Selective Laser Trabeculoplasty (SLT)

Merits and Mechanisms

Prof. S. Melamed
Background and Rationale for SLT

• Lasers have a long history of use in the management of glaucoma

• Argon laser trabeculoplasty (ALT) was initially utilized in patients who failed medical therapy

• Glaucoma Laser Trial (GLT) established efficacy of ALT in lowering IOP in primary open-angle glaucoma patients
Background and Rationale for SLT

- Limitations of ALT
  - Post-treatment increase in IOP; PAS
  - Limited efficacy of ALT re-treatment
  - Coagulative damage to the trabecular meshwork; may limit efficacy of further non-surgical therapy
- Selective laser trabeculoplasty (SLT) developed as an alternative to ALT
Selective Laser Trabeculoplasty

- A treatment for Open Angle Glaucoma
- Q-Switched frequency doubled (532 nm) Nd:YAG Laser
- Permits selective targeting of pigmented trabecular meshwork cells without causing structural or coagulative damage to the TM
Trabecular Meshwork

- Cellular and Structural Components
- TM cells are phagocytic and contain variable amounts of melanin
- ALT induces focal scarring and coagulation damage with reduced flow through the lasered site
Trabecular Meshwork
Argon Laser Coagulation of TM
TEM 1 hr after ALT
TEM – enhanced phagocytosis
4 weeks after ALT (monkey)
SEM - 4 weeks after ALT
ALT – induced trabeculitis
ALT – scarred lasered region
ALT – non lasered region (ferritin)
ALT - Biological effects

- Increased phagocytic activity of TM cells
- Induced "trabeculitis"
- Shift of aqueous flow
- Up – regulation of mmp’s
However, You do not need the “Over-Kill” of ALT in order to induce biological enhancement of the TM…

A more gentle Rx of Pigmented Cells alone will achieve similar effects!
To Achieve Selective Targeting of TM Cells

• Scheme of Selective Photothermolysis
  – Requirements
    • Intracellular target chromophore - MELANIN
    • Targets must absorb laser energy better than surrounding tissues
    • Short Laser Pulse to generate and confine heat
  – Only pigmented cells within the irradiation zone will be targeted
Mixture of Pigmented and Non-pigmented TM cells

M. Latina, M.D.
TM Cells
post 532 Nd:YAG pulse

M. Latina, M.D
TM Cells
532 Nd:YAG pulse -fluorescence

M. Latina, M.D
TM Cells
Argon Laser 0.1 sec pulse

M. Latina, M.D
SLT – intracellular pigment targeting

M. Latina, M.D
SLT
Selective Rx of Melanin – containing trabecular cells only.

• No coagulative necrosis
• Induced synthesis of IL – 1 alpha and beta
• Recruitment of macrophages
Mechanisms of SLT

- Recruitment of macrophages (large, blue) that remove cellular debris and extra-cellular melanin from the meshwork.\(^4\)

- Macrophages stimulate the release of cytokines (small, blue/yellow), which:\(^3\)
  - Induce cell division
  - Up-regulate synthetic metalloproteinases
  - Increase the porosity of the endothelial layers of the trabecular meshwork and Schlemm’s canal
  - Stimulate re-synthesis of the extra-cellular matrix

ALT spot vs. SLT spot size

Courtesy M. Berlin, M.D.
Human TM

ALT

SLT

R. Noecker, T. Kamm
## Comparison of SLT vs ALT

<table>
<thead>
<tr>
<th></th>
<th>SLT</th>
<th>ALT</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of spots</td>
<td>50</td>
<td>50</td>
<td>1:100</td>
</tr>
<tr>
<td>Energy</td>
<td>0.8-1.4 mj</td>
<td>400-600 mw</td>
<td>1:6000</td>
</tr>
<tr>
<td>Fluence (mj/mm²)</td>
<td>6</td>
<td>40,000</td>
<td></td>
</tr>
<tr>
<td>Exposure Time</td>
<td>3 nsec</td>
<td>0.1 sec</td>
<td></td>
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</table>
SLT compared to ALT

Spot size comparison:

