Star Trek Medicine in suburban general practice

...low-level laser therapy for the treatment of pain

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Disclosure

I have no financial interest in any of the products or companies discussed or referred to in the following presentation.

I am President of the Australian Medical Laser Association (AMLA) – an interdisciplinary group including doctors, dentists, physios.
Outline

• History/context
• Photobiology and mechanisms
• Tissue effects of light
• Clinical effects
• Evidence
• Application in general practice
• Things you can consider immediately
• Some politics
Low-level laser therapy

.....is not really this...
LASER SURGERY
- cutting, heating and ablative
...but it’s not this either
Synonyms

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 of the comparison with surgical “HIGH” power lasers….but it does not really describe the true nature of the lasers.
Light based therapies

...we are getting closer

- Photodynamic therapy
- Light therapy (e.g. for SAD)
- PUVA for psoriasis
- UV light for neonatal hyperbilirubinaemia
LASER MEDICINE

- Is the use of laser light with no gross thermal effect or tissue destruction which causes cellular and tissue changes which result in physiological effects with a therapeutic benefit such as:
  - Pain relief
  - Anti-inflammatory effects
  - Tissue healing
  - Nerve injury repair
  - Promotion of lymphatic drainage
WHAT IS LASER?

Einstein
1916

Light
Amplification by
Stimulated
Emission of
Radiation

Maiman
1960
WHAT IS LASER?

- Light
- Amplification by
- Stimulated
- Emission of
- Radiation
Laser: Basic Elements

Energy

Lasing Medium

Laser Radiation

Mechanical Structure/Controller Device
Diode laser model

Basic structure of a laser diode:

Note: Chip size may be varied.
WHAT IS LASER?

- Monochromatic i.e. single wavelength e.g. red, blue, infrared
- Coherence
- Lack of divergence

Part of the electromagnetic spectrum – from the red to infrared range
The PHOTON is the active ingredient

- a discrete bundle (or quantum) of electromagnetic (or light) energy.
- always in motion at the constant speed of light
- can have particle-like interactions (i.e. collisions) with electrons and other particles
- both a wave and a particle all the time
LASER PARAMETERS

Wavelength  e.g. 632.8nm (red), 830nm (infrared), 904nm (infrared)

Power: 1mW to 500mW

Mode: pulsed or continuous wave

Duration of stimulation: seconds to minutes

Area over which it is applied
Laser Formula

• Energy unit: **joules** (J) is a basic unit of measurement of laser “dose”

\[
\text{Joules} = \text{Watts} \times \text{seconds}
\]

e.g. 100mW (0.1W) \times 10 \text{ seconds} = 1 \text{ joule}
# Laser Classification

**IEC 60825-1**

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
<th>Used for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1/1M</td>
<td>Very low power lasers which are inherently safe because their power is so low.</td>
<td><em>Used in barcode readers</em></td>
</tr>
<tr>
<td>Class 2 /2M</td>
<td>Low power lasers emitting visible light limited to &lt;1 mW</td>
<td><em>Used in laser pointers</em></td>
</tr>
<tr>
<td>Class 3R</td>
<td>Low power lasers emitting visible light limited to &lt;5mW</td>
<td><em>Used in laser printers</em></td>
</tr>
<tr>
<td>Class 3b</td>
<td>Lasers emitting 5mW to 500mW, and some lasers emitting infra-red light below 5mW</td>
<td><strong>Laser Therapy</strong></td>
</tr>
<tr>
<td>Class 4</td>
<td>Lasers emitting over 500mW</td>
<td>Used in surgery</td>
</tr>
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</table>
Laser Acupuncture - *(the stimulation of acupuncture points with laser instead of needles)*

is not the same as

* Low-level laser therapy
The photobiological basis of low-level laser therapy - where quantum physics meets biology

The First Law of Photochemistry states that “for light to exert an effect it must be absorbed”

...and something must absorb it

(Kendric Smith 1991)
Photons are absorbed by molecules called photoacceptors (syn. Chromophores). Electromagnetic energy is transduced to electrophysical and/or electrochemical energy, not heat!!

Retinal neurons are highly specialised photoreceptors.
Chromophores (..that we know) are molecules which absorb photons

- Cytochrome C oxidase *
- Porphyrins and Flavins
- Adenine Nucleotides (NADH)
- ....and are located in mitochondrial and plasma membranes
- and others.....
Mitochondria are thought to be the primary site of laser energy transduction. Chromophores (including cyt c oxidase) are present in mitochondrial membranes and are a primary site of laser energy absorption.
The respiratory chain in mitochondria is the primary site of absorption

\[ \text{O}_2 + 4 \text{Cyt c}^{3+}_\text{out} + 8 \text{H}^+ \rightarrow 2 \text{H}_2\text{O} + 4 \text{Cyt c}^{3+}_\text{out} + 4 \text{H}^+ \text{out} \]
Other mechanisms of laser energy transduction

- Mitochondria act as waveguides
  

- Polarized light interacts with birefringent collagen
Absorption is the **PRIMARY** event common to all cell types

- This initiates several intramitochondrial events
  - Production of reactive oxygen species (ROS) (singlet oxygen, nitric oxide displacement etc)
    - Especially for visible wavelengths
  - Vibrational overtone excitation of enzymes
    - Especially for infrared wavelengths
  - Conformational change in enzymes Especially for infrared wavelengths
  - Ion channel activity
CONFORMATIONAL CHANGE IN ENZYMES CAN OCCUR AFTER ABSORPTION OF LASER ENERGY RESULTING IN CHANGE IN ENZYME ACTIVITY

[Science, 2006, 313, 1638]

DNA topoisomerase 1 reaction
SECONDARY EFFECTS

✧ ATP synthesis/inhibition
✧ DNA & RNA Synthesis
✧ Gene regulation – up or down
✧ Expression of growth factors
✧ bFGF, VEGF, TGFβ
✧ Increased inducible nitric oxide synthase
cDNA Microarray Analysis of Gene Expression Profiles in Human Fibroblast Cells Irradiated with Red Light

0.88 J/cm² 628-nm
HS27 human fibroblasts
74 genes up > 2-fold
37 genes down > 0.5 fold
Nitric Oxide (NO) is an important inter- and intracellular messenger involved in a variety of physiological and pathophysiological conditions.

Biphasic Dose Response in Low Level Light Therapy
Ying-Ying Huang, Aaron C-H Chen, James Carroll and Michael R Hamblin
Harvard Med School, USA
TERTIARY EFFECTS

Cell-specific effects initiated by the primary absorption of laser by the mitochondria

- Cell proliferation
- Decreased apoptosis and cell death
- Cell migration
- Differentiation eg myofibroblasts
- Neurotransmitter synthesis
- Endorphin peptide synthesis
- Increased “fertilisability” of sperm
TERTIARY EFFECTS

Are cell-specific and *dose* and *wavelength* dependent – for example

**STIMULATORY**
- Fibroblast *Wound healing*
- Chondrocyte *Cartilage repair*
- Sperm cells *Increased fertilisation*
- Mast cells *Anti-inflammatory*
- Neutrophils *Wound healing*

**INHIBITORY**
- Neurons *Pain relief, Anti-inflammation*
- Fibroblasts
  - *Reduction in keloid scarring*
Cascade of Primary, Secondary, Tertiary and Quaternary Responses

- Cells
- Tissues
- Mitochondria
- Respiratory Chain
- Tissue and whole body response
Quaternary effects

- **Reduces pain**
  - by direct anti-nociceptive effects
- **Reduces inflammation**
  - reduce PGE$_2$ (and other inflammatory markers)
- **Reduces muscle spasm**
  - direct spasmolytic effects
- **Reduces swelling**
  - improve motoricity of lymphatics
- **Stimulates tissue repair/wound healing**
  - Stimulates fibroblast activity; increased procollagen production, release of growth factors; angiogenesis
- **Stimulates central effects**
  - Causes release of β-endorphins, 5HIAA end-products, down regulated long term potentiation
- **Systemic effects**
DIFFERENT TYPES OF PAIN

- Nociceptive
  - Aδ & C fibre
- Neuropathic
  - nerve damage
  - central sensitisation
- Can be mixture
Pain and laser - from skin to brain

Ch 23.1 Introduction to Pain Mechanisms in Neural Blockade in Clinical Anesthesia and Management of Pain
Siddal PJ & Cousins MJ 1998
LASER EFFECTS ON NERVES – a mechanism for the pain relieving effects

LASER (at the right dose!) has direct inhibitory effects on nerves sufficient to cause conduction block

i.e. LLLT causes an “anaesthetic effect”
MICROSCOPIC ANATOMY OF PERIPHERAL NERVES

Cross section of myelinated & unmyelinated nerves

Nerves, such as the sciatic nerve, can be up to 1 metre in length e.g. sciatic n
PERIPHERAL NERVE CONDUCTION

A compound action potential is made up of the electrical activity of all the different nerve types within the nerve fascicle or bundle.

