DOI: 10.24292/01.OT.291217.02

Selective laser trabeculoplasty for open angle glaucoma

Joanna Liput[1,2], Weijen Tan[1]

[1] Harrogate and District NHS Foundation Trust, United Kingdom

[2] York Teaching Hospital NHS Foundation Trust, United Kingdom

Head of Glaucoma Service at York Teaching Hospital NHS: Joanna Liput, MD, PhD

HIGHLIGHTS

SLT is effective and safe treatment as first line as well as adjunctive treatment of open angle glaucoma.

ABSTRACT

Selective laser trabeculoplasty (SLT) is an important treatment option in open angle glaucoma. It has been shown to be as effective as argon laser trabeculoplasty in primary open angle glaucoma while having an improved safety profile. Its use is also indicated for other subtypes of open angle glaucoma (OAG) such as pseudoexfoliation (PXE) and pigmentary glaucoma. In this review, we present the current literature on the role of SLT in treating OAG. The indications, duration of effect, repeatability, cost effectiveness and clinical effectiveness of SLT were reviewed. Available evidence comparing SLT with ALT and medical treatment are also presented. We also discuss the applicability of SLT for PXE, pigmentary glaucoma, normal tension glaucoma and advanced OAG. Lastly, the complications of SLT and areas of further research are discussed.

Key words: selective laser trabeculoplasty, primary open glaucoma, safety, efficacy

INTRODUCTION

Trabeculoplasty is the application of laser to the trabecular meshwork and is now a well-recognised form of treatment for glaucoma. Continuous wave argon laser trabeculoplasty (ALT) was first reported by Worthen and Wickham in 1973 [1]. The photocoagulation of the trabecular meshwork produced a temporary reduction in IOP which lasted several months. A lower energy form of ALT was later pioneered by Wise in 1979 which unlike earlier versions of ALT only produced superficial scarring of the meshwork [2]. The use of ALT for treating primary open angle glaucoma (POAG), ocular hypertension (OHT) and secondary open angle glaucoma (OAG) later became recognised due to its proven efficacy at reducing IOP [3]. ALT is now largely superseded by selective laser trabeculoplasty (SLT) owing to its similar efficacy while utilising less than 1% of the energy required for ALT contributing to lower rates of complications [4]. SLT was first described by Latina and Park in 1995 [5]. It uses a Q-switched frequency-doubled short pulse Nd:YAG laser which selectively targets the pigmented trabecular meshwork cells [6]. As the pulse duration of the laser is only about 3 ns while the thermal relaxation time of melanin within the pigmented cells are in the microseconds range, the laser energy cannot be converted to thermal energy. This prevents any collateral damage to the microstructure of the trabecular meshwork and the surrounding tissues. The actual mechanism of IOP lowering by SLT is not completely known. The original hypothesis of trabeculopuncture is unlikely to be correct as electron microscopy studies demonstrated minimal disruption to the trabecular meshwork [7]. The improvement in trabecular meshwork outflow after laser trabeculoplasty may stem from biochemical and cellular changes [8]. Bylsma et al. observed that there may have been an increase in trabecular meshwork cell division following trabeculoplasty [9]. The upregulation of inflammatory cytokines induced by trabeculoplasty also leads to the induction of matrix metalloproteinases and the recruitment of phagocytic macrophages [10]. These processes are thought to aid in the removal of excess extracellular matrix and debris in the trabecular meshwork of glaucomatous eyes.

It is believed that SLT has a similar mechanism of action to prostaglandin analogues (PGE). The histology of Schlemm's canal cells exposed to SLT or PGE demonstrated similar cell junction disassembly, which was not observed in cells exposed to timolol, dorzolamide and brimonidine [11]. The poorer success of SLT in patients on prostaglandins is still controversial. A study by Latina and Gulati showed that SLT induced a 7% drop in IOP in patients taking PGE [12]. However among patients who are not taking PGE, the reduction in IOP achieved was 20%. Kara et al. showed that the success rate of SLT was 78.6% at 1 year in patients who were on dorzolamide/timolol combinations and only 50% in patients who were on PGE [13]. However, Ayala and Chen demonstrated no difference in IOP reduction between eyes that had received PGE and eyes that did not receive PGE [14].

INDICATIONS OF SLT

SLT is recommended not only in the treatment of POAG and OHT but also pseudoexfoliation (PXE), pigmentary glaucoma, normal tension glaucoma (NTG), steroid-induced glaucoma and as prophylaxis for anticipated steroid-induced ocular hypertension [15–20]. It was also successfully performed after deep sclerectomy, trabectome, trabeculectomy and retinal detachment repair with silicone oil [21–23].

ADVANTAGES OF SLT

SLT is a safe, non-invasive procedure which can be effective at lowering IOP for patients with OAG including POAG and OHT which make up for the majority of glaucoma patients worldwide [24, 25]. Therefore, SLT can be safely recommended to most patients with OAG and OHT following careful discussion of risks and expectations with patients. One important benefit of SLT is the potential for patients to refrain, cease or reduce usage of anti-glaucoma medications. This is especially useful for patients who are susceptible to eye drop toxicity or medication side-effects. It was estimated that up to 43% of patients may have ocular discomfort from instillation of glaucoma eye drops which mostly contain preservatives such as benzalkonium chloride [26]. This is often a significant barrier to patient compliance as up to 55% of patients with ocular irritation may discontinue their eye drops within a few months of prescription[27]. The *Collaborative Initial Glaucoma Treatment Study* (CIGTS) has also showed that 75% of patients were using 2 or more medications within 2 years of initial glaucoma treatment [28]. This polypharmacy is a factor for non-compliance which can be especially problematic among increasingly elderly patients. Although the IOP-lowering effect of SLT wanes with time, some patients still saw a significant drop in their IOP lasting several years [4]. At 6 months after SLT, 67–75% of patients had an IOP reduction of ≥ 20% from baseline. This reduced to 38–74% at 3 years and 11–31% at 5 years [29]. Therefore the potential for SLT to reduce patients' dependence for medications is particularly invaluable. Several studies have also demonstrated that SLT was safe to be repeated [30, 31]. This may prolong the period of IOP control without medications. Four retrospective studies studying the repeatability of SLT concluded that a 2nd SLT treatment yielded a statistically significant absolute reduction in IOP from baseline (prior

to 1st SLT) [30–33]. However, there were differences among the studies regarding the success rates of the 2nd SLT when compared with the 1st SLT. Francis et al. found a higher success rate when the interval between the 1st and 2nd SLT was shorter than 1 year [33]. Avery et al. reported that 35% of eye that responded to the 1st SLT did not respond to the 2nd SLT [34]. Additionally, 68% of eyes that failed to respond to the 2nd SLT were successfully treated following the 2nd SLT.

