

# Selective laser trabeculoplasty: current perspectives

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**Abstract:** Selective laser trabeculoplasty (SLT) has been used in the treatment of glaucoma for just over a decade. Here, we review the current literature in terms of suggested mechanism, efficacy, method of treatment, predictors of success, adverse events, repeatability, and cost of SLT. The exact mechanism by which SLT lowers intraocular pressure (IOP) remains unknown although circumstantial evidence has come in many forms in relation to structural alteration; oxidative stress and inflammatory responses; tight junction integrity; proliferative responses; and microbubble formation. SLT is as effective as argon laser trabeculoplasty and medications in reducing IOP in glaucoma and ocular hypertension. The treatment is not uniformly effective in all eyes, and its IOP-lowering effect decreases over time. High pretreatment IOP is the strongest predictor of success; however, significant pressure reduction has also been shown in normal-tension glaucoma and in patients already taking multiple antiglaucoma drops. Mild, transient adverse effects are common. Transient IOP spikes usually resolve quickly with or without antiglaucoma treatment but may be problematic in pigmented angles. The limited available evidence suggests SLT is repeatable and cost-effective for the treatment of glaucoma and ocular hypertension.

**Keywords:** glaucoma, SLT, ocular hypertension, intraocular pressure

## Key principles

Selective laser trabeculoplasty (SLT) was designed to selectively target pigmented trabecular meshwork (TM) cells while sparing adjacent cells and tissues from thermal damage and maintaining TM architecture. In vitro investigation showed that nonpigmented cells did not experience collateral thermal or structural damage when a culture of mixed pigmented and nonpigmented TM cells were irradiated with frequency-doubled Nd:YAG laser at pulse durations less than 1  $\mu$ s.<sup>1</sup> The SLT parameters used clinically (532 nm frequency doubled Q-switched Nd:YAG laser with a 3 ns pulse and 400  $\mu$ m beam diameter) were based on the principle of selective photothermolysis, which relies on selective absorption of laser energy by pigmented TM cells and a pulse duration sufficiently short to prevent heat transfer and collateral tissue damage. This is because the nanosecond pulse duration is shorter than the time for the heat generated by the chromophore (melanin) to flow into the surroundings, which is in the range of microseconds.<sup>2</sup> The selective targeting of pigmented TM cells, and the safety and morphologic effects of SLT in vivo were confirmed in owl monkeys.<sup>3</sup>

SLT was preceded by argon laser trabeculoplasty (ALT), a widely accepted treatment for open-angle glaucoma (OAG) providing successful intraocular pressure (IOP) control in 44% of eyes at 2 years,<sup>4</sup> as well as experimental laser therapies to the TM dating back over 40 years. In 1974, Q-switched ruby laser goniopuncture of the anterior chamber angle was used to reduce IOP in 50 of 52 eyes by an average of 8.3 mmHg, with the effect lasting for a period of 3 months.<sup>5</sup>

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The similar efficacy of both SLT and ALT<sup>6</sup> has led to speculation that they produce their IOP-lowering effect through similar mechanisms, hence the coagulative damage to the TM with ALT may be unnecessary.<sup>7</sup>

## Suggested mechanisms

### Structural alteration

The exact mechanism by which SLT lowers IOP remains incompletely understood. Circumstantial evidence has come in many forms.<sup>8,9</sup> Histological studies have shown coagulative and mechanical damage occur minimally or not at all after SLT. Examination of human eye bank eyes with light microscopy, scanning, and transmission electron microscopy showed ALT caused crater formation, destruction of the rope-like components of the TM, and whitening of the surrounding collagen indicative of coagulative damage. The TM treated with SLT remained intact except for crack-like defects on the corneoscleral meshwork sheets; some of the endothelial cells contained disrupted intracytoplasmic pigment granules and some were vacuolated.<sup>8</sup>

Similarly, morphologic examination by light and transmission electron microscopy comparing ALT and SLT in patients 1–5 days prior to enucleation showed the extent of damage to the TM to be smaller after SLT. Post-ALT, trabeculae were markedly fragmented and the inner wall of Schlemm's canal was disrupted. Minor damage to trabeculae was seen after SLT; however, Schlemm's canal was well preserved and endothelial cells appeared less damaged with better-preserved nuclei than after ALT.<sup>9</sup>