<table>
<thead>
<tr>
<th>Axon type</th>
<th>Aα</th>
<th>Aβ</th>
<th>Aδ</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (µm)</td>
<td>13-20</td>
<td>6-12</td>
<td>1-5</td>
<td>0.2-1.5</td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>80-120</td>
<td>35-75</td>
<td>5-35</td>
<td>0.5-2.0</td>
</tr>
</tbody>
</table>

*Peripheral Neuropathy 1999 2nd Ed Dyck & Thomas*
SYSTEMATIC REVIEW OF THE EFFECTS OF LASER ON NERVES

• 18 human studies - LI slowed conduction velocity and decreased CAP amplitude

• *Message: establishes the principle that transcutaneous laser can inhibit underlying nerves in humans* eg Median nerve (carpal tunnel)

• 25 animal studies - demonstrated Aδ and C fibre inhibition and anti-inflammatory activity

• *Message: LI can selectively suppress nociceptors and inflammation*

Studies showing inhibition of neural stimuli following noxious stimuli

- Suppression of noxious stimuli, including turpentine injection into rat paw
  - Tsuchiya et al 1994 -

- Effect of multiple unit discharges by pinch stimulation in the sural nerve of rabbit
  - Kasai et al 1994
Ga-Al-As laser irradiation inhibits neuronal activity associated with inflammation.
Sato T, Kawatani M, Takeshige C, Matsumoto I
Acupunct Electrother Res 1994 Jun-Sep 19(2-3) 141-51
Neuronal discharge

Laser to peripheral nerve has central effects

Fig. 1. Schema of the electrophysiological experiment in rats. The pulp of the lower incisor was electrically stimulated and the evoked action potentials were extracellularly recorded in the ipsilateral caudal neurons. The GaAlAs semiconductor laser was irradiated on the cervical surface of the stimulated incisor toward the tooth pulp.
GaAlAs (830nm) low-level laser enhances peripheral endogenous opioid analgesia in rats.
Hagiwara et al (2007) 39(10) 797-802

Fig. 2. Rat withdrawal latency in the hot plate test after injection of saline or FCA in the hind paw followed by LLLT or no treatment. Circles represent values measured for the saline group, triangles represent the control group, and squares represent the LLLT group. Data are expressed as mean ± SEM (n = 6–8 rats/group). *P < 0.05, compared with the control group.

Fig. 3. Rat withdrawal latency on the hot plate test with naloxone administration 2 days after injection of saline or FCA in the hind paw followed by LLLT or no treatment. Circles represent values measured for the saline group, triangles the control group, and squares represent the LLLT group. Data are expressed as mean ± SEM (n = 6/group). *P < 0.05, compared with the control group.

This study was undertaken with an NHMRC Grant 2009 – to study the effects of laser on nerves
• Somatosensory evoked potentials (SSEPs) and

• Compound muscle action potentials (CMAPs) were both measured
Latency and amplitude of SSEPs following 30s of 650 nm LI at 4 points over sciatic nerve

**Graphs:**

**a) 650 nm LI on SSEP latency**
- Latency (ms) measured at baseline, 10 min, 20 min, 24 h, and 48 h.
- Significant changes indicated with *P*<0.001.

**b) 650 nm LI on SSEP amplitude**
- Amplitude (uV) measured at baseline, 10 min, 20 min, 24 h, and 48 h.
- Significant changes indicated with *P*<0.05 and *P*<0.01.
Latency and hip/ankle ratios of CMAPs following 30s of 650 nm LI at 4 points over sciatic nerve

650 nm LI on CMAP latency

Latency (ms)

Baseline Control LI

650 nm LI on CMAP amplitude

H/A ratio

Baseline Control LI
808 nm LI at 4 points over sciatic nerve

**808 nm LI on SSEP latency**

- c: Latency (ms)
- P<0.001
- P<0.001

**808 nm LI on SSEP amplitude**

- d: Amplitude (µV)
- P<0.001
- P<0.05
Latency and hip/ankle ratios of CMAPs following 30s of 808 nm LI at 4 points over sciatic nerve

808 nm LI on CMAP latency

Baseline Control LI

808 nm LI on CMAP amplitude
LASER CAUSES CHANGES IN THE CYTOSKELETON

- **Immunohistochemistry**
  - Cultured, neonatal rat dorsal root ganglion neurons
  - Immunohistochemistry - anti-β tubulin antibodies

- **Live cell imaging - JC 1**
  - Measured Mitochondrial Membrane potential
  - Fast axonal flow

- **650nm, 808nm & 830nm LI**

Representative photomicrograph of control cultures showing nerve cell bodies and smooth axonal arrays.

MICROTUBULE POLYMERISATION AND TRANSPORT FUNCTION

*Polymerisation and maintenance of the cytoskeleton is ATP dependent*

*Images of microtubule arrays (Alberts - Molecular Biology of the Cell 3rd edition)*

*Microtubule Associated Proteins (MAPS) are ATPases*
AFTER LI

Before LI

*diagram not to scale*
Laser-irradiated axon showing varicosity in real time over 10 minutes of observation - confocal microscopy using JC-1 staining.
Control axon showing normal fast axonal flow
• The pain relieving effects of laser therapy are (in part) mediated by the (strongly evidence based) neural blockade effects of light on nerves
Quaternary effects

- Reduces pain
  - by direct anti-nociceptive effects
- Reduces inflammation
  - reduce PGE$_2$ (and other inflammatory markers)
- Reduces muscle spasm
  - direct spasmolytic effects
- Reduces swelling
  - improve motoricity of lymphatics
- Stimulates tissue repair/wound healing
  - Stimulates fibroblast activity; increased procollagen production, release of growth factors; angiogenesis
- Stimulates central effects
  - Causes release of $\beta$-endorphins, 5HIAA end-products, down regulated long term potentiation
- Systemic effects
ANTI-INFLAMMATORY EFFECTS

LLLT has anti-inflammatory effects equivalent to those of (some) oral anti-inflammatory agents
ANTHI-INFLAMMATORY EFFECTS

Pathways for acute pain relief and anti-inflammatory effects by red or infrared LI

Local LLLT effects after first irradiation, enhanced effect by repeated irradiation

Effects on biochemical inflammatory markers

<table>
<thead>
<tr>
<th>Effect</th>
<th>Number of Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced PGE$_2$ levels (5)</td>
<td></td>
</tr>
<tr>
<td>Reduced TNF$\alpha$ levels (2)</td>
<td></td>
</tr>
<tr>
<td>Reduced IL1$\beta$ levels (3)</td>
<td></td>
</tr>
<tr>
<td>Reduced COX-2 mRNA levels (2)</td>
<td></td>
</tr>
<tr>
<td>Reduced plasminogen activator levels (1)</td>
<td></td>
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</tbody>
</table>

Effects on cells and soft tissue

<table>
<thead>
<tr>
<th>Effect</th>
<th>Number of Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced oedema formation (7)</td>
<td></td>
</tr>
<tr>
<td>Reduced hemorrhagic formation (5)</td>
<td></td>
</tr>
<tr>
<td>Reduced neutrophil cell influx (4)</td>
<td></td>
</tr>
<tr>
<td>Enhanced local microcirculation (4)</td>
<td></td>
</tr>
</tbody>
</table>

Anti-inflammatory effects found in 21/24 laboratory studies

Bjordal et al. 2006, Photomed Laser Surg
Anti-inflammatory effects demonstrated in human Achilles microdialysis study

A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E$_2$ concentrations

J M Bjordal, R A B Lopes-Martins, V V Iversen

Cytokine mRNA expression is decreased in the subplantar muscle of rat paw subjected to carrageenan-induced inflammation after LLLT. 

