Selective Laser Trabeculoplasty


SLT for Compliance

SLT’s Role in the Armamentarium

Preserving the Trabecular Meshwork

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BY ROBERT J. NOECKER, MD, MBA

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Patients’ compliance with prescribed medical therapy is a thorny issue with any chronic disease. Studies of individuals who require long-term drug treatment (eg, for glaucoma, arthritis, or systemic hypertension) reveal that their adherence to prescribed therapy is not nearly as strict as physicians imagine.1-3 Because glaucoma is initially asymptomatic, it can be particularly difficult for ophthalmologists to impress upon patients their need for treatment.

The obstacles to compliance are many. Tsai et al4 attempted to create a systematic classification of barriers to compliance in glaucoma. They found that social and environmental factors such as a change in daily routine or travel negatively affected nearly half of the study subjects’ adherence to prescribed therapy. Approximately one-third of patients cited factors related to the regimen, including the cost and side effects of the drugs and the complexity of the dosing regimen, as the reason they did not regularly take their medications. For an additional 19% of subjects, the issues were related to themselves (eg, problems with memory or difficulty instilling the drops) or to their physicians (eg, inadequate education about the disease or patients’ dissatisfaction with their doctor). Another issue in the study, of course, was that many patients perceive no short-term gain from taking glaucoma medications; they neither see nor feel better, but their medications may be costly and can produce undesirable side effects.

Some newer agents have superior efficacy at lowering IOP than drugs of the past when taken once daily. The former have undoubtedly improved patients’ compliance by simplifying their dosing schedules (Figure 1). Tsai et al,4 however, asked subjects if only needing to administer an eye drop once daily would improve their compliance with prescribed therapy. Half said no. Related research5 demonstrated just a 70% persistence rate among patients taking prostaglandin analogues, drugs typically instilled once a day. Selective laser trabeculoplasty (SLT) is a means of guaranteeing patients’ compliance with glaucoma therapy.

EFFICACY
Prospective studies have shown that SLT as primary therapy can decrease IOP by 30% to 35%,6,7 similar to the reduction in pressure achieved with the most effective, current topical medications. After SLT, however, no compliance on the part of the patient is required to continue the treatment’s efficacy or prevent complications. At the 7-year follow-up in the Glaucoma Laser Trial,8 subjects who first underwent treatment with an argon laser versus medication had a slightly lower IOP, and the status of their visual fields and optic nerve was somewhat better. Although a number of the laser-first patients eventually required medication to maintain control of their IOP, by the end of follow-up, these individuals achieved a 38% reduction in the total number of days requiring medication compared with subjects first treated with medical therapy. In all, undergoing initial treatment with a laser versus medication reduced subjects’ dependence on drug therapy. In light of the issues with compliance outlined earlier, these results favor the use of laser therapy earlier in the course of glaucoma treatment.

PERSONAL EXPERIENCE
Despite the results of the Glaucoma Laser Trial, the use of laser therapy as a first-line treatment for glaucoma has not gained widespread acceptance for various reasons, including ophthalmologists’ concerns about the modali-

Figure 1. This graph depicts patients’ rate of compliance with common dosing schedules. (Data adapted from Cramer JA. Overview of methods to measure and enhance patient compliance. In: Cramer JA, Spilker B, eds. Patient Compliance in Medical Practice and Clinical Trials. New York, NY: Raven Press; 1991: 3-10.)

SLT for Compliance
This modality is the only means by which to guarantee patients’ adherence to glaucoma treatment.

BY MICHAEL C. STILES, MD
Selective Laser Trabeculoplasty

Figure 2. Scanning electron micrographs were taken of the trabecular meshwork after ALT (A) and after SLT (B).

SLT has allowed me to avoid medications in some patients whose medical history suggests that they will not comply with prescribed treatment. The procedure has also enabled me to reduce the number of medications for individuals who have trouble with their current drug regimen, even if it is controlling their IOP. Such patients are happy after SLT, because they require fewer medications and experience fewer side effects.