Absent or minimal structural damage to the TM structure favors theories that SLT lowers IOP on a cellular level without mechanical or thermal effects.<sup>7,8</sup> This could occur either through migration and phagocytosis of TM debris by macrophages, or by stimulating the growth of healthy TM to optimize the outflow pathway architecture.<sup>10,11</sup>

### Oxidative stress and inflammatory responses

A rabbit model showed that a transient increase in aqueous lipid peroxide occurred between 3 hours and 7 days after SLT, which had predominantly normalized within 24 hours. This finding suggested that SLT may lead to liberation of free oxygen radicals, which then induce peroxidation of lipids or fatty acids. Potential sites of lipid peroxidation include the corneal endothelium and iris, which are rich in polyunsaturated fatty acids. Reactive oxygen metabolites also appear to participate in amplifying an inflammatory cascade and have direct cytotoxic effects.<sup>12</sup>

### Tight junction integrity

An *in vitro* study showed the disassembly of ZO-1 tight junctions in cultured Schlemm's canal cells that were exposed to media conditioned by lasered TM cells,<sup>13</sup> suggesting a role for intercellular junction changes in mediating the IOP-lowering effect of SLT by altering transendothelial aqueous flow across Schlemm's canal cells. Changes in ZO-1 tight junction staining were also seen in the corneal endothelium after SLT in cadaveric human donor corneas.<sup>14</sup>

### Proliferative responses

Immunofluorescent staining of human cadaveric anterior segments exposed to media conditioned by ALT showed that intracellular IL-1 $\alpha$ , IL-1 $\beta$ , and TNF $\alpha$  increased in conditioned trabecular cells. Western immunoblot analysis of the culture media showed augmented levels of the matrix metalloproteinase stromelysin and cytokines IL-1 $\beta$  and TNF $\alpha$ . This provided support to the theory that the therapeutic effect of laser trabeculoplasty is mediated by cytokine release, and proposed IL-1 $\beta$  and TNF $\alpha$  as the responsible factors. Blocking these two cytokines blocked the post-laser trabeculoplasty rise in stromelysin, a matrix metalloproteinase which may increase outflow facility by remodeling the juxtacanalicular extracellular matrix.<sup>15</sup>

A fivefold increase in monocyte population at the TM in eyes treated with SLT prior to enucleation and, in a separate experiment, a twofold increase in Schlemm's canal endothelial conductivity in cell cultures exposed to mononuclear cells from peripheral blood has been shown.<sup>16</sup> Chemokines released during SLT may trigger monocyte recruitment to the TM which in turn then release cytokines, such as TNF $\alpha$ , that could in turn modulate TM cells or alter the permeability of Schlemm's canal.

Laser trabeculoplasty to human corneoscleral explants in organ culture increased trabecular DNA replication by 80% during the first 2 days after ALT.<sup>17</sup> A second study showed a fourfold increase in cell division,<sup>18</sup> localized to the anterior nonfiltering TM, and migration of 60% of the new cells to the laser burn sites over the following 2 weeks. These findings support a hypothesis that laser trabeculoplasty causes early cell division by a population of cells from the anterior TM; these new cells then migrate and repopulate the treatment sites over the next few weeks.

The evidence supporting a cellular theory for the mechanism of SLT action correlates with the clinically observed time frame of IOP reduction occurring days to weeks after SLT.

## Microbubble formation

Clinically, the energy level used for SLT is usually titrated according to the appearance of microbubbles.<sup>3</sup> Selective photodamage of the retinal pigment epithelium (RPE) is a new technique to treat a variety of retinal diseases without causing adverse effects to surrounding tissues such as the neural retina and choroid. There is histological evidence for RPE cell death occurring at the energy threshold for microbubble formation after this treatment. The most probable mechanism of cell damage is thought to be formation of transient microbubbles arising more or less simultaneously around melanosomes once the boiling point of the intracellular plasma is reached. Subsequently, the cell volume significantly increases transiently which leads to mechanically disrupted cell structures. Two weeks after laser exposure, lesions are covered by a new population of RPE cells. Four weeks after treatment, a morphologically restored RPE was found.<sup>19</sup>

## Efficacy

The SLT pilot study<sup>20</sup> was a nonrandomized prospective trial that followed 53 eyes of 53 patients with uncontrolled OAG, including 23 eyes previously treated with ALT. Seventy percent of eyes achieved an IOP reduction of at least 3 mmHg and at 26 weeks; the treatment response group showed a mean IOP reduction of 23.8% (5.9 mmHg).

