



## Laser Therapy (LLLT) relief for chronic pain

**Anti-inflammatory** (reduced prostaglandin E2, interleukin 1 $\beta$  and TNF alpha).

**Analgesic** (temporary nerve block, long term altered nociception, reduced central sensitisation)

**Promotes repair**(increasedATP; reduced oxidative stress, increased cell metabolism)

**Favourable systematic reviews** The Lancet, BMJ and the International Assoc for the Study of Pain

## Introduction to Low Level Light Therapy (LLLT) for pain relief

James D Carroll

THOR Photomedicine Ltd (UK)

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## Low Level Laser Therapy (LLLT) Digest

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## Introduction to Low Level Laser Therapy (LLLT) for pain relief

LLLT improves tissue repair, reduces pain and inflammation wherever the beam is applied. Usually applied by a doctor, therapist or technician, treatments take about 10 minutes and should be applied two or more times a week.

LLLT has been used for many years on sports injuries, arthritic joints, neuropathic pain syndromes, back and neck pain. Over 200 randomised clinical trials have been published on LLLT, half of which are on pain.

Customers include British and US military, Premier Division soccer teams, Olympic teams, Formula 1, rugby and cricket team therapists as well as specialist pain clinics in the UK and USA.

In the last 3 years five systematic reviews have found in favour of LLLT.

- BMJ sports medicine journal, systematic review of surgical and conservative interventions for frozen shoulder "strong evidence" for LLLT. 2010 [click here](#)
- The International Association for the Study of Pain found "strong evidence" for LLLT on myofascial pain syndrome. 2010 [click here](#)
- American Physical Therapy Association guidelines recommend LLLT for Achilles tendonitis. 2010 [click here](#)
- Lancet systematic review: "LLLT reduces pain immediately after treatment in acute neck pain and up to 22 weeks after completion of treatment in patients with chronic neck pain". 2009 [click here](#)
- World Health Organisation (Bone and Joint Task Force) For neck pain LLLT "more effective than no treatment, sham, or alternative interventions" 2008 [click here](#)

In August 2010 The Lancet reported that the systematic review of LLLT for neck pain was in their top 20 most downloaded papers for 2010. [click here](#)

## How Low Level Laser Therapy (LLLT) works

There are two mechanisms of action for LLLT pain relief:

1. **Anti-inflammatory.** LLLT reduces oxidative stress: Mitochondria in stressed or ischaemic tissues produce nitric oxide (mtNO) that binds to cytochrome c oxidase competitively displacing oxygen leading to oxidative stress and reduced ATP production. Light of suitable wavelength, sufficient irradiance and time when applied to injuries is absorbed by cytochrome c oxidase displacing mtNO thereby reducing oxidative stress and increasing ATP production. A cascade of downstream metabolic effects lead to a reduction in inflammatory markers including prostaglandin E<sub>2</sub>, interleukin 1 $\beta$  and tumour necrosis factor  $\alpha$ .
2. **Analgesia.** LLLT creating a nerve block. Higher irradiance / energy treatments can induce an analgesic effect by disrupting fast axonal transport in small diameter fibres, in particular nociceptors. This temporary (reversible) inhibition of A-delta and C fibre transmission reduces tonic peripheral nociceptive afferent input and facilitates reorganisation of the modulation of synaptic connections. Repeated treatments lead to a reduction in central sensitisation.

# Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials

*Roberta T Chow, Mark 'Johnson, Rodrigo A B Lopes-Martins, Jan M Bjordal*

## Summary

Background Neck pain is a common and costly condition for which pharmacological management has limited evidence of efficacy and side-effects. Low-level laser therapy (LLLT) is a relatively uncommon, non-invasive treatment for neck pain, in which non-thermal laser irradiation is applied to sites of pain. We did a systematic review and metaanalysis of randomised controlled trials to assess the efficacy of LLLT in neck pain.

## Methods

We searched computerised databases comparing efficacy of LLLT using any wavelength with placebo or with active control in acute or chronic neck pain. Effect size for the primary outcome, pain intensity, was defined as a pooled estimate of mean difference in change in mm on 100 mm visual analogue scale.

