SD reported)	—	18	1% prednisolone acetate only in eyes with increased inflammation after SLT
Solu et al[38]	Prospective	Ellex, Adelaide, Australia	15	POAG	0.4–1.2	0.6 (no SD reported)	180 degrees	49 (no SD reported)	—	6	—
Raj et al[39]	Prospective		34	PACG	0.6–1.2	—	360 degrees	At least 100 (no SD reported)	—	12	—
Schlote et al[40]	Retrospective		71	POAG, PE, OHT, pigmentary	0.6–1.0	—	180 degrees	50–70 (no SD reported)	—	12	NSAIDs 4 times daily for 1 wk
Wang et al[41]	Retrospective	Ellex, Adelaide, Australia	52	POAG, NTG, pigmentary	0.8–1.5	—	360 degrees	70–85 (no SD reported)	—	—	Topical prednisolone 0.1% twice daily for 3 d

TABLE 1. (*continued*)

References	Methodology	Laser Manufacturer	Sample Size	Glaucoma Type	Energy Range (mJ)	Energy per Spot in mJ (Mean ± SD)	Pattern	No. Spots (Mean ± SD)	Total Energy in mJ (Mean ± SD)	Follow-up (mo)	Medications After SLT
Zhang et al[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 degrees	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

	No. Glaucoma Medications		IOP (mm Hg)					
References	Pre-SLT (Mean ± SD)	Post-SLT (Mean ± SD)	Pre-SLT (Mean ± SD)	Post-SLT (Mean ± SD)	Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Lee et al[27]	1.9 ± 1.1	—	17.1 ± 2.9	13.5 ± 2.8	—	None	IOP reduction ≥ 20% at 1 mo post-SLT	There was a 20.2% ± 14.6% in IOP reduction and a 57.1% success rate
Tang et al[22]	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 mo	—	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
Habib et al[28]	2.03 ± 1.01	2.0 ± 1.2	19.62 ± 3.69	16.11 ± 5.82 at 3 y	3.44 ± 6.58	—	—	Higher energy was associated with higher IOP reduction at 36 mo
Mao et al[29]	—	—	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 mo after SLT	Neither high-energy SLT (> 41 mJ) nor low-energy SLT (< 41 mJ) was associated with higher IOP reduction in univariate analysis
Xu et al[30]	1.5 ± 0.7	—	—	19.8 ± 3.9	16.5 ± 2.8 at 2 y	—	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 mo and 55.2% at 2 y
Elahi et al[31]	1.5 ± 1.2	1.0 ± 1.2 at 2 y	18.6 ± 4.8	15.4 ± 3.2 at 2 y	—	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 a 20% difference from baseline or a reduction in IOP-lowering medications	There was 16.8% complete success and 24.4% qualified success at 2 y. Higher energy was associated with longer duration of qualified success
Hong et al[32]	—	—	20.1 (no SD reported) for the first SLT	16.2 (no SD reported), at 5–8 mo	4.0 (no SD reported)	—	≥ 20% peak IOP reduction	54.5% eyes that reached > 20% reduction after the first SLT

References	No. 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)			
Khouri et al[33]	1.7 ± 0.9	1.5 ± 0.8 at 24 mo	19.7 ± 2.3	17.3 ± 3.2 at 24 mo	2.8 ± 3.4	—	—	There were 55% eyes with IOP reduction > 20% from baseline
Lee et al[34]	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 mo	—	—	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
Lee et al[35]	1.5 ± 0.8	0.9 ± 0.9	16.2 ± 2.3	12.6 ± 2.7 at 24 mo	—	—	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 mo
Liu et al[36]	—	—	27.05 ± 3.57 in young patients (age < 40)	18.83 ± 3.12 in young patients (age < 40), at 12 mo	8.22 ± 3.11	IOP spikes, conjuctival hyperemia, anterior chamber flashing, epithelial punctate keratitis	≥ 20% in IOP with no change in pharmaceutical treatment or additional surgery needed at 1-year follow-up	There was 30.4% IOP reduction and 71.4% success rate in young patients' eyes (vs. 25.2% and 56.5%, respectively, in elderly patients)
Melamed et al[37]	None	None	25.6 ± 2.5	17.9 ± 2.8 at 18 mo	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 mm Hg
Solu et al[38]	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 mo	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 mo from baseline at the time of diagnosis. Success was achieved in all eyes (100% success rate). In 87% of eyes topical medications were discontinued
Raj et al[39]	—	—	23.76 ± 1.92	16.96 ± 2.82 at 12 mo	6.82 ± 3.49	None	-	20% or more reduction in IOP was achieved in 51.51% eyes at 6 mo and 46.42% at 12 mo, without any medications.
Schlote et al[40]	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 mo	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 mo	—	None	Early: IOP < 21 mm Hg and > 20% of the initial IOP, and eyes with discomfort from antiglaucoma medication but controlled IOP should achieve a reduction in the number of medications ≥ 1 and an IOP <21 mm Hg. Advanced: IOP reduction <18 mm Hg and > 30% of the baseline IOP	63% of eyes in the early glaucoma group had IOP reduction <21 mm Hg/ > 20% of the preoperative IOP and reduction in medication. 50% of eyes in the advanced glaucoma group had IOP reduction <18 mm Hg and > 30% reduction from baseline IOP