Another advantage of SLT is the potential to reduce healthcare cost. Using a Markov model, Cantor et al. estimated the 5 year cost of various glaucoma treatment modalities on POAG patients who were not adequately controlled with two medications [35]. Cost estimations were calculated from the predicted course of glaucoma management derived from published literature with pricing based on Medicare fee schedules in the United States. The mean treatment cost over 5 years for patients treated with medications, laser trabeculoplasty and surgery was $6553, $4849 and $6386 respectively. In another study based on the Ontario Health Insurance Plan in Canada showed that the use of primary SLT produced a 6 year cumulative cost savings of $206.54, $1668.64, and $2992.67 per patient over monotherapy, bi-therapy and tri-therapy with anti-glaucoma drugs [36].

HOW DOES SLT COMPARE WITH ALT?

Large randomised controlled trials (RCT) which demonstrated the efficacy of laser trabeculoplasty such as the *Glaucoma Laser Trial, Early Manifest Glaucoma Trial* and *Advanced Glaucoma Intervention Study* utilised ALT as intervention [37–40]. As SLT was introduced later, there is still a shortage of level 1 evidence on the effectiveness of SLT [41]. Therefore, it is important to determine whether SLT is comparable or superior to ALT in treating OAG. There have been at least 8 RCTs comparing the outcomes of SLT versus ALT [17, 42–49]. Damji et al. published an RCT comparing 87 eyes receiving ALT and 89 eyes receiving SLT which did not demonstrate a significant difference in IOP reduction between the two groups at all time points including 1 month, 3 months, 6 months and 12 months [43]. A meta-analysis by Wong et al. did not significantly show that SLT is more effective at reducing IOP compared to ALT, indicating that the difference in pooled mean reduction in IOP by SLT compared to ALT was -0.5 mmHg (95% confidence interval -1.5 to 0.4) [41]. The meta-analysis also showed no statistical significance in the difference seen in reduction of medications and success rates between SLT and ALT. A Cochrane systematic review showed comparable results of IOP reduction between SLT and ALT [3]. Therefore, the current evidence suggests that the efficacy of SLT is not inferior to ALT.

IS SLT MORE EFFECTIVE THAN MEDICAL THERAPY?

SLT can be introduced into a patient's glaucoma management as a primary intervention in treatment-naïve patients or as an adjunct to control IOP when a patient is already on medical treatment. Several RCTs have attempted to clarify the role of SLT in glaucoma treatment algorithms by comparing the efficacy of SLT against medical treatment.

Nagar et al. [50] performed 2 prospective randomised trials comparing the effectiveness of SLT with latanoprost. In the first study, 167 eyes with OHT or primary or secondary OAG were recruited. Eighty five eyes (50.8%) had a diagnosis of OHT, 76 eyes (45.5%) had a diagnosis of POAG, 4 eyes (2.4%) had a diagnosis of pigment dispersion syndrome (PDS) and 2 eyes (1.2%) had a diagnosis of PXE. They were either newly diagnosed or medically treated. Patients already on medical therapy underwent a 5 week "washout" period. The patients were randomised to 4 groups receiving the following treatment: 90° of SLT to the trabecular meshwork (35 eyes), 180° of SLT (49 eyes), 360° of SLT (44 eyes) and latanoprost 0.005% (39 eyes). At 1, 6 and 12 months, the medical treatment group achieved a significantly lower mean IOP than 90° SLT. The medical treatment group also had significantly lower mean IOP than 180° SLT at 1, 3, 6 and 12 months. The medical treatment group had significantly lower mean IOP than the 360° SLT at 12 months. 90% percent of eyes in the medical treatment group achieved more than 20% IOP reduction from baseline with no additional IOP-lowering treatment. This is significantly greater than the proportion of eyes with more than 20% IOP reduction in the 90° and 180° SLT group but the medical treatment group did not reach statistical significance with the 360° SLT group. To achieve at least a 20% reduction in IOP, the investigators administered additional SLT or medical treatment to a number of eyes at their discretion. The proportion of eyes which required additional SLT or IOP-lowering eye drops were 10%, 66%, 35% and 25% in the medical treatment group, 90° SLT, 180° SLT and 360° SLT groups respectively.

In the second study, Nagar et al. [51] compared 360° SLT with latanoprost 0.005% for a period of 4 to 6 months. 40 patients with OHT or POAG were randomised to have a single SLT treatment (20 patients) or started solely on latanoprost treatment (20 patients). The mean reduction of IOP for the SLT group at 4 to 6 month follow up was 6.2 mmHg while for the medical treatment group this was 7.8 mmHg. The mean reduction in IOP was not statistically different between the SLT group and the medical treatment group at day 3, week 1 and month 4–6. However, at 1 month follow up, there was a significant difference in IOP lowering within the medical treatment group (7.2 mmHg) compared to the SLT group (3.2 mmHg). At the final follow up, there was also no significant difference in the percentage of patient who achieved successful IOP control (defined by

a reduction in IOP of ≥ 20%) between the treatment groups (75% in SLT group and 73% in medical treatment group).

