

“Selective Laser Trabeculoplasty – Past, Present and Future”

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ABSTRACT

Over the past two decades, selective laser trabeculoplasty (SLT) has increasingly become an established laser treatment used to lower intraocular pressure in open angle glaucoma and ocular hypertensive patients. The purpose of this review is to perform an up to date evaluation of SLT. We trace its' origins from previous derivatives of laser trabeculoplasty and review the current role SLT has in clinical practice by summarizing the existing literature. We outline future directions of SLT research and present emerging technologies that are further developing this treatment modality underpinning its importance in the treatment paradigm of glaucoma.

INTRODUCTION

Glaucoma is a progressive multifactorial disease characterised by damage to the optic nerve. It is strongly associated with elevated intraocular pressure (IOP) but may also occur with IOP in the normal range. Glaucoma results in progressive visual field loss and is a leading cause of blindness worldwide, second only to cataract. It is predicted by the end of the decade, close to 80 million people will have glaucoma, the majority by open angle glaucoma (OAG)([1](#))

The mainstay of glaucoma treatment is lowering of IOP to prevent further progression and visual loss. This may be achieved by either medical, laser or surgical means.

Over the past two decades, selective laser trabeculoplasty (SLT) has increasingly become an established laser treatment used to lower intraocular pressure in open angle glaucoma and ocular hypertensive patients.

In this review, we trace the origins of SLT from argon laser trabeculoplasty, review the current role of SLT and outline future directions of research and emerging technologies.

“PAST”

Lasers were first used to lower IOP in the 1970s with early attempts meeting with limited success. Goniopuncture using the Q-switched ruby laser produced a temporary IOP reduction, whilst high-energy argon laser photocoagulation of the trabecular meshwork (TM) caused acute post-laser IOP spikes(2). In 1979, Wise and Witter used argon laser at lower energy levels and reported successful short-term IOP reduction by approximately 10 mmHg in 40 phakic eyes, despite 65% of these eyes eventually requiring additional medication (3).

In 1983, Anderson and Parrish (4) found applied radiation energy could be selectively absorbed by a pigmented cell population within a tissue to cause damage. This process was known as Selective Photothermolysis (SP). The inherent properties of the tissue provided target selectivity reducing collateral damage.

Selective photothermolysis had two principle requirements; the desired target needed an intracellular chromophore with greater optic absorption at the laser wavelength than surrounding tissue. Secondly, laser duration could not exceed the time required for thermal diffusion into the tissue (thermal relaxation time) (5).

ALT fulfilled the first requirement of SP, as melanin within the pigmented trabecular meshwork acted as the chromophore. However, the laser duration of ALT (~0.1sec) was longer than the thermal relaxation time of melanin (1microsecond) allowing heat generated within pigmented cells to dissipate and damage surrounding TM(5).

ALT - Mechanism of Action

Intraocular pressure reduction seen in ALT was mediated by an increase in aqueous outflow, confirmed by both tonographic and aqueous dynamic studies (6, 7). A mechanical mechanism was postulated in which laser induced thermal burns of the TM caused collagen and tissue contraction. This reduced the diameter of the inner trabecular ring, reversing collapse of the meshwork, maintaining aqueous outflow(3). Electron microscopy demonstrated focal coagulative TM disruption with connective tissue and cellular debris deposited within the intra-trabecular spaces (8). Importantly, ultrastructural TM changes occurred before IOP lowering response, suggesting the mechanism of action was unlikely to be by mechanical means alone. 'Biological' theories were suggested once ALT was found to modify local cellular signalling pathways to enable increased aqueous outflow(9).

ALT - Efficacy

ALT induced an initial 30% reduction in IOP. The response seemed related to pretreatment IOP and thus eyes with normal tension glaucoma (NTG) showed a smaller effect (2). ALT was successful as both primary treatment (10) and as an adjunct to maximal medical treatment (6) with IOP reductions reported between 6.4-9.7mmHg (26-33%).

There were limitations. ALT effect diminished over time. Schwartz et al performed 360-degree ALT on 72 patients with uncontrolled OAG on maximal medical treatment and found the 77% success rate at 2 years had fallen to 46% at 5 years (11). Spaeth and Baez treated 109 eyes with uncontrolled OAG on maximal medical treatment with ALT: 32% needed filtration surgery at 1 year, 65% at 5 years and 95% at 10 years (12). Failure was highest in the first year and subsequently occurred at 10% per year (13).

Repeatability of ALT on failed eyes was also less successful than initial treatment. Richter et al performed 180-degree ALT retreatment to 40 eyes that had previously undergone 360-degree ALT and found only 32% of eyes demonstrated at least 3mmHg reduction in IOP (14).

Baseline predictors of ALT success were: higher pre-treatment IOP and increased age. Race was also relevant: black patients had a lower success rate (32%) at 5 years compared to white (65%) (11). Pigmentary and exfoliative glaucoma showed similar efficacy to POAG, but the largest IOP reductions and earlier failures were noted in exfoliative glaucoma. Other forms of secondary open angle glaucoma had limited response to ALT with uveitic and developmental glaucomas often showing little or no useful fall in IOP (15).

ALT – Adverse Effects

The main adverse events related to ALT were transient acute IOP spikes post-laser, development of peripheral anterior synechiae (PAS), corneal endothelial changes and acute anterior uveitis (2). In one study of 271 eyes, a rise of more than 5mmHg occurred in 34% of patients and of more than 10mmHg in 12% after 180 degrees of ALT. (16)

The frequency and severity of IOP elevations were positively associated with higher energy levels, 360-degree treatment, posterior placement of burns, greater angle pigmentation, and a low preoperative outflow facility. Most post-treatment IOP peaks occurred within 2 hours and postulated to be due to TM swelling or obstruction of the trabecular spaces by debris (17).