CONCLUSION
It is difficult to determine whether patients are complying with prescribed medical therapy. Many overstate how regularly they administer their eye drops. Primary SLT can eliminate this problem when it achieves the target IOP. Alternatively, the procedure can help patients follow their drug regimen by reducing the number of medications they require.

Ophthalmologists’ initial approach to managing glaucoma has evolved, especially with respect to laser trabeculoplasty. Ten years ago, a newly diagnosed glaucoma patient likely would have received a prescription for a topical beta-blocker (assuming no contraindications). If this therapeutic agent proved insufficient, many ophthalmologists would have added pilocarpine to the patient’s drug regimen.

Using multiple antiglaucoma medications prior to considering laser therapy was standard in many practices a decade ago, despite the publication in 1990 of the Glaucoma Laser Trial’s results. This landmark study compared argon laser trabeculoplasty (ALT) to topical medicine for controlling IOP in patients with newly diagnosed primary open-angle glaucoma. The investigators looked at 271 patients over a 2-year follow-up period and found that the eyes treated with a laser first consistently had lower mean IOPs than those initially treated with medication. Certainly, as a result of this study, some eye doctors initiated glaucoma treatment with ALT in appropriate candidates. The 1995 Glaucoma Laser Trial follow-up study confirmed this course of action. Investigators reported that initial treatment with ALT was at least as efficacious as initial treatment with topical medication, even at 7 years mean follow-up. Despite these reports, however, by the mid- to late 1990s, many ophthalmologists performed ALT only after first prescribing multiple topical medications.

Why did ALT fail to gain widespread use as an initial therapy for glaucoma? On the one hand, the procedure is associated with initial success rates of up to 85%. After 5 years, however, success rates drop to between 19% and 31%. Of greater concern is that repeat ALT is successful in only 33% of eyes in which primary ALT is successful. Furthermore, repeat ALT poses a significant risk (12%) of major IOP elevation. The tendency of ALT to be a “one-shot deal” led many ophthalmologists to save the procedure until later in the course of glaucoma treatment, perhaps only as an attempt to avoid the OR.

MEDICAL TREATMENT REGIMENS TODAY

Today, the medical options for treating glaucoma differ vastly from 10 years ago. Topical carbonic anhydrase inhibitors were introduced in late 1995. The first prostaglandin analogue, latanoprost, and the alpha-2 agonist, brimonidine, were available in the US by 1996. Ophthalmologists prescribe parasympathomimetics to increasingly fewer patients, and practitioners have become more cautious about topical beta-blockers, because other topical medications with fewer potential systemic side effects are available. For most physicians, a once-a-day hypotensive lipid is their first choice when beginning glaucoma treatment. Many then choose alpha agonists or topical carbonic anhydrase inhibitors as second-line glaucoma therapy.

SELECTIVE LASER TRABECULOPLASTY

Background

LaTina et al first described selective laser trabecuoplasty (SLT) more than 5 years ago. They analyzed the safety and efficacy of using a Q-switched, 532-nm Nd:YAG laser to treat glaucoma in a multicenter study. The investigators noted a significant decrease in IOP in patients responding to SLT. Of interest, this pressure reduction occurred in eyes that had previously undergone ALT as well as in those with a history of only medical treatment.
Selective Laser Trabeculoplasty

**Mechanism of Action**

ALT causes thermal coagulative damage to the trabecular meshwork. Electron microscopy shows the procedure disrupts the trabecular beams and significantly harms adjacent tissue. SLT’s effect on the trabecular meshwork appears to be different. Its selective photothermolysis uses an ultra-short laser pulse to generate and confine heat at explicit pigmented targets—the melanin contained in the trabecular meshwork’s cells. The laser pulse’s short duration (3 nanoseconds) minimizes the associated heat of the laser shot and thus prevents collateral damage, because the pulse time is shorter than the thermal relaxation time of melanin (1 microsecond). Electron microscopy of trabecular meshwork treated by SLT shows none of the disruption seen with ALT.

