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Nes A G, Posso M B. Patients with moderate chemotherapy-induced mucositis: pain therapy using low intensity lasers. Int Nurs Rev. 2005; 52 (1): 68-72.

The study by Nes was performed as a clinical test with a sample consisting of 13 adult patients receiving oncology treatment. The patients were treated during a 5-day period, and the pain was measured before and after each laser application. A 830 nm 250 mW laser was used. The energy given was 35 J/cm². There was a 67% decrease in the daily average experience of pain felt before and after each treatment, confirming that LPT can relieve pain among patients who have developed mucositis. The low number of COM patients at the hospital did not allow a control group to be included in the study, and therefore the results contain a potential placebo effect.

Tumilty S, Munn J, Abbott J H, McDonough S, Hurley D A, Baxter G D. Laser therapy in the treatment of achilles tendinopathy: a pilot study. Photomed Laser Surg. 2008; 26 (1): 25-30.

In feasibility study by Tumilty twenty patients were randomized into an active laser or placebo group; all patients, therapists, and investigators were blinded to allocation. All patients were given a 12-week eccentric exercise program and irradiated three times per week for 4 wk with either an active or placebo laser at standardized points over the affected tendons. Irradiation parameters in the active treatment group were: 810 nm, 100 mW, applied to six points on the tendon for 30 s, for a total dose of 3 J per point and 18 J per session. Outcome measures were the VISA-A questionnaire, pain, and isokinetic strength. Patients were measured before treatment and at 4 and 12 wk. Within groups, there were significant improvements at 4 and 12 wk for all outcome measures, except eccentric strength for the placebo group at 4 wk.

Carrasco T G, Mazzetto M O, Mazzetto R G, Mestriner W Jr. Low intensity laser therapy in temporomandibular disorder: a phase II double-blind study. Cranio. 2008; 26 (4): 274-281.

Carrasco selected fourteen patients and divided them into two groups (active and placebo). Infrared laser (780 nm, 70 mw, 60s, 4.2 J/point, 105 J/cm²) was applied precisely and continuously into five points of the temporomandibular joint (TMJ) area: lateral point (LP), superior point (SP), anterior point (AP), posterior point (PP), and posterior-inferior point (PIP) of the condylar position. This was performed twice per week, for a total of eight sessions. A Visual Analogue Scale and a colorimetric capsule method were employed. Data were obtained three times: before treatment (Ev1), shortly after the eighth session (Ev2), and 30 days after the first application (Ev3). Statistical tests revealed significant differences at one percent (1%) likelihood, which implies that superiority of the active group offered considerable TMJ pain improvement. Both groups presented similar masticatory behavior, and no statistical differences were found. With regard to the evaluation session, Ev2 presented the lowest symptoms and highest masticatory efficiency throughout therapy.

da Cunha L A, Firoozmand L M, da Silva A P, Esteves S A, Oliveira W. Efficacy of low-level laser therapy in the treatment of temporomandibular disorder. Int Dent J. 2008; 58 (4): 213-217.

In a study by da Cunha the sample consisted of 40 patients, divided into an experimental group (G1) and a placebo group (G2). The treatment was done with an infrared laser (830nm, 500mW, 20s, 4J/point) at the painful points, once a week for four consecutive weeks. The patients were evaluated before and after the treatment through VAS and the Craniomandibular Index (CMI). The baseline and post therapy values of VAS and CMI were compared by the paired T-test, separately for the placebo and laser groups. A significant difference was observed between initial and final values in both groups. Baseline and post-therapy values of pain and CMI were compared in the therapy groups by the two-sample T-test, yet no significant differences were observed regarding VAS and CMI. After either placebo or laser therapy, pain and temporomandibular symptoms were significantly lower, although there was no significant difference between groups. **The actual energy is 500 x 20 seconds = 10 J/point. The two studies above appear to be rather similar, but the study delivering positive results treated twice a week, the negative study once a week. The longer time used in the positive study may also be of importance, even though the energy per point was lower than in the negative study.**

França C M, Núñez S C, Prates R A, Noborikawa E, Faria M R, Ribeiro M S. Low-intensity red laser on the prevention and treatment of induced-oral mucositis in hamsters. J Photochem Photobiol B. 2009; 94 (1): 25-31.

França divided a group of hamsters into four groups: preventive cryotherapy, preventive laser, therapeutic laser and therapeutic control group. Mucositis was induced in hamsters by intraperitoneal injection of 5-fluorouracil (5-FU) and superficial scratching. All preventive treatment was performed on the right cheek pouch mucosa. The left pouch mucosa was used for a spontaneous development of mucositis and did not receive any preventive therapy. Laser parameters were: 660 nm, 30 mW, 1.2 J/cm², 40 s, spot size 3 mm². Cryotherapy was done positioning ice packs in the hamster mucosa 5 min before 5-FU infusion and 10 min afterwards. To study the healing of mucositis, the left pouch mucosa of each of the hamsters in the TLG received laser irradiation on the injured area. Irradiation parameters were kept the same as above mentioned. The control hamsters in the TCG did not receive any treatment. The mucositis degree and the animal's body mass were evaluated. An assessment of blood vessels was made based on immunohistochemical staining. The CG animals lost 15.16% of their initial body mass while the LG animals lost 8.97% during the first 5 days. The laser treated animals had a better clinical outcome with a faster healing, and more granulation tissue. The quantity of blood vessels at both LG and CG were higher than in healthy mucosa. Regarding the therapeutic analysis, the severity of the mucositis in the TLG was always lower than TCG. TLG presented higher organization of the granulation tissue, parallel collagen fibrils, and increased angiogenesis.

Mirzaii-Dizgah I, Ojaghi R, Sadeghipour-Roodsari HR, Karimian SM, Sohanaki H. Attenuation of morphine withdrawal signs by low level laser therapy in rats. Behav Brain Res. 2009; 196 (2): 268-270.

In the study by Mirzaii-Dizgah the effects of LPT on naloxone-induced withdrawal signs of morphine-dependent rats were examined. A GaAlAs laser with a power density of 12.5 J/cm² was used. One-way ANOVA showed that the LPT applied immediately or 15min prior to naloxone injection significantly decreased total withdrawal score (TWS). These results suggest that LPT prior to naloxone injection attenuates the expression of withdrawal signs in morphine-dependent rats.

Pozza D H, Fregapani P W, Weber J B, de Oliveira M G, de Oliveira M A, Ribeiro Neto N, de Macedo Sobrinho J B. Analgesic action of laser therapy (LLLT) in an animal model. Med Oral Patol Oral Cir Bucal. 2008; 13 (10): 648-652.