Anti-inflammatory effects

The anti-inflammatory effects of laser and anti-inflammatory drugs in animal studies are very similar

Albertini, Lopes-Martins et al.  
Photochem PhotoBiol 2004

Aimbire, Lopes-Martins, Bjordal et al.  
Photomed Laser Surg 2006

Diclofenac = Voltaren®
Laser (655nm) dose 7.5 Joules

Celecoxib = Celebra®, Celebrex®
Dexamethasone = Glucocorticoid
Laser (650nm) dose 2.5 Joules
Analgesic effect of GaAlAs diode laser irradiation on hyperalgesia in carrageenin-induced inflammation.


Fig. 1. The effect of the low-power laser irradiation in the acute first phase of the carrageenin-induced inflammation on the occurrence of hyperalgesia. The vertical axis shows changes in the pressure-pain threshold of hind paws of rats. The horizontal axis shows the time. In the saline-laser group (n = 6) and carrageenin-laser group (n = 6), the right hind paw was irradiated immediately before and after the injection (a total of 6 minutes) of 0.1 ml saline or 0.1 ml 2% carrageenin. In the carrageenin control (n = 6), indomethacin (IMC: 4 mg/kg, i.o.) was administered. In the carrageenin control (n = 4) and the carrageenin IMC groups, rats were held against the probe but were not irradiated. Values were given by the mean ± SR. *; significantly different not only from the value at -1 hour (P < 0.01), but also the value in the intact left hind paw (P < 0.01).
A clinical study on serum PGE$_2$ with LLLT

Mizutani 2004 Photomed Laser Surg 22(6) 537-539

“The serum PGE2 levels are therefore considered to directly reflect nociceptive pain.”
IN ACUTE INJURY - LI SUPPRESSES PERIPHERAL NERVE SENSITISATION AND REDUCES SENSITIVITY TO BRADYKININ, PGE2

- Block nociceptors
- Suppresses peripheral nerve sensitisation
- Suppresses neurogenic inflammation
- Reduce pain
- Reduce oedema
- Prevent progression of acute to chronic pain

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>NGF</td>
<td>TrkA</td>
</tr>
<tr>
<td>Bradykinin</td>
<td>EKβ2</td>
</tr>
<tr>
<td>Serotonin</td>
<td>5-HT3</td>
</tr>
<tr>
<td>ATP</td>
<td>P2X3</td>
</tr>
<tr>
<td>H+</td>
<td>ASIC3/VR1</td>
</tr>
<tr>
<td>Lipids</td>
<td>PGE2/CB1/VR1</td>
</tr>
<tr>
<td>Heat</td>
<td>VR1/VRL-1</td>
</tr>
<tr>
<td>Pressure</td>
<td>DEG/E NaC</td>
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</table>
NEUROGENIC INFLAMMATION

Neurogenic inflammation:

- Is inflammation resulting from the release of bioactive substances, *substance P*, *CRGP* & *Prostaglandins* from primary sensory nerve terminals (in the periphery), which in turn act on mast cells, immune cells, and vascular smooth muscle.

- Contributes to chronic pain states by increasing synaptic activity in second order neurons.

- 40% of back pain is “neuropathic”
Suppression of neural excitability suppresses mast cell degranulation leading to decrease in neurogenic inflammation (*unpublished data*)

Representative histost showing reduction in mast cell density 1 hr after pre-emptive 30s x1 650 & 808 nm laser and immediately prior to inj of 48/80 (mast cell activator)
Reduction in mast cell degranulation, 30s immediately prior to inj of 48/80
Reduction in PGE2 levels in skin following 30s LI to normal rat skin

PGE levels following 650nm LI

PGE levels following 808nm LI

* 1 h or 48 h post LI to baseline: P < 0.05
** 4 h post LI to baseline: P < 0.01

* 1h post LI to baseline: P < 0.05
** 24 h or 48 h post LI: P < 0.01
Reduction in degranulation in peritoneal mast cells in vitro following 48/80 at 3 strengths

(48/80 stimulates mast cell degranulation)
Reduction in PGE2 levels in skin following 30s LI to normal rat skin

**PGE levels following 650nm LI**

- Baseline
- 1 h post LI
- 4 h post LI
- 24 h post LI
- 48 h post LI

**PGE levels following 808nm LI**

- Baseline
- 1 h post LI
- 4 h post LI
- 24 h post LI
- 48 h post LI

* 1 h or 48 h post LI to baseline: P < 0.05
** 4 h post LI to baseline: P < 0.01

* 1h post LI to baseline: P < 0.05
** 24 h or 48 h post LI: P < 0.01
Inflammation in active trigger points in neck pain

Acidity (pH) and increased levels of neurotransmitter substance P in trigger points of upper trapezius muscle

Increased inflammatory markers in active trigger points of upper trapezius muscle

Shah et al. (2009), Arch Phys Med Rehab
Quaternary effects – whole person effects

- **Reduces pain**
  - by direct anti-nociceptive effects
- **Reduces inflammation**
  - reduce PGE$_2$ (and other inflammatory markers)
- **Reduces muscle spasm**
  - direct spasmolytic effects
- **Reduces swelling**
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- **Stimulates central effects**
  - Causes release of $\beta$-endorphins, 5HIAA end-products, down regulated long term potentiation
- **Systemic effects**
Effects on muscle

Trigger points

New hypothesis about myofascial trigger points:
A taut band in muscles in myofascial pain syndromes is caused by inflammation of muscle spindles and consequently a positive feedback loop for III- and IV-fferent-driven skeletofusimotor activity resulting in contracture of extrafusal muscle fibres.

Partanen et al (2009), J Pathophys
doi:10.1016/j.pathophys.2009.05.001
LASER REDUCES MUSCLE SPASM

- Duration of effect - minutes
  - reduction in pain and ppt (Airaksinen et al 1989)
  - By a direct effect on motor end plate activity in vitro models (Nicolau 2004 a & b)
  - By an indirect effect on inflammation within trigger points

Siddall & Cousins 1998

Muscle spindle

A taut band in muscles in myofascial pain syndromes is caused by inflammation of muscle spindles and consequently a positive feedback loop for III- and IV-afferent-driven skeletofusimotor activity resulting in contracture of extrafusal muscle fibres.

Increased inflammatory markers in active trigger points of upper trapezius muscle
Myofascial Trigger Points

- Abnormal depolarization of motor end plates
- EMG studies show spontaneous electrical activity in MTPs
- Adjacent muscle tissues are electrically silent

Effects of helium-neon laser irradiation on skin resistance and pain in patients with trigger points in the neck or back.

Muscle Fatigue

Effect of 655-nm low-level laser therapy on exercise-induced skeletal muscle fatigue in humans.
Leal Junior EC et al
University of Caxias do Sul, Caxias do Sul, RS, Brazil,
Effect of 655-nm Low-Level Laser Therapy on Exercise-Induced Skeletal Muscle Fatigue in Humans

Quaternary effects

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- **Systemic effects**
The lymphatic system -

• In patients with poor lymphatic transport function laser to any part of the body causes stimulation of the pumping action of the lymph vessels of the whole body.