TABLE 1. (continued)

References	No. Glaucoma Medications Pre-SLT (Mean ± SD)	No. Glaucoma Medications Post-SLT (Mean ± SD)	IOP (mm Hg) Pre-SLT (Mean ± SD)	IOP (mm Hg) Post-SLT (Mean ± SD)	IOP (mm Hg) Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Wang et al[41]	—	—	23 ± 4.6	18 ± 3.2 at 4 mo	—	—	—	SLT resulted in a mean of 27% IOP reduction at 4–8 wk follow-up and 79% response rate. Mean time to failure was 22.2 mo.
Zhang et al[21]	—	—	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 mo	—	—	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

IOP indicates intraocular pressure; NSAIDs, Non-steroidal anti-inflammatory drugs; NTG, normal tension glaucoma; OAG, open angle glaucoma; OHT, ocular hypertension; PACG, primary angle closure glaucoma; PE, pseudo-exfoliation; POAG, primary open angle glaucoma; SLT, selective laser trabeculoplasty.

There were 2 studies that reported on positive associations between total SLT energy dosage and IOP reduction. Habib an colleagues 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 the greater IOP reduction for up to 36 months post-treatment. Although 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[28] reported that patients in the high-energy group had a higher baseline IOP levels, 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 and colleagues carried out post-SLT follow-up of 126 patients with POAG or OHT. Although no association was found between the 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 et al[28] and Elahi et al,[31] 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),[31] which is more frequently used as a criterion for a successful SLT treatment.[44]

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[30] 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. In contrast, Hong et al[32] and Khouri et al[33] 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 the greater reduction in IOP or with the 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 532 nm 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 ALT.[48,49] In some studies, the choice of energy level was indeed based on the level of TM pigmentation.[25,46] This could be partially explained by the fact that SLT, when performed in heavily pigmented eyes,

TABLE 2. SLT Dose-response and TM Pigmentation

References	Methodology	Laser Manufacturer	Sample Size	Pigmentation	Glaucoma Type	Energy Range (mJ)	Energy per Spot in mJ (Mean ± SD)	Pattern	No. Spots (Mean ± SD)	Total Energy in mJ (Mean ± SD)	Follow-up (mo)	Medications After SLT
Ayala et al[45]	Retrospective	Ellex, Adelaide, Australia	120	0.77 ± 0.66	POAG, PE, pigmentary, OHT	06–1.0	0.88 ± 0.11	90 degrees	26.9 ± 4.8	—	24	Apraclonidine instilled once
Kuley et al[46]	Retrospective	—	667	—	PACG, POAG, PE, pigmentary	—	—	360 degrees	97.4 ± 9.4	64.9 ± 22.0	12	—
McIlraith et al[47]	Prospective	—	100	—	OAG	—	—	180 degrees	50 ± 5	—	12	1 drop of brimonidine 0.2% and either prednisolone acetate 1% or ketorolac 0.5% postlaser. Prednisolone acetate 1% or ketorolac 1% 4 times daily for 5 d
Hodge et al[43]	Prospective	—	89	2.5 ± 0.9	POAG, PE, pigmentary	0.8–1.4	—	180 degrees	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% 4 times a day for 5 d
Hirabayashi et al[25]	Retrospective	—	198	—	POAG, NTG, SOAG	0.6–1.4	—	180 and 360 degrees	—	64.2 ± 24.5 in successful cases	6	None
Chen et al[48]	Prospective	—	64	1* (no SD reported)	POAG, PE, pigmentary, OHT	—	0.9 (no SD reported)	90 and 180 degrees	25 in the 90-degree group and 50 in the 180-degree group	—	7	1 drop of 1% Iopidine [apraclonidine]. Dexamethasone eye drops 3 times daily for 5 d

References	Number of Glaucoma Medications: Pre-SLT (Mean ± SD)	Number of Glaucoma Medications: Post-SLT (Mean ± SD)	IOP (mm Hg): Pre SLT (Mean ± SD)	IOP (mm Hg): Post-SLT (Mean ± SD)	IOP (mm Hg): Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Ayala et al[45]	—	—	24.7 ± 4.6	—	—	—	—	Higher TM pigmentation was not associated with longer time to failure of SLT treatment
Kuley et al[46]	—	—	19.6 ± 5.2	16.0 ± 4.5 at 12 mo	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 mm Hg and IOP reduction > 20%). Greater angle pigment and higher IOP at baseline were associated with success on univariate analysis
McIlraith et al[47]	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 mo (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.
Hodge et al[43]	—	—	23.84 ± 4.88	16.6 ± 3.39 in the success group and 20.0 ± 5.78 in the no success group, at 12 mo	—	—	IOP reduction of > 20% at 1-year posttreatment follow-up.	TM pigmentation was not a predictor of success. There was no significant difference between success and no success in terms of total energy applied

TABLE 2. (*continued*)

