
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. There is strong evidence from 19 out of 22 controlled laboratory studies that laser irradiation can modulate inflammatory pain by reducing levels of biochemical markers (PGE2, 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/cm², range 0.3-19 J/cm²). Four comparisons with non-steroidal anti-inflammatory drugs (NSAIDs) in animal studies found optimal doses of laser irradiation 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 cm² 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 laser irradiation 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, 1.8-3.9) in a fixed effects model. In conclusion, laser irradiation 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 laser irradiation doses are needed to precisely estimate the effect size for laser irradiation in acute pain.


In a double blind, randomised, placebo controlled study Schlager has previously documented the effectiveness of point P6 acupuncture on postoperative vomiting in children undergoing strabismus (eye) surgery was studied. A 10 mW 670 nm laser was used and the P6 point was irradiated for 30 seconds 15 minutes before anesthesia and 15 minutes after arriving in the recovery room. In the laser group the incidence of vomiting was 25% and in the placebo group 85%. These results are confirmed by Butkovic in a pediatric group scheduled for hernia repair, circumcision or orchidopexy. Laser acupuncture was equally effective as metoclopramide in preventing post operative vomiting.


A study by Chow was undertaken to test the efficacy of 300 mW, 830 nm laser in a prospective double-blind, randomised, placebo-controlled trial in patients with chronic neck pain. 90 patients were enrolled. Laser was applied using the contact method over tender areas in the neck musculature, twice a week for 7 weeks. The primary outcome measure was change in a 10 cm Visual Analogue Scale for pain. Other measures used included a Self-Reported Improvement in pain, measured by a VAS, Short-Form 36 Quality-of-Life questionnaire,
Northwick Park Neck Pain Questionnaire, Neck Pain and Disability Scale and the McGill Pain Questionnaire. Measurements were taken at baseline, at the end of 7 weeks treatment and at 12 weeks from baseline. Patients in the treated group experienced a mean self reported improvement of 48.5% compared with 3.99% in the placebo group.


The course of arthritis was investigated by Gottlieb on an animal-experimental arthritis model considering macroscopic aspects, and the proteoglycan and the glycosaminoglycan contents. Based on these parameters, the influence of a diode laser of 692.6 nm, 20 mW, on the progress of arthritis was investigated. Thirty days following joint instability surgery another operation was made during which the femoral condyles were irradiated using different energy densities (1 or 4 J/cm²). Seven days after the second operation, macroscopic findings were made and the proteoglycan content was established. Macroscopically, a progressively increasing severity of cartilage changes during the course of arthritis was detected and the proteoglycan content was found to decrease. The changes in the irradiated joints proved to be less severe, with the higher energy density having a greater positive influence of statistical significance.


In a study by Medrado dorsal fat pads of normal adult rats were submitted to laser irradiation applied locally through intact skin, with four different dose schedules (4, 8, 12 and 16 J/cm²), with a further group being sham-irradiated. Histology, morphometry, immunofluorescence, and electron microscopy were all used to analyze irradiated tissues. Changes were restricted to the brown fatty tissue, in which a tendency was shown for multivacuolar cells to be transformed into the unilocular type. The number of cells which exhibited enlargement and fusion of small vacuoles was greater in the 4- and 16-J/cm² groups. Increased vascular proliferation and congestion was another more evident finding in laser-treated animals compared to non-treated animals. Laser irradiation at therapeutic levels cause brown adipose fat droplets to coalesce and fuse. Additionally, it stimulated proliferation and congestion of capillaries in the extra cellular matrix.


Carati has previously performed a randomised, double blind study on the effect of GaAs laser on postmastectomy lymphedema. There was no immediate effect of the irradiation but at 1 and 3 months follow up, after 2 cycles of laser treatment. About 30% of the patients had a clinically significant reduction of the arm volume and there was a significant softening of the tissue. Treatment did not appear to improve range of movement of the affected arm. Similar, but not quite as positive results are now reported by Kaviani using 890 nm, 1.5 J/cm² over the arm and axillary areas.

