A Decade of Selective Laser Trabeculoplasty

Examining the role of SLT in the glaucoma treatment arsenal

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Examining the role of SLT in the glaucoma treatment arsenal

The Panel

Moderator

Dr Keith Barton, MD, FRCP, FRCS, FRCOphth is glaucoma service director and consultant ophthalmologist at Moorfields Eye Hospital and honorary senior lecturer, department of epidemiology, Institute of Ophthalmology at University College London, UK. Dr Barton owns a Lumenis Selecta Trio

Participants

Dr Mark A. Latina, MD, associate clinical professor at Tufts University, Boston, Massachusetts, USA, is the inventor of selective laser trabeculoplasty (SLT). Dr Latina owns a Lumenis Selecta 7000, a Lumenis Selecta II and a Lumenis Selecta Duet.

Dr Jorge Alvarado, MD is a glaucoma specialist and professor of ophthalmology at UC San Francisco, California, USA. Dr Alvarado owns a Lumenis Selecta 7000 and a Lumenis Selecta II.

Dr Sanjay Asrani, MD, associate professor of ophthalmology at Duke University Eye Center in Durham, North Carolina, USA. Dr Asrani owns a Lumenis Selecta II.

Dr Kate Coleman, BSc, FRCSEd, FRCOphth, PhD is an eye surgeon at the Blackrock Clinic, Dublin, Ireland, specializing in cataract and oculoplastic surgery; she is the executive chairperson of Right to Sight, which she founded in 2006. Dr Coleman is also heading up the African multicentre glaucoma and SLT trial. She owns a Lumenis Selecta II.

Dr Frank Howes, MB, ChB, MMed, FCS, FRCS, FRCOphth, FRANZCO, Vision Group, Australia, conducted some early SLT studies in 2000. Dr Howes owns a Lumenis Selecta 7000 and a Lumenis Selecta Duet.

Dr L. Jay Katz, MD is Chief of Glaucoma at the Wills Eye Institute and professor of Ophthalmology at Thomas Jefferson University in Philadelphia, Pennsylvania, USA. Dr Katz owns a Lumenis Selecta II.

Dr Madhu Nagar, MBBS, FRCSOphth, MSOphth is a consultant ophthalmologist and glaucoma specialist at Mid-Yorkshire Hospital Trust, Wakefield, West Yorkshire, UK. Dr Nagar, an early adopter of Lumenis SLT therapy, has been using it since 1999 and has worked with a Lumenis Selecta 7000, a Lumenis Selecta Duet and a Lumenis Selecta II.

Dr Rob Noecker, MD conducted some of the early histopathology studies on laser/tissue interactions in SLT, and is now in private practice in Connecticut, USA. Dr Noecker owns a Lumenis Selecta Duet and a Lumenis Selecta II.

Laser trabeculoplasty has been continuously used for the treatment of glaucoma in the US since its introduction in 1979.[1] Adoption of the technique gradually slowed when prostaglandins were introduced to the market in the 1990s. However, a steady and significant increase was seen in SLT procedures after it had gained FDA approval in March 2001 (according to US reimbursement codes data). This increase has continued to this day, indicating the growing adoption and acceptance of SLT procedures in the US as a viable treatment modality for managing primary open-angle glaucoma (POAG).

By comparison, Europe has been a slower adopter. Instead, European ophthalmologists have relied almost exclusively on medical treatments to combat glaucoma, in spite of the associated drawbacks. The hesitation to implement laser therapy, particularly as primary treatment, can be explained by a diverse range of reasons, including (but not limited to) perceived economic barriers, heavy promotion of medical treatments, convenience and lack of physician familiarity with laser treatment.

Ten years after the introduction of selective laser trabeculoplasty (SLT) in the US, however, with its favourable safety and efficacy profile in comparison to both medical and alternative laser therapies, it may be time to re-examine the role of lasers in the treatment of glaucoma in Europe.

In June 2011 Lumenis (the company that devloped and introduced SLT to the market) convened a panel of experts for a roundtable discussion about SLT, how it compares to other currently available glaucoma treatment options and to consider whether it deserves greater prominence as a potential first-line therapy in the future.

The science of SLT

Designed with the aim of avoiding scarring to the trabecular meshwork (TM) caused by other laser therapies, SLT has very short pulse duration and uses low levels of energy.

Table 1: Major differences between SLT and ALT.

	SLT	ALT	Ratio
Energy (mJ)	0.8–1.4	40–70	1:100
Fluence (mJ/mm²)	6	40 000	1:6000
Exposure time	3 ns	100 000 000 ns	1:33 000 000

Images courtesy of Lumenis

Its wavelength is in the visible range, and it has a specific chromophore target: the pigment granules inside TM cells.

Despite its much larger spot size, SLT eliminates the necrotic death of contiguous cells that is a feature of both ALT and micropulse laser trabeculoplasty (MLT).[2,3] And, unlike the aforementioned technologies, the lack of thermal damage and the preservation of TM architecture allows for the procedure to be repeated when necessary.

Mechanism of action

SLT uses a Q-switched (i.e., pulsed), 3 nanosecond, frequency-doubled Nd:YAG; 532 nm wavelength green laser. The large beam diameter of SLT has two functions: It reduces the need for focus, allowing the physician to more easily focus the laser onto the TM, and it distributes the laser energy evenly, meaning that all targeted cells receive equivalent doses of laser energy.[3–7] However, in comparison to other laser therapies, SLT is of extremely low intensity, particularly when considering the increase in spot size. Commonly, an SLT procedure requires energies of just 0.6–1.2 mJ; conversely, ALT requires 40–70 mJ per pulse.[1,2] The major differences between SLT and ALT can be seen in Table 1.

