What’s new in laser treatment for glaucoma?

Jay J. Meyer and Scott D. Lawrence

Purpose of review
This review highlights recently published studies on prevailing and newer laser therapies in glaucoma and critically evaluates their roles in the treatment algorithm.

Recent findings
Recently published studies suggest a role for selective laser trabeculoplasty (SLT) as initial therapy for open-angle glaucoma and ocular hypertension and have demonstrated efficacy in other glaucoma subtypes. Novel laser applications (micropulse diode laser trabeculoplasty, titanium sapphire laser trabeculoplasty and excimer laser trabeculotomy) have shown favorable early results. Endoscopic and transscleral cyclophotocoagulation (ECP, TCP) are generally reserved for refractory glaucomas, although some recent studies report its use in patients with good visual acuity. The effectiveness of laser iridotomy with or without iridoplasty for long-term prevention of primary angle closure glaucoma is undetermined. Laser goniopuncture is an important adjunct to nonpenetrating surgery, but wide adoption of the procedure is lacking.

Summary
The use of lasers in glaucoma continues to evolve, with a trend towards primary and earlier intervention. SLT is assuming an expanded role in the treatment of additional subtypes of glaucoma, whereas ECP and TCP are generally reserved for refractory glaucomas. Newer laser modalities show promise as alternatives and adjuncts to topical medications and nonpenetrating surgery. Additional research is needed to better define their safety and efficacy.

Keywords
cyclophotocoagulation, glaucoma, goniopuncture, laser, trabeculoplasty

INTRODUCTION
Initial demonstration by Wise and Witter [1,2] that argon laser trabeculoplasty (ALT) could effectively lower intraocular pressure (IOP) led to the development of new laser techniques and applications for the treatment of glaucoma. Refinements in technology as well as studies demonstrating strong safety profiles and efficacies of newer laser modalities have led to an expanding role for lasers in the treatment of glaucoma. Trabeculectomy with mitomycin-C (MMC) remains the gold standard for advanced cases of open-angle glaucoma. However, there is a trend towards using lasers earlier in the course of treatment of open-angle glaucoma. Recent developments and insights into their use in glaucoma are reviewed.

SELECTIVE LASER TRABECULOPLASTY
Initially described by Latina and Park [3], selective laser trabeculoplasty (SLT) is a Q-switched 532-nm, frequency-doubled neodymium:yttrium-aluminium-garnet (Nd:YAG) laser applied to the trabecular meshwork. Early prospective studies demonstrated the safety and efficacy of SLT to reduce IOP [4–9]. The laser’s parameters (400-μm spot, 0.4–1.2 mJ bursts, 3-ns duration) facilitate selective treatment of the pigmented trabecular meshwork cells, a process commonly referred to as selective photothermolysis [10]. As a result, the fluence levels delivered to the trabecular meshwork are thousands of times lower than that achieved by ALT, resulting in decreased thermal damage to the trabecular meshwork [11].
SELECTIVE LASER TRABECULOPLASTY VS. MEDICATIONS AS INITIAL TREATMENT FOR GLAUCOMA

The Glaucoma Laser Trial [12] provided some support for the concept of laser trabeculoplasty as an initial treatment for open-angle glaucoma. When applied to previously untreated eyes, SLT typically achieves an IOP reduction of approximately 30%, comparable with the IOP-lowering effect of prostaglandin analogues [13–15]. Successful reduction of IOP in the first eye is highly predictive of success in the fellow eye [16].

Katz et al. [17**] recently conducted a multicenter, prospective, randomized trial comparing SLT with medical therapy as initial treatment for open-angle glaucoma and ocular hypertension (OHT). IOP reduction from baseline was 26.4% for the SLT group and 27.8% for the medical group at 9–12 months follow-up. Additional treatment requirements due to failure of IOP control were greater in the medical arm of the study (24 vs. 11%). Table 1 [13–15,17**] provides a summary of studies of SLT as initial therapy.