The aim of a study by Goulart was to evaluate, through a double-blind study, the effect of GaAlAs laser irradiation on the speed of orthodontic movement in canine premolars. Eighteen dogs were divided into two groups, and their third molars were extracted. An orthodontic device was placed between the first molar and the second premolar for stabilisation purpose. Group I was irradiated with a dosage of 5.25 J/cm² on the right side, whereas the left side was used as the control group. Group II was submitted to the same procedure, but was irradiated with a dosage of 35.0 J/cm². Irradiations were done every 7 days, for a total of nine irradiations. The orthodontic space was measured every 21 days. The 5.25 J/cm² dosage accelerated orthodontic movement during the first observation period, from 0 to 21 days, whereas the 35.0 J/cm² dosage retarded the orthodontic movement in the treated group when compared with the control group, during both the first and second observation periods, from 0 to 42 days. The results suggest that photoradiation may accelerate orthodontic movement at a dosage of 5.25 J/cm², whereas a higher dosage, 35.0 J/cm², may retard it.

However, the experimental study by Seifi [Seifi M, Shafeei HA. Effects of two types of low level lasers (KLO3 and Optodan) on the orthodontic tooth movements in rabbits. JIDA, The J of the Islamic Dental Association of Iran. 2005; 17 (3).] has come to the opposite conclusion. The study was conducted on 18 male albino rabbits divided into three equal groups: Laser 1 (5 mW, 850 nm wavelength, 3 minutes per session, pulsed, frequency of 3000 Hz, duration of pulse 100 nsec, total energy in experiment 2.43 J) and Laser 2 (10 mW, continuous, wave length 630 nm, 5 minutes per session, total energy in experiment 27 J) and a non irradiated group. The first mandibular molars, in all groups were under a four ounce tension using NiTi-Closed coil springs. The control group was not irradiated but the laser groups were irradiated for nine days. After sixteen days, following the termination of therapeutic regime; samples were sacrificed. The distance between the distal surface of the first molar and the mesial surface of the second molar was measured with 0.05 mm accuracy. The mean orthodontic tooth movements of the first mandibular molars were 1.7±0.16 mm in control group, 0.69±0.16 mm in Laser 1 group and 0.86±0.13 mm in Laser 2 group. These results indicate that the orthodontic movement velocity was actually reduced by the laser irradiation.

The two studies above suggest that low dose may accelerate orthodontic tooth movement and higher doses after completed movement may create a more compact bone around the tooth.


A double-blind, placebo-controlled study by Craig using male subjects (n=60), was conducted to investigate the efficacy of three different frequencies of combined phototherapy/low-intensity laser therapy (CLILT) in alleviating the signs and symptoms of delayed-onset muscle soreness (DOMS). After screening for relevant pathologies, recent analgesic or steroid drug usage, current pain, diabetes, or current involvement in regular weight-training activities, subjects were randomly allocated to one of five experimental groups: Control, Placebo, or 2.5 Hz, 5 Hz, or 20 Hz CLILT groups (660-950 nm; 31.7 J/cm²; pulsed at the given frequencies for a duration of 12 min; n=12 all groups). Once baseline measurements were obtained, DOMS was induced in the nondominant arm, which was exercised in a standardised fashion until exhaustion, using repeated eccentric contractions of the elbow flexors. The procedure was repeated twice more to ensure exhaustion was achieved, after which subjects were treated according to group allocation. In the CLILT/placebo groups, the treatment head was applied...
directly to the affected arm at the level of the musculotendinous junction. Subjects returned on two consecutive days for further treatment and assessment. The range of variables used to assess DOMS included range of movement), mechanical pain threshold/tenderness and pain. Measurements were taken before and after treatment on each day, except for the McGill Pain questionnaire, which was completed at the end of the study. Analysis of results using repeated measures and one-factor analysis of variance with relevant post hoc tests showed significant changes in ranges of movement accompanied by increases in subjective pain and tenderness for all groups over time; however, such analysis failed to show any significant differences between groups on any of the days.