Katz et al. [52] implemented a RCT involving 69 patients (127 eyes) which was based on the CIGTS design. All patients had no glaucoma medications for at least 4 weeks before recruitment. Patients with POAG, PXE glaucoma, mixed mechanism OAG with narrow angle and OHT were included. The authors did not quantify the number of patients with these diagnoses. No sub-group analysis was performed for these different diagnoses. The 69 patients were randomised to receive SLT treatment (67 eyes) or medical treatment (60 eyes). If the target IOP (determined using the CIGTS formula) was not achieved following the initial treatment, further SLT was performed in the SLT group in pre-determined step-wise increments. Similarly, if the target IOP is not reached in the medical treatment group, additions or substitutions of IOP-lowering eye drops were made. 54 patients (100 eyes) completed 9 to 12 months of observation. At 9 to 12 months, there was a mean IOP reduction of 6.3 mmHg for the SLT group and 7.0 mmHg for the medical treatment group. The percentage IOP reduction at 9 to 12 months for the SLT group was 26.4% and 27.7% for the medical treatment group. The difference in IOP reduction between the 2 groups was statistically insignificant. In the SLT group, 11% of eyes required additional SLT to maintain target IOP while 27% of eyes in the medical treatment group required additional medications. None of the patients in this study required intraocular surgery to meet the target IOP during the 12 months of study.

Lai et al. [53] prospectively evaluated the effectiveness of SLT versus topical medications in 29 Chinese patients. They recruited 29 patients of which 17 have POAG and 12 have OHT. One eye from each patient was randomised to receive SLT while the fellow eye would receive medical treatment. Only 1 course of SLT was performed for each patient in the SLT group. Treatment failure (defined as IOP > 21 mmHg) following SLT was controlled by administration of IOP-lowering eye drops. A follow up of 5 years was achieved for 24 patients. At 5 years, the SLT group obtained a mean IOP reduction of 8.6 ± 6.7 mmHg while the medical treatment group saw a mean IOP reduction of 8.7 ± 6.6 mmHg. The percentage IOP reduction at 5 years was 32.1% and 33.2% for the SLT group and medical treatment respectively. There was no statistically significant differences for the IOP reduction achieved between the 2 groups at all time points within the 5 years of follow up. However, 8 eyes (26.7%) from the SLT group required additional medical treatment to prevent treatment failure. One of these eyes was started on IOP-lowering drops at 4 weeks after SLT while the other 7 required supplementary medications one year after SLT. The mean number of medications used by the SLT group to maintain IOP of less than 21 mmHg was still significantly lower than the medical treatment group at annual follow-up within the 5 years. They range from 0.46 to 0.55 in the SLT group and from 1.45 to 1.63 in the medical treatment group. Filtration surgery was required by 5 eyes (17.2%) in the SLT group and 8 eyes (27.6%) in the medical treatment group although there was no statistically significant difference in failure rates following commencement of maximum medications between the 2 groups. Although it cannot be concluded from this study that SLT treatment is as superior as medical treatment due to the use of additional medications in the SLT group and also filtration surgery, this study provided some evidence supporting the use of SLT as a means to reduce dependence on multiple IOP-lowering eye drops. Another flaw is the possibility of cross-over effect from SLT and topical medications to the contra-lateral eye which may reduce the difference in outcomes observed between both eyes [6, 54, 55].

McIlraith et al. [54] recruited 61 patients with newly diagnosed POAG in a prospective non-randomised trial. The treatment-naïve patients were offered either SLT or topical latanoprost 0.005% following a discussion of the risks and benefits of both treatments. Patients with advanced visual field defects (split fixation or a scotoma within 10° of fixation) were excluded. 74 eyes were allocated to have SLT treatment while 26 eyes received latanoprost. The follow-up period was 12 months. The average absolute reduction in IOP for the SLT group was 8.3 mmHg and the latanoprost group was 7.7 mmHg. The average percentage reduction was 31.0% and 30.6% for the SLT group and latanoprost respectively. 83% of eyes in the SLT group had at least a 20% reduction in IOP and 84% of the latanoprost group also achieved this. In short, there was no statistically significant difference in IOP reduction between the SLT and latanoprost groups throughout the 12 months of observation.

In conclusion, SLT appears to offer similar efficacy in IOP reduction compared to medical treatment. Discrepancies were observed by Nagar et al who noted superiority of latanoprost over SLT but this effect was diminished when latanoprost was compared to 360° SLT rather than 90° and 180° SLT. However, the significant heterogeneity in methodology and outcomes of the trials discussed above should be taken into account.

IS SLT EFFECTIVE FOR PATIENTS WITH ADVANCED OPEN ANGLE GLAUCOMA?

There are few studies which specifically examined whether SLT is suitable for patients with advanced POAG [3]. Several studies have also excluded patients with advanced OAG [50, 54]. SLT is conventionally recommended to patients at the earlier stages of OAG. When IOP is uncontrolled in patients with advanced POAG, there is a tendency by clinicians to gravitate towards surgical treatments. However, there are

currently no studies which directly compare SLT with trabeculectomy or glaucoma drainage implants. Schlote et al. [56] retrospectively examined the efficacy of SLT on patients with early OAG and advanced OAG. The study included patients with POAG, PXE, PDS and OHT who are mostly already on topical medications. Patients with previous ALT or intraocular surgeries were excluded. The retrospective follow-up duration was 1 year. Glaucoma staging is established by the vertical cup-disc ratio (vCDR) and enhanced glaucoma staging system (GSS2). The GSS2 is based on the global indices (mean deviation, pattern standard deviation or loss variance) from either Humphrey or Octopus threshold tests [57]. 27 eyes of 27 patients were categorised to the early glaucoma group (vCDR < 0.8 and GSS2 stage ≤ 1). The advanced glaucoma group included 44 eyes from 44 patients with: vCDR ≥ 0.9 and GSS2 stage ≥ 3 or vCDR 0.6–0.8 and GSS2 ≥ 2. An overall IOP reduction of >20% and <21 mmHg was observed in 17 eyes (63%) of the early glaucoma group and 26 eyes (59.1%) of the advanced glaucoma group. However, it is not possible to conclude that SLT is similarly effective in both early and advanced glaucoma groups as patients from both groups had received additional treatments following the first SLT exposure. This included alterations to medical therapies and further SLT. In fact, 8 eyes (18.8%) from the advanced glaucoma underwent trabeculectomy.

IS SLT EFFECTIVE FOLLOWING FAILED TRABECULECTOMY?