Some researchers have hypothesized that ALT works in part by mechanically changing the meshwork (ie, laser-induced microscars reverse the pathologic laxity and collapse of trabecular tissues). Both ALT and SLT are hypothesized to increase drainage through the trabecular meshwork by releasing chemotactic factors such as interleukin-1a, interleukin-1b, and tumor necrosis factor-alpha. The resultant recruitment of macrophages affects aqueous outflow facility and thus lowers the IOP.

The key difference between the procedures is the apparent absence of significant coagulative damage to the meshwork in SLT-treated eyes. Also, SLT can have a crossover effect, in which the IOP of the untreated eye decreases after its fellow undergoes the procedure. This observation argues for a totally biological rather than mechanical mechanism of action in SLT. One might hypothesize that activated macrophages collect in the spleen and are then released into the blood stream, where some act upon the contralateral trabecular meshwork. SLT’s ostensible stimulation of this system without the destructive collateral thermal damage seen in ALT is probably the basis for the procedure’s potential repeatability.

**Our Experience**

Since the initial report by Latina et al, other investigators have demonstrated that SLT is as effective as ALT over a 5-year period in patients receiving maximum medical therapy. Melamed et al showed that SLT as the primary treatment for open-angle glaucoma was safe and effective in eyes not previously treated with glaucoma medicines. IOP dropped an average of 7.7 ± 3.5 mm Hg after SLT.

In our hands, SLT and ALT lower IOP similarly as well. Additionally, we found that SLT decreases IOP equally in pseudophakic and phakic eyes, an interesting result considering that ALT is less effective in pseudophakic versus phakic patients (Figure 1). For us, SLT has also been successful in 66% to 75% of eyes with a prior history of both successful and unsuccessful ALT (Figure 2). Of importance, none of these patients experienced serious complications.

**CONCLUSION**

We routinely offer SLT rather than a second medicine as a second-line treatment option for most of our glaucoma patients with open angles. We also offer the procedure as first-line treatment in patients who have budgetary concerns or who are not good candidates for medicine (ie, due to severe arthritis, early dementia, a history of significant forgetfulness with other prescribed medicines). We have repeated SLT up to two times with no complications and achieved a drop in IOP similar to that with the original treatment. As our experience grows, we can envision performing SLT even earlier in the stepped treatment of glaucoma.

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13. Werner MA, Smith MF, Doyle JW. Effectiveness of selective laser trabeculoplasty in eyes that have had previously successful vs. unsuccessful argon laser trabeculoplasty. Poster presented at: The AAO Annual Meeting; October 25-26, 2004; New Orleans, LA.
The development of selective laser trabeculoplasty (SLT) has prompted many ophthalmologists to re-evaluate the role of laser treatment to the angle. After the demonstration of SLT’s equivalent efficacy to argon laser trabeculoplasty (ALT),\(^1\)\(^3\) discussion has focused on the procedures’ safety, repeatability, and long-term implications. These issues can be reduced to a single consideration: the structural alteration of the architecture of the normal trabecular meshwork and Schlemm’s canal.

**THE MECHANISM OF ACTION**

When the IOP is elevated in open-angle glaucoma, the pathologically increased resistance to aqueous outflow is at the level of the juxtacanalicular trabecular meshwork.\(^4\) Most current glaucoma therapies rely on mechanisms independent of this primary disease process. Common topical medications either suppress aqueous outflow or enhance uveoscleral outflow. Pilocarpine, although now rarely used, is an exception.

Laser trabeculoplasty treats the site of the pathology by reducing the resistance to outflow in the trabecular meshwork and Schlemm’s canal. Early experience with ALT led Van Buskirk et al\(^5\) in 1984 to suggest three potential mechanisms for lowering IOP. First, they posited a mechanical effect in which focal shrinkage of the anterior meshwork puts the posterior filtering meshwork on stretch between the laser scar and the scleral spur, thereby widening the meshwork’s outflow channels. A second option was a cellular effect, a diffuse loss of meshwork cells (even in untreated areas between burns) as noted after laser treatment. Third, they proposed a biochemical effect by which an alteration in both the rate and composition of the trabecular meshwork’s extracellular matrix might favor the clearance of outflow-obstructing material.