In a later study with different light parameters Craig used thirty-six subjects (18 M; 18 F) who were randomly allocated, under double-blind conditions, to one of three experimental conditions: Control, Placebo, and CLILT (660-950 nm; 11 J/cm²; pulsed at 73 Hz). DOMS was induced in a standardised fashion in the non-dominant elbow flexors using repeated eccentric contractions until exhaustion was reached. Subjects returned on five consecutive days, and two days during the following week, for treatment according to group, and assessment of outcome variables including range of motion, pain, and tenderness. While analysis of results using repeated measures and one-factor ANOVA with post-hoc tests showed significant changes in all variables over time as a result of the induction procedure, there were no significant differences observed between groups.


Vinck treated DOMS with 950 nm LED, 160 mW, 3.2 J/cm² and did not find any statistically significant effect.


Lopes-Martins investigated if 655 nm laser irradiation can reduce muscular fatigue during tetanic contractions in rats. 32 male Wistar rats were divided in 4 groups receiving laser doses of 0 (control group), 0.5, 1.0 and 2.5 J/cm². Irradiation lasted 32, 80 and 160 seconds respectively with a fixed power density of 31.25 mW/cm². The total energy doses were 0.08, 0.2 and 0.4 Joules respectively. Electrical stimulation induced 6 tetanic muscle contractions in the tibial anterior muscle. Contractions were stopped when the muscle force fell to 50% of the initial value for each contraction (T50%). There was no significant difference between the 2.5 J/cm² laser-irradiated groups and the control group in mean T50%-values. Laser-irradiated groups 0.5 J/cm² and 1.0 J/cm² had significantly longer T50% values than the control group. The relative peak force for the 6th contraction in the laser irradiated groups were significantly higher at 92.2 % for 0.5 J/cm², 83.2 % for 1.0 J/cm² and 82.9 % for 2.5 J/cm² respectively, than for the control group. 50% Laser groups receiving 0.5 J/cm² and 1.0 J/cm², showed significant increases in mean performed work compared both to the control group and their 1st contraction values. Groups receiving laser irradiation with doses of 1 and 2.5 J/cm² also
showed significantly lower levels of Creatine Kinase in plasma than the non-irradiated control group.

**In conclusion, only coherent light has so far been documented as effective for DOMS.**


Sixteen patients with 34 resistant patches that had not responded to different treatment modalities for alopecia areata were enrolled in this study. In patients with multiple patches, one patch was left as a control for comparison. Patients were treated on a four-session basis, once a week, with a pulsed diode laser (904 nm) at a pulse rate of 40/s. A photograph was taken of each patient before and after treatment. The treated patients were 11 males and five females (31.25%). Their ages ranged between 4 and 50 years, and the durations of their disease were between 12 months and 6 year. Regrowth of hair was observed in 32 patches while only two patches failed to show any response. No regrowth of hair was observed in the control patches. The regrowth of hair appeared as terminal hair with its original color in 29 patches while three patches appeared as a white villous hair. In patients who showed response, the response was detected as early as 1 week after the first session in 24 patches while eight patients started to show response from the second session.

Nikiforova N. B. **The low intensive laser therapy of alopecia.** Municipal Polyclinic, Vladivostok, Russia (Unpublished material found online).

Therapeutic laser apparatus with the wavelength of 0.63 and 0.89 mm were used for the treatment. A course of therapy consists of 10-15 procedures. Depending on a complication of the disease a patient underwent 1 to 3 courses with the intervals of 1, 3 and 6 months. 78 patients (17 men and 61 women) at the age of 16 to 49 years old have been treated. Diseases have been caused by strong stresses, after-effects of surgical treatment, ovary and thyroid gland dysfunctions, gastroenteric diseases etc. A considerable improvement of hair quality, recovery of pigment, increase in thickness and rate of hair growth (50-100%) were observed in all cases. An intensive alopecia was ceased among 100% of patients. By the end of the first course a daily number of fallen hairs were in accordance with the norm. By the end of the third week an appearance of new hairs was observed along the front line of growth in 90% of patients. Out of 24 patients underwent three medical treatments the problem was completely solved for 23 of them.


