

# History and Scientific Evidence of Selective Laser Trabeculoplasty (SLT)

## Histórico e Evidência Científica da Trabeculoplastia Seletiva a Laser (SLT)

Marcelo Hatanaka<sup>1</sup>

1. Setor de Glaucoma, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil.

### KEYWORDS:

Open-angle glaucoma; Ocular hypertension; intraocular pressure; Hypotensive eye drops; Selective laser trabeculoplasty.

### ABSTRACT

Sustained reduction of intraocular pressure is the only strategy known to be effective in slowing or, ideally, halting the progression of open-angle glaucoma. Recent evidence has repositioned selective laser trabeculoplasty as an initial alternative to drug treatment by demonstrating that, in selected patients, it leads to a reduction in intraocular pressure comparable to drug therapy and less dependence on hypotensive eye drops while exhibiting a good safety profile and better cost-effectiveness. This review discusses the historical evolution and mechanisms of action of selective laser trabeculoplasty, and the main clinical evidence supporting its use in the management of open-angle glaucoma and ocular hypertension, with an emphasis on randomized clinical trials, systematic reviews, meta-analyses, and international guidelines, including the Laser in Glaucoma and Ocular Hypertension (LiGHT) study and its six-year extension.

### PALAVRAS-CHAVE:

Glaucoma de ângulo aberto; Hipertensão ocular; Pressão intraocular, colírios hipotensores; Trabeculoplastia seletiva a laser.

### RESUMO

A redução sustentada da pressão intraocular é a única estratégia comprovadamente eficaz para retardar, ou, idealmente, interromper a progressão do glaucoma de ângulo aberto. Evidências recentes repositionaram a trabeculoplastia seletiva a laser como alternativa inicial ao tratamento medicamentoso, demonstrando que, em pacientes selecionados, a trabeculoplastia seletiva a laser promove redução da pressão intraocular comparável à terapia medicamentosa, menor dependência de colírios hipotensores, perfil de segurança favorável e melhor relação custo-efetividade. Esta revisão aborda a evolução histórica, os mecanismos de ação e as principais evidências clínicas que fundamentam o uso da trabeculoplastia seletiva a laser no manejo do glaucoma de ângulo aberto e da hipertensão ocular, com ênfase em ensaios clínicos randomizados, revisões sistemáticas, meta-analises e diretrizes internacionais, incluindo o estudo *Laser in Glaucoma and Ocular Hypertension (LiGHT)* e sua extensão de seis anos.

## INTRODUCTION

Open-angle glaucoma (OAG) is one of the leading causes of irreversible blindness globally, with an estimated prevalence of 3.54% in individuals aged 40-80 years, and with over 110 million individuals estimated to be affected by 2040<sup>1</sup>. The only effective strategy for delaying onset and progression of

glaucomatous optic neuropathy is sustained reduction in intraocular pressure (IOP)<sup>2</sup>.

This classic therapeutic regimen, starting with hypotensive eye drops, followed by laser, and finally, surgical procedures, has been increasingly questioned due to recent evidence that supports repositioning selective laser trabeculoplasty (SLT)

**Corresponding author:** Marcelo Hatanaka. Email: marcelohatanaka@gmail.com

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as the initial treatment in applicable cases with an open angle.

## 1. LASER TRABECULOPLASTY: FROM ARGON TO ND:YAG

### Argon laser trabeculoplasty: mechanism of action, efficacy, and limitations

The first successful efforts to reduce IOP with an argon laser or via argon laser trabeculoplasty (ALT) date back to the late 1970s when Wise et al. demonstrated that applying a low-energy argon laser to the trabecular meshwork reduced IOP by approximately 10mmHg in phakic eyes and eyes with OAG, although a majority (65%) of patients required additional treatment<sup>3</sup>.

Tonographic and aqueous humor dynamics studies showed an easier outflow after ALT and led to the “mechanical” theory that thermal photocoagulation of the pigmented trabecular meshwork caused collagen retraction and tissue contraction, with the consequent opening of filtration spaces<sup>4,5</sup>. However, ultrastructural changes and signs of modulation of inflammatory pathways and remodeling of the extracellular matrix suggested the presence of a relevant “biological” component, involving recruitment of macrophages, expression of metalloproteinases, and reorganization of the trabecular matrix<sup>6,7</sup>.