During the panel discussion, Dr Noecker explained how SLT works. In common with all other laser therapies, SLT achieves its effect by triggering a cascade of events, which is initiated when pigment-containing trabecular cells absorb laser energy. The laser energy targets pigmented trabecular meshwork endothelial cells (TMEs); as this targeting is highly specific, the laser energy does not cause coagulative damage to the TM or other collateral thermal effects to the trabecular beams.[3–7]

In addition to the high degree of selectivity of the laser, SLT prevents thermal reactions by using a comparatively short pulse duration, which lasts for just nanoseconds rather than milliseconds. Dr Noecker explained, "The pulse duration is below the thermal relaxation time, so there really is no appreciable heating occurring in the cells that are targeted. There's a quiet, focal cell death without a lot of necrotic cell death surrounding that."

Hence, the TM is left intact; however, the treated TME's are prompted to release cytokines in response to the laser insult. As these newly-released cytokines bind with the Schlemm's canal endothelial cells (SCEs), they compromise the cellular tight-junction barrier previously formed by these cells (Figure 1), which had been acting as a 'control' site for aqueous outflow. The opening of the SCE barrier, therefore, leads to increased aqueous outflow and, consequently, a decrease in intraocular pressure (IOP).[3–7]

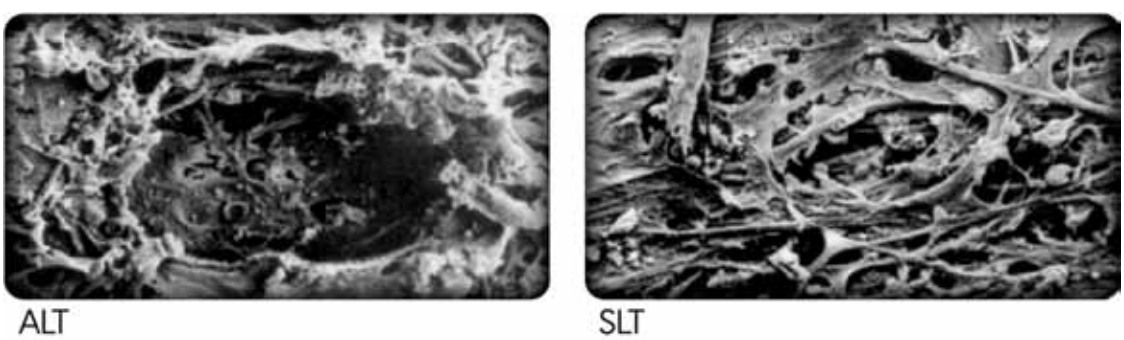
"SLT causes really no thermal damage to the adjacent cells or structures compared to MLT or ALT,"

Dr Mark Latina

Dr Alvarado described a supporting theory about the indirect effect of laser treatment on pressure. As previously revealed, cytokines, such as interleukin 1-alpha, are released after laser treatment has been performed and Dr Alvarado explained that these factors not only open the SCE barrier but also act as chemoattractants to recruit circulating monocytes to the lasering site. These monocytes become macrophages, which perform phagocytosis to pigmented and cellular debris while circulating in the TM. As the TM is cleared the aqueous outflow through the Schlemm's canal becomes easier and IOP is reduced.

Figure 1: The trabecular meshwork endothelial cells treated with SLT release cytokines, which bind with the Schlemm's canal endothelial cells (SCEs) and open up the cellular barrier. (Adapted from references 3, 4–7.)

Figure 2: ALT causes thermal damage to the TM, while SLT has no associated necrotic cell death outside of the targeted cells. (Adapted from T.R. Kramer, R. Noecker *et al.*, *Ophthalmology*, 2001;**108**:773–779.)



SLT versus ALT

"So, SLT is more like a sniper rifle than a hand grenade going off?" questioned Dr Barton, regarding the difference between the laser techniques. The panel agreed that the analogy was apt, since, as its name suggests, SLT targets TME cells selectively. By comparison, ALT uses higher levels of energy to target cells indiscriminately, resulting in high thermal absorption to all cells.[5] ALT, therefore, causes coagulative damage that leads to scarring of the TM, and potentially various other clinical adverse events, such as PAS formation, while SLT treatment does not.[2,3]

"Largely the problem with SLT is we're burdened by the history of ALT. I think if SLT came first or ALT never existed, that the uptake in SLT would be infinitely higher,"
Dr Rob Noecker

"SLT causes really no thermal damage to the adjacent cells or structures compared to MLT or ALT," Dr Latina stated. (Figure 2) This is in spite of the fact that the beam diameter used for SLT is many times larger than that used for ALT (Figure 3), or indeed for MLT. He added, "As thermal damage is not occurring, the Schlemm's canal is not fused together, the process can theoretically be repeated in the same eye."

In terms of success rates for IOP reduction, ALT and SLT were comparable. However, in addition to eliminating the damage to the TM, SLT has been shown to have a better overall long-term success rate (Figure 4),[8] further indicating that it is a far more suitable treatment option than ALT.