• These people can usually feel the gentle pulsing in their lymph vessels distal to the place of application of the laser.
Submandibular Lymph Nodes
INCREASES MOTORICITY OF LYMPHATICS

- Oedema is associated with stiffness and pain
- Increased motoricity leads to decreased swelling
- Decreased swelling leads to decreased pain
- Decreased pain leads to earlier mobilisation
  - Lievens 1991; Carati et al 2003
Scanning Laser

Pilot trial completed Flinders Medical Centre  1995
Hand Held Laser

Double Blind Crossover Trial Completed Flinders Medical Centre - 2002

Cancer 2003

31 October 2013
A systematic review of the effect of low-level laser therapy in the management of breast cancer-related lymphedema

Mohammed Taher Ahmed Omar • Afaf Ahmed Mohamed Shaheen • Hamayun Zafar

Received: 2 February 2012 / Accepted: 23 July 2012
© Springer-Verlag 2012

Abstract
Purpose The purpose of this study was to review the effect of low-level laser therapy (LLLT) in the management of breast cancer-related lymphedema (BCRL).
Methods A systematic review of seven databases for clinical trials for LLLT in the management of BCRL published between 1990 and 2011 was performed.
Results A total of eight studies on 230 patients were found. The methodological qualities of the selected studies were assessed with the Physiotherapy Evidence Database scale, and the studies were categorized according to Sackett’s levels of evidence. Five studies were graded at evidence level II. Two studies were graded at evidence level III, and the remaining study was graded at evidence level V.
Conclusions There is moderate to strong evidence for the effectiveness of LLLT for the management of BCRL from five small studies of acceptable methodological quality. A dose of 1–2 J/cm² per point applied to several points covering the fibrotic area can reduce limb volume following BCRL. Further well-designed, large-scale studies are required to determine more precisely how effective LLLT may be in BCRL.

Keywords Breast cancer • Lymphedema • Low-level laser therapy
Treatment of Post-Mastectomy Lymphoedema with Laser Therapy: Double Blind Placebo Control Randomized Study

Omar et al
Journal of Surgical Research 2010
Oedema in ankle sprains

Low-Level Laser Treatment Can Reduce Edema in Second Degree Ankle Sprains Stergioulas A
University of Peloponnese, Greece

Volume measurement (ml) differences
72h

RICE = Rest
Ice
Compression
Elevation
Quaternary effects – whole person effects

- **Reduces pain**
  - by direct anti-nociceptive effects

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- **Systemic effects**
LLLT **CAN** ACCELERATE THE RESOLUTION OF ACUTE INFLAMMATION and TISSUE REPAIR ....... provided that the correct parameters are used

.....POSSIBLY BY STIMULATING THE SECRETION OF SOLUBLE PROTEIN MEDIATORS by INFLAMMATORY (IMMUNE) CELLS & NON-INFLAMMATORY CELLS
EXAMPLES OF EFFECTS OF LIGHT ON IMMUNE CELLS WHICH FACILITATE HEALING

Changes have been reported in:

• Neutrophils
• Monocytes
• Macrophages
• Lymphocytes
• Mast cells
An example: wavelength effects on mediator secretion & calcium uptake (macrophages)

**STIMULATORY**

- 660 nm (non-coherent)
- 820 nm (coherent)
- 870 nm (non-coherent)

**INEFFECTIVE**

- 880 nm (noncoherent)

COHERENCE IS NOT ESSENTIAL
MACROPHAGES

- LLLT (632.8 nm, 0.2 W/cm²) for 5 to 180s increases cellular TNF-alpha in murine macrophages in vitro.
- IL-6 production increased by 5s exposure, but not by 60 to 180s

Thus energy level and possibly treatment time matter.
Effect of wavelength on macrophage-induced fibroblast proliferation by 5 days in vitro (2J/cm²)
EFFECT OF LLLT ON WOUND CONTRACTION

At 5 days post-op:
700 Hz is inhibitory
1200 Hz is stimulatory
Cell counts 5 days post-op

- poly
- macro
- myofibro
- endo

control
700 Hz
1200 Hz
LLLT for stimulation of wound healing

LLLT transforms fibroblasts to myofibroblasts

Michael R Hamblin PhD
Photonics West: BIOS
2006
• RED LIGHT can affect all cells
• INFRARED is more specific:
  – Some wavelengths affect some cell types
  – Other wavelengths affect other cell types
LLLT CAN STIMULATE ANGIOGENESIS

Number of blood vessels & endothelial cell proliferation is increased in granulation tissue of skin wounds treated with red LEDs

Ghali L & Dyson M 1992
Direct effects of LLLT on endothelial cell proliferation in vitro

- 660 or 820nm, 15mW, 1 – 8 J/cm²
- Endothelial proliferation stimulated by all treatments, 4 J/cm² being the most effective at both wavelengths

(Sehgal 1998)
Indirect effects on endothelial cells in vitro via angiogenic factors released from LLLT treated macrophages

- 660nm or 820nm, 15 mW, 1-8 J/cm²
- 2, 4 & 8 J/cm² stimulated endothelial cell proliferation indirectly
- 660 nm more effective than 820 nm
- 660 nm, 2 J/cm² optimum
- 1 J/cm² ineffective (i.e. sub-threshold) (Sehgal 1998)

If this also occurs in vivo then angiogenesis would be stimulated.
LED Therapy
RCT
14 patients
23 diabetic leg ulcers
Cleaned, dressed with 1% silver sulfadiazine cream
LLLT twice per week

Phototherapy promotes healing of chronic diabetic leg ulcers that failed to respond to other therapy
Minatel DG, Frade MA, Franca SC, Enwemeka CS
Lasers Surg Med 2009 Aug 41(6) 433-41
Stage 4 pressure sore
before Laser Therapy

Male, 49 MS
Wheelchair bound
2 Year old pressure sore
4 x 6 cm x 6 cm cavity

Packing cavity & dressing
Aquacel & Pressure Plus

Pressure reliving mattress and cushion

Lydia Jacks, Tissue Viability Nurse Specialist, Inverclyde Royal Hosp

Wounds UK 2006 Vol2, No1, pg74-75
Stage 4 pressure sore after Laser Therapy

Cavity reduced to 3cm 5 weeks

Full healing 7 months

Laser treatment twice week 1 min per area

Lydia Jacks, Tissue Viability Nurse Specialist, Inverclyde Royal Hosp

Wounds UK 2006 Vol2, No1, pg74-75
LED Therapy
Stage 2 pressure ulcers
RCT.
> 64 years

Stage 2 pressure ulcers n = 62
Differences were statistically significant
to 50% healing P = 0.001
to 90% healing p < 0.01
complete healing p = 0.01

Effects of phototherapy on pressure ulcer healing in elderly patients after a falling trauma. A prospective, randomized, controlled study.
Schubert V.
Karolinska Institutet, Department of Clinical Neuroscience, Occupational Therapy and Elderly Care Research, Huddinge University Hospital, Stockholm, Sweden.
Photodermatol Photoimmunol Photomed 2001 Feb;17(1):32-8
Venous Ulcer healing

The use of low energy photon therapy (LEPT) in venous leg ulcers: a double-blind, placebo-controlled study.
Gupta AK, Filonenko N, Salansky N, Sauder DN
• Light non-coherent or coherent can affect multiple cells involved in tissue repair and would healing
Quaternary effects

- **Reduces pain**
  - by direct anti-nociceptive effects
- **Reduces inflammation**
  - reduce PGE₂ (and other inflammatory markers)
- **Reduces muscle spasm**
  - direct spasmolytic effects
- **Reduces swelling**
  - improve motoricity of lymphatics
- **Stimulates tissue repair/wound healing**
  - Stimulates fibroblast activity; increased procollagen production, release of growth factors; angiogenesis
- **Stimulates central effects**
  - Causes release of β-endorphins, 5HIAA end-products, down regulated long term potentiation
- **Systemic effects**
Laser Blood Irradiation

Alters rheology of blood
Summary

• Photons of particular wavelengths and at a particular “dose” can relieve pain by
  – Direct neural blockade
  – Anti-inflammatory effects
  – Relief of muscle spasm
  – Reduction in oedema
  – Tissue repair

........ so what are the clinical applications?
Why do we need this?

