Bone Healing – Formation - Resorption

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Effects of low-level laser therapy on bone formed after distraction osteogenesis.

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This study evaluated the effect of low-level laser therapy (LLLT) on the chemical composition, crystallinity and crystalline structure of bone at the site of distraction osteogenesis. Five rabbits were subjected to distraction osteogenesis (latency = 3 days; rate and frequency = 0.7 mm/day for 7 days; consolidation = 10 days), and three were given LLLT with arsenide-gallium-aluminum (AsGaAl; 830 nm, 40 mW): 10 J/cm(2) dose per spot, applied directly to the distraction osteogenesis site during the consolidation stage at 48 h intervals. Samples were harvested at the end of the consolidation stage. X-ray fluorescence and X-ray diffraction were used to analyze chemical composition, crystallinity and crystalline structure of bone at the distraction osteogenesis site. The analysis of chemical composition and calcium (Ca) and phosphorus (P) ratios revealed greater mineralization in the LLLT group. Diffractograms showed that the crystalline structure of the samples was similar to that of hydroxyapatites. Crystallinity percentages were greater in rabbits that were given LLLT. Crystallinity (41.14% to 54.57%) and the chemical composition of the bone at the distraction osteogenesis site were similar to the that of the control group (42.37% to 49.29%). The results showed that LLLT had a positive effect on the biomodulation of newly formed bone.

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Superpulsed laser irradiation increases osteoblast activity via modulation of bone morphogenetic factors.

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BACKGROUND AND OBJECTIVE: Laser therapy is a new approach applicable in different medical fields when bone loss occurs, including orthopedics and dentistry. It has also been used to induce soft-tissue healing, for pain relief, bone, and nerve regeneration. With regard to bone synthesis, laser exposure has been shown to increase osteoblast activity and decrease osteoclast number, by inducing alkaline phosphatase (ALP), osteopontin, and bone sialoprotein expression. Studies have investigated the effects of continuous or pulsed laser irradiation, but no data are yet available on the properties of superpulsed laser irradiation. This study thus aimed to investigate the effect of superpulsed laser irradiation on osteogenic activity of human osteoblast-like cells, paying particular attention to investigating the molecular mechanisms underlying the effects of this type of laser radiation. STUDY DESIGN/MATERIALS AND METHODS: Human osteoblast-like MG-63 cells were exposed to 3, 7, or 10 superpulsed laser irradiation (pulse width 200 nanoseconds, minimum peak power 45 W, frequency 30 kHz, total energy 60 J, exposure time 5 minutes). The following parameters were evaluated: cell growth and viability (light microscopy, lactate dehydrogenase release), calcium deposits (Alizarin Red S staining), expression of bone morphogenetic factors (real-time PCR). RESULTS: Superpulsed laser irradiation decreases cell growth, induces expression of TGF-beta2, BMP-4, and BMP-7, type I collagen, ALP, and osteocalcin, and increases the size and the number of calcium deposits. The stimulatory effect is maximum on day 10, that is, after seven applications. CONCLUSIONS: Reported results show that superpulsed laser irradiation, like the continuous and pulsed counterparts, possesses osteogenic properties, inducing the expression of molecules known to be important mediators of bone formation and, as a consequence, increasing calcium deposits in human MG-63 cells. Moreover, the data suggest a new potential role for PPARgamma as a regulator of osteoblast proliferation.

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Nd:YAG laser biostimulation in the treatment of bisphosphonate-associated osteonecrosis of the jaw: clinical experience in 28 cases.

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OBJECTIVE: To research an efficient treatment for the management of bisphosphonate-associated osteonecrosis. BACKGROUND DATA: Necrosis of the jawbone has recently been described in association with systemic bisphosphonate therapy with drugs including zoledronic acid, pamidronate, and alendronate. The extent and clinical characteristics of bisphosphonate-associated osteonecrosis (BON) of the jaw are extremely variable, and range from the presence of fistulae in the oral mucosa or orofacial tissues, to large exposed areas of necrotic bone within the oral cavity. Clinical signs and symptoms commonly reported include pain, swelling, the presence of pus, loose teeth, ill-fitting dentures, and paresthesias of the inferior alveolar nerve when the necrosis affects the mandible. Fractures have also been reported. The treatment of BON of the jaw is still controversial since no therapy has proven to be efficacious as shown by the literature on the subject. MATERIALS AND METHODS: In this study we report results achieved with 28 patients affected by BON of the jaw, who received treatment with the Nd:YAG laser alone or in combination with conventional medical or surgical treatment. Clinical variables such as severity of symptoms, presence of pus, and closure of mucosal flaps before and after therapy were evaluated to establish the effectiveness of laser irradiation. The 28 patients with BON were subdivided into four groups: eight patients were treated with medical therapy only (antibiotics with or without antimycotics and/or antiseptic rinses), six patients were treated with medical and surgical therapy (necrotic bone removal and bone curettage), six patients were treated with medical therapy associated with laser biostimulation, and eight patients were treated with medical therapy associated with both surgical therapy and laser biostimulation. RESULTS: Of the 14 patients who underwent laser biostimulation, nine reported complete clinical success (no pain, symptoms of infection, or exposed bone or draining fistulas), and three improved their symptomatology only, with a follow-up of between 4 and 7 mo. CONCLUSIONS: While the results reported in this study are not conclusive, they indicate that laser therapy has potential to improve management of BON.

Acta Biomed. 2006 Aug;77(2):109-17.

Bone necrosis of the jaws associated with bisphosphonate treatment: a report of twenty-nine cases.

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Bone necrosis of the jaws is often related to head and neck radiotherapy, to surgical procedures at maxillary or mandibular level but also to various local and systemic factors such as haematological diseases, haemoglobinopathies and systemic lupus eritematosus; its pathogenesis maybe associated with defects of vascularization. Bisphosphonate are synthetic analogues of pyrophosphate used for the treatment of hypercalcemia in patients with malignancies and bone metastasis and for the treatment of many other disorders such as metabolic bone diseases, Paget's disease, and osteoporosis; their pharmacological activity is related to the inhibition of the osteoclastic function which leads to resorption and reduction of bone vascularization. Since the end of 2003 Bisphosphonate-associated Osteonecrosis (BON) has become an increasing problem and the test of that is the increase of the relative published case report and case series. Here we report 29 cases of bone necrosis of the jaws in patients treated with pamidronate (Aredia), zoledronate

(Zometa) and alendronate: 15 underwent surgical procedures and 14 occurred spontaneously. Among these patients (21 females, 8 males; mean age between 45 and 83 years); 14 were treated for bone metastasis, 12 for multiple myeloma and 3 for osteoporosis. Bone necrosis involved only maxilla in 7 patients, only mandible in 20 patients and both in 2 patients. Six patients had multiple osteonecrotic lesions, 3 contemporary lesions and 3 non contemporary. In these patients we performed 3 kinds of therapy, associated or not: medical therapy (with antibiotic drugs, antimycotics and antiseptic mouthwashes), surgical therapy with curettage or sequestrectomy and Nd:YAG laser biostimulation.

Lasers Med Sci. 2008 Jul;23(3):313-7. Epub 2007 Sep 20.

Effect of IR laser photobiomodulation on the repair of bone defects grafted with organic bovine bone.

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A major problem on modern dentistry is the recovery of bone defects of different etiologies. Biomaterials are used to improve the repair of these defects. Previous studies have shown positive effects of Laser Photobiomodulation (LPBM) on the repair of both soft and bone tissues. This study assessed histologically the effect of LPBM 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 + LPBM). The animals on the irradiated groups received 16 J/cm(2) 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. It is concluded that LPBM has positive biomodulative effect on the healing process bone defects.

Photomed Laser Surg. 2005 Aug;23(4):382-8

Assessment of bone repair associated with the use of organic bovine bone and membrane irradiated at 830 nm.