Despite the use of anti-metabolites, the failure rate of trabeculectomy was estimated at around 20–40% at 5 years and 40–50% at 15 years [58, 59]. Treatment options to control IOP following trabeculectomy failure can be challenging and often involve a bleb revision before medical treatment is started [60]. The role of SLT in treating post-trabeculectomy patients is unclear and there has been few studies investigating its effectiveness.

In a case series of 16 Chinese patients with trabeculectomy failure for advanced POAG (mean deviation > -12 dB), Zhang et al. [61] investigated whether SLT resulted in an adequate reduction in IOP. All patients were on at least 2 IOP-lowering eye drops and had a mean pre-SLT IOP of 21 mmHg (±3.4). Following SLT, the mean IOP at 3 months and 9 months were 15.9 mmHg (±3.1) and 16.2 mmHg (±3.0) respectively. 13 out of 16 patients had an IOP reduction of >20% 1 day after SLT. At 9 months, 10 out of 16 patients had an IOP reduction of >20%.

The reduction in IOP observed by Zhang and colleagues following SLT may not be generalised to other post-trabeculectomy patients considering the low number of participants and the non-randomised nature of this study. Nonetheless, SLT may serve as a non-invasive treatment option if there is inadequate success from surgical revision or medical treatment following trabeculectomy failure.

THE USE OF SLT FOR OTHER FORMS OF GLAUCOMA

Most trials studying the effects of SLT have focussed on POAG and OHT. Hence there is a relative scarcity of evidence surrounding the use of SLT on other subtypes of OAG. Prior studies have demonstrated that factors such as baseline IOP, trabecular meshwork pigmentation and patient age may influence the success of SLT [62–64]. This would suggest that SLT may produce different therapeutic responses in eyes with PXE glaucoma, pigmentary glaucoma and NTG compared to POAG.

PSEUDOEXFOLIATION GLAUCOMA

Lindegegger et al. [65] compared the effects of SLT on 94 eyes with PXE glaucoma against 250 eyes with other subtypes of OAG which included 198 eyes with POAG, 26 eyes with NTG, 6 eyes with PDS and 19 eyes with OHT. In a retrospective review, IOP was analysed at 3 monthly intervals up to 60 months. There was no significant statistical difference between PXE glaucoma group and non-PXE glaucoma group at all time points except at 12 months. At 12 months, a mean IOP reduction of 4.8 mmHg (20.6% reduction from baseline) was found in the PXE glaucoma group while an IOP reduction of 2.7 mmHg (10.4% reduction from baseline) was observed in the non-PXE group. The greater IOP reductions seen in the PXE glaucoma group remained statistically significant when compared with individual glaucoma subtypes within the non-PXE glaucoma group at 12 months after SLT. It should be noted that 70% of patients in both groups were already prescribed one topical medication prior to SLT treatment although there was no significant difference between the anti-glaucoma medications taken by both groups.

A prospective non-randomised study by Ayala et al. [66] recruited 30 patients with PXE glaucoma and 30 patients with POAG. Only 1 eye from each patient was included in the study. When both eyes were treated, 1 eye was randomly selected. There was no statistical difference in IOP reduction between the PXE glaucoma patients and the POAG patients. At 1 month, mean reduction of IOP for the PXE patients was 6.19 mmHg whereas the mean IOP reduction for the POAG patients was 6.87 mmHg. No further IOP measurements were made beyond 1-month of follow-up.

Shazly et al. [67] prospectively compared patients with PXE glaucoma and POAG over the course of about 30 months. They included 19 eyes from 13 patients with POAG and 18 eyes from 13 patients with PXE glaucoma. No eyes with prior anti-glaucoma medication, glaucoma surgery or laser trabeculoplasty were included. There was no statistical significance between the difference in IOP reduction of the two groups at all follow up intervals (3 months, 9–15 months, 21–27 months and 30–42 months). The cumulative probability of PXE glaucoma patients remaining off

medications at 30 months was 77% while the POAG patients had a cumulative probability of 74%.

NORMAL TENSION GLAUCOMA

Lee et al. [68] studied the effects of SLT on patients with NTG in a prospective case series over a period of 1 year. 41 eyes from 41 NTG patients of Chinese ethnicity were included. Prior to SLT treatment, all patients underwent a 1 month "washout" period where all anti-glaucoma medications were stopped. The investigators also attempted to account for IOP fluctuations by recording their subjects' IOPs at 9 am, 1 pm and 5 pm to calculate the average IOP. This IOP phasing was only done prior to SLT and at 1 month after SLT. During the 1 year follow-up, topical medications were prescribed if the individual patient's target IOP was not met. Two patients required an additional SLT treatment. Prior to the study, the mean IOP for the 41 eyes was 14.3 mmHg (±3.4) while on medical treatment. After cessation of medical treatment (1 month washout period), the mean IOP was 16.2 mmHg (±2.2). At 1 month after SLT, the mean IOP was 12.4mmHg (±2.0) which represented a 14.7% reduction to pre-study levels. At 3, 6, 9 and 12 months, the mean IOP ranged between 11.2 mmHg and 12.2 mmHg. There was also a reduction in the mean number of medications used from a pre-SLT number of 1.5 (±0.8) eye drops to 0.9 (±0.9) and 1.1 (±0.9) at 1 month and 12 months respectively. The reduction in IOP and number of eye drops used was statistically significant at all time points except at 1 week. 34 of the 41 eyes had further follow up at 24 months [69]. At 24 months, their mean IOP was 12.6 mmHg which equate to an IOP reduction of 11.5% from pre-study levels (while still on pre-study medications) or a reduction of 22.0% from pre-SLT levels (after medications were stopped).

De Keyser et al. [70] compared the reduction of IOP following SLT in NTG patients with POAG and OHT patients. All patients were already medically controlled prior to SLT treatment. Following SLT, medications were gradually withdrawn if the IOP was 2 mmHg below target IOP. 56 eyes with NTG and 79 eyes with POAG/OHT were included. There was no significant difference when IOP reductions in NTG eyes were compared with POAG/OHT eyes at 1, 3, 6 and 12 months following SLT. However at 18 months, NTG eyes obtained a significantly greater IOP reduction from baseline than POAG/OHT eyes. Following SLT, there was also a reduction in the mean number of medications used in both NTG and POAG/OHT groups but this was not statistically significant when compared between both groups.

Other studies have investigated for IOP fluctuations in NTG patients following SLT. Tojo et al. [18] and Lee et al. [71] used the SENSIMED Triggerfish which is a wireless silicon contact lens sensor to continuously track for IOP-related pattern over a 24 h period. Tojo et al. included 10 eyes of 10 patients with NTG and expressed IOP fluctuations by calculating the range of IOP (difference between highest IOP and lowest IOP within 24 h). Lee et al. included 18 eyes of 18 patients and expressed IOP fluctuations as "global variability" which was derived from cosinor modelling of IOP-related amplitude fluctuations. Both studies did not demonstrate a significant change in IOP fluctuations at 1 week and 1 month post-SLT treatment.

PIGMENTARY GLAUCOMA

Ayala et al. [72] undertook a retrospective case series of 30 eyes from 30 patients with pigmentary glaucoma. The average number of medications was 2.06 (±0.73) prior to SLT. Following the first and only session of 180° SLT, the mean IOP reduction at 1 month was 7.5 mmHg. At 12 months, the success rate (success after SLT was defined by ≥20% reduction in IOP without alteration of pharmaceutical treatment or addition of further SLT or glaucoma surgery) was 85%. This gradually decreased to 67%, 44% and 14% at 24 months, 36 months and 48 months respectively. 2 out of the 30 patients had a spike in their IOP of >6 mmHg at 2 h following SLT but returned to pre-treatment levels the next day. There has also been another case series of 3 patients with pigmentary glaucoma which developed IOP spikes after SLT [64].

SAFETY PROFILE OF SLT

SLT is a safe procedure with a low risk of permanent or serious complications. Most of the commonly reported side-effects are transient. One of these side-effects is the rise of IOP post-operatively. This was estimated to occur in 3–8.5% of cases and would usually occur within the day of SLT treatment [73]. However, most IOP spikes can be expected to return to pre-operatively levels by next day with medical treatment [74]. The laser operator should avoid using high laser energies in patients with increased angle pigmentation as there has been case reports of uncontrollable IOP spikes requiring trabeculectomy surgery [64]. Transient anterior chamber flare and cells can usually be observed immediately following SLT [74]. Some clinicians regularly prescribe topical steroids to reduce this anterior chamber inflammation but most would resolve spontaneously within 5 days without any clinical sequela [17]. There have also been sporadic case reports of patients developing significant anterior uveitis following SLT requiring frequent topical steroid administration [75, 76]. Case reports of patients developing hyphaema and peripheral anterior synechiae (PAS) following SLT have been published but such cases remain rare and are more common following

ALT [77–80]. Cystoid macular oedema was also reported as a complication of SLT in case reports of patients with pre-existing ocular morbidities such as diabetic maculopathy, retinal vein occlusion and recent cataract surgery [81–84]. Therefore, patients with pre-disposing risk factors for macula oedema should be cautioned before SLT treatment. Corneal endothelial changes may also be detected in up to 50% of patients immediately following SLT [85]. However, these changes are usually self-limiting [86]. Corneal side-effects which are more serious such as corneal thinning, persistent corneal oedema and myopic/hyperopic shifts remain rare [87–89].

CONCLUSIONS AND FUTURE DIRECTIONS

The published literature has suggested that SLT is as effective as ALT at lowering the IOP of patients with OAG. The use of SLT is not limited to POAG as it is also indicated for other subtypes of OAG including PXE, NTG and pigmentary glaucoma. There is also evidence to suggest that SLT is not inferior to medical treatment although the therapeutic effect of SLT reduces with time. Therefore, the use of SLT may reduce patients' dependence on medical treatment and prevent non-compliance with eye drops. Several studies have also demonstrated SLT to be a cost-effective treatment in comparison to medical and surgical treatments. Despite the excellent safety profile of SLT, clinicians should be aware of rare adverse events when consenting patients for the procedure.

Further robust clinical trials are needed to determine whether most patients with OAG can be initially treated with SLT before the introduction of medical therapy. One such trial is *The Laser in Glaucoma and Ocular Hypertension* (LiGHT) study which is currently conducted in the United Kingdom [90]. It is a multicentre RCT which will randomise patients to either medical therapy without SLT or initial treatment with SLT followed by conventional medical treatment as needed. The aim of this study is to establish the health-related quality of life, clinical effectiveness and cost effectiveness of SLT compared to current medical treatment. There is also little research comparing SLT with glaucoma surgery. Further evidence in this field will be especially helpful towards improving the treatment algorithm of patients with moderate to severe glaucoma. As more glaucoma surgical devices such as Schlemm's canal stents and subconjunctival stents are developed, the use of SLT will need to be continually evaluated [91].

CORRESPONDENCE
Joanna Liput MD, PhD
Head of Glaucoma Service at York Teaching Hospital NHS Foundation Trust and Harrogate and District NHS Foundation Trust, United Kingdom
York Teaching Hospital
Wigginton Rd
YO31 8HE
e-mail: joanna.liput@york.nhs.uk

References

1. Worthen D, Wickham M. Argon laser trabeculotomy. Transactions-American Academy of Ophthalmology and Otolaryngology. American Academy of Ophthalmology and Otolaryngology 1973; 78(2): OP371-375.
2. Wise JB, Witter SL. Argon laser therapy for open-angle glaucoma: a pilot study. Archives of Ophthalmology 1979; 97(2): 319-322.
3. de Moura R, Paranhos CA Jr., Wormald R. Laser trabeculoplasty for open angle glaucoma. Cochrane Database Syst Rev 2007; (4): CD003919.
4. Samples JR, Singh K, Lin SC, et al. Laser trabeculoplasty for open-angle glaucoma: a report by the american academy of ophthalmology. Ophthalmology 2011; 118(11): 2296-2302.
5. Latina MA, Park C. Selective targeting of trabecular meshwork cells: in vitro studies of pulsed and CW laser interactions. Experimental Eye Research 1995; 60(4): 359-371.
6. Latina MA, Sibayan SA, Shin DH, et al. Q-switched 532-nm Nd: YAG laser trabeculoplasty (selective laser trabeculoplasty): A multicenter, pilot, clinical study. Ophthalmology 1998; 105(11): 2082-2090.
7. Kramer TR, Noecker RJ. Comparison of the morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. Ophthalmology 2001; 108(4): 773-779.
8. Alvarado JA, Katz LJ, Trivedi S, Shifera AS. Monocyte modulation of aqueous outflow and recruitment to the trabecular meshwork following selective laser trabeculoplasty. Archives of Ophthalmology 2010; 128(6): 731-737.
9. Bylsma SS, Samples JR, Acott TS, Van Buskik EM. Trabecular cell division after argon laser trabeculoplasty. Archives of Ophthalmology 1988; 106(4): 544-547.