Development of PAS was another important complication noted more frequently with higher powers (18). One study found a three times higher incidence of encapsulated blebs in eyes previously treated with ALT (15.4%) compared to eyes without laser (4.7%) (19).

Role of ALT

The benefit of ALT was as an outpatient procedure that was quick, well tolerated and safe. It avoided the inconvenience and side effects of regular medical treatment and delayed the risks of surgery. However, loss of effect with time and association with bleb encapsulation in drainage surgery meant ALT was considered an adjunct to maximal tolerated medical treatment and a means of delaying surgery.

One pivotal study evaluated ALT's role as a primary treatment: The Glaucoma Laser Trial Research Group found better IOP control with ALT alone compared to a single medication at 6 months, 1 year and 2 years but inferior control at 5 years or if 2 medications were used(10). Compared to surgery, trabeculectomy achieved significantly lower IOPs with reduced diurnal IOP fluctuation (20).

“PRESENT”

SLT: Introduction

Introduced by Latina & Park in 1995, SLT uses a 532nm Q switched, frequency-doubled Nd:YAG laser that delivers a shorter pulse duration (3nanoseconds). It satisfies the dual criteria of selective photothermolysis, preventing heat dissipation outside of pigmented TM cells and causing less collateral damage ([21](#)).

Since receiving FDA approval in 2001, SLT has increasingly been adopted into practice. In the USA, 75 647 trabeculoplasties performed in 2001 increased to 142 682 procedures in 2012 ([22](#)).

The benefits are clear. The procedure is short, outpatient-based with quick recovery and good safety profile.

The role of SLT in the treatment paradigm of glaucoma is still not well defined. In this section we review the literature to give current perspectives on aspects related to SLT relevant to its role in clinical practice.

SLT – Mechanism of Action

Tonographic and aqueous dynamic studies demonstrate SLT increases aqueous outflow through the TM(23)(24).

Histopathological comparisons of human eyes that have undergone SLT vs. ALT (25) report lesser disruption to the TM in eyes post SLT. Higher power SLT can cause more extensive TM damage than lower power suggesting (26) that damage could be energy dose dependent.

Since limited structural damage occurs to the TM, the mechanical and structural theories which underpin ALT's mechanism of action do not fully apply to SLT. Moreover, SLT has been demonstrated to induce biological changes that modulate increased aqueous outflow through the TM, including changes in gene expression, cytokine secretion, matrix metalloproteinase induction and trabecular meshwork remodelling (5).

Using microarray analysis, SLT has been shown to modulate expression of genes related to cell motility, extracellular matrix production, membrane repair & reactive oxygen species production (27). In vitro studies have demonstrated an increase in pro-inflammatory cytokine expression including interleukin-1-alpha, interleukin-1-beta, tumour necrosis factor-alpha and interleukin-8 post SLT (9).

These cytokines increase stromelysin-1 expression (MMP-3), a matrix metalloproteinase implicated in TM extracellular matrix remodelling to increase aqueous outflow through the juxtacanalicular meshwork (28).

Increased TM monocyte recruitment has also been noted post SLT, a result of increased chemokine production (29). Monocytes increase aqueous outflow in vivo and increase Schlemm's canal permeability in vitro, by further cytokine secretion or directly phagocytosing debris within the TM. Local increases in endothelin-1 are thought to contribute to the acute IOP rise seen post SLT(30) whilst rises in lipid peroxide levels and decrease in antioxidant enzymes may be due to the increased inflammatory response precipitated after laser (31).

In vitro studies demonstrate that SLT and prostaglandin analogues may share a common pathway of action by inducing intercellular junction disassembly in Schlemm's canal and TM cells thus increasing aqueous permeability(32).

CLINICAL TECHNIQUE

Laser Treatment

SLT is performed using topical anaesthetic and a gonioscopic lens with coupling medium. The spot size (400 microns) is fixed but number of shots, energy level, total energy delivered and laser pulse duration are variable.

In their pilot study, Latina et al used 50 non-overlapping shots placed over 180° of the TM (21). The energy level was set at 0.8mJ and decreased by 0.1mJ increments until no visible effects or bubbles were observed. In current practice, typical treatment parameters are 50-100 shots applied over 180°-360° with energy adjusted to 0.6-1.4mJ and an expected endpoint of no visible tissue reaction or small microbubbles.

Studies have evaluated whether treating different degrees of the TM with SLT influences IOP lowering. Chen et al compared OAG patients that received 90° SLT vs. 180° SLT and found no significant difference in IOPs at 1, 4 and 7 months between groups ($p=0.21$)(33). In a RCT comparing 180° SLT vs. 360° SLT in patients with untreated POAG/OHT, mean IOP reduction at 1 month was 6.9mmHg and 8.2mmHg in the two groups respectively, with no significant difference noted($p= 0.35$)(24). Nagar et al compared IOP lowering of 90°, 180° and 360° SLT and found no difference between 180° and 360° SLT treatments at 12 months follow up (34). Both groups were more effective than the 90° SLT group.

Energy settings have also been investigated. Tang et al compared 39 patients receiving 100 shots of 360° SLT using low energy settings (0.3-0.5mJ) vs. 35 patients who received 100 shots of 360° SLT using standard energy settings (0.6-1.0mJ) (35). No difference in IOP lowering

between groups at all time points up to 1 year was noted. Furthermore, there was reduced incidence of adverse events in the lower energy group. In contrast, Lee et al found greater total SLT energy was associated with a greater IOP lowering, but this study was limited by small sample size and short follow up duration (1 month) ([36](#)).

A recent study has evaluated using a shorter laser pulse duration of 1ns compared to conventional 3-5ns and found no difference in IOP lowering or adverse events between the two arms in treatment naïve POAG, OHT and NTG patients with 6 month follow up ([37](#)).

