Potential Treatment for Cognitive Dysfunction using Transcranial Laser / Light Emitting Diodes

Margaret Naeser, Ph.D., L.Ac.

Neuroimaging in Aphasia, and Transcranial Magnetic Stimulation to Treat Aphasia
VA Boston Healthcare System

Harold Goodglass Boston University Aphasia Research Center
Department of Neurology
Boston University School of Medicine

Four Parts to this Lecture

1. **Laser Basics**, including some **Cellular Effects**

2. **Case Report**, Transcranial LEDs to Treat Cognitive Dysfunction in Chronic TBI

3. Previous Research: Low-Level Laser Therapy (Acupuncture) to treat
   *Paralysis in stroke*;
   and *Pain in Carpal Tunnel Syndrome*

4. Two Studies where Low-Level Laser Therapy was used to treat *Fibromyalgia*

Naeser, RAC-GWI Presentation, 6-30-09
Endre Mester, M.D., Budapest, Hungary, early 1960’s. Father of Low-Level Laser Therapy, especially known for studies of red-beam, HeNe laser for treatment of non-healing wounds.

Part 1. Laser Basics
Sample gallium arsenide laser diode. Naeser Lecture Notes®

Laser light has photons that are monochromatic and coherent.

Laser Wavelengths (nm), and Depth of Laser Penetration

Fig. 1 Transmission in skin. Approximate skin transmission depth at which the incident radiant exposure has decreased by 90%. The transmission depth for a 99% decrease can be calculated by doubling the corresponding 90% depth. Data shown are for fair Caucasian skin. Graph drawn from data presented in [29].

How to Calculate the Number of Sec. Required to Produce 1 Joule of Energy

Three variables are listed below which you must know about a specific laser, before using it. You will also need to know the beam spot size in cm², which is explained later.

1. **The wavelength, in nanometers (nm, one billionth of a meter).** For "laser acupuncture," the wavelength is usually in the red-to-infrared range of 600-1,000 nm. Otherwise, the hemoglobin or water may block the laser beam. The laser manufacturer supplies information on the nm wavelength for each laser.

2. **The number of watts, or milliwatts (mw).** Usually only 5 or 500 mw (always less than 500 mw). If the laser is greater than 500 mw, it will cause an "ouch" response, and will burn the skin. The laser manufacturer supplies information on the number of milliwatts for each laser.

3. The number of seconds exposure = 1 joule of energy (A “joule” is a unit of work energy - for example, the energy expended by a current of 1 ampere flowing for 1 second through a resistance of 1 ohm.)

Some low-level laser research or clinical papers are published showing only the number of Joules (J) used, per point on the skin. **It is better, however, to know treatment protocols in J/cm², per point, or per cm² on the skin,** as is explained on additional pages in this handout. When J/cm² is calculated for a specific laser, the beam spot size must also be known (in cm²). It is important, however, to understand the basic concept of Joule, or unit of work energy.
### Energy Density Dosages (Joules/cm²) for Various Treatment Effects

- **Analgesic effect**: Muscular pain —— 2 to 4 joules/cm²  
  Joint pain —— 4 to 8 joules/cm²
- **Anti-inflammatory effect**: Acute and subacute 1 to 6 joules/cm²  
  Chronic —— 4 to 8 joules/cm²
- **Eutrophic effect**: —— 3 to 6 joules/cm²
- **Circulatory effect**: —— 1 to 3 joules/cm²

---


---

For a 5 mW laser, it takes **200 Sec**. to produce 1 Joule of energy.

Why beam spot size, cm², is important:

<table>
<thead>
<tr>
<th>Laser Aperture</th>
<th>1 Joule = 200 Sec</th>
<th>1 Joule = 200 Sec</th>
<th>1 Joule = 200 Sec</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diameter</strong></td>
<td>1.14 cm</td>
<td>.5 cm</td>
<td>.1 cm</td>
</tr>
<tr>
<td><strong>Radius</strong></td>
<td>.57</td>
<td>.25</td>
<td>.05</td>
</tr>
<tr>
<td><strong>Beam Spot Size</strong></td>
<td>1.02 cm²</td>
<td>0.196 cm²</td>
<td>0.0078 cm²</td>
</tr>
<tr>
<td></td>
<td>( \pi (3.14) \times r^2 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1 J/cm² = cm²/W</strong></td>
<td>1.02 cm²/0.005</td>
<td>0.196 cm²/0.005</td>
<td>0.0078 cm²/0.005</td>
</tr>
<tr>
<td><strong>1 J/cm²</strong></td>
<td>204 Sec</td>
<td>39.2 Sec</td>
<td>1.56 Sec</td>
</tr>
<tr>
<td><strong>Used for 200 Sec</strong></td>
<td>200/204 = .98 cm²</td>
<td>200/39.2 = 5.1 J/cm²</td>
<td>200/1.56 = 128.2 J/cm²</td>
</tr>
</tbody>
</table>
For a 500 mW laser, it takes 2 Sec. to produce 1 Joule of energy.

Why beam spot size, cm², is important:

<table>
<thead>
<tr>
<th>Laser Aperture</th>
<th>1 Joule = 2 Sec</th>
<th>1 Joule = 2 Sec</th>
<th>1 Joule = 2 Sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>1.14 cm</td>
<td>.5 cm</td>
<td>.1 cm</td>
</tr>
<tr>
<td>Radius</td>
<td>.57</td>
<td>.25</td>
<td>.05</td>
</tr>
<tr>
<td>Beam Spot Size</td>
<td>1.02 cm²</td>
<td>0.196 cm²</td>
<td>0.0078 cm²</td>
</tr>
<tr>
<td>[(3.14) \times r^2]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 J/cm² = (\frac{cm^2}{W})</td>
<td>1.02 cm²</td>
<td>0.196 cm²</td>
<td>0.0078 cm²</td>
</tr>
<tr>
<td>1 J/cm²</td>
<td>2.04 Sec</td>
<td>.392 Sec</td>
<td>.0156 Sec</td>
</tr>
<tr>
<td>Used for 2 Sec.</td>
<td>2/2.04 =</td>
<td>2/.392 =</td>
<td>2/.0156 =</td>
</tr>
<tr>
<td></td>
<td>.98 J/cm²</td>
<td>5.1 J/cm²</td>
<td>128.2 J/cm²</td>
</tr>
</tbody>
</table>

Naeser Lecture Notes®


**Table 1. Cellular Effects of Low-energy Laser Irradiation (Blackard, 1992)**

<table>
<thead>
<tr>
<th>Phenomenon</th>
<th>Change and reported</th>
<th>Model</th>
<th>Laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen and protein synthesis</td>
<td>Increase &amp; decrease</td>
<td>Human fibroblasts, muscle, human skin, bony cartilage</td>
<td>NaN</td>
</tr>
<tr>
<td>Cell proliferation</td>
<td>Increase &amp; decrease</td>
<td>Mouse fibroblasts, human fibroblasts</td>
<td>NaN</td>
</tr>
<tr>
<td>Cell morphology</td>
<td>Increase</td>
<td>Human muscle</td>
<td>NaN</td>
</tr>
<tr>
<td>Cell death</td>
<td>Increase</td>
<td>Human skin</td>
<td>NaN</td>
</tr>
<tr>
<td>Cell migration</td>
<td>Increase</td>
<td>Rat laser microtensiometers, human fibroblasts</td>
<td>NaN</td>
</tr>
<tr>
<td>Cell signaling</td>
<td>Increase</td>
<td>Human lymphocytes and fibroblasts</td>
<td>NaN</td>
</tr>
<tr>
<td>Neurotransmitter release</td>
<td>Increase</td>
<td>Human lymphocytes</td>
<td>NaN</td>
</tr>
<tr>
<td>Oxygenation</td>
<td>Increase</td>
<td>Human lymphocytes</td>
<td>NaN</td>
</tr>
<tr>
<td>A TP synthesis</td>
<td>Increase</td>
<td>Rat laser microtensiometers</td>
<td>NaN</td>
</tr>
<tr>
<td>Intervalocorticis</td>
<td>Increase</td>
<td>Mice retina</td>
<td>NaN</td>
</tr>
<tr>
<td>Propagation of synthesis</td>
<td>Increase</td>
<td>Rat retina</td>
<td>NaN</td>
</tr>
</tbody>
</table>