.........don’t we have enough tools ??
NSAIDS AND SIDE EFFECTS

Miscarriage risk prompts warning on NSAID use in pregnancy

Anna Evangeli

A STUDY finding an increased risk of miscarriage in women taking non-steroidal anti-inflammatory drugs (NSAIDs) has raised questions about the use of these drugs during pregnancy.

High-risk NSAIDs remain popular worldwide

Dickenson should be removed from essential medicine lists (EMLs) worldwide, according to the authors of a report published in *PLOS Medicine*. Using data from published meta-analyses, the authors correlated the relative risk of cardiovascular events associated with specific non-steroidal anti-inflammatory drugs (NSAIDs) with the EMLs of 100 countries and sales information for NSAIDs in 15 countries. Apart from countries that were not available, the NSAID was the NSAID most associated with an increased risk of cardiovascular events (40%–60% higher relative risk compared with non-use). Yet it remains on the EMLs of 74 countries, including Australia. In contrast, naproxen, was the safest of the NSAIDs, features on only 27 EMLs. An accompanying editorial said that "emerging evidence about NSAID risk is poorly translated into practice and sales in countries around the world, raising questions about the use and promotion of potentially harmful drugs".

doi: 10.1371/journal.pmed.1001398

Study links low-dose NSAIDs to stroke risk in healthy population

David Brill

EXPERT opinion remains divided on risks versus benefits of NSAIDs, after research shows even low doses may raise the risk of stroke in healthy individuals.

David Henry, conjoint professor at the University of Newcastle, NSW, said there was "no reason for (diclofenac) to stay on the market" when naproxen was a safer alternative.

NSAIDs: study suggests no safe dose post-MI

NSAIDs used to treat patients quickly after a heart attack may not be as safe as previously thought.

There is no safe dose of NSAIDs for people with a history of myocardial infarction, research finds, signaling doubt about the risks of over-the-counter NSAIDs.

The Danish study of almost 65,000 patients with prior MI found both short- and long-term use of NSAIDs increased the risk of a further MI and death. Those taking any NSAIDs over the eight-year study period faced a 65% increased risk of death or MI at the beginning of treatment, and the risk persisted throughout the treatment duration.

The authors called for trials on NSAID use, noting the increased risk with diclofenac (Voltaren) was higher than for celecoxib (Celebrex), which was withdrawn in 2004.

"The present results indicate that there is no apparent safe therapeutic window for NSAIDs in patients with prior MI," they wrote in *Circulation*. Professor Lars Wiklund, head of cardiology at Concord Hospital in Sydney, said the study added to mounting evidence that increased cardiovascular risk, but said he did not support an outright ban for CVD patients.

"The advice would be to avoid the drugs where possible, to base them for the shortest period of time possible and to take them under supervision of a family doctor," he said.

"The most important thing is there is a warning to patients ... and it's much better that patients informed verbal and written, [acknowledged] this risk so that patients knows what it's doing."
**In brief**

**NSAIDs and aspirin role in preventing GI cancers**

There may be a role for NSAIDs in prevention of adenocarcinomas of the oesophagus and oesophago-gastric junction say the authors of a review (link) that found a 40% lower risk of cancer among frequent and or long term aspirin and NSAID users.

*Gastroenterology* (online Nov 19)
Doctors should think twice about recommending paracetamol for patients with osteoarthritis due to safety concerns over the drug, UK guidelines warn.

The recommendation, dubbed “excessive” by one expert, was made in the UK National Institute for Health and Care Excellence’s (NICE) draft guidelines on osteoarthritis.

Citing concern about the “very definite trend” linking paracetamol to adverse cardiovascular, gastrointestinal and renal events, NICE said osteoarthritis patients should not be routinely advised to use the drug, even intermittently when the condition flares up.

Clinicians were instead encouraged to offer proven interventions, such as weight management and exercise for strengthening and aerobic fitness.

Topical NSAIDs were the analgesic of choice, ahead of oral NSAIDs or opioids, according to the document, which was drafted by a multidisciplinary panel including rheumatologists and GPs.
Editorial: Arthroscopy to treat OA of the knee? Changing clinical beliefs and behaviour in response to credible evidence of lack of treatment efficacy remains highly challenging. *Buchbinder & Harris MJA 197(7) Oct 2012*

“Action is needed to change the current situation of making novel but untested non-drug treatments available to patients before their rigorous evaluation. The use of arthroscopy for knee osteoarthritis has been allowed to continue, exposing patients to an intervention that is at best ineffective, and at worst, harmful.”

“…..it has remained difficult to shift convictions of many surgeons. This may be due to cognitive dissonance: the need to refute or reject information that is inconsistent with ingrained beliefs.”
What about the clinical evidence for low-level laser therapy?
Over 300 (RCT) clinical trials
Over 3000 laboratory studies
Over 30 new research papers a month
Most published literature - >10 RCTs published in peer-reviewed journals

- Tendinopathy
- Osteoarthritis
- Neck Pain
- Oral Mucositis (of chemotherapy)
- Dental pain
- Also a reasonable amount of literature on
  - Neuropathic pain
  - Non-healing wounds
  - Lymph phoedema
A systematic review of low level laser therapy with location-specific doses for pain from chronic joint disorders


**Figure 1.** Effect of low level laser therapy on pain (mm on a 100 mm VAS).

**Figure 2.** Effect of low level laser therapy on health status (Relative risk of not improving).
Application in arthritis

• Prevalent condition, becoming more prevalent in aging population
• Common conditions
  – Osteoarthritis
  – Rheumatoid arthritis
  – Mechanical spine disorders
  – Patella femoral pain
  – TMJ disorders
• Can involve impaired muscular stabilisation, reduced range of motion and inflammation of the joint capsule
Frozen shoulder: the effectiveness of conservative and surgical interventions—systematic review

M M Favejee,1,2 B M A Huisstede,1,3 B W Koes3

ABSTRACT

Background A variety of therapeutic interventions is available for restoring motion and diminishing pain in patients with frozen shoulder. An overview article concerning the evidence for the effectiveness of these interventions is lacking.

Objective To provide an evidence-based overview regarding the effectiveness of conservative and surgical interventions to treat the frozen shoulder.

Methods The Cochrane Library, PubMed, Embase, Cinahl and Pedro were searched for relevant systematic reviews and randomised clinical trials (RCTs). Two reviewers independently selected relevant studies, assessed the methodological quality and extracted data. A best-evidence synthesis was used to summarise the results.

Results Five Cochrane reviews and 18 RCTs were included studying the effectiveness of oral medication, injection therapy, physiotherapy, acupuncture, arthrographic distension and suprascapular nerve block (SSNB).

Conclusions We found strong evidence for the effectiveness of steroid injections and laser therapy in short-term and moderate evidence for steroid injections in mid-term follow-up. Moderate evidence was found in favour of mobilisation techniques in the short and long term, for the effectiveness of arthrographic distension alone and as an addition to active physiotherapy in the short term, for the effectiveness of oral steroids compared with no treatment or placebo in the short term, and for the effectiveness of SSNB compared with acupuncture, placebo or steroid injections. For other commonly used interventions no or only limited evidence of effectiveness was found. Most of the included studies reported short-term results, whereas symptoms of frozen shoulder may last up to 4 years. High quality RCTs studying long-term results are clearly needed in this field.

the glenohumeral joint in all directions), frozen phase (stiffness reaches its maximum) and the thawing phase (range of motion (ROM) returns to normal). Although frozen shoulder is often considered to be self-limiting, full resolution of symptoms does not always occur. Only 59% of the patients had a near normal shoulder after 4 years. However, persistent symptoms are commonly mild.

No therapeutic intervention is currently universally accepted as most effective for restoring motion and diminishing pain in patients with frozen shoulder. An overview regarding the effectiveness of possible conservative and surgical interventions is lacking. Therefore, this study aimed to provide an evidence-based overview on the effectiveness of interventions for primary frozen shoulder.