SLT has an enhanced safety profile compared with ALT and is an attractive alternative to topical glaucoma medications as a first-line treatment for open-angle glaucoma. This situation is in part due to the potential side-effects, long-term cost of treatment and compliance issues inherent with medical treatment. Numerous studies have confirmed that a significant number of patients do not take their glaucoma medications as scheduled and that patients’ perceptions and behavior often do not correlate [18–20]. SLT can be used to reduce or eliminate the need for medications in some patients with open-angle glaucoma [21]. However, a decrement in IOP reduction over time is also well documented [22].

SELECTIVE LASER TRABECULOPLASTY IN DIFFERENT SUBTYPES OF GLAUCOMA

SLT is commonly used to treat patients with open-angle glaucoma [i.e. primary open-angle glaucoma (POAG), pigmentary glaucoma, exfoliative glaucoma]. However, recent studies have examined the efficacy and safety of SLT to lower IOP in other glaucoma subtypes as well. Although limited by

Table 1. Summary of studies of selective laser trabeculoplasty as initial therapy

<table>
<thead>
<tr>
<th>Authors</th>
<th>Comparison</th>
<th>Number of eyes</th>
<th>Glaucoma subtype</th>
<th>Degrees of treatment</th>
<th>% IOP reduction</th>
<th>% Eyes with IOP reduction &gt;20%</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melamed et al. **</td>
<td>None</td>
<td>45</td>
<td>OAG, OHT</td>
<td>180</td>
<td>30%</td>
<td>Not reported</td>
<td>18</td>
</tr>
<tr>
<td>McIlraith et al.</td>
<td>Latanoprost</td>
<td>100 (26 latanoprost)</td>
<td>OAG, OHT</td>
<td>180</td>
<td>SLT: 31% Latanoprost 30.6%</td>
<td>SLT: 83% Latanoprost: 84%</td>
<td>12</td>
</tr>
<tr>
<td>Nagar et al. [13]**</td>
<td>Latanoprost</td>
<td>167 (39 latanoprost)</td>
<td>OAG, OHT</td>
<td>90 (n = 35)</td>
<td>180 (n = 49)</td>
<td>360 (n = 44)</td>
<td>9–12</td>
</tr>
<tr>
<td>Katz et al. [17**]</td>
<td>Medication</td>
<td>127 (60 medication)</td>
<td>OAG, OHT, mixed mechanism</td>
<td>360</td>
<td>SLT: 26.4% Medication: 27.8%</td>
<td>Not reported</td>
<td>9–12</td>
</tr>
</tbody>
</table>

IOP, intraocular pressure; OAG, open-angle glaucoma; OHT, ocular hypertension; SLT, selective laser trabeculoplasty.

**Prospective, randomized, controlled trial.
small sample sizes and lack of control groups, these studies suggest an expanding clinical role for laser trabeculoplasty.

El Mallah et al. [23] performed a retrospective study of SLT in 31 eyes of 18 patient diagnosed with normal tension glaucoma. The mean postoperative IOP was 12.2 ± 1.7 mmHg from a baseline of 14.3 ± 2.6 mmHg. SLT-treated eyes also showed decreased IOP fluctuation of 2.5 ± 1.9 (during 1-year posttreatment) vs. 4.5 ± 2.5 mmHg (pretreatment).

Meanwhile, Bozkurt et al. [24] examined the efficacy of SLT in preventing an IOP increase after intravitreal triamcinolone acetonide injections in patients treated for diabetic macular edema. Fifteen eyes (15 patients) underwent SLT a mean of 8.3 days before intravitreal triamcinolone acetonide injection and 16 eyes (16 patients) received only intravitreal triamcinolone acetonide injection. Postinjection IOP was higher in the control group at all time points up to 6 months. No SLT-treated patients required glaucoma medications, whereas 50% required glaucoma medications in the control group during follow-up. Finally, Ho et al. [25] studied the use of SLT in 60 eyes (60 patients) with primary angle closure glaucoma, a patent iridotomy and at least 90° of visible pigmented trabecular meshwork. At 6 months, the mean IOP reduction was 24% with no statistical change in medications.