Post Laser Treatment

Topical IOP lowering medications are commonly prescribed pre-operatively or immediately post SLT to prevent IOP spikes. A meta-analysis of 22 trials involving 2112 patients investigated efficacy of perioperative medications to prevent increased IOP post laser ([38](#)). Patients receiving medication had a lower risk of IOP increase of 10 mmHg or greater within first 2 hours compared with those receiving no medication or placebo (risk ratio (RR) 0.05, 95% confidence interval (CI) 0.01 to 0.20) and up to 24 hours (RR 0.22, 95% CI 0.11 to 0.42). There was no advantage to medication being administered before or after laser and no difference in effectiveness between different alpha2-agonists.

Topical anti-inflammatory drops are commonly prescribed post trabeculoplasty to mitigate early inflammation. Since SLT's effects are purported to act partly via a biological pathway (including production of pro-inflammatory cytokines), could topical anti-inflammatories post procedure be counter-productive?

A prospective RCT of 132 eyes evaluated usage of topical Indomethacin 0.1% or Dexamethasone 0.1% TDS for 1 week vs. control (no treatment) post SLT ([39](#)). No statistically significant difference in anterior chamber reaction, conjunctival redness, reported pain or IOP lowering between groups at all time points was found. This supports previous studies that have concluded anti-inflammatory drops after SLT do not cause a significant reduction in inflammation or altered IOP lowering efficacy ([40](#), [41](#)).

Clinical Efficacy of SLT in POAG and OHT patients

The first SLT efficacy data reported by Latina et al ([42](#)) who treated 180 degrees of TM demonstrated 6mmHg mean IOP reduction in uncontrolled POAG eyes previously treated with ALT and 5.8mmHg in eyes without prior ALT. Overall, 70% of eyes exhibited an IOP reduction of greater than or equal to 3mmHg.

Average IOP reduction following SLT is reported as 21.8-29.4% at 6 months, 16.9-30% at 12 months, 7.7-27.8% at 2 years, 24.5-25.1% at 3 years, 23.1%-29.3% at 4 years, 22.6-32.1% at 5 years and 22.8% at 6 years ([43](#)).

The IOP lowering effect of SLT diminishes with time. Based on the commonly adopted success criteria of IOP reduction >20% from baseline IOP, success rates vary from 66.7-75% eyes at 6 months, 58-94% at 12 months, 40-85% at 2 years, 38-74% at 3 years, 38-68% at 4 years, 11.1-31% at 5 years ([43](#)).

SLT vs ALT in OAG/OHT patients

To date, there are at least 10 RCTs comparing SLT vs. ALT ([44](#)). All studies have reported no difference in IOP reduction between the two treatments. A meta-analysis ([45](#)) evaluated 4 RCTs comparing efficacy of SLT and ALT([46-49](#)). Studies included patients with primary open angle glaucoma (POAG), pseudoexfoliation (PXF), pigment dispersion syndrome (PDS), uveitic glaucoma and normal tension glaucoma. In all studies, patients had uncontrolled IOP despite maximally tolerated medical treatment or previous ALT. Patients received 180 degrees of treatment in both groups. Overall, there was a pooled total of 150 eyes in the SLT group and 140 eyes in the ALT group. Definition of success varied between the studies. 3 out of 4 studies aimed for >20% IOP lowering without need for further surgery ([46, 47, 49](#)) whereas one study was less stringent – opting for 15% IOP reduction ([48](#)).

Difference in pooled mean IOP reduction between both groups was not significant - 0.5mmHg (95% CI: -1.5mmHg, 0.4mmHg). 2 studies ([46, 47](#)) calculated the effect of SLT vs. ALT in reducing the number of medications but was also not significantly different. Achievement of treatment success for SLT vs. ALT was similar between both groups ($p>0.05$). Overall, SLT demonstrated comparable efficacy with ALT in patients on maximally tolerated medical treatment ([45](#)).

These findings agree with 2 previous meta-analyses evaluating SLT vs. ALT ([50, 51](#)) but a third, analysing 6 studies reported SLT to have a superior IOP lowering efficacy to ALT([52](#)). The difference could have arisen since this study included quasi-randomised controlled trials as part of their analysis.

SLT vs. Topical Medication in OAG/OHT patients

Multiple trials have compared SLT against topical medication in treating OAG and OHT patients (44). Within SLT groups, there is often variability in the degree of TM treated. Common parameters used by studies include either 90°, 180° or 360° SLT.

Nagar et al performed a RCT comparing 90°, 180°, 360° SLT vs. latanoprost in OAG/OHT patients(34). Success rates were significantly higher in the latanoprost group compared to 90° and 180° SLT groups but similar to the 360° SLT group. This was confirmed in a subsequent RCT where 20 patients receiving 360° SLT were compared against 20 patients taking 0.005% latanoprost (53). SLT decreased IOP by 4.7mmHg (95% CI 3.6 to 5.7mmHg; p<0.01) with a similar reduction from latanoprost. Both were found to reduce daily IOP fluctuation with no difference in treatment success at last follow up (4-6 months) between groups (p=0.4).

To date, 2 meta-analyses comparing SLT with medication have been performed (45, 54). Both include 4 RCTs, but Li et al (54) also included one further prospective non-randomised trial(55). In 4 out of 5 studies, 360 degree SLT was performed. Definition of success varied between studies - 4 studies compared SLT with medication in terms of IOP reduction whilst one study classified success as meeting target IOP. Using IOP reduction as a success criterion, one study chose IOP reduction as IOP <21mmHg after intervention(56) whilst the remaining 3 used at least 20% IOP reduction from baseline(34, 53, 55).

Analysis included 492 eyes of 366 patients with OAG. SLT showed no significant difference in IOP reduction compared to medication (weighted mean difference (WMD) 0.6, 95% CI: -0.24, 1.43). There was no significant difference in achieving target endpoint success rates between

groups (pooled OR 0.84, 95% CI: 0.42, 1.68). Similar analyses performed by Wong et al also demonstrated no significant difference between SLT and medication ([45](#)).