ALT promotes initial reductions in IOP of 26%-33%, with a better response in eyes with higher baseline IOP and older patients. However, the durability of the hypotensive effect is limited, and classic series have shown a success rate of 77% in 2 years, 46% in 5 years, with up to 95% of eyes requiring filtering surgery within 10 years in cohorts with advanced OAG patients, under maximum medical therapy<sup>8</sup>.

Repeat ALT is less effective than the first administration<sup>9</sup>, which, combined with the complications of the technique, limits treatment to just two administrations—180° at a time and not repeated on previously treated areas.

Complications include IOP peaks of >5mmHg after the procedure in a third of cases and >10mmHg in 10%-12% of eyes, specifically when using higher energies, 360° treatment, greater angular pigmentation, or low preoperative outflow facility. There is also a significant risk of peripheral anterior synechiae (PAS), acute anterior inflammation, and corneal endothelial alterations, with a higher risk in heavily pigmented eyes<sup>8</sup>.

Thus, ALT showed that trabeculoplasty was effective as primary or adjuvant therapy but with a risk of irreversible structural damage, gradually decreasing benefit, and a limited safety profile, which prompted the development of more selective approaches.

### SLT

From a physical perspective, ALT is capable of causing selective photothermolysis because melanin present in trabecular meshwork cells acts as a chromophore with high absorption in the argon laser spectral range. However, the duration of the argon laser pulse (approximately 0.1 s) substantially exceeds the thermal relaxation time of melanin (approximately 1  $\mu$ s), which leads to the diffusion of heat to adjacent tissues, with consequent collateral thermal damage to the trabeculae and adjacent structures<sup>10</sup>.

SLT was developed to preserve the principles of selective photothermolysis, while overcoming the temporal limitations of ALT. It uses a 532 nm Q-switched Nd:YAG laser with a pulse duration of nanoseconds, which is shorter than the thermal relaxation time of melanin. The energy is confined to the melanosomes of the pigmented trabecular cells, thus minimizing heat dissipation and collateral damage<sup>10</sup>.

Histologically, SLT does not cause obvious coagulation craters in the trabecular meshwork<sup>11</sup> but it does trigger a biological cascade mediated by cytokines, a transient increase in inflammatory cells in the meshwork, upregulation of metalloproteinases and remodeling of the extracellular matrix, resulting in increased porosity and ease of outflow. This predominantly biological and “nondestructive” nature explains the greater possibility of repeating SLT over time as well as a more favorable safety profile compared to ALT<sup>10</sup>.

Data from series and clinical trials over the last two decades have shown that SLT reduces IOP by 20%-30% and its efficacy is similar to that of prostaglandin analogs as monotherapy in multiple studies. Moreover, the incidence of clinically significant spikes of IOP and PAS is significantly lower than with ALT, which has led to the gradual replacement of ALT by SLT as the standard trabeculoplasty technique<sup>8,12-17</sup>.

## 2. The LiGHT study and its influence on glaucoma treatment

The Laser in Glaucoma and Ocular Hypertension (LiGHT) study<sup>18</sup> is a randomized, multicenter, examiner-blinded trial conducted in six hospitals in the United Kingdom, which compared primary SLT with hypotensive eye drops as the initial treatment for patients who had not been treated for OAG or ocular hypertension (OHT) and had no ocular comorbidities. Participants were randomized to initial SLT, with the possibility of repetition, or to stepwise drug treatment, with pre-defined IOP targets according to the severity of the glaucomatous damage. The primary endpoint was health-related quality of life (EQ-5D) at 3 years. Secondary outcomes included clinical efficacy, safety, and cost-effectiveness<sup>18</sup>.

After 36 months, the LiGHT study showed that SLT was not inferior to eye drops in terms of quality of life (EQ-5D; 0.89 vs. 0.90; 95% CI –0.01 to 0.03;  $p=0.23$ ), thus confirming their equivalence from the patient's perspective<sup>18</sup>.

However, in terms of clinical outcomes, SLT showed substantial advantages: after 36 months, 74.2% of patients in the SLT group maintained their target IOP without the need for eye drops while in the drug group 64.6% of eyes were on monotherapy and 25.6% of eyes were on 2-4 drugs<sup>18</sup>.