10. Kagan DB, Gorfinkel NS, Hutnik CM. Mechanisms of selective laser trabeculoplasty: a review. Clinical & Experimental Ophthalmology 2014; 42(7): 675-681.
11. Alvarado JA, Iguchi R, Martinez J, et al. Similar effects of selective laser trabeculoplasty and prostaglandin analogs on the permeability of cultured Schlemm canal cells. American Journal of Ophthalmology 2010; 150(2): 254-264.
12. Latina MA, Gulati V. Selective laser trabeculoplasty: stimulating the meshwork to mend its ways. International Ophthalmology Clinics 2004; 44(1): 93-103.
13. Kara N, Altan C, Satana B, et al. Comparison of selective laser trabeculoplasty success in patients treated with either prostaglandin or timolol/dorzolamide fixed combination. Journal of Ocular Pharmacology and Therapeutics 2011; 27(4): 339-342.
14. Ayala M, Chen E. The influence of topical prostaglandin analogues in inflammation after selective laser trabeculoplasty treatment. Journal of Ocular Pharmacology and Therapeutics 2012; 28(2): 118-122.
15. Goldenfeld M, Geyer O, Segev E, et al. Selective laser trabeculoplasty in uncontrolled pseudoexfoliation glaucoma. Ophthalmic Surgery, Lasers and Imaging Retina 2011; 42(5): 390-393.
16. Juzych MS, Chopra V, Banitt MR, et al. Comparison of long-term outcomes of selective laser trabeculoplasty versus argon laser trabeculoplasty in open-angle glaucoma. Ophthalmology 2004; 111(10): 1853-1859.
17. Damji KF, Shah KC, Rock WJ. Selective laser trabeculoplasty vargon laser trabeculoplasty: a prospective randomised clinical trial. British Journal of Ophthalmology 1999; 83(6): 718-722.
18. Tojo N, Oka M, Miyakoshi A, et al. Comparison of fluctuations of intraocular pressure before and after selective laser trabeculoplasty in normal-tension glaucoma patients. Journal of Glaucoma 2014; 23(8): e138-e143.
19. Lee JW, Gangwani RA, Chan JC, Lai JS. Prospective study on the efficacy of treating normal tension glaucoma with a single session of selective laser trabeculoplasty. Journal of Glaucoma 2015; 24(1): 77-80.
20. Bozkurt E, Kara N, Yazici A, et al. Prophylactic selective laser trabeculoplasty in the prevention of intraocular pressure elevation after intravitreal triamcinolone acetonide injection. American Journal of Ophthalmology 2011; 152(6): 976-981.e2.
21. Baykara M, Hamidi NA, Akova-Budak B, et al. Early results of selective laser trabeculoplasty in patients resistant to deep sclerectomy. European Journal of Ophthalmology 2014; 24(3): 371-374.
22. Töteberg-Harms M, Rhee DJ. Selective laser trabeculoplasty following failed combined phacoemulsification cataract extraction and ab interno trabeculectomy. American Journal of Ophthalmology 2013; 156(5): 936-940.e2.
23. Alkin Z, Satana B, Ozkaya A, et al. Selective laser trabeculoplasty for glaucoma secondary to emulsified silicone oil after pars plana vitrectomy: a pilot study. BioMed Research International 2014; 2014.
24. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. British Journal of Ophthalmology 2006; 90(3): 262-267.
25. Stein JD, Challa P. Mechanisms of action and efficacy of argon laser trabeculoplasty and selective laser trabeculoplasty. Current Opinion in Ophthalmology 2007; 18(2): 140-145.
26. Pisella P, Pouliquen P, Baudouin C. Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication. British Journal of Ophthalmology 2002; 86(4): 418-423.
27. Chawla A, McGalliard JN, Batterbury M. Use of eyedrops in glaucoma: how can we help to reduce non-compliance? Acta Ophthalmologica 2007; 85(4): 464-464.
28. Lichter PR, Musch DC, Gillespie BW, et al. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. Ophthalmology 2001; 108(11): 1943-1953.
29. Leahy KE, White AJ. Selective laser trabeculoplasty: current perspectives. Clinical Ophthalmology (Auckland, NZ) 2015; 9: 833.
30. Hong BK, et al. Repeat selective laser trabeculoplasty. Journal of Glaucoma 2009; 18(3): 180.
31. Polat J, Grantham L, Mitchel K, Realini T. Repeatability of selective laser trabeculoplasty. British Journal of Ophthalmology 2016; 100(10): 1437-1441.
32. Khouri AS, Lari HB, Berezina TL, et al. Long term efficacy of repeat selective laser trabeculoplasty. Journal of Ophthalmic & Vision Research 2014; 9(4): 444.
33. Francis BA, Loewen N, Hong B, et al. Repeatability of selective laser trabeculoplasty for open-angle glaucoma. BMC Ophthalmology 2016; 16(1): 128.
34. Avery N, Ang GS, Nicholas S, Wells A. Repeatability of primary selective laser trabeculoplasty in patients with primary open-angle glaucoma. International Ophthalmology 2013; 33(5): 501-506.
35. Cantor LB, Katz LJ, Cheng JW, et al. Economic evaluation of medication, laser trabeculoplasty and filtering surgeries in treating patients with glaucoma in the US. Current Medical Research and Opinion 2008; 24(10): 2905-2918.
36. Lee R, Hutnik CM. Projected cost comparison of selective laser trabeculoplasty versus glaucoma medication in the Ontario Health Insurance Plan. Canadian Journal of Ophthalmology/Journal Canadien d'Ophtalmologie 2006; 41(4): 449-456.