In summary, meta-analysis data suggests SLT is as effective as medication for IOP control of with similar success rates. Limitations to consider include data being derived and pooled from trials of different durations with missing data during follow up as well as different definitions being used to define success.

SLT vs. Surgical Treatments in OAG/OHT patients

No studies have evaluated SLT vs. glaucoma surgery. ALT has been evaluated against trabeculectomy and found to be inferior at IOP lowering ([20](#)). Similar comparisons would be expected to yield similar results.

More recently, Fea et al compared 25 eyes receiving SLT vs. 31 eyes receiving placement of Hydrus microstent, a microinvasive glaucoma surgery (MIGS) device ([57](#)). At 12 months, a significant decrease in IOP was noted in both groups. Comparison between groups revealed no significant difference in mean IOP reduction between groups but a 3-fold greater reduction in medication use in the Hydrus group compared with SLT was found (-1.4 ± 0.97 vs. -0.5 ± 1.05 , $P = 0.001$). 47% of patients were medication free at 12 months in the Hydrus group vs. only 4% in the SLT group.

A higher frequency of post-operative complications were seen in the Hydrus group - three patients experienced a temporary reduction of visual acuity post-operatively and two patients had post-operative IOP spikes vs. no complications noted in the SLT group.

These results suggest MIGs devices have a similar IOP lowering efficacy to SLT and can reduce the number of medications that patients take. However, MIGs insertion is a surgical procedure performed in theatre associated with an increased adverse events profile. Further studies are needed to fully compare MIGs vs. SLT to evaluate effectiveness and safety.

SLT as Primary Treatment in OAG/OHT patients

Most studies investigating primary SLT have compared efficacy against topical medication. They have found primary SLT has a similar IOP lowering efficacy and success rate as topical medication.

However, many of these studies have included patients taking topical medications stopped for a variable duration (4 weeks to 3 months) prior to SLT ([34](#), [47](#), [55](#)). Such patients are not truly treatment naïve. Despite a washout period to mitigate against residual effects of prior topical treatment, some studies have shown SLT to be less effective when used following topical treatment. McIlraith et al reported clinical outcomes in 87 eyes on topical glaucoma medication discontinued 4 weeks prior to SLT([55](#)). IOP reduction was significantly less compared to the treatment naïve group (8.1mmHg vs. 6.4mmHg, $p<0.001$). Explanations include inadequate washout time or simply that SLT is more effective as a primary treatment. Further research is required to investigate primary SLT efficacy in treatment naïve patients.

SLT as Adjunct Treatment in OAG/OHT patients

Similar to ALT, SLT has been investigated as an adjunct treatment for patients on concurrent topical therapy as a means of further IOP reduction. Weinand et al reported clinical outcomes of 52 POAG eyes that received adjunct SLT whilst on topical medical treatment ([58](#)). Average IOP reduction from baseline was 24.3% (6.0 mmHg) at 1 year, 27.8% (6.12 mmHg) at 2 years,

24.5% (5.53 mmHg) at 3 years, and 29.3% (6.33 mmHg) at 4 years. In a RCT of 41 medically controlled POAG patients evaluating the effect of adjuvant SLT vs. medication alone ([59](#)), At 6 months, average IOP post SLT was 7.6% lower than the medication group ($p=0.03$) with the SLT group requiring significantly fewer anti-glaucoma medications compared with the medication group ($p=0.02$). Adjuvant SLT in POAG patients with uncontrolled IOPs despite medical therapy has also been shown to be effective([60](#))([61](#)), whilst other studies have demonstrated a reduction in number of concurrent glaucoma medications needed to control IOP following SLT ([60](#), [62](#)).

Woo et al investigated the effects of concurrent topical medication on efficacy of first-time adjunct SLT ([63](#)). Patients were grouped into different groups (0-3) based on the number of medications they were taking prior to SLT and then followed up for 5 years. Average IOP reduction following SLT varied between 21.8- 29% across all groups at 6 months and between 23.6 - 25.6% at 5 years with no statistically significant difference noted between groups. Mixed model analysis demonstrated no significant interactions between number of medications and post-treatment IOP response over time and was in agreement with previous studies demonstrating this. Importantly, of the 206 patients initially in the study, only 55 patients remained at 5 years due to loss to follow up and patients requiring additional intervention. This makes interpretation of the longer-term outcomes difficult and reiterates that the effect of SLT is largely temporary.

SLT post other treatment interventions

SLT is effective as an adjunct in patients who have previously undergone ALT. Mean IOP reduction at 1 year in 30 OAG patients receiving primary SLT (23%) was no different to 27 OAG patients receiving SLT after prior ALT (19.3%) ([64](#)).

Zhang et al investigated the efficacy of SLT in advanced POAG patients who despite previous trabeculectomy had uncontrolled IOPs requiring additional topical treatment (65). In 18 eyes, mean IOP was reduced from 21.3mmHg to 16.2mmHg at last follow up with 77.7% of patients achieving a reduction of >20% from pre-treatment IOP. The study was small with a short follow up (9 months) limiting the conclusions that can be made.

In conclusion, SLT is effective as an adjunct in OAG patients on medical treatment. It is effective at delaying the need for surgery in uncontrolled OAG patients but also may have a role in post-surgical patients as a means of further IOP reduction.

IOP fluctuation reduction with SLT

Large diurnal IOP fluctuations are an independent risk factor for glaucoma progression (66). Nagar et al reported SLT and prostaglandins are successful at reducing IOP fluctuation in POAG patients, but prostaglandins are more effective (3.6mmHg, 95% CI 3.2-3.9mmHg vs. 2.5mmHg, 95% CI 2.2-2.9mmHg, p =0.04) (53). Kiddee et al confirmed this in POAG and NTG patients and also demonstrated prostaglandins reduce IOP fluctuation throughout a 24-hour period whereas SLT's effect is pronounced at night (67). The extent of SLT treatment may also influence IOP fluctuation (68) with 360° SLT being shown to reduce IOP fluctuation greater than 180° treatment.