## Findings

We identified 16 randomised controlled trials including a total of 820 patients. In acute neck pain, results of two trials showed a relative risk (RR) of 1.69 (95% CI 1.22-2.33) for pain improvement of LLLT versus placebo. Five trials of chronic neck pain reporting categorical data showed an RR for pain improvement of 4.05 (2.74-5.98) of LLLT. Patients in 11 trials reporting changes in visual analogue scale had pain intensity reduced by 19.86 mm (10.04-29.68). Seven trials provided follow-up data for 1-22 weeks after completion of treatment, with short-term pain relief persisting in the medium term with a reduction of 22.07 mm (17.42-26.72). Side-effects from LLLT were mild and not different from those of placebo.

Interpretation We show that LLLT reduces pain immediately after treatment in acute neck pain and up to 22 weeks after completion of treatment in patients with chronic neck pain.

Lancet. 2009 Dec 5;374(9705):1897-908.

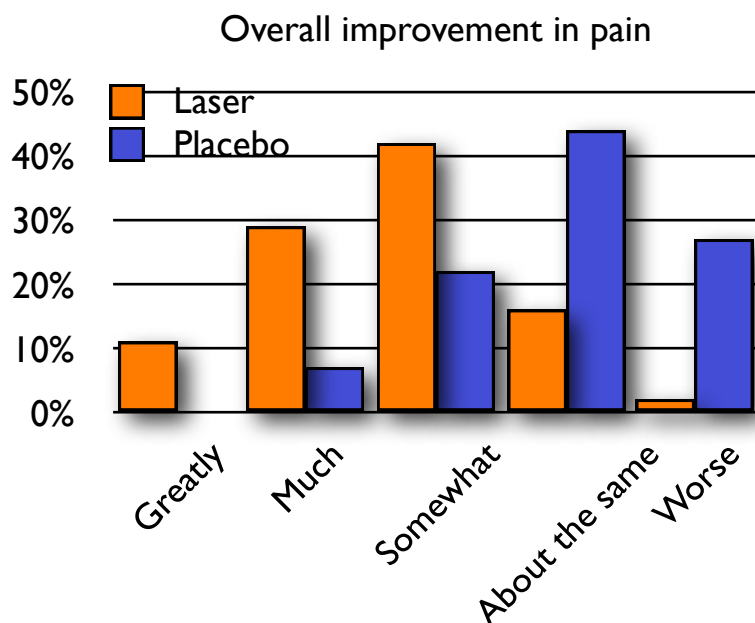
# The effect of 300 mW, 830nm laser on chronic neck pain: a double-blind, randomized, placebo-controlled study.

*Chow RT, Heller GZ, Barnsley L.*

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A randomized, double-blind, placebo-controlled study of low-level laser therapy (LLLT) in 90 subjects with chronic neck pain was conducted with the aim of determining the efficacy of 300 mW, 830 nm laser in the management of chronic neck pain. Subjects were randomized to receive a course of 14 treatments over 7 weeks with either active or sham laser to tender areas in the neck. The primary outcome measure was change in a 10 cm Visual Analogue Scale (VAS) for pain. Secondary outcome measures included Short-Form 36 Quality-of-Life questionnaire (SF-36), Northwick Park Neck Pain Questionnaire (NPNQ), Neck Pain and Disability Scale (NPAD), the McGill Pain Questionnaire (MPQ) and Self-Assessed Improvement (SAI) in pain measured by VAS. Measurements were taken at baseline, at the end of 7 weeks' treatment and 12 weeks from baseline. The mean VAS pain scores improved by 2.7 in the treated group and worsened by 0.3 in the control group (difference 3.0, 95% CI 3.8-2.1). Significant improvements were seen in the active group compared to placebo for SF-36-Physical Score (SF36 PCS), NPNQ, NPAD, MPQVAS and SAI. The results of the SF-36 - Mental Score (SF36 MCS) and other MPQ component scores (afferent and sensory) did not differ significantly between the two groups. Low-level laser therapy (LLLT), at the parameters used in this study, was efficacious in providing pain relief for patients with chronic neck pain over a period of 3 months.