### ALTERNATIVE LASERS IN TRABECULOPLASTY

Micropulse diode laser trabeculoplasty (MDLT) uses an 810-nm diode laser and includes the OcuLight SLx and IQ810 (Iridex Corporation, Mountain View, California, USA). This technology employs micropulsed emission of laser energy interrupted by ‘interval’ off times to create sublethal thermal injury to cells of the trabecular meshwork. A phase 2 pilot study of 180° treatment of trabecular meshwork with MDLT found a mean IOP reduction of 22.1% at 1 year [26]. A subsequent prospective, randomized study comparing MDLT and ALT showed decreased IOP reduction in the MDLT group at 3 months follow-up (12.2 ± 11.9 vs. 21.8 ± 11.1%) [27]. Further studies with larger sample size and variations in degrees of treatment are required to better understand the efficacy of MDLT. Like SLT, MDLT causes no evident morphologic change, including no coagulative damage, to the trabecular meshwork in human cadaver tissue [28].

Titanium sapphire laser trabeculoplasty (TLT) is currently undergoing trial and uses a 790-nm laser (SOLX, Inc., Waltham, Massachusetts, USA) that emits flashlamp-pumped, near-infrared energy in pulses that last 5–10 μs – a duration intermediate to ALT and SLT (Table 2). A pilot study with a mean follow-up of 15 months demonstrated that eyes treated with TLT achieved an average IOP reduction of 32 vs. 25% in the ALT comparison group [29].

### ENDOSCOPIC CYCLOPHOTOCOAGULATION

Endoscopic cyclophotocoagulation (ECP, Endo Optiks, Little Silver, New Jersey, USA) employs a fiber optic cable to deliver pulsed, continuous-wave diode laser energy to the ciliary processes under direct endoscopic visualization using a video monitor. It is generally accepted that the direct visualization gives the surgeon greater control over the procedure, potentially reducing overtreatment and the subsequent risk of late phthisis. Lin [30] recently published a comprehensive review of this surgical technique.

ECP is typically reserved for patients with refractory glaucomas, often having failed maximum tolerated medical therapy and prior glaucoma surgery. Francis et al. [31] recently performed a prospective, nonrandomized interventional case series of 25 consecutive eyes with uncontrolled glaucoma and prior tube shunt surgery treated with ECP. At 1 year, the mean IOP decreased from a baseline of 24.02 to 15.36 mmHg, and the mean IOP reduction was 30.8%. The study also found a decrease in glaucoma medications from 3.2 to 1.5 during the follow-up period. ECP has also been combined with phacemulsification in patients with less advanced glaucoma. Lima et al. [32] retrospectively reviewed 368 eyes (243 patients) with POAG that underwent

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**Table 2. Comparison of typical laser trabeculoplasty parameters**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Laser</th>
<th>Spot size (μm)</th>
<th>Duration</th>
<th>Power/energy</th>
<th>Number of spots</th>
<th>Degrees</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>Argon, blue-green 488/514 nm</td>
<td>50</td>
<td>0.1 s</td>
<td>300–900 mW</td>
<td>50–100</td>
<td>180</td>
</tr>
<tr>
<td>SLT</td>
<td>Nd:YAG, 532 nm</td>
<td>400</td>
<td>3 ns</td>
<td>0.6–1.2 mJ</td>
<td>50–100</td>
<td>180–360</td>
</tr>
<tr>
<td>MDLT</td>
<td>Diode, 810 nm</td>
<td>200</td>
<td>0.2 s (15% duty cycle)</td>
<td>1–2 W</td>
<td>50–100</td>
<td>180–360</td>
</tr>
<tr>
<td>TLT</td>
<td>Titanium sapphire, 790 nm</td>
<td>200</td>
<td>7 μs</td>
<td>30–50 mJ</td>
<td>50</td>
<td>180</td>
</tr>
</tbody>
</table>

**Note:** ALT, argon laser trabeculoplasty; MDLT, micropulse diode laser trabeculoplasty; SLT, selective laser trabeculoplasty; TLT, titanium laser sapphire trabeculoplasty.
combined phacoemulsification with ECP and had a mean follow-up of 35.15 months. They found a significant decrease in IOP at all time points with a mean final IOP of 12.29 mmHg, from a mean prelaser IOP of 23.07 mmHg. Mean visual acuity was significantly increased and mean glaucoma medications significantly decreased in these patients. Reported side-effects in this study included immediate postoperative IOP spike (14.4%), fibrin exudates in the anterior chamber (7.06%) and cystoid macular edema (4.34%).

