Safety and Efficacy of SLT as Primary Therapy
Ellex Nanopulse Laser Innovations Symposium

Carlo Lovisolo, MD
Quattroelle Custom Eye Clinics
Milan, Italy
Medical therapy quite effective, but critically relies on regular & proper administration of drugs

Quigley’s land-mark studies
While patients self-reported a 95% adherence, objective methods showed that only 55% of them were taking more than 75% of the prescribed dose of medications.… 45% of patients were not taking three-quarters of their drops or more”


Dreer LE, Girkin C, Mansberger SL. Determinants of medication adherence to topical glaucoma therapy J Glaucoma 2012 Apr-May;21(4):234-40


Sherwood’s 4 Hurdles to Achieving Adherence to a Medication Regimen

1. **Acceptance** – > 50% have no visual symptoms at all

2. **Compliance** – requires a change in life-style

3. **Persistence** – very long term

4. **Execution** – difficulties in administering drops


Normal psychological reaction: > 80% reported negative feelings after learning they have glaucoma

Old patients: 9 out of 10 Unable to Instill their Drops Correctly…

Young patients?

Telematic generation: although reminder apps are available for smartphones to schedule glaucoma medications, 38% still miss a dose at least once a week

(Lovisolo C. unpublished data)
25% experienced adverse effects of moderate or high intensity

- Bronchospasm - asthma
- Bradycardia, arrhythmia
- Masked hypoglycemia in IDDM
- Elevated serum lipids
- Drowsiness, fatigue
- Depression
- Nocturnal hypotension
- Shortness of breath
- Reduced libido

- α-adrenergic agonists
- Burning, stinging, fatigue
- Headache, drowsiness, dry mouth
- Allergy
- Hypo-or hypertension
- Fatigue
- Sleepiness
- Dry mouth/nose
- Apnea/bradycardia in children
- Changes in eye color and eyelid skin
- Stinging, eye redness, itching, burning
- Growth & increased thickness of eyelashes
- Blurred vision
- Hypertension
- Chest « tightness »

- J-Blockers
- Eye drops
  - Stinging, burning, eye discomfort
  - Bitter taste

- Prostaglandin analogues
  - Tingling hands and feet
  - Stomach upset, nausea
  - Memory problems, depression
  - Frequent urination, kidney stones
  - Bone marrow depression, thrombocytopenia
  - Haemolytic anemia, leucopenia

- CA Inhibitors
- Pills
  - Tingling hands and feet
  - Stomach upset, nausea
  - Memory problems, depression
  - Frequent urination, kidney stones
  - Bone marrow depression, thrombocytopenia
  - Haemolytic anemia, leucopenia
SLT as Primary Therapy

SLT interesting alternative, particularly as primary therapy in OHT & POAG

<table>
<thead>
<tr>
<th>Interval</th>
<th>Cumulative Probability of Success</th>
<th>Incidence of 1st Repeat SLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>97%</td>
<td>3%</td>
</tr>
<tr>
<td>2 years</td>
<td>95%</td>
<td>3%</td>
</tr>
<tr>
<td>3 years</td>
<td>93%</td>
<td>2%</td>
</tr>
<tr>
<td>4 years</td>
<td>85%</td>
<td>8%</td>
</tr>
<tr>
<td>5 years</td>
<td>82%</td>
<td>4%</td>
</tr>
<tr>
<td>6 years</td>
<td>72%</td>
<td>1%</td>
</tr>
<tr>
<td>7 years</td>
<td>52%</td>
<td>3%</td>
</tr>
<tr>
<td>8 years</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interval</th>
<th>Cumulative Probability of Success</th>
<th>Incidence of 1st Repeat SLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>2 years</td>
<td>54%</td>
<td>25%</td>
</tr>
<tr>
<td>3 years</td>
<td>41%</td>
<td>25%</td>
</tr>
<tr>
<td>4 years</td>
<td>34%</td>
<td>17%</td>
</tr>
<tr>
<td>5 years</td>
<td>30%</td>
<td>12%</td>
</tr>
<tr>
<td>6 years</td>
<td>24%</td>
<td>19%</td>
</tr>
<tr>
<td>7 years</td>
<td>24%</td>
<td>0%</td>
</tr>
<tr>
<td>8 years</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Lawrence F. Jindra, Columbia University, Winthrop University Hospital – results presented at Venezuelan Congress of Ophthalmology, July 2012 – analysis of nearly 4,000 treated eyes over more than 10 years
High Safety Profile ("Primum Non Nocere")