SLT provides a clinically significant IOP reduction in patients with OAG. A recent meta-analysis<sup>21</sup> identified 35 studies including eight randomized control trials (RCTs) assessing IOP reduction at 12 months or more post-SLT. Among patients with primary OAG (POAG), pseudoexfoliation (PXF), pigmentary, uveitic, steroid-induced, and normal-tension glaucoma (NTG) as well as ocular hypertension (OHT), ranging from treatment-naïve to those on maximum tolerated medical therapy, SLT resulted in a 6.9%–35.9% reduction in IOP.

The average reduction in IOP following SLT is 21.8%–29.4% at 6 months,<sup>22–25</sup> 16.9%–30.0% at 12 months,<sup>6,24,26–30</sup> 7.7%–27.8% at 2 years,<sup>24,28,31</sup> 24.5%–25.1% at 3 years,<sup>24,28</sup> 23.1%–29.3% at 4 years,<sup>24,28</sup> 22.6%–32.1% at 5 years,<sup>24,32</sup> and 22.8% at 6 years.<sup>24</sup>

The IOP-lowering effect of SLT decreases over time. SLT is effective in reducing IOP  $\geq 20\%$  below baseline pressure in 66.7%–75% eyes at 6 months,<sup>25,33,34</sup> 58%–94% at 12 months,<sup>24,28,29,35,36</sup> 40%–85% at 2 years,<sup>24,28,31</sup> 38%–74% at 3 years,<sup>24,28,36,37</sup> 38%–68% at 4 years,<sup>24,28,37</sup> and 11.1%–31% at 5 years.<sup>23,36,37</sup> The mean survival time (time for 50% of eyes to fail) is around 2 years.<sup>28,37</sup> An IOP reduction  $\geq 30\%$  is seen in 48%–59% eyes at 12 months.<sup>29,35</sup>

## SLT versus medical treatment

Four RCTs have compared SLT to medication. Meta-analysis of these studies showed that there was no statistically significant difference in IOP reduction (0.85 mmHg, 95% confidence interval [CI] –0.2 to 1.9) or treatment success (odds ratio [OR] 0.8, 95% CI 0.33–2.0).<sup>21</sup>

SLT has the advantage of not relying on adherence with glaucoma medications, which has been found to be low in several studies. Electronic eye drop monitoring revealed 76%–86% drop compliance, and evaluation of prescription claims showed patients had glaucoma drops available to use 69% of the time. Persistence (time until the patient first discontinues their medication) was observed to range from 20% to 64%.<sup>38</sup>

## SLT versus ALT

Ten RCTs comparing SLT to ALT showed that there was no significant difference in IOP reduction between the two types of laser trabeculoplasty.<sup>39</sup> One RCT reported better outcomes with SLT after 1 year, but no difference after 2 years.<sup>31</sup> Meta-analysis of four studies showed there was no statistically significant difference in absolute IOP reduction (–0.5 mmHg, 95% CI –1.5 to 0.4), number of antiglaucoma drops (–0.2 medications, 95% CI –0.08 to 0.5), or treatment success (OR 1.2, 95% CI 0.7–1.8).<sup>21</sup>

## SLT after prior ALT

SLT can produce a clinically useful decrease in IOP, similar to that of SLT as a first laser procedure, in patients who have had prior ALT. A prospective, non-RCT found no significant difference in the IOP reduction at 1 year in patients receiving SLT as a first laser procedure or SLT after prior ALT. Mean IOP reductions were 23% (SLT) and 19.3% (SLT after ALT).<sup>26</sup>

## SLT as initial treatment

SLT is effective as a first-line therapy to lower IOP and eliminates the issue of adherence to medications when used as an initial treatment.<sup>40</sup> The limited research on SLT as primary treatment in newly diagnosed POAG, PXF, and OHT suggests that the majority of patients maintain the IOP-lowering effect of SLT for up to 30 months<sup>41</sup> and even 5 years.<sup>32</sup>

## Concurrent medications

A retrospective review of 206 patients found that the number of coexisting antiglaucoma medications did not shorten the duration of the clinically significant pressure reduction after SLT. At 5 years, the cumulative proportion of patients not

requiring further intervention (such as additional medications, repeat SLT, or trabeculectomy) was 60.2%, 39.8%, 57.4%, and 45.7% of patients taking none, one, two, or three or more glaucoma medications, respectively.<sup>23</sup> This correlates with an earlier retrospective review which found that specific classes of antiglaucoma medications were not associated with SLT success.<sup>33</sup> These findings confirm a role for SLT as an adjunct to antiglaucoma medications, including prostaglandin analogs, which had been suggested may impair the effectiveness of SLT by competing for a common pathway to lower pressure.<sup>13</sup>