**EFFECTS ON THE MESHWORK’S TISSUE**

**Laser Energy**

The Q-switched, 3-nanosecond, frequency-doubled Nd:YAG SLT laser delivers a fraction of the laser energy (< 1%) to tissue that ALT does. That the SLT pulse is shorter than the thermal relaxation time of tissue minimizes destruction of the ocular tissue. Moreover, SLT’s targeting of the trabecular meshwork’s pigmented cells helps minimize collateral damage to angle structures.

![Figure 1](https://example.com/figure1.jpg)

Figure 1. Peeling the inner wall of Schlemm’s canal shows greater fibrosis in an eye previously treated with ALT (A) versus SLT (B).
Selective Laser Trabeculoplasty

This photothermolysis of melanin-laden cells results in a release of cytokines and the recruitment of macrophages, which in turn enable the clearance of the trabecular meshwork.

Laboratory Findings

Based on SLT’s selective nature and its use of less laser energy than ALT, one would expect the former procedure to cause less structural damage to the trabecular meshwork and Schlemm’s canal. Evidence from in vitro cell cultures as well as ultrastructural, histological, and in vivo clinical results prove that SLT is indeed less harmful. Using culture models of trabecular-meshwork cells irradiated with laser energy, Latina and Park showed much more generalized and higher thermal transfer with ALT than SLT, which caused a localized thermal uptake only in cells containing melanin.

Using scanning electron microscopy of human cadaveric eyes, Kramer and Noecker compared the effects of ALT and SLT on the trabecular meshwork’s structure and found distinct differences. ALT burns coagulated tissue and caused the formation of craters, whereas SLT did not significantly physically alter the meshwork. Another histopathologic comparison of low-energy ALT versus SLT on the human trabecular meshwork and Schlemm’s canal used light and transmission electron microscopy. The study found less fragmentation of the trabecular beams and better preservation of the inner wall of Schlemm’s canal with SLT. Similarly, Douglas Johnson, MD, noted that he had found herniation of the juxtacanalicular trabecular meshwork into Schlemm’s canal. He also discerned lost integrity of Schlemm’s canal’s inner wall, with ALT burns visible on histological sectioning.

Clinical Evidence

Preliminary in vivo work conducted by Dr. Ahmed and his colleagues compared anatomical differences in Schlemm’s canal and the external trabeculum in eyes undergoing nonpenetrating surgery that had previously been treated with either SLT or ALT. This ongoing, controlled, prospective study has revealed important qualitative differences upon examination and peeling of the inner wall of Schlemm’s canal (Figure 1). A greater number of the ALT-treated eyes exhibited visible fibrosis at the inner wall, and peeling was more difficult due to the presence of adhesions between the trabecular meshwork and Schlemm’s canal. The investigators found no difference between SLT-treated eyes and controls upon unroofing Schlemm’s canal or peeling the inner wall. Dissecting the juxtacanalicular trabecular meshwork as well as the inner and outer walls of Schlemm’s canal easily achieved desirable flow in these eyes as opposed to ALT-treated eyes due to the latter’s fibrotic trabecular meshwork.

One could argue that the laser’s mechanical effects are less important than its cellular and/or biochemical/immunological impact in terms of the mechanism of action of lowering IOP.

Clinical Relevance

From a practical standpoint, the differences between ALT and SLT described herein relate mainly to retreatments and patients’ safety. The repeatability of ALT has been limited by the cumulative destruction and fibrosis of the trabecular meshwork and Schlemm’s canal with successive retreatments, which eventually raised IOP. ALT and SLT generate similar primary IOP reductions, but the latter does not structurally alter the trabecular meshwork and Schlemm’s canal. SLT, then, has the theoretical advantage and may be a more repeatable procedure that poses less risk of IOP spikes. Although preliminary data appear promising, the results of properly controlled studies on these topics are pending.