References	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)			
Hirabayashi et al[25]	2.0 ± 1.3	2.0 ± 1.3 at 6 mo	17.8 ± 4.4	15.2 ± 4.9 at 6 mo	—	IOP spikes	≥ 20% IOP reduction or ≥ 1 medication reduction without an IOP-lowering procedure	Success rate at 6 mo was 38.5%. TM pigmentation was not a predictive factor for success
Chen et al[48]	—	—	25.44 ± 1.41 in the 90-degree group and 26.06 ± 1.73 in the 180-degree group	18.43 ± 1.38 in the 90-degree group and 19.90 ± 1.59 in the 180-degree group, at 7 mo	—	—	—	There was no difference in IOP reduction between the groups. TM pigmentation was associated with successful SLT only at 7 mo (but not at 1 and 4 mo)

* Median.

IOP indicates intraocular pressure; NTG, normal tension glaucoma; OAG, open angle glaucoma; OHT, ocular hypertension; PACG, primary angle closure glaucoma; PE, pseudo-exfoliation; POAG, primary open angle glaucoma; SLT, selective laser trabeculoplasty; SOAG, secondary open angle glaucoma; TM, trabecular meshwork.

could lead to severe IOP spikes in patients with pigmentary glaucoma or pseudoexfoliative glaucoma. For such patients, lower energy settings were recommended.[23] 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[45] (0.88 mJ), and the mean total energy over these 6 studies ranged between 43.87 and 64.9 mJ.

Ayala and colleagues 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. Although 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.[45] McIlraith et al[47] found no differences in the IOP-lowering effect of SLT on the basis of TM pigmentation. In a prospective study of 89 OAG patients, Hodge et al[43] 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 nonsuccess groups (44.95 and 43.87 mJ, respectively). Hirabayashi and colleagues retrospectively followed 198 patients with POAG, normal tension glaucoma, or secondary open angle glaucoma 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%. Although 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, whereas others had 360 degrees. TM pigmentation was thus not a predictor for successful SLT treatment.[25]

In a retrospective case-series of 667 patients with OAG or primary angle closure glaucoma, Kuley and colleagues attempted to define predictors for successful SLT treatment. Both baseline IOP and greater angle pigmentation were found to be associated with the 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.[46] In another study (not included in Table 2), Martow et al[42] 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.

The only study in this category that reported some association between TM pigmentation and successful SLT was conducted by Chen and colleagues 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 mo). Nevertheless, no difference in IOP reduction was found between the study groups.[48]

Currently, there is no strong scientific evidence suggesting that the 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

TABLE 3. SLT Dose-Response and Race/Ethnicity

References	Methodology	Laser Manufacturer	Sample Size	Race/ Ethnicity	Glaucoma Type	Energy Range (mJ)	Energy per Spot in mJ (mean ± SD)	Pattern	No. Spots (Mean ± SD)	Total Energy in mJ (Mean ± SD)	Follow-up (mo)	Medications After SLT
Shibata et al[50]	Retrospective	Lumenis, Inc Coherent Inc, Palo Alto, CA	54	Japanese	POAG, PE	0.8–1.4	—	180 and 360 degrees	75 ± 22 and 121 ± 19 in 180 and 360 degrees, respectively	73 ± 29 and 125 ± 30 in 180 and 360 degrees, respectively	36	Apraclonidine 1% once. Fluorometholone 0.1% eye drops 4 times/d for 7 d
Al-busaidi et al[51]	Retrospective	Ellex, Adelaide, Australia	36	Omani	OHT, OAG	0.4–0.9	—	360 degrees	99.52 ± 10.31	64.03 ± 10.26	3	Apraclonidine 0.5% once
Lai et al[52]	Prospective	Coherent Inc., Palo Alto CA	32	Chinese	POAG, OHT	—	1.0 ± 0.1	360 degrees	Approximately 100 (no SD reported)	73.6 ± 16.4	60	One drop of 1% apraclonidine and 1% prednisolone acetate immediately postlaser. Prednisolone acetate 4 times daily for 7 d
Miki et al[53]	Retrospective	Ellex, Adelaide, Australia	78	Japanese	POAG, NTG, PE, SOAG	—	—	360 degrees	—	71.7 ± 20.2	12	Steroid eye drops administered at the discretion of the physician
Ono et al[54]	Retrospective	—	65	Japanese	POAG, NTG, PE	0.7–1.0	—	360 degrees	~100 (no SD reported)	—	12	—
Realini et al[55]	Prospective	Lumenis	64	African	POAG	—	—	360 degrees	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
Soboka et al[56]	Prospective	Lumenis Inc., Santa Clara, CA	61	Ethiopian	POAG, PE, OHT	0.4–1.5	0.79 ± 0.23	360 degrees	100 (no SD reported)	89.82 ± 29.64	12	Daily topical NSAIDs for 1 wk
Goosen et al[57]	Retrospective	Lumenis; Yokneam, Inc., Israel	82	African, Indian (21/84), White (3/84)	—	1.1–1.4	—	360 degrees	120–140 (no SD reported)	—	12	Ketoralac eye drops 3 times daily for 28 d
Funarunart et al[58]	Retrospective	Optimis Fusion, Quantel Medical, Cournon d'Auvergne, France	96 eyes (exact number of patients was not reported)	Thai	POAG, NTG, OHT, PE, JOAG	0.5–1.0	0.73 ± 0.11	180 and 360 degrees (depending on the surgeon's preference)	—	56.83 ± 19.77	24	—
Realini et al[59]	Retrospective	Lumenis Selecta II	265 eyes	Afro-Caribbean	OAG	—	—	360 degrees	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 mo was 71.2% and 71.7% in right and left eye