A prospective, nonrandomized study showed that SLT reduced the number of medications required to control IOP by an average of 2.0 (95% CI 1.8–2.3) at 6 months and 1.5 (95% CI 1.27–1.73) at 12 months. Ninety-seven percent of eyes attained a reduction in medications.<sup>42</sup>

## Reduction of diurnal IOP fluctuation

SLT is effective in reducing diurnal IOP fluctuation<sup>34,43</sup> although it may not be as effective as prostaglandin analogs in this respect. A prospective study showed mean diurnal IOP fluctuation was 5.5 mmHg before treatment and this reduced by 2.5 mmHg 4–6 months after SLT and by 3.6 mmHg in the latanoprost group. Fifty percent of patients in the SLT group achieved at least a 50% reduction in IOP fluctuation.<sup>34</sup> A retrospective study found 100% of eyes with 360° SLT and 84% eyes with 180° treatment maintained an IOP fluctuation <3 mmHg during the period 6–24 months after SLT. A statistically significant difference was found between the 180° and 360° treatment regimes in the number of eyes achieving an IOP fluctuation ≤2 mmHg (86% after 360° SLT compared to 52% of eyes after 180° SLT).<sup>43</sup> A recent study measuring IOP fluctuations in patients with NTG using a contact lens sensor found a statistically significant decrease in the range of nocturnal IOP fluctuation 1–2 months after SLT.<sup>44</sup>

## NTG

Although the strongest predictor determining SLT success is a higher pretreatment IOP, a significant IOP reduction can still be achieved in patients with NTG. IOP was shown to decrease from 13.5±2.5 mmHg to 11.3±2.7 mmHg ( $P=0.018$ ) 3 months after SLT,<sup>44</sup> although there is a paucity of data in this area.

## PXF glaucoma

SLT in eyes with PXF has a similar efficacy and adverse event profile to other types of OAG.<sup>41,45–48</sup> Studies have reported a mean IOP reduction for eyes with PXF in the

range of 31.5% at 12 months,<sup>46</sup> 16.6% at 16 months,<sup>47</sup> and 31.4% at 18 months,<sup>45</sup> with a cumulative probability of maintaining ≥20% IOP reduction in 64% of patients at 18 months<sup>45</sup> and 47% at 36 months,<sup>49</sup> and successfully remaining off medical therapy without further SLT in 74% at 30 months.<sup>41</sup> Where comparisons were made to POAG or other glaucoma subtypes, no statistically significant difference in IOP reduction or treatment success was found. PXF does not appear to be a risk factor for post-laser complications or transient IOP elevation.<sup>41,46–48</sup>

## Pigmentary glaucoma

A diagnosis of pigmentary glaucoma or the degree of TM pigmentation does not appear to affect the success rate of SLT;<sup>6,47,50</sup> however, patients with a deeply pigmented TM may be at higher risk of post-SLT complications such as, importantly, sustained IOP elevations. A series of four cases of post-SLT IOP spikes in patients with heavily pigmented angles has been reported, three of whom had pigment dispersion syndrome. The duration of post-SLT IOP elevation was 4 days to 3 months, and three of the four patients went on to require trabeculectomy. The patients were relatively young, taking two to three glaucoma medications prior to SLT, and one had a history of ocular trauma. Laser settings were 30–52 spots at 0.6–1.0 mJ laser energy. The authors theorized that it may be necessary to reduce the energy level or number of shots for heavily pigmented angles.<sup>51</sup> A prospective study found a significantly higher rate of mild pain and inflammation and a post-SLT IOP spike of >6 mmHg, as well as a higher need for surgical intervention in patients with pigmentary glaucoma, compared with POAG and PXF.<sup>47</sup> TM pigmentation was associated with pressure rises after ALT as well.<sup>52</sup>

## Steroid-induced glaucoma

A small study including ten eyes with steroid-induced OHT showed SLT to be effective at lowering IOP in these patients, with a 12-month mean IOP reduction of 35.9%, which was not significantly different to the IOP reduction for other glaucoma subgroups in this study.<sup>53</sup> Another small, prospective case control study of 31 eyes showed that prophylactic SLT in patients with a baseline IOP ≥21 mmHg prevented IOP elevation after intravitreal triamcinolone injection for diabetic macular edema.<sup>54</sup>