Pain. 2006 Sep;124(1-2):201-10. Epub 2006 Jun 27



# Low-level laser therapy for acute neck pain with radiculopathy: a double-blind placebo-controlled randomized study.

Konstantinovic LM, Cutovic MR, Milovanovic AN, Jovic SJ, Dragin AS, Letic MDj, Miler VM. Clinic for Rehabilitation, Medical School, University of Belgrade, Sokobanjska 13, Belgrade, Serbia.

## Abstract

**Objective.** The objective of the study was to investigate clinical effects of low-level laser therapy (LLLT) in patients with acute neck pain with radiculopathy. **Design.** Double-blind, randomized, placebo-controlled study. **Setting.** The study was carried out between January 2005 and September 2007 at the Clinic for Rehabilitation at the Medical School, University of Belgrade, Serbia. **Patients and Intervention.** Sixty subjects received a course of 15 treatments over 3 weeks with active or an inactivated laser as a placebo procedure. LLLT was applied to the skin projection at the anatomical site of the spinal segment involved with the following parameters: wavelength 905 nm, frequency 5,000 Hz, power density of 12 mW/cm<sup>2</sup>, and dose of 2 J/cm<sup>2</sup>, treatment time 120 seconds, at whole doses 12 J/cm<sup>2</sup>. **Outcome measures.** The primary outcome measure was pain intensity as measured by a visual analog scale. Secondary outcome measures were neck movement, neck disability index, and quality of life. Measurements were taken before treatment and at the end of the 3-week treatment period. **Results.** Statistically significant differences between groups were found for intensity of arm pain ( $P = 0.003$ , with high effect size  $d = 0.92$ ) and for neck extension ( $P = 0.003$  with high effect size  $d = 0.94$ ). **Conclusion.** LLLT gave more effective short-term relief of arm pain and increased range of neck extension in patients with acute neck pain with radiculopathy in comparison to the placebo procedure.

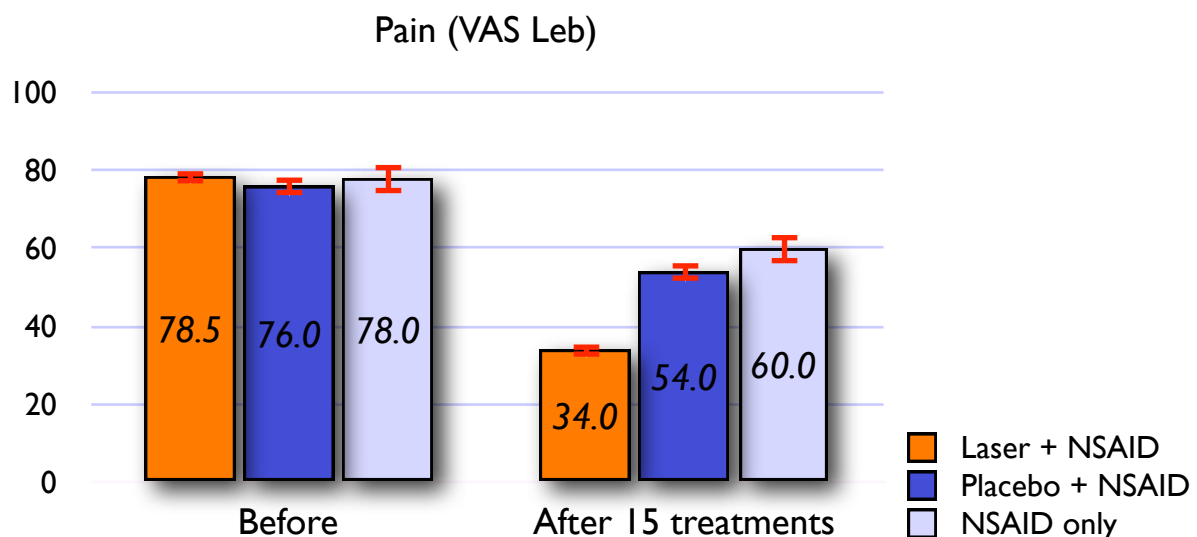
Pain Med. 2010 Aug;11(8):1169-78.