---

**RELIEF FROM CHRONIC PAIN BY LOW POWER LASER IRRADIATION**

J. WALKER

_The Pain Institute, 1904 Waxwood Boulevard, Suite 230, Los Angeles, CA 90025 (U.S.A.)_ (Received September 5th, 1983; Revised version received October 13th, 1983; Accepted October 17th, 1983)

**Key words:** chronic pain - serotonin metabolism - helium-neon laser - 5-hydroxytryptamine acid

**SUBJECTS EXPERIENCING PAIN RELIEF AS A RESULT OF LASER TREATMENT**

<table>
<thead>
<tr>
<th>Experimental <em>t</em> number</th>
<th>% of pain relief</th>
<th>Experiment</th>
<th>No. of sessions</th>
<th>Pain relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigeminal neuralgia</td>
<td>66%</td>
<td>7</td>
<td>8</td>
<td>85%</td>
</tr>
<tr>
<td>Post-hypoxic neuralgia</td>
<td>50%</td>
<td>2</td>
<td>2</td>
<td>60%</td>
</tr>
<tr>
<td>Osteoarthritic</td>
<td>50%</td>
<td>5</td>
<td>5</td>
<td>72%</td>
</tr>
<tr>
<td>Radicular</td>
<td>33%</td>
<td>6</td>
<td>4</td>
<td>72%</td>
</tr>
<tr>
<td>Diabetic neuropathy</td>
<td>33%</td>
<td>3</td>
<td>3</td>
<td>82%</td>
</tr>
<tr>
<td>26</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trigeminal neuralgia</td>
<td>50%</td>
<td>3</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>Post-hypoxic neuralgia</td>
<td>25%</td>
<td>2</td>
<td>3</td>
<td>8%</td>
</tr>
<tr>
<td>Osteoarthritic</td>
<td>11%</td>
<td>3</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Radicular</td>
<td>11%</td>
<td>1</td>
<td>3</td>
<td>12%</td>
</tr>
<tr>
<td>19</td>
<td>65</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A 6 month follow-up of the patients indicated that 15 of the 19 originally pain-free patients were pain-free via pain scale estimate [8, 9] without additional treatment. Analgesic use was virtually eliminated. Confirmation of these results is under...
FIG. 8. Action and absorption spectra in the far red and near infrared range for oxidized cytochrome c oxidase (15), relative cytochrome c oxidase activity, and relative ATP content in TTX-treated neurons exposed to LED treatments at different wavelengths expressed as percentages of controls (present study). Note the correspondence of effective wavelengths (especially 670 and 830 nm) with the absorption spectrum of oxidized cytochrome c oxidase and the non-correspondence of the least effective wavelength (728 nm).

Wong-Riley et al., J. Biological Chemistry, 2005
Low-Level Laser Therapy (LLLT), 1.4 J/cm² of 810 nm IR light delivered at 10 mW/cm² has bigger effect in increasing ATP in hypoxic cells (1 hour under N₂)

A. Mean luminescence values (+/- SD) from 12 wells of HeLa cells (a human cervical cancer cell line often used to demonstrate LLLT effects) treated or not with 1.4 J/cm² of 810 nm light in either normoxic conditions (regular atmosphere) or hypoxic conditions (1 hour exposure to pure nitrogen after 3 cycles of vacuum).

B. Ratio of ATP in illuminated, compared to dark wells, as described in A.

Michael Hamblin, Ph.D., R.Rox Anderson, M.D., Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA

Effect of red or near IR light on cellular respiration, oxygenation

Explains why:
Normal cells and tissue generally do not respond
Hypoxic cells, damaged cells, and tissue at risk of death respond well
Effects continue for long time after light is switched off
Released nitric oxide temporarily increases blood flow in illuminated area
Released nitric oxide reduces swelling by dilating lymphatics and increasing drainage

Michael Hamblin, Ph.D., R.Rox Anderson, M.D., Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA
Video of a mouse fibroblast cell, seeking out a pulsating near IR laser light.
Source: Guenter Albrecht-Buehler, Ph.D., Physicist
Northwestern University Medical School, Chicago

Video of a mouse fibroblast cell, seeking out a pulsating near IR laser light.
Note, the cell maneuvers around an obstacle, to get to the laser light.
Source: Guenter Albrecht-Buehler, Ph.D., Physicist
Northwestern University Medical School, Chicago
Video of a mouse fibroblast cell, seeking out a pulsating near IR laser light. The nucleus has been removed from this cell (an enucleated cell), yet the remainder of the cell still seeks out the light - the mitochondria are outside the nucleus. Source: Guenter Albrecht-Buehler, Ph.D., Physicist Northwestern University Medical School, Chicago

low level laser light in the auditory canal, middle, and inner ear

Some of the photons from laser or LEDs will penetrate through bone, probably because bone has a crystalline structure. Data and Figures from: Dr. med. Lutz Wilden, Bad Fussing, Germany
Recent studies have reported a single, transcranial, low-level laser therapy (LLLT) treatment to have a significant, beneficial effect when used to treat acute stroke in humans.

Zivin, Albers, Bornstein, et al., *Stroke*, 2009
Transcranial, Laser Therapy Protocol with Acute, Human Stroke Patients:
(Lampl, et al., *Stroke*, 2007)
Treated only once, about 18 hours post-stroke (non-hemorrhagic, no tPA)

NeuroThera Laser System (NTS), PhotoThera Laser Co., San Diego, CA
Class IV Laser (>500 mW), 808 nm, near-infrared

Shaved all hair off of the head, of the stroke patient.
Train operator placed the handheld device for 2 minutes on 20 points all over the head, both hemispheres, regardless of side of stroke.

Energy Dose to the Brain Cortex estimated to be only 1 Joule/cm²
Sham device used on 1/3 of the patients. No perceptible heat, Real or Sham

Significant (p < .05)

Transcranial, Laser Therapy Protocol with Acute, Human Stroke Patients:
(Zivin, et al., *Stroke*, 2009)
Treated only once, < 24 hours post-stroke (non-hemorrhagic, no tPA)

NeuroThera Laser System (NTS), PhotoThera Laser Co., San Diego, CA
Class IV Laser (>500 mW), 808 nm, near-infrared

Shaved all hair off of the head, of the stroke patient.
Train operator placed the handheld device for 2 minutes on 20 points all over the head, both hemispheres, regardless of side of stroke.

Energy Dose to the Brain Cortex estimated to be only 1 Joule/cm²
Sham device used on 1/2 of the patients. No perceptible heat, Real or Sham

Significant (p = .04), beneficial results only in patients receiving Real (vs. Sham) with NIH Stroke Severity scores of Moderate to Moderate-Severe, at Baseline entry.
Naeser & Saltmarche, NAALT, 2009
Conclusions from two, transcranial LLLT studies with human stroke patients:

Transcranial, laser therapy in human stroke patients was safe.

Possible mechanisms of action included:
- Stimulation of mitochondria
- Increase in ATP production
- Mitigation of apoptosis
- Possible enhancement of neurorecovery mechanisms.