- Excellent Risk profile
  - selective absorption of laser energy by pigmented chromophores in TM prevents thermal damage seen with ALT
- No Acceptance, Compliance, Execution issues
- Minimal side effects
  - Mild inflammation common, 1 hr after SLT, decreasing by day 1, resolving in all cases 3-5 days with NSAI drops
  - Mild ocular discomfort in 1/3 of eyes, resolving by day 1
  - IOP spike (>5 mmHg) rare (<5% of eyes) 1 hr after SLT, resolved with medication


- Positive psychological reaction to SLT
  - Most of treated patients "felt" some improvement

Efficacy of SLT as Primary Therapy

Expect:

- 30-35% IOP reduction from baseline
  - Relationship between eye pigment and ↓ IOP
- equivalent to ALT, even in younger patients
- equivalent to medical therapy in pressure-lowering capability
- the higher baseline IOP, the better the result
- I have not found that pre-treatment with prostaglandins ↓ effect
Efficacy of SLT as Primary Therapy

Expect

- a decrease of diurnal fluctuations of IOP

- ~90% success rate at 1 year

- Safe/effective combo with adj drug: 20-30% ↓ IOP

- 70-85% response rate at 1 year

- may delay surgical option

- safe & effective (?) use after ALT or surgery
**SLT is Repeatable**

**Results**

<table>
<thead>
<tr>
<th>Interval</th>
<th>Cumulative Probability of Success</th>
<th>Incidence of 2nd Repeat SLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>98%</td>
<td>2%</td>
</tr>
<tr>
<td>2 years</td>
<td>96%</td>
<td>3%</td>
</tr>
<tr>
<td>3 years</td>
<td>70%</td>
<td>27%</td>
</tr>
<tr>
<td>4 years</td>
<td>47%</td>
<td>33%</td>
</tr>
<tr>
<td>5 years</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>6 years</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interval</th>
<th>Cumulative Probability of Success</th>
<th>Incidence of 2nd Repeat SLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>94%</td>
<td>6%</td>
</tr>
<tr>
<td>2 years</td>
<td>85%</td>
<td>9%</td>
</tr>
<tr>
<td>3 years</td>
<td>70%</td>
<td>18%</td>
</tr>
<tr>
<td>4 years</td>
<td>50%</td>
<td>28%</td>
</tr>
<tr>
<td>5 years</td>
<td>27%</td>
<td>46%</td>
</tr>
<tr>
<td>6 years</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Lawrence F. Jindra, M.D.,** Columbia University, Winthrop University Hospital

Presented at the Venezuelan Congress of Ophthalmology, July 2012
SLT does not prevent application of future treatments

Better Surgical Outcome Expected

Filtering Operations

- Long-term topical medication:
  a risk factor for postop scarring after trab


- Prostaglandin analogues induce collagen contraction


Canaloplasty

- Uneasy pass thru scarred Schlemm Canal after ALT

- after SLT, no additional risks
SLT = Flexible Approach

SLT works on different open angle types of glaucoma

- effective in various population types (Asia, Latin America, Europe, Middle East, Africa…)
- POAG & Pseudoexfoliation glaucoma (PEXG)
  - Equally effective
- Pigmentary Glaucoma
  - SLT effective but lower duration of ↓ IOP
Normal Tension Glaucoma

- Low IOP reduction but nice stabilization
  El Mallah MK et al. SLT reduces mean IOP and IOP variation in normal tension glaucoma patients *Clin Ophthalmol* 2010; 4:889-93

POAG refractory to medical therapy

- Effective in avoiding further surgery
  Babighian S et al: Excimer laser trabeculotomy vs SLT in POAG. A 2-year controlled trial. Eye (Lond) 2010 Apr; 24:632-8

Silicone Oil-related Glaucoma (Uveitis?)

- Effective
  Vukosavljevic M et al: Belgrade, Serbia (unpublished data)

Iatrogenic ↑ IOP (Steroid Responders)

- Effective in preventing / treating IOP raise
  Yuki K et al: SLT for elevated IOP following subtenon injection of acetonide *Clin Ophthalmol* 2010 Apr 26;4:247-9
Distinct Individual and Societal economic advantages

5-year cumulative costs:

- **SLT** = $4,838
- **Medication** = $6,571
- **Surgery** = $6,363


Assumed 2 year repeat rate, 6 year cumulative saving vs.

- Monotherapy $ 206.54
- Dual therapy $1,668.64
- Triple therapy $2,992.67

SLT in local comorbidities?