TCP remains an important treatment modality for refractory glaucoma, particularly when other surgical treatments have failed to control IOP. Further refinements in the technology, including variations in the modulations of energy delivery, might allow conservative treatments to be performed in patients with useful vision, particularly in areas of the world where patient follow-up or access to care is limited.

**TRANSCLERAL CYCLOPHOTOCOAGULATION**

Transcleral cyclophotocoagulation (TCP) is an effective treatment for lowering IOP. Owing to the risk of hypotony and phthisis, however, the modality has been generally reserved for refractory pediatric and adult glaucoma cases, particularly when visual prognosis is poor. Some recent studies seem to suggest interest in applying TCP in eyes with good vision.

Agrawal et al. [33] surveyed ophthalmologists in the UK (47% of respondents were glaucoma subspecialists) on use of diode laser. Sixty percent of respondents reported performing the procedure at any visual acuity, whereas 22% performed combined cyclodiode treatment and cataract surgery. Another study in the UK retrospectively examined patients with visual acuity better than or equal to 20/60 (mean 20/30) treated with diode laser. At 5 years follow-up, the mean visual acuity was 20/60 and 30% of eyes lost two or more lines of Snellen visual acuity. In 16.3% of patients, final visual acuity was less than 20/200. Causes of decreased visual acuity included progression of glaucoma and macular edema. IOP was controlled in 79.6% of eyes with no cases of hypotony at final follow-up [34].

There has been some recent interest in combining TCP with intravitreal anti-vascular endothelial growth factor injections for the treatment of neovascular glaucoma. Initial studies suggest improvement in IOP but are limited by small sample sizes and short follow-ups. More work is needed to evaluate for long-term efficacy and complications [35,36].

A new form of TCP has been described, which uses a micropulse diode laser and trans-pars plana treatment with a novel contact probe (Iris Medical Instruments, Mountain View, California, USA). Although most of the data are preliminary, one prospective study of 40 eyes with refractory glaucoma found a relative success (IOP 6–21 mmHg or 30% decrease in IOP with or without glaucoma medications) of 80% at last follow-up after a mean of 1.3 treatments. There were no cases of hypotony or loss of best-corrected visual acuity at 18 months [37].

**LASER IRIDOTOMY AND IRIDOPLASTY**

Laser iridotomy (LPI), with or without iridoplasty, is used to treat nearly all types of narrow or closed-angle glaucoma. The Nd:YAG laser alone is frequently used to perform the iridotomy but may follow pretreatment with an argon laser, particularly for thick, heavily pigmented irises or patients on blood thinners in whom the risk of bleeding may be increased. A recent prospective randomized trial compared 1064-nm pulsed Nd:YAG laser with and without pretreatment with a 532-nm continuous-wave Nd:YAG green laser in dark irides. Mean pulsed YAG power was 37.5 mJ in the standard treatment group and 22.5 mJ in the sequential treatment group. Iris hemorrhages occurred in 43% of the standard group and in only 13% of the sequential treatment group [38], suggesting an enhanced safety profile of the combined technique.

LPI has also been utilized in the treatment of pigmentary dispersion syndrome (PDS) based on the theory of reverse pupillary block as a primary mechanism. Scott et al. [39] conducted a prospective, randomized, controlled trial assigning patients who had PDS with OHT to either Nd:YAG LPI or observation. A total of 52 patients in the laser treatment group and 53 patients in the observation group were followed for 3 years, and no differences were found in the proportion of eyes started on medical treatment between the two groups (15% in the laser group and 17% in the control group). Survival analyses failed to show any difference in time to visual field progression or commencement of medical treatment.