Low-Level Laser Therapy Applied Transcranially to Mice following Traumatic Brain Injury Significantly Reduces Long-Term Neurological Deficits

AMIR GIRON,1 URI GIRON,2 JACKSON STRUETER,2 LUIS DE TAVEDA,2 ALEXANDER ALEXANDROVICH,3 VICTORIA TRUMBOLEV,2 and ESTHER SHORHAM³

FIG 1. Neurological score (NSS) of control/non-laser-treated (gray columns) and laser-treated (black columns) mice at different time intervals after induction of brain trauma. Results are expressed as mean ± SD. *Statistical significance level is p < 0.05.
Traumatic Brain Injury (TBI)

- Significant socio-economic burden in the U.S.

- 80,000 to 90,000 individuals sustain long-term disabilities annually. (Thurman et al., 1999)

- With closed-head TBI, **diffuse axonal injury (DAI)** is one of the main consequences. These injuries result when shearing, stretching, and/or angular forces pull on axons and small vessels. Normal structural CT or MRI scan.
  Taber, Warden, Hurley, 2006; Medana, Esiri, 2003
  Naeser & Saltmarche, NAALT, 2009

Traumatic Brain Injury (TBI)

**Often results in Cognitive Dysfunction**

- Chronic, mild TBI (mTBI) is associated with persistent post-concussive symptoms, and problems with:
  - attention
  - cognitive manipulation of temporal information
  - processing speed
  - *working memory*, i.e., the ability to hold information in mind, and to manipulate it in light of incoming material.

- These “Executive Functions” are sensitive to damage of frontal lobe - orbital, medial (anterior cingulate), and dorsolateral, prefrontal cortex.
  Naeser & Saltmarche, NAALT, 2009
Functional Brain Imaging (PET) Study in Chronic TBI
Kato et al., J. of Neurotrauma, 2007

Significantly low, regional glucose metabolism (rCM) observed in 36 chronic TBI cases, DAI; mean age=36.3 Yr., SD=9.8; at 6-38 months post-motor vehicle accident (MVA), compared to normal controls.

Fig 1. Brain PET studies during resting state, with chronic TBI cases (> 6 months post-TBI) (Kato et al, 2007).
(Left) Regions of decreased cerebral metabolism (p<0.001) in TBI group compared with normal controls are displayed on a glass brain.
(Right) Red areas show decreased cerebral metabolism in bilateral medial prefrontal cortex (top row, white arrows), as well as other areas, including anterior superior temporal gyrus (bottom rows) during resting PET scans.

Fig 2. Solid white areas, in bilateral, medial prefrontal cortex and ant. cingulate gyrus mark the location of significant (p<0.01) positive correlation with Full-Scale IQ, and regional cerebral metabolism for these cortical areas in the chronic TBI cases. Results for regression analysis for Full-Scale IQ and cerebral metabolism in the TBI patients are superimposed on a normal magnetic resonance imaging (MRI) template (Kato et al, 2007).

Naeser & Saltmarche, NAALT, 2009

FRONTAL HYPOACTIVATION IN WORKING MEMORY AFTER DIFFUSE TBI
Functional MRI Study with Chronic, Traumatic Brain Injury (TBI) Cases.

FIG. 3. Areas where patients showed significantly lower activation than did controls for the 2-back > 0-back comparison after-correction for performance. Significant differences were observed in right superior and left middle frontal gyri (p = 0.006).

Digits Backwards and Letter-Number Sequencing subtests from the WAIS-III.
Sanchez-Carrion et al., J. of Neurotrauma, 2008

Naeser & Saltmarche, NAALT, 2009
### Case Report: Transcranial LED to Treat Cognitive Dysfunction in Chronic, mild TBI

#### Summary of Accident:


She was the driver (small, compact car) hit from behind, while stopped at a red light. Hit by a large, heavy car driven at a high rate of speed. Her head snapped back, and *hit a very rigid, head-rest*. She was wearing the seat-belt, and did not lose consciousness.

She called the Police; but drove herself home.

Later that evening, the increasing headache caused her to seek medical attention in an ER, at her local hospital.

**Head X-Rays and Brain MRI scan were normal.**

(Brain MRI scans continued to be considered normal, even years later.)

Returned home with pain meds for the headache and sub-occipital neck pain.

---

### Case Report: Transcranial LED to Treat Cognitive Dysfunction in Chronic, mild TBI

#### Summary of initial 2 Months, post-Accident

She was told to stay home and *rest for 2 months*. She also slept a great deal.

She *tried to return to work after 2 months*, but could not function, due to confusion, inability to remember what people said to her, and inability to focus on her computer work.

She had 2 Master's Degrees; had written 3 books; knew 3 languages; in Mensa. She had been Director of Marketing and a Sales Development Specialist for an Internet Marketing Company.

She had also *taught web-design on the graduate level, at a university*.

She had to *resign from all work*, due to "cognitive dysfunction."

She was diagnosed by a Neurologist as having "Post-Concussive Syndrome," and was told she might never recover, even for 5 years.

---

*Naeser & Saltmarche, NAALT, 2009*
Case Report: Transcranial LED to Treat Cognitive Dysfunction in Chronic, mild TBI

Summary of Cognitive Behavioral Evaluation and Treatment Programs

At 2 years post-MVA, her cognitive abilities were evaluated for 40 hours at a rehabilitation institute.

Her Divergent Reasoning abilities were significantly impaired across all verbal tasks.

Her Executive Function ability was severely impaired, where a task required that she plan moves ahead in her mind (such as in a game of chess).

She had a vulnerability to emotional distress, and depression, (not uncommon with this disorder)

Naeser & Saltmarche, NAALT, 2009

Case Report: Transcranial LED to Treat Cognitive Dysfunction in Chronic, mild TBI

Summary of Cognitive Behavioral Treatment Programs, 2 - 4 Yr. post-MVA

At 2 Yr. post-MVA, she underwent two, 20-week “Remedial Training for Cognitive Function” programs with peers of similar education and background, who had similar cognitive deficits due to TBI or myocardial infarction with hypoxia to brain.

However, few of her old skills returned, no new skills were acquired, and her original disabilities remained.

After completion of the second, 20-session program, she was still unable to perform any work. There was a suicide attempt with drug overdose.

At 4 Yr. post-MVA, she received further “Behavioral Therapy Sessions,” at a rehabilitation institute in a different state.

39 one-hour (one-on-one) “Cognitive Training Sessions,” followed by 39 one-hour “Personal TBI Acceptance Sessions”

She could work on her computer for 20 minutes.

Naeser & Saltmarche, NAALT, 2009
Case Report: Transcranial LED to Treat Cognitive Dysfunction in Chronic, mild TBI
Beginning of LED Treatments, at 7 Yr. post-MVA

At 5 Yr. post-MVA, she and her husband moved to another state.

At 7 Yr. post-MVA, she answered an Ad for "Free LED treatments for Pain."

Following the MVA, she had developed painful, knee arthritis.

She received two, LED treatments on both knees, one week apart. Resulted in “…a reduction of swelling by 66% and a reduction in pain by 80%.”

She then requested that the doctor place the LED cluster heads on her head, “to treat her brain.”

After consultation with A. Saltmarche, RN, MHSc, in Toronto, and appropriate “Informed Consent” was obtained, the transcranial, LED treatments were initiated.

1st Transcranial, LED Treatment (May, 2004) 7 years post-MVA (in Dr.’s Office)

High Intensity, LED Cluster Head Device, used at Office:
MBM1100 Console, with 3 Square-shaped LED Cluster Heads

Each Square-shaped Cluster-head dimension: 4.4 cm x 4.4 cm (approximately 1.75 inch x 1.75 inch)

Treatment Area: 19.39 cm²

Each cluster head contained 49 diodes:
40 near-infrared 870 nm diodes, 12.25 mW each
9 red 633 nm red diodes, 1 mW each

Total Power: 500 mW (+20%) Continuous Wave, CW

Power density: 25.8 mW/cm² (+20%)
1 J = 2 sec
1 J/cm² = 38.8 sec

Naeser & Saltmarche, NAALT, 2009
1st Transcranial, LED Treatment (May, 2004)  
7 years post-MVA (in Dr.’s Office)

Office Notes:

Treatment Loci: Left and Right Forehead areas  
8 J/cm^2 to each area  
Treatment Time: 5 minutes, 10 seconds per area

Patient Reaction:  
Drove herself home (30 minutes)  
Slept through dinner, could not get up.  
Slept most of the next day.