# Acute Low Back Pain with Radiculopathy: A Double-Blind, Randomized, Placebo-Controlled Study.

*Konstantinovic LM, Kanjuh ZM, Milovanovic AN, Cutovic MR, Djurovic AG, Savic VG, Dragin AS, Milovanovic ND.*

**Abstract Objective:** The aim of this study was to investigate the clinical effects of low-level laser therapy (LLLT) in patients with acute low back pain (LBP) with radiculopathy. **Background Data:** Acute LBP with radiculopathy is associated with pain and disability and the important pathogenic role of inflammation. LLLT has shown significant anti-inflammatory effects in many studies. **Materials and Methods:** A randomized, double-blind, placebo-controlled trial was performed on 546 patients. Group A (182 patients) was treated with nimesulide 200 mg/day and additionally with active LLLT; group B (182 patients) was treated only with nimesulide; and group C (182 patients) was treated with nimesulide and placebo LLLT. LLLT was applied behind the involved spine segment using a stationary skin-contact method. Patients were treated 5 times weekly, for a total of 15 treatments, with the following parameters: wavelength 904 nm; frequency 5000 Hz; 100-mW average diode power; power density of 20 mW/cm<sup>2</sup> and dose of 3 J/cm<sup>2</sup>; treatment time 150 sec at whole doses of 12 J/cm<sup>2</sup>. The outcomes were pain intensity measured with a visual analog scale (VAS); lumbar movement, with a modified Schober test; pain disability, with Oswestry disability score; and quality of life, with a 12-item short-form health survey questionnaire (SF-12). Subjects were evaluated before and after treatment. Statistical analyses were done with SPSS 11.5. **Results:** Statistically significant differences were found in all outcomes measured ( $p < 0.001$ ), but were larger in group A than in B ( $p < 0.0005$ ) and C ( $p < 0.0005$ ). The results in group C were better than in group B ( $p < 0.0005$ ). **Conclusions:** The results of this study show better improvement in acute LBP treated with LLLT used as additional therapy.

Photomed Laser Surg.





# Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain.

*Gur A, Karakoc M, Cevik R, Nas K, Sarac AJ, Karakoc M*

*Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey.*

**BACKGROUND AND OBJECTIVES:** The aim of this study was to determine whether low power laser therapy (Gallium-Arsenide) is useful or not for the therapy of chronic low back pain (LBP). **STUDY DESIGN/MATERIALS AND METHODS:** This study included 75 patients (laser + exercise-25, laser alone-25, and exercise alone-25) with LBP. Visual analogue scale (VAS), Schober test, flexion and lateral flexion measures, Roland Disability Questionnaire (RDQ) and Modified Oswestry Disability Questionnaire (MODQ) were used in the clinical and functional evaluations pre and post therapeutically. A physician, who was not aware of the therapy undertaken, evaluated the patients. **RESULTS:** Significant improvements were noted in all groups with respect to all outcome parameters, except lateral flexion ( $P < 0.05$ ). **CONCLUSIONS:** Low power laser therapy seemed to be an effective method in reducing pain and functional disability in the therapy of chronic LBP.

