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**830 nm laser irradiation induces varicosity formation, reduces mitochondrial membrane potential and blocks fast axonal flow in small and medium diameter rat dorsal root ganglion neurons: implications for the analgesic effects of 830 nm laser.**

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**Abstract**

We report the formation of 830 nm (cw) laser-induced, reversible axonal varicosities, using immunostaining with beta-tubulin, in small and medium diameter, TRPV-1 positive, cultured rat DRG neurons. Laser also induced a progressive and statistically significant decrease ( $p < 0.005$ ) in MMP in mitochondria in and between static axonal varicosities. In cell bodies of the neuron, the decrease in MMP was also statistically significant ( $p < 0.05$ ), but the decrease occurred more slowly. Importantly we also report for the first time that 830 nm (cw) laser blocked fast axonal flow, imaged in real time using confocal laser microscopy and JC-1 as mitotracker. Control neurons in parallel cultures remained unaffected with no varicosity formation and no change in MMP. Mitochondrial movement was continuous and measured along the axons at a rate of 0.8 microm/s (range 0.5-2 microm/s), consistent with fast axonal flow. Photoacceptors in the mitochondrial membrane absorb laser and mediate the transduction of laser energy into electrochemical changes, initiating a secondary cascade of intracellular events. In neurons, this results in a decrease in MMP with a concurrent decrease in available ATP required for nerve function, including maintenance of microtubules and molecular motors, dyneins and kinesins, responsible for fast axonal flow. Laser-induced neural blockade is a consequence of such changes and provide a mechanism for a neural basis of laser-induced pain relief. The repeated application of laser in a clinical setting modulates nociception and reduces pain. The application of laser therapy for chronic pain may provide a non-drug alternative for the management of chronic pain.

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**Assessment of feasibility and efficacy of Class IV laser therapy for postoperative pain relief in off-pump coronary artery bypass surgery patients: A pilot study.**

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## Abstract

### **BACKGROUND:**

Laser therapy, for its established analgesic properties with minimal side effects, has been used for the treatment of chronic pain. However, it has not been used for the treatment of acute postoperative pain. This pilot study was designed to assess the feasibility and efficacy of Class IV laser on postoperative pain relief following off-pump coronary artery bypass graft (OPCABG) surgery, as a component of multimodal analgesia (MMA) technique.

### **METHODS:**

This open observational prospective study comprised of 100 adult patients (84 male, 16 female) who underwent OPCABG through sternotomy. For postoperative analgesia, they were subjected to laser therapy in addition to the standard institutional pain management protocol comprising of IV infusion/bolus of tramadol and paracetamol and fentanyl bolus as rescue analgesic. Pain intensity was measured by Verbal Rating Scale (VRS). The laser therapy was scheduled as once a day regime for three consecutive postoperative days (PODs) starting on POD 1, 30 min following tracheal extubation. The subsequent laser applications were also scheduled at the same time of the day as on day 1 if VRS was  $\geq 5$ . 10 W Class IV laser was applied over 150 cm<sup>2</sup> sternal wound area for 150 s. VRS was used to assess pain severity and was recorded for statistical analysis using Friedman Test.

### **RESULTS:**

The mean (standard deviation [SD]) VRS of all the 100 patients just before application of the first dose of laser was 7.31 (0.94) while on MMT; the same fell to 4.0 (1.279) and 3.40 (2.697) at 1 h and 24 h respectively following first dose of laser. The change of VRS over first 24 h among all the 100 patients was statistically significant ( $P = 0.000$ ). Laser was re-applied in 40 patients whose VRS was  $\geq 5$  (mean [SD] - 6.38 [0.868]) at 24th h. After receiving the 2nd dose of laser the VRS scores fell significantly ( $P = 0.000$ ) and became 0 at 54th h. No patients required 3rd dose of the laser. No patient required rescue analgesic while on laser therapy.

### **CONCLUSION:**

Class IV laser can be an effective technique for postoperative analgesia following OPCABG surgery through sternotomy when included as a component of MMA technique.