Day 3, post- 1st LED Tx: Improved concentration and focus.  
Able to work at her computer, 40 minutes  
Previously (for 7 Yr. post-MVA), able to work at her computer for only 20 minutes.

Naeser & Saltmarche, NAALT, 2009

High Intensity, LED Treatment Considerations

Only 2 to 3% of energy penetration from skin on the scalp surface, is estimated to reach brain cortex 1 cm deep, from the scalp or skin surface.

Only 0.2 to 0.3% energy penetration from scalp on skin surface, is estimated to reach 2 cm deep (into the white matter).  
(M. Hamblin, Ph.D., Wellman Center for Photomedicine, MGH, personal communication; Wan, Parrish, Anderson et al., 1981)  
Thus, 3% of 8 J/cm^2 delivered to skin on L and R temple areas, would deliver only 0.24 J/cm^2 to brain cortex.  
This is a very low dose.

If there is an effect, it is unclear whether the effect may be related to:  
a. The photons reaching the grey and white matter of the brain?  
OR  
b. The photons may be stimulating shallow acupuncture points located on the surface of the scalp or skin?  
OR  
c. Possible “Systemic Effects” (Mary Dyson, Ph.D., personal communication)

Naeser & Saltmarche, NAALT, 2009
1st LED Treatment:  L & R Forehead areas
8 J/cm^2 per area (0.24 J/cm^2 to cortex)

Red areas show low cortical activation on functional MRI in chronic, TBI cases (post-MVA) with "cognitive dysfunction."
Sanchez-Carrion et al., 2008

Location of Gyral Areas of Brain Cortex, in Relationship to Bone Suture Lines of Skull.
(Gray1197.png)

Naeser & Saltmarche, NAALT, 2009

2nd Transcranial LED Treatment (1 Week Later)
7 years post-MVA (in Dr.’s Office)

Office Notes:

Treatment Loci:  Left and Right Forehead areas

8 J/cm^2, each area (0.24 J/cm^2)

Treatment Time:  5 min, 10 sec per area

Patient Reaction:

Her husband drove her to the appointment.  
She had no return of excess sleepiness.  
Continued to have improved concentration and focus.
Able to work at her computer, 40 minutes

Naeser & Saltmarche, NAALT, 2009
3rd LED Treatment: L & R Forehead; midline at hairline; and L & R Temples, 8 J/cm^2 per area (0.24 J/cm^2 to cortex)

Red areas show cortical locations of low glucose metabolism on PET scans, in chronic, TBI cases (post-MVA) with cognitive dysfunction.

Kato et al., 2007

 Weeks 3 - 8 of Treatments (1x / Week) at Dr.’s Office

Office Notes:

Treatment Loci: Left and Right Forehead areas above eyebrows; plus a midline forehead area, at the front hairline; Left and Right Temple areas.

Total = 5 areas

Gradually increased from 8 J/cm^2 per area, up to 20 J/cm^2 per area

Treatment Time: Gradually increased from 5 min, 10 sec to up to 12 min, 54 sec, per area.

Patient Reaction:

She had no return of excess sleepiness.
Continued to have improved concentration and focus.

*After 8 Weeks, able to work at her computer, 3 hours*

Naeser & Saltmarche, NAALT, 2009
For 5 more Months, the patient continued with 1x / Week, Transcranial LED Treatments in the Dr.’s Office (7 Months)

**Patient Overall Reaction:**
Able to drive herself to and from appointments.

Her time on the *computer was focused for 3 hours at a time*.

Her *mood became more stabilized,*
and *outbursts of anger, greatly reduced.*

She had received a total of approximately 28 transcranial, LED treatments.

---

After 7 Months of LED Tx.’s, 1x / Wk. at Dr.’s Office, in January, 2005, she *obtained Home Treatment Unit* [Off-label MedX Device use] with a single LED Cluster Head (7 Yr., 9 Mo. post-MVA)

Circular-shaped, Cluster-head diameter: 53.45 mm (2.1 inches)
Treatment Area: 22.48 cm^2
Single cluster head contained **61 diodes:**
- 52 near-infrared **870 nm** diodes
- 9 red **633 nm** diodes

Each diode was 12–15 mW
**Total optical output power:** 500 mW (+20%) CW
**Power density:** 22.2 mW/cm^2 (+20%)
1 J = 2 sec
1 J/cm^2 = 45 sec

She treated 6 spots per night, 10 min per area; 13.3 J/cm^2 per area (0.4 J/cm^2 to brain cortex).  
Naeser & Saltmarche, NAALT, 2009
Hypothetical direction of penetration of 2 - 3% of photons, from high-intensity LED cluster head, on L and R forehead. 

Sample placement locations for transcranial treatment with the high-intensity LED cluster head. (The model demonstrating the LED placement locations is not in this case report. No medical claims of cures are made or implied.)

Naeser & Saltmarche, NAALT, 2009
Here, two LED cluster heads are held in place on the head, with a loose-fitting elastic cap.

The LED cluster head placed on the sole of the foot (acupuncture point, Kidney 1), is held in place with a soft, flexible, elastic band, secured with a velcro strap.

The MedX Console Unit has three LED Cluster Heads.

*Three LED cluster heads may be used in three different locations, at the same time.*

The usual treatment time is 10 minutes per location.

---

**Notes from Patient, following Home Treatments:**

**Treatment Loci:**

- Left & Right Forehead areas; Left and Right Temple areas
- Midline at front hairline (Combined with foot points, see below.)
- Left and Right areas posterior-superior to the ears (Angular gyrus area), "Able to remember what she read."
- Left and Right base of skull, "Removed sensitivity of L scalp area when hair was being cut there (had been present for previous 7 years); improvement in reflexes on left side of body."
- Center, top of her head, "Able to work better with numbers, and math."

**Treatment Time:**

- 10 minutes per area, CW; **13.3 J/cm^2 per area**
  - (0.4 J/cm^2 to brain cortex)

*Prefers to treat at bedtime,* as her sleep improves.

She treats 6 scalp areas per night (locations vary). (Also acupuncture points, on sole of foot - Kidney 1; or top, base of toes - Ba Feng.)
**Patient's Overall Reaction:**

Able to drive.

Able to perform computer work for 3 hours at a time.

"Decision-making and verbal memory, incredibly better."

"Improved self-awareness of both limitations and successes."

Also continues to treat pain in her knees (arthritis), if pain is present in the mornings.

**Remaining Cognitive Problems:**

She *still cannot multi-task well*, her chief complaint now, after 4 years of home treatments with the LED cluster head.

She still needs to make notes, to be sure all things are accomplished, but her *overall quality of life is much improved*.

---

**She needs to treat almost daily.**

*If she stops* the transcranial LED treatment for 2 to 7 weeks, *she slowly regresses.*

Her focus and attention become compromised.

She cannot work for hours on her computer and her balance becomes poor.

As is common with TBI, she has fallen sometimes, since the MVA.

This includes 2x, since acquiring LED home treatment unit.

Using the *LED cluster head, transcranially, as soon as possible after the fall,* helps her to *recover faster.*

**When re-starting transcranial LED treatments,** she starts with a *shorter treatment time* and lower J/cm^2.

Initial Treatment Time, Round Cluster: 6 min per area; 8 J/cm^2; 0.24 J/cm^2 to brain cortex

Preferred Treatment Time (at night): 10 min per area; 13.3 J/cm^2 (estimated 0.4 J/cm^2 to brain cortex).
High Intensity, LED Treatment Considerations

Only 2 to 3% of energy penetration from skin on the scalp surface, is estimated to reach brain cortex 1 cm deep, from the scalp or skin surface.