Lasers Surg Med 2003 32(3) 233-8

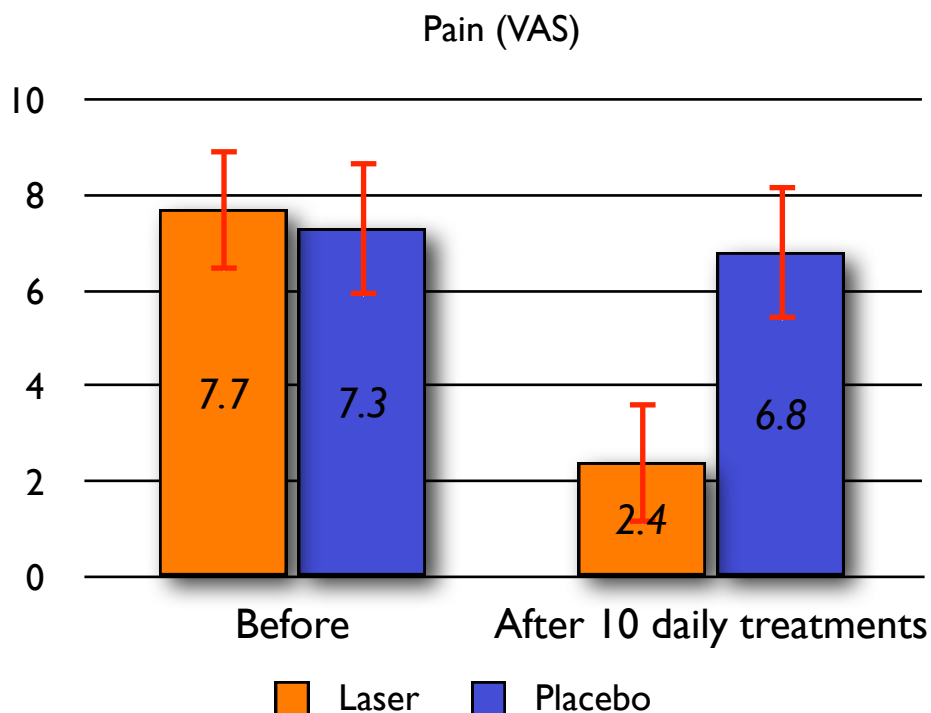
# The clinical efficacy of low-power laser therapy on pain and function in cervical osteoarthritis.

*Ozdemir F, Birtane M, Kokino S*

*Department of Physical Therapy and Rehabilitation, Medical Faculty of Trakya University, Edirne, Turkey.*

Pain is a major symptom in cervical osteoarthritis (COA). Low-power laser (LPL) therapy has been claimed to reduce pain in musculoskeletal pathologies, but there have been concerns about this point. The aim of this study was to evaluate the analgesic efficacy of LPL therapy and related functional changes in COA. Sixty patients between 20 and 65 years of age with clinically and radiologically diagnosed COA were included in the study. They were randomised into two equal groups according to the therapies applied, either with LPL or placebo laser. Patients in each group were investigated blindly in terms of pain and pain-related physical findings, such as increased paravertebral muscle spasm, loss of lordosis and range of neck motion restriction before and after therapy. Functional improvements were also evaluated. Pain, paravertebral muscle spasm, lordosis angle, the range of neck motion and function were observed to improve significantly in the LPL group, but no improvement was found in the placebo group. LPL seems to be successful in relieving pain and improving function in osteoarthritic diseases.

Clin Rheumatol 2001 20(3) 181-4



# DOUBLE BLIND CROSSOVER TRIAL OF LOW LEVEL LASER THERAPY IN THE TREATMENT OF POST HERPETIC NEURALGIA

*Kevin C Moore MB ChB FRCA Naru Hira. Parswanath Kramer, Copparam Jayakumar & Toshio Ohshiro Department of Anaesthesia, The Royal Oldham Hospital*

Post herpetic. neuralgia can be an extremely painful condition which in many cases proves resistant to all the accepted forms of treatment. It is frequently most severe in the elderly and may persist for years with no predictable course. This trial was designed as a double blind assessment of the efficacy of low level laser therapy in the relief of the pain of post herpetic neuralgia with patients acting as their own controls. Admission to the trial was limited to patients with established post herpetic neuralgia of at least six months duration and who had shown little or no response to conventional methods of treatment. Measurements of pain intensity and distribution were noted over a period of eight treatments in two groups of patients each of which received four consecutive laser treatments. The results demonstrate a significant reduction in the pain intensity and distribution following a course of low level laser therapy.

Laser Therapy. 1988; 1: 7.

# EFFICACY OF LASER IRRADIATION ON THE AREA NEAR THE STELLATE GANGLION IS DOSE-DEPENDENT: DOUBLE-BLIND CROSSOVER PLACEBO-CONTROLLED STUDY.