References	No. 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)			
Shibata et al[50]	3.0 ± 1.0 and 2.8 ± 0.7 in 180 and 360 degrees, respectively	—	19.5 ± 4.3 and 21.0 ± 4.1 in 180 and 360 degrees, respectively	—	2.6 ± 4.0 and 5.6 ± 4.3 and in 180 and 360 degrees at 6 mo, respectively	IOP spikes	IOP reduction by ≥ 20% of pretreatment IOP without additional medications, laser or surgery	IOP reduction was significantly greater in the 360 degree group than in the 180 degree group. Response rate between groups was similar. Success rate was higher in the 360 degree group at 1 and 2 y than in the 180 degree group. Total energy was not associated with IOP reduction.

TABLE 3. (*continued*)

	No. Glaucoma Medications		IOP (mm Hg)					
References	**Pre-SLT (Mean ± SD)**	**Post-SLT (Mean ± SD)**	**Pre-SLT (Mean ± SD)**	**Post-SLT (Mean ± SD)**	**Reduction (Mean ± SD)**	**Adverse Events**	**Definition of Success**	**Main Results**
Al-busaidi et al[51]	1 ± 0.4	—	25.77 ± 4.57	18.82 ± 4.68, at 3 mo	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 wk and 72.7% at 12 wk postlaser
Lai et al[52]	—	—	26.8 ± 5.6	—	8.6 ± 6.7 at 5 y	—	—	There was 32.1% reduction in IOP in the SLT group at 5 y. Eyes treated with SLT needed substantially fewer anti-glaucoma medications
Miki et al[53]	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.
Ono et al[54]	2.6 ± 1.2 in the SLT group	2.38 (no SD reported) in the SLT group, at 12 mo	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 mo and 18.5% reduction in IOP at 12 mo in the SLT group
Realini et al[55]	—	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 mo	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)
Soboka et al[56]	1.29 ± 1.01	1.03 ± 0.70 at 12 mo	24.3 ± 2.5	17.6 ± 3.4 at 12 mo	6.7 ± 4.2	-	IOP lowering of > 20% from baseline without repeat treatment	There was a 25.9% reduction at 12 mo with 60% success rate. There was a significant reduction in antiglaucoma medications
Goosen et al[57]	—	—	27.7 in right eyes and 25.9 in left eyes (no SD reported)	13.6 at 12 mo (no SD reported)	—	None	—	There was 49% reduction of IOP from pre-SLT baseline levels, at 12 mo. 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 mo

TABLE 3 *(continued)*

References	No. Glaucoma Medications: Pre-SLT (Mean ± SD)	No. Glaucoma Medications: Post-SLT (Mean ± SD)	IOP (mm Hg): Pre-SLT (Mean ± SD)	IOP (mm Hg): Post-SLT (Mean ± SD)	IOP (mm Hg): Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Funarunart et al[58]	2.74 ± 1.09	2.16 ± 1.31 at 24 mo	19.31 ± 3.59	14.79 ± 3.67 at 24 mo	—	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 mo, where 33.3% of treated eyes had at least 20% IOP reduction and 30.2% needed fewer antiglaucoma drugs
Realini et al[59]	R: 1.14 ± 0.55 L: 1.14 ± 0.54	0—study exculsion	R: 21.2 ± 3.4 L: 21.2 ± 3.9	At 8 years R: 15.7 ± 2.6 L: 14.7 ± 2.5	At 8 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 13–16 mm Hg in more than 70% of the patients over 8 y

IOP indicates intraocular pressure; JOAG, Juvenile open angle glaucoma; NSAIDs, Non-steroidal anti-inflammatory drugs; NTG, normal tension glaucoma; OAG, open angle glaucoma; OHT, ocular hypertension; PE, pseudo-exfoliation; POAG, primary open angle glaucoma; SLT, selective laser trabeculoplasty; SOAG, secondary open angle glaucoma.