Only 0.2 to 0.3% energy penetration from scalp on skin surface, is estimated to reach 2 cm deep (into the white matter).

(M. Hamblin, Ph.D., Wellman Center for Photomedicine, MGH, personal communication; Wan, Parrish, Anderson et al., 1981)

Thus, 3\% of 8 J/cm^2 delivered to skin on L and R temple areas, would deliver only 0.24 J/cm^2 to brain cortex. This is a very low dose.

If there is an effect, it is unclear whether the effect may be related to:

a. The photons reaching the grey and white matter of the brain?

OR

b. The photons may be stimulating shallow acupuncture points located on the surface of the scalp or skin?

OR

c. Possible “Systemic Effects” (Mary Dyson, Ph.D., personal communication)

Naeser & Saltmarche, NAALT, 2009

The red, and near infra-red photons may penetrate best through suture lines in the skull, and through emissary veins located throughout the skull.

The emissary veins communicate with the Arachnoid Granulations (Villi), which exchange CSF into the veins in the cerebral sinuses.

Thus, the photons may enter the emissary veins and CSF, and the venous drainage system (which leads to the jugular vein). This system may also be a factor in Transcranial, Laser or LED therapy.

Mary Dyson, Ph.D., King’s College, London
Personal Communication

Williams, Warwick, Dyson, Bannister. Gray’s Anatomy,
Functional magnetic resonance imaging detects activation of the visual association cortex during laser acupuncture of the foot in humans

Christian M. Siedentopf, Stefan M. Golaszewski, Felix M. Mottaghy, Christian C. Ruff, Stephan Felber, Andreas Schlager

Abstract

The aim of this study was to investigate the effect of laser acupuncture on cerebral activation. Using functional magnetic resonance imaging (fMRI) control activation during laser acupuncture at the left foot (Bladder 67) and dummy acupuncture, were compared employing a block design in ten healthy male volunteers. All experiments were done on a 1.5 Tesla magnetic resonance scanner equipped with a circular polarized head coil. During laser acupuncture, we found activation in the cuneus corresponding to Bodenmann Area (BA 18) and the medial occipital gyrus (BA 19) of the ipsilateral visual cortex. Placebo stimulation did not show any activation. We could demonstrate that laser acupuncture of a specific acupuncture point, empirically related to sphincteric disorders, leads to activation of visual brain areas, whereas placebo acupuncture does not. These results indicate that fMRI has the potential to elucidate effects of acupuncture on brain activity. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Laser acupuncture, Acupuncture Bladder 67, Functional magnetic resonance imaging, Visual cortex

Fig. 2. Ipsilateral, occipital cerebral activation pattern induced by laser acupuncture to Bl 67. Naeser & Saltmarche, NAALT, 2009
Considerations for Future Transcranial, High-intensity LED Treatments

With current LED treatment protocol, the energy density and the power density may be too low.

Treatment for only 10 minutes per area (13.3 J/cm²) at scalp surface, is likely only delivering 0.4 J/cm² to local brain cortex (estimate is 3% of NIR photons will reach local brain cortex).


Therefore, it is estimated that MedX LED clusters would deliver approximately 1 J/cm² in 25 minutes, or 4 J/cm² in 100 minutes.

The patient states that she is “comfortable with the LED in place for 10 minutes, but is not comfortable with longer than that.”

Naeser & Saltmarche, NAALT, 2009
Suggestions, Future High-intensity LED Treatments:

Stronger LED clusters with higher power density, could reduce the necessary overall treatment time, per area.

Optimal J/cm^2 (and mW/cm^2) still to be determined, as well as number of treatments, and duration of treatment periods. Possible need for long-term, home-treatment programs.

Treatment for other CNS disorders where “cognitive dysfunction” is present include Stroke, Dementia (vascular or Alzheimer’s), Sports-related traumatic brain injury, Football and Soccer players, etc. Further research with randomized, controlled trials is necessary.
REVIEW, Eight Cellular Effects of LLLT/LED relevant to TBI:

Michael Hamblin, PhD, Wellman Center for Photomedicine, Massachusetts General Hospital

1. Induction of reactive oxygen species and NF-kB activation

The present hypothesis is that LLLT produces low levels of reactive oxygen species (ROS) in mitochondria of illuminated cells, and that these ROS cause NF-kB activation via the redox sensitive sensor enzyme protein kinase D1 (Storz, 2007).

Induction of low levels of ROS by LLLT may actually prevent major ROS-mediated damage occurring in the brain after TBI.

The mitochondrial superoxide dismutase (MnSOD) is one of the most upregulated genes after NF-kB activation (Sompol et al., 2006).

Another highly upregulated gene after NF-kB activation and after LLLT is heat-shock protein 70 (Zhang et al., 1994).

This is a molecular chaperone for protein molecules and prevents mis-folding and unwanted protein aggregation.

Heat stress preconditioning (Shein et al., 2007) and various mild stresses (Guo et al., 2001) have been shown to prevent neuronal death after TBI.

2. Increased ATP formation and improved mitochondrial function

in injured brain will allow ATPase pumps to pump out Na+/Ca++ ions and prevent neuronal death

Impaired cerebral energy metabolism may be a major contributor to the secondary injury cascade that occurs after TBI.

Significant reductions in mitochondrial function have been found after TBI in both animals (Verweij et al., 1997) and humans (Verweij et al., 2000).

Many reports studying effects of LLLT on isolated mitochondria and on multiple cell lines including neurons (Oron et al., 2007), have shown increased ATP production, and increased mitochondrial respiration and function

(Karu et al., 1995; Passarella et al., 1984; Pastore et al., 1996).

Michael Hamblin, PhD
3. The **anti-apoptotic effects**, and increase in mitochondrial potential due to LLLT, **will reduce neuronal and glial cell death**

*Traumatic axonal injury* causes *neuronal and glial cell death*, and apoptotic and necrotic neurons have been identified within contusions in the acute post-traumatic period, *and in regions remote from the site of impact in the days and weeks after trauma.*

Many studies demonstrate the *anti-apoptotic effect of LLLT* especially on *neurons subjected to various toxic insults* such as

- **cyanide** (Liang et al., 2006)
- **tetrodotoxin** (Wong-Riley et al., 2005)
- **methanol** (Eells et al., 2003)

Michael Hamblin, PhD

4. The **anti-inflammatory effects of LLLT** will reduce key inflammatory mediators (TNFα, PGE2) in the injured brain

Animal studies described *up-regulation of COX-2, PGE and PGD expression* in two rat models of TBI (Kunz et al., 2002).

Reports (Castano et al., 2007) demonstrate that *LLLT reduces COX-2* expression levels and *reduces prostaglandins* in multiple animal models as well as in vitro (Aimbire et al., 2005; Albertini et al., 2007; Sakurai et al., 2000).

Another key inflammatory mediator that has been implicated in pathogenesis of TBI is the cytokine tumor necrosis factor alpha (TNFα).

*There are multiple reports showing that LLLT reduces TNFα levels in arthritis* (Aimbire et al., 2006) and other animal models of inflammation.

Michael Hamblin, PhD
5. **LLLT is expected to reduce brain edema** and hence *ameliorate neuronal damage*

Brain edema resulting from TBI or ischemia exhausts volume reserve and leads to raised intracranial pressure and brain herniation.

Studies of LLLT in both various animal models (Albertini et al., 2004) and in rat arthritis (Castano et al., 2007) and in numerous clinical applications (Carati et al., 2003; Markovic et al., 2007) have demonstrated that *LLLT is particularly effective in reducing edema.*

Michael Hamblin, PhD

---

6. **LLLT has been shown to increase antioxidant capacity in ischemic tissues**

Many reports show that *reactive oxygen species or oxidative stress* is involved in the *pathogenesis of brain damage after TBI.*

**LLLT treatment** of ischemic gastrocnemius muscle in rats gave a significant *increase in global antioxidant measure* and an *increase in heat shock protein 70* (Avni et al., 2005).