*Hashimoto T, Kemmotsu O, Otsuka H et al.*

In the present study we evaluate the effects of laser irradiation on the area near the stellate ganglion on regional skin temperature and pain intensity in patients with postherpetic neuralgia. A double blind, crossover and placebo-controlled study was designed to deny the placebo effect of laser irradiation. Eight inpatients (male 6, female 2) receiving laser therapy for pain attenuation were enrolled in the study after institutional approval and informed consent. Each patient received three sessions of treatment on a separate day in a randomised fashion. Three minutes irradiation with a 150 mW laser (session 1), 3 minutes irradiation with a 60 mW laser (session 2), and 3 minutes placebo treatment without laser irradiation. Neither the patient nor the therapist was aware which session type was being applied until the end of the study. Regional skin temperature was evaluated by thermography of the forehead, and pain intensity was recorded using a visual analogue scale (VAS). Measurements were performed before treatment, immediately after (0 minutes) then 5, 10, 15, and 30 min after treatment. Regional skin temperature increased following both 150 mW and 60mW laser irradiation, whereas no changes were obtained by placebo treatment. VAS decreased following both 150 mW and 60 mW laser treatments, but no changes in VAS were obtained by placebo treatment. These changes in the temperature and VAS were further dependent on the energy density, i.e the dose. Results demonstrate that laser irradiation near the stellate ganglion produces effects similar to stellate ganglion block. Our results clearly indicate that they are not placebo effects but true effects of laser irradiation.

Laser Therapy 1997 (1): 9:7-- 12

# 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

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Medicine, Odense University Hospital, Denmark*

Neurogenic facial pain has been one of the more difficult conditions to treat, but the introduction of laser therapy now permits a residual group of patients hitherto untreatable to achieve a life free from or with less pain. The present investigation was designed as a doubleblind, placebo controlled study to determine whether low reactive-level laser therapy (LLLT) is effective for the treatment of trigeminal neuralgia. Two groups of patients (14 and 16) were treated with two probes. Neither the patients nor the dental surgeon were aware of which was the laser probe until the investigation had been completed. Each patient was treated weekly for five weeks. The results demonstrate that of 16 patients treated with the laser probe, 10 were free from pain after completing treatment and 2 had noticeably less pain, while in 4 there was little or no change. After a one year follow-up, 6 patients were still entirely free from pain. In the group treated with the placebo system, i.e. the non-laser probe, one was free from pain, 4 had less pain, and the remaining 9 patients had little or no recovery. After one year only one patient was still completely free from pain. The use of analgesics was recorded and the figures confirmed the fact that LLLT is effective in the treatment of trigeminal neuralgia. It is concluded that the present study clearly shows that LLLT treatment, given as described, is an effective method and an excellent supplement to conventional therapies used in the treatment of trigeminal neuralgia.

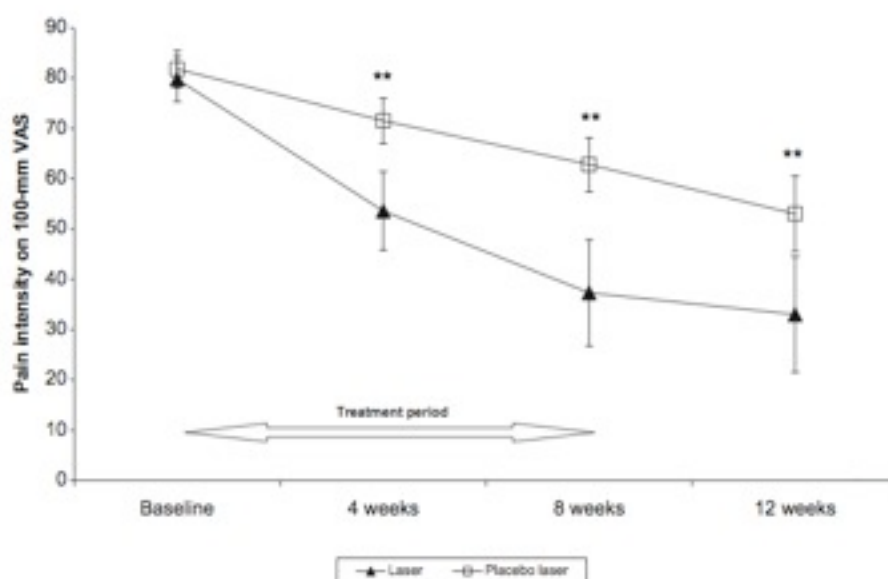
Laser Therapy, 1996: 8: 247-252

# Effects of Low-Level Laser Therapy and Eccentric Exercises in the Treatment of Recreational Athletes With Chronic Achilles Tendinopathy.