Contact lens sensors (CLS) (SENSIMED Triggerfish, Sensimed, Switzerland) have been used to measure 24-hour IOP fluctuation post SLT. At 1 month, in 18 NTG patients treated with 360° SLT(69) who achieved treatment success (greater than or equal to 20% IOP reduction), there was a 24.6% reduction in 24-hour IOP variability whereas in unsuccessful patients, the IOP

variability increased by 19.2%. This differs to a study by Tojo et al ([70](#)) who also investigated 24-hour IOP fluctuations using CLS in 10 NTG patients. They found the range of IOP fluctuations was not significantly changed between pre and post SLT over 24 hours ($p=0.77$) or during the daytime diurnal period ($p=0.92$). However, the range of IOP fluctuations during the nocturnal periods significantly decreased ($P=0.014$). SLT was shown to significantly lower IOP and decrease fluctuations during nocturnal periods in NTG patients supporting the findings of Kiddee et al ([67](#)).

REPEATABILITY OF SLT

The IOP lowering effect of SLT diminishes with time. As SLT causes minimal structural TM damage, repeat treatment has been considered feasible in suitable patients requiring further IOP reduction. To date, 7 studies report outcomes of repeat 360° SLT.

Ayala et al performed a RCT to evaluate the effect of repeat SLT in POAG/PXF glaucoma patients ([71](#)). Patients were treated initially with 180° SLT in the lower half of the TM and then randomly received further SLT in the previously treated TM or in the 180° upper untreated TM. 40 patients were included in both groups. The study found no significant differences in IOP between the retreatment groups at all time points but follow up was only 6 months ($p = 0.66$). This suggests repeat SLT can be applied to any TM area with similar efficacy and supports the theory that SLT retreatment is similarly effective to primary treatment.

Francis et al retrospectively evaluated 137 eyes with POAG or secondary OAG (excluding uveitic glaucoma) that had undergone two 360° SLT treatments at least 6 months apart ([72](#)). Percentage IOP reduction between the 2 treatments at 12-15 months was not significantly different (14.5% vs. 10.9%, $p=0.11$). A sub-analysis of 62 patients where baseline IOPs were

matched demonstrated 20% success at 12 months following both initial and repeat SLT (success criteria: IOP between 5-21mmHg and IOP reduction greater than or equal to 20% from baseline at 12 months).

Hong et al investigated 44 eyes with uncontrolled OAG on maximum tolerated medical therapy where primary 360° SLT had initially been successful (success criteria: greater than or equal to 20% peak IOP reduction). Repeat 360° SLT achieved success in 43.2% of eyes at 5-8 months compared to 50% success at initial SLT (73). There was no statistically significant difference between primary SLT and repeat SLT success rates. These findings are supported by Polat et al (74), who performed a retrospective review of 38 eyes with OAG uncontrolled on medical therapy that had undergone 2 successive 360° SLT treatments. They found a significant IOP reduction from baseline after both treatments up to 24 months follow up. Kaplan Meier survival analysis demonstrated median survival time of 9 months for initial SLT and 12 months for repeat SLT when using a definition of success as greater than or equal to 20% reduction in IOP from baseline.

In a separate study of newly diagnosed POAG patients, repeat SLT had a similar mean IOP reduction and treatment success rate (IOP reduction greater than or equal to 20%) compared to primary SLT in 42 eyes (75). Mean duration of success in repeat treatment (13.1 months) was longer than initial treatment (6.9 months). This difference was not statistically significant.

Repeat SLT can be successful irrespective prior SLT success. Khouri et al performed repeat 360° SLT after initial SLT in 51 OAG eyes(76). Eyes were stratified into those that had a successful response to initial SLT (greater than or equal to 20% IOP reduction from baseline) vs. a modest response (<20% IOP reduction from baseline). 41 % of eyes met the success

criteria after primary SLT and 43% after repeat SLT. In the 22 eyes with treatment success after repeat SLT, the proportion of eyes with initial successful response (11 eyes) and modest response (11 eyes) was the same. In a different study ([27](#)) of longer term outcomes of repeat 360° SLT, 29% of eyes achieved IOP reduction > 20% at 24 months compared to 36% of eyes following initial treatment – this was not statistically significant.

Overall, repeat SLT appears to be comparable to initial SLT. It achieves a similar absolute level of IOP control but mean IOP reductions following repeat SLT appear to be smaller. This could be explained due to residual effects of initial SLT not typically wearing off before retreatment. In addition, selection bias could apply with repeat SLT where patients who respond to initial SLT are offered retreatment. Larger prospective studies investigating repeat SLT are required to investigate this further.

SLT in PACG

SLT is not commonly performed in Primary Angle Closure Glaucoma (PACG) patients.

Visualisation of the TM within the angle is required, which can be limited in these patients.

Nonetheless, the efficacy of SLT in PAC/PACG patients where some of the angle is open and visible for treatment has been evaluated.

Narayanaswamy et al performed a prospective RCT to evaluate the effect of SLT in PAC/PACG patients that had previously undergone laser iridotomy (78). Following iridotomy, the angle was opened (at least 180° visible posterior TM on gonioscopy) but IOPs were still greater than 21mmHg. 96 eyes were randomized to SLT and 99 eyes to prostaglandin (PGA) therapy. At 6 months, IOP decreased by 4.0 mm Hg (95% CI, 3.2-4.8) in the SLT group ($P < .001$) and by 4.2 mm Hg (95% CI, 3.5-4.9) in the PGA group ($P < .001$). There were no differences between groups in the absolute mean reduction of IOP (4.0 vs 4.2 mm Hg, respectively; $p = 0.78$) or in percentage IOP reduction (16.9% vs 18.5%, respectively; $p = 0.52$). The procedure appeared safe in PAC/PACG patients with only one patient suffering from a transient IOP spike.