<table>
<thead>
<tr>
<th></th>
<th>ALT</th>
<th>SLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spot Size</td>
<td>50 micron</td>
<td>400 micron</td>
</tr>
<tr>
<td>Energy Output</td>
<td>500 – 1,000 mW</td>
<td>0.8 – 1.5 mJ</td>
</tr>
<tr>
<td>Pulse Duration</td>
<td>10 ms</td>
<td>3 ns</td>
</tr>
<tr>
<td>Fluence</td>
<td>60,000 mJ/cm²</td>
<td>600 mJ/cm²</td>
</tr>
</tbody>
</table>

*Latina MA, Tumbocon JA. Selective Laser Trabeculoplasty: The Evolution of Laser Treatment for Open Angle Glaucoma
Alternative to ALT

Clinical Trial Results Comparing IOP reduction between SLT and ALT

\[\text{IOP mm Hg}\]

\[\text{Week}\]

\[\text{SLT}\]

\[\text{ALT}\]

## SLT – Clinical Experience

<table>
<thead>
<tr>
<th>Study</th>
<th>no. of patients</th>
<th>IOP reduction</th>
<th>FU time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latina et al</td>
<td>120 MTMT + s/p ALT</td>
<td>17.10%</td>
<td>26 w</td>
</tr>
<tr>
<td>Howes</td>
<td>107 MTMT</td>
<td>20%</td>
<td>11 m</td>
</tr>
<tr>
<td>Damji</td>
<td>118 MTMT</td>
<td>6.5 mmHg</td>
<td>24 m</td>
</tr>
<tr>
<td>Larsson</td>
<td>60 MTMT</td>
<td>6.2 mmHg (24%)</td>
<td>6 m</td>
</tr>
</tbody>
</table>
SLT – Other Studies

* 90 deg. is as effective as 180 deg. Rx (Chen et al. 2004)

* 5 year FU of Chinese patients – SLT is equal to medical Rx (Lai et al., 2004)

* SLT as effective as ALT, but associated with less inflammation and better tolerated by patients (Martinez de la Casa et al., 2004)
Alternative to ALT

- SLT is equivalent to ALT in lowering intraocular pressure (IOP) at all time points.
- For patients on maximally tolerated medical therapy and baseline IOP of 24mm Hg, you can expect a sustained reduction in IOP of 22% (6mm Hg).
- Over 70% of patients respond.
SLT Patient Selection

- Open Angle Glaucoma
  - Primary Open-Angle Glaucoma
  - Ocular Hypertension
  - Pigmentary Glaucoma
  - Pseudo-exfoliative glaucoma
- Poorly compliant to drug therapy
- Intolerant or unresponsive to drug therapy
- Failed ALT
- Patients currently undergoing drug therapy who wish to use SLT in conjunction with glaucoma medications
- Post-filtration surgery patients requiring additional treatment
SLT Treatment Regime

Approximately 50 confluent spots are applied during the procedure in order to treat a 180° angle.
SLT Treatment Regime
Efficacy of SLT (Damji et al., 2003)
SLT – Clinical Experience

• In all studies only minor complications reported such as:
  – IOP spikes (in 3-11%)
  – Limited AC reaction

• No PAS formation!
Why should we use SLT as a primary treatment in Glaucoma?...
Reasons:

- GLT study supports ALT as primary Rx
- SLT is effective in MTMT and even post ALT patients
- SLT is extremely safe
- SLT may be repeated more than twice
- Avoiding side effects and cost of chronic drug use
Selective Laser Trabeculoplasty (SLT) as Primary Treatment in Open Angle Glaucoma

Shlomo Melamed, Guy J. Ben Simon & Hana Levkovitch-Verbin

The Sam Rothberg Glaucoma Center
Goldschleger Eye Institute, ISRAEL
SLT – its use as a primary treatment in Open Angle Glaucoma and OHT

A pilot study of 45 eyes
Inclusion criteria

- IOP $\geq 23$ mmHg
- Newly diagnosed cases (OAG and OHT)
- History of single topical anti-glaucoma medication (discontinued)
- No previous intra-ocular surgery or laser
- All patients signed an informed consent
Methodology