## Method of treatment

Topical anesthetic and a Gonio Laser lens, such as Latina SLT lens (Ocular Instruments, Bellevue, WA, USA), with a



methylcellulose coupling medium are used. With SLT, the spot size (400  $\mu\text{m}$ ) and duration (3 ns) are fixed, with the only variable being delivered energy. Compared to the small, 50  $\mu\text{m}$  spot diameter in ALT, the SLT spot covers the entire width of the TM making aiming easier. The SLT pilot study<sup>20</sup> used approximately 50 non-overlapping laser spots placed over 180° of TM. In this study, the energy level was initially set at 0.8 mJ and decreased by 0.1 mJ increments until no visible effects or bubble formation were observed. Typical treatment parameters are 50 (or 100) applications over 180° (or 360°) and laser energy is adjusted to 0.6–1.4 mJ, with an expected endpoint of no visible tissue reaction or small microbubbles.<sup>3,6,33,55,56</sup> It is assumed that bubble formation is important for the procedure to be effective, but too much bubble formation may lead to a higher rate of inflammation. As transient post-SLT IOP spikes may occur in some patients, apraclonidine 0.5% (Iopidine; Alcon Laboratories, Inc., Fort Worth, TX, USA) given 1 hour before treatment<sup>3,21</sup> is common practice. Topical anti-inflammatory drops are not advocated as the induction of an inflammatory response may be involved with the IOP-lowering effect of SLT, and various anti-inflammatory regimens do not correlate with better IOP-reduction post-SLT.<sup>3,57</sup> The symptomatic anterior chamber inflammation occurring in some patients after SLT usually resolves within a few days without treatment.<sup>20,35,47,58–60</sup>

A small, prospective study of 64 patients found no difference between 90° (25 spots) or 180° (50 spots) SLT in terms of IOP reduction in the treatment success group (7.01 mmHg versus 6.16 mmHg) and number of eyes requiring retreatment because of unsatisfactory IOP reduction (47% versus 41% eyes) at 7 months.<sup>61</sup> A more recent RCT of 167 patients randomized to 90°, 180°, or 360° of SLT found that 90° treatment was significantly less successful than latanoprost and generally ineffective. In the 90° group, 34% of eyes achieved  $\geq 20\%$  IOP reduction compared to 65% in the 180° and 82% in the 360° groups. The 90° group was discontinued 9 months after randomization because of apparent lack of treatment efficacy.<sup>35</sup>

Two RCTs and one retrospective review<sup>23,35,62</sup> comparing 180° with 360° SLT found no statistically significant difference in IOP reduction between the two groups.

Novel regimens reported at scientific congresses showed similar efficacy compared with traditional protocols. Laser applied around the limbus on the sclera overlying the TM without a Gonio lens and using the same laser parameters as conventional SLT (100 shots over 360°) reduced IOP from an average of 20.21 mmHg before treatment to 15.50 mmHg at 6 months (n=16), which was not statistically different from

the conventional SLT group (21.14 mmHg to 15.00 mmHg, n=16). The direct trans-scleral treatment group experienced a significantly lower rate of complications including superficial punctate keratitis and anterior chamber inflammation.<sup>63</sup> In a different study, 360° low-power SLT (0.4 mJ, 50–60 shots) repeated every year for 3–10 years (mean 6.5 years) maintained a higher number of patients on no antiglaucoma medications (84% patients) and a longer mean time to initiation of medical therapy (6.2 years) compared with a conventional 360° SLT regime (47% of patients taking no antiglaucoma medications and 3.3 years to initiation of medical therapy).<sup>64</sup>

## Predictors of success

The strongest predictor of success is baseline (pre-SLT) IOP. A RCT showed that higher baseline IOP correlated well with a  $\geq 20\%$  IOP reduction 12 months after SLT (OR 1.58; 95% CI 1.2–2.1). Baseline IOP in the treatment success group ranged from 18 to 36 mmHg and for the nonsuccess group from 16 to 28 mmHg.<sup>50</sup> A retrospective study using the same definition of treatment success and 6-months follow-up similarly found that SLT efficacy is positively associated with the degree of IOP elevation before SLT treatment. The treatment success group had significantly higher baseline IOP before SLT than the non-success group (21.75 $\pm$ 4.53 mmHg versus 16.65 $\pm$ 4.32 mmHg) with an OR of 1.3 (95% CI 1.16–1.46).<sup>33</sup>