In agreement Dr Howes stated, "I now try to avoid ALT as a result of the amount of damage we see in the angle and the progressive nature of the formation of peripheral anterior synchiae (PAS) with time. I think that we should no longer be using ALT."

Dr Noecker in fact believes that the legacy of ALT is one of the reasons accounting for lack of enthusiasm about SLT. "Largely the problem with SLT is we're burdened by the history of ALT. I think if SLT came first or ALT never existed, that the uptake in SLT would be infinitely higher," he said.

However, Dr Alvarado interjected that the upsurge of prostaglandin analogues (PGAs) must also be considered when examining why SLT has not been more readily adopted.

SLT and prostaglandins

As the current gold standard first-line therapy, PGAs are both efficacious in controlling IOP and convenient for the ophthalmologist to prescribe. However, there is a significant drawback — patient compliance.

SLT is as effective as one glaucoma medication[9–12] and may be associated with fewer drawbacks.[10] For instance, SLT avoids the compliance (Sidebar 1), side effect (Sidebar 2) and inconvenience issues associated with medical interventions.[10] In a study comparing SLT and medication as primary therapy options it was shown that over a 12-month period, SLT provided a comparative mean IOP reduction to that achieved with latanoprost (Figure 5).[9]

Figure 3: The larger beam diameter of SLT compared with ALT. (Courtesy of Michael S. Berlin, MD.)

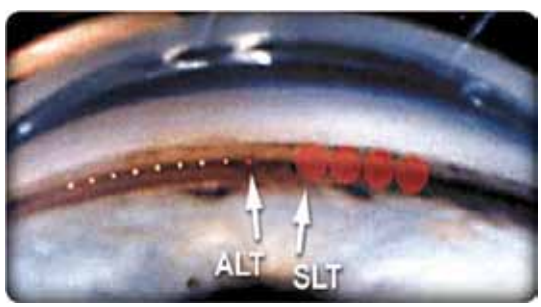
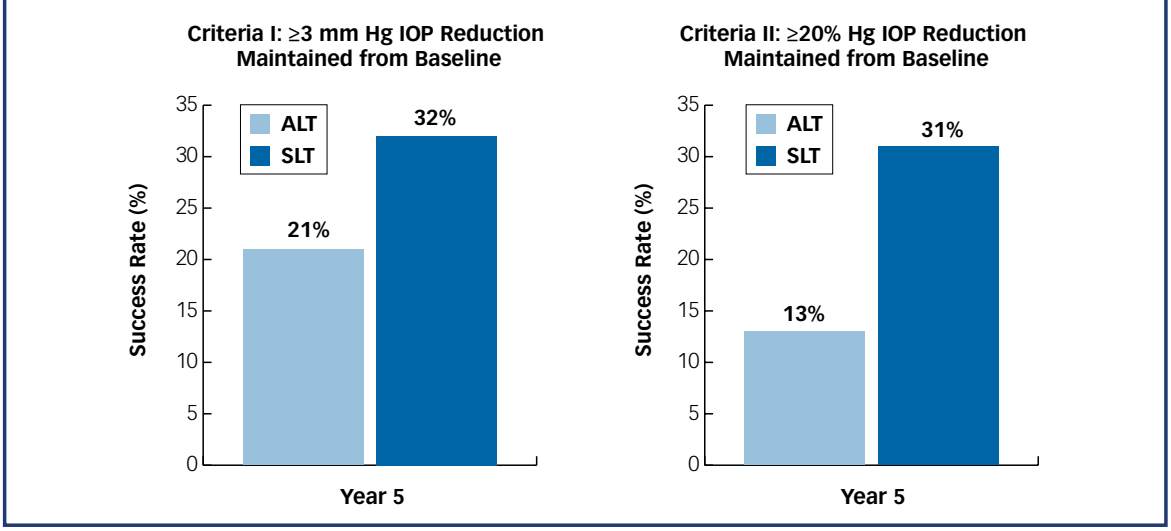


Figure 4: SLT vs ALT: long-term success rates. (Adapted from M.S Juzych *et al.*, *Ophthalmology*, 2004;**111**:1853–1859.)



In a study by Dr Nagar and colleagues the effect of SLT on reducing IOP fluctuation was examined. She revealed that both SLT and latanoprost had a significant impact on IOP control and fluctuation. There was a slightly higher reduction in IOP as a result of latanoprost but she explained that SLT offers the benefit of being a one-time intervention not requiring ongoing patient compliance.[13]

Further studies have also demonstrated that SLT as a primary treatment offers sustained reductions in IOP over 18 months,[11] and five years.[14] "The best thing SLT can do for you is stop the use of the prostaglandin analogues," Dr Alvarado claimed.

"I think there is a factor that we need to employ more, and that is the diminishment of conjunctival scarring as a result of medication use which can be ameliorated by the regular use of SLT. From the moment patients start using PGAs, or any topical hypotensive agent for that matter, particularly if preserved with benzalkonium chloride, a scarring crisis begins," said Dr Howes.

SLT, however, effectively sidesteps this crisis, maintaining the integrity of the ocular surface, as well as maintaining the integrity of the TM.

Clinical indications and patient selection

"Since its introduction as a new laser for open-angle glaucoma (OAG), SLT has been shown to be a safe and effective therapy in several forms of the disease," affirmed Dr Latina.