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.[60–62] Investigators at Moorfields Eye Hospital in London suggested that primary SLT could be more efficacious in Caucasians, whereas the Glaucoma Laser Treatment (GLT) Study suggested that primary ALT could be more efficacious in patients of African-American descent.[4,63] 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 9 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 and colleagues reported the clinical results of SLT in 54 Japanese OAG patients. Although both IOP reductions and success rates were greater in patients who had undergone 360- than 180-degree SLT, total energy was not associated with IOP reduction.[50] Al-Busaidi and colleagues 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 and colleagues, whereas the success rates were significantly higher (51.5% at 5 wk and 72.7% at 12 wk vs. 46% and 29% in the 360-degree SLT group, at 1 and 2 y, respectively).[50,51] Although the definitions of success in both studies were similar, differences in their follow-up periods may account for their different results, as in most studies the IOP-reducing effect of SLT is found to wane with time. Lai et al[52] 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. Miki an colleagues reported treatment outcomes and prognostic factors of SLT in Japanese OAG patients on maximal tolerable therapy. Although 85.8% of eyes showed > 20% reduction in IOP during the 12-month follow-up period, energy dose was not associated with treatment failure.[53] In another post hoc analysis of 8 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.[59]

It is difficult to carry out valid comparisons between different studies for the various reasons mentioned above,

TABLE 4. SLT Dose-Response at Different Patterns of Application

References	Methodology	Laser Manufacturer	Sample Size	Glaucoma Type	Energy Range (mJ)	Energy per Spot in mJ (Mean ± SD)	Pattern	No. Spots (Mean ± SD)	Total Energy in mJ (Mean ± SD)	Follow-up (mo)	Medications After SLT
Nagar et al[66]	Prospective	Lumenis, Coherent, Inc, Palo Alto, CA	167	OHT, OAG	—	—	90, 180, and 360 degrees	25–30 (90 deg), 48–53 (180 deg), 93–102 (360 deg), no SD reported	—	12	Dexamethasone 0.1% eye drops 4 times/d for 5 d or ketorolac eye drops 4 times/d for 5 d
Shibata et al[50]	Retrospective	Lumenis, Coherent, Inc, Palo Alto, CA	54	POAG, PE	0.8–1.4	—	180 and 360 degrees	75 ± 22 and 121 ± 19 in 180 and 360 degrees, respectively	73 ± 29 and 125 ± 30 in 180 and 360 degrees, respectively	36	Apraclonidine 1% once, fluorometholone 0.1% eye drops 4 times/d for 7 d
Ozen et al[67]	Prospective	Lightmed SeLecTor Deux	26	POAG	0.7–0.9	—	180 degrees in group 1 and 360 degrees in group 2	50 in group 1 and 100 in group 2 (no SD reported)	—	6	None
Tawfique et al[68]	Prospective	Ellex, Adelaide, Australia	67	POAG, PE, OHT, pigmentary	—	—	90 and 360 degrees	25 in the 90-degree group and 100 in the 360-degree group	—	24	—
Tufan et al[69]	Prospective	Lumenis, Coherent, Inc., Palo Alto, CA	40	POAG	—	—	180 and 360 degrees	56.0 ± 6.5 in the 180-degree group and 97.5 ± 11.5 in the 360-degree group	65.6 ± 17.2 in the 180-degree group and 116.0 ± 31.7 in the 360-degree group	6	Apraclonidine 1% once postlaser
George et al[70]	Retrospective	Lumenis, Coherent Inc, Palo Alto, CA	284	POAG, PE	05–1.6 in the overlapping SLT group and 0.7–1.1 in the nonoverlapping SLT group	1.03 ± 0.17 in the overlapping SLT group and 0.89 ± 0.1 in the nonoverlapping SLT group	180 degrees in the overlapping SLT group and 360 degrees in the non-overlapping SLT group	104 ± 18.67 in the overlapping SLT group and 105 ± 12.83 in the nonoverlapping SLT group	—	14	Diclofenac sodium 0.1% drops 4 times daily for 5 d
Wong et al[71]	Retrospective	Ellex, Adelaide Australia	199	POAG, PACG, OHT, NTG, PE,	0.8–1.2	—	360 degrees	119.39 ± 4.23 and 159.56 ± 3.56	—	12	Brimonidine tartrate 0.15%/ apraclonidine hydrochloride 0.5% postlaser for 4 d
Pukl et al[72]	Prospective	OptoSLT M DPSS, 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)	360 degrees	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 d, oral Acetazolamide 125 mg immediately post-laser, with an additional 125 mg given 6–8 h postoperatively