METHODS

A search of systematic reviews on primary frozen shoulder was performed in the Cochrane Library. In addition, reviews and randomised clinical trials (RCTs) in PubMed, Embase, Cinahl and Pedro were searched for interventions included in the systematic reviews from the date of the search strategy of the review up to April 2008 (ie, recent RCTs) and from the beginning of the database up to April 2008 for interventions not (yet) included in systematic reviews (ie, additional RCTs). See supplementary appendix I (available online only) for the complete search strategy.

Inclusion criteria

Systematic reviews and RCTs were included if they fulfilled all of the following criteria: (1) the study included patients with frozen shoulder; (2)
Conclusions: We found strong evidence for the effectiveness of steroid injections and laser therapy in short-term and moderate evidence for steroid injections in mid-term follow-up. For other commonly used interventions no or only limited evidence of effectiveness was found.

Frozen shoulder: the effectiveness of conservative and surgical interventions— systematic review
**CRP response**

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*Units: mg/L*
A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations

J M Bjordal, R A B Lopes-Martins, V V Iversen
RCT60 Patients (20 - 65 years of age)
Cervical Osteoarthritis
Treatment daily treatment for 10 days
830nm 50mW 12 points
12 application points @ 15 seconds
6 each side midline of the paravertebral muscles.

Neck Pain

The clinical efficacy of low-power laser therapy on pain and function in cervical osteoarthritis. Ozdemir et al Clin Rheumatol 2001 20(3)
181-4 Medical Faculty of Trakya University, Turkey
Efficacy of 904 nm Gallium Arsenide Low Level Laser Therapy in the Management of Chronic Myofascial Pain in the Neck: A Double-Blind and Randomize-Controlled Trial


Fig. 2. Perceived percentage improvement in pain at the end of treatment in both actual and placebo laser groups.
LLLT in non-specific neck pain

Efficacy of low-level laser therapy (LLLT) in the management of neck pain: a systematic review & meta-analysis of randomised, placebo & active treatment controlled trials.

Prof R. Lopes-Martins  Prof M Johnson  Prof JM Bjordal

The Lancet seeks to publish high-quality clinical research that will alter medical practice:

The Lancet is one of the world's leading Independent general medical journal.
Impact factor 30,75
Outcomes assessed

- **Primary**
  - pain relief along a 0-100mm visual analogue scale (VAS) or a numerical rating scale (NRS) or
  - patient reported improvement (e.g. categorical report of no change to complete relief of pain)

- **Secondary**
  - Functional measures of disability (e.g. neck pain disability questionnaire)

- **Adverse events** (where reported)

- **Duration** of follow-up
  - short-term (less than 1 month)
  - medium (1 to 6 months) and
  - long-term (over 6 months)

- **Laser irradiation parameters** and application
Sites treated

- Laser irradiation was applied to points in the neck identified as
  - trigger points (6) or
  - tender points (Ah Shi) (4) or
  - local acupuncture points (3) or
  - predetermined points on a grid (1) or
  - unspecified (2)
Results - Acute neck pain

- two studies - one clearly positive
- RR for improvement in acute neck pain is 1.69
Chronic neck pain

Subgrouped by methodological score (cut off $\geq 3/5$)

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Laser Therapy Mean (SD)</th>
<th>Placebo Mean (SD)</th>
<th>Weight</th>
<th>WMD (random) 95% CI</th>
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<td>63.60 (26.05, 83.91)</td>
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<td>Chow</td>
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<td>40.00 (26.80)</td>
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<td>360</td>
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Effect size was larger in studies with higher method scores ($\geq 3/5$)
### Chronic neck pain

Duration of effects after end of treatment

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<th>Study or sub-category</th>
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<th>Placebo Mean (SD)</th>
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</tr>
<tr>
<td>Test for overall effect: Z = 7.28 (P &lt; 0.00001)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Total (95% CI)</td>
<td>171</td>
<td>175</td>
<td>100.00</td>
<td>22.07</td>
<td>[17.42, 26.72]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Ch² = 38.08, df = 7 (P &lt; 0.00001), P = 81.8%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 9.29 (P &lt; 0.00001)</td>
<td></td>
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</tbody>
</table>

- **Effect size duration 1-4 weeks**: 20.5 mm [95% CI: 13.6 to 27.3]
- **Effect size duration 10-22 weeks**: 23.4 mm [95% CI: 17.1 to 29.8]
Chronic neck pain
Subgroup with laser acupuncture treatment procedure
(not in the published paper)

Must have treated local acupuncture points in the neck
Pain reduction over placebo: 20.7 mm [95% CI: 10.0 to 31.4]
Results - Chronic neck pain

- **VAS reduced by 19.9 mm** (95% CI: 10.4 - 29.68) irrespective of methodological quality of trials at the end of treatment (*correction - 16.6 mm*)

- **VAS reduced by 20.5 mm** (95% CI: 13.6 - 27.3) at 1 to 4 weeks follow-up after treatment

- **VAS reduced by 23.4 mm** (95% CI: 17.1 - 29.8) at follow up from 10 to 22 weeks
Results -

secondary outcome measures

• 5 studies provided data for improvement in disability at the end of treatment

➢ used several outcome measures (e.g. the neck pain and disability scale (NPDS), Northwick Park neck pain questionnaire (NPNQ), Short Form 36 (SF36), Nottingham Health Profile and neck disability index (NDI))
Chronic neck pain
Disability scores - end of treatment

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Laser Mean (SD)</th>
<th>Placebo Mean (SD)</th>
<th>SMD (random) 95% CI</th>
<th>Weight %</th>
<th>SMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ozdemir</td>
<td>26.60 (17.60)</td>
<td>6.60 (13.60)</td>
<td>17.25</td>
<td>4.60</td>
<td>[3.61, 5.59]</td>
</tr>
<tr>
<td>Gur</td>
<td>30</td>
<td>30</td>
<td>20.55</td>
<td>0.79</td>
<td>[0.21, 1.28]</td>
</tr>
<tr>
<td>Chow</td>
<td>18.20 (12.10)</td>
<td>3.10 (14.10)</td>
<td>20.95</td>
<td>0.91</td>
<td>[0.47, 1.34]</td>
</tr>
<tr>
<td>Ibusa</td>
<td>19.10 (12.30)</td>
<td>7.10 (12.90)</td>
<td>20.85</td>
<td>0.79</td>
<td>[0.18, 1.42]</td>
</tr>
<tr>
<td>Dundar</td>
<td>19.60 (10.90)</td>
<td>7.10 (12.90)</td>
<td>20.59</td>
<td>0.29</td>
<td>[-0.20, 0.78]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1.57</td>
<td>1.57</td>
<td>100.00</td>
<td>1.88</td>
<td>[1.88, 2.87]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 59.65, df = 4 (P < 0.00001), I² = 93.3%
Test for overall effect: Z = 2.74 (P = 0.006)

Active laser groups had an effect size of 1.4 [0.4 to 2.4] over placebo.
Comparison with other Rxs

- **Oral NSAIDs** - “largely negative” - 10.5 mm
  (20mm reduction in VAS recognised as clinically relevant)
- **Paracetamol** - no evidence of benefit
- **Diazepam (valium)** - no evidence of benefit
- **GP rx (ed/analg/antiflam)** - no benefit
- **Inj Botox** - evidence of no benefit
- **Inj of lignocaine to muscles** - 40mm
  - *Peloso et al 2008 Issue 3 - Medicinal and injection therapies for mechanical neck pain - Cochrane Library*
Acute Low Back Pain with Radiculopathy: A Double-Blind, Randomized, Placebo-Controlled Study
Konstantinovic, et al
Photomedicine and Laser Surgery

RCT
546 Patients
Acute Low Back Pain with Radiculopathy
5 times a week for 3 weeks

904nm
100mW
4 points
150 sec per point

Back Pain

Pain (VAS Leb)

![Graph showing pain levels before and after treatments for Laser, Placebo, and NSAID only conditions.](source)