In a retrospective study comparing SLT in 59 eyes with PAC/PACG post PI vs. 59 eyes with POAG (79), SLT achieved an average IOP reduction of 38% from baseline in the PAC/PACG group vs. 32.7% in the POAG group. ($p=0.08$). Treatment criteria in the PAC/PACG group required at least 180 degrees of visible TM. In both groups, SLT was performed as either a primary treatment for uncontrolled IOP or as an adjunct for patients with uncontrolled IOP on maximal tolerated medical therapy or for those intolerant to medical therapy. Average postoperative follow was 10-11 months. In both groups, SLT permitted reduction of glaucoma medication (1.6 medications in PAC/PACG vs. 1.5 medications in POAG, $p=0.40$). There was no significant difference in frequency of post laser IOP spike between groups.

SLT in NTG

SLT can be of benefit in NTG patients. Patients have lower pre-treatment baseline IOPs compared to POAG patients, so the absolute IOP reduction is often less. Moreover, when using commonly used success criteria (IOP reduction > 20% from baseline), the success rates in NTG patients appear lower.

Lee et al performed a prospective study of 41 eyes with NTG patients evaluating 360° SLT efficacy ([80](#), [81](#)). At 12 months, average IOP reduction was 14.7% from baseline levels. Absolute success (IOP reduction of >20% from baseline washout IOP without addition of additional medication) was 22 % at 12 months and 11.1% at 24 months.

SLT in Pseudoexfoliation Glaucoma

SLT in PXF patients demonstrates comparable IOP lowering to OAG patients([82](#), [83](#)). In their review, Kennedy et al reported a mean IOP reduction for PXF eyes of approximately 31.5% at 12 months and 31.4% at 18 months. 64% of patients maintained greater than or equal to 20% IOP reduction at 18 months and 47% at 36 months ([84](#)). PXF also does not appear to be a risk factor for post-laser complications including inflammation.

SLT in Pigmentary Glaucoma

Koucheiki et al assessed the efficacy of 360° SLT in a cohort of patients with pigmentary glaucoma (PG), POAG and PXFG ([85](#)). At ~16 months, mean IOP reduction was 16.7% in POAG, 16.6% with PEX, and 14.5% in the PG group. Percentage of IOP reduction was not significantly different between groups ($P=0.696$) and no significant difference in success rates were noted ($p=0.597$).

Interestingly, increased post procedure pain, inflammation and IOP spikes were noted in the PG group. A higher rate of further interventions eg. repeat SLT or trabeculectomy was observed in the PG group (26.1%) vs the other 2 groups (POAG 16.5%, PXF 13.6%, $p < 0.001$). Similar associations have been found previously where increased post laser IOP spikes were noted in patients with heavily pigmented TM (86). Increased TM pigmentation in PG could cause more energy absorption following SLT resulting in increased pain. This has led to suggestions that lower energy settings be used in PG patients.

In a different study assessing time to failure in 30 PG eyes that had received 180° SLT (87), average time to failure was 27.4 months. 2 eyes experienced a post-laser IOP spike however only 180° of TM was treated in this study and lower energy was used limiting comparisons with other studies.

SLT in Secondary Glaucoma

Few studies have investigated SLT efficacy in secondary glaucoma. Rubin et al (88) reported the results of 7 secondary steroid induced glaucoma eyes that underwent SLT after intravitreal triamcinolone injections for macular oedema (6 eyes) or post central retinal vein occlusion (1 eye). Patients had elevated IOP despite maximum tolerated medical therapy (Mean pre-operative IOP 38.4mmHg±7.3) but following SLT, IOP decreased to 25.9mmHg±8.8 at 1 month ($P < 0.007$), 23.9mmHg±10.6 at 3 months ($P < 0.006$), and 15.7mmHg±2.2 at 6 months ($P < 0.001$). Four patients required repeat SLT and two patients failed after the 3-month visit.

Bozkurt et al investigated whether prophylactic SLT could reduce or prevent the IOP rise often seen following intravitreal steroid injection ([89](#)). In their prospective study, 15 eyes underwent 360° SLT approximately 8 days prior to intravitreal triamcinolone injection for diabetic macular oedema. IOP rise from 1-3 months was reduced and this effect was maintained up to 6 months.

In a study of 15 uveitic eyes that had received intravitreal steroid to control inflammation, the efficacy of SLT to reduce IOP was evaluated ([90](#)). Mean IOP prior to SLT was 30.57mmHg and was lowered to 14.85mmHg (51.4% reduction) at 1 month, 13.42 mmHg (55.7% reduction) at 6 months, and 15.14mmHg (50.4% reduction) at 12 months. Seven eyes (46.7%) achieved success criteria (IOP < 22 mmHg and/or a 20% or more reduction in IOP from the pre-SLT IOP) at 1-month, 6-month, and 12-month follow-up visits. One treated eye developed a prolonged IOP spike but there were no other adverse events.

Zhang et al evaluated the efficacy of SLT in 42 eyes with silicone oil induced secondary glaucoma ([91](#)). 360° SLT was performed and mean IOP decreased from 23.1 ± 1.9 mmHg pre-treatment to 18.4 ± 3.7 mmHg after treatment ($p < 0.05$). Mean number of anti-glaucoma medications used for IOP control also decreased from 2.17 ± 1.21 to 1.25 ± 0.89 ($p < 0.05$).

Overall, SLT appears to have some clinical efficacy in secondary glaucoma patients. Further large-scale studies are required to fully investigate this further.

Predictors of Success – SLT

SLT is not successful in all treated eyes. Studies have analysed baseline patient factors that may predict success, frequently by performing univariate and multivariate regression analyses to seek associations.