The aim of the study by Pozza was to evaluate the analgesic effect of laser therapy on healthy tissue of mice. 45 animals were divided in three groups of 15: A: infrared laser irradiation (830 nm), B: red laser irradiation (660 nm) and C: sham irradiation with laser unit off. After laser application, the mice remained immobilized for the injection of 30 microl of 2% formalin in the plantar pad of the irradiated hind paw. The time that the mouse kept the hind paw lifted was measured at 5 min intervals for 30 minutes. Results showed statistically significant differences comparing the control group with the infrared laser group at 5, 20, 25 and 30 accumulated minutes, and with the red laser group at all time points. The analysis of partial times, at each 5 minutes, showed statistically significant differences between the control and the laser groups up to 20 minutes. Thus, laser irradiation had an analgesic effect and red laser had the best results.

Blaya D S, Guimarães M B, Pozza D H, Weber J B, de Oliveira M G. Histologic study of the effect of laser therapy on bone repair. J Contemp Dent Pract. 2008; 9 (6): 41-48.

This study used histologic analysis and HE staining to evaluate laser biomodulation of bone repair in cavities made in the femurs of rats that underwent non-ablative laser irradiation. METHODS AND MATERIALS: Eighteen male Wistar rats weighing 300 to 400 grams were randomly assigned to three groups of six animals each. A surgical defect site was produced with a trephine about 2 mm in diameter under abundant irrigation. In Group I the complete surgical protocol to produce a bone defect was followed but without laser radiation (control). In Group II a continuous wave 830 nm infrared laser was used at 10 J/cm² and 50 mW at each point of the surgical site. In Group III a continuous wave 685 nm infrared laser at 10J/cm² and 35 mW was used at each point of surgical site. The animals were irradiated at intervals of 48 hours beginning immediately after the preparation of the defect and were sacrificed on the 15th, 21st, and 30th days. Slides were studied by means of descriptive analysis. RESULTS: Greater degrees of new bone formation and vertical regeneration were found in the irradiated groups than in the control group. Laser therapy in this study protocol was efficient in promoting bone repair.

Shirani A M, Gutknecht N, Taghizadeh M, Mir M. Low-level laser therapy and myofascial pain dysfunction syndrome: a randomized controlled clinical trial. Lasers Med Sci. 2008; Nov 12. [Epub ahead of print]

Myofascial pain dysfunction syndrome (MPDS) is the most common reason for pain and limited function of the masticatory system. The aim of a study by Shirani was to

evaluate the efficacy of a particular source producing 660 nm and 890 nm wavelengths that was recommended to reduce of the pain in the masticatory muscles. This was a double-blind and placebo-controlled trial. Sixteen MPDS patients were randomly divided into two groups. For the laser group, two diode laser probes (660 nm, 6.2 J/cm², 6 min, CW and 890 nm, 1 J/cm², 10 min, 1,500 Hz) were used on the painful muscles. For the control group, the treatment was similar, but the patients were not irradiated. Treatment was given twice a week for 3 weeks. The amount of patient pain was recorded at four time periods (before and immediately after treatment, 1 week after, and on the day of complete pain relief). A visual analog scale was selected as the method of pain measurement. In each group the reduction of pain before and after the treatment was meaningful, but, between the two groups LPT was more effective

Shooshtari S M, Badiie V, Taghizadeh SH, Nematollahi A H, Amanollahi A H, Grami M T. The effects of low level laser in clinical outcome and neurophysiological results of carpal tunnel syndrome. Electromyogr Clin Neurophysiol. 2008; 48 (5): 229-231.

The study by Shooshtari evaluated the effects of LPL through nerve conduction measurement and clinical signs and symptoms. A total of 80 patients were included. Diagnosis of CTS was based on both clinical examination and electromyographic (EMG) findings. Patients were randomly assigned into two groups. Test group (group A) underwent laser therapy (9-11 joules/cm²) over the carpal tunnel area. Control group (group B) received sham laser therapy. Pain, hand grip strength, median proximal sensory and motor latencies, transcarpal median sensory nerve conduction (SNCV) were recorded. After fifteen sessions of irradiation (five times per week), parameters were recorded again and clinical symptoms were measured in both groups. Pain was evaluated by VAS; day-night. Hand grip was measured by Jamar dynamometer. There was a significant improvement in clinical symptoms and hand grip in group A. Proximal median sensory latency, distal median motor latency and median sensory latencies were significantly decreased. Transcarpal median SNCV increased significantly after laser irradiation. There were no significant changes in group B except changes in clinical symptoms.

Chen K H, Hong C Z, Kuo F C, Hsu H C, Hsieh Y L. Electrophysiologic effects of a therapeutic laser on myofascial trigger spots of rabbit skeletal muscles. Am J Phys Med Rehabil. 2008; 87 (12): 1006-1014.

To better understand the mechanisms of therapeutic lasers for treating human myofascial trigger points, Chen designed a blinded controlled study of the effects of a therapeutic laser on the prevalence of endplate noise (EPN) recorded from the myofascial trigger spot (MTrS) of rabbit skeletal muscle. In eight rabbits, one MTrS in each biceps femoris muscle was irradiated with a 660 nm at 9 J/cm². The contralateral side of muscle was treated with a sham laser. Each rabbit received six treatments. The immediate and cumulative effects were assessed by the prevalence of EPN with electromyographic (EMG) recordings after the first and last treatments. Compared with pretreatment values, the percentages of EPN prevalence in the experimental side after the first and last treatments were significantly reduced. The change in EPN prevalence in the experimental side was significantly greater than in the control side immediately after the first and last treatments. However, no

significant differences were noted between the first and last treatments. It seems that laser irradiation may inhibit the irritability of an MTrS in rabbit skeletal muscle. This effect may be a possible mechanism for myofascial pain relief with LPT.

Zhang L, Xing D, Zhu D, Chen Q. Low-power laser irradiation inhibiting Abeta25-35-induced PC12 cell apoptosis via PKC activation. Cell Physiol Biochem. 2008; 22 (1-4): 215-222.

Apoptosis is a contributing pathophysiological mechanism of Alzheimer's disease (AD). In a study by Zhang the techniques of fluorescence resonance energy transfer (FRET) and real-time quantitative RT-PCR were used to investigate the anti-apoptotic mechanism of LPT. Rat pheochromocytoma (PC12) cells were treated with amyloid beta 25-35 (Abeta(25-35)) for induction of apoptosis before LPT treatment. The cell viability assays and morphological examinations show that low fluence of LPT (0.156 J/cm²-0.624 J/cm²) could inhibit the cells apoptosis. An increase of PKC activation was dynamically monitored in the cells treated with PMA (specific activator of PKC), LPT only or Abeta(25-35) followed by 5 min LPT treatment, respectively. However, the effect of LPT activating PKC could be inhibited by Go 6983 (specific inhibitor of PKC). Furthermore, LPT involved an increase in mRNA of the cell survival member bcl-xl and a decrease in the up-regulation of cell death member bax mRNA caused by Abeta(25-35). Further data show that low fluence of LPT could reverse the increased level of bax/bcl-xl mRNA ratio caused by Abeta(25-35) treatment. In addition, Go 6983 could inhibit the decreased level of bax/bcl-xl mRNA ratio. Taken together, these data clearly indicate that LPT inhibited Abeta(25-35)-induced PC12 cell apoptosis via PKC-mediated regulation of bax/bcl-xl mRNA ratio.