Questions remain regarding when to perform LPI in patients with narrow or closed angles without symptoms or evidence of glaucoma. In a single-masked, randomized, controlled trial in a Mongolian population, 4597 patients were screened for angle closure based on measurement of anterior chamber depth (ACD). One hundred and fifty-six participants received a prophylactic LPI after being found to have an ACD less than 2.53 mm and subsequent closed...
angles on gonioscopy. At 6 years of follow-up, no difference in the incidence of angle closure glaucoma was found in the screened group (19 patients) and the nonscreened group (14 patients, $P=0.47$) [40]. A prospective trial is currently underway in China to determine if LPI is well tolerated and effective at preventing pathological angle closure in asymptomatic eyes with narrow angle configurations [41].

Primary angle closure is the leading cause of glaucoma in China and has high prevalence in other parts of east Asia. Angle closure may occur secondary to pupillary block or from other mechanisms such as plateau iris or lens position. Sun et al. [42] compared the efficacy and safety of LPI with or without laser iridoplasty for the treatment of primary angle closure or primary synchial angle closure glaucoma. Both iridotomy alone and iridotomy combined with iridoplasty provided significant reductions in IOP with no significant difference between treatment groups in terms of IOP, medications, need for surgery or visual function at 1-year follow-up.

**Nd:YAG Goniopuncture**

Nd:YAG goniopuncture following deep sclerectomy converts a nonpenetrating procedure into a full-thickness surgery with the goal of producing a lower IOP. The initial surgery is often performed with MMC and may involve a space-maintaining implant. Goniopuncture is employed to augment filtration through the trabeculo-Descemet's membrane when greater IOP lowering is required or when a bleb begins to fail. Previous prospective randomized clinical trials comparing deep sclerectomy with trabeculectomy have found significant IOP lowering with both surgeries, but with superior IOP lowering in the trabeculectomy group [43,44]. Ollikainen et al. [45] recently performed a 3-year prospective, consecutive case series of deep sclerectomy with collagen implant and MMC in patients with POAG and exfoliative glaucoma. Nd:YAG laser gonipuncture was performed in 87% of exfoliative eyes and in 61% of the POAG cases. At 36 months, 74 and 73% of surgeries were a complete success in the POAG and exfoliative groups, respectively.

Anand and Pilling [46] reviewed 258 eyes of 258 consecutive patients who underwent deep sclerectomy or combined phacoemulsification and deep sclerectomy with a mean follow-up of 40 months after initial deep sclerectomy and 31 months after laser goniopuncture. Laser goniopuncture was performed in 67.0% of cases, and the mean interval between surgery and goniopuncture was 10.3 ± 8.7 months. At 2 years following laser goniopuncture, nearly 50% of patients maintained an IOP less than 15 mmHg with a 20% decrease in prelaser IOP. Complications following laser included peripheral anterior synchiae (13.2%), hypotony (4%) and late IOP rise (1.7%).

Iris occlusion and fibrous tissue over the gonipuncture site have been reported complications [46,47]. The latter has been confirmed by confocal microscopy in cases of treatment failure [47]. Additional treatment measures such as laser iridoplasty and bleb needling may be required to ensure long-term success of the procedure.

**Excimer Laser Trabeculotomy**

Excimer laser trabeculotomy (ELT, Glautec AG, Nurnberg, Germany) is designed to enhance outflow facility by creating microperforations in trabecular meshwork and inner wall of Schlemm's canal to access the outflow collector channels. The device utilizes a xenon chloride laser with a wavelength of 308 nm and pulsed delivery of 1.2 mJ over 80-ns duration. ELT has been shown to have minimal thermal effects on the trabecular meshwork [48,49]. An initial study found an IOP reduction of approximately 22% in ELT and 26.7% in ELT combined with phacoemulsification. Failure was significantly higher in the ELT alone group and increased with length of follow-up [50]. More recently, Babighian et al. [51] performed a randomized, controlled trial comparing ELT with SLT (180° treatment) in patients with POAG. At 2 years, complete success (≥20% reduction in IOP without additional medications) was achieved in 53.3% of patients with ELT and 40% for the SLT group, whereas qualified success was 33.3% for ELT and 26.6% for SLT. The mean IOP reduction was 29.6% in the ELT group and 21% in the SLT. Complications noted in the ELT arm of the study included temporary anterior chamber bleeding lasting less than 5 days without functional consequences (80%) and transient IOP increase less than 5 mmHg (20%).