Dr Noecker reiterated one of the benefits of the large beam size. "The nice thing is," he said, "it's very forgiving because even with an open-angle, you're offered overlapping peripheral cornea and often the iris." By virtue of this, the safety zone is larger and, hence, a wider range of patients can be treated.

However, patient selection still plays an important role. Dr Nagar raised the critical point that the patients most likely to have a significant response to SLT are those with the highest baseline pressure, regardless of any prior medical or therapeutic interventions.

"In my experience it is the baseline pressure that has an impact. The higher the pressure, the better the response to SLT," she summarized. Dr Nagar's rule of thumb was that she expected a 20% drop in IOP when the baseline pressure was 20 mmHg, and a 30% drop for a baseline of 30 mmHg.

"In my experience it is the baseline pressure that has an impact. The higher the pressure, the better the response to SLT,"

Dr Madhu Nagar

Dr Latina mentioned that other studies[15,16] had also previously indicated that the best predictor for success was high baseline pressure. However, among pre-treated patients, good PGA response also seems to predict good SLT response, although this is an unreliable criterion because of potential concerns over non-compliance. "I'm not sure I would totally disengage from the possibility of doing an SLT if somebody didn't appear to respond to a prostaglandin," pointed out Dr Katz.

In terms of unsuitable patients, Dr Latina recommends not treating patients with 360° synechial closure with SLT. However, patients with intermittent PAS are suitable candidates for the treatment, provided there is some open angle. Unlike with ALT — in which PAS is an inevitable consequence when the angle is narrow, according to Dr Noecker — as long as the TM is visible, PAS will not be a problem with SLT.

Treatment-naïve patients

Patients who are newly diagnosed with OAG and have as yet received no therapeutic intervention are ideal candidates for SLT, particularly if they have a high baseline IOP.[15,16] In fact, Dr Nagar commented that she will perform SLT on treatment-naïve patients with normal tension

Sidebar 1: Common reasons for non-compliance with prescribed medical treatment regimens

- Complicated prescription regimens
- Polypharmacy
- Medication costs
- Unpleasant side effects
  - ◊ See Sidebar 2
- Not following appropriate dosing instructions
  - ◊ Too much medication
  - ◊ Too little medication
  - ◊ Waiting 5 minutes between applications of different medications
- Physical or material barriers
  - ◊ Adverse weather preventing prescription being filled
  - ◊ Problems administering drops due to arthritis
  - ◊ Reading small print on label
- Changes in routine

Sidebar 2: Side effects associated with commonly-prescribed glaucoma treatment medications

- Allergic reactions
- Blurred vision
- Compromised ocular surface: burning or stinging pain, or other ocular discomfort or itching
- Dry nose, mouth, sore throat, coughing
- Headaches
- Fatigue, drowsiness
- Low blood pressure
- Reduced pulse rate
- Dim vision
- Changes in sense of taste (dysgeusia)
- Increased pigmentation of iris, eyelid and eyelashes
- Hyperaemia
- Shortness of breath (in patients with respiratory disorders)

glaucoma (NTG) only if their pressures were in the high teens.

Approximately 93% of patients are anticipated to respond to SLT as primary therapy, demonstrating a mean IOP reduction of 31%, and more than half of all patients treated with SLT as replacement therapy will not need any medication post-treatment.[14]

The different subsets of glaucoma

While the experts reached a consensus about the overall effectiveness of SLT, some issues were raised regarding certain variations of the condition — specifically, NTG, pseudoexfoliative glaucoma and pigment dispersion syndrome.

"So, SLT is more like a sniper rifle than a hand grenade going off?"
Dr Keith Barton

Normal tension glaucoma: Compared with high-tension glaucoma patients, Dr Nagar found a higher non-responder rate among NTG patients (25–30% versus 20–22%) as well as a lower five-year survival rate (30% versus 50%). Therefore, in patients with NTG and IOP in the low teens, Dr Nagar does not recommend SLT, unless she has significant concerns about either compliance or intolerance to PGAs or significant IOP fluctuations.

Dr Asrani had initially worked with SLT in the early 2000s on NTG patients. "Following the SLT there was no significant pressure drop in the mean IOP but there was incredible stabilization," he said. As IOP fluctuation has been shown to be a major factor in glaucoma progression,[17] dampening this activity is beneficial for the patient, even without a significant associated drop in IOP.

Dr Asrani also noted that the pressure standard deviation and range dropped much more significantly than the mean pressure.[18] "This effect endures for 18–24 months, after which SLT may be repeated if necessary," he stated. Even after up to three SLT treatments and no significant changes in the mean pressure, his NTG patients have maintained their visual fields since the initial treatment, which now represents a period of 10 years.

Pseudoexfoliation: IOP response to SLT has been found to be the same among pseudoexfoliation patients (PXF) as among POAG patients. However, in a 30-month follow-up, the failure rate was higher among PXF patients, who tended to experience a rise in IOP at approximately 15 months. As the duration of response is likely to be shorter for PXF patients than for POAG patients, the interval until retreatment is also anticipated to be shorter.

For PXF patients, the responses seen are similar to ALT in the short-term. Patients continued to have PXF, despite the drop in IOP, and material continues to build up over time.

In an effort to tailor the treatment, Dr Latina stated that he treats PXF eyes with lower energies and fewer spots (60–65 versus 100) compared with his treatment for OAG.