Gál P, Mokry M, Vidinsky B, Kilik R, Depta F, Harakaľová M, Longauer F, Mozeš S, Sabo J. Effect of equal daily doses achieved by different power densities of low-level laser therapy at 635 nm on open skin wound healing in normal and corticosteroid-treated rats. Lasers Med Sci. 2008 Aug 21. [Epub ahead of print]

In a study by Gál four, round, full-thickness skin wounds were made on the backs of 48 rats that were divided into two groups (non-steroid laser-treated and steroid laser-treated). Three wounds were stimulated daily with a diode laser (daily dose 5 J/cm²), each with different power density (1 mW/cm², 5 mW/cm², and 15 mW/cm²), whereas the fourth wound served as a control. Two days, 6 days, and 14 days after surgery, eight animals from each group were killed and samples were removed for histological evaluation. In the non-steroid laser-treated rats, significant acceleration of epithelization and collagen synthesis 2 days and 6 days after surgery was observed in laser-stimulated wounds. In steroid laser-treated rats, 2 days and 14 days after surgery, a decreased leucocyte/macrophage ratio and a reduction in the area of granulation tissue were recorded, respectively. LPT improved wound healing in the non-steroid laser-treated rats, but it was not effective after corticosteroid treatment.

Doin-Silva R, Baranauskas V, Rodrigues-Simioni L, da Cruz-Höfling M A. The Ability of Low Level Laser Therapy to Prevent Muscle Tissue Damage Induced by Snake Venom. Photochem Photobiol. 2008 Jul 17. [Epub ahead of print]

In a study by Doin-Silva the tibialis anterior muscle of rats was injected with venom diluted in 0.9% saline solution or saline solution alone. Sixty minutes after venom

injection, HeNe treatment was administered at three incident energy densities: dose 1, a single exposure of 3.5 J/cm²; dose 2, three exposures of 3.5 J/cm², dose 3, a single exposure of 10.5 J/cm². Muscle function was assessed through twitch tension recordings whereas muscle damage was evaluated through histopathologic analysis, morphometry of area of tissue affected and creatine kinase (CK) serum levels, and compared to unirradiated muscles. Laser application at the dose of 3.5 J/cm² reduced the area of injury by 64%, decreased the neuromuscular blockade (NMB) by 62% and reduced CK levels by 58% , when compared with unirradiated controls. Dose 2 showed a poorer benefit than dose 1, and dose 3 was ineffective in preventing the venom effects. Measurements of the absorbance of unirradiated and irradiated venom solution showed no difference in absorption spectra. In addition, no difference in the intensity of partial NMB in nerve-muscle preparation was shown by unirradiated and irradiated venom. The results indicate that the laser light did not alter venom toxicity.

Hagiwara S, Iwasaka H, Hasegawa A, Noguchi T. Pre-Irradiation of blood by gallium aluminum arsenide (830 nm) low-level laser enhances peripheral endogenous opioid analgesia in rats. *Anesth Analg.* 2008; 107 (3): 1058-1063.

Hagiwara investigated whether pre-irradiation of blood by LPT enhances peripheral endogenous opioid analgesia. The effect of LPT pretreatment of blood on peripheral endogenous opioid analgesia was evaluated in a rat model of inflammation. Additionally, the effect of LPT on opioid production was also investigated in vitro in rat blood cells. The expression of the beta-endorphin precursors, proopiomelanocortin and corticotrophin releasing factor, were investigated by reverse transcription polymerase chain reaction. LPT pretreatment produced an analgesic effect in inflamed peripheral tissue, which was transiently antagonized by naloxone. Correspondingly, beta-endorphin precursor mRNA expression increased with LPT, both in vivo and in vitro. These findings suggest that that LPT pretreatment of blood induces analgesia in rats by enhancing peripheral endogenous opioid production, in addition to previously reported mechanisms.

Hagiwara S, Iwasaka H, Okuda K, Noguchi T. GaAAs (830 nm) low-level laser enhances peripheral endogenous opioid analgesia in rats. *Lasers Surg Med.* 2007; 39 (10): 797-802.

The study by Hagiwara investigated whether LPT may enhance peripheral endogenous opioid analgesia. The effect of LPT on opioid analgesia and production was evaluated in vivo in a rat model of inflammation as well as in vitro in Jurkat cells, a human T-cell leukemia cell line. mRNA expression of the beta-endorphin precursors proopiomelanocortin and corticotrophin releasing factor was assessed by reverse transcription polymerase chain reaction. LPT produced an analgesic effect in inflamed peripheral tissue which was transiently antagonized by naloxone. Beta-endorphin precursor mRNA expression increased with LPT, both in vivo and in vitro. This study demonstrates that LPT produces analgesic effects in a rat model of peripheral inflammation. The researchers also revealed an additional mechanism of LPT-mediated analgesia via enhancement of peripheral endogenous opioids. These findings suggest that LPT induces analgesia in rats by enhancing peripheral endogenous opioid production in addition to previously reported mechanisms.

Lapchak P A, Han M K, Salgado K F, Streeter J, Zivin J A. Safety profile of transcranial near-infrared laser therapy administered in combination with thrombolytic therapy to embolized rabbits. Stroke. 2008; 39 (11): 3073-3078.

Transcranial near-infrared laser therapy (TLT) is currently under investigation in a pivotal clinical trial that excludes thrombolytic therapy. To determine if combining tissue plasminogen activator (tPA; Alteplase) and TLT is safe, this study assessed the safety profile of TLT administered alone and in combination with Alteplase. The purpose for a study by Lapchak was to determine if the combination of TLT and thrombolysis should be investigated further in a human clinical trial. The researchers determined whether postembolization treatment with TLT in the absence or presence of tPA would affect measures of hemorrhage or survival after large clot embolism-induced strokes in rabbits. TLT did not significantly alter hemorrhage incidence after embolization, but there was a trend for a modest reduction of hemorrhage volume (by 65%) in the TLT-treated group compared with controls. Intravenous administration of tPA, using an optimized dosing regimen, significantly increased hemorrhage incidence by 160%. The tPA-induced increase in hemorrhage incidence was not significantly affected by TLT, although there was a 30% decrease in hemorrhage incidence in combination-treated rabbits. There was no effect of TLT on hemorrhage volume measured in tPA-treated rabbits and no effect of any treatment on 24-hour survival rate. In the embolism model, TLT administration did not affect the tPA-induced increase in hemorrhage incidence. TLT may be administered safely either alone or in combination with tPA because neither treatment affected hemorrhage incidence or volume. These results support the study of TLT in combination with Alteplase in patients with stroke.