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## **Inhibitory effects of visible 650-nm and infrared 808-nm laser irradiation on somatosensory and compound muscle action potentials in rat sciatic nerve: implications for laser-induced analgesia.**

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## Abstract

Low-level laser therapy (LLLT) has been shown in clinical trials to relieve chronic pain and the World Health Organization has added LLLT to their guidelines for treatment of chronic neck pain. The mechanisms for the pain-relieving effects of LLLT are however poorly understood. We therefore assessed the effects of laser irradiation (LI) on somatosensory-evoked potentials (SSEPs) and compound muscle action potentials (CMAPs) in a series of experiments using visible ( $\lambda = 650$  nm) or infrared ( $\lambda = 808$  nm) LI applied transcutaneously to points on the hind limbs of rats overlying the course of the sciatic nerve. This approximates the clinical application of LLLT. The 650-nm LI decreased SSEP amplitudes and increased latency after 20 min. CMAP proximal amplitudes and hip/ankle (H/A) ratios decreased at 10 and 20 min with increases in proximal latencies approaching significance. The 808-nm LI decreased SSEP amplitudes and increased latencies at 10 and 20 min. CMAP proximal amplitudes and H/A ratios decreased at 10 and 20 min. Latencies were not significantly increased. All LI changes for both wavelengths returned to baseline by 48 h. These results strengthen the hypothesis that a neural mechanism underlies the clinical effectiveness of LLLT for painful conditions.

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## **Inhibitory effects of laser irradiation on peripheral mammalian nerves and relevance to analgesic effects: a systematic review.**

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### **Abstract**

#### **OBJECTIVE:**

The objective of this review was to systematically identify experimental studies of non-ablative laser irradiation (LI) on peripheral nerve morphology, physiology, and function. The findings were then evaluated with special reference to the neurophysiology of pain and implications for the analgesic effects of low-level laser therapy (LLLT).

#### **BACKGROUND:**

LLLT is used in the treatment of pain, and laser-induced neural inhibition has been proposed as a mechanism. To date, no study has systematically evaluated the effects of LI on peripheral nerve, other than those related to nerve repair, despite the fact that experimental studies of LI on nerves have been conducted over the past 25 years.

#### **METHODS:**

We searched computerized databases and reference lists for studies of LI effects on animal and human nerves using a priori inclusion and exclusion criteria.

#### **RESULTS:**

We identified 44 studies suitable for inclusion. In 13 of 18 human studies, pulsed or continuous wave visible and continuous wave infrared (IR) LI slowed conduction velocity (CV)

and/or reduced the amplitude of compound action potentials (CAPs). In 26 animal experiments, IR LI suppressed electrically and noxiously evoked action potentials including pro-inflammatory mediators. Disruption of microtubule arrays and fast axonal flow may underpin neural inhibition.

### **CONCLUSIONS:**

This review has identified a range of laser-induced inhibitory effects in diverse peripheral nerve models, which may reduce acute pain by direct inhibition of peripheral nociceptors. In chronic pain, spinal cord changes induced by LI may result in long-term depression of pain. Incomplete reporting of parameters limited aggregation of data.

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## **Pre-conditioning with low-level laser (light) therapy: light before the storm.**

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#### **Abstract**

Pre-conditioning by ischemia, hyperthermia, hypothermia, hyperbaric oxygen (and numerous other modalities) is a rapidly growing area of investigation that is used in pathological conditions where tissue damage may be expected. The damage caused by surgery, heart attack, or stroke can be mitigated by pre-treating the local or distant tissue with low levels of a stress-inducing stimulus, that can induce a protective response against subsequent major damage. Low-level laser (light) therapy (LLLT) has been used for nearly 50 years to enhance tissue healing and to relieve pain, inflammation and swelling. The photons are absorbed in cytochrome(c) oxidase (unit four in the mitochondrial respiratory chain), and this enzyme activation increases electron transport, respiration, oxygen consumption and ATP production. A complex signaling cascade is initiated leading to activation of transcription factors and up- and down-regulation of numerous genes. Recently it has become apparent that LLLT can also be effective if delivered to normal cells or tissue before the actual insult or trauma, in a pre-conditioning mode. Muscles are protected, nerves feel less pain, and LLLT can protect against a subsequent heart attack. These examples point the way to wider use of LLLT as a pre-conditioning modality to prevent pain and increase healing after surgical/medical procedures and possibly to increase athletic performance.

#### **KEYWORDS:**

LLLT; Mitochondria; Photobiomodulation; Pre-conditioning; Reactive Oxygen Species; Remote Ischemic Pre-conditioning

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