Predictors of success comparisons between studies is difficult since multiple variations exist within studies including study size, patient demographics, glaucoma subtype treated, SLT parameters, follow up length and definition of 'success' itself. This creates difficulty in establishing 'definite' robust predictors of SLT success and is reflected in the literature, where multiple studies have varying results.

The most consistently reported patient factor which predicts SLT success is elevated baseline IOP ([84](#)). This is partly explained by the commonly used definition of success (IOP reduction greater than or equal to 20% from baseline) tending to favour elevated baseline IOPs, since the magnitude of IOP reduction post treatment is often greater with higher IOPs. This is reflected in NTG studies where baseline IOPs are lower and both absolute IOP reductions and success rates are also lower compared to other subtypes ([80](#), [81](#)). One recent study suggested that patients with pre-treatment baseline of <14mmHg may not benefit from SLT at all ([92](#)).

A limitation of such success criteria is that though they are a marker of IOP reduction, they may not reflect real world clinical practice. Patients may achieve >20% IOP reduction from baseline following SLT, but following treatment, IOP may still be relatively elevated and too high to prevent glaucoma progression. Few studies have used pragmatic individualised target IOPs and assessed 'pursuit of control' for different treatments to obtain target IOPs ([93](#)).

Higher pre-treatment baseline IOPs may in fact be associated with increased treatment failure post SLT (94). Patients with higher pre-treatment IOPs are more likely to need repeat SLT or surgery as the magnitude of IOP reduction to control disease progression is larger and unachievable by single SLT treatment alone. Other patient factors including sex, race, age, glaucoma type, TM pigmentation, lens status and central corneal thickness have been investigated and found not to be predictive of SLT success (84, 92). Corneal biomechanical markers such as corneal hysteresis (CH) and corneal resistance factor (CRF) may be useful in helping to model the IOP lowering effect of SLT (95).

Investigating the effect of pre-existing topical medication on SLT success, Woo et al found no significant difference in success rate based on number of concurrent topical medications (63). In contrast, Lee et al found using multiple topical medications particularly topical carbonic anhydrase inhibitors was associated with SLT treatment success (96). Bruen et al found that pretreatment with prostaglandins was associated with a decreased IOP lowering response (97). This is feasible as both SLT and prostaglandins have been purported to share a common mechanism of action (32).

COMPLICATIONS + ADVERSE EVENTS

SLT is a safe procedure which is well-tolerated with low complication rates. Complications associated with SLT are usually transient and self-limiting.

IOP spikes immediately post laser can occur, with reported rises of greater than or equal to 5mmHg being reported in up to 28% of eyes (84). An association between IOP spikes has been noted in patients with pigmentary glaucoma and heavily pigmented TMs (85).

Anterior chamber inflammation is also common post SLT with up to 83% of eyes demonstrating some degree of inflammation ([98](#)). Considering the biological changes that SLT induces, including release of pro-inflammatory cytokines, some regard acute anterior uveitis as a predictable consequence of treatment. This inflammation is usually transient and self-limiting.

Unlike ALT, the development of peripheral anterior synechiae (PAS) is uncommon post SLT. In their meta-analysis, Wong et al noted only 2.86% of cases developed PAS ([45](#)) with increased occurrence after repeat SLT ([99](#)). Retinal changes post SLT are rare, but those described include cystoid macular oedema, development of subretinal fluid and choroidal effusions ([98](#)).

Transient corneal endothelial changes are well described post SLT. These can occur acutely, within an hour of treatment and are self-limiting with no lasting changes to visual acuity, central corneal thickness or endothelial cell count ([100](#)). A few case reports of transient corneal oedema and haze have been reported with and without residual corneal stromal scarring and hyperopic shift ([101-103](#)).

COST EFFECTIVENESS OF SLT

The treatment of OAG/OHT imposes significant costs on healthcare systems. The total annual costs in Australia for 2005 were \$1.9 billion, of which \$355 million were health system costs (104). Direct and indirect costs are higher for severe disease states (US\$623 for mild POAG to US\$2511 for severe POAG) suggesting early effective IOP control could reduce future costs (105).

In the USA, Cantor et al compared costs of uncontrolled glaucoma treated with either further medications vs. SLT followed by medications or surgery (106). Using Markov modelling and cost assumptions based on Medicare fee schedules, they found 5-year cumulative costs per patient were \$6571, \$4838 and \$6363 in the medication, SLT and surgery arms respectively. An Australian study modelled the cost benefit of laser trabeculoplasty as primary treatment compared to conventional medical treatment and found a saving of \$2.50 for every \$1 spent on laser treatment, compared to initial medical therapy (104, 107). Furthermore, cost savings were projected to continue increasing over time since with an ageing population, the prevalence, burden and treatment needed for POAG was also going to increase(104).

Seider et al calculated the time threshold at which bilateral SLT would become less costly than bilateral use of topical medication by dividing total costs of SLT by monthly costs of each medication (108). They found SLT became less costly than most brand-name medications within 1 year and less costly than generic latanoprost and generic timolol after 13 and 40 months respectively. This is supported by Lee & Hutnik who compared projected 6-year costs of primary SLT vs. primary medical therapy in OAG treatment in a Canadian healthcare model (109). If primary SLT had to repeated between 2-3 years, use of primary SLT over mono-, bi-, and tri-drug therapy produced a 6-year cumulative cost-saving between \$580.52, \$2042.54

and \$3366.65 dollars per patient respectively. Guedes et al confirmed this, using modelling to show primary SLT demonstrated better cost-effectiveness than topical treatment in the management of both mild and moderate glaucoma disease states ([110](#)).

In a separate analysis comparing 5 year costs of initiating OAG patients on 3 different treatment arms – initial medication, initial SLT or insertion of x2 MIGs (iStent) devices ([111](#)), the projected average cumulative cost at 5 years was lower in the SLT arm (\$4730) vs. medications arm (\$6217). The iStent arm was projected to be cheapest (\$4420) despite highest initial year zero costs.