Leal Junior E C, Lopes-Martins R A, Dalan F, Ferrari M, Sbabo F M, Generosi R A, Baroni B M, Penna S C, Iversen V V, Bjordal J M. Effect of 655-nm low-level laser therapy on exercise-induced skeletal muscle fatigue in humans. Photomed Laser Surg. 2008; 26 (5): 419-24.

Leal Junior investigated if development of skeletal muscle fatigue during repeated voluntary biceps contractions could be attenuated by LPT. Twelve male professional volleyball players were entered into a randomized double-blind placebo-controlled trial, for two sessions (on day 1 and day 8) at a 1-wk interval, with both groups performing as many voluntary biceps contractions as possible, with a load of 75% of the maximal voluntary contraction force (MVC). At the second session on day 8, the groups were either given LPT (655 nm) of 5 J at an energy density of 500 J/cm² administered at each of four points along the middle of the biceps muscle belly, or placebo LLLT in the same manner immediately before the exercise session. The number of muscle contractions with 75% of MVC was counted by a blinded observer and blood lactate concentration was measured. RESULTS: Compared to the first session (on day 1), the mean number of repetitions increased significantly by 8.5 repetitions (+/- 1.9) in the active LPT group at the second session (on day 8), while in the placebo LPT group the increase was only 2.7 repetitions (+/- 2.9) (p = 0.0001). At the second session, blood lactate levels increased from a pre-exercise mean of 2.4 mmol/L, to 3.6 mmol/L in the placebo group, and to 3.8 mmol/L in the active LPT group after exercise, but this difference between groups was not statistically significant. It is concluded that LPT appears to delay the onset of muscle fatigue and exhaustion by a local mechanism in spite of increased blood lactate levels.

Ribeiro D A, Matsumoto M A. Low-level laser therapy improves bone repair in rats treated with anti-inflammatory drugs. J Oral Rehabil. 2008; 35 (12) :925-933.

The aim of a study by Ribeiro was to evaluate the action of anti-COX-2 selective drug (celecoxib) on bone repair associated with LPT. A total of 64 rats underwent surgical bone defects in their tibias, being randomly distributed into four groups: Group 1) negative control; Group 2) animals treated with celecoxib; Group 3) animals treated with LPT and Group 4) animals treated with celecoxib and LPT. The animals were killed after 48 h, 7, 14 and 21 days. The tibias were removed for morphological, morphometric and immunohistochemistry analysis for COX-2. Statistical significant differences were observed in the quality of bone repair and quantity of formed bone between groups at 14 days after surgery for Groups 3 and 4. COX-2 immunoreactivity was more intense in bone cells for intermediate periods evaluated in the laser-exposed groups. Taken together, such results suggest that low-level laser therapy is able to improve bone repair in the tibia of rats as a result of an up-regulation for cyclooxygenase-2 expression in bone cells.

Dos Reis F A, Belchior A C, de Carvalho P D, da Silva B A, Pereira D M, Silva I S, Nicolau R A. Effect of laser therapy (660 nm) on recovery of the sciatic nerve in rats after injury through neurotmesis followed by epineural anastomosis. Lasers Med Sci. 2008 Dec 23. [Epub ahead of print]

The aim of a study by dos Reis was to analyze the influence of 660 nm laser light on the myelin sheath and functional recovery of the sciatic nerve in rats. The sciatic nerves of 12 Wistar rats were subjected to injury through neurotmesis and epineural anastomosis, and the animals were divided into two groups: group 1 was the control and group 2, underwent LPT. After the injury, 660 nm, 4 J/cm², 26.3 mW and beam area of 0.63 cm² was administered to three equidistant points on the injury for 20 consecutive days. In the control group the mean area of the myelin impairment was 0.51 on day 21 after the operation, whereas this value was 1.31 in the LPT group. Comparison of the sciatic functional index (SFI) showed that there was no significant difference between the pre-lesion value in the laser therapy group and the control group. The use of 660 nm LPT provided significant changes to the morphometrically assessed area of the myelin sheath, but it did not culminate in positive results for functional recovery in the sciatic nerve of the rats after injury through neurotmesis.

Hou J F, Zhang H, Yuan X, Li J, Wei Y J, Hu S S. In vitro effects of low-level laser irradiation for bone marrow mesenchymal stem cells: proliferation, growth factors secretion and myogenic differentiation. Lasers Surg Med. 2008; 40 (10):726-733.

Bone marrow derived mesenchymal stem cells (BMSCs) have shown to be an appealing source for cell therapy and tissue engineering. Previous studies have confirmed that the application of LPT could affect the cellular process. However, little is known about the effects of LPT on BMSCs. The aim of study by Zhang was designed to investigate the influence of LPT at different energy densities on BMSCs proliferation, secretion and myogenic differentiation. BMSCs were harvested from rat fresh bone marrow and exposed to a 635 nm diode laser (60 mW; 0, 0.5, 1.0, 2.0, or

5.0 J/cm²). The lactate dehydrogenase (LDH) release was used to assess the cytotoxicity of LPT at different energy densities. Cell proliferation was evaluated by using 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) and 5-bromo-2'-deoxyuridine (BrdU) assay. Production of vascular endothelial growth factor (VEGF) and nerve growth factor (NGF) were measured by enzyme-linked immunosorbent assay (ELISA). Myogenic differentiation, induced by 5-azacytidine (5-aza), was assessed by using immunocytochemical staining for the expression of sarcomeric alpha-actin and desmin. Cytotoxicity assay showed no significant difference between the non-irradiated group and irradiated groups. LPT significantly stimulated BMSCs proliferation and 0.5 J/cm² was found to be an optimal energy density. VEGF and NGF were identified and LPT at 5.0 J/cm² significantly stimulated the secretion. After 5-aza induction, myogenic differentiation was observed in all groups and LPT at 5.0 J/cm² dramatically facilitated the differentiation. LPT may provide a novel approach for the preconditioning of BMSCs in vitro prior to transplantation.

Lasers Med Sci. 2008 Nov 22. [Epub ahead of print] Enhancement of light propagation depth in skin: cross-validation of mathematical modeling methods. Kwon K, Son T, Lee KJ, Jung B.