37. Group GLTR, The Glaucoma Laser Trial (GLT). 2. Results of argon laser trabeculoplasty versus topical medicines. Ophthalmology 1990; 97(11): 1403-1413.
38. Group GLTR, The Glaucoma Laser Trial (GLT) and glaucoma laser trial follow-up study. 7. Results. American Journal of Ophthalmology 1995; 120(6): 718-731.
39. Leske MC, Heijl A, Hyman L, Bengtsson B. Early manifest glaucoma trial. Ophthalmology 1999; 106(11): 2144-2153.
40. The Advanced Glaucoma Intervention Study (AGIS). 7. The relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. Am J Ophthalmol 2000; 130: 429-440.
41. Wong MO, Lee JW, Chay BW, et al. Systematic review and meta-analysis on the efficacy of selective laser trabeculoplasty in open-angle glaucoma. Survey of Ophthalmology 2015; 60(1): 36-50.
42. Martinez-de-la-Casa J, Garcia-Feijoo J, Castillo A, et al. Selective vs argon laser trabeculoplasty: hypotensive efficacy, anterior chamber inflammation, and postoperative pain. Eye 2004; 18(5): 498.
43. Damji KF, Bovell AM, Hodge WG, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty: results from a 1-year randomised clinical trial. British Journal of Ophthalmology 2006; 90(12): 1490-1494.
44. Birt CM. Selective laser trabeculoplasty retreatment after prior argon laser trabeculoplasty: 1-year results. Canadian Journal of Ophthalmology/Journal Canadien d'Ophtalmologie 2007; 42(5): 715-719.
45. Russo V, Barone A, Cosma A, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty in patients with uncontrolled open-angle glaucoma. European Journal of Ophthalmology 2009; 19(3): 429.
46. Almeida ED, Moreira Pinto L, Brant Fernandes RA, Prata TS. Pattern of intraocular pressure reduction following laser trabeculoplasty in open-angle glaucoma patients: comparison between selective and nonselective treatment. Clinical Ophthalmology (Auckland, NZ) 2011; 5: 933.
47. Liu Y, Birt CM. Argon versus selective laser trabeculoplasty in younger patients: 2-year results. Journal of Glaucoma 2012; 21(2): 112--115.
48. Kent SS, Hutnik CM, Birt CM, et al. A randomized clinical trial of selective laser trabeculoplasty versus argon laser trabeculoplasty in patients with pseudoexfoliation. Journal of Glaucoma 2015; 24(5): 344-347.
49. Rosenfeld E, Shemesh G, Kurtz S. The efficacy of selective laser trabeculoplasty versus argon laser trabeculoplasty in pseudophakic glaucoma patients. Clinical Ophthalmology (Auckland, NZ) 2012; 6: 1935.
50. Nagar M, Ogunyomade A, O'Brart DP, et al. A randomised, prospective study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma. British Journal of Ophthalmology 2005; 89(11): 1413-1417.
51. Nagar M, Luhishi E, Shah N. Intraocular pressure control and fluctuation: the effect of treatment with selective laser trabeculoplasty. British Journal of Ophthalmology 2009; 93(4): 497-501.
52. Katz LJ, Steinmanna WC, Kabir A, et al. Selective laser trabeculoplasty versus medical therapy as initial treatment of glaucoma: a prospective, randomized trial. Journal of Glaucoma 2012; 21(7): 460-468.
53. Lai JS, Chua J, Tham C, Lam D. Five-year follow up of selective laser trabeculoplasty in Chinese eyes. Clinical & Experimental Ophthalmology 2004; 32(4): 368-372.
54. McIlraith I, Strasfeld M, Colev G, Hutnik CM. Selective laser trabeculoplasty as initial and adjunctive treatment for open-angle glaucoma. Journal of Glaucoma 2006; 15(2): 124-130.
55. Best U, Domack H, Schmidt V. Pressure reduction after selective laser trabeculoplasty with two different laser systems and after argon laser trabeculoplasty – a controlled prospective clinical trial on 284 eyes. Klinische Monatsblatter fur Augenheilkunde 2007; 224(3): 173-179.
56. Schlote T, Kynigopoulos M. Selective laser trabeculoplasty (SLT): 1-year results in early and advanced open angle glaucoma. International Ophthalmology 2016; 36(1): 55-61.
57. Brusini P, Filacorda S. Enhanced Glaucoma Staging System (GSS 2) for classifying functional damage in glaucoma. Journal of Glaucoma 2006; 15(1): 40-46.
58. Law SK, Shih K, Tran DH, et al. Long-term outcomes of repeat vs initial trabeculectomy in open-angle glaucoma. American Journal of Ophthalmology 2009; 148(5): 685-695e1.
59. Suzuki R, Dickens CJ, Iwach AG, et al. Long-term follow-up of initially successful trabeculectomy with 5-fluorouracil injections. Ophthalmology 2002; 109(10): 1921-1924.
60. Landers J, Sarkies N, Bourne R, Watson P. A twenty-year follow-up study of trabeculectomy: risk factors and outcomes. Ophthalmology 2012; 119(4): 694-702.
61. Zhang H, Yang Y, Xu J, Yu M. Selective laser trabeculoplasty in treating post-trabeculectomy advanced primary open-angle glaucoma. Experimental and Therapeutic Medicine 2016; 11(3): 1090-1094.