It is also relevant to consider the phrase “do no harm” from the Hippocratic oath. When selecting a glaucoma therapy, ophthalmologists must always consider its effect on future intervention. ALT’s destruction and alteration of the trabecular meshwork and Schlemm’s canal will likely compromise the success of most if not all treatment modalities currently in development. One should therefore consider SLT for the sake of preserving this ocular tissue, not only for the present but also for the near future.

My experience with selective laser trabeculoplasty (SLT) began with laboratory research on how lasers affect ocular tissue, prior to the FDA’s clearance of the Selecta Duet laser (Lumenis Inc., Santa Clara, CA) in 2001. Since that time, I have been serving as the principal investigator in the SLT/Med study, which is ongoing. This prospective, multicenter, randomized, controlled clinical trial is designed to compare SLT with stepped medications as the initial monotherapy for open-angle glaucoma.

In my daily practice, I rely on SLT for patients who fail or do not comply with medical therapy and for those who prefer laser treatment to medications. Although I predominantly perform 360º SLT treatments, I would suggest that physicians consider 180º treatments for certain patients.

WHY 180º?

The main reason to perform 180º SLT treatment is to limit the potential risk of large, sustained IOP spikes, the greatest concern with any form of laser trabeculoplasty. The risk of sudden transient or ongoing rises in pressure is simply less with a 180º versus 360º treatment area.

Certain patients are at greater risk for an IOP spike after (Continued on page 11)

Point/Counterpoint:
180º Versus 360º Treatment

In many patients, 180º is more appropriate.

BY L. JAY KATZ, MD

Why I prefer 360º for selective laser trabeculoplasty.

BY ROBERT J. NOECKER, MD, MBA

For selective laser trabeculoplasty (SLT), I prefer to perform a 360º treatment of the trabecular meshwork in one session. When managing glaucoma, it is most efficient to select the therapy that has the highest chance of success in order to minimize subsequent changes in treatment and the number of follow-up visits.

EFFICACY

There are no prospective, published, head-to-head studies demonstrating that 360º SLT lowers IOP to a greater degree or for a longer duration than treatment protocols. Nonetheless, the consensus among experts participating in the SLT/Med study is that SLT may represent the most efficacious way to treat open-angle glaucoma, and the study employs 360º versus 180º treatments.

“Because SLT does not produce the severe, long-term complications of ALT, it makes sense for ophthalmologists to maximize the procedure’s efficacy, and 360º treatment seems to be more effective than 180º.”

In this prospective, randomized, controlled clinical trial, investigators such as myself are comparing SLT with medication as initial monotherapy for open-angle glaucoma. The study involves 16 sites in the US and Canada and 340 patients (680 eyes). Subjects are enrolled for 18 months: 6 months for recruitment and 12 months for follow-up. Within 2 weeks of enrollment, SLT subjects (Continued on page 10)
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(Continued from page 9)

receive treatment at parameters of a mean 100 pulses for 360° degrees. If an eye’s pigmentation grade is 1 or 2, the starting point of laser energy is 0.8 mJ, a level titrated according to the targeted response (when the energy level is high enough, “champagne bubbles” are seen wafting into the anterior chamber in front of the site of laser application). The investigators adjust the power by 0.1-mJ steps until the treatment achieves the visible response (whereupon titration is not then decreased). This treatment method is the protocol that I have adopted into my clinical practice.

TRADITION

The reason that ophthalmologists consider performing 180° SLT is based on history. The standard treatment for argon laser trabeculoplasty (ALT) evolved to be 180° in one setting, because patients were at increased risk of dangerous IOP elevations after the treatment, especially before alpha agonists were widely available.1,2 Due to the obvious similarities between the procedures, the initial treatment parameters for early clinical trials of the current SLT device (Selecta 7000 Glaucoma Laser System; Lumenis Inc., Santa Clara, CA) more or less mimicked those used for ALT.3 Nevertheless, it is important to point out that, despite similarities in the mechanism of action for ALT and SLT, there are distinct differences in the collateral damage and side effects of the two procedures.