Nitric oxide (NO) has been shown to be neurotoxic while transforming growth factor-beta 1 (TGF-beta1) is neuroprotective in the stroke model. The study BY Leung investigated the effects of laser therapy on nitric oxide synthase (NOS) and TGF-beta1 activities after cerebral ischemia and reperfusion injury. Cerebral ischemia was induced for 1 hour in male adult rats with unilateral occlusion of middle cerebral artery. Laser irradiation was then applied to the cerebrum at different durations (1, 5, or 10 minutes). The wavelength of the laser was 660 nm, 8.8 mW, 2.64 J/cm2, 10 kHz. The activity of NOS and the expression of TGF-beta1 were evaluated in groups with different durations of laser irradiation. After ischemia, the activity of NOS was gradually increased from day 3, became significantly higher from day 4 to 6 but
returned to the normal level after day 7. The activity and expression of the three isoforms of NOS were significantly suppressed to different extents after laser irradiation. In addition, laser irradiation was shown to trigger the expression of TGF-beta1.


A study by Fillipin investigated the effects of laser therapy on oxidative stress and fibrosis in an experimental model of Achilles tendon injury induced by a single impact trauma. Rats were randomly divided into four groups (n=8): control, trauma, trauma+laser for 14 days, and trauma+laser for 21 days. Achilles tendon traumatism was produced by dropping down a load with an impact kinetic energy of 0.544 J. A GaAs laser of 45 mW average power was used, 5 J/cm² dosage, for 35 seconds duration, continuously. Studies were carried out at day 21. Histology showed a loss of normal architecture, with inflammatory reaction, angiogenesis, vasodilatation, and extracellular matrix formation after trauma. This was accompanied by a significant increase in collagen concentration when compared the control group. Oxidative stress was also significantly increased in the trauma group. Administration of laser for 14 or 21 days markedly alleviated histological abnormalities reduced collagen concentration and prevented oxidative stress. Superoxide dismutase activity was significantly increased by laser treatment over control values.


Drugova studied the effects of low-intensity red light (HeNe and broadband) on lipid peroxidation in isolated rat heart in the postischemic period were studied. It was established that both laser and wideband luminescent irradiation applied during reperfusion reduced the content of lipid peroxidation products in tissues to a near-control level. Acc. to the researchers of the study, the effect is possibly associated with reactivation of antioxidant enzymes.


The aim of the study by Fontana was to evaluate temperature variation induced by a diode laser in periodontal repair. The temperature variation induced by a 810-nm diode laser was investigated in an in vitro study, varying the soft tissue thickness, and in an in vivo study for soft periodontal and bone tissues. The laser powers used were 600 mW, 800 mW, 1.0 W, and 1.2 W, and the light was delivered by a 300-microm fiber. The laser parameters and irradiation time used did not induce a temperature variation high enough to cause thermal irreversible damage to the periodontal tissues investigated.

The aim of the study by Schuhfried was to examine the effects of helium–neon laser irradiation on the mechanical (pressure algometry) and electrical (1 ms monophasic square-wave pulses, 50 Hz) pain threshold. 32 pain-free subjects were randomly assigned to either the experimental group (helium–neon laser stimulation: 5 mW, 10 min) or the placebo group (sham stimulation). Laser or sham stimulation and pain threshold ascertainment were carried out on the dorsal aspect of the forearm area. The contra lateral arm served as an untreated control. The groups were compared with each other and with the control arm. No significant differences were found between the laser stimulation and the sham stimulation in changes of either the mechanical or the electrical pain threshold. There were no changes in the mechanical pain threshold through laser stimulation and sham stimulation with respect to the untreated contra lateral arm. After laser stimulation electrical pain threshold was significantly higher (p<0.01) in the treated arm than in the untreated contra lateral arm, because this threshold decreased in the contra lateral arm. This was not the case in sham treatment.


Souza divided 60 amputated worms in three study groups: a control group and two other groups submitted to daily 1 and 3 min long laser treatment sections at approximately 910 W/m2 power density. A 685 nm diode laser with 35 mW optical power was used. Samples were sent to histological analysis at the 4th, the 7th and the 15th days after amputation. A remarkable increase in stem cells counts for the fourth day of regeneration was observed when the regenerating worms was stimulated by the laser radiation. regeneration.