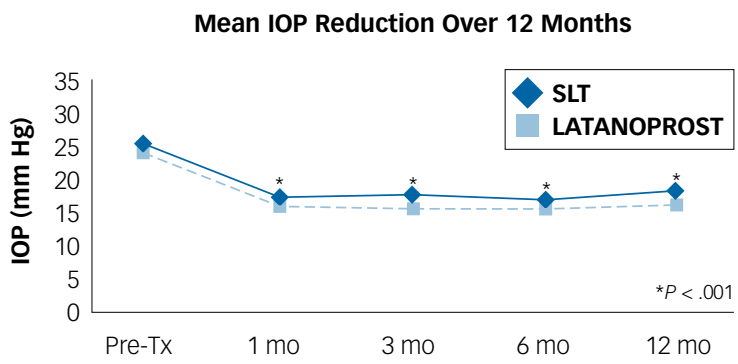
Pigmentary dispersion syndrome: SLT is extremely efficient at targeting melanin granules. According to Dr Latina, the degree of pigmentation does not affect the outcome, however, because of certain histological factors relating to pigmentary glaucoma, certain adjustments to the treatment algorithm are necessary.

"In pigmentary glaucoma there is a greater degree of melanin granules both intracellularly and extracellularly, and trabecular beams become fused, as melanin is toxic to the TM cell," Dr Latina said. "However, the laser is designed to target melanin granules, and so if there is too much energy used and/or too many spots, the TM can become overwhelmed, leading to a sustained increase in IOP, which will then require trabeculectomy."

To avoid this, he recommends using very low energies (0.4–0.5 mJ) to treat no more than 12 shots over 90°, 24 shots over 180° or 48 per 360°. Additionally, it is not necessary to observe microcavitation bubbles when treating pigmentary eyes, and the pulse energies should be adjusted such that microcavitation bubbles are not seen.

These precautions allow for pigmentary glaucoma patients to be retreated, should that become necessary. "It's better to

Figure 5: IOP control with SLT versus medication (current gold standard, latanoprost). (Adapted from I. McIlraith *et al.*, *J. Glaucoma*, 2006;**15**:124–130.)



retreat them to get your pressure lowering than to get the risk of a sustained pressure spike," asserted Dr Latina.

"However, the degree of pigmentation of the angle does not correlate with response to SLT," Dr Latina once again cautioned. "The amount of melanin present can be minimal and you can still get an absorption with the laser, which is the beauty of the laser over really any other treatment."

"But, that said, that's why we titrate in the treatment, as you can apply too much energy," supplied Dr Noecker. Dr Alvarado disagreed, claiming that taking these precautionary steps leads to under-treatment of pigmentary glaucoma. "All you need to do is stage your treatment sessions, giving the full treatment at a low energy level while simultaneously controlling the pressure," he said.

SLT in the treatment algorithm

Although the most commonly prescribed first line therapy for glaucoma is medication, it is at this stage when SLT is most effective. However, SLT is an effective second-line treatment after prior treatment with either medication or ALT, and is an effective adjunct to medical therapy.

Nevertheless, as with all therapies, the success rate of SLT tends to decrease when used later in the treatment algorithm (for instance, for advanced glaucoma patients on maximal medical therapy). This is because these patients may have an obstructed or damaged outflow system caused by prior treatment with drops, thereby limiting the effect of SLT.

The SLT advantage

Already the therapeutic benefit of SLT in comparison with other treatment options is clear. SLT also offers wider advantages for patients and physicians in terms of: compliance; cost savings; efficacy; repeatability; safety profile and reduction of side effects; suitability for use in developing nations; and simplicity of the technique.

Compliance

"One very strong argument for laser has always been in the patients who are non-compliant," Dr Barton asserted, and this statement was not greeted with any argument.

"The best assumption we have out there is that 50% of our patients are truly compliant with medical therapy," was the shocking assessment by Dr Katz, a claim that is supported by published statistics (see Figure 6).[19–21]

Previous studies have demonstrated that, of all patients prescribed drops to treat glaucoma, over 90% are non-adherent and nearly 50% are non-persistent, when 'adherence' is defined as 'the prevalence of use of the initial medication at various time points' and 'persistence' is defined as 'continuous treatment with initially prescribed medication'.[20]

There are various reasons for non-compliance (see Sidebar 1), and SLT avoids all of them. As SLT is a single intervention and does not require the patient to commit to an ongoing treatment regime (or, in many cases, ongoing financial expenditure), there is no question of compliance to be addressed.

"I now try to avoid ALT as a result of the amount of damage we see in the angle and the progressive nature of PAS formation. I think that we should no longer be using ALT,"

Dr Frank Howes

Cost savings

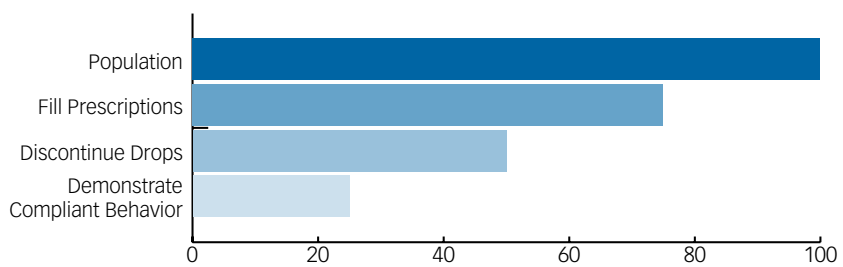
With healthcare expenditures becoming a topic of concern for governments across the world, the cost-effectiveness of laser therapy is a timely issue.