A higher proportion of follow-up visits met the predefined intraocular pressure target in the SLT group (93.0% vs. 91.3). There was a lower rate of disease progression in the SLT group than in the eye drops group (23 eyes, 3.8% vs. 36 eyes, 5.8%). No patient in the SLT group required filtering surgery to control IOP, in contrast to 11 patients in the drug group. Additionally, more patients treated with eye drops required cataract surgery compared to the SLT group (25 vs. 13 surgeries). As expected, ocular adverse effects were more evident in the group using hypotensive eye drops. Among the 776 SLTs performed, there was one clinically relevant hypertensive peak<sup>18</sup>.

As for the economic profile, the cost-effectiveness analysis showed a 97% probability of the "SLT first" strategy being more cost-effective than "eye drops first" for a threshold of £20,000 per quality-adjusted life year gained, when considering direct ophthalmic costs<sup>18</sup>.

Thus, the authors suggest that SLT should be offered as a first-line treatment for OAG and ocular hypertension, which involves a change in clinical practice<sup>18</sup>.

## LiGHT study: 6-year extension

The 6-year extension of the LiGHT study confirms and extends the initial findings.<sup>19</sup> A total of 633 patients completed the 3-year follow-up and entered the extension phase, 524 of whom completed the 6 years follow-up (73% of those randomized initially). Patients in the SLT group could receive up to a third session of SLT, whereas patients in the eye drops group could receive exchange therapy or SLT as escalation<sup>19</sup>.

After 6 years, there were no significant differences between the groups in the EQ-5D, the Glaucoma Utility Index, or the Glaucoma Quality of Life-15 (GQL-15), although the SLT group scored better on the Glaucoma Symptom Scale, which indicates a lower burden of subjective symptoms related to the disease and/or treatment<sup>19</sup>.

In terms of efficacy, 69.8% of eyes in the SLT group remained at the target IOP without the need for drug or surgical treatment, thus confirming the longer durability of the "laser first" strategy. Disease progression was more frequent in the drug group (26.8% vs. 19.6%;  $p=0.006$ ), and the number of trabeculectomies was significantly higher in patients initially treated with eye drops (32 vs. 13;  $p<0.001$ ). During the extension, 11 and no minimally invasive glaucoma surgeries (MIGS) were performed in the drug and laser groups, respectively<sup>19</sup>.

Additionally, a higher number of cataract surgeries were performed in the drug group, possibly as a result of the greater need for filtering interventions and/or the effect of chronic eye drops on the ocular surface and anterior segment inflammation, although this causal relationship cannot be definitively established based on the study design<sup>19</sup>.

Collectively, the 3- and 6-year results of LiGHT represent a paradigm shift, i.e., when used as the initial treatment, SLT provides at least equivalent pressure control, less need for eye drops, a lower rate of structural and functional progression, and less need for filtering surgery as well as clearly superior cost-effectiveness. This combination of outcomes supports the re-evaluation of traditional therapeutic escalation.

## 3. Evidence from the literature

### Cochrane review 2022

The 2022 Cochrane review on laser trabeculoplasty for OAG and OHT evaluated studies comparing laser trabeculoplasty with three treatment

strategies: drug treatment, glaucoma surgery, and no intervention. Fourteen studies comparing laser with topical medication were included; seven were conducted only in primary OAG and seven in primary or secondary OAG and five of these trials also included ocular hypertensive subjects. Among the studies comparing laser and eye drops, six used ALT and eight used SLT.

The interpretation of pressure outcomes showed high heterogeneity. The risk ratios for failure to control IOP at 24 months ranged from 0.43 in favor of laser to 1.87 in favor of medication. This range is possibly due to significant differences between the studies, often related to lack of blinding, non-standardized measurement strategies, and the use of less effective hypotensive drugs in the older ALT studies. Thus, the certainty of the evidence for IOP control was classified as low, i.e., with residual uncertainty and the impossibility of more assertive conclusions.

However, the evidence regarding functional progression assessed by visual field outcomes showed greater consistency. Two studies with ALT, totaling 624 eyes, reported a lower rate of failure to stabilize the visual field at 24 months (7% vs. 11%; RR 0.70; CI 95% 0.42-1.16). Additionally, a study evaluating SLT at 48 months reported a lower risk of functional progression in the laser group (17% vs. 26%; RR 0.65; CI 95% 0.52-0.81). The overall certainty of the evidence for this outcome was classified as moderate. In both cases, results suggest an advantage of laser in preserving visual function, although the exact magnitude of the effect still depends on further studies.