Michael Hamblin, PhD
7. LLLT has been shown to be effective in stimulating repair of neurons (both peripheral and in spinal cord) and could increase neurogenesis in TBI.

In recent years it has become realized that neurogenesis in damaged brain after TBI is not the rare event it was once thought to be (Richardson et al., 2007).

Byrnes and colleagues (Byrnes et al., 2005) showed that adult rats that underwent a T9 dorsal hemisection, followed by treatment with an 810-nm, 150 mW diode laser showed significant improvement in axonal regeneration and functional recovery.

Michael Hamblin, PhD

8. LLLT increases expression (and activation) of growth factors such as TGF-β and VEGF that may contribute to positive brain remodeling after TBI

There has been a report (Leung et al., 2002) that in a rat stroke model, transcranial LLLT triggered the expression of TGF-β (as well as reducing NO levels).

Tuby et al. (2006) showed that in a rat heart infarcts model, LLLT significantly increased VEGF expression levels and this correlated with increased angiogenesis.

Michael Hamblin, PhD

Hua Shan Hospital
Shanghai, China, 1985.

Neurological and Dermatological Research Institute

Laser Acupuncture to Treat Paralysis in Stroke

Red-beam laser used on acupuncture points to treat paralysis due to stroke.
Shoulder Abduction


BEFORE TREATMENT:  Right Hand spasticity still present, 1.5 Yr. Poststroke

Microamps TENS device (MicroStim 100) will be used for 20 Minutes, on two Acupuncture Points:  HRT 8 and TW 5

High Frequency, 292 Hz., 2 min. (subthreshold)

Low Frequency, 0.3 Hz., 18 min. (subthreshold)

PLUS, Red-Beam Laser Acupuncture on the finger tips, 4 J/cm² per point
Step 4: Place the tip of the laser directly on each acupuncture point. With red-beam laser treat each point at 4 Joules/cm² - Hrt 8, PC 9, Lu 9, Hrt 7. See special instructions below for *PC 7.

Step 3: Place the tip of the laser directly on each acupuncture point. With red-beam laser treat each point at 4 Joules/cm² - Lu 11, LI 1, PC 9, TW 1, Hrt 9, SI 1.

This graph simulates the effects of direct micropulse on ATP concentration in Cheng's study. It displays that the increase in ATP concentration peaks at around 5000 A, with a 50% increase noted (ATP) in contrast to the unstimulated control group. In addition, at current above 4 mA, ATP dropped below that of the unstimulated group (Barrett et al.), indicating a long-term decrease in ATP concentration in patients treated with conventional (milliamperes) TENS. (Cheng et al., 1992)

Hand Diagram #1.

Right Hand (Palm)

Hrt 8

Right Hand (Back)

Step 3) Place the tip of the laser directly on each acupuncture point. With red-beam laser treat each point at 4 Joules/cm² - Lu 11, LI 1, PC 9, TW 1, Hrt 9, SI 1.

Step 4) Place the tip of the laser directly on each acupuncture point. With red-beam laser treat each point at 4 Joules/cm² - Hrt 8, PC 9, Lu 9, Hrt 7. See special instructions below for *PC 7.

Note: For stroke patients, place the circular electrode over Hrt 8.

BEFORE TREATMENT:
Hand spasticity still present
1.5 Yr. Poststroke
1st Treatment
Naeser Laser Hand Treatment
Microamps TENS (Hrt 8, TW 5) and
Red-beam Laser (Jing-Well Pts.)

AFTER TREATMENT:
Post- 1st, 20-Minute Treatment
Hand opens
Fingers have more extension and less spasticity
Requires more treatments, to retain more lasting effect.
Patient can treat him/herself.
Patient’s hand with carpal tunnel syndrome was treated with laser acupuncture and microamps TENS, behind a hanging black curtain, so that the patient did not know if the laser and microamps TENS devices were turned on (Real), or off (Sham). The patient felt nothing, even when the devices were turned on.

VA Boston Healthcare System, 1997

Naezer Lecture Notes®

Table 2. Melzack Pain Scores

<table>
<thead>
<tr>
<th>Cases</th>
<th>Real Treatments</th>
<th>Sham Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Entry Baseline</td>
<td>Post Test #2</td>
</tr>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± Post mins Pre (%)</td>
</tr>
<tr>
<td>1</td>
<td>Mld CT S</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Mld CT S</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>Mld CT S</td>
<td>23 *</td>
</tr>
<tr>
<td>4</td>
<td>Mld CT S</td>
<td>20</td>
</tr>
<tr>
<td>Mean (n=5)</td>
<td>21.3</td>
<td>0.33</td>
</tr>
<tr>
<td>S.D.</td>
<td>5.09</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Real 1st

<table>
<thead>
<tr>
<th>Cases</th>
<th>Real Treatments</th>
<th>Sham Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Entry Baseline</td>
<td>Post Test #2</td>
</tr>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± Post mins Pre (%)</td>
</tr>
<tr>
<td>6</td>
<td>Med CT S</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>Med CT S</td>
<td>1 *</td>
</tr>
<tr>
<td>8</td>
<td>Med CT S</td>
<td>21</td>
</tr>
<tr>
<td>9</td>
<td>Med CT S</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>Med CT S</td>
<td>20</td>
</tr>
<tr>
<td>11</td>
<td>Med CT S</td>
<td>2 *</td>
</tr>
<tr>
<td>Mean (n=5)</td>
<td>22.21</td>
<td>5.80</td>
</tr>
<tr>
<td>S.D.</td>
<td>11.28</td>
<td>7.36</td>
</tr>
</tbody>
</table>

Real 2nd

- Case was a placebo responder during First or Second Sham Treatment Series; data excluded from t-test comparisons.

Table 3. Median Nerve, Sensory Peak Latencies

<table>
<thead>
<tr>
<th>Cases</th>
<th>Pre Treatment</th>
<th>Post Treatment</th>
<th>Δ Post minus Pre Treatment</th>
<th>Real Treatments</th>
<th>Sham Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre (ms)</td>
<td>Post (ms)</td>
<td>Δ Post minus Pre (ms)</td>
<td>Pre (ms)</td>
<td>Post (ms)</td>
</tr>
<tr>
<td>Real 1st</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Mild CTS</td>
<td>4.32</td>
<td>4.90</td>
<td>0.58</td>
<td>4.00</td>
<td>3.92</td>
</tr>
<tr>
<td>2 Mild CTS</td>
<td>3.76</td>
<td>3.60</td>
<td>0.16</td>
<td>3.60</td>
<td>3.60</td>
</tr>
<tr>
<td>3 Mild CTS</td>
<td>Absent *</td>
<td>5.00 *</td>
<td>- *</td>
<td>5.00</td>
<td>5.00</td>
</tr>
<tr>
<td>4 MILD CTS</td>
<td>3.60</td>
<td>3.60</td>
<td>0.00</td>
<td>3.60</td>
<td>3.60</td>
</tr>
<tr>
<td>Mean (ms)</td>
<td>3.89</td>
<td>3.73</td>
<td>0.16</td>
<td>4.05</td>
<td>3.95</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.38</td>
<td>0.23</td>
<td>0.16</td>
<td>0.66</td>
<td>0.34</td>
</tr>
<tr>
<td>Real 2nd</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Moderate/Severe CTS</td>
<td>5.20</td>
<td>5.30</td>
<td>0.10</td>
<td>5.50</td>
<td>5.40</td>
</tr>
<tr>
<td>6 MILD CTS</td>
<td>3.92</td>
<td>3.84</td>
<td>-0.08</td>
<td>4.00</td>
<td>3.92</td>
</tr>
<tr>
<td>7 MILD CTS</td>
<td>4.16</td>
<td>4.08</td>
<td>-0.08</td>
<td>4.16</td>
<td>4.10</td>
</tr>
<tr>
<td>8 MILD CTS</td>
<td>3.20</td>
<td>3.30</td>
<td>0.10</td>
<td>No Data *</td>
<td>3.20 *</td>
</tr>
<tr>
<td>9 MILD CTS</td>
<td>Absent *</td>
<td>5.36 *</td>
<td>- *</td>
<td>Absent *</td>
<td>5.36 *</td>
</tr>
<tr>
<td>10 MILD CTS</td>
<td>Absent *</td>
<td>5.36 *</td>
<td>- *</td>
<td>Absent *</td>
<td>5.36 *</td>
</tr>
<tr>
<td>11 MILD CTS</td>
<td>5.26</td>
<td>4.90</td>
<td>0.36</td>
<td>5.26</td>
<td>5.26</td>
</tr>
<tr>
<td>Mean (ms)</td>
<td>3.95</td>
<td>3.75</td>
<td>-0.25</td>
<td>4.02</td>
<td>3.95</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.93</td>
<td>0.82</td>
<td>0.18</td>
<td>0.55</td>
<td>0.36</td>
</tr>
</tbody>
</table>