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OBJECTIVE: The aim of the present investigation was to assess histologically the effect of LLLT (GaAIAs, 830 nm, 40 mW, CW, (Phi) approximately 0.6 mm, 16 J/cm(2) per session) on the repair of surgical defects created in the femur of the Wistar Albinus rat. The defects were filled to lyophilized bovine bone (Gen-ox), organic matrix) associated or not to GTR (Gen-derm). BACKGROUND DATA: A major problem on modern Dentistry is the recovery of bone defects caused by trauma, surgical procedures or pathologies. Several types of biomaterials have been used in order to improve the repair of these defects. These materials are often associated to procedures of GTR. Previous studies have shown positive effects of LLLT on the repair of soft tissue wounds, but there are a few on its effects on bone healing. METHODS: Surgical bone defects were created in 42 animals divided into five groups: Group I (control, 6 animals); Group II (Gen-ox, 9 animals); Group III (Gen-ox + Laser, 9 animals); Group IV (Gen-ox + Gen-derm, 9 animals); Group V (Gen-ox + Gen-derm + Laser, 9 animals). The animals on the irradiated group received 16 J/cm(2) per session divided into four points around the defect (4 J/cm(2)) being the first irradiation immediately after surgery and repeated seven times at every 48 h. The animals were humanly killed after 15, 21, and 30 days. RESULTS: The results of the present investigation showed histological evidence of improved amount of collagen fibers at early stages of the bone healing (15 days) and increased amount of well organized bone trabeculae at the end of the experimental period (30 days) on irradiated animals compared to non irradiated ones. CONCLUSIONS: It is concluded that a positive biomodulative effect on the healing process of one defect associated or not to the use of organic lyophilized bone and biological bovine lyophilized membrane on the femur of the rat.

Photomed Laser Surg. 2008 Aug;26(4):401-4

Evaluation of low-level laser therapy of osteoblastic cells.

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Abstract Objective: The purpose of the present study was to evaluate the effect of biomodulation on osteoblastic cells using a gallium-aluminium-arsenide diode laser. Background Data: Low-level laser therapy (LLLT) is a non-pharmacological therapeutic resource to which biological tissues respond well, producing such effects as the acceleration of bone formation and bone repair. Materials and Methods: Osteoblastic cell cultures (OFCOL II) were irradiated with a gallium-aluminium-arsenide diode laser (GaAlAs lambda = 830 nm; 50 mW; 3 J/cm(2); 600-mum-diameter optical fiber) and divided into two groups: group 1-irradiated cells, and group 2-non-irradiated cells. Irradiation occurred at 24-h intervals for a total of 3 d. After each interval, the cells were marked with Mito Tracker Orange dye to assess the biostimulatory effect on mitochondrial activity and cell proliferation using an MTT assay. Results: Intense

grouping of mitochondria in the perinuclear region was observed at 24 h and 48 h following irradiation. Changes from a filamentous to a granular appearance in mitochondrial morphology and mitochondria distributed throughout the cytoplasm were observed 72 h following proliferation. Such changes led to an in vitro proliferation process, as confirmed by the MTT assay. Conclusion: LLLT has shown itself capable of altering mitochondrial activity and the population of OFCOL II cells.

Wien Klin Wochenschr. 2008 Feb;120(3-4):112-117

Initial effects of low-level laser therapy on growth and differentiation of human osteoblast-like cells.

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Low-level laser therapy is a clinically well established tool for enhancement of wound healing. In vitro studies have also shown that low level laser therapy has a biostimulatory effect on cells of different origin. The aim of this in vitro study was to investigate the initial effect of low-level laser therapy on growth and differentiation of human osteoblast-like cells. SaOS-2 cells were irradiated with laser doses of 1 J/cm(2) and 2 J/cm(2) using a diode laser with 670 nm wave length 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/cm(2) compared with untreated control cells. Increasing the laser dose to 2 J/cm(2) 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/cm(2), but their expression was increased by treatment with 2 J/cm(2) after 72 h. These results indicate that low-level laser therapy has a biostimulatory effect on human osteoblast-like cells during the first 72 h after irradiation. Further studies are needed to determine the potential of low-level laser therapy as new treatment concept in bone regeneration.

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Low-level laser therapy modulates cyclo-oxygenase-2 expression during bone repair in rats.

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The goal of this study was to analyze the role of cyclo-oxygenase-2 following bone repair in rats submitted to low-level laser therapy. A total of 48 rats underwent surgery to inflict bone defects in their tibias having been randomly distributed into two groups: negative control and laser exposed group, i.e., the animals were treated with low-level laser therapy by means of gallium arsenide laser at 16 J/cm(2). The animals were killed after 48 h, 7 days, 14 days, or 21 days. The tibias were removed for morphological, morphometric, and immunohistochemistry analysis for cyclo-oxygenase-2. Statistical significant differences ($P < 0.05$) were observed in the quality of bone repair and quantity of formed bone between groups 14 days after surgery in the laser exposed group. In the same way, cyclo-oxygenase-2 immunoreactivity was more intense in bone cells for intermediate periods evaluated in this group. Taken together, such results suggest that low-level laser therapy is able to improve bone repair in the tibia of rats after 14 days of surgery as a result of an up-regulation for cyclo-oxygenase-2 expression in bone cells.

Photomed Laser Surg. 2007 Dec;25(6):487-94

Effect of lower-level laser therapy on rabbit tibial fracture.

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Objective: The purpose of the study was to demonstrate the biological effects of low-level laser therapy (LLLT) on tibial fractures using radiographic, histological, and bone density examinations. Methods: Fourteen New Zealand white rabbits with surgically induced mid-tibial osteotomies were included in the study. Seven were assigned to a group receiving LLLT (LLLT-A) and the remaining seven served as a sham-treated control group (LLLT-C). A low-energy laser apparatus with a wavelength of 830 nm, and a sham laser (a similar design without laser diodes) were used for the study. Continuous outflow irradiation with a total energy density of 40 J/cm(2) and a power level of 200 mW/cm(2) was directly delivered to the skin for 50 seconds at four points along the tibial fracture site. Treatment commenced immediately postsurgery and continued once daily for 4 weeks. Results: Radiographic findings revealed no statistically significant fracture callus thickness difference between the LLLT-A and LLLT-C groups ($p > 0.05$). However, the fractures in the LLLT-A group showed less callus thickness than those in LLLT-C group 3 weeks after treatment. The average tibial volume was 14.5 mL in the LLLT-A group, and 11.25 mL in the LLLT-C group. The average contralateral normal tibial volume was 7.1 mL. Microscopic changes at 4 weeks revealed an average grade of 5.5 and 5.0 for the LLLT-A group and the LLLT-C group, respectively. The bone mineral density (BMD) as ascertained using a grey scale (graded from 0 to 256) showed darker coloration in the LLLT-A group (138) than in the LLLT-C group (125). Conclusion: The study suggests that LLLT may accelerate the process of fracture repair or cause increases in callus volume and BMD, especially in the early stages of absorbing the hematoma and bone remodeling. Further study is necessary to quantify these findings.

Photomed Laser Surg. 2007 Aug;25(4):275-80.

The effects of laser irradiation on osteoblast and osteosarcoma cell proliferation and differentiation in vitro.

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OBJECTIVE: The aim of this study was to investigate the effects of 670-nm, 780-nm, and 830-nm laser irradiation on cell proliferation of normal primary osteoblast (MC3T3) and malignant osteosarcoma (MG63) cell lines in vitro. BACKGROUND: Some studies have shown that laser phototherapy is able to stimulate the osteogenesis of bone tissue, increasing osteoblast proliferation and accelerating fracture consolidation. It has been suggested that laser light may have a biostimulatory effect on tumor cells. However, the mechanism by which the laser acts on cells is not fully understood. MATERIALS AND METHODS: Neonatal, murine, calvarial, osteoblastic, and human osteosarcoma cell lines were studied. A single laser irradiation was performed at three different wavelengths, at the energies of 0.5, 1, 5, and 10 J/cm(2). Twenty-four hours after laser irradiation, cell proliferation and alkaline phosphatase assays were assessed. RESULTS: Osteoblast proliferation increased significantly after 830-nm laser irradiation (at 10 J/cm(2)) but decreased after 780-nm laser irradiation (at 1, 5, and 10 J/cm(2)). Osteosarcoma cell proliferation increased significantly after 670-nm (at 5 J/cm(2)) and 780-nm laser irradiation (at 1, 5, and 10 J/cm(2)), but not after 830-nm laser irradiation. Alkaline phosphatase (ALP) activity in the osteoblast line was increased after 830-nm laser irradiation at 10 J/cm(2), whereas ALP activity in the osteosarcoma line was not altered, regardless of laser wavelength or intensity. CONCLUSION: Based on the conditions of this study, we conclude that each cell line responds differently to specific wavelength and dose combinations. Further investigations are required to investigate the physiological mechanisms responsible for the contrasting outcomes obtained when using laser irradiation on cultured normal and malignant bone cells.

Photomed Laser Surg. 2006 Dec;24(6):735-40.

Comparative study of how low-level laser therapy and low-intensity pulsed ultrasound affect bone repair in rats.

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Objective: This study aimed to compare the consequences of low-level laser therapy (LLLT) and low-intensity pulsed ultrasound (LIPUS) on bone repair. Background Data: Many studies have assessed the effects of LLLT and LIPUS on bone repair, but a comparison of them is rare. Methods: Male Wistar rats (n = 48) with tibial bone osteotomy were used. One group had the osteotomized limb treated with LLLT (GaAlAs laser, 780 nm, 30 mW, 112.5 J/cm(2)) and the second group with LIPUS (1.5 MHz, 30 mW/cm(2)), both for 12 sessions (five times per week); a third group was the control. After 20 days, rats were sacrificed and had their tibias submitted to a bending test or histomorphometric analysis. Results: In the bending test, maximum load at failure of LLLT group was significantly higher ($p < 0.05$). Bone histomorphometry revealed a significant increase in osteoblast number and surface, and osteoid volume in the LLLT group, and a significant increase in eroded and osteoclast surfaces in the LIPUS group. Conclusion: LIPUS enhanced bone repair by promoting bone resorption in the osteotomy area, while LLLT accelerated this process through bone formation.

Photomed Laser Surg. 2006 Oct;24(5):642-5

Effects of 830-nm Laser Light on Preventing Bone Loss after Ovariectomy.

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Objective: The aim of this study was to investigate the effects of low-level laser therapy (LLLT; infrared, 830 nm) on the bone properties and bone strength of rat femora after ovariectomy (OVX). Background Data: Osteoporosis affects 30% of postmenopausal women, and it has been recognized as a major public health problem. Based on the stimulatory effects of LLLT on proliferation of bone cells, we hypothesized that LLLT would be efficient in preventing bone mass loss in OVX rats. Methods: Forty female rats were divided into four groups: sham-operated control (SC), OVX control (OC), sham-operated irradiated at a dose of 120 J/cm(2) (I120), and OVX irradiated at a dose of 120 J/cm(2) (O120). Animals were operated at the age of 90 days. Laser irradiation was initiated 1 day after the operation and was performed three times a week, for 2 months. Femora were submitted to a biomechanical test and a physical properties evaluation. Results: Maximal load of O120 was higher than in control groups. Wet weight, dry weight, and bone volume of O120 did not show any difference when compared with SC. Conclusion: The results of the present study indicate that LLLT was able to prevent bone

loss after OVX in rats. However, further studies are needed to investigate the effects of different parameters, wavelengths, and sessions of applications on OVX rats.

Photomed Laser Surg. 2006 Feb;24(1):38-44.

Laser therapy improves healing of bone defects submitted to autologous bone graft.

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OBJECTIVE: The aim of the present study was to assess histologically the effect of low-level laser thrapy (LLLT) (lambda 830 nm) on the healing of bone defects associated with autologous bone graft. BACKGROUND DATA: LLLT has been used on the modulation of bone healing because of the photo-physical and photochemical properties of some wavelengths. The use of correct and appropriate parameters has been shown to be effective in the promotion of a positive biomodulative effect on the healing bone. METHODS: Sixty male Wistar rats were divided into four groups: G1 (control), G2 (LLLT on the surgical bed), G3 (LLLT on the graft), and G4 (LLLT on both the graft and the surgical bed). The dose per session was 10 J/cm(2), and it was applied to the surgical bed (G2/G4) and on the bone graft (G3/G4). LLLT was carried out every other day for 15 days (lambda 830 nm, phi = 0.5 cm(2), 50 Mw, 10 J/cm(2)). The dose was fractioned in four points. The animals were sacrificed 15, 21, and 30 days after surgery; specimens were taken and routinely processed (wax, cut, and stain with H&E and Sirius red stains). Light microscopic analysis was performed by a pathologist. RESULTS: In the groups in which the LLLT was used trans-operatively on the surgical bed (G2/G4), bone remodeling was both quantitatively and qualitatively more evident when compared to subjects of groups G1 and G3. CONCLUSION: The present study indicates that the use of LLLT trans-operatively resulted in a positive biomodulative effect on the healing of bone defects associated with autologous bone grafts.

J Craniofac Surg. 2006 Mar;17(2):297-301

Repair of bone defects treated with autogenous bone graft and low-power laser.

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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, and irradiated with 10.2 J/cm. The laser (2.4 mW, 735 nm, 3.4 x 10 W/cm, 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. 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.

Photomed Laser Surg. 2006 Apr;24(2):169-78

Photoengineering of bone repair processes.

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OBJECTIVE: This paper aims to report the state of the art with respect to photoengineering of bone repair using laser therapy. BACKGROUND DATA: Laser therapy has been reported as an important tool to positively stimulate bone both in vivo and in vitro. These results indicate that photophysical and photochemical properties of some wavelengths are primarily responsible for the tissue responses. The use of correct and appropriate parameters has been shown to be effective in the promotion of a positive biomodulative effect in healing bone. METHODS: A series of papers reporting the effects of laser therapy on bone cells and tissue are presented, and new and promising protocols developed by our group are presented. RESULTS: The results of our studies and others indicate that bone irradiated mostly with infrared (IR) wavelengths shows increased osteoblastic proliferation, collagen deposition, and bone neorformation when compared to nonirradiated bone. Further, the effect of laser therapy is more effective if the treatment is carried out at early stages when high cellular proliferation occurs. Vascular responses to laser therapy were also suggested as one of the possible mechanisms responsible for the positive clinical results observed following laser therapy. It still remains uncertain if bone stimulation by laser light is a general effect or if the isolate stimulation of osteoblasts is possible. CONCLUSION: It is possible that the laser therapy effect on bone regeneration depends not only on the total dose of irradiation, but also on the irradiation time and the irradiation mode. The threshold parameter energy density and intensity are biologically independent of one another. This independence accounts for the success and the failure of laser therapy achieved at low-energy density levels.

Arq Bras Endocrinol Metabol. 2005 Dec;49(6):891-6. Epub 2006 Mar 16.

[Evidences of physical agents action on bone metabolism and their potential clinical use]

[Article in Portuguese]

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The action of physical agents such as low level laser therapy, low-intensity pulsed ultrasound and electrical and electromagnetic fields on bone have been often studied, showing that they are able to promote osteogenesis, accelerate fracture consolidation and augment bone mass. The use of these therapeutic modalities was first based on the finding that bone is a piezoelectric material, that means it can generate polarization when deformed, transforming mechanical energy into electric energy, and this has widen therapeutic possibilities to bony tissue. The present work aims to present evidences of physiologic effects and mechanisms of action of these physical agents on bone metabolism, based on articles published in international scientific literature.

Swed Dent J Suppl. 2005;(172):1-63.

The effect of low level laser irradiation on implant-tissue interaction. In vivo and in vitro studies.

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Low-level laser therapy (LLLT) is increasingly used in medicine and dentistry. It has been suggested that LLLT may be beneficial in the management of many different medical conditions, including pain, wound healing and nerve injury. The present thesis is based on a series of in vivo and in vitro experimental studies investigating whether LLLT has the potential to enhance titanium-implant interaction. Information about LLLT effect on bone healing is fundamental to understand whether LLLT may improve implant-tissue interaction. Thus in the initial study (I), the effect of LLLT on bone healing and growth in rat calvarial bone defects was investigated. It was found that LLLT may accelerate metabolism and/or mineralization during early bone healing. Based on these findings, study II explored the hypothesis that LLLT can enhance implant integration in the rabbit tibial bone. It was shown that LLLT stimulated the mechanical strength of the interface between the implant and bone after a healing period of 8 weeks. Histomorphometrical and mineral analyses showed that the irradiated implants had greater bone-to-implant contact than the controls. In the in vitro experiments, cellular responses to LLLT were studied in two cell types: primary cultures of human gingival fibroblasts and human osteoblast-like cells, with special reference to attachment, proliferation, differentiation

and production of transforming growth factor beta1 (TGF-beta1). The objectives of studies III & IV were to develop a standardized, reproducible in vitro model for testing a GaAlAs diode laser device and to document the influence of single or multiple doses of LLLT, as a guide to defining the optimal laser dose for enhancing cell activity. A further objective was to investigate the effect of LLLT on initial attachment and subsequent behaviour of human gingival fibroblasts cultured on titanium. While both multiple doses (1.5 and 3 J/cm2) and a single dose (3 J/cm2) enhanced cellular attachment, proliferation increased only after multiple doses (1.5 and 3 J/cm2). Study V concerned the response to LLLT of osteoblast-like cells, derived from human alveolar bone cultured on titanium implant material. In this study LLLT significantly enhanced cellular attachment. Greater cell proliferation in the irradiated groups was observed first after 96 h indicating that the cellular response is dose dependent. Osteocalcin synthesis and TGF-beta1 production were significantly stimulated on the samples exposed to 3 J/cm2. The following conclusions are drawn from the results of these five studies: LLLT can promote bone healing and bone mineralization and thus may be clinically beneficial in promoting bone formation in skeletal defects. It may be also used as additional treatment for accelerating implant healing in bone. LLLT can modulate the primary steps in cellular attachment and growth on titanium surfaces. Multiple doses of LLLT can improve LLLT efficacy, accelerate the initial attachment and alter the behaviour of human gingival fibroblasts cultured on titanium surfaces. The use of LLLT at the range of doses between 1.5 and 3 J/cm2 may modulate the activity of cells interacting with an implant, thereby enhancing tissue healing and ultimate implant success.

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Molecular structure of the bony tissue after experimental trauma to the mandibular region followed by laser therapy.

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OBJECTIVE: We investigated the therapeutic efficiency of laser irradiation and Bio-Oss, both and separately, on the post-traumatic regeneration of bone tissue in rats using infrared spectroscopy as an informative and accurate measuring method. BACKGROUND DATA: The therapeutic effect of low-power laser irradiation on bone tissue regeneration processes in animal models has been studied using morphogenic, biochemical, roentgenographic and electron microscopic measurements. Natural bone minerals, such as Bio-Oss collagen, were recommended for the reconstruction of bone defects in the alveolar process. MATERIALS AND METHODS: 29 male Wistar rats, divided into four random groups in a blinded manner were operated on the right alveolar process. A bone defect was made by penetrating the right alveolar process of the mandible bone using a 3-mm drill. The rats were divided into four groups as follows:

Group I, left side served as intact bone and right injured side as the control; Group II, right injured side was treated by organic bovine bone (Bio-Oss); Group III, right side bone defect was treated by HeNe laser (632.8 nm, 35 mW) applied transcutaneously for 20 min to the injured area daily for the following 14 consecutive days; and Group IV, Bio-Oss was placed loosely in the right side defect followed by laser treatment. After 2 weeks, the intact bone and bone replicas of the trauma area were removed and analyzed by infra-red spectroscopy technique. The composition and the structure of the bone tissue mineral substances were determined and compared among the four groups. For quantitative analysis of the regenerative bone process, the Mineralization index was used. An increase in this index indicates regenerative bone processes. RESULTS: The normal state analysis of the IR spectra of the normal alveolar bone tissue within the intervals of 400 to 4000 cm(-1) revealed characteristic absorption bands for the inorganic bone component in spectrum regions 450-1480 cm(-1), and the organic component at 1540-3340 cm(-1). In the case of trauma, the intensity of absorption of the inorganic component was decreased by 54%, and the absorption band became narrow, which can be interpreted as quantitative changes of the bone tissue mineral content. The wavelength characteristics of the inorganic component remained unchanged; that is, the induced trauma under these experimental conditions did not provoke alterations in the structure of the phosphate framework. The organic component showed decreased absorption by 10-15%, compared to the normal bone, and slight displacement of the wavelength, which can be interpreted as changes occurring in the quality of the organic content of the bone tissue. In the Bio-Oss-treated group, the intensity of absorption of the inorganic component increased by 43%, compared to the control injured area; however, there was a decrease of 22.6% in the normal bone. The wavelength characteristics of the inorganic component remained unchanged. The organic component showed similar absorption results in the injured non-treated group and absorption was 10-15% less than in the normal bone. Mineralization Index in the Bio-Oss-treated group was 0.93, compared to 0.63 in the control group and 2.04 in the normal bone. In the laser-treated group, the intensity of absorption of the inorganic component increased by 62, compared to the control injured area, and decreased only 11.4% in the normal bone. The wavelength characteristics of the organic component remained unchanged; that is, the organic component was similar to that of normal bone. Mineralization Index in the laser-treated group increased significantly to 1.86, compared to 0.63 in the control group and 2.04 in the normal bone. In the combined laser and Bio-Oss-treated groups, the intensity of absorption of the inorganic component and organic component was similar to that of normal bone. Mineralization Index in this group increased significantly to 1.98, compared to 0.63 in the control group and 2.04 in the normal bone. CONCLUSION: The results suggest that low-power laser irradiatults suggest that low-power laser irradiation alone and in combination with Bio-Oss enhances bone healing and increases bone repair.

Bone Stimulation by Low Level Laser - A Theoretical Model for the Effects

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Abstract

The anecdotal and researched evidence for the effects of Low Level Laser Therapy (LLLT) on the stimulation of bone have been reported for over 20 years. This has been in the form of local as well as systematic effects - including contra-lateral effects. Reports of stimulation of rabbit radii fractures and mice femurs were made as early as 1986 and 1987 with irradiated bones healing faster than controls and contra-lateral non-treated fractures similarly demonstrating faster healing times. Over the following decade and a half, further studies have also investigated and demonstrated that LLLT is effective for the stimulation of bone tissue.

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The reasons for this have been attributed to the general effects of LLLT and its ability to increase the rates of healing through mitochondrial ATP production and alteration in the cellular lipid bi-layer. Additional hypothesis include the subsequent capacity of irradiated cells to alter their ion exchange rate and thus influence the catalytic effects of the specific enzymes and substrates. These in turn initiate and promote the healing process completing the cascading cycle of events.

In the area of bone specific research, Dr. Tony Pohl of the Royal Adelaide Hospital in South Australia, has provided a new theory that postulates that the majority of fluid transfer and exchange within living bone is predominantly influenced by the lymphatic circulation.

LLLT is well documented and known as having effects that influence the lymphatic circulation and wound healing process. A coupling of these two areas of theory can demonstrate a positive description and explanation of the predominant effects of LLLT in bone stimulation. In reality, LLLT's effects on bone may well be a further consequence of its actions on the lymphatic circulation.

Reports of stimulation of Rabbit radii fractures were made by Tang in 1986 and similar reports by Trelles in 1987 on mice femurs. In both situations the irradiated bones healed faster than the controls. In another study by Hernandez-Ros, in 1987, LLLT demonstrated stimulation of fresh fractures on Sprague-Dawley rats that were fractured bilaterally. The unexpected results of this study were that the contra-lateral fractured non-treated limb also healed faster than the control group. Over the following decade and a half further studies (Yamada 1991; Pyczek, Sopala et al. 1994; Ozawa 1995; Horowitz 1996; Yaakobi 1996; Saito and Shimizu 1997) have also investigated and demonstrated that LLLT is effective for promoting the stimulation of bone healing. Recently Nicolau and colleagues (2002) from Brazil demonstrated the positive effect of LLLT on the stimulation of bone in mice with latent promotion of bone remodulation at injury sites without changes in bone architecture, increased bone volume and increased osteoblast surface through increased resorption and formation of bone with higher apposition rates. A positive effect on bony implants has been demonstrated by Dörtbudak (2002) and

Guzzardella (2003). The effect of laser irradiation on osteoblastic cells has been reported by Yamamoto (2001) and Guzzardella (2002).

The reasoning for this amelioration in all experimental circumstances, based on electron microscopy as well as macroscopic histological evidence, was concluded to be due to i.a. improved vascularisation as a consequence of blood vessel formation, absorption of the haematoma, macrophage action, fibroblast proliferation, chondrocyte activity, bone remodeling from increased osteoblastic activity and deposition of calcium salts.

These changes and evidence based studies attribute the macro- and microscopic effects to the known and accepted general actions of LLLT and its ability to increase rates of healing through stimulation of ATP production, (Karu 1989; Smith 1990) promoting repair and polarization of the cellular lipid bilayer (Fenyo 1990) as well as LLLT's capacity to affect cells through alterations in their exchange rate of ions (Robinson and Walters 1991) and influences the catalytic effects of the specific enzymes and substrates (Pouyssegur 1985; Karu 1988) which in turn initiate and promote the healing process.

More recent work by Dr. Tony Pohl, an internationally renowned Orthopaedic Surgeon from the Royal Adelaide Hospital in South Australia and lecturer at the Adelaide and South Australian Universities, has given rise to a new theory on bone circulation through reconsideration of fluid and protein transfer within bone (Pohl 1999). This theory suggests that the general understanding of the circulatory action within bone has been incorrect. Pohl postulates that the majority of fluid transfer and exchange within the living bone is predominantly influenced by the lymphatic rather than the vascular circulation. This is justified through studies on bone fluid input and output levels that have demonstrated that the venous and arterial aspect of circulation alone cannot account for the demonstrated levels of output nor the presence of free radical molecules which exceed those of the vascular input. Furthermore, the diameter of large protein cells within the bone exceed the diameter of the vessels that form the terminal aspects of the circulatory system making it impossible for them to have been delivered via this system. Consequently, an additional circulatory system must be present that will account for both the increased output and the presence of the large diameter protein cells as well as the free radicals.

If LLLT is then considered within the context of this new theory on bone circulation and the contribution of the lymphatic circulation then a further logical reasoned deduction for the action of LLLT on bone stimulation can be made. LLLT has a well documented and known effect influencing the lymphatic circulation. This has been demonstrated from the early works of Lievens, (1985) that demonstrated the influence of "Laser Irradiation" on the motricity of the lymphatic system and on the wound healing process. This is supported by several wound studies that demonstrate that the levels of protein rich exudates in non-healing wounds increase markedly from exposure to LLLT. This demonstrated action is determined to be as a result of the increase in lymphatic circulation (Robinson and Walters 1991; Gabel 1995). More recent work at the Flinders Medical Center in Adelaide South Australia has been completed and presented at the World Association of Laser Therapy conference in Tokyo Japan (Anderson, Carati et al.

2002). This study has demonstrated the positive effects of LLLT on the lymphatic circulation and its consequential benefits to the post mastectomy patient.

An understanding of the existing knowledge of the effects of LLLT on the lymphatic system combined with the hypothesis of bone fluid transport provides a coupled theory that would demonstrate a positive description and explain of the predominant effects of LLLT in bone stimulation.

In the trauma situation of direct or indirect damage to the bone, including fractures and periosteal induced damage such as stress fractures, the tissue damage leads to compromises that include but are not limited to, physical blockage from the trauma and waste / debris, increased fluid and circulatory viscosity from added cellular content within the lymphatics, lower speed motility and energy deficit in the tissue and cells from the loss of ATP production as a general effect from the trauma, cell changes and inability of mitochondria to function at the normal higher level to promote self repair and regeneration.

LLLT with its known general effects and specific direct effects on the lymphatic system would act to stimulate mitochondria ATP that increases cellular and circulatory motility as well as directly influencing lymphatic flow. LLLT also promotes increased permeability in interstitial tissue and facial layers (Gabel 1995) reducing stagnation and blockage. These actions would assist the increase in lymphatic flow and consequently the circulation within the affected bone. There is also a hypothetical potential that the presence of LLLT by increasing lymphatic circulation does so by virtue of an increase in the diameter of the lymphatic vessels, not just by increased flow rates within the vessel at an unchanged diameter. This diameter increase, if definitively present, would also explain the presence of large diameter protein cells within the normal bone circulation that cannot be attributed to the vascular circulation and would additionally explain a facilitated process for removal of debris and larger protein cells passing out of traumatized areas that is additionally stimulated by the use of LLLT.

Stimulation of bone healing by LLLT has till now has been generally classified as a consequence of the general healing effects of LLLT. In reality LLLT's effect on bone may well be a further consequence of its actions on the lymphatic circulation.

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Photomed Laser Surg. 2005 Aug;23(4):382-8

Assessment of bone repair associated with the use of organic bovine bone and membrane irradiated at 830 nm.

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OBJECTIVE: The aim of the present investigation was to assess histologically the effect of LLLT (GaAIAs, 830 nm, 40 mW, CW, (Phi) approximately 0.6 mm, 16 J/cm(2) per session) on the repair of surgical defects created in the femur of the Wistar Albinus rat. The defects were filled to lyophilized bovine bone (Gen-ox), organic matrix) associated or not to GTR (Gen-derm). BACKGROUND DATA: A major problem on modern Dentistry is the recovery of bone defects caused by trauma, surgical procedures or pathologies. Several types of biomaterials have been used in order to improve the repair of these defects. These materials are often associated to procedures of GTR. Previous studies have shown positive effects of LLLT on the repair of soft tissue wounds, but there are a few on its effects on bone healing. METHODS: Surgical bone defects were created in 42 animals divided into five groups: Group I (control, 6 animals); Group II (Gen-ox, 9 animals); Group III (Gen-ox + Laser, 9 animals); Group IV (Gen-ox + Gen-derm, 9 animals); Group V (Gen-ox + Gen-derm + Laser, 9 animals). The animals on the irradiated group received 16 J/cm(2) per session divided into four points around the defect (4 J/cm(2)) being the first irradiation immediately after surgery and repeated seven times at every 48 h. The animals were humanly killed after 15, 21, and 30 days. RESULTS: The results of the present investigation showed histological evidence of improved amount of collagen fibers at early stages of the bone healing (15 days) and increased amount of well organized bone trabeculae at the end of the experimental period (30 days) on irradiated animals compared to non irradiated ones. CONCLUSIONS: It is concluded that a positive biomodulative effect on the healing process of one defect associated or not to the use of organic lyophilized bone and biological bovine lyophilized membrane on the femur of the rat.

J Clin Laser Med Surg. 2003 Dec;21(6):383-8.

Effect of 830-nm laser light on the repair of bone defects grafted with inorganic bovine bone and decalcified cortical osseous membrane.

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OBJECTIVE: The aim of this study was to assess histologically the effect of LLLT (lambda830 nm) on the repair of standardized bone defects on the femur of Wistar albinus rats grafted with inorganic bovine bone and associated or not to decalcified bovine cortical bone membrane. BACKGROUND DATA: Bone loss may be a result of several pathologies, trauma or a consequence of surgical procedures. This led to extensive studies on the process of bone repair and development of techniques for the correction of bone defects, including the use of several types of grafts, membranes and the association of both techniques. There is evidence in the literature of the positive effect of LLLT on the healing of soft tissue wounds. However, its effect on bone is not completely understood. MATERIALS AND METHODS: Five randomized groups were studied: Group I (Control); Group IIA (Gen-ox); Group IIB (Gen-ox + LLLT); Group IIIA (Gen-ox + Gen-derm) and Group IIIB (Gen-ox + Gen-derm + LLLT). Bone defects were created at the femur of the animals and were treated according to the group. The animals of the irradiated groups were irradiated every 48 h during 15 days; the first irradiation was performed immediately after the surgical procedure. The animals were irradiated transcutaneously in four points around the defect. At each point a dose of 4 J/cm2 was given (phi approximately 0.6 mm, 40 mW) and the total dose per session was 16 J/cm2. The animals were humanely killed 15, 21, and 30 days after surgery. The specimens were routinely processed to wax, serially cut, and stained with H&E and Picrosirius stains and analyzed under light microscopy. RESULTS: The results showed evidence of a more advanced repair on the irradiated groups when compared to non-irradiated ones. The repair of irradiated groups was characterized by both increased bone formation and amount of collagen fibers around the graft within the cavity since the 15th day after surgery, through analysis of the osteoconductive capacity of the Gen-ox and the increment of the cortical repair in specimens with Gen-derm membrane. CONCLUSION: It is concluded that LLLT had a positive effect on the repair of bone defect submitted the implantation of graft.

Lasers Med Sci. 2003;18(2):89-94.

Effect of low-power GaAlAs laser (660 nm) on bone structure and cell activity: an experimental animal study.

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Low-level laser therapy (LLLT) is increasingly being used in the regeneration of soft tissue. In the regeneration of hard tissue, it has already been shown that the biomodulation effect of lasers repairs bones more quickly. We studied the activity in bone cells after LLLT close to the site of the bone injury. The femurs of 48 rats were perforated (24 in the irradiated group and 24 in the control group) and the irradiated group was treated with a GaAlAs laser of 660 nm, 10 J/cm2 of radiant exposure on the 2nd, 4th, 6th and 8th days after surgery (DAS). We carried out histomorphometry analysis of the bone. We found that activity was higher in the irradiated group than in the control group: (a) bone volume at 5 DAS (p=0.035); (b) osteoblast surface at 15 DAS (p=0.0002); (c) mineral apposition rate at 15 and 25 DAS (p=0.0008 and 0.006); (d) osteoclast surface at 5 DAS and 25 DAS (p=0.049 and p=0.0028); and (e) eroded surface (p=0.0032). We concluded that LLLT increases the activity in bone cells (resorption and formation) around the site of the repair without changing the bone structure.

J Clin Laser Med Surg. 2003 Oct;21(5):271-7. Links

Effects of pulse frequency of low-level laser therapy (LLLT) on bone nodule formation in rat calvarial cells.

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OBJECTIVE: The purpose of this study was to determine the effect of pulse frequencies of low-level laser therapy (LLLT) on bone nodule formation in rat calvarial cells in vitro. BACKGROUND DATA: Various photo-biostimulatory effects of LLLT, including bone formation, were affected by some irradiation factors such as total energy dose, irradiation phase, laser spectrum, and power density. However, the effects of pulse frequencies used during laser irradiation on bone formation have not been elucidated. MATERIALS AND METHODS: Osteoblast-like cells isolated from fetal rat calvariae were irradiated once with a low-energy Ga-Al-As laser (830 nm, 500 mW, 0.48-3.84 J/cm2) in four different irradiation modes: continuous irradiation (CI), and 1-, 2-, and 8-Hz pulsed irradiation (PI-1, PI-2, PI-8). We then investigated the effects on cellular proliferation, bone nodule formation, alkaline phosphatase (ALP) activity, and ALP gene expression. RESULTS: Laser irradiation in all four groups significantly stimulated cellular proliferation, bone nodule formation, ALP activity, and ALP gene expression, as compared with the non-irradiation group. Notably, PI-1 and -2 irradiation markedly stimulated these factors, when compared with the CI and PI-8 groups, and PI-2 irradiation was the best approach for bone nodule formation in the present experimental conditions. CONCLUSION: Since low-frequency pulsed laser irradiation significantly stimulates bone formation in vitro, it is most likely that the pulse frequency of LLLT an important factor affecting biological responses in bone formation.

Clin Orthod Res. 2001 Feb;4(1):3-14

The effects of low level laser irradiation on osteoblastic cells.

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Low level laser therapy has been used in treating many conditions with reports of multiple clinical effects including promotion of healing of both hard and soft tissue lesions. Low level laser therapy as a treatment modality remains controversial, however. The effects of wavelength, beam type, energy output, energy level, energy intensity, and exposure regime of low level laser therapy remain unexplained. Moreover, no specific therapeutic window for dosimetry and mechanism of action has been determined at the level of individual cell types. The aim of this study was to investigate the effects of low level laser irradiation on the human osteosarcoma cell line, SAOS-2. The cells were irradiated as a single or daily dose for up to 10 days with a GaAlAs continuous wave diode laser (830 nm, net output of 90 mW, energy levels of 0.3, 0.5, 1, 2, and 4 Joules). Cell viability was not affected by laser irradiation, with the viability being greater than 90% for all experimental groups. Cellular proliferation or activation was not found to be significantly affected by any of the energy levels and varying exposure regimes investigated. Low level laser irradiation did result in a heat shock response at an energy level of 2 J. No significant early or late effects of laser irradiation on protein expression and alkaline phosphatase activity were found. Investigation of intracellular calcium concentration revealed a tendency of a transient positive change after irradiation. Low level laser irradiation was unable to stimulate the osteosarcoma cells utilised for this research at a gross cell population level. The heat shock response and increased intracellular calcium indicate that the cells do respond to low level laser irradiation. Further research is required, utilising different cell and animal models, to more specifically determine the effects of low level laser irradiation at a cellular level. These effects should be more thoroughly investigated before low level laser therapy can be considered as a potential accelerator stimulus for orthodontic tooth movement.

Clin Oral Implants Res. 2003 Apr;14(2):226-32.

Osseointegration of endosseous ceramic implants after postoperative low-power laser stimulation: an in vivo comparative study.

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Stimulation with low-power laser (LPL) can enhance bone repair as reported in experimental studies on bone defects and fracture healing. Little data exist concerning the use of LPL postoperative stimulation to improve osseointegration of endosseous implants in orthopaedic and dental surgery. An in vivo model was used for the present study to evaluate whether Ga-Al-As (780 nm) LPL stimulation can improve biomaterial osseointegration. After drilling holes, cylindrical implants of hydroxyapatite (HA) were placed into both distal femurs of 12 rabbits. From postoperative day 1 and for 5 consecutive days, the left femurs of all rabbits were submitted to LPL treatment (LPL group) with the following parameters: 300 J/cm2, 1 W, 300 Hz, pulsating emission, 10 min. The right femurs were sham-treated (control group). Three and 6 weeks after implantation, histomorphometric and microhardness measurements were taken. A higher affinity index was observed at the HA-bone interface in the LPL group at 3 ($P<0.0005$) and 6 weeks ($P<0.001$); a significant difference in bone microhardness was seen in the LPL group vs. the control group ($P<0.01$). These results suggest that LPL postoperative treatment enhances the bone-implant interface.

Lasers Surg Med. 1998; 22: 97-102.

Laser therapy plays a role in bone healing

Luger et al. studied the effect of HeNe laser on the healing of tibial bone fractures in rats. 63 J (35 mW) was given transcutaneously daily over the fracture area. After 4 weeks the tibia was removed and tested at tension up to failure. The maximal load at failure and the structural stiffness of the tibia were found to be elevated significantly in the irradiated group, whereas the extension maximal load was reduced. In addition, gross non-union was found in four fractures in the contol group, compared to none in the irradiated group.

Clin Laser Med Surg. 2002; 20: 83-87

Computerized morphometric assessment of the effect of low-level laser therapy on bone repair: an experimental animal study.

Silva Júnior AN, Pinheiro AL, Oliveira MG, Weismann R, Ramalho LM, Nicolau RA. J

The aim of this study was to evaluate morphometrically the amount of newly formed bone after GaAlAs laser irradiation of surgical wounds created in the femur of rats. Low-level laser therapy (LLLT) has been used in several medical specialties because of its biomodulatory effects on different biological tissues. However, LLLT is still controversial because of contradictory reports. This is a direct result of the different methodologies used in these works. In this study, 40 Wistar rats were divided into four groups of 10 animals each: group A (12 sessions, 4.8 J/cm2 per session, observation time of 28 days); group C (three sessions, 4.8 J/cm2 per session, observation time of 7 days).

Groups B and D acted as nonirradiated controls. The specimens were routinely processed to wax and cut at 6-microm thickness and stained with H&E. For computerized morphometry, Imagelab software was used. RESULTS: Computerized morphometry showed a significant difference between the areas of mineralized bone in groups C and D (p = 0.017). There was no difference between groups A and B (28 days; p = 0.383).

Laser Med Surg Abstract issue, 2002: 11.

Effects of visible NIR low intensity laser on implant osseointegration in vivo.

Blay A, Blay C C, Groth E B et al.

The effects of 680 and 830 nm lasers on osseointegration was studied by Blay. 30 adult rats were divided into three groups; two laser groups and one control. The rats in the two laser groups had pure titanium Frialit-2 implants implanted into each proximal metaphysis of their respective tibias, inserted with a 40 Ncm torque. The initial stability was monitored by means of a resonance frequency analyser. Ten irradiations were performed, 48 hours apart, 4 J/cm2 on two points, starting immediately after surgery. Resonance frequency analysis indicated a significant difference between frequency values at 3 and 6 weeks, as compared to control. At 6 weeks the removal torque in the laser groups was much higher than in the control group.

Laser Surg Med. Abstract Issue 2002. abstract 303.

Bone repair of the periapical lesions treated or not with low intensity laser (wavelenght=904 nm).

Sousa G R, Ribeiro M S, Groth E B.

The effect of bone repair in periapical lesions has been studied by Sousa []. 15 patients with a total of 18 periapical lesions were divided into two groups. One group received endodontic treatment and/or periapical surgery. The patients in the other group were submitted to the same procedure and in addition the lesions were irradiated by GaAs laser, 11 mW, 9 J/cm2. This therapy was performed during 10 sessions with an interval of 72 hours. Bone regeneration was evaluated through X-ray examination. The results showed a significant difference between the laser and the control group in favour of the laser group.

J Photochem Photobiol B. 2003 May-Jun;70(2):81-9.

Low-power laser irradiation improves histomorphometrical parameters and bone matrix organization during tibia wound healing in rats.

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The influence of daily energy doses of 0.03, 0.3 and 0.9 J of He-Ne laser irradiation on the repair of surgically produced tibia damage was investigated in Wistar rats. Laser treatment was initiated 24 h after the trauma and continued daily for 7 or 14 days in two groups of nine rats (n=3 per laser dose and period). Two control groups (n=9 each) with injured tibiae were used. The course of healing was monitored using morphometrical analysis of the trabecular area. The organization of collagen fibers in the bone matrix and the histology of the tissue were evaluated using Picrosirius-polarization method and Masson's trichrome. After 7 days, there was a significant increase in the area of neoformed trabeculae in tibiae irradiated with 0.3 and 0.9 J compared to the controls. At a daily dose of 0.9 J (15 min of irradiation per day) the 7-day group showed a significant increase in trabecular bone growth compared to the 14-day group. However, the laser irradiation at the daily dose of 0.3 J produced no significant decrease in the trabecular area of the 14-day group compared to the 7-day group, but there was significant increase in the trabecular area of the 15-day controls compared to the 8-day controls. Irradiation increased the number of hypertrophic osteoclasts compared to non-irradiated injured tibiae (controls) on days 8 and 15. The Picrosirius-polarization method revealed bands of parallel collagen fibers (parallel-fibered bone) at the repair site of 14-day-irradiated tibiae, regardless of the dose. This organization improved when compared to 7-day-irradiated tibiae and control tibiae. These results show that low-level laser therapy stimulated the growth of the trabecular area and the concomitant invasion of osteoclasts during the first week, and hastened the organization of matrix collagen (parallel alignment of the fibers) in a second phase not seen in control, non-irradiated tibiae at the same period. The active osteoclasts that invaded the regenerating site were probably responsible for the decrease in trabecular area by the fourteenth day of irradiation.

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The effects of low level laser irradiation on osteoblastic cells.

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Low level laser therapy has been used in treating many conditions with reports of multiple clinical effects including promotion of healing of both hard and soft tissue lesions. Low level laser therapy as a treatment modality remains controversial, however. The effects of wavelength, beam type, energy output, energy level, energy intensity, and exposure regime of low level laser therapy remain unexplained. Moreover, no specific therapeutic window for dosimetry and mechanism of action has been determined at the level of individual cell types. The aim of this study was to investigate the effects of low level laser irradiation on the human osteosarcoma cell line, SAOS-2. The cells were irradiated as a single or daily dose for up to 10 days with a GaAlAs continuous wave

diode laser (830 nm, net output of 90 mW, energy levels of 0.3, 0.5, 1, 2, and 4 Joules). Cell viability was not affected by laser irradiation, with the viability being greater than 90% for all experimental groups. Cellular proliferation or activation was not found to be significantly affected by any of the energy levels and varying exposure regimes investigated. Low level laser irradiation did result in a heat shock response at an energy level of 2 J. No significant early or late effects of laser irradiation on protein expression and alkaline phosphatase activity were found. Investigation of intracellular calcium concentration revealed a tendency of a transient positive change after irradiation. Low level laser irradiation was unable to stimulate the osteosarcoma cells utilised for this research at a gross cell population level. The heat shock response and increased intracellular calcium indicate that the cells do respond to low level laser irradiation. Further research is required, utilising different cell and animal models, to more specifically determine the effects of low level laser irradiation at a cellular level. These effects should be more thoroughly investigated before low level laser therapy can be considered as a potential accelerator stimulus for orthodontic tooth movement.

Stomatologiia (Mosk). 2001;80(2):33-5.

[Prevention of inflammatory complications after mandibular osteosynthesis by a combination of low-frequency ultrasound and laser exposure]

[Article in Russian]

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Clinical and laboratory study of the efficiency of separate and combined use of low-frequency ultrasound and laser exposure of the operative wound for prevention of pyoinflammatory complications during mandibular osteosynthesis was carried out. Clinical parameters of wound reparation in the course of healing and microbiological and cytological findings in various methods of treatment are presented. The results evidence a high efficiency of these physical methods, particularly of their combination.

Bull Exp Biol Med. 2001 Apr;131(4):399-402.

Healing of bone fractures of rat shin and some immunological indices during magnetic laser therapy and osteosynthesis by the ilizarov method.

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The effect of magnetic and laser therapy on healing of bone fractures and blood levels of T and B lymphocytes was studied in rats during osteosynthesis by the Ilizarov method.

Laser therapy induced changes in cells attesting to stimulation of reparative processes and normalization of immunological parameters.

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Effect of 830-nm laser light on the repair of bone defects grafted with inorganic bovine bone and decalcified cortical osseous membrane.

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OBJECTIVE: The aim of this study was to assess histologically the effect of LLLT (lambda830 nm) on the repair of standardized bone defects on the femur of Wistar albinus rats grafted with inorganic bovine bone and associated or not to decalcified bovine cortical bone membrane. BACKGROUND DATA: Bone loss may be a result of several pathologies, trauma or a consequence of surgical procedures. This led to extensive studies on the process of bone repair and development of techniques for the correction of bone defects, including the use of several types of grafts, membranes and the association of both techniques. There is evidence in the literature of the positive effect of LLLT on the healing of soft tissue wounds. However, its effect on bone is not completely understood. MATERIALS AND METHODS: Five randomized groups were studied: Group I (Control); Group IIA (Gen-ox); Group IIB (Gen-ox + LLLT); Group IIIA (Gen-ox + Gen-derm) and Group IIIB (Gen-ox + Gen-derm + LLLT). Bone defects were created at the femur of the animals and were treated according to the group. The animals of the irradiated groups were irradiated every 48 h during 15 days; the first irradiation was performed immediately after the surgical procedure. The animals were irradiated transcutaneously in four points around the defect. At each point a dose of 4 J/cm2 was given (phi approximately 0.6 mm, 40 mW) and the total dose per session was 16 J/cm2. The animals were humanely killed 15, 21, and 30 days after surgery. The specimens were routinely processed to wax, serially cut, and stained with H&E and Picrosirius stains and analyzed under light microscopy. RESULTS: The results showed evidence of a more advanced repair on the irradiated groups when compared to non-irradiated ones. The repair of irradiated groups was characterized by both increased bone formation and amount of collagen fibers around the graft within the cavity since the 15th day after surgery, through analysis of the osteoconductive capacity of the Gen-ox and the increment of the cortical repair in specimens with Gen-derm membrane. CONCLUSION: It is concluded that LLLT had a positive effect on the repair of bone defect submitted the implantation of graft.

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Effects of pulse frequency of low-level laser therapy (LLLT) on bone nodule formation in rat calvarial cells.

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OBJECTIVE: The purpose of this study was to determine the effect of pulse frequencies of low-level laser therapy (LLLT) on bone nodule formation in rat calvarial cells in vitro. BACKGROUND DATA: Various photo-biostimulatory effects of LLLT, including bone formation, were affected by some irradiation factors such as total energy dose, irradiation phase, laser spectrum, and power density. However, the effects of pulse frequencies used during laser irradiation on bone formation have not been elucidated. MATERIALS AND METHODS: Osteoblast-like cells isolated from fetal rat calvariae were irradiated once with a low-energy Ga-Al-As laser (830 nm, 500 mW, 0.48-3.84 J/cm2) in four different irradiation modes: continuous irradiation (CI), and 1-, 2-, and 8-Hz pulsed irradiation (PI-1, PI-2, PI-8). We then investigated the effects on cellular proliferation, bone nodule formation, alkaline phosphatase (ALP) activity, and ALP gene expression. RESULTS: Laser irradiation in all four groups significantly stimulated cellular proliferation, bone nodule formation, ALP activity, and ALP gene expression, as compared with the non-irradiation group. Notably, PI-1 and -2 irradiation markedly stimulated these factors, when compared with the CI and PI-8 groups, and PI-2 irradiation was the best approach for bone nodule formation in the present experimental conditions. CONCLUSION: Since low-frequency pulsed laser irradiation significantly stimulates bone formation in vitro, it is most likely that the pulse frequency of LLLT an important factor affecting biological responses in bone formation.

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Effect of low-level laser irradiation on osteoglycin gene expression in osteoblasts.

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Many studies have attempted to elucidate the mechanism of the biostimulatory effects of low-level laser irradiation (LLLI), but the molecular basis of these effects remains obscure. We investigated the stimulatory effect of LLLI on bone formation during the early proliferation stage of cultured osteoblastic cells. A mouse calvaria-derived osteoblastic cell line, MC3T3-E1, was utilised to perform a cDNA microarray hybridisation to identify genes that induced expression by LLLI at the early stage. Among those genes that showed at least a twofold increased expression, the osteoglycin/mimecan gene was upregulated 2.3-fold at 2 h after LLLI. Osteoglycin is a small leucine-rich proteoglycan (SLRP) of the extracellular matrix which was previously called the osteoinductive factor. SLRP are abundantly contained in the bone matrix, cartilage cells and connective tissues, and are thought to regulate cell proliferation, differentiation and adhesion in close association with collagen and many other growth factors. We investigated the time-related expression of this gene by LLLI using a reverse transcription polymerase chain reaction (RT-PCR) method, and more precisely with a real-time PCR method, and found increases of 1.5-2-fold at 2-4 h after LLLI compared with the non-irradiated controls. These results suggest that the increased expression of the osteoglycin gene by LLLI in the early proliferation stage of cultured osteoblastic cells may play an important role in the stimulation of bone formation in concert with matrix proteins and growth factors.

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Effect of low-power laser irradiation on bony implant sites.

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This study was designed to examine the effects of low-energy laser irradiation on osteocytes and bone resorption at bony implant sites. Five male baboons with a mean age of 6.5 years were used in the study. Four holes for accommodating implants were drilled in each iliac crest. Sites on the left side were irradiated with a 100 mW low-energy laser (690 nm) for 1 min (6 Joule) immediately after drilling and insertion of four sandblasted and etched (Frialit-2 Synchro) implants. Five days later, the bone was removed en bloc and was evaluated histomorphometrically. The mean osteocyte count per unit area was 109.8 cells in the irradiated group vs. 94.8 cells in the control group. As intra-individual cell counts varied substantially, osteocyte viability was used for evaluation. In the irradiated group, viable osteocytes were found in 41.7% of the lacuna vs. 34.4% in the non-irradiated group. This difference was statistically significant at $P < 0.027$. The total resorption area, eroded surface, was found to be 24.9% in the control group vs. 24.6% in the irradiated group. This difference was not statistically significant. This study showed that osteocyte viability was significantly higher in the samples that were subjected to laser irradiation immediately after implant site drilling and implant insertion, in comparison to control sites. This may have positive effects on the integration of implants. The bone resorption rate, in contrast, was not affected by laser irradiation.

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Laser technology in orthopedics: preliminary study on low power laser therapy to improve the bone-biomaterial interface.

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Low Power Laser (LPL) seems to enhance the healing of bone defects and fractures. The effect of LPL in other orthopedic areas such as osteointegration of implanted prosthetic bone devices is still unclear. In the present study, 12 rabbits were used to evaluate whether Ga-Al-As (780 nm) LPL stimulation has positive effects on osteointegration. Hydroxyapatite (HA) cylindrical nails were drilled into both distal femurs of rabbits. From postoperative day 1 and for 5 consecutive days, the left femura of all rabbits were given LPL treatment (Laser Group-LG) with the following parameters: 300 Joule/cm2, 1 Watt, 300 Hertz, pulsating emission, 10 minutes. The right femura were sham-treated (Control Group-CG). At 4 and 8 weeks after implantation, histologic and histomorphometric investigations evaluated bone-biomaterial-contact. Histomorphometry showed a higher degree of osteointegration at the HA-bone interface in the LG Group at 4 ($p < 0.0005$) and 8 weeks ($p < 0.001$). These preliminary positive results seem to support the hypothesis that LPL treatment can be considered a good tool to enhance the bone-implant interface in orthopedic surgery.