References	No. Glaucoma Medications: Pre-SLT (Mean ± SD)	No. Glaucoma Medications: Post-SLT (Mean ± SD)	IOP (mm Hg): Pre-SLT (Mean ± SD)	IOP (mm Hg): Post-SLT (Mean ± SD)	IOP (mm Hg): Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Nagar et al[66]	—	—	29.3 (SD not reported)	17–25 in all groups, at 12 mo (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 360-degree SLT than 90-degree SLT and 180-degree SLT. Success rates were greater with 180-degree and 360-degree than with 90-degree SLT. With 360-degree SLT, 82% of eyes achieved a 20% IOP reduction and 59% a 30% reduction from baseline. Although success rates were better with 360-degree than with 180-degree 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 180-degree and 360-degree SLT treatments.
Shibata et al[50]	3.0 ± 1.0 and 2.8 ± 0.7 in 180 and 360 degrees, respectively	—	19.5 ± 4.3 and 21.0 ± 4.1 in 180 and 360 degrees, respectively	—	2.6 ± 4.0 and 5.6 ± 4.3 and in 180 and 360degrees at 6 mo, respectively	IOP spikes	IOP reduction by ≥ 20% of pretreatment IOP without additional medications, laser or surgery	IOP reduction was significantly greater in the 360-degree group than in the 180-degree group. Response rate between groups was similar. Success rate was higher in the 360-degree group at 1 and 2 y than in the 180-degree group. Total energy was not associated with IOP reduction.
Ozen et al[67]	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 mo	—	—	Reduction of 20% or more in IOP at 6 mo	There was 33.0% reduction in IOP in group 1 and 37.1% reduction in IOP in group 2. At 6 mo, 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 2 groups in terms of antiglaucoma drug numbers.
Tawfique et al[68]	—	—	24.9 ± 3.6 in the 90-degree group and 24.8 ± 4.2 in the 360-degree group	—	—	—	—	Distributions of survival times for the 2 treatment extents were not significantly different. The mean survival of the treatment effect was similar in the 90-degree and 360-degree SLT groups.
Tufan et al[69]	2.2 ± 0.4 in the 180-degree group and 2.4 ± 0.5 in the 360-degree group	—	17.3 ± 2.3 in the 180-degree group and 17.0 ± 2.9 in the 360-degree group	16.8 ± 2.4 in the 180-degree group and 17.6 ± 3.1 in the 360-degree group, at 6 mo	—	Mild anterior chamber inflammation	—	There were no significant differences in IOP reductions between the groups
George et al[70]	2.51 in the 180-degree overlapping SLT group and 2.48 in the 360-degree nonoverlapping SLT group (no SD reported)	2.0 in the 360- degree nonoverlapping SLT group at 14 mo, no SD reported (change was not observed in the other groups)	18.44 in the 180-degree overlapping SLT group and 19.35 in the 360-degree nonoverlapping SLT group, no SD reported	—	—	—	—	The percentage of responders was ~20% greater for nonoverlapping SLT than for overlapping SLT (50% vs. 30%, respectively

TABLE 4. (*continued*)

	No. Glaucoma Medications		IOP (mm Hg)					
References	Pre-SLT (Mean ± SD)	Post-SLT (Mean ± SD)	Pre-SLT (Mean ± SD)	Post-SLT (Mean ± SD)	Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Wong et al[71]	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 y	—	≥ 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.
Pukl et al[72]	None	None	24.1 ± 3.72 in the 1 ns group and 24.3 ± 3.71 in the 3–5 ns group	18.28 ± 3.32 in the 1 ns group and 18.41 ± 3.53 in the 3–5 ns group, at 6 mo	5.8 in the 1 ns group and 5.9 in the 3–5 ns group (no SD reported)	—	≥ 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 group and 72% in the 3–5 ns group at 6 mo

IOP indicates intraocular pressure; NTG, normal tension glaucoma; OAG, open angle glaucoma; OHT, ocular hypertension; PACG, primary angle closure glaucoma; PE, pseudo-exfoliation; POAG, primary open angle glaucoma; SLT, selective laser trabeculoplasty.

but 2 studies,one by Realini and colleagues and the other by Soboka and colleagues,show striking similarities. Both studies are prospective, with similar patterns of application, numbers of spots, sample sizes, and follow-up periods. Realini and colleagues studied POAG patients of West African descent whereas Soboka and colleagues studied POAG, OHT, and pseudoexfoliative glaucoma patients from Ethiopia. The most important differences between the 2 studies were in the mean total energy and in the fact that SLT was performed in both eyes by Realini and colleagues and in one eye by Soboka and colleagues After 12 months, Realini and colleagues 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[56] 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).[55] One possible explanation for the significantly better results of Realini and colleagues could be that IOP-lowering treatment of 1 eye has been shown to produce an IOP-lowering effect on the contralateral eye.[64,65] The impressive efficacy of SLT reported in these 2 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 and colleagues 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 with 50% of the Indians, had > 20% reduction in IOP.[57] This highlights the 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, ~100, 50, or 25, although 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 although 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 and colleagues compared the efficacies of SLT, and 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[66] concluded that total energy level was not associated with treatment success. Shibata and colleagues retrospectively compared the results of 180- and 360-degree SLT in 54 OAG patients. Similarly to the findings of Nagar and colleagues, both IOP reduction and success rates were highest with 360-degree SLT, and total energy was not associated with IOP reduction.[50]

Ozen and colleagues compared the efficacies of 180- and 360-degree SLT in 26 POAG patients. Both groups showed an 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.[67] Tufan and colleaguues, 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 2 groups were not significantly different. Associations between energy level and IOP reduction were not examined in that study.[69] In contrast to Ozen and colleagues and Tufan and colleagues, Tawfique and colleagues 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 2 groups were reported. No significant differences were found between the 2 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).[68]