* Data excluded from test comparisons.


Part 4. Review two LLLT Studies to Treat Fibromyalgia.

Long-term efficacy of low level laser therapy in women with fibromyalgia: A placebo-controlled study

Onur Armağan*, Funda Tascigil, Ayse Ekim and Cengiz Onzer
Osmanagazi University, Faculty of Medicine, Departments of Physical Therapy and Rehabilitation, Eskisehir, Turkey

Abstract. Aim: To investigate the efficacy of low level laser therapy (LLLT) in fibromyalgia patients.

Materials and Methods. Thirty-four fibromyalgia patients were randomly assigned to LLLT (n = 18) and placebo laser groups (n = 18). Outcome measures included number of tender points (NTP), Fibromyalgia Impact Questionnaire (FIQ), morning stiffness, global improvement as reported on a visual analog scale (VAS), and total myalgia score. Clinical evaluations were performed before, immediately after, and six months after the treatment.

Results: In the LLLT group, significant improvement was observed in clinical parameters at the end of the treatment (p < 0.01). On the other hand, significant improvements were observed only in the number of tender points and morning stiffness in the placebo group (p < 0.05). In comparing the groups, significant improvements were detected in scores of FIQ, VAS, and total myalgia in the active laser group (p < 0.05). The clinical evaluations performed after six months demonstrated improvements in the clinical parameters only in the LLLT group (p < 0.05). When the groups were compared with each other, significant improvements were found in the LLLT group (p < 0.05).

Conclusion. Our results suggest that LLLT has both short- and long-term effectiveness in the treatment of fibromyalgia.

Laser Parameters Used:
Armagan et al., 2006, Treat Fibromyalgia in Women

Wavelength: 830 nm (Near infra-red, NIR)

Laser Power: 50 mW, continuous wave, CW

Diameter of Laser Beam: 1 mm
Beam spot size: 0.0078 cm^2

Power Density: 6,410 mW/cm^2 (M. Naeser calculations)

Energy Density: 1 J/cm^2 = 0.156 sec (M. Naeser calculations)

Laser Treatment Time: 60 sec per tender spot
(2 Joules per tender spot, authors’ information provided)

384.6 J/cm^2 per tender spot (M. Naeser calculations)

Total = 11 - 18 tender spots associated with fibromyalgia pain were treated

Treatment Schedule: 1x Day, 5 Days/Week; 2 Weeks
**Fibromyalgie in der Schmerztherapie**

*Mechanismen und Behandlungschancen durch Lasertherapie*

**Einführung**


Das Wort Fibromyalgie leitet sich mit seinen Bestandteilen *fibra* = Faser, *myos* = Muskel und *algos* = Schmerz ab und weist damit bereits in der Namensgebung auf die Lokalisation der Beschwerden hin.

Im prospektiven Schenkel der Beobachtung haben 72 Patienten eine Laserbehandlung, entweder als reine perkutane Therapie an spezifischen Akupunkturpunkten oder als kombiniertes Verfahren mit intravasaler Blutbestrahlung erhalten.

**Zur Anwendung**

Weber Medical Laser System

Laser light emitted in various wavelengths for use on Acupuncture Points, “Laser Acupuncture.”

Michael Weber, MD
Lauenförde, Germany
weber@webermedical.com

Celle, Germany

Red laser light hypothesized to have modulating effect on leucocytes.

These authors cite research from Russia suggesting that I.V. laser blood irradiation can promote physiological leucocytolysis similar to immunomodulating therapies.

Michael Weber, MD
Lauenförde, Germany
Results for Treatment of Pain in Fibromyalgia.  N = 72  
T. E. Wieden, MD, Celle, Germany  
Note: Best Results were obtained in cases treated with 
10 Laser Acupuncture Treatments (Red and Infrared on Acupuncture Points) 
Plus 
3 I.V. Laser Therapy Sessions (Red and Green). (5 Weeks)  

1. Schmerzen  
Im Lauf der Behandlung nahm die durchschnittliche Schmerzstärke auf der Visuellen Analogskala (VAS) in allen Behandlungsgruppen im Vergleich zur Erstuntersuchung deutlich ab, wobei die Ausprägung der Schmerzen in der zusätzlich mit Laserlicht behandelten Gruppe die geringsten Werte zeigte.  

<table>
<thead>
<tr>
<th></th>
<th>Beginn</th>
<th>Ende</th>
</tr>
</thead>
<tbody>
<tr>
<td>MED</td>
<td>8,7</td>
<td>6,8</td>
</tr>
<tr>
<td>AKU</td>
<td>8,5</td>
<td>6</td>
</tr>
<tr>
<td>LAS</td>
<td>8,5</td>
<td>4,4</td>
</tr>
<tr>
<td>LAS+IV</td>
<td>8,9</td>
<td>2,9</td>
</tr>
</tbody>
</table>

I.V. Red laser, beneficial effect on Platelets and modulating effect on Leucocytes.  
Green laser, beneficial effect on Erythrocytes.  

MED = medikamentöse Verfahren, AKU = Nadelakupunktur, LAS = Laserakupunktur, LAS+IV = kombinierte Laserakupunktur mit intravasaler Laserbestrahlung.

Results for Treatment of Depression in Fibromyalgia.  N = 72  
T. E. Wieden, MD, Celle, Germany  
Note: Best Results were obtained in cases treated with 
10 Laser Acupuncture Treatments (Red and Infrared on Acupuncture Points) 
Plus 
3 I.V. Laser Therapy Sessions (Red and Green). (5 Weeks)  

5. Depressionsindex  
Die in Begleitung einer Fibromyalgie häufig auftretende Depression nahm insbesondere in den Gruppen mit Laserakupunktur bzw. mit Laserakupunktur und intravenöser Laserbestrahlung am deutlichsten ab.  