A persistent increase in calcitonin gene-related peptide (CGRP) immunoreactivity in motoneurons may serve as an indicator for regeneration after peripheral nerve injury Snyder [1] examined the effects of laser treatment (633 nm) on axotomy-induced changes in alpha-CGRP mRNA and long-term neuronal survival in facial motoneurons. A quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) assay for alpha-CGRP mRNA was used to detect changes in the response to axotomy and laser irradiation. Cell counts of neurons in injured and non-injured facial motor nuclei of laser-treated and non-treated rats were done to estimate neuronal survival. A 10-fold increase in mRNA for alpha-CGRP at 11 days post-transection and an almost threefold increase in neuronal survival at 6-9 months post-transection were found in 633 nm light treated rats. These findings demonstrate that 633 nm laser light upregulates CGRP mRNA and support the theory that laser irradiation increases the rate of regeneration, target reinnervation, and neuronal survival of the axotomised neuron.


The subjects of this investigation consisted of 83 female patients that were treated in this department during the 2-year period from January 1999 to December 2002. Laser irradiation was applied for 3 min either every day or every other day for a total of 10 times. A diode
A semiconductor laser with a wavelength of 830 nm and a photointensity of 1 W was used. Evaluations were performed before and after the series of 10 exposures to laser irradiation. The evaluation included the measurement of pain using the visual analog scale (VAS) and serum prostaglandin E2 (pg/mL). The analgesic effects were observed in 67 of 83 cases. The VAS scores for the effective cases decreased after the irradiation series from 8.5 +/- 0.2, to 2.8 +/- 0.2. The post-irradiation PGE2 levels were lower than the pre-irradiation PGE2 levels in the effective cases, which were 5.8 +/- 0.3 and 7.1 +/- 0.4 pg/mL, respectively. The post-irradiation PGE2 levels for the effective cases were lower than those for the ineffective cases, which were 5.8 +/- 0.3 and 7.3 +/- 0.9 pg/mL, respectively.


Thirty-four adult rabbits were used in a study by Ihsan. Two of the rabbits were considered 0-h reading group, while the rest were divided into two equal groups, with 16 rabbits each: control and those treated with laser. Each rabbit underwent two surgical operations; the medial aspect of each thigh was slit, the skin incised and the femoral artery exposed and ligated. The site of the operation in the treated group was irradiated directly following the operation and for 3 d after, one session daily for 10 min/session. The laser system used was a GaAs laser with a wavelength of 904 nm and power of 10 mW. Blood samples collected from the femoral artery above the site of the ligation were sent for examination with high-performance liquid chromatography (HPLC) to determine the levels of adenosine, growth hormone (GH) and fibroblast growth factor (FGF). Tissue specimens collected from the site of the operation, consisting of the artery and its surrounding muscle fibres, were sent for histopathological examination to determine the fibre/capillary (F/C) ratio and capillary diameter. Blood samples and tissue specimens were collected at 4, 8, 12, 16, 20, 24, 48 and 72 h postoperatively from the animals of both groups, control and treated. Rapid increases in the level of adenosine, GH, and FGF occurred. The F/C ratio and capillary diameter peaked at 12-16 h; their levels declined gradually, reaching normal values 72 h after irradiation in the treated group. Numerous collateral blood vessels proliferated the area, with marked increases in the diameters of the original blood vessels.


An investigation was made of applying pulsed 890 nm laser radiation in the treatment for early diagnosed periodontitis. The investigation was made on 65 patients (47 patients constituted the experimental group and 18 patients constituted a control group affected by periodontitis). Clinical and functional tests revealed that laser therapy produced a strong effect on the course of the illness. It reduced bleeding, inflammation, and pruritus. Biomicroscopic examinations and periodontium rheography revealed that the gingival blood flow became normal after the course of laser therapy. The capillary permeability and venous congestion decreased, which was confirmed by the increased time of vacuum tests, raised gingival temperature, reduced tissue clearance, and increased oxygen tension. Apart from that, laser therapy subsided fibrinolysis, proteolytic tissue activity, and decreased the exudative inflammation of the periodontium.