Various techniques to enhance light propagation in skin have been studied in low-level laser therapy. In this study, three mathematical modeling methods for five selected techniques were implemented so that we could understand the mechanisms that enhance light propagation in skin. The five techniques included the increasing of the power and diameter of a laser beam, the application of a hyperosmotic chemical agent (HCA), and the whole and partial compression of the skin surface. The photon density profile of the five techniques was solved with three mathematical modeling methods: the finite element method (FEM), the Monte Carlo method (MCM), and the analytic solution method (ASM). We cross-validated the three mathematical modeling results by comparing photon density profiles and analyzing modeling error. The mathematical modeling results verified that the penetration depth of light can be enhanced if incident beam power and diameter, amount of HCA, or whole and partial skin compression is increased. In this study, light with wavelengths of 377 nm, 577 nm, and 633 nm was used.

Igić M, Kesić L, Apostolović M, Kostadinović L. [Low-level laser efficiency in the therapy of chronic gingivitis in children] [in Serbian]. Vojnosanit Pregl. 2008; 65 (10): 755-757.

The aim of a study by Igić was to determine the efficiency of a LPT in the therapy of chronic gingivitis in children. The study included 100 children with permanent dentition and suffering from chronic gingivitis. They were divided into two groups: group I-50 children with chronic gingivitis, who underwent the basic therapy; group II-50 children with chronic gingivitis, who underwent the basic therapy and also LPT. Evaluation of the condition of oral hygiene, the health of gingiva and periodontium was done using appropriate index before and after the therapy. For the plaque index (PI) following results were obtained: in the group I PI = 1.94, and in the group II PI = 1.82. After the therapy in both groups PI was 0. In the group I sulcus plaque index (SPI) was 2.02 before the therapy and 0.32 after the therapy. In the group II SPI was 1.90 before the therapy and 0.08 after the therapy. In the group I Community

Periodontal Index of Treatment Needs (CPITN) was 1.66 before the therapy and 0.32 after the therapy, and in the group II CPITN was 1.60 before the therapy and 0.08 after the therapy. Chronic gingivitis in children can be successfully cured by the basic treatment but the use of LPT can significantly improve this effect.

Aimbire F, de Lima F M, Costa M S, Albertini R, Correa J C, Iversen V V, Bjordal J M. Effect of low level laser therapy on bronchial hyper-responsiveness. Lasers Med Sci. 2008 Nov 12. [Epub ahead of print]

The objective of a study by Aim bire was to investigate whether LPT could reduce bronchial hyper-responsiveness (BHR) induced by tumour necrosis factor-alpha (TNF-alpha) modulating the metabolism of inositol phosphate (IP) in bronchial smooth muscle cells (BSMCs). The study was on 28 Wistar rats, randomly divided into four groups. Irradiation (1.3 J/cm²) was administered 5 min and 4 h after bronchial smooth muscle (BSM) had been suspended in TNF-alpha baths, and the contractile response-induced calcium ion (Ca²⁺) sensitization was measured. The BSMCs were isolated, and the IP accumulation was measured before and after TNF-alpha immersion in the groups that had been irradiated or not irradiated. BSM segments significantly increased contraction 24 h after TNF-alpha immersion when exposed to carbachol (CCh) as Ca²⁺, but it was significantly reduced by 64% and 30%, respectively, after laser treatment. The increase in IP accumulation induced by CCh after TNF-alpha immersion was reduced in the BSMCs by LPT. The dose of 2.6 J/cm² reduced BHR and IP accumulation in the rats' inflammatory BSMCs.

Evid Based Complement Alternat Med. 2008 Dec;5(4):383-9. Epub 2007 Sep 13. Blinding techniques in randomized controlled trials of laser therapy: an overview and possible solution. Relf I, Chow R, Pirotta M.

Low-level laser therapy has evidence accumulating about its effectiveness in a variety of medical conditions. We reviewed 51 double blind randomized controlled trials (RCTs) of laser treatment. Analysis revealed 58% of trials showed benefit of laser over placebo. However, less than 5% of the trials had addressed beam disguise or allocation concealment in the laser machines used. Many of the trials used blinding methods that rely on staff cooperation and are therefore open to interference or bias. This indicates significant deficiencies in laser trial methodology. We report the development and preliminary testing of a novel laser machine that can blind both patient and operator to treatment allocation without staff participation. The new laser machine combines sealed preset and non-bypassable randomization codes, decoy lights and sound, and a conical perspex tip to overcome laser diode glow detection.

Gorgey A S, Wadee A N, Sobhi N N. The effect of low-level laser therapy on electrically induced muscle fatigue: a pilot study. Photomed Laser Surg. 2008; 26 (5): 501-506.

The purpose of a pilot study by Gorgey was to determine if LPT could attenuate skeletal muscle fatigue induced by surface neuromuscular electrical stimulation (NMES) in healthy volunteers. Five college-age participants underwent three cross-

over randomized trials: two (LLLT + NMES) test trials and a control trial (NMES only), in which NMES was applied to their dominant knee extensor muscle group. The LPT doses, 500 mW at 808 nm, were either adjusted to deliver a total energy of 7 J for 10 min or 3 J for 5 min in a blinded fashion. Following LPT irradiation, the NMES protocol was immediately delivered for 3 min to induce fatigue in the knee extensor muscle group. The five participants completed the three trials. After the control trial, torque significantly decreased at the end of 3 min. There was no significant difference between the 7 J and 3 J trials on muscle fatigue. Following both LPT trials, torque significantly decreased at the end of 3 min. Although there was a difference (11%) in fatigue between the two LPT trials and the control trial, this difference did not attain statistical significance

Cressoni M D, Dib Giusti H H, Casarotto R A, Anaruma C A. The Effects of a 785-nm AlGaInP Laser on the Regeneration of Rat Anterior Tibialis Muscle After Surgically-Induced Injury. Photomed Laser Surg. 2008 Sep 18. [Epub ahead of print]

A study by Cressoni aimed to investigate the effects of LPT on muscle regeneration. For this purpose, the anterior tibialis muscle of 48 male Wistar rats received treatment (785 nm) after surgically-induced injury. The animals were randomized into four groups: uninjured rats (UN); uninjured and laser-irradiated rats (ULI); injured rats (IN); and injured and laser-irradiated rats (ILI). The direct contact laser treatment was started 24 h after surgery. A laser emitting 75 mW of continuous power at 785 nm was used for irradiation. The laser probe was placed at three treatment points to deliver 0.9 J per point, for a total dose of 2.7 J per treatment session. The animals were euthanized after treatment sessions 1, 2, and 4. Mounted sections were stained with hematoxylin and eosin and used for quantitative morphological analysis, in which the number of leukocytes and fibroblasts were counted over an area of 4480 μm^2 . Quantitative data showed that the number of both polymorphonuclear and mononuclear leukocytes in the inflammatory infiltrate at the injury site was smaller in the ILI(1), ILI(2), and ILI(4) subgroups compared with their respective control subgroups (IN(1), IN(2), and IN(4)) for sessions 1, 2, and 4, respectively. On the other hand, the number of fibroblasts increased after the fourth treatment session. With regard to the regeneration of muscle fibers following injury, only after the fourth treatment session was it possible to find muscle precursor cells such as myoblasts and some myotubes in the ILI(4) subgroup. Thus, in the acute inflammatory phase, the laser treatment was found to have anti-inflammatory effects, reducing the number of leukocytes at the injury site and accelerating the regeneration of connective tissue.