Potential advantages of ELT include the reported simplicity of the procedure as well as the ab-interno approach that spares the conjunctiva. Intraoperative hemorrhage is common in the early postoperative period, although hypotony does not appear to be a major risk with the procedure. ELT is approved by the European Union but is not currently available for use in the USA.

**Conclusion**

Glaucoma management has traditionally followed a step-wise algorithm that begins with medications and progresses to laser and, when necessary, to lower IOP, incisional surgery. Recent literature is
challenging this approach with early data supporting the use of SLT as an option for initial therapy in patients with open-angle glaucoma or OHT. Patients with mild-to-moderate glaucomatous optic neuropathy who cannot tolerate medical therapy might particularly benefit from earlier trabeculoplasty. The body of literature describing the use of SLT in other subtypes of glaucoma is growing, with limited studies suggesting efficacy in patients with normal tension glaucoma, prior to intravitreal steroid injections as prophylaxis for steroid-induced glaucoma, and in selected cases of primary angle closure glaucoma following iridotomy. Additional randomized, prospective studies are necessary to better define the role of SLT as initial or adjunctive therapy in various subtypes of glaucoma. Novel laser modalities are being developed and refined, with favorable initial results using MDLT, TLT and ELT, although limited data regarding these modalities exist at this time.

In addition to trabeculoplasty, other laser applications have been developed to treat many different types of glaucoma. The indications for treatment and potential complications of therapy vary by application (Table 3). ECP and TCP remain effective treatments for lowering IOP with recent literature describing the use of ECP in combination with phacoemulsification and TCP for patients with neovascular glaucoma. The ability to modulate TCP with an emphasis on micropulse delivery is promising, but more work is required to better understand its potential benefits. LPI with or without iridoplasty is used to treat nearly all types of narrow or closed-angle glaucoma. Its use in pigmentary glaucoma may be of limited benefit, although its role as a prophylactic treatment for narrow angles in countries such as China needs further investigation. Nd:YAG gonipuncture following deep sclerectomy has been described as a useful procedure to improve filtration when greater IOP lowering is required or when a bleb begins to fail, although late occlusion of the gonipuncture site is a well described late complication.

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Conflicts of interest
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REFERENCES AND RECOMMENDED READING
Papers of particular interest, published within the annual period of review, have been highlighted as:
- of special interest
- of outstanding interest
Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

Selective laser trabeculoplasty (SLT) is a minimally invasive procedure used to treat primary open-angle glaucoma (POAG) as an alternative to traditional surgical treatments. The procedure involves the use of a laser to create microinjuries in the trabecular meshwork, leading to increased aqueous humor outflow through the peripheral iridocorneal angle. The goal is to lower intraocular pressure (IOP) and prevent disease progression.

The procedure is performed by a surgeon or an ophthalmologist using a handheld laser device. The laser delivers a series of low-energy pulses to the trabecular meshwork, typically at a wavelength of 532 nm. The treatment is usually performed on both eyes, as painless, low-risk procedures that can be repeated as needed to reach target IOP.

Benefits of SLT include:
- Minimally invasive procedure
- No incision or external drainage device
- Reduced risk of complications
- Potential for reduced medication requirements

However, SLT may not be suitable for all patients. Patients with narrow angles or those at high risk for angle closure glaucoma are not recommended to receive SLT. Additionally, patients should be monitored closely to ensure the procedure is effective and to avoid any potential side effects, such as increased IOP in the fellow eye or reduced visual fields.

In conclusion, SLT is a viable option for the treatment of primary open-angle glaucoma, offering a minimally invasive approach to lowering IOP. For patients and providers, the decision to use SLT should be discussed with regards to the patients’ overall health and glaucoma disease severity.

References: