

LaserWorld Science December 2007

Gottlieb T, Jörgensen B, Rohde E et al. The influence of irradiation with low-level diode laser on the proteoglycan content in arthrotically changed cartilage in rabbits. Medical Laser Application, 2006; 21 (1): 53-59.

The course of arthrosis was investigated on an animal-experimental arthrosis model considering macroscopic aspects, and the proteoglycan and the glycosaminoglycan contents. Based on these parameters, the influence of a low-power diode laser of 692.6 nm wavelength on the progress of arthrosis was investigated. Thirty days following joint instability surgery another operation was made during which the femoral condyles were irradiated using different energy densities. Seven days after the second operation, macroscopic findings were made and the proteoglycan content was established based on the quantitative determination according to Taylor and Jeffre. This method is based on various spectrophotometric absorption behaviours of different concentrations of sulphatized glycosaminoglycans in the presence of dimethylmethylene blue. Macroscopically, a progressively increasing severity of cartilage changes during the course of arthrosis 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.

Baumann M, Jörgensen B, Rohde E et al. Influence of wavelength, power density and exposure time of laser radiation on chondrocyte cultures – An in-vitro investigation. Medical Laser Application. 2006; 21 (3): 191-198.

The influence of laser radiation on human osteoarthrotically changed chondrocytes was investigated using various wavelengths, power density and dependence on the exposure time in order to confirm the positive results obtained in an animal experiment. It was manifested that, if there was a specific parameter constellation (2 W; 16 W/cm²; 60 s; 120 J), an enhanced matrix synthesis (cartilage material from 36 patients) could be achieved. The proof succeeded by applying the radioisotope marking method (3H-proline).

Interestingly enough it turned out that the application of too high a power density but constant energy density resulted in a reduced matrix synthesis rate (reduction of 28%). In this study, it was demonstrated for the first time that laser radiation may have a positive influence on human cartilage thus contributing to future in-vivo application.

Müller K P, Rodrigues C R, Núñez S C et al. Effects of low power red laser on induced-dental caries in rats. Archives of Oral Biology. 2007; 52 (7): 648-654.

Dental caries were induced in molars of 40 rats divided into five groups: control group (CG), the teeth were not submitted to any treatment; laser group (LG), teeth were irradiated with a red laser (LPRL), power of 30 mW and dose of 5 J/cm²; fluoride group (FG), teeth were treated with topical acidulated phosphate fluoride (APF) 1.23% applied for 4 min; laser + fluoride group (LFG), teeth were irradiated with LPRL followed by APF; fluoride + laser group (FLG), teeth were treated with APF followed by LPRL. The animals were killed after 48 days, and the first and second molars were extracted to analyze the caries lesion area, microhardness, and calcium and phosphorus ratio. There were no statistical differences among FG, LFG, SLMS – Swedish Laser-Medical Society

and FLG regarding to caries area and microhardness, although the caries area were smaller in LFG. Ca/P ratio did not show significant differences among all groups. Although LPRL before APF application appeared to diminish the caries progression, LPRL did not present any additional benefit compared with acidulated phosphate fluoride on the prevention of induced-dental caries in rats.

Fereira M C, Brito V N, Gameiroa J et al. Effects of HeNe laser irradiation on experimental paracoccidioidomycotic lesions. Journal of Photochemistry and Photobiology B: Biology. 2006; 84 (2): 141-149.

Paracoccidioidomycosis (PCM) is the most prevalent human mycosis in Latin America. The infection is thought to take place firstly in the lungs and then may disseminate to other organs and tissues. Treatment by currently available antifungals is lengthy, the drugs may have undesirable side effects, and some are costly. Occasional resistant strains of *Paracoccidioides brasiliensis*, the causative agent of PCM, have been reported. So, the search for more efficient treatments or adjuvant therapies has to be continued. In this work, we evaluated the effects of HeNe laser irradiation on cutaneous inflammatory lesions caused by the inoculation of $5 \times 10^6/0.1$ ml yeasts cells into the back footpad of Balb/c mice. HeNe irradiation (3 mW, 3 J/cm^2) was applied at days 7, 8 and 9 post-infection and histological and immunohistochemical analysis were done. Unirradiated animals were used as controls. The results showed that laser-treated mice presented reduction of footpad edema, faster cutaneous wound healing, confluent granuloma, diffuse- and more loosely distributed immunolabeling for TNF- α , enhanced labeling of IFN- γ and any *P. brasiliensis* form detected, whereas multiple viable fungi were seen in diffuse widespread granulomas obtained from non-treated mice foot-pad. Fungi that were harvested from laser-treated animals presented no capability of growth in vitro as compared to those obtained from non-treated mice. We conclude that HeNe laser irradiation was able to inhibit the progress of inflammatory local reaction produced by *P. brasiliensis* infection and influence local cytokines production. We suggest that this treatment modality can be a useful coadjuvant tool to be combined with antifungal agents in the treatment of PCM ulcerations. The mechanisms involved in laser therapy of PCM lesions need further investigation.

Chow R, Heller G Z, Barnsley L. The effect of 300 mW, 830 nm laser on chronic neck pain: A double-blind, randomized, placebo-controlled study. Pain. 2006; 124 (1-2): 201-210.

A randomized, double-blind, placebo-controlled study of low-level laser therapy 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 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.

Kamalia F, Bayat M, Torkamanc G et al. The therapeutic effect of low-level laser on repair of osteochondral defects in rabbit knee. Journal of Photochemistry and Photobiology B: Biology. 2007; 88 (1): 11-15.

Osteochondral defects with 5 mm diameter and 4 mm in depth induced by drilling in right femoral patellar grooves of 41 adolescent male rabbits. They were divided into experimental and control groups. Experimental group received pulsed 890 nm laser irradiation with energy density of 4.8 J/cm². The rabbits in the control group received placebo LLLT with shut-down equipment. The control defects were allowed to heal spontaneously. Each group was divided into three subgroups: A, B and C. Subgroups A, B and C were sacrificed on 4, 8, and 16 weeks after surgery. The knee joints were removed, and the defects were examined biomechanically by in situ-indentation method. The thickness, instantaneous and equilibrium indentation stiffness was measured during the test. Data were analysed using ANOVA and independent sample t-test. While no difference was observed in the repaired cartilage biomechanical properties among 4th, 8th, 16th weeks in study groups, the equilibrium indentation stiffness of the experimental group was significantly higher in the 8th week in comparison with control group.

Lilveria P, Syeck E L, Pinhoa R A. Evaluation of mitochondrial respiratory chain activity in wound healing by low-level laser therapy. Journal of Photochemistry and Photobiology B: Biology. 2007; 86 (3): 279-282.

In this work, researchers evaluated mitochondrial respiratory chain complexes II and IV and succinate dehydrogenase activities in wounds after irradiation with low-level laser. The animals were divided into two groups: group 1, the animals had no local nor systemic treatment and were considered as control wounds; group 2, the wounds were treated immediately after they were made and every day after with a GaAs laser for 10 days. The results showed that laser therapy improved wound healing. Besides, their results showed that laser therapy significantly increased the activities of complexes II and IV but did not affect succinate dehydrogenase activity. These findings are in accordance to other works, where cytochrome c oxidase (complex IV) seems to be activated by laser therapy. Besides, researchers showed, for the first time, that complex II activity was also activated.

Djavid GE, Mehrdad R, Ghasemi M, Hasan-Zadeh H et al. In chronic low back pain, low level laser therapy combined with exercise is more beneficial than exercise alone in the long term: a randomised trial. Aust J Physiother. 2007; 53 (3): 155-160.

This was a randomised trial with concealed allocation, blinded assessors and intention-to-treat analysis. Sixty-one patients who had low back pain for at least 12 weeks. INTERVENTION: One group received laser therapy alone, one received laser therapy and exercise, and the third group received placebo laser therapy and exercise. Laser therapy was performed twice a week for 6 weeks. Outcomes were pain severity measured using a 10-cm visual analogue scale, lumbar range of motion measured by the Schober Test and maximum active flexion, extension and lateral flexion, and disability measured with the Oswestry Disability Index on admission to the study,

after 6 weeks of intervention, and after another 6 weeks of no intervention. There was no greater effect of laser therapy compared with exercise for any outcome, at either 6 or 12 weeks. There was also no greater effect of laser therapy plus exercise compared with exercise for any outcome at 6 weeks. However, in the laser therapy plus exercise group pain had reduced by 1.8 cm lumbar range of movement increased by 0.9 cm on the Schober Test and by 15 deg of active flexion, and disability reduced by 9.4 points (more than in the exercise group at 12 weeks. In chronic low back pain low level laser therapy combined with exercise seems to be more beneficial than exercise alone in the long term.

Mazzetto MO, Carrasco TG, Bidinelo EF, de Andrade Pizzo RC, Mazzetto RG. Low intensity laser application in temporomandibular disorders: a phase I double-blind study. Cranio. 2007; 25 (3): 186-192.

The purpose of this study was to evaluate the effectiveness of low intensity laser therapy for the control of pain from temporomandibular disorder (TMD) in a random and double-blind research design. Forty-eight patients presenting temporomandibular joint (TMJ) pain were divided into an experimental group (GI) and a placebo group (GII). The sample was submitted to the treatment with infrared laser (780 nm, 70 mW, 10 s, 0.7 J, 89.7 J/cm²) applied in continuous mode on the affected temporomandibular region, at one point: inside the external auditive duct toward the retrodiskal region, twice a week, for four weeks. For the control group, two identical probes (one active and one that does not emit radiation) were used unknown by the clinician and the subjects. A tip planned for laser acupuncture was used and connected to the active point of the probe. The parameter evaluated was the intensity of pain after palpation of the condylar lateral pole, pre-auricular region and external auditive duct, according to the Visual Analogue Scale (VAS). Four evaluations were performed: Ev1 (before laser application), Ev2 (after 4th application), Ev3 (after 8th application) and Ev4 (30 days after the last application). The results showed a decrease in the pain level mainly for the active probe. Among the evaluations, the Ev3 exhibited lower sensitivity to palpation. In conclusion, the results show that low intensity laser is an effective therapy for the pain control of subjects with painful TMJ.

Simões A, Nicolau J, de Souza DN, Ferreira LS, de Paula Eduardo C, Apel C, Gutknecht N. Effect of defocused infrared diode laser on salivary flow rate and some salivary parameters of rats. Clin Oral Investig. 2007 Jul 12; [Epub ahead of print]

This study aims to investigate whether infrared laser therapy (LLLT) increased salivary flow rate and altered pH value, protein concentration, and peroxidase and amylase activities in saliva of rats. Wistar rats were used and divided into three groups. Experimental groups (A and B) had their parotid, submandibular and sublingual glands submitted to diode laser, 808 nm wavelength, on two consecutive days. The doses were 4 and 8 J/cm² respectively. A red guide light was used to visualize the irradiated area. Group C was irradiated only with the red pilot beam and served as control. The saliva samples were collected after each irradiation step (first and second collection days) and 1 week after the first irradiation (seventh day). Statistical analysis was performed, and differences were observed according to different days of salivary collection. The results showed that salivary flow rate for

groups A and B was higher on the seventh day if it is compared to data obtained for the first day.

Saygun I, Karacay S, Serdar M, Ural AU, Sencimen M, Kurtis B. Effects of laser irradiation on the release of basic fibroblast growth factor (bFGF), insulin like growth factor-1 (IGF-1), and receptor of IGF-1 (IGFBP3) from gingival fibroblasts. *Lasers Med Sci.* 2007 Jul 10; [Epub ahead of print]

The aim of the present study was to determine whether the laser irradiation can enhance the release of basic fibroblast growth factor (bFGF), insulin-like growth factor-1 (IGF-1), and receptor of IGF-1 (IGFBP3) from human gingival fibroblasts (HGF). The number of all samples in the study were 30, and the samples were randomly divided into three equal groups; In the first group (single dose group), HGF were irradiated with 685 nm, for 140 s, 2 J/cm² for one time, and in the second group, energy at the same dose was applied for two consecutive days (double dose group). The third group served as nonirradiated control group. Proliferation, viability, and bFGF, IGF-1, IGFBP3 analysis of control and irradiated cultures were compared with each other. Both of the irradiated groups revealed higher proliferation and viability in comparison to the control group. Comparison of the single-dose group with the control group revealed statistically significant increases in bFGF and IGF-1, but IGFBP3 increased insignificantly. When the double dose group was compared with the control group, significant increases were determined in all of the parameters. In the comparison of the differences between the two irradiated groups (one dose and two doses), none of the parameters displayed any statistically significant difference. In both of the laser groups, LLLT increased the cell proliferation and cell viability. The results of this study showed that LLLT increased the proliferation of HGF cells and release of bFGF, IGF-1, and IGFBP3 from these cells. LLLT may play an important role in periodontal wound healing and regeneration by enhancing the production of the growth factors.

Albertini R, Aimbire F, Villaverde AB, Silva JA Jr, Costa MS. Inflamm Res. COX-2 mRNA expression decreases in the subplantar muscle of rat paw subjected to carrageenan-induced inflammation after low level laser therapy. 2007; 56 (6): 228-229.

Herein we studied the effect of LLLT on the COX-2 mRNA expression in subplantar tissue taken from rats treated with carrageenan. The groups consisted of 32 rats: A(1) (Saline), A(2) (Carrageenan), A(3) (Carrageenan + laser 660 nm) and A(4) (Carrageenan + laser 684 nm). A(3) and A(4) were irradiated in the first hour after carrageenan. The edema was measured by a plethysmometer and COX-2 mRNA was by RT-PCR. Carrageenan increased both edema (A 1)= 0.6 +/- 0.04 vs. A(2)= 2.24 +/- 0.08) and COX-2 mRNA (A(1)= 1.1 +/- 0.26 vs. A(2)= 3.52 +/- 0.69). Irradiation reduced the edema (A(3)= 0.84 +/- 0.09; A(4)= 1.31 +/- 0.05) and the COX-2 mRNA (A(3)= 2.16 +/- 0.28; A(4)= 1.86 +/- 0.20).

Liu YH, Cheng CC, Ho CC, Pei RJ, Lee KY, Yeh KT, Chan Y, Lai YS. Effects of diode 808 nm GaAlAs low-power laser irradiation on inhibition of the proliferation of human hepatoma cells in vitro and their possible mechanism. *Res Commun Mol Pathol Pharmacol.* 2004; 115-116:185-201.

The cytoskeleton plays important roles in cell function and therefore is implicated in the pathogenesis of many human liver diseases, including malignant tumors. In our previous study, we found the stability of cytokeratin molecules in human hepatocytes was related to the intact microtubule network that was influenced by colchicine. In this study, we are going to search the effect of LPLI on proliferation of human hepatoma cell line HepG2 and J-5 cells. In addition, the stability of cytokeratin and synemin (one of the intermediate filament-associated proteins) were analyzed under the action of LPLI to evaluate the possible mechanism of LPLI effects on proliferation of human hepatoma cells. In experiment, HepG2 and J-5 cells were cultured in 24-well plate for 24 hours. After irradiation by 130 mW diode 808 nm GaAlAs continuous wave laser in different time intervals, the cell numbers were counted. Western blot and immunofluorescent staining examined the expression and distribution of PCNA, cytokeratin and synemin. The cell number counting and PCNA expression were evaluated to determine the proliferation. The organization and expression of cytokeratin and synemin were studied to identify the stability of cytoskeleton affected by LPLI. The results revealed that proliferation of HepG2 and J-5 cells was inhibited by LPLI since the cell number and PCNA expression was reduced. Maximal effect was achieved with 90 and 120 seconds of exposure time (of energy density 5.85 J/cm^2 and 7.8 J/cm^2 , respectively) for HepG2 and J-5, respectively. The decreased ratio of cell number by this dose of irradiation was 72% and 66% in HepG2 and J-5 cells, respectively. Besides that, the architecture of intermediate filaments in these cells was disorganized by laser irradiation. The expression of intermediate filament-associated protein, synemin, was also reduced. Two significant findings are raised in this study: (1) 808 nm GaAlAs continuous wave laser has an inhibitory effect on the proliferation of human hepatoma cells line HepG2 and J-5. (2) The mechanism of inhibition might be due to down-regulation of synemin expression and alteration of cytokeratin organization that was caused by laser irradiation.

Kim YD, Kim SS, Hwang DS, Kim SG et al. Effect of low-level laser treatment after installation of dental titanium implant-immunohistochemical study of RANKL, RANK, OPG: an experimental study in rats. *Lasers Surg Med.* 2007; 39 (5): 441-450.

This experiment using an animal experimental model was conducted in order to investigate the effect of LLLT on the healing of the dental titanium implant. The experimental group received LLLT for a week and the control group did not. Each group consisted of 10 rats. Two rats from the groups were euthenized on the days 1, 3, 7, 14, and 21 of the experiment. The expression of receptor activator of nuclear factor κ B ligand (RANKL), osteoprotegerin (OPG), and receptor activator of nuclear factor κ B (RANK) were investigated. RESULTS: The expression of RANKL was observed from the initial stage of the installation of the implant for both the experimental and control groups. However, the degree of expression was higher in the experimental group. The degree of expression of OPG increased remarkably in the experimental group, while in the control group the degree of expression increased only slightly. In the experimental group, the expression of RANK was observed from the first day, but in the control group, it was weakly observed after day 3. The overall expression within the bone was slight on day 7 in the control group, while an active expression was observed in the experimental group. Bone density after installation of dental titanium implant during osseointegration in the experimental group was higher than the control group. The surface and structure of the titanium implant was not damaged

by low-level laser (LLL). From the above results, the expression of OPG, RANKL, and RANK during the osseointegration of the dental titanium implant was observed within bone tissue. The application of the LLL influenced the expression of OPG, RANKL, and RANK, and resulted in the expansion of metabolic bone activity and increased the activity of bone tissue cells.

Jakse N, Payer M, Tangl S, Berghold A, Kirmeier R, Lorenzoni M. Influence of low-level laser treatment on bone regeneration and osseointegration of dental implants following sinus augmentation. An experimental study on sheep. Clin Oral Implants Res. 2007 Aug;18(4):517-24. Epub 2007 Apr 19.

The aim of this experimental study was to evaluate if LLLT enhances bone regeneration and osseointegration of dental implants in a sinus graft model. Twelve sheep underwent a bilateral sinus floor elevation procedure with cancellous bone from the iliac crest. Implant insertion followed 4 weeks (six sheep) and 12 weeks (six sheep) later. Sixteen weeks after second-stage surgery, animals were sacrificed. Unilaterally, the grafted sinus and during the second-stage surgery the implant sites were irradiated intraoperatively and three times during the first postoperative week with a diode laser (75 mW, 680 nm). The overall energy density per irradiation was 3-4 J/cm². Biopsies of the augmented area were obtained during implant insertion and after scarification. Bone regeneration within the grafted sinus histomorphometric analysis hardly differed between control and test side both 4 and 12 weeks after sinus grafting. Osseointegration measurements resulted in a significantly higher bone/implant contact (BIC) on the test side. Further evaluation of peri-implant bone tends to amount in significant higher percentage on the laser side. The presented experimental study on sheep did not confirm a positive LLLT effect on bone regeneration within a cancellous sinus graft. Nevertheless, LLLT possibly has a positive effect on osseointegration of dental implants inserted after sinus augmentation.

Schubert MM, Eduardo FP, Guthrie KA, Franquin JC, Bensadoun RJ, Migliorati CA, Lloid CM, Eduardo CP, Walter NF, Marques MM, Hamdi M. A phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation. Support Care Cancer. 2007;15(10):1145-1154. Epub 2007 Mar 29.

This phase III randomized double-blind placebo-controlled study was designed to compare the ability of 2 different low level GaAlAs diode lasers (650 nm and 780 nm) to prevent oral mucositis in HCT patients conditioned with chemotherapy or chemoradiotherapy. Seventy patients were enrolled and randomized into 1 of 3 treatment groups: 650 nm laser, 780 nm laser or placebo. All active laser treatment patients received daily direct laser treatment to the lower labial mucosa, right and left buccal mucosa, lateral and ventral surfaces of the tongue, and floor of mouth with energy densities of 2 J/cm². Study treatment began on the first day of conditioning and continued through day +2 post HCT. Mucositis and oral pain was measured on days 0, 4, 7, 11, 14, 18, and 21 post HCT. The 650 nm wavelength reduced the severity of oral mucositis and pain scores. Low level laser therapy was well-tolerated and no adverse events were noted.

Zyciński P, Krzemińska-Pakuła M, Peszyński-Drews C, Kierus A, Trzos E, Rechciński T, Figiel L, Kurpesa M, Plewka M, Chrzanowski L, Drozd J. Laser biostimulation in end-stage multivessel coronary artery disease--a preliminary observational study. [Article in English, Polish]. *Kardiol Pol.* 2007; 65 (1): 13-21; discussion 22-23.

The introductory assessment of the effects of laser biostimulation applied to patients with advanced multivessel CAD. 39 patients with advanced CAD were assigned (mean age 64.8+/-9.6, male gender 64%, CCS class 2.5+/-0.5, EF=46+/-11%, 69% with a history of acute myocardial infarction), to undergo two sessions of irradiation of low-energy laser light on skin in the chest area from helium-neon B1 lasers. The time of irradiation was 15 minutes while operations were performed 6 days a week for one month. Before including the patients in the experimental group a full clinical evaluation, basic biochemical tests, ECG, 24h Holter recordings, 6-minute walk test, treadmill test using Bruce protocol and full echocardiographic examination were performed. After the first and second period of laser therapy with a one-month break between them analogical parameters with the initial examination were measured. No side effects associated with the laser biostimulation or performed clinical tests were noted. Lower CCS class higher exercise capacity longer exercise time, less frequent angina symptoms during the treadmill test longer distance of 6-minute walk test lower systolic blood pressure and trend towards less frequent 1 mm ST depression lasting 1 min during Holter recordings were noted. An improvement of functional capacity and less frequent angina symptoms during exercise tests without a significant change in the left ventricular function were observed. Laser biostimulation in short-term observation was a very safe method.

Martinasso G, Mozzati M, Pol R, Canuto RA, Muzio G. Effect of superpulsed laser irradiation on bone formation in a human osteoblast-like cell line [Article in English, Italian]. *Minerva Stomatol.* 2007; 56 (1-2): 27-30.

The effect OF superpulsed GaAs laser therapy on bone regeneration has been the focus of recent research. This preliminary study investigated the effect of GaAs laser irradiation on proliferation and bone formation in human osteoblast-like cells MG-63. Human osteoblast-like cells MG-63 were exposed every 24 h to superpulsed low-level laser. The experimental protocol comprised 4 days of treatment. At each experimental time, cell proliferation and some markers of osteoblast activity were evaluated. Numbers of laser-treated cells increased starting from day 2 of treatment. The ability of GaAs irradiation to stimulate bone production was evaluated by determining the expression of osteocalcin and alkaline phosphatase, proteins involved in calcium nodule formation. These proteins increased markedly after 3 days of laser treatment. These preliminary results show that repeated GaAs irradiation stimulates cell proliferation in human osteoblast-like cells and, importantly, increases the expression of proteins essential for bone formation.

Miloro M, Miller JJ, Stoner J A. Low-level laser effect on mandibular distraction osteogenesis. *J Oral Maxillofac Surg.* 2007; 65 (2):168-176.

Nine adult female New Zealand white rabbits underwent bilateral mandibular corticotomies and placement of unidirectional distraction devices. Each rabbit served as its own internal control. After a latency of 1 day, distraction progressed bilaterally at 1 mm per day for 10 days. Immediately after each device activation, the

experimental side, chosen randomly, was treated with real LLL of 6.0 J x 6 transmucosal sites in the area of the distraction gap. Radiographs were taken presurgically, immediately postsurgically, and weekly until sacrifice, and the bone was analyzed using a semiquantitative 4-point scale (Bone Healing Score [BHS]). Three animals each were sacrificed at 2, 4, and 6 weeks postdistraction, and each hemimandible was prepared for histologic examination in a blinded fashion. Ten millimeters of distraction was achieved in each rabbit bilaterally. Radiographically, the BHS was higher for the LLL-treated group at all time periods. Histologically, the area of new bone trabeculation and ossification was more advanced for the LLL-treated group, with less intervening fibrovascular intermediate zone in the bony regenerate, at all time periods. The formation of a complete inferior border occurred sooner in the treatment group than in the controls. LLL accelerated the process of bone regeneration during the consolidation phase after distraction osteogenesis. The adjunctive use of LLL may allow a shortened period of consolidation and therefore permit earlier device removal, with the avoidance of morbidity associated with prolonged device.

Matsui S, Tsujimoto Y, Matsushima K. Stimulatory effects of hydroxyl radical generation by Ga-Al-As laser irradiation on mineralization ability of human dental pulp cells. Biol Pharm Bull. 2007; 30(1): 27-31.

The present study was conducted to investigate the effects of Ga-Al-As laser irradiation on the mineralization ability of human dental pulp (HDP) cells. HDP cells in vitro were irradiated once with a GaAlAs laser at 0.5 W for 500 s and at 1.0 W for 500 s in order to investigate free radicals as one mechanism for transmission of laser photochemical energy to cells. Production of the hydroxyl radical (*OH) was measured using the ESR spin-trapping method and was found to be increased by laser irradiation. The DMPO-OH was not detected in the presence of dimethyl sulfoxide (DMSO), a *OH scavenger. The formation of calcification nodule was also investigated by von Kossa staining. The number of calcified nodules was increased by 1.0 W-laser irradiation. Alkaline phosphatase (ALP) activity was higher in the 1.0 W-laser irradiation group. Expression of mRNAs for heat shock protein 27, bone morphogenetic proteins (BMPs) and ALP were greater in the 1.0 W-laser irradiation group. Expression of BMPs in the conditioned medium was also higher in the 1.0 W-laser irradiation group. In particular, DMSO decreased the number of calcified nodule produced by 1.0 W-laser irradiation. These results supposed that the mineralization of HDP cells is stimulated by laser irradiation, and that *OH generated by laser irradiation is a trigger for promotion of HDP cell mineralization.

Bulyakova NV, Azarova VS. Regeneration of skeletal muscles and state of thymus in gamma-irradiated rats under laser therapy of the area of muscle trauma. Minim Invasive Ther Allied Technol. 2006; 15 (5):277-285.

The gamma-irradiation of adult rats with a semi-lethal dose (6 Gy) suppressed the posttraumatic regeneration of skeletal muscles and brought about considerable destructive changes in the thymus. The effect of HeNe laser radiation at a total dose 4.5-5.4 J/cm² at each operated leg in irradiated rats stimulated the regenerative capacity of skeletal muscle tissue, the healing of skin-muscle wound, and the processes of postradiation recovery in thymus cells (a decrease of chromosome aberrations). The histological structure of regenerates had more muscle pattern. At the

same time, the positive dynamics of regenerative processes in muscles was achieved by an increased functional load on the thymus. To stimulate the regeneration of irradiated muscles on the background of a more moderate load on the thymus, the prolonged period of laser therapy and fragmentary distribution of laser exposures during muscle regeneration were preferable. Wound healing improved visibly. No formation of chronic radiation ulcers on operated shins was observed.

de Araújo CE, Ribeiro MS, Favaro R, Zezell DM, Zorn TM. Ultrastructural and autoradiographical analysis show a faster skin repair in HeNe laser-treated wounds. J Photochem Photobiol B. 2007; 86 (2): 87-96. Epub 2006 Oct 9.

To better understand the photobiological effects of laser radiation, this study investigated by electron microscopy, immunohistochemistry and autoradiography the morphological and functional features of irradiated and non-irradiated injured mice skin. Full-thickness skin lesions were created on the back of mice and irradiated on days 1, 5, 8, 12, and 15 post-wounding with a HeNe laser, dose $1\text{J}/\text{cm}^2$, exposure time 3min. Non-irradiated lesions were used as a control. The mice were inoculated with $(3)\text{H}$ -proline and sacrificed one hour after on the 8th, 15th and 22nd days to histological and radioautographical analysis. The irradiated-lesions showed a faster reepithelization compared with control lesions. The irradiated dermis contained a higher number of activated fibroblasts compared to control group and, most of them showed several cytoplasmic collagen-containing phagosomes. In irradiated-lesions, smooth muscle alpha-actin positive cells predominated, which correspond to a higher number of myofibroblasts observed in the electron microscope. Moreover, laser radiation reduced the local inflammation and appears to influence the organization of collagen fibrils in the repairing areas. Quantitative autoradiography showed that the incorporation of $(3)\text{H}$ -proline was significantly higher in irradiated-dermis on the 15th day post-wounding. These results suggest that laser radiation may accelerate cutaneous wound healing in a murine model.

Prado RP, Liebano RE, Hochman B, Pinfield CE, Ferreira LM. Experimental model for low level laser therapy on ischemic random skin flap in rats. Acta Cir Bras. 2006; 21 (4): 258-262.

The sample was 24 Wistar-EPM rats. The random skin flap measured 10×4 cm and a plastic sheet was interposed between the flap and donor site. Group 1 (control) underwent sham irradiation with diode laser (830 nm). Group 2 was submitted to laser irradiation with diode laser (830 nm). The animals were submitted to Laser therapy with $36\text{J}/\text{cm}^2$ energy density (72 seconds) immediately after the surgery and on the four subsequent days. The probe was usually held in contact with the skin flap surface on a point at 2.5 cm cranial from the flap base. On the seventh postoperative day, the percentage of necrotic area was measured and calculated. Group 1 reached an average necrotic area of 48.86%, Group 2 - 23.14%. After the statistic analysis, compared with the control group, Group 2 showed a statistically significant increase in survival area. The experimental model proved to be reliable to be used in the study of effects of low level laser therapy in random skin flap in rats.

da Silva R V, Camilli J A. Repair of bone defects treated with autogenous bone graft and low-power laser. J Craniofac Surg. 2006; 17 (2):297-301.

Because bone healing at the graft site is similar to a fracture repair, the purpose of the present study was to evaluate the effects of low-power laser irradiation on the repair of rat skull defects treated with autogenous bone graft. A defect measuring 3 mm in diameter was produced in the left parietal bone and filled with an autogenous bone graft obtained from the right parietal bone. The animals were divided into 3 groups of 20 rats each: nonirradiated control, irradiated with 5.1 J/cm^2 , and irradiated with 10.2 J/cm^2 . The laser (2.4 mW, 735 nm, $3.4 \times 10 \text{ W/cm}^2$, 3-mm spot size) was applied three times per week for 4 weeks. Greater volume of newly formed bone was observed in the irradiated group with 10.2 J/cm^2 . In both irradiated groups, a greater volume of newly formed bone occurred only in the first 2 weeks. The results demonstrated that laser irradiation at the grafted site stimulated osteogenesis during the initial stages of the healing process in a skull defect of the rat and that this effect was dose dependent.

Fujihara NA, Hiraki KR, Marques MM. Irradiation at 780 nm increases proliferation rate of osteoblasts independently of dexamethasone presence. Lasers Surg Med. 2006; 38 (4): 332-336.

Our objective was to study the effect of phototherapy on osteoblast-like cells in culture treated with dexamethasone. Rat calvaria osteoblast-like cells were previously treated or not with dexamethasone and then, they were irradiated or not with a GaAlAs diode laser (wavelength of 780 nm, 10 mW, 3 J/cm^2). Adhesion, proliferation, and osteonectin synthesis were analyzed. Phototherapy increased the proliferation rate of cells independently of dexamethasone presence. Adhesion and osteonectin synthesis were not significantly influenced by laser and/or dexamethasone. Based on the conditions of this study we concluded that phototherapy acts as a proliferative stimulus on osteoblast-like cells, even under the influence of dexamethasone. Thus, we suggest that phototherapy can be of importance as co-adjuvant in bone clinical manipulation in order to accelerate bone regeneration.

Novoselova E G, Glushkova O V, Cherenkov D A, Chudnovsky V M, Fesenko E E. Effects of low-power laser radiation on mice immunity. Photodermatol Photoimmunol Photomed. 2006; 22 (1): 33-38.

To study of the possible side effects of laser immunotherapy we monitored the productions of cytokines, nitric oxide (NO), and heat shock protein 70 (Hsp70) in mice subjected to a periodic laser exposure for 1 month. Helium-neon laser radiation with the power of 0.2 mW/cm^2 and wavelength of 632.8 nm was applied on two different mouse skin surfaces, i.e. a thymus projection area or a hind limb. Healthy NMRI male mice were irradiated repeatedly with laser light for 1 min with 48-h intervals for 30 days. The animals were divided into three groups of 25 mice. The first and the second groups were exposed to laser light, on the thymus and hind limb area, respectively. The third, sham-irradiated group served as a control. Early and prolonged effects of laser radiation on the levels of NO Hsp70 tumor necrosis factors (TNF-alpha and TNF-beta) and interleukin-2 (IL-2) were determined. The dynamics of immune responses to low-power laser light intensity was shown to be dependent on two factors, i.e. the cumulative dose and the localization of the irradiated surface. Besides, various populations of cells demonstrated different sensitivity to laser radiation, with T cells being more responsive among examined populations of the cells. Laser light induced an immune cell activity when the exposure duration did not

exceed 10 days, while a more prolonged period of treatment generated more severe changes in the immune system, up to immunosuppression. The treatment of the thymus zone resulted in more pronounced changes in the cytokine production as well as in NO and Hsp70 synthesis. Low-level laser irradiation showed more effective immunomodulatory effects when applied on the thymus projection area. The rise in IL-2 and Hsp70 production related to a short-term effect of laser application may be reversed after repeating laser treatment. We suggest that for the support of immune system stability, the prolonged laser therapy should be accompanied by supplementary methods.

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