Abramoff M M, Lopes N N, Lopes L A, Dib L L, Guilherme A, Caran E M, Barreto A D, Lee M L, Petrilli A S. Low-level laser therapy in the prevention and treatment of chemotherapy-induced oral mucositis in young patients. Photomed Laser Surg. 2008; 26 (4): 393-400.

Patients undergoing chemotherapy (22 cycles) and still without mucositis were randomized into a group receiving prophylactic laser-irradiation (group 1), and a group receiving placebo light treatment (group 2). Patients who had already presented with mucositis were placed in a group receiving irradiation for therapeutic purposes (group 3, with 10 cycles of CT). Serum granulocyte levels were taken and compared to the progression of mucositis. In group 1, most patients (73%) presented with

mucositis of grade 0 and 18% presented with grade 1. In group 2, 27% had no OM and did not require therapy. In group 3, the patients had marked pain relief, and a decrease in the severity of OM, even when they had severe granulocytopenia.

Krechina E K, Shidova A V, Maslova V V. [Comparative evaluation of influence of low-intensity laser radiation of different spectrum components and regimen of laser work upon microcirculation in comprehensive treatment of chronic parodontitis]. [Article in Russian] Stomatologiia (Mosk). 2008; 87 (3): 24-27

A comparative study of the influence details of low-intensity pulse and continuous oscillation of laser radiation of red and infrared parts of spectrum upon microcirculation indices in comprehensive treatment of chronic parodontitis of light and middle severity was performed by Krechina For the first time the predominantly activating influence upon microcirculation in gingival tissues of the pulsed laser radiation in the red part of spectrum was established.

Wu C S, Hu S C, Lan C C, Chen G S, Chuo W H, Yu H S. Low-energy helium-neon laser therapy induces repigmentation and improves the abnormalities of cutaneous microcirculation in segmental-type vitiligo lesions. Kaohsiung J Med Sci. 2008; 24 (4): 180-189.

Since segmental-type vitiligo lesions (SV) are resistant to conventional forms of therapy, its management represents a challenge for dermatologists. HeNe laser, wavelength 632.8 nm has been employed as a therapeutic instrument in many clinical situations, including vitiligo management and repair of nerve injury. The purpose of the study by Wu was to evaluate the effectiveness and safety of HeNe lasers in treating SV, and determine the effects on the repair of sympathetic nerve dysfunction. Forty patients with stable-stage SV on the head and/or neck were enrolled in this study. He-Ne laser irradiation was administered locally at 3.0 J/cm² with point stimulation once or twice weekly. Cutaneous microcirculatory assessments in six SV patients were performed using a laser Doppler flowmeter. The sympathetic adrenoceptor response of cutaneous microcirculation was determined by measuring cutaneous blood flow before, during and after iontophoresis with sympathomimetic drugs (phenylephrine, clonidine and propranolol). All measurements of microcirculation obtained at SV lesions were simultaneously compared with contralateral normal skin, both before and after HeNe laser treatment. After an average of 17 treatment sessions, initial repigmentation was noticed in the majority of patients. Marked repigmentation was observed in 60% of patients with successive treatments. Cutaneous blood flow was significantly higher at SV lesions compared with contralateral skin, but this was normalized after HeNe laser treatment. In addition, the abnormal decrease in cutaneous blood flow in response to clonidine was improved by HeNe laser therapy.

Stein E, Koehn J, Sutter W, Wendtlandt G, Wanschitz F, Thurnher D, Baghestanian M, Turhani D. Initial effects of low-level laser therapy on growth and differentiation of human osteoblast-like cells. Wien Klin Wochenschr. 2008; 120 (3-4): 112-117.

The aim of the in vitro study by Stein was to investigate the initial effect of LPT on growth and differentiation of human osteoblast-like cells. SaOS-2 cells were

irradiated with laser doses of 1 J/cm² and 2 J/cm² using a laser with 670 nm wavelength and an output power of 400 mW. Untreated cells were used as controls. At 24 h, 48 h and 72 h post irradiation, cells were collected and assayed for viability of attached cells and alkaline phosphatase specific activity. In addition, mRNA expression levels of osteopontin and collagen type I were assessed using semi-quantitative RT-PCR. Over the observation period, cell viability, alkaline phosphatase activity and the expression of osteopontin and collagen type I mRNA were slightly enhanced in cells irradiated with 1 J/cm² compared with untreated control cells. Increasing the laser dose to 2 J/cm² reduced cell viability during the first 48 h and resulted in persistently lower alkaline phosphatase activity compared with the other two groups. The expression of osteopontin and collagen type I mRNA slightly decreased with time in untreated controls and cells irradiated with 1 J/cm², but their expression was increased by treatment with 2 J/cm² after 72 h. These results indicate that LPT has a biostimulatory effect on human osteoblast-like cells during the first 72 h after irradiation.

Acupunct Electrother Res. 2007;32(1-2):81-6. Depth of penetration of an 850nm wavelength low level laser in human skin. Esnouf A, Wright PA, Moore JC, Ahmed S.

Low Level Laser Therapy is used for a wide variety of conditions including superficial skin sores, musculoskeletal and joint problems, and dentistry. Knowledge of the penetration depth of laser radiation in human skin is an essential prerequisite to identifying its method of action. Mathematical simulations and estimates from the literature suggest that the depth of penetration of laser radiation using wavelengths from 630nm up to 1100nm may be up to 50mm. The aim of this study is to directly measure the penetration depth of a Low Level Laser in human tissue. Human abdominal skin samples up to 0.784mm thickness were harvested by dermatome following abdominoplasty procedures. These samples were irradiated by a Gallium Aluminium Arsenide Laser (Wavelength 850nm near infra-red invisible light, 100mW, 24kHz, 0.28mm diameter probe) and the transmitted radiation measured with an Ophir Optronics 'Nova' external energy meter. The intensity of laser radiation reduced by 66% after being transmitted through a 0.784mm sample of human abdominal tissue. In this study most laser radiation was absorbed within the first 1mm of skin.