The review showed significant differences between ALT and SLT. ALT showed a higher incidence of PAS. IOP spikes after the procedure were more frequent in the studies involving ALT, whereas SLT only showed transient hypertensive events that were usually mild and manageable, with no consistent serious adverse events reported. The review found no evidence of recurrent severe complications associated with SLT in the controlled trials included.

Moreover, the Cochrane review concluded that laser trabeculoplasty (ALT and SLT) has similar pressure efficacy to topical drugs in several trials and may reduce the risk of functional progression in certain contexts. The Cochrane review also notes that although laser is a valid therapeutic alternative to initial drug treatment, especially due to the favorable safety profile of SLT, there are still important gaps

in the literature, specifically with regard to the consistency of long-term pressure control. When comparing ALT with filtering surgery, the review shows a greater likelihood of not achieving adequate pressure control with ALT at 24 months, reinforcing that laser does not replace trabeculectomy in cases that require more aggressive pressure reduction.

### Other evidence

A meta-analysis conducted by Chen et al.<sup>16</sup> evaluated the efficacy and safety of SLT in controlling primary OAG. Overall, 50 studies were included, totaling a quantitative base of 8,934 eyes followed up for 12-60 months<sup>16</sup>.

Pressure control with laser therapy was equivalent to that obtained with drug therapy between 6 and 12 months, with a pooled mean difference of 0.04 mmHg (95% CI -0.27 to 0.34). The reduction in the number of eye drops was 0.87 per patient (95% CI -1.13 to -0.62), suggesting the ability of laser treatment to reduce therapeutic dependence. As for the functional analysis, campimetric progression showed a significant benefit in the SLT group, with a grouped mean difference of 0.79 dB (95%CI 0.76-0.82) in the mean deviation parameter, suggesting that SLT not only keeps IOP under control but also contributes to preserving visual function. The safety profile remained favorable throughout the period analyzed: no study reported serious adverse events or irreversible visual loss, and the complications observed were limited to mild anterior chamber inflammation and transient IOP elevation<sup>16</sup>.

Chavez et al.<sup>14</sup> performed a meta-analysis involving 14 randomized clinical trials (RCTs) and 1706 patients, 936 of whom underwent SLT. There was no difference in terms of functional assessment and quality of life. Data from RCTs allowed a comparison at specific follow-up times, and it was observed that drug therapy was associated with significantly greater pressure reduction in the first month of treatment and a higher proportion of patients achieving  $\geq 20\%$  IOP reduction (RR 0.79; 95% CI, 0.64-0.97;  $p=0.02$ ;  $I^2=44\%$ ); however, pressure control was similar between the groups at most follow-ups. Moreover, treatment with eye drops showed better IOP control compared to SLT in the group of patients who had not been treated. However, SLT led to a mean reduction of 1.09 eye drops (95% CI -1.21 to -0.97;  $p<0.01$ ), which is a substantial reduction in long-term therapeutic dependence<sup>14</sup>.

The safety analysis showed a similar incidence of adverse effects between SLT and eye drops (RR **0.94**; 95% CI 0.84-1.06;  $p=0.34$ ), with no evidence of an increase in relevant complications in the laser group. The review also showed a lower cumulative requirement for glaucoma surgery in the SLT group (RR **0.42**; 95% CI 0.24-0.73;  $p<0.01$ ), suggesting a structural impact on the course of the disease by reducing the need for filtering interventions. The author concludes that SLT is an effective and safe treatment for OAG and OHT<sup>14</sup>.

#### 4. International guidelines and SLT position

Rapid evolution of scientific evidence has led to a revision of the recommendations in the main international guidelines. A systematic review of OAG guidelines published in 2025 evaluated 11 guidelines (out of a total of 55) published between 2017 and 2024, in English or Spanish, using the AGREE-II instrument<sup>20</sup>.

An analysis of the recommendations of the different guidelines showed relative convergence with regard to IOP targets, structural and functional monitoring, and the central role of pressure reduction in preventing progression. However, significant variability has been identified in the indications for SLT and minimally invasive surgery (MIGS)<sup>20</sup>.

The most recent European guidelines tend to consider SLT as the first-line option equivalent to topical therapy in OAG and OHT, especially when considering factors such as adherence, side effects, and drug costs. The American guidelines, which have historically maintained eye drops as the first choice, began to more explicitly admit SLT as an initial alternative in the post-LiGHT study versions, with a high level of evidence (Level I). Asian and Latin American guidelines, although heterogeneous, have also gradually incorporated SLT as an early option for patients with adherence difficulties, polypharmacy, or economic barriers to the continuous use of eye drops<sup>20</sup>.