Cost-effectiveness studies have yet to be performed in the UK. A SLT cost-effectiveness analysis would be useful to evaluate whether SLT would be similarly efficacious and cost-effective in an NHS setting.

QUALITY OF LIFE & SLT

The benefits of SLT are clear. It is a proven alternative to medication with comparable clinical efficacy, avoiding medication related side-effects and compliance issues. Despite this, there is little evidence to evaluate whether these benefits manifest as a difference in quality of life.

In a RCT of 41 medically controlled POAG patients randomly allocated to receive either additional 360° SLT (n=22) or continue with their usual treatment (n=19), quality of life outcomes were measured at baseline and 6 months using the Glaucoma Quality of Life-15 (GQL-15) and Comparison of Ophthalmic Medications for Tolerability (COMTOL) survey

scores. No statistically significant difference in the 6-month GQL-15 or COMTOL score as compared to baseline ($P \geq 0.4$) or between the two treatment groups ($P \geq 0.2$) was noted despite greater IOP reduction and reduction in number of medications in the SLT group. This is different to De Keyser et al ([112](#)) who used a different validated assessment tool for quality of life – the ‘Treatment Satisfaction Survey for Intraocular Pressure (TSS-IOP) and found significant improvement in parameters including side effects, eye appearance, convenience of use, ease of administration at 12 months compared to topical treatment.

Further large-scale studies are needed to evaluate whether SLT has a better quality of life compared to topical treatments.

“FUTURE”

Newer laser trabeculoplasty procedures are currently under investigation. Pilot studies have compared their efficacy against conventional SLT though further large-scale research is required to establish whether any of these newer modalities could supersede SLT in the future.

Micropulse Diode Laser Trabeculoplasty (MDLT)

MDLT was first described by Ingvaldstad et al in 2005 ([113](#)). This technique uses trabeculoplasty with subvisible (subthreshold) applications of repetitive short diode (532nm, 577nm or 810nm) laser pulses spaced by a long relaxation time with spot size of 300microns. MDLT does not cause coagulative damage to the trabecular meshwork ([114](#)) and there is no blanching or bubble formation over the TM during the treatment. Post treatment inflammation is minimal hence no anti-inflammatory medications are required. MDLT results are variable - some studies reporting limited IOP lowering success ([115](#)) whilst others report better results mean IOP reduction between 19.5-22% with a good safety profile ([116](#), [117](#)). In a comparison with ALT, the percentage of eyes with IOP reduction >20% from baseline was lower with MDLT compared with ALT([118](#)). No large studies exist comparing its use with SLT.

Titanium Sapphire Laser Trabeculoplasty (TLT)

TLT uses near infrared energy (790nm) in short pulses (5-10microseconds) with a spot size of 200microns. The near infrared wavelength is believed to penetrate deeper (~200microns) to the inner and outer walls of Schlemm's canal as well as the collector channels and ciliary body. The laser is believed to be selectively absorbed by pigmented phagocytic cells, preserving the trabecular meshwork tissue([119](#))

The total radiation energy of TLT is approximately 250 times that of SLT but is delivered over a longer time period, resulting in a longer thermal relaxation time, causing minimal collateral coagulative damage as a result ([120](#)).

In a small RCT comparing TLT vs. SLT in OAG/OHT patients, 18 patients received 360° TLT vs. 19 patients received 360° SLT. At 12 months, mean IOP reduction was 22% from baseline in TLT group and 20% in SLT group. At 2 years, mean IOP reduction was 35% in TLT group and 25% from baseline. No statistically significant differences in IOP or success rates were noted between groups. Treatments had a similar adverse events profile but despite this, some concerns remain about the long burn duration and deeper penetration of TLT compared to SLT ([120](#)).

Pattern Scanning Laser Trabeculoplasty (PSLT)

The PASCAL photocoagulator (OptiMedica Inc, Santa Clara, California) was introduced in 2006 for semi-automated photocoagulation of the retina ([121](#)). This technology uses short pulse durations (10-20msec), 100 micron spot size and computer guided predetermined pattern of spots. This results in reduction of thermal diffusion and surrounding tissue damage whilst permitting many more shots to be applied per area of TM ([114](#)). In a recent RCT ([122](#)), the safety, tolerability and IOP lowering efficacy of PSLT was compared against SLT. 29 OAG patients underwent PSLT in one eye and SLT in the fellow eye. There was no significant difference in mean IOP reduction at latest follow up (6 months).

Trans-scleral SLT without Gonioscopy Lens

Trans-scleral or Direct SLT allows 360° treatment around the perilimbal sclera overlying the TM without a gonioscopy lens. This eliminates corneal and gonioscopy related side effects

([123](#), [124](#)). It utilizes similar laser settings to conventional SLT and has similar IOP lowering efficacy but shots are fired simultaneously in less than 1 second reducing procedure duration. Direct SLT could potentially enable treatment to lower IOP in angle closure/ angle closure glaucoma patients as visible access to the TM is not required using this technique. If successful, direct SLT could be widely implemented including in the developing world. Further larger scale studies are underway to evaluate Direct SLT- the GLAUrious trial is a prospective multicentre RCT comparing SLT vs. direct SLT. A separate trial evaluating its' use is currently recruiting in Israel.

CONCLUSIONS

SLT is as effective as ALT and topical medication in POAG/OHT patients. It can be used as primary or adjunct treatment and has effect in other glaucoma subtypes. It has been shown to reduce IOP fluctuation but its effect does subside over time. SLT is repeatable as it causes minimal damage to the TM and IOP lowering is present even if initial response with primary SLT is limited. Adverse events are uncommon but most of these are transient and self-limiting. SLT has been shown to be a cost-effective option for primary treatment of glaucoma patients and evidence exists to show it is associated with better quality of life. Newer technologies are emerging to further develop SLT but these require further investigation with larger scale studies.

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