<table>
<thead>
<tr>
<th></th>
<th>Beginn</th>
<th>Ende</th>
</tr>
</thead>
<tbody>
<tr>
<td>MED</td>
<td>34</td>
<td>23</td>
</tr>
<tr>
<td>AP</td>
<td>37</td>
<td>24</td>
</tr>
<tr>
<td>LAS</td>
<td>42</td>
<td>12</td>
</tr>
<tr>
<td>LAS+IV</td>
<td>40</td>
<td>12</td>
</tr>
</tbody>
</table>

MED = medikamentöse Verfahren, AKU = Nadelakupunktur, LAS = Laserakupunktur, LAS+IV = kombinierte Laserakupunktur mit intravasaler Laserbestrahlung.
Results for Treatment of Depression in Fibromyalgia. N = 72
T. E. Wieden, MD, Celle, Germany

Laser Acupuncture Plus Laser Blood Irradiation

<table>
<thead>
<tr>
<th></th>
<th>Beginn</th>
<th>Ende</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affektive Komp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Veg. Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wohlbefinden</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In the U.S., using the Weber Medical Laser System:

Peter T. Dorsher, MS, MD
Mayo Clinic Florida
4500 San Pablo Road
Jacksonville, FL 32224

Ph: 904-953-2823
Fax: 904-953-0276
Email: dorsher.peter@mayo.edu

Primarily treats orthopedic disorders, and uses Laser Acupuncture on skin points.
Some National and International Laser Therapy Organizations

www.naalt.org  North American Association for Laser Therapy (NAALT)

Annual meetings are informative and educational.

www.walt.org  World Association for Laser Therapy

www.laser.nu  Swedish Laser Medical Society

Journals:  Photomedicine and Laser Surgery
Lasers in Surgery and Medicine, Am. Soc. for Laser Medicine & Surgery

Team of Investigators and Collaborators
Proposed Study, Transcranial LED Tx. TBI (Not yet Funded)

VA Boston Healthcare System, JP:
Margaret Naeser, Ph.D., L.Ac.  Maxine Krengel, Ph.D.
Henry Lew, M.D., Ph.D.  Terence M. Keane, Ph.D.
Jeffrey Knight, Ph.D.  David Salat, Ph.D.
Kim Sullivan, Ph.D.  Errol Baker, Ph.D.

Massachusetts General Hospital, Boston, MA
Wellman Center for Photomedicine (formerly, Wellman Laser Center)

R. Rox Anderson, M.D.  Director, Wellman Center for Photomedicine
Michael Hamblin, Ph.D.,  Cell Biologist and Biochemist, Wellman Center Photomedicine

Spaulding Rehabilitation Hospital, Boston, MA
Ross Zafonte, D.O., Chief, Rehabilitation Medicine
Harvard Medical School
Case Study:
Low-level laser therapy (LLLT) to heal a chronic, venous leg ulcer.

FIG. 1. A venous leg ulcer (2 cm x 0.7 cm and 0.4 cm deep) from a 62-year-old woman with hypertension is shown. All previous treatments had failed. Pulsed 904 nm, GaAr laser, once per day, for 5 days, 2 days off; repeat cycle for 12 Tx.’s.

FIG. 2. After 7 applications, the depth of the ulcer was reduced.

FIG. 4. After the 12th application, the ulcer was nearly healed.
Sample Light-emitting diode device used on the face (cheek) for the prevention of oral mucositis in pediatric bone marrow transplant patients.

Whelan et al., 2002 (see previous slide).

Quantum WARP 75 Features:

- High intensity 60 mW/cm² illuminated surface produces 5 Joules/cm² dose in 88 seconds
- Large 75 cm² treatment area
- Dose accuracy controlled by an electronic timing circuit (timer) with audible end of cycle alarm
- Remains cool to the touch
- Easy to operate with one hand
- Mounted to articulated arm (upon request)
- Certified wavelength (676 nm) and power output - AC power

The WARP 75 is a larger and more powerful version of the WARP 10. System controls are located on the top panel for easy light dose delivery. Placement is directly against the skin where treatment is to occur. This is the clinical device being used in a double blind clinical trial at the Medical College of Wisconsin and University of Alabama - Birmingham Hospitals for the treatment of oral mucositis in patients undergoing bone marrow transplants. Oral Mucositis is a very painful and life threatening side effect of intense chemotherapy and radiation.
Red-beam, He Ne laser used in the mouth to treat mouth ulcer in BeiJing China, 1985.

Naeser Lecture Notes®

Treatment of Alopecia Areata with LLLT. The LLLT decreases inflammation.
50 J per cm2, per cm2 of no hair; 780 nm, 20 mW, Unilaser, Denmark.

Pre-LLLT Tx.; and post- 4 weeks, post- 8 weeks and post- 12 weeks of LLLT. Treat every other day, 3 times per week.

New hair growth 9 Mo. after the hair began to grow back in, following 4 weeks of LLLT (50 J per cm², per cm² of no hair; 780 nm, 20 mW, Unilaser). She moved to another state, after she had received 3 Mo. of LLLT treatments in Boston; she received no additional LLLT.
Another case study, where LLLT was used to treat the hair loss in alopecia areata.

The same laser parameters were used in this case, as in the previous case.

More effective if treated within first two years of hair loss.

Historical timepoints

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Laser Parameters</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1967</td>
<td>Hungary</td>
<td>Mester</td>
<td>Hair growth in mice</td>
</tr>
<tr>
<td>1970s</td>
<td>Hungary</td>
<td>Mester</td>
<td>Wound healing in patients</td>
</tr>
<tr>
<td>1980s</td>
<td>Russia</td>
<td>Karu</td>
<td>Action spectrum</td>
</tr>
<tr>
<td>1980s</td>
<td>Italy</td>
<td>Pasarellia</td>
<td>Mitochondria &amp; ATP</td>
</tr>
<tr>
<td>1980s</td>
<td>Various</td>
<td>Various</td>
<td>Arthritis in patients</td>
</tr>
<tr>
<td>1992</td>
<td>Norway</td>
<td>Larsen</td>
<td>Clinical trial tennis elbow</td>
</tr>
<tr>
<td>1990s</td>
<td>Various</td>
<td>Various</td>
<td>Pain relief, nerve conduction</td>
</tr>
<tr>
<td>1998</td>
<td>Belgium</td>
<td>Kipshidze</td>
<td>Inhibit restenosis</td>
</tr>
<tr>
<td>2001</td>
<td>Israel</td>
<td>Oron</td>
<td>Heart attack in animals</td>
</tr>
<tr>
<td>2002</td>
<td>USA</td>
<td>MicroLight</td>
<td>FDA approval- carpal tunnel</td>
</tr>
<tr>
<td>2003</td>
<td>USA</td>
<td>Whelan</td>
<td>Retinal toxicity</td>
</tr>
<tr>
<td>2004</td>
<td>Italy</td>
<td>Geuna</td>
<td>Peripheral nerve repair</td>
</tr>
<tr>
<td>2004</td>
<td>USA</td>
<td>Streeter</td>
<td>Prevent damage from stroke</td>
</tr>
<tr>
<td>2005</td>
<td>USA</td>
<td>Anders</td>
<td>Regenerate spinal cord rats</td>
</tr>
</tbody>
</table>

Endre Mester       Tiina Karu
What’s in a name?

Low level laser therapy
Low reactive-level laser therapy
Low intensity laser therapy
Low level light therapy
Low energy laser irradiation
Photobiomodulation
Photobiostimulation
Biomodulation
Biostimulation
Cold laser
Soft laser
Laser therapy

It is called “LOW” because a little light is better than a lot of light

First law of photobiology

hv, 600-950-nm,

Cellular photoreceptor

Wound healing
Tissue repair
Prevention of tissue death
Relief of inflammation
Pain, edema
Acute injuries
Chronic diseases
Neurogenic pain
Neurological problems
Acupuncture
## Medical applications

### Healing:
- leg ulcers, radiation mucositis, sports injuries, dentistry, gastric ulcers

### Prevention of tissue death:
- myocardial infarction, stroke, retinal toxicity

### Chronic orthopedic:
- carpal tunnel, arthritis, tennis elbow, temporal-mandibular joint disorder

### Pain relief:
- trigeminal neuralgia, post-herpetic, chronic and acute traumatic pain

### Edema:
- lymphedema after BrCa, sports injuries

### Miscellaneous:
- acupuncture, tinnitus, hair regrowth, smoking cessation

### Contra-indications:
- directly on cancer tumor; or infection