Age, sex, race, glaucoma type, previous ALT, myopia, hypertension, diabetes, family history of glaucoma, concurrent antiglaucoma eye drops (including prostaglandin analogs), visual acuity, TM pigmentation, angle grade, lens status (phakic versus pseudophakic), and central corneal thickness were not found to be significant predictors.<sup>33,50,65</sup>

## Adverse events

The reported incidence of mild, transient side effects, presumably related to anterior chamber inflammation, ranges between studies from none to affecting the majority of patients. Although redness, discomfort or pain, and photophobia may occur commonly after SLT, they resolve, without treatment, within a few days.<sup>18,33,45,56–58</sup>

A transient IOP rise of  $\geq 5$  mmHg occurs in 0%–28% eyes,<sup>6,20,25,27,32,35,41,42,46,60,66–68</sup> and  $\geq 10$  mmHg in up to 5.5% eyes.<sup>41,42,67,69</sup> It resolves quickly with or without topical antiglaucoma treatment, usually within 24 hours. A systematic review found that empirical, prophylactic treatment reduced the incidence of transient IOP elevation (28.8% with treatment compared with 62% overall incidence).<sup>21</sup> Following

ALT, IOP rises of greater than 5 mmHg occurred in 34% of eyes and IOP rises greater than 10 mmHg in 12%.<sup>52</sup>

Peripheral anterior synechiae (PAS) occur rarely following SLT, and less often than was observed after ALT. PAS were found in one eye (1.1%–2.85% of eyes) in two of the nine studies that reported on the presence or absence of PAS after SLT.<sup>20,27,29,32,59,66,70–72</sup> Forty-six percent of eyes developed PAS after ALT.<sup>52</sup>

There are a few isolated case reports of less common adverse events following SLT, including two occurrences of hyphema,<sup>73,74</sup> a bilateral anterior uveitis,<sup>75</sup> and a choroidal effusion.<sup>76</sup> Four patients with pigmented angles encountered sustained IOP spikes after SLT, as detailed above.

There is one case report of cystoid macular edema after SLT.<sup>77</sup> However, a prospective study of 64 eyes in which macular thickness was measured by OCT in nine areas (as per the Early Treatment of Diabetic Retinopathy Study protocol), found no significant alteration in retinal thickness at any follow-up visit after SLT and did not prescribe any anti-inflammatory treatment.<sup>56</sup>

A few isolated cases of transient corneal stromal edema,<sup>78</sup> and one case of diffuse lamellar keratitis in a patient with prior laser in situ keratomileusis<sup>79</sup> were reported. In practice, transient changes in the corneal endothelium have been noted routinely on slit-lamp examination. This clinical finding has been described as a variable number of white spots in the endothelium which have resolved as early as 24 hours after treatment. The corneal endothelium has been evaluated with specular and confocal microscopy before, immediately after, and 1 month to 6 weeks after SLT. Specular microscopy found dark spots appeared immediately after laser treatment and had resolved by 1 month.<sup>80</sup> Confocal microscopy revealed areas of hyper-reflectivity corresponding to the location of an individual endothelial cell, and a slight increase in intercellular spacing, 30 minutes after SLT in 88% of eyes. These changes had resolved before the 6-week follow-up visit.<sup>81</sup> Both studies showed no significant change in endothelial cell count at 1 month or 6 weeks post-SLT.

## Repeatability

The theoretical advantage of SLT over ALT is that its absence of coagulative damage (fibrosis and scarring) to the TM allows treatment to be repeated. Retrospective studies have looked at the efficacy of repeat SLT after failed primary SLT.<sup>82–84</sup> Two studies showed that the repeat SLT treatment was at least as effective and may last longer than the initial treatment. In 42 eyes of 42 patients with newly diagnosed POAG,<sup>82</sup> repeat SLT had similar efficacy to primary SLT