62. Lee JW, Liu CC, Chan JC, Lai JS. Predictors of success in selective laser trabeculoplasty for primary open angle glaucoma in Chinese. Clinical Ophthalmology (Auckland, NZ) 2014; 8: 1787.
63. Hodge W, Damji KF, Rock W, et al. Baseline IOP predicts selective laser trabeculoplasty success at 1 year post-treatment: results from a randomised clinical trial. British Journal of Ophthalmology 2005; 89(9): 1157-1160.
64. Harasymowycz PJ, Papamatheakis DG, Latina M, et al. Selective laser trabeculoplasty (SLT) complicated by intraocular pressure elevation in eyes with heavily pigmented trabecular meshworks. American Journal of Ophthalmology 2005; 139(6): 1110-1113.
65. Lindegger DJ, Funk J, Jaggi G. Long-term effect of selective laser trabeculoplasty on intraocular pressure in pseudoexfoliation glaucoma. Klinische Monatsblätter für Augenheilkunde 2015; 232(04): 405-408.
66. Ayala M, Chen E. Comparison of selective laser trabeculoplasty (SLT) in primary open angle glaucoma and pseudoexfoliation glaucoma. Clinical Ophthalmology (Auckland, NZ) 2011; 5: 1469.
67. Shazly TA, Smith J, Latina MA. Long-term safety and efficacy of selective laser trabeculoplasty as primary therapy for the treatment of pseudoexfoliation glaucoma compared with primary open-angle glaucoma. Clinical Ophthalmology (Auckland, NZ) 2011; 5: 5.
68. Lee JW, Ho WL, Chan J, Lai J. Efficacy of selective laser trabeculoplasty for normal tension glaucoma: 1 year results. BMC Ophthalmology 2015; 15(1): 1.
69. Lee JW, Shum JJ, Chan JC, Lai JS. Two-year clinical results after selective laser trabeculoplasty for normal tension glaucoma. Medicine 2015; 94(24): e984.
70. Keyser D, Belder D, De Groot V. Prospective study on the effect of selective laser trabeculoplasty in normal tension glaucoma. International Journal of Ophthalmology & Eye Science 2016; S1:008: 36-41.
71. Lee JW, Fu L, Chan J, Lai J. Twenty-four-hour intraocular pressure related changes following adjuvant selective laser trabeculoplasty for normal tension glaucoma. Medicine 2014; 93(27): e238. DOI: 10.1097/MD.0000000000000238.
72. Ayala M. Long-term outcomes of selective laser trabeculoplasty (SLT) treatment in pigmentary glaucoma patients. Journal of Glaucoma 2014; 23(9): 616-619.
73. De Keyser M, De Belder M, De Groot V. Randomized prospective study of the use of anti-inflammatory drops after selective laser trabeculoplasty. Journal of Glaucoma 2017; 26(2): e22-e29.
74. Song J. Complications of selective laser trabeculoplasty: a review. Clinical Ophthalmology (Auckland, NZ) 2016; 10: 137.
75. Koktekir BE, Gedik S, Bakbak B. Bilateral severe anterior uveitis after unilateral selective laser trabeculoplasty. Clinical & Experimental Ophthalmology 2013; 41(3): 305-307.
76. Kim DY, Singh A. Severe iritis and choroidal effusion following selective laser trabeculoplasty. Ophthalmic Surgery, Lasers and Imaging Retina 2008; 39(5): 409-411.
77. Rouhiainen HJ, Teräsvirta ME, Tuovinen EJ. Peripheral anterior synechiae formation after trabeculoplasty. Archives of Ophthalmology 1988; 106(2): 189-191.
78. Shihadeh WA, Ritch R, Liebmann JM. Hyphema occurring during selective laser trabeculoplasty. Ophthalmic Surgery, Lasers and Imaging Retina 2006; 37(5): 432-433.
79. Traverso CE, Greenidge KC, Spaeth GL. Formation of peripheral anterior synechiae following argon laser trabeculoplasty: a prospective study to determine relationship to position of laser burns. Archives of Ophthalmology 1984; 102(6): 861-863.
80. Kitazawa Y, Shirato S, Yamamoto T, Eguchi S. Argon Laser Trabeculoplasty. Variation of Methods and Immediate Complications in Second European Glaucoma Symposium, Helsinki, May 1984. Springer Netherlands1985.
81. Wechsler D, Wechsler I. Cystoid macular oedema after selective laser trabeculoplasty. Eye 2010; 24(6): 1113-1113.
82. Ha JH, Bowling B, Chen SD. Cystoid macular oedema following selective laser trabeculoplasty in a diabetic patient. Clinical & Experimental Ophthalmology 2014; 42(2): 200-201.
83. Wu Z, Huang J, Sadda S. Selective laser trabeculoplasty complicated by cystoid macular edema: report of two cases. Yǎnkē xuébào 2016; 27(4): 193-197.
84. Klamann MK, Maier AK, Gonnermann J, Ruokonen PC. Adverse effects and short-term results after selective laser trabeculoplasty. Journal of Glaucoma 2014; 23(2): 105-108.
85. Ong K, Ong L, Ong LB. Corneal endothelial abnormalities after selective laser trabeculoplasty (SLT). Journal of Glaucoma 2015; 24(4): 286-290.
86. White AJ, Mukherjee A, Hanspal I, et al. Acute transient corneal endothelial changes following selective laser trabeculoplasty. Clinical & Experimental Ophthalmology 2013; 41(5): 435-441.
87. Regina M, Bunya VY, Orlin SE, Ansari H. Corneal edema and haze after selective laser trabeculoplasty. Journal of Glaucoma 2011; 20(5): 327-329.

88. Song J, Song A, Palmares T, Song M. Myopic Shift Following Selective Laser Trabeculoplasty: A Case Report. British Journal of Medicine & Medical Research 2014; 4(4): 1008-1013.
89. Moubayed SP, Hamid M, Choremis J, Li G. An unusual finding of corneal edema complicating selective laser trabeculoplasty. Canadian Journal of Ophthalmology/Journal Canadien d'Ophtalmologie 2009; 44(3): 337-338.
90. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial. A multicentre, randomised controlled trial: design and methodology. Br J Ophthalmol. 2017: DOI: 10.1136/bjophthalmol-2017-310877.
91. Pillunat LE, Jungeman AGM, Kimmich F. Micro-invasive glaucoma surgery (MIGS): a review of surgical procedures using stents. Clinical Ophthalmology (Auckland, NZ) 2017; 11: 1583.