- **dry eye**: ocular surface disease real issue with topical therapy
- A diminishment of **conj scarring** helpful for future success of surgery
- Efficacy affected by **cataract** surgery? Apparently not...


### Table 2 Percentage of IOP reduction following SLT

<table>
<thead>
<tr>
<th>Percentage of IOP reduction following SLT</th>
<th>Phakic group (n = 18)</th>
<th>Pseudophakic group (n = 76)</th>
<th>t-test P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>At 2 weeks</td>
<td>27.4</td>
<td>11.5</td>
<td>19.8</td>
</tr>
<tr>
<td>At 3 months</td>
<td>29.8</td>
<td>13.1</td>
<td>26.5</td>
</tr>
<tr>
<td>At 6 months</td>
<td>28.0</td>
<td>13.4</td>
<td>24.3</td>
</tr>
<tr>
<td>At 9 months</td>
<td>27.7</td>
<td>13.1</td>
<td>23.2</td>
</tr>
<tr>
<td>At 12 months</td>
<td>27.4</td>
<td>13.5</td>
<td>22.5</td>
</tr>
<tr>
<td>At 18 months</td>
<td>26.2</td>
<td>13.3</td>
<td>22.8</td>
</tr>
<tr>
<td>At 30 months</td>
<td>27.3</td>
<td>12.9</td>
<td>25.9</td>
</tr>
</tbody>
</table>

**Note:** "Statistically significant difference at P < 0.05.
**Abbreviations:** IOP, intraocular pressure; SD, standard deviation; SLT, selective laser trabeculoplasty.
SLT in Systemic Co-morbidities?

**Advantage**: No worries about potential influence on comorbidity

Statistical correlations of POAg & PEXG with:
- Reduced life expectancy
- Cardiovascular diseases
  - arterial hypertension / hypotension
  - heart arrhythmia
  - silent myocardial ischemia
- Thyroid Disorders (Hyper/Hypo)
- Diabetes
  - SLT less effective
- Alzheimer disease
- Hypoacusis
- Obstructive Sleep Apnea Syndrome
- Reduced pulmonary function
  - Asthma

Topical β-blocker: ±90% systemic absorption; 1 drop 0.50% Timolol = 10 mg per os

β-Blockers
- Bronchospasm - asthma
- Bradycardia, arrhythmia
- Elevated serum lipids
- Masked hypoglycemia in IDDM
- Drowsiness, fatigue
- Depression
- Nocturnal hypotension

ALL Combination drugs contain β-blocker!

α-adrenergic agonists
- Systemic hypo-or hypertension
- Fatigue
- Sleepiness
- Dry mouth
- Apnea in children
- Bradycardia in children

Prostaglandin analogues
- Hypertension
- Chest « tightness »

CA Inhibitors
- Paresthesia
- Anaphylaxis
- GI disturbance, nausea
- Kidney stones
- Bone marrow depression
- Thrombocytopenia
- Hemolytic anemia
- Leucopenia
- Nephrolitiasis (topical)
- Allergy (topical)
- Bitter taste (topical)
Pregnancy great indication for SLT

Brimonidine? NO
Prostaglandin analogues? NO
Topical & systemic CAI? NO
Myotics? NO
β-blockers? NO (only selective betaxolol)
“In a busy refractive clinic, patients are younger, more affluent and more active than the average glaucoma patient”

“The Baby Boomer generational segment is getting older, but keeps on being confident, independent, self-reliant, and goal-oriented. They welcome exciting, challenging projects”

“In a competitive clinical environment, economic success in a practice is largely dependent on the ability to offer innovative, appealing treatments that guarantee the highest level of care at a reasonable cost”
SLT in My Practice

- “As our mission, at Quattroelle, we individualize every treatment to impact our patient’s quality of life”
- “Provide glaucoma management tailored to the individual needs of the patients” (EGS Guidelines, 2008)
- “SLT as an alternative to medication for primary treatment fits perfectly and is highly welcome among my patient cohort”
- “Almost everybody, even glaucoma patients who have good IOP on medications are candidates for SLT”

SLT/YAG in My Practice

- Beauty of Ellex Tango™ laser
  - switch between SLT/YAG at the touch of a button
  - unsurpassed photodisruptor
    - vitreous floaters, retina disease
  - complies with all international regulations

- The number of treatments are constantly growing

- In the easy forecast of growth of non-medical, minimvasive options

SLT will remain a proven, well-tested friend
Thank You so much for Attention

Ellex Nanopulse Laser Innovations Symposium

Carlo Lovisolo, MD
Quattroelle Custom Eye Clinics
Milan, Italy