Though drug prices vary throughout Europe, laser treatment has been suggested to represent a more cost-effective first-line treatment option than medical therapy,[22,23] which may comprise up to four separate sets of PGAs, or even incisional surgery.

"Laser trabeculoplasty is not terribly costly," explained Dr Katz. "The machinery lasts for a long time and it's repeatable. So, it does seem to make sense on first pass. Careful economic modelling analysis seems to verify that."

One study concluded that the only way to reduce the cost of glaucoma treatment was to use laser therapy as a first-line option.[22] This was also supported by Augusto Azuara-Blanco's editorial in the British Journal of Ophthalmology, which

Figure 6: Patient compliance is a serious issue with 75% admitting to some form of non-compliant behaviour. (Adapted from 1. National Community Pharmasists Association Website. Take as Directed: A Prescription Not Followed. December 15, 2006, 2. B.L. Nordstrom *et al.*, *Am. J. Ophthalmol.*, 2005;**140**:598–606, 3. L. Osterberg and T. Blaschke, *N. Engl. J. Med.*, 2005;**353**(5):484–497. Review.)



Only 25% of glaucoma patients on medical therapy were both adherent and persistent with their hypotensive medications

bemoaned the lack of SLT as an initial therapy in light of the rising healthcare costs in the UK and Ireland.[24]

Dr Coleman and Dr Katz suggested that the financial benefits of SLT might extend further than the direct costs of therapy. They agreed that SLT has the potential to prevent the blindness that can result from poor adherence to medical therapies. This led them to assert that SLT can ultimately prevent some patients from entering the dependency sector, thereby creating cost savings for the wider economy.

"The best thing SLT can do for you is stop the use of the prostaglandin analogues,"
Dr Jorge Alvarado

Dr Katz went on to suggest that eliminating further medical interventions associated with side effects of medical therapy would also generate cost savings. "I think the consensus is that, when you're looking at laser trabeculoplasty as an initial therapy, it seems to be a winner on cost-effectiveness," he concluded.

Efficacy

Particularly when used as a first-line therapy, SLT offers IOP control equivalent to (or slightly greater than) latanoprost, the current 'gold-standard' therapy (see Figure 5), without the side effects or compliance concerns associated with medication.

SLT also offers equivalent short-term IOP control to other laser therapies, including ALT and MLT, but with better long-term success (see Figure 4) and without the associated insult to the TM and the long-term complications.

Repeatability

If necessary, SLT can be repeated without endangering the TM or compromising the treatment. Repeat 360° SLT may be safe and efficacious even after initial treatment has failed (Figure 7),[25] though there is evidence that the probability of success on a second SLT is equivalent to the success of the first. A waiting period of three months between SLT treatments is recommended, to ensure that the full effect of the initial treatment can be appreciated.

"When we looked at the repeatability studies that are coming out now, whether they're retrospective or not, they all seem to indicate that you can get the effect to continue for years, unlike with ALT," noted Dr Katz.

SLT can also be performed after prior ALT or treatment with PGAs. "In the original FDA clinical trials, we had a specific study group containing patients who had previously undergone ALT," said Dr Latina. "The results really did show that there was about a 65% success rate in that group, which was similar to those patients who were taking medications. So, they did as well as patients who were on prior medications."

Although it is safe and potentially effective, Dr Nagar put forward that she would not repeat an SLT if it had not been successful the first time (i.e., 360° treatment), as she believes that non-responders remain non-responders. She would also not repeat if the effect of the initial SLT had not been sustained, and a pressure drop of 20–25% had not been maintained for at least 9–12 months. However, if the effect of an initial SLT had been substantial but wears off with time, she would repeat the treatment. She enhances SLT through treating the second half of the TM after the initial 180° treatment and performs repeat SLT (i.e., retreats previously treated TM following 360° treatment).

Safety profile and side effects

Side effects associated with SLT include:

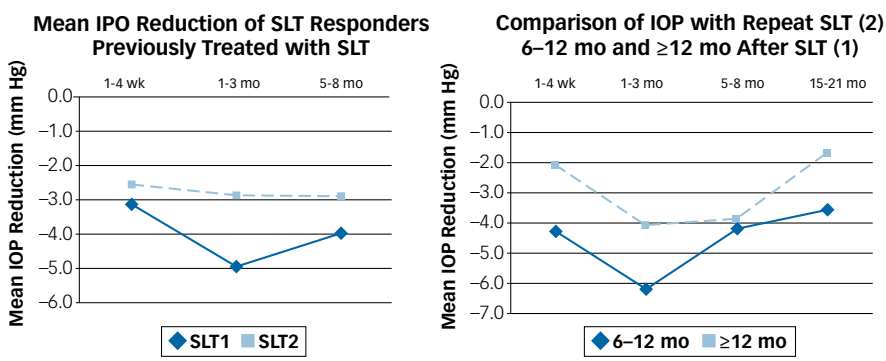
- An initial IOP spike (which can be seen one hour post-therapy and may not be statistically significant; >2 mmHg).
- Slightly blurred vision.
- Mild photophobia for 2–3 days.

SLT produces:

- Minimal pain and discomfort.
- Minimal inflammatory reaction.
- No systemic side effects.