Gottschling S, Meyer S, Gribova I, Distler L, Berrang J, Gortner L, Graf N, Shamdeen M G. Laser acupuncture in children with headache: a double-blind, randomized, bicenter, placebo-controlled trial. Pain. 2008; 137 (2): 405-412.

The aim of the study by Gottschling was to investigate whether laser acupuncture is efficacious in children with headache and if active laser treatment is superior to placebo laser treatment, in a prospective, randomized, double-blind, placebo-controlled trial of low level laser acupuncture in 43 children with headache, either migraine (22 patients) or tension type headache (21 patients)). Patients were randomized to receive a course of 4 treatments over 4 weeks with either active or placebo laser. The treatment was highly individualised based on criteria of Traditional Chinese medicine (TCM). The primary outcome measure was a difference in numbers of headache days between baseline and the 4 months after randomization. Secondary

outcome measures included a change in headache severity using a 10 cm Visual Analogue Scale for pain and a change in monthly hours with headache. Measurements were taken during 4 weeks before randomization (baseline), at weeks 1-4, 5-8, 9-12 and 13-16 from baseline. The mean number of headaches per month decreased significantly by 6.4 days in the treated group) and by 1.0 days in the placebo group. Secondary outcome measures headache severity and monthly hours with headache decreased as well significantly at all time points compared to baseline and were as well significantly lower than those of the placebo group at all time points.

Jaguar G C, Prado J D, Nishimoto I N, Pinheiro M C, de Castro D O Jr, da Cruz Perez D E, Alves F A. Low-energy laser therapy for prevention of oral mucositis in hematopoietic stem cell transplantation. Oral Dis. 2007; 13 (6): 538-543.

In a study by Jaguar 24 patients received prophylactic laser therapy (L+ group). The applications started from the beginning of the conditioning regimen up to day +2. The oral assessment was performed daily until day +30. This group was compared with historical controls, namely 25 patients, who did not receive laser therapy (L- group). All patients developed some grade of mucositis. However, the L- group presented initial mucositis by 4.36 days, whereas the L+ group presented it in 6.12 days. The maximum mucositis occurred between day +2 and day +6 with healing by day +25 in the L- group and between day +2 and day +7 with healing by day +14 for the L+ group. Laser therapy also reduced the time of oral pain from 5.64 to 2.45 days and decreased the consumption of morphine.

M E, Pinheiro A L, Ramalho L M. Effect of IR laser photobiomodulation on the repair of bone defects grafted with organic bovine bone. Lasers Med Sci. 2008; 23(3): 313-317.

The study by Márquez Martínez assessed histologically the effect of LPT on the repair of surgical defects on the femur of rats filled with lyophilized bovine bone. The animals were divided into three groups: group I (control); group II (graft); group III (graft + LPT). The animals on the irradiated groups received 16 J/cm² per session divided into four points around the defect being the first irradiation immediately after surgery and repeated at every 48 h during 2 weeks. Animal death occurred 15, 21, and 30 days after surgery. The specimens were routinely processed and stained with H/E and Sirius red and analyzed by light microscopy. There was histological evidence of improved collagen fiber deposition at early stages of the healing; increased amount of well-organized bone trabeculae at the end of the experimental period on irradiated animals.

Yasukawa A, Hrui H, Koyama Y, Nagai M, Takakuda K. The effect of low reactive-level laser therapy (LLLT) with helium-neon laser on operative wound healing in a rat model. J Vet Med Sci. 2007; 69 (8): 799-806.

The effect of low reactive-level laser therapy (LLLT) with a He-Ne laser on operative wound healing was investigated in a rat model. 10-millimeter surgical wounds were created on the backs of Sprague Dawley rats, and animals were assigned to one of eleven groups (n=5). Ten groups received either 8.5 mW or 17.0 mW irradiation of 15 seconds LLLT a day with one of five different irradiation frequencies, i.e. daily (from the 1st to 6th day following surgery), every other day (the 1st, 3rd, and 5th day), on

only the 1st day, on only the 3rd day, and on only the 5th day; the 1st day was the day following the surgery. The control group received no irradiation. A skin specimen was harvested from the dorsal thoracic region on the 7th day to measure the rupture strength. The control group had the lowest rupture strength (5.01 N), and the 17.0 mW every other day irradiation group had the highest rupture strength (13.01 N). Statistical differences were demonstrated in the 8.5 mW irradiation setting between the every other day irradiation group and the control group ($p < 0.05$); and in 17.0 mW irradiation setting between the everyday irradiation, the every other day, and the 1st day only groups vs. the control group ($p < 0.01$). Histological examination demonstrated that wound healing in the 17.0 mW every other day irradiation group was promoted most significantly such as the prevention of excessive inflammation, increased formation of collagen fibers, and recovery in continuity of tissues. The control group showed poor wound healing and the other experimental groups showed intermediate healing. Thus LLLT with a He-Ne laser was found to promote the healing of operative wounds in the present rat model, in which the most favorable application of LLLT was the 17.0 mW setting of 15 seconds a day with a frequency of every other day.

Ng G Y, Fung D T. Combining therapeutic laser and herbal remedy for treating ligament injury: an ultrastructural morphological study. Photomed Laser Surg. 2008; 26 (5): 425-432.

Ng examined the ultrastructural morphology (number of collagen fibrils, mean and mass-averaged diameter) of isolated and combined treatments of a therapeutic laser and herbs for medial collateral ligament (MCL) injury in rats. Twenty-eight rats, divided into seven groups: laser (L), herb (H), laser + herb (LH), laser control (LC), herb control (HC), laser sham (LS) and herb sham (HS), were studied. Right MCL of groups L, H, LH, LC and HC were transected, while that of LS and HS remained intact. Group L received 9 treatment sessions of GaAlAs laser with a dosage of 3.5 Jcm²; group H received herbal plaster treatment; groups LH had combined treatments of laser and herb; group LC had placebo laser; group LS had no treatment; groups HC and HS received only bandage without herb. All MCLs were analyzed using transmission electron microscopy at 3 weeks. Differences ($p < 0.05$) existed in mean fibril diameters among groups. Core mass-averaged diameters of groups L and H were larger than the control groups (LC and HC). Fibril diameter of group LH (combined treatment) was even larger and approaching that of the intact MCL. Combined therapeutic laser and herbal treatment hastened collagen fibril maturation in MCL repair.

Karu T, Pyatibrat L, Kalendo G. Irradiation with He-Ne laser increases ATP level in cells cultivated in vitro. J Photochem Photobiol B. 1995; 27 (3): 219-223.