• IOP measurements, SLE before and after SLT (1h, 1d, 1w, 1m, 3m, 6m, 12m, 15m, 18m, 2y)
• Visual Acuity, gonioscopy and Visual Field analysis (Humphrey 24-2) before, 6 mo and 1 yr after SLT
Selective Laser Trabeculotherapy
Treatment Procedure

• 180 degrees (nasal)
• Average 50 spots
• Starting pulse energy 0.8 mJ (0.6-1.2 mJ)
• Endpoint: mini-bubbles or no visible effect
• No pre or post-op medications
• NO Iopidine pre-treatment
Patients Demographics

- 31 patients, 14 bilateral SLT (45 eyes)
- Age 54±10 yrs (32-76)
- Diagnosis: POAG 66.3%, PXFG 10.6%, PDG 6.4%, NTG 4.3%, OHT 12.8%
Results

- Mean FU time - 11±5.3 months (41/45 patients longer than 6 months)
- Pre SLT IOP – 25.6 ±2.5 mmHg
- Post SLT IOP – 17.9 ±2.8 mmHg
- Mean IOP decrease – 7.7 ±3.5 mmHg (30%)
- VA, gonioscopy and VF remained unchanged
## Extent of IOP reduction

<table>
<thead>
<tr>
<th>IOP Reduction (mmHg from Baseline)</th>
<th>(N=45) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>2 (4.4%)</td>
</tr>
<tr>
<td>&gt;2 to 4</td>
<td>3 (6.7%)</td>
</tr>
<tr>
<td>≥5</td>
<td>40 (88.9%)</td>
</tr>
</tbody>
</table>
Complications

- Conjunctival redness and injection (1 day) – 66%
- Ocular discomfort (1 day) – 58%
- IOP rise above 5 mmHg (1 hour) – 11%
- IOP rise between 2 and 5 mmHg (1 hour) – 6.7%
Interestingly…

• IOP reduction over 5 mmHg within 1 hour was detected in 33% of eyes

• Mechanism?…
  – Mechanical effect of photodisruption
  – Early recruitment of inflammatory mediators
SLT as initial and adjunctive study for OAG

McIlraith et al., J Glaucoma, 2006

* Prospective, Multi-Center, Non-Randomized Study
* Newly diagnosed OAG assigned to Primary SLT or Latanoprost
* Similar effect of SLT as Latanoprost
* 30% IOP reduction in both groups!!
SLT vs. latanoprost

147 patients / eyes

- Newly diagnosed
- Medically controlled then washed out

- **SLT 90, 180, 360**

<table>
<thead>
<tr>
<th></th>
<th>SLT 90</th>
<th>SLT 180</th>
<th>SLT 360 (n=44)</th>
<th>Latanoprost (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year response rate 20%</td>
<td>34%</td>
<td>65%</td>
<td>82%</td>
<td>90%</td>
</tr>
<tr>
<td>p vs. latanoprost</td>
<td>&lt;.001</td>
<td>&lt;.01</td>
<td>&lt;0.5</td>
<td></td>
</tr>
</tbody>
</table>

Nagar et al. 2005
SLT/MED initial results

- 94 eyes (47 patients) virgin
- SLT vs. meds
  - SLT 360 – 180 -180 – meds
  - Lipids – β-blocker – Brimonidine - CAI

<table>
<thead>
<tr>
<th></th>
<th>SLT</th>
<th>Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>58</td>
<td>36</td>
</tr>
<tr>
<td>IOP decrease</td>
<td>6.7</td>
<td>7.6</td>
</tr>
<tr>
<td>Treatment changes</td>
<td>1.1</td>
<td>1.3</td>
</tr>
</tbody>
</table>
Cost effectiveness of SLT

- Ontario Health Insurance Plan
- Assumed 2 year repeat rate
  - SLT $373.98
- 6 year cumulative saving vs.
  - Monotherapy $206.54
  - Dual therapy $1,668.64
  - Triple therapy $2,992.67

Lee 2006
Conclusions

- SLT is safe and effective
- SLT can be used as a primary treatment modality in OAG or OHT
- Only a randomized, multi-center study comparing SLT with medical therapy as primary treatment in glaucoma will provide a more definitive role for SLT in such patients.