In several studies, laser application regimens differed from the commonly accepted regimens described in the literature. George and colleagues, for example, compared 180-degree SLT and overlapping treatment spots with 360-degree SLT and nonoverlapping treatment spots, in 284 OAG patients. The rate of responders to the treatment was found to be ~20% higher in the nonoverlapping SLT group,[70] 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 nonoverlapping spots with similar spot numbers and similar mean energy per spot. Furthermore, in the study conducted by George et al,[70] the mean energy per spot was higher in the nonoverlapping 180-degree SLT group, and the total treatment energy in the 2 groups was similar. 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 and colleagues examined the efficacy of 360-degree SLT at different spot numbers (120 spots vs. 160 spots). Although IOP reduction was greater with 160 spots, success rates between the 2 groups did not differ.[71] 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 2 groups. Unsurprisingly, during the 6 months of follow-up visits, no significant difference in IOP reduction were found between the 2 groups.[72]

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

Although 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.[73] 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.[74] The physical disruption caused by argon laser treatment does not seem to be necessary to reduce the IOP equally, supporting the hypothesis of nondisruptive levels of laser to create biological stimulation of the meshwork.[75]

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 although 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 and 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, despite the rarity of the procedure's serious side effects[20] (see Appendix).

APPENDIX 1

SLT Dose Response Versus Topical Treatment

The effectiveness of SLT versus topical antiglaucoma treatment was compared in eight studies (Table 5). While such comparisons are not strictly related to the energy levels

TABLE 5. SLT Dose-Response Versus Topical Antiglaucoma Treatment

References	Methodology	Laser Manufacturer	Sample Size	Glaucoma Type	Energy Range (mJ)	Energy per Spot in mJ (Mean ± SD)	Pattern	No. of Spots (Mean ± SD)	Total energy in mJ (Mean ± SD)	Follow-up (mo)	Medications After SLT
Nagar et al[66]	Prospective	Lumenis, Coherent, Inc, Palo Alto, CA	167	OHT, OAG	—	—	90, 180, and 360 degrees	25–30 (90 deg), 48–53 (180 deg), 93–102 (360 deg), no SD reported	—	12	Dexamethasone 0.1% eye drops 4 times/d for 5 d or ketorolac eye drops 4 times/d for 5 d
Nagar et al[76]	Prospective	Ellex, Adelaide, Australia	40	OHT, OAG	0.2–1.4	—	360 degrees	100 ± 5	—	6	Ketorolac tromethamine 4 times/d for 5 d
Lai et al[52]	Prospective	Coherent, Palo Alto, CA	32	POAG, OHT	—	1.0 ± 0.1	360 degrees	~100 (no SD reported)	73.6 ± 16.4	60	One drop of 1% apraclonidine and 1% prednisolone acetate immediately postlaser. Prednisolone acetate was continued 4 times daily for 7 d
Narayanaswamy et al[77]	Prospective	—	100	PACG	—	—	360 degrees	117.6 ± 25.6	90.2 ± 33.2	6	Prednisolone acetate 1% eyedrops 4 times daily for 1 wk
Ono et al[54]	Retrospective	—	65	POAG, NTG, PE	0.7–1.0	—	360 degrees	~100 (no SD reported)	—	12	—
Katz et al[78]	Prospective	—	69	POAG, PE, OHT	0.2–1.2	—	360 degrees	100 (no SD reported)	—	12	—
Gazzard et al[11]	Prospective	—	718	POAG, OHT	0.3–1.4	—	360 degrees	100 (no SD reported)	—	36	—
De-Keyser et al[79]	Prospective	Lumenis, Dreieich, Germany	143	POAG, OHT	—	1.1 ± 0.3	360 degrees	102.6 ± 9.2	—	18	Indomethacin/ Dexamethasone or no drops

	No. Glaucoma Medications		IOP (mm Hg)					
References	Pre-SLT (Mean ± SD)	Post-SLT (Mean ± SD)	Pre-SLT (mean ± SD)	Post-SLT (Mean ± SD)	Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
Nagar et al[66]	—	—	29.3 (SD not reported)	17–25 in all groups, at 12 mo (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 antiglaucomatous interventions	Mean IOP was significantly lower in eyes receiving latanoprost than 90, 180, and 360-degree SLT. Mean IOP was lower with 360-degree SLT than 90-degree SLT. Differences in success rates with latanoprost and 360 degrees were not significant
Nagar et al[76]	—	—	26.1 ± 4.0 in the SLT group	—	6.2 ± 0.8 in the SLT group at 4–6 mo	—	20% decrease in IOP	There was no significant difference between IOP reduction with SLT and with latanoprost
Lai et al[52]	—	—	26.8 ± 5.6	—	8.6 ± 6.7 at 5 y	—	—	IOP reduction was similar between eyes treated with SLT and those with antiglaucoma medications. Eyes treated with SLT needed substantially fewer anti-glaucoma medications
Narayanaswamy et al[77]	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 mo	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	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