A monolayer of HeLa cells was irradiated with an He-Ne laser (632.8 nm, 100 J m⁻², 10 s) and the amount of adenosine triphosphate (ATP) was measured by the luciferin-luciferase bioluminescent assay technique at different times (5-45 min) after irradiation. The amount of ATP in the log phase of cultured cells remained at the control level (0.79 ± 0.09) x 10⁽⁻¹⁵⁾ mol per cell) during the first 15 min after irradiation; it then increased sharply and, after reaching a maximum (170.8%) 20 min after irradiation, decreased slowly to the control level. The ability of monochromatic red light to induce an increase in the cellular ATP level was found to depend on the

growth phase of the culture, being insignificant in the lag phase of cultured cells, increasing in the log phase of cultured cells and reaching a maximum (about 190%) in cells at the late logarithmic and early plateau phase.

Mochizuki-Oda N, Kataoka Y, Cui Y, Yamada H, Heya M, Awazu K. Effects of near-infra-red laser irradiation on adenosine triphosphate and adenosine diphosphate contents of rat brain tissue. *Neurosci Lett.* 2002; 323 (3): 207-210.

To investigate the cellular mechanisms by near-infra-red laser on the nervous system, Mochizuki-Oda examined the effect of 830 nm laser irradiation on the energy metabolism of the rat brain. The laser was applied for 15 min with an irradiance of 4.8 W/cm². Tissue adenosine triphosphate (ATP) content of the irradiated area in the cerebral cortex was 19% higher than that of the non-treated area, whereas the adenosine diphosphate (ADP) content showed no significant difference. Laser irradiation at another wavelength (652 nm) had no effect on either ATP or ADP contents. The temperature of the tissue was increased by 4.4-4.7 degrees C during the irradiation of both wavelengths. These results suggest that the increase in tissue ATP content did not result from the thermal effect, but from a specific effect of the laser operated at the 830 nm wavelength.

Ahmed N A, Radwan N M, Ibrahim K M, Khedr M E, El Aziz M A, Khadrawy Y A. Effect of three different intensities of infrared laser energy on the levels of amino acid neurotransmitters in the cortex and hippocampus of rat brain. *Photomed Laser Surg.* 2008; 26 (5): 479-488.

The aim of a study By Ahmed was to investigate the effects of three different intensities of infrared diode laser radiation on amino acid neurotransmitters in the cortex and hippocampus of rat brain. Lasers are known to induce different neurological effects such as pain relief, anesthesia, and neurosuppressive effects; however, the precise mechanisms of these effects are not clearly elucidated. Amino acid neurotransmitters (glutamate, aspartate, glutamine, gamma-aminobutyric acid [GABA], glycine, and taurine) play vital roles in the central nervous system (CNS). The shaved scalp of each rat was exposed to different intensities of infrared laser energy (500, 190, and 90 mW) and then the rats were sacrificed after 1 h, 7 d, and 14 d of daily laser irradiation. The control groups were exposed to the same conditions but without exposure to laser. The concentrations of amino acid neurotransmitters were measured by high-performance liquid chromatography (HPLC). The rats subjected to 500 mW of laser irradiation had a significant decrease in glutamate, aspartate, and taurine in the cortex, and a significant decrease in hippocampal GABA. In the cortices of rats exposed to 190 mW of laser irradiation, increases in aspartate accompanied by a decrease in glutamine were observed. In the hippocampus, other changes were seen. The rats irradiated with 90 mW showed a decrease in cortical glutamate, aspartate, and glutamine, and an increase in glycine, while in the hippocampus an increase in glutamate, aspartate, and GABA were recorded. It is concluded that daily laser irradiation at 90 mW produced the most pronounced inhibitory effect in the cortex after 7 d. This finding may explain the reported neurosuppressive effect of infrared laser energy on axonal conduction of hippocampal and cortical tissues of rat brain.

Shen-Zheng, Xiao-Jian, Lin S Z, Wang L H. Effects of laser guided by optic fiber into rat brain on conditioned avoidance response and brain chemistry. *Lasers Surg Med.* 1983; 2 (3): 231-239.

Low power lasers were guided by optic fibers into the rat caudate nucleus or frontal cortex, during conditioned avoidance response (CAR) training. The changes in striatal monoamine and amino acid concentrations were subsequently determined. Of six training groups tested, only the experimental group with helium-neon laser radiation to the caudate nucleus exhibited the formation of CAR and an increase of unconditioned leg contractions. The striatal concentrations of dopamine (DA) and norepinephrine (NE) were increased simultaneously in the group.

Igarashi H, Inomata K. Effects of low-power gallium aluminium arsenide diode laser irradiation on the development of synapses in the neonatal rat hippocampus. *Acta Anat (Basel).* 1991; 140 (2): 150-155.

Igarashi studied the effect of LPT on the development of synapses in the radiatum layer and the lacunosum-molecular layer of field CA3 of the neonatal rat hippocampus. Neonatal rats were irradiated with a laser (830 nm, 60 mW) at two points located above the hippocampi, for 15 s, respectively, twice per day from birth (day 1) to day 5. The mean body weights of the laser-irradiated animals were found to be lower than those of the control animals, the deficit at day 20 being 22.6%. Moreover, the density of synaptic junctions stained by ethanolic phosphotungstic acid per unit area of the radiatum layer and the lacunosum-molecular layer of the neonatal rat hippocampus was significantly reduced at day 20. It was suggested that the low-power diode laser irradiation affected the development of synapses in the neonatal rat brain.

Majlesi G. GaAs laser treatment of bilateral eyelid ptosis due to complication of botulinum toxin type A injection. *Photomed Laser Surg.* 2008; 26 (5): 507-509.

The widespread use of botulinum toxin type A (BTX-A) for aesthetic procedures in recent years has brought about some unwanted side effects that, though they are self-limited, cause inconvenience for patients. Injection of this paralytic toxin inactivates target muscle(s) for many months and unwanted facial movements will thus be prevented. Spreading of the toxin beyond the target muscles sometimes involves muscles necessary for other facial movements, such as the levator palpebrae, inactivation of which causes upper eyelid ptosis. Mild cases resolve after 2-3 wk, but in severe cases the complication may last as long as the cosmetic results persist (3-4 mo), and until now there has been no medical intervention to accelerate healing. In an effort to achieve more rapid recovery from eyelid ptosis due to overdose of BTX-A in the glabella, laser therapy was used by Majlesi [] in a 46-year-old woman with bilateral eyelid ptosis (partial on the right side and complete on the left) 12 d after injection. A GaAs laser was used and the protocol consisted of irradiation of three points on the upper lid just above the levator, and one point on the corrugator muscle on each side in contact mode, with three sessions per week (890 nm, peak power 94 W, average power 28 mW, pulse duration 200 ns, spot size 3 mm, pulse repetition rate 3000 Hz, duration of irradiation 40 sec per point, energy per point 1.1 J, total energy per session 8.8 J, dose 16 J/cm²). The result was complete recovery from ptosis after 10 sessions, but the cosmetic results persisted for several months.

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