Before
After 15 treatments
- Laser: 78.5, 34.0
- Placebo: 76.0, 54.0
- NSAID only: 78.0, 60.0
Outcome measures - between group differences in Acute low back pain with radiculopathy: a double-blind, randomised, placebo-controlled study

Konstantinovic et al 2010

Statistically sign diff for almost all measured outcomes
Chronic Achilles Tendinopathy

RCT
52 Recreational athletes
chronic Achilles tendinopathy for a min of 6 months duration
eccentric exercises

820nm
30mW
0.5cm²
60mW/cm²
6 points
0.9J per point
15 sec
12 treatments
8 weeks

University of Peloponnese, Greece
Low Level Laser Treatment of Tendinopathy: A Systematic Review with Meta-analysis


FIG. 3. Lateral epicondylitis grip strength. The upper graph includes both comparisons from Oken et al. 20 (2008) and therefore pooling of data is not shown.
When LLLT does not work

A systematic review with procedural assessments and meta-analysis of Low Level Laser Therapy in lateral elbow tendinopathy (tennis elbow) Bjordal et al

8 out of 13 trials (62%) reported one or more outcome measures in favour of LLLT

38% failed

Over treatment

LLLT for the Treatment of Tendinopathy: A Systematic Review, Tumilty et al

9 out of 20 trials (45%) reported one or more outcome measures in favour of LLLT

55% failed/ inconclusive

Over treatment
Chronic Neuropathic Pain
Post Herpetic Neuralgia
(Crossover Trial)

20 patients
4 x twice weekly treatments
1 min per point

A Double Blind Crossover Trial of Low Level Laser Therapy in the treatment of Post Herpetic Neuralgia
Moore et al
Laser Therapy 1998
The effects of infrared laser and medical treatments on pain and serotonin degradation products in patients with myofascial pain syndrome: a controlled trial

Ceylan et al 2004 Rheumatol Int 24: 260-263
Efficacy of LLLT in myofascial pain syndrome: an algometric and thermographic evaluation


Hot spot on the thermographic image before LLLT and regression of the spot 3 weeks after LLLT

*Moore et al Laser Ther 1992: 145-149*
Diagnosis and Treatment
Management of myofascial trigger points is multimodal. The most commonly used interventions are as follows:

- Massage, ischemic compression, pressure release, and other soft tissue interventions (such as muscle energy) have shown moderately strong evidence for immediate pain relief.
- Dry needling of trigger points has shown clinical benefits, but more studies are needed.
- Laser therapy shows strong evidence of effectiveness for pain relief.
- Transcutaneous electrical nerve stimulation and magnet therapy have shown moderate evidence for immediate effects over myofascial trigger points.
- Exercise has shown moderate benefit and can include stretching and range of motion, strengthening, endurance, or coordination exercises.
- Ultrasound therapy has weak evidence for effectiveness in management of trigger points.
Can low reactive-level laser therapy be used in the treatment of neurogenic facial pain? A double-blind, placebo controlled investigation of patients with trigeminal neuralgia.

Eckerdal and Bastian Laser Therapy (1996) 8: 247-252

Daily analgesic consumption index over 30 days comparing the LLLT Rxd group (Group B) with the sham-irradiated placebo group (Group A).
Meta-analysis of pain relief by laser irradiation on joint areas

The Effect of Low-Level Laser in Knee Osteoarthritis: A Double-Blind, Randomized, Placebo-Controlled Trial
Efficacy of Different Therapy Regimes of Low-Power Laser in Painful Osteoarthritis of the Knee: A Double-Blind and Randomized-Controlled Trial

Use Clusters to Cover Large Muscles or Low Level Laser moving slowly around the muscle

Masseter  Temporalis
Practical Applications

Where to treat?
What to treat?
How long to treat?
What wavelength to use?
How many treatments?
What to expect........?
Principles of Pain Rx

• Make a provisional diagnosis – assess nociceptive processing – central sensitisation or not? (hyperalgesia/allodynia)
• Rx tender points in the region of clinical interest as well as those in the dermatomal, myotomal and muscle bellies
• Rx “centrally” – over tips of spinous process of relevant nerve root
• Rx lymphatics draining the region
• Rx twice a week for two weeks and then re-evaluate
Treatment targets

- **Musculoskeletal targets**
  - Entheses
  - muscle bellies
  - facet joints
  - Ligaments
  - Trigger points

- **Neural targets**
  - cutaneous nerves
  - Stellate ganglion,
  - brachial plexus,
  - medial branch of cervical nerve to facet joints

- **Acupuncture points**

- **Lymphatics**
Test, Treat and Test again (3 Ts)

- Identify a clinical target – e.g. ROM, VAS, functional improvement, limits to range of movement
- Treat as described
- Test again (and then “chase” pain)
Site of treatment (post aspect)

- Rx tender points
  - Over spinous processes
  - At the insertion of the occiput and nuchal line
  - Origins and insertions of muscles in muscles of ant/post Δs of neck
  - Over thoracic cervical and thoracic spine
  - Shoulder girdle
  - Over the lateral articular pillars of facet jts
Anterior aspect of neck

3.2
Anterior aspect of the neck: bones and muscles
1 Ramus of mandible
2 Angle of mandible
3 Sternal notch
4 Manubrium
5 Clavicle
6 Sternoclavicular joint
7 Sternocleidomastoid muscle—sternal head
8 Sternocleidomastoid muscle—clavicular head

LATERAL HEAD & NECK ACUPUNCTURE POINTS & CUTANEOUS NERVES
Modes of nociceptive processing –

Mode 1 “normal”
- Pain: hyperalgesia & allodynia
- Abnormal sensory processing but no pain
- Normal somatosensory processing

Mode 2 “facilitated”
- Pain: hyperalgesia & allodynia
- Abnormal sensory processing but no pain
- Normal somatosensory processing

Mode 2 “suppressed”
- Pain: hyperalgesia & allodynia
- Abnormal sensory processing but no pain
- Normal somatosensory processing

Fibromyalgia

Athletes
5mW cw 650nm
Recommended irradiation times range between 30 and 600 seconds depending on output.

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Minimum area</th>
<th>Minimum total dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpal-tunnel</td>
<td>2-3</td>
<td></td>
</tr>
<tr>
<td>Lateral epicondylitis</td>
<td>1-2</td>
<td>1</td>
</tr>
<tr>
<td>Biceps humeri cap.lo</td>
<td>1-2</td>
<td>2</td>
</tr>
<tr>
<td>Supraspinatus</td>
<td>2-3</td>
<td>3</td>
</tr>
<tr>
<td>Infraspinatus</td>
<td>2-3</td>
<td></td>
</tr>
<tr>
<td>Trochanter major</td>
<td>2-3</td>
<td>2</td>
</tr>
<tr>
<td>Patellartendon</td>
<td>2-3</td>
<td></td>
</tr>
<tr>
<td>Tract. Iliotibialis</td>
<td>2-3</td>
<td></td>
</tr>
<tr>
<td>Achilles tendon</td>
<td>2-3</td>
<td></td>
</tr>
<tr>
<td>Plantar fasciitis</td>
<td>2-3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Arthritis</th>
<th>Points or cm²</th>
<th>Joules 904nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finger PIP or MCP</td>
<td>1-2</td>
<td>2</td>
</tr>
<tr>
<td>Wrist</td>
<td>2-3</td>
<td>3</td>
</tr>
<tr>
<td>Humeroradial joint</td>
<td>1-2</td>
<td>2</td>
</tr>
<tr>
<td>Elbow</td>
<td>2-3</td>
<td>3</td>
</tr>
<tr>
<td>Glenohumeral joint</td>
<td>2-3</td>
<td>6</td>
</tr>
<tr>
<td>Acromioclavicular</td>
<td>1-2</td>
<td>2</td>
</tr>
<tr>
<td>Temporomandibular</td>
<td>1-2</td>
<td>2</td>
</tr>
<tr>
<td>Cervical spine</td>
<td>2-3</td>
<td>6</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>2-3</td>
<td>10</td>
</tr>
<tr>
<td>Hip</td>
<td>2-3</td>
<td>10</td>
</tr>
<tr>
<td>Knee anteromedial</td>
<td>2-4</td>
<td>6</td>
</tr>
<tr>
<td>Ankle</td>
<td>2-4</td>
<td>6</td>
</tr>
</tbody>
</table>
Understanding skin pigmentation and laser absorption