Both ALT and SLT cause damage to the trabecular meshwork that leads to a stress response in which cytokines are released and macrophages are activated and recruited. The resultant increase in outflow reduces IOP. The minimal damage that SLT causes is limited to trabecular cells containing pigment, but it is sufficient to activate the biologic responses that increase outflow. By contrast, ALT delivers a greater amount of laser energy for a longer duration. This procedure heats the pigmented tissue that absorbs the laser energy. As the energy level is high enough, “champagne bubbles” are seen wafting into the anterior chamber in front of the site of laser application. The investigators adjust the power by 0.1-mJ steps until the treatment achieves the visible response (whereupon titration is not then decreased). This treatment method is the protocol that I have adopted into my clinical practice.

CAVEATS

Despite the argument for maximal treatment, SLT should be performed with caution in certain patients. Because individuals with pigmentary glaucoma are at risk for IOP spikes, their initial treatment with SLT should be limited to 180° or less. The pigment in these eyes is mostly extraculляр, so a tremendous amount of it may be disturbed without the laser energy reaching the target tissue, the pigmented trabecular endothelial cells. For this reason, in the SLT/Med study, the starting point may be as low as 0.4 mJ in patients with a pigment grade of 3 or 4. Depending on the tissue’s response and the amount of pigment present in the angle, investigators will raise or lower the laser application by 0.1-mJ increments to a maximum of 1.2 mJ or a minimum of 0.3 mJ.

CONCLUSION

SLT marks an advance in the treatment of glaucoma. The procedure is extremely safe and, unlike ALT, is not limited by collateral damage to the eye’s outflow structure. For the greatest reduction in IOP, ophthalmologists should treat the greatest amount of the trabecular meshwork, except when contraindicated (eg, cases of pigmentary glaucoma). Maximizing efficacy minimizes the frequency of retreatment and follow-up as well as the amount of additional therapy required to control IOP.

laser trabeculoplasty. Among them are individuals who have heavily pigmented angles, pigmentary glaucoma, or pseudoexfoliation glaucoma, because the melanin in their eyes easily absorbs laser energy. This absorption of energy may lead to trabeculitis and a reduction in aqueous outflow. Also at elevated risk of sustained rises in IOP are patients on maximal medical therapy (eg, multiple glaucoma drugs) whose pressure remains inadequately controlled. Finally, it is questionable whether to risk even a short-term IOP spike in patients with advanced disease, a small central island of vision, and a seriously damaged optic nerve.

For many individuals, 180º of SLT will be sufficient to achieve their target IOP or reduce their dependence on medication. Theoretically, some ophthalmologists may prefer a 180º treatment area, because it will leave an additional 180º for future SLT. This practice is common with argon laser trabeculoplasty, but the proper course is less clear with SLT, because one could potentially repeat SLT after 360º treatment.

The only drawback to limiting SLT to 180º is logistical. There may be a dose-response curve with 360º treatment, which is generally more effective at lowering IOP than 180º treatment. Therefore, if 180º SLT does not achieve the desired results, the patient will have to return to the clinic for additional therapy. For some individuals, multiple trips may pose a hardship.

**CONCLUSION**

SLT is a relatively safe procedure for treating open-angle glaucoma. The most common concern with this form of therapy is the potential for an IOP spike after laser therapy. The risk of this complication is less with 180º than 360º of trabeculoplasty. For that reason, limited 180º SLT seems a more sensible approach in eyes that have heavy pigmentation of the angle, compromised eyes with poor IOP control despite treatment with multiple glaucoma medications, and eyes that have tenuous central visual acuity due to significant glaucomatous damage.