References	No. Glaucoma Medications Pre-SLT (Mean ± SD)	No. Glaucoma Medications Post-SLT (Mean ± SD)	IOP (mm Hg) Pre-SLT (mean ± SD)	IOP (mm Hg) Post-SLT (Mean ± SD)	IOP (mm Hg) Reduction (Mean ± SD)	Adverse Events	Definition of Success	Main Results
							6 mo. Qualified success—those with IOP < 21 mm Hg and who required IOP-lowering medication.	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
Ono et al[54]	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 mo	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 mo and an 18.5% reduction in IOP after 12 mo in the SLT group. The SLT group required significantly fewer medications at 1, 3 and 9 mo than those who took ripasudil. There was no significant association between treatment success in the SLT group vs. the ripasudil group
Katz et al[78]	—	—	24.5 ± 2.2 in the SLT group	18.2 ± 2.8 in the SLT group, at 12 mo	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
Gazzard et al[11]	—	—	24.5 ± 5.2	18.2 ± 3.73 in OHT patients, 14.4 ± 3.07 in moderate OAG patients, at 36 mo	—	Inflammation, IOP spikes	—	Target IOPi was achieved by 36 mo in 95% of eyes in the SLT group and in 93.1% in the eye drops group. By 36 mo,. 78.2% eyes in the SLT group did not require any medications. There were no significant differences in IOP reduction between the 2 groups
De-Keyser et al[76]	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 mo	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 mo	—	—	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 mo, and in 74.1% after 18 mo. 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 mo. With > 30% reduction used as the criterion, SLT was a success in 86.2% of patients

IOP indicates intraocular pressure; NTG, normal tension glaucoma; OAG, open angle glaucoma; OHT, ocular hypertension; PACG, primary angle closure glaucoma; PE, pseudo-exfoliation; PGA, prostaglandin analogues; POAG, primary open angle glaucoma; SLT, selective laser trabeculoplasty.

applied during treatment, it is interesting to look at the different energy levels across different studies. Across all of the studies summarized in Table 5, four reported on the energy range used for treatment, which varied between 0.2 and 1.4 mJ per treatment spot.[11,68–70] The mean total energy was reported in two studies as 73.6 and 90.2 mJ.[50,71] Another study compared the effectiveness of SLT at 90, 180 or 360 degrees to that of topical treatment,[58] while in the other seven studies the energy was applied to 360 degrees of the TM.

In the previously mentioned study by Nagar et al., the effectiveness of SLT performed at different application patterns was compared to topical treatment. Eyes treated with latanoprost showed greater IOP reductions than those with 90- or 180-degree SLT, yet similar IOP reductions compared to 360-degree SLT.[58] In another study, Nagar et al compared the effects of IOP control and fluctuation in patients with OHT or OAG and who were treated with SLT or latanoprost. While IOP reduction was greater and control of IOP was more successful in the latanoprost-treated eyes at 1 month of follow-up, these differences failed to reach statistical significance at all other follow-up visits, including at 4−6 months.[69] Lai et al compared SLT and topical antiglaucoma treatment in 32 Chinese patients with POAG or OHT. IOP reduction in both groups was similar at 5 years of follow-up, but the SLT patients required significantly fewer medications for IOP reduction during follow-up.[50] Narayanaswamy et al. conducted a prospective study in 100 PACG patients with at least 180 degrees of open angle post-laser peripheral iridotomy, comparing the efficacy of SLT and prostaglandin analogs (PGAs). After adjustment for baseline IOP, differences in mean IOP reduction between the groups were not significant. Complete success (defined as IOP < 21 mmHg without any additional antiglaucoma medications) was significantly greater in the PGA group (84% versus 60%).[71] In a retrospective study of 65 POAG, NTG and pseudo-exfoliative glaucoma patients, with uncontrolled IOP, Ono et al compared the IOP-lowering effect of ripasudil or SLT as adjuvant therapy. Mean IOP reduction and success rates were similar in the two groups; however, similarly to the publication by Lai et al, SLT patients required significantly fewer antiglaucoma medications at 1, 3 and 9 months of follow-up.[68] In a prospective study, Katz et al compared SLT and topical treatment as an initial IOP-lowering therapy. Mean IOP reduction was found to be similar in both groups.[70]

The most significant study in the context of the efficacy of SLT compared to that of topical treatment is the previously mentioned LiGHT trial. In this randomized controlled trial, Gazzard et al followed 718 patients with POAG or OHT for 36 months after treatment with SLT or with eye drops. The two groups showed similar levels of IOP reduction at 36 months of follow-up. Furthermore, patients' eyes were found to be within target IOP at more visits in the SLT group than in the eye-drops group, and neither clinically assessed angle pigmentation nor race were predictors of success.[11] De-Keyser et al examined SLT as a replacement therapy in 143 patients with POAG or OHT with medically controlled IOP. Full replacement of antiglaucoma medications was achieved in 74.1% of the patients at 18 months of follow-up, and no patient remained on the same number of medications.[72]

Differences in methodologies of the various studies pose a challenge to attempts at comparing them, especially with respect to energy levels and IOP-reducing efficacies of treatment. It is evident, however, that across different energy ranges, SLT is as efficacious as topical treatment, and differences between them are mostly minor. The authors of the LiGHT trial suggested that SLT should be considered as first-line treatment,[11] and to that end, standardized protocols defining optimal energy levels should be generated. Further research will clearly be required for that purpose, and studies comparing high- and low-energy SLT with topical treatments should be conducted.

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