*Stergioulas A, Stergioula M, Aarskog R, Lopes-Martins RA, Bjordal JM  
Peloponnese University, Sparta, Laconia, Greece.*

**BACKGROUND:** Eccentric exercises (EEs) are recommended for the treatment of Achilles tendinopathy, but the clinical effect from EE has a slow onset. **HYPOTHESIS:** The addition of low-level laser therapy (LLLT) to EE may cause more rapid clinical improvement. **STUDY DESIGN:** Randomized controlled trial; Level of evidence, 1. **METHODS:** A total of 52 recreational athletes with chronic Achilles tendinopathy symptoms were randomized to groups receiving either EE + LLLT or EE + placebo LLLT over 8 weeks in a blinded manner. Low-level laser therapy ( $\lambda = 820$  nm) was administered in 12 sessions by irradiating 6 points along the Achilles tendon with a power density of 60 mW/cm<sup>2</sup> and a total dose of 5.4 J per session. **RESULTS:** The results of the intention-to-treat analysis for the primary outcome, pain intensity during physical activity on the 100-mm visual analog scale, were significantly lower in the LLLT group than in the placebo LLLT group, with 53.6 mm versus 71.5 mm ( $P = .0003$ ) at 4 weeks, 37.3 mm versus 62.8 mm ( $P = .0002$ ) at 8 weeks, and 33.0 mm versus 53.0 mm ( $P = .007$ ) at 12 weeks after randomization. Secondary outcomes of morning stiffness, active dorsiflexion, palpation tenderness, and crepitation showed the same pattern in favor of the LLLT group. **CONCLUSION:** Low-level laser therapy, with the parameters used in this study, accelerates clinical recovery from chronic Achilles tendinopathy when added to an EE regimen. For the LLLT group, the results at 4 weeks were similar to the placebo LLLT group results after 12 weeks.

Am J Sports Med 2008 Feb 13



# The effect of infrared laser irradiation on the duration and severity of postoperative pain: a double blind trial

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\*Department of Anaesthesia, The Royal Hallamshire Hospital, Sheffield, U.K., General Practitioner, Pennymeadow Clinic, Ashton-under-Lyne, U.K.

This trial was designed to test the hypothesis that LLLT reduces the extent and duration of postoperative pain. Twenty consecutive patients for elective cholecystectomy were randomly allocated for either LLLT or as controls. The trial was double blind. Patients for LLLT received 6-8-min treatment (GaAlAs: 830 nm: 60 mW CW: CM) to the wound area immediately following skin closure prior to emergence from GA. All patients were prescribed on demand postoperative analgesia (IM or oral according to pain severity). Recordings of pain scores (0-10) and analgesic requirements were noted by an independent assessor. There was a significant difference in the number of doses of narcotic analgesic (IM) required between the two groups. Controls n = 5.5: LLLT n = 2.5. No patient in the LLLT group required IM analgesia after 24 h. Similarly the requirement for oral analgesia was reduced in the LLLT group. Controls n = 9: LLLT n = 4. Control patients assessed their overall pain as moderate to severe compared with mild to moderate in the LLLT group. The results justify further evaluation on a larger trial population.