Notably, despite this convergence, the review shows that the methodological quality of the guidelines is not uniform and that national policies can delay the full incorporation of SLT as the first-line standard, even in the face of robust evidence<sup>20</sup>.

Incorporation of a new therapeutic paradigm depends not only on guidelines but also on the attitudes and preferences of specialists. A recent survey of American Glaucoma Society members

evaluated treatment preferences for OAG in the United States, focusing on the choice between SLT and eye drops<sup>21</sup>.

Among 136 eligible respondents, 65%-71% reported preferring SLT as initial treatment in treatment-naïve patients with ocular hypertension, mild to moderate primary OAG, pseudoexfoliation, or pigmentary glaucoma. For mild to moderate OAG treated with eye drops, 75% of respondents were in favor of SLT as the next step. For advanced OAG under the most intensive drug therapy, 57% of respondents preferred surgery (typically trabeculectomy or non-penetrating filtering procedures), while 38% still considered SLT<sup>21</sup>.

The factors most cited as facilitators for recommending SLT included reducing medication non-adherence (93%), appropriateness of the type/stage of glaucoma (88%), and personal experience with SLT (83%). The following barriers stood out: the patient's inability to position themselves properly for the procedure (78%), unsuitable type/stage of glaucoma (67%), and comorbidities or contraindications for SLT (55%)<sup>21</sup>.

Multivariate analyses showed that ophthalmologists in private practice, trained more recently, and treating a higher volume of treatment-naïve patients were substantially more likely to prefer SLT over the use of eye drops<sup>21</sup>.

#### 5. Critical synthesis and implications for practice

The trajectory of laser trabeculoplasty in OAG clearly illustrates technological evolution, which combined with high-level clinical trials and systematic reviews can reshape well-established therapeutic paradigms. ALT inaugurated the concept of laser modulation of the trabecular meshwork and showed that increased flow could be achieved without filter surgery, but at the cost of irreversible thermal damage, limited repeatability, and decreasing benefit over time<sup>3-10</sup>.

By applying the principles of selective photothermolysis more rigorously, SLT minimizes structural damage and allows for a predominantly biological approach to trabeculation. In terms of efficacy, SLT delivered IOP reductions comparable to those obtained with monotherapy with prostaglandin analogs, both in randomized trials and in observational series. In terms of safety, it maintains a favorable profile, with infrequent IOP peaks and rare serious events<sup>11-17</sup>.

The LiGHT study and its 6-year extension show that, when used as the primary intervention, SLT reduces the need for eye drops on a sustained basis, maintains a greater proportion of patients within the target IOP, reduces functional and structural progression, and significantly reduces the need for filtering surgery, all without loss of quality of life and with superior cost-effectiveness<sup>18-19</sup>.

The outcomes of reduced progression, reduced use of eye drops, and less need for surgical procedures are particularly relevant for populations with low adherence to topical therapy and for public health management.

The most recent Cochrane review and meta-analyses consolidate and extend these findings, confirming the applicability of laser trabeculoplasty in OAG and ocular hypertension<sup>12,16,17</sup>.

At the regulatory level, more methodologically rigorous guidelines have already incorporated SLT as the first-line treatment option, and the global trend is toward increasing convergence in this direction, albeit with heterogeneity depending on regional contexts, availability of equipment, training, and funding<sup>20</sup>.

A survey of US specialists shows that clinical practice is shifting, with the majority already preferring SLT for patients who have not undergone treatment or are using eye drops, although in advanced disease the predominance of conventional surgical procedures persists<sup>21</sup>. Data on SLT in the Brazilian population, published in indexed journals, will be discussed in the next editorials<sup>13,15</sup>.

Considering the evidence discussed herein, SLT as initial therapy in applicable cases is not only acceptable but also a recommended therapeutic option for patients with initial or moderate OAG and ocular hypertension, specifically when there is a risk of poor compliance, use of multiple hypotensive eye drops, significant treatment costs, or socioeconomic barriers.

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## AUTHOR INFORMATION



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### » **Marcelo Hatanaka**

<http://orcid.org/0000-0002-0244-3652>  
<http://lattes.cnpq.br/2626412495906464>