

Laser therapy literature 2006