By comparison, there are several side effects associated with medical treatments, which are highlighted in Sidebar 2.

Figure 7: SLT retreatment results. (Adapted from B.K. Hong *et al.*, *J. Glaucoma*, 2009;**18**(3):180–183.)



Lumenis Selecta Duet (YAG/SLT combination).

Dr Asrani asserted that the glaucoma patient population typically has a high incidence of ocular surface disease (OSD). This incidence increases with age and becomes increasingly severe if the patient is taking other topical medications, as the ocular surface may have become compromised. "We found that when offering SLT as primary therapy the number of complaints dropped and we could just treat the dry eye at base level rather than worsening it with drops," he added.

"We're loading these conjunctivae with more and more benzalkonium chloride, producing OSD and other problems. We're managing to control the glaucoma, but creating another problem," continued Dr Howes. "The answer to that, then, is SLT, because we're removing those things."

Suitability for use in developing nations

There are many advantages to SLT making it a preferable option to PGAs in the developing world, not least the cost-effectiveness implications, the elimination of the requirement to pay for long-term medical therapy, the durability of the equipment and the simplicity of the procedure. Additionally, patients in developing nations seem to be eminently well-suited to SLT treatment.

"We're getting extraordinary results in the short-term," claimed Dr Coleman, of her initial experiences with SLT in Africa. This is explained at least partially because many patients in developing nations will not have received any treatment for their glaucoma. Dr Coleman concurred with Dr Nagar's earlier statement about patient selection, that high IOP on presentation makes this group of patients' excellent candidates for SLT.

Dr Barton said that in his experience, even among treatment-naïve patients, it isn't possible to get pressure below 21 mmHg with SLT alone, although this was not Dr Coleman's experience. "I can think of one patient who was in last week with normal OAG, and we managed to get the pressure down from 35 to 15," she countered.

Dr Coleman also pointed out that there is often a quality control issue with medications available in developing nations, particularly in rural areas, as the drugs are frequently diluted to make them last longer or to allow them to be distributed more widely. This introduces an additional level of safety risk and inefficacy with medical treatments, which is again eliminated by using SLT.

Summarizing the situation, Dr Coleman concluded, "The need for glaucoma treatments in the developing world is huge and SLT is coming in with something to offer that no-one else is offering."

Simple technique

"SLT is a straightforward technique," according to Dr Nagar. The large beam diameter and spot size means that it is not necessary to locate a specific zone on the TM, so the learning curve of the technique is short.

Lumenis conducts various educational seminars and sponsorships for physicians to increase their familiarity with the treatment. Also, patient education is not as difficult as some might believe as there are many resources available in the forms of brochures and on-line facilities.

"I think the consensus is that, when you're looking at laser trabeculoplasty as an initial therapy, it seems to be a winner on cost-effectiveness,"

Dr L. Jay Katz

The equipment itself is also easy to use. The portable, durable unit can be transported in a briefcase-sized container, making it particularly suitable for use in developing nations, where it is more likely to be employed as part of a travelling clinic.

Achieving optimal outcomes with SLT

The panel reached a general consensus about the benefits and patient selection criteria for SLT; nevertheless, each of the experts implemented the technique in their own way, and had tweaked the procedure to suit their patients' needs.

For example, according to Dr Alvarado, medical interventions and laser therapies share a common final pathway concerning the junction disassembly. "There is only a certain amount of barrier disassembly that can be induced," he said. "PGAs can only reach the same maximum level of barrier disassembly as SLT (approximately 35%) if the full spectrum is used, which cannot be done as a result of side-effects." Therefore, Dr Alvarado offers his patients PGAs initially, to test for likely SLT response. Also, if a patient did not respond to PGAs, Dr Alvarado stated he would not proceed to SLT.

Dr Asrani commented that he offers SLT as first-line therapy to treatment-naïve patients, but once they have agreed he places them onto a prostaglandin sample immediately. "The reason I do this is to predict the response rate of SLT and also to give the patient the opportunity to choose the medical therapy," he stated.

However, among Dr Nagar's patients those who received SLT as a replacement therapy (because of compliance or tolerance issues with medication) had a much better response (at 18 months) than patients who were uncontrolled on medical treatment. Thereafter, she began washing off

the medication (following EGS guidelines)[26] to achieve higher baseline pressures and then, using SLT as an adjunctive treatment, had noted much higher rates of success. In Dr Nagar's experience, adding SLT to PGA treatment produced an excellent response when baseline pressure was high.

> **"The need for glaucoma treatments in the developing world is huge and SLT is coming in with something to offer that no-one else is offering,"**
> Dr Kate Coleman

The optimal clinical outcomes are achieved when following the more aggressive treatment protocol of 360° (100 pulses) versus 180° (50 pulses). (For the recommended treatment protocol, see Sidebar 3.) However, Dr Nagar treated a few of her patients with 50 shots over 360° either because of the presence of PAS or due to narrow angles and was amazed at the excellent response. Dr Nagar is now conducting a study of 50 shots versus 100 shots to determine whether success is dependent on the number of shots or the area treated.

Pre- and postoperative recommendations

Both pre- and post-therapy, medication recommendations depend on physician preference, but the following are suggested as a guideline:

Pre-therapy medications:

- Topical anaesthesia (e.g., proxymetacaine hydrochloride).
- Prophylactic application of alpha agonist or equivalent agent to avoid postoperative pressure spike — recommended (particularly with heavily pigmented angles/TM and/or when performing 360°).