with respect to IOP reduction ( $\geq 20\%$ ) and treatment success (reduction of IOP  $\geq 20\%$  and below an individually determined target pressure). The treatment success rate between patients undergoing a second treatment (66%) was higher but not statistically different to success after primary treatment (55%). Similarly, mean duration of success after second (13.1 months) and first treatments (6.9 months) was longer but did not reach statistical significance. Survival analysis, however, showed that eyes undergoing repeat SLT had a longer duration of clinical benefit and this was statistically significant. Duration of clinical benefit after SLT was relatively short in this study and repeat treatment was performed at as early as 1 month, which may be related to the treatment regime used (40–50 shots over 360° compared to 100 shots used more commonly). In 44 eyes of 35 patients with OAG uncontrolled on maximum medical therapy where primary SLT had been successful for at least 6 months,<sup>83</sup> repeat SLT achieved  $\geq 20\%$  IOP reduction in 43.2% of eyes at 5–8 months, which was not as marked as success rate at first treatment (50%) although the difference was not statistically significant. The interval between first and second treatment did not affect success rate.<sup>83</sup>

One study showed that not all eyes responding to primary SLT responded to repeat SLT. Fifty-one eyes of 34 patients that responded to primary SLT received repeat SLT between 7 and 72 months after their initial treatment. Forty-three percent of eyes achieved a  $\geq 20\%$  reduction in the average of all IOP readings in the following 12 months. Forty-one percent of eyes that responded to primary SLT achieved the same degree of IOP reduction after repeat SLT.<sup>84</sup> The posttreatment complication rate for repeat SLT was comparable to that reported in other studies for primary SLT.

## Cost

Economic modeling shows that if SLT and topical medications have similar efficacy, SLT alone as primary, rather than second-line, treatment for POAG is cost-saving, and the associated savings increase over time in an aging population as more people are diagnosed and treated.<sup>85</sup>

The projected cost over a 6-year period to a health service provider (Ontario Health Insurance Plan) predicted a modest cost saving with SLT over medical therapy as primary treatment for OAG. The cost of performing 180° bilateral SLT was 370 Canadian Dollars (CAD), taken from the Schedule of Benefits for Physician Services. Average annual costs for generic versions of six medication classes (prostaglandins, beta-blockers, carbonic anhydrase inhibitors, alpha-agonists, combination drugs, and pilocarpine) were calculated with

reference to a retrospective study of prescription refill frequency of 27,000 patients, in order to account for misadministration and noncompliance. Charts of 707 glaucoma patients were randomly selected to determine a representative utilization rate of glaucoma medications. The annual cost per medication ranged from 17.66 CAD for pilocarpine to 305.74 CAD for a dorzolamide–timolol combination, with the most commonly prescribed group, prostaglandin analogs, costing 271.81 CAD per annum. Forty-two percent of patients were taking two or three medications, making the yearly mean cost for all glaucoma medications 344 CAD per patient. The 6-year cumulative cost saving between SLT and medical treatment assumed that SLT was repeatable every 2 or 3 years. Using the scenario that SLT would be repeated after 2 years, SLT produced a 6-year saving over mono-, bi-, and tri-drug therapy of 206.54, 1,668.64, and 2,992.67 CAD per patient, respectively. If duration between SLT treatments were 3 years, the savings would be 580.52, 2,042.82, and 3,366.65 CAD, respectively. This study used the theoretical scenario in which every patient will respond to SLT, and patients who fail SLT and require adjunctive medication were not included. Using the results of studies examining duration of SLT success, the outcomes would be valid for up to 85% of patients treated every 2 years and 74% of patients treated every 3 years, assuming the repeatability of SLT shown in retrospective studies.<sup>82,83</sup> Costs associated with drop toxicity and allergy were also not included and their incorporation could potentially increase the cost of medical treatment.

## Conclusion

SLT is as effective as medications and ALT at lowering IOP in OHT, primary open-angle, PXF, pigmentary, and steroid-induced glaucoma. It is successful as both initial and adjunctive treatment in these patients. SLT does not rely on patients' compliance with eye drops, which is traditionally low, and side effects associated with drop toxicity are also avoided. Common adverse effects – namely discomfort and redness – are mild and transient. Sustained IOP spikes are rare and associated with heavily pigmented angles. Lower energy settings are recommended for pigmented angles as SLT selectively targets pigment in the TM. SLT is not uniformly effective in all eyes, and its IOP-lowering effect decreases over time. High pretreatment IOP is the strongest predictor of SLT success; however, significant IOP reduction has also been shown in patients with NTG and patients already taking multiple antiglaucoma drops. Available evidence suggests that repeat SLT achieves a good pressure reduction after successive treatments, and this makes SLT a cost-effective glaucoma treatment.

## Disclosure

The authors report no conflicts of interest in this work.

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