Laser Therapy 1992 Vol 4; Number 4 , pg 145-150

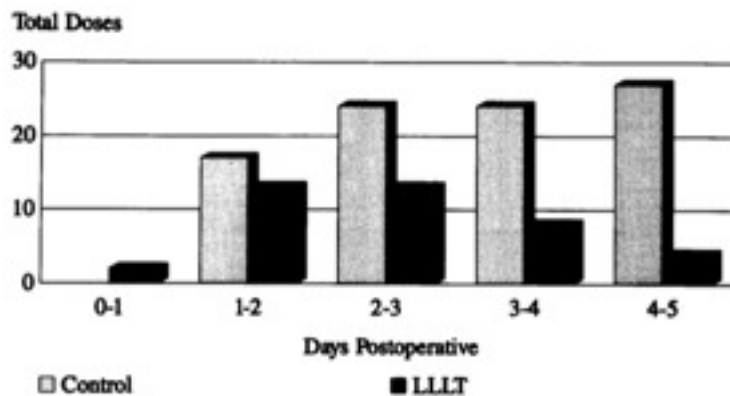


Figure 4. Analgesia—coproxamol

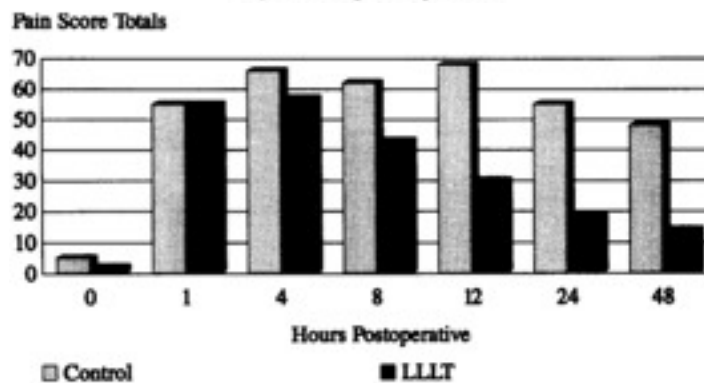


Figure 1. Pain score summation

# Low-Level Laser Therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomized placebo-controlled trials.

*Bjordal JM, Johnson MI, Iversen V, Aimbire F, Lopes-Martins RA*

*Section of Physiotherapy Science, University of Bergen, Bergen University College, Norway.*

**OBJECTIVE:** The aim of this study was to review the biological and clinical short-term effects of Low Level Laser Therapy (LLLT) in acute pain from soft-tissue injury. **BACKGROUND DATA:** It is unclear if and how LLLT can reduce acute pain. **METHODS:** Literature search of (i) controlled laboratory trials investigating potential biological mechanisms for pain relief and (ii) randomized placebo-controlled clinical trials which measure outcomes within the first 7 days after acute soft-tissue injury. **RESULTS:** There is strong evidence from 19 out of 22 controlled laboratory studies that LLLT can modulate inflammatory pain by reducing levels of biochemical markers (PGE(2), mRNA Cox 2, IL-1beta, TNFalpha), neutrophil cell influx, oxidative stress, and formation of edema and hemorrhage in a dose-dependent manner (median dose 7.5 J/cm(2), range 0.3-19 J/cm(2)). Four comparisons with non-steroidal anti-inflammatory drugs (NSAIDs) in animal studies found optimal doses of LLLT and NSAIDs to be equally effective. Seven randomized placebo-controlled trials found no significant results after irradiating only a single point on the skin overlying the site of injury, or after using a total energy dose below 5 Joules. Nine randomized placebo-controlled trials (n = 609) were of acceptable methodological quality, and irradiated three or more points and/or more than 2.5 cm(2) at site of injury or surgical incision, with a total energy of 5.0-19.5 Joules. Results in these nine trials were significantly in favor of LLLT groups over placebo groups in 15 out of 18 outcome comparisons. Poor and heterogeneous data presentation hampered statistical pooling of continuous data. Categorical data of subjective improvement were homogeneous (Q-value = 7.1) and could be calculated from four trials (n = 379) giving a significant relative risk for improvement of 2.7 (95% confidence interval [CI], 1.8-3.9) in a fixed effects model. **CONCLUSION:** LLLT can modulate inflammatory processes in a dose-dependent manner and can be titrated to significantly reduce acute inflammatory pain in clinical settings. Further clinical trials with adequate LLLT doses are needed to precisely estimate the effect size for LLLT in acute pain.

Photomed Laser Surg 2006 Apr 24(2) 158-68



# 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.

*Chow RT, David MA, Armati PJ*

*Castle Hill Medical Centre, Discipline of Medicine, The University of Sydney, Sydney, Australia*

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.

J Peripher Nerv Syst. 2007 Mar;12(1):28-39.

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