Selective Laser Trabeculoplasty (SLT): When and How

BRIAN A. FRANCIS, MD, MS
RIFFENBURGH PROFESSOR OF GLAUCOMA
DOHENY EYE INSTITUTE
KECK SCHOOL OF MEDICINE
UNIVERSITY OF SOUTHERN CALIFORNIA

Key Topics

• SLT Mechanism of Action
• SLT as Primary Therapy
• SLT as Adjunctive Therapy
• SLT as Replacement Therapy
• SLT Retreatment Therapy
• SLT in Clinical Practice
SLT Mechanism of Action

The Science Behind SLT

SLT uses a Q-switched, 3 nanosecond pulsed, frequency-doubled Nd:YAG; 532 nm wavelength green laser

Larger beam diameter with SLT
- Reduces need for focus
- Evenly distributes laser energy

The Advantages of Selectivity

- ALT causes coagulative damage that leads to scarring of the trabecular meshwork
- SLT treatments do not cause the coagulative damage associated with ALT. Therefore, SLT is believed to improve aqueous outflow and regeneration of the trabecular meshwork

Mechanism of Action

Laser energy selectively targets pigmented trabecular meshwork endothelial cells (TMES) with no coagulative damage or collateral thermal effects

References:
Mechanism of Action

Cytokines activate macrophages, which travel to the area of injury and phagocytize cellular debris in the intertrabecular spaces of the TM.


Treated TMEs release cytokines, which bind with the Schlemm’s canal endothelial cells (SCEs) and open up the cellular barrier formed by these cells.

Mechanism of Action

The SCE barrier acts as a “control” site for aqueous outflow. The opening of the SCE barrier cells leads to increased aqueous outflow and a decrease in IOP.

Insights into cellular regulation of aqueous outflow: TM and SC endothelial cells

JA Alvarado, RG Alvarado, RF Yeh et al, Br J Ophthalmol 2005

- TME cells Rx SLT
- Medium added to SCE
- SCE permeability (flow meters)
- Gene expression (PCR)
- SCE exposed to TME media show ↑ gene expression
- SCE permeability ↑ 4x
- Cytokines IL-1α, IL-1β, TNF-α, IL-8 directly ↑ SCE permeability
- Action of TME media nullified by boiling
Schlemm’s Canal Endothelial Cells

Exposure to tissue media from TM cells treated with Frequency Doubled YAG laser

Hydraulic Conductivity of SCE cells

Treatment: Frequency Doubled YAG Laser
SCE Cells Treated with Prostaglandin Analog Drugs

SCE Cell Hydraulic Conductivity after PGA Exposure

![Graph showing hydraulic conductivity](image)
Clinical Application of SLT Therapy

- SLT as Primary Therapy
- SLT as Adjunctive Therapy
- SLT as Replacement Therapy
- Potential SLT Retreatment Therapy

SLT as Primary Therapy

Equivalent Efficacy to Medication
Effective Long-term Results
Primary Therapy: SLT vs Medication

Mean IOP Reduction Over 12 Months

- SLT provided a mean IOP reduction of 31% (vs a mean IOP reduction of 30.6% with LATANOPROST)

SLT therapy provides IOP reduction equivalent to that of medications


Comparison of Selective Laser Trabeculoplasty (SLT) vs. Medical Therapy for Initial Therapy for Glaucoma or Ocular Hypertension

Katz LJ, Steinmann WC, Marcellino G and the SLT/MED Study Group
Overview

- **Study Design**: Multi-center (17 sites), prospective, randomized, controlled clinical trial to compare medical therapy and selective laser trabeculoplasty (SLT) as initial therapy for glaucoma.

- **Subjects**: untreated primary open angle glaucoma or high risk ocular hypertensive patients.

- **Treatment groups**: patients are randomized to receive either: 1) SLT and repeat SLT; or, 2) Stepwise addition of topical glaucoma medications. Both eyes are to receive the same treatment assignment.