Certain physicians advocate a washout period of any prostaglandin topical medication of 6–8 weeks prior to the SLT procedure, due to the hypothesized competing mechanism of action.

Post-therapy medications may be unnecessary and should be judged on specific patient comfort and need, but the following recommendations may be useful:

- One drop of NSAID immediately after surgery to avoid inflammation; 1–2 drops up to 2–3 days postoperatively if needed.
- Do not use a steroid (recommended), as it will potentially interfere with the SLT mechanism of action.

The panel universally rejected steroid use post-therapy, agreeing that non-steroidal options worked just as well.

Patients should be followed up one hour after therapy, to examine for IOP spikes; two weeks after therapy, to monitor IOP reduction; and, one month after therapy to check for target IOP reduction. It may take up to three months post-therapy for individual target IOP reductions to be reached, and other interventions during this time period are not recommended.

Sidebar 3: SLT treatment protocol

Laser settings:

- Duration: 3 nanoseconds (preset)
- Spot Size: 400 microns (preset). As the spot size is so large, some 'overspill' (for instance, above Schwalbe's line) is to be expected and is not a source of concern
- Energy range: 0.3–2.0 mJ
- Aim to cover AC angle (not on iris)
- Plan to treat 360° (100 applications total or 25/quadrant)

Contact placement:

- No magnification
  - ◊ Latina SLT Gonio lens
  - ◊ Goldmann 3 mirror
  - ◊ Ritch (small × mirror)
- Please use contact lenses with zero magnification factors, as changes in magnification will alter beam diameter and laser energy, thereby resulting in over-treatment or under-treatment.

Therapy degrees:

- 360° provides best results for primary therapy
- 180° can be effective for primary therapy

Optimal clinical outcomes are achieved when following the more aggressive treatment protocol of 360° (100 pulses) versus 180° (50 pulses). If treating only 180°, it is recommended to treat the inferior or the nasal half of the TM, due to variations in pigmentation levels.

Therapy energy level:

- Starting at 0.8 mJ and leading up to higher energy, as needed, until clinical endpoint (cavitation bubbles) is identified.
- Titrate energy per angle pigmentation level. Consider the following energy levels as starting point and titrate accordingly:
  - ◊ Highly pigmented angles: 0.6–0.8 mJ
  - ◊ Lightly pigmented angles: 1.0 - 1.2 mJ

Pigmentary glaucoma cases need to be treated conservatively:

- Degrees: 90°
- Energy: 0.4 mJ

Therapy endpoint:

Cavitation bubbles ("Champagne bubbles"). When reaching the treatment endpoint, scale down the energy level by 0.1 mJ. Once you lower energy, cavitation bubbles will no longer be visible (i.e. treatment is now considered sub-threshold). As pigmentation varies along the TM (especially inferior and superior areas of the TM), power settings need to be reassessed at least every quadrant to avoid under-treatment.

Patient follow-up

- As required
- Minimum: 1-hour, 2-weeks, 6-weeks, 3-months post-treatment

SLT: The future of glaucoma treatment?

Medication compromises the ocular surface and is characterized by very low patient compliance; and higher-energy laser treatments compromise the TM. Conversely, SLT is a far less traumatic option for the eye, and has equivalent efficacy to other treatment options, with reduced concerns surrounding cost-effectiveness, compliance and repeatability.

In spite of all the evidence for SLT, and the fact that its risk–benefit profile is unparalleled among currently available treatment options, medication still has the upper hand as a first-line treatment.

Dr Barton puts this 'disconnect' down to convenience on the part of the ophthalmologists. "It's easier to give the patient drops than to talk them into something that sounds like an invasive procedure, even though it really isn't," he argues.

"Also, we have a hundred plus years of a track record of using medical therapy as our first line therapy. It's hard to get people to disengage from that, both on the part of the physician and the patient," agreed Dr Katz. "But if it were a drug, we wouldn't even be having this conversation because it would be a slam dunk."

Dr Barton continued, "You've got to change your clinic structure if you want to have somebody to talk to a patient about laser trabeculoplasty, whereas it's easier with drops. They just read the information sheet."

"I think that's part of it," Dr Katz responded. "If you're in a busy practice, it's a lot easier going with the grain. In fact, I don't think a lot of physicians really even bring up laser trabeculoplasty as a first line option. If they did, I think a lot of the patients would opt for it. The role of the physician should be to provide the patient with the benefits and drawbacks of the reasonable choices available and let the patients make the informed decision regarding their care."

Dr Asrani disagreed, "The theoretical barrier, at least in the US, is the perception of the patient. On their first visit being offered a procedure rather than being treated with eye drops is like they're being sold a procedure. Also, it may sound more aggressive than medication."

Dr Nagar, however, agreed with Dr Katz that the burden of sub-optimal uptake seemed to lie more on the shoulders of the physicians than the patients, who, in her experience, were willing to adopt SLT.

Thanks to an excellent safety and efficacy profile, coupled with building economic pressure to decrease healthcare expenditure, it appears that SLT is finally becoming not just a viable but an increasingly attractive and sensible option for first-line glaucoma therapy, regardless of disease subtype and regardless of market.

"In normal tension glaucoma following the SLT there was no significant pressure drop in the mean IOP but there was incredible stabilization,"

Dr Sanjay Asrani

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