• Study designed based on Fitzpatrick Skin Typing Scale (Fitzpatrick, 1975)
Fitzpatrick Scale

Type I: white; very fair; red or blond hair; blue eyes; freckles; always burns, never tans

Type II: white; fair; red or blond hair; blue, hazel or green eyes; usually burns, tans with difficulty

Type III: cream white; fair, any hair or eye colour; sometimes mild burs, gradually tans

Type IV: dark brown; rarely burns, tans with ease

Type V: dark brown; very rarely burns, tans very easily

Type VI: black; never burns, tans very easily
Understanding skin pigmentation and laser absorption

- Melanin is most significant chromophore (light sensitive molecule) in the epidermis
- Skin colour is the biological result of varying amount of melanin in the skin
- Absorption spectrum of melanin (250-1200 nm) allows for the absorption of visible light, UV light and IR light (Battle, 2007)
- Dermis contains haemoglobin and subcutaneous lipids as chromophores, in addition to melanin (Nussbaum, 2005)
Understanding skin pigmentation and laser absorption

- During therapeutic use of laser, melanin in the skin absorbs light.
- Greater melanin density will result in greater light absorption.
- Darker skin will therefore have a greater superficial absorption of light.
- Hence more heating of epidermal tissues and less light reaching intended subcutaneous chromophores (Battle, 2007).
- Efficacy of laser in persons with darker skin may be reduced at equivalent fluences.
Understanding skin pigmentation and laser absorption

CURRENTLY:

• Simonovic (1998) recommended the use of:
  – 50% higher radiant exposure for highly pigmented skin and
  – 50% lower radiant exposure for lightly pigmented skin compared with “average” skin

• Nussbaum (2007) with LED transmission in skinfolds, found that red light was more reduced than IR
Understanding skin pigmentation and laser absorption

LED transmission through different skin types

Ethne Nussnaum, Jeff Van Zuylen
University of Toronto
Understanding skin pigmentation and laser absorption

Variation in percent transmission of infrared 904 nm LLLT through the cheek of subjects with different skin types

Variation in percent transmission of infrared 904 nm LLLT through the thenar web of subjects with different skin types
Understanding skin pigmentation and laser absorption

CONCLUSION

When adjusting for dose response in very dark skin people, dose must be increased by 26% and by 13% for medium dark skin people.
Precautions and Contraindications

• No laser into eyes
• No laser to tumorous tissues (but studies generally suggest inhibitory effects - if any)
• No laser to fontanelles of infants

• No laser to thyroid and other endocrine glands
• ? Laser therapy in pregnancy (rats bigger, healthier)
• ? In cancer (prostate, breast survival rates not affected or improved)
Eye protection

- Lasers all labelled with their “class” according to the Australian Standard
- Overseas standards are different
- Up to Class IIIa lasers - no need to wear glasses
- Class IIIb and above - required to wear glasses
- CE standards to be introduced later
Adverse effects

- Dizziness
- Faintness
- Extreme tiredness
- Nausea
- Burn
  - (if at upper limit of “low” power especially around the hair line in patients with dark hair)
- Headaches
- Change in the site of pain
- Stiffness
- Increased pain “treatment reaction”
- Reassure “can it cause cancer?”
Treatment Reactions (Kert & Rose)

Reaction pattern for the same patient show in Fig. 6.5. The dosage is the same. The difference is that only 3 treatments are given during the first 8 weeks. During this period, the patient will experience a much more moderate reaction as compared to that shown in Fig. 6.5.

The patient in this example has a severe chronic condition. The initial dosage is correct in that it provokes a treatment reaction. Subsequent treatments on the same regular basis illustrated in previous examples will cause pronounced treatment reactions. 9 treatments are given during the course of 8 weeks.
Factors that may interfere...

• Corticosteroids

• Calcium channel antagonists

  – Do these studies translate to a clinical phenomenon?
WHICH MACHINE?

• Infra-red or visible?
• Pulsed/non-pulsed?
• Variable time
• Variable power
• With/without optical power meter?
• Cost
• Ease of use
• “Repairability”
• Portability
• With/without glasses?
• Recharging time
• Warranty
Hand held lasers for home use
The context

• Most medical practitioners know nothing about laser therapy
• Most pain specialists, in particular, no nothing about laser therapy
• Most physiotherapists know nothing about laser therapy…..

....and more importantly all the above groups will rubbish it without having any knowledge of the literature
Words of advice

• Don’t bulk bill
• Charge for laser
• Use a nurse to assist
• Care with item numbers
• Laser will not do everything ...but can do a lot that nothing else can
• Use as a monotherapy or adjunctive therapy
Where LLLT is going?

Strong evidence
• MS pain, injury and Dysfunction
• Oral mucositis
• muscle fatigue

Moderate evidence
• lymphoedema
• wound healing
• neuropathic pain (trigeminal neuralgia and PHN)
• stroke
• depression
• PTSD
• Traumatic Brain Injury

Moderate evidence (cont)
• Age related Mac Degeneration
• Tuberculosis
• nerve regeneration

In the lab
• spinal cord injury
• Alzheimer’s disease
• Parkinson’s disease
• Stroke
• Glaucoma
• Sperm motility
“Third-generation” laser “acupuncture”

- FIBREOPTIC DELIVERY OF LASER THERAPY
LLLT for prevention of damage after heart attack

Uri Oron lab

Angiogenesis

Effect of low energy laser irradiation on infarct size following (3 weeks) induction of myocardial infarction in the rat

Nitric oxide synthase

LLLT for prevention of damage after heart attack

**Effect of LLT, 7 days before MI, on the reduction of infarct size**

<table>
<thead>
<tr>
<th>Laser Irradiation</th>
<th>1 week</th>
<th>Myocardial Infarction</th>
<th>3 weeks</th>
<th>Sacrifice</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 or 12mW/cm²</td>
<td></td>
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</tbody>
</table>

**Desmin expression in the infarcted porcine heart**

- Control: 8%
- Laser (5mW/cm²): 62%
- Laser (12mW/cm²): 50%

- *: Significant difference
- **: Highly significant difference

Michael R Hamblin PhD
Photonics West: BIOS
2006
LLLT for prevention of damage after stroke

Laser treatment
10mW/cm² 2min 1.2 J/cm² 808-nm CW

Significant at
p<0.001*

Average Total Neurological Score

Days Post Stroke

Control n=44  Laser n=39

Michael R Hamblin PhD
Photonics West: BIOS
2006
LLLT for repair of injury to spinal cord

Byrnes/Anders lab

Ladder Beam Cross
Time

Axons/mm

Control Light Treated

Pre Surgery 1 Week Post Surgery 3 Weeks Post Surgery

Baseline

Control

810 nm

mm Caudal to T9 Lesion

Michael R Hamblin PhD
Photonics West: BIOS 2006
LlLT for protection of retina from toxicity

Methanol consumption produces the mitochondrial toxin formate that damages the retina - 4 J/cm² 670-nm LED light to whole rat reduces damage

PNAS | March 18, 2003 | vol. 100 | no. 6 | 3441

Action spectrum of reversal of Tetrodotoxin neuron toxicity by LEDs in culture
Laser Medicine offers the potential to treat many different conditions in primary care practice – it is the medicine of the future....be excited!

Thank you

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robertachow@iinet.net.au
roberta.chow@sydney.edu.au
Where to learn more?

- AMLA runs courses from time to time
  http://www.amla.org.au/
- Take care about who does run other courses
- Journals – Photomedicine Laser Surgery
  Lasers in Surgery and Medicine
- THOR laser website
Thank you

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roberta.chow@sydney.edu.au