- **Outcome measures**: The primary outcome to be measured is whether selective laser trabeculoplasty is equal to medical therapy for initial IOP lowering effect based on target levels using formula devised for the Collaborative Initial Glaucoma Treatment Study (CIGTS). The study investigators will collect this data depending on the measure at baseline and at 2, 4, 6, 9, or 12 month intervals.

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**Treatment Groups and Sequence of Steps**

- **Group 1**: SLT
  - 37 subjects (74 eyes)
  - Step 1: SLT 360 100 Applications
  - Step 2: SLT Naked 180 50 Applications
  - Step 3: SLT Temporal 180 50 Applications
  - Step 4: Treatment, clinician choice of next therapy for intervention failure

- **Group 2**: Medical Therapy
  - 35 patients (70 eyes)
  - Step 1: prostaglandin analog, latanoprost, tafluprost, or travoprost
  - Step 2: Add a beta blocker or timolol beta blocker
  - Step 3: Add or substitute brimonidine
  - Step 4: Add or substitute dorzolamide, brinzolamide, or a fixed combination
Results

- A total of 72 patients (136 eyes) were enrolled and randomized.
- Group 1 (the SLT arm) had 37 patients (69 eyes) and Group 2 (the medical arm) had 35 subjects (67 eyes).
- Data for at least 8 months of follow-up was available for 47 patients (94 eyes): 29 (58 eyes) were in Group 1 (SLT) and 18 (36 eyes) in Group 2 (medical).

Primary Therapy: SLT MED Study

Mean IOP Reduction: SLT vs Medical Therapy

- SLT Therapy: 6.7 mm Hg mean IOP reduction (58 eyes)
- Medical Therapy: 7.6 mm Hg mean IOP reduction (36 eyes)

Equivalent IOP reduction with less concern about side effects and patient compliance

SLT as Adjunctive Therapy

Benefits of SLT Adjunctive to Topical Medication

SLT Clinical Investigation
United States

Mark Latina, M.D. – Boston, MA
Robert Ritch, M.D. – New York, NY
Jeffrey Liebman, M.D. – New York, NY
Dong Shin, M.D., Ph.D – Detroit, MI
Robert Noecker, M.D. – Tucson, AZ
Objective (US Study)

- To establish the safety and effectiveness of selective laser trabeculoplasty to reduce IOP in patients with open-angle glaucoma
- Patient population
  - Uncontrolled on max meds
  - Failed ALT

Selective Laser Trabeculoplasty
U.S. Clinical Trial Results

SLT-Treated Eyes Mean IOP Reductions at 26 weeks
Responders (> 3mmHg IOP reduction) - 71/101 patients

Latina, et al - US
**SLT: Conclusions**

- Difficult cases, uncontrolled IOP
  - Prior ALT
  - Maximum tolerated medications
- Potentially repeatable
- Effective and less destructive alternative to ALT
- FDA Status: Cleared for Clinical Use

**IOP Fluctuation: Visual Field Progression**

- Significant progression was observed in eyes with high fluctuation

*Visual field loss progression is increased by 30% with each 1 mm Hg increase in IOP fluctuation*

IOP Fluctuations: Glaucoma

- Large fluctuations (>5 mm Hg) in IOP are a significant risk factor for disease progression in glaucoma patients
- IOP fluctuations are an independent risk factor

Fluctuating IOP has been shown to be a major factor in glaucoma progression


Circadian Control

Laser trabeculoplasty adjunctive to medications has shown 24-hour IOP control with significant additive IOP reduction in the nocturnal period

SLT as Replacement Therapy
SLT Benefits Beyond Achievement of Target IOP

SELECTIVE LASER TRABECULOPLASTY (SLT) AS A REPLACEMENT FOR MEDICAL THERAPY IN OPEN ANGLE GLAUCOMA

Francis BA, Ianchulev T, Schofield JK, Minckler DS
American Journal of Ophthalmology, September 2005
Methods: Doheny Replacement Study

Inclusion Criteria:
- Primary Open Angle Glaucoma or
- Exfoliation glaucoma
- Both phakic and pseudophakic eyes
- IOP of newly diagnosed patients higher than 20
- Group A: Patients without treatment with drops or ALT or
- Group B: Previously diagnosed patients currently controlled on medications or
- Group C: Patients diagnosed with POAG and uncontrolled on maximum medications

Exclusion Criteria:
- Monocular patients (fellow eye with vision worse than 20/400)
- Advanced visual field defects that jeopardize fixation (within 10 degrees)
- Previous glaucoma surgery (except ALT, PI)
- Aphakia
- IOP so poorly controlled that if not lowered immediately may result in visual deterioration within a 3 month period
Methods: Doheny study

**SLT**

- No. of shots: 50-70 over 180 deg
- Duration: 3 nsec
- Spot size: 400 um
- Power: 0.7 - 1.3 mJ
  - (Mean= 0.8 mJ)

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Replacement Therapy (cont’d)

- 87% of eyes maintained reduction in medication use by at least 1 medication at 12 months

**SLT therapy can help reduce patient dependence on topical medications**

Results: Doheny Replacement Study

SLT Replacement Treatment Success

ARM 2 (Substitute RX)
Controlled reduction of 1 or more medications

6 mo = 98% (65/66)
12 mo = 87% (52/60)

N=56 on 2 or more meds; 44 (79%) able to DC 2 or more meds.
N=10 on 1 medication; 8 (80%) able to DC

Glaucoma Costs

- Glaucoma medications are a major factor toward the total direct cost of glaucoma

Early diagnosis and treatment may lead to potential cost savings for both patients and overall health care systems

SLT Patients Previously Treated with ALT

- 57% of SLT responders previously treated with ALT achieved a mean IOP reduction of $\geq 5$ mm Hg

* Achieved an IOP reduction of $\geq 3$ mm Hg

The safety profile and clinical data suggest that SLT may be an effective retreatment therapy, in contrast with ALT.

REPEAT SELECTIVE LASER TRABECULOPLASTY (SLT) IN OPEN ANGLE GLAUCOMA

Francis, BA, Hong B, Katz LJ, Iwach A, Shields MB, Bacharach J
In press

SLT Repeatability
Multicenter Study

- Doheny Eye Institute, USC
- Wills Eye Hospital
- Yale University
- California Pacific Medical Center
- Pacific Eye Institute
SLT Repeatability
Multicenter Study

• SLT 1 360
• Successful IOP lowering (3 mmHg)
• Effect lasting 1 year
• Effect wearing off over time
• SLT 2 360 performed
• Change in IOP, meds
• N=137 patients, one eye randomly selected

SLT Repeatability
Doheny Study

• Patient Demographics
• Age = 72.5 (11.9) years
• Gender = Female 61.3%
• Race
  Caucasian 76.5%
  African American 7.4%
  Latino 8.8%
• Diagnosis
  POAG 80.3%    XFG 12.4%
  PG 4.4%       OHTN 1.5%  JOAG 1.5%
• Prior ALT 8.8%
SLT Repeatability

• SLT 1
  • Baseline IOP = 20.3 (5.2) mmHg
  • 6 months, IOP = 16.3* (4.3)mmHg; p<.001
  • 12 months, IOP = 16.4* (3.9)mmHg; p<.001

• SLT 2
  • Baseline IOP = 19.4 (5.0) mmHg; p=.03
  • 6 months, IOP = 16.3* (4.8) mmHg; p<.001
  • 12 months, IOP = 16.7* (4.7) mmHg; p<.001

SLT Repeatability

• SLT 1
  • Baseline meds = 2.2 (1.2)
  • 6 months meds = 1.9 (1.3)
  • 12 months meds = 2.1 (1.3)

• SLT 2
  • Baseline meds = 2.1 (1.3)
  • 6 months meds = 1.9 (1.4)
  • 12 months meds = 2.2 (1.2)
SLT Repeatability

- Subanalysis: Equal Baselines
  - SLT 1
    - Baseline IOP = 18.7 (3.8) mmHg
    - 6 months, IOP = 16.0* (4.3) mmHg; p<.001
    - 12 months, IOP = 15.8* (3.3) mmHg; p<.001
  - SLT 2
    - Baseline IOP = 18.7 (3.5) mmHg
    - 6 months, IOP = 15.3* (3.8) mmHg; p<.001
    - 12 months, IOP = 16.6* (4.5) mmHg; p<.001

SLT Repeatability

- Success SLT 2 = IOP lowered > 20%
  - 6 months = 37.0%
- Equal baselines
  - 6 months = 44.2%

- Success SLT 2 = IOP lowering > 20% or ↓meds
  - 6 months = 47.9%
- Equal baselines
  - 6 months = 51.9%
Patient Adherence and Persistence

- Over 90% of patients are nonadherent
  - Adherence: The prevalence of use of the initial medication at various time points
- Nearly 50% of patients are not persistent
  - Persistence: Continuous treatment with initially prescribed medication

Majority of glaucoma patients have trouble staying **committed** to their prescription regimens

Common Reasons for Noncompliance

- Complicated prescription regimens
- Polypharmacy
- Medication costs
- Unpleasant side effects
- Not following appropriate dosing instructions
  - Too much medication
  - Too little medication
  - Waiting 5 minutes between applications of different medications
- Inability to correctly apply drops, independently


SLT Best Practices

Consensus on SLT Therapy
Appropriate Patient Types

**Patient type:**
- Selective laser trabeculoplasty is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma (OAG)
- Highest success rate when used as primary therapy
- Effective results as adjunctive therapy
  - Patients on medications who need further IOP control
- Effective results as replacement therapy
  - Patients with controlled IOP who want to reduce medications
- Success rate tends to decrease when performed later in the glaucoma treatment algorithm (as with all therapies)

Laser Settings and Contact Placement

**Laser settings:**
- Duration: 3 nanoseconds (preset)
- Spot Size: 400 microns (preset)
- Energy: 1.0 mJ/pulse
- Aim to cover angle (not on iris)
- Plan to treat 360 degrees (100 applications total or 25/quadrant)

**Contact placement:**
- NO (1X) magnification
  - Latina SLT
  - Goldmann 3 mirror
  - Ritch (small x mirror)
- Changes in magnification will alter beam diameter and energy
SLT Therapy Procedures

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

Therapy energy level:
  - Starting at .4 to .8 millijoules
  - Titrate energy per angle pigment and treatment effect

Pigmentary glaucoma cases need to be treated conservatively:
  - Degrees: 90°
  - Energy: 0.4 millijoules

Therapy endpoint:
  - “Champagne bubbles”

Recommended SLT Pre- and Post-Therapy

Pre-therapy medications:
  - Depends on physician preference
    - NSAID (recommended)
    - Nothing
    - Do not use a steroid (recommended)

Post-therapy medications:
  - Depends on physician preference
    - Patients may not need medications based on specific patient comfort
    - One drop of brimonidine (0.2% or 0.15%)
    - One drop of NSAID immediately after surgery; 1–2 drops on the next day if needed (mostly to ease patients’ minds about mild irritation)
    - Do not use a steroid (recommended)
### SLT Patient Follow-up

**Patient follow-up:**
- One hour after therapy to check IOP
- Two weeks after therapy to check IOP reduction
- One month after therapy to check for target IOP reduction
  - It may take up to 3 months after therapy to reach individual target IOP reductions (advised to wait before switching to new therapy)

### SLT Treatment Pearls

**Narrow angle, poor visibility of TM:**
- Patient looks towards treating mirror
- Pilocarpine preoperatively
- Penlight to fellow eye (consensual pupil response)
- Laser PI or iridoplasty

**Corneal epithelial injury:**
- Use artificial tear gel instead of goniosol

**Severely anxious patient:**
- Identify prior to laser treatment
- Oral sedation
  - Alprazolam (Xanax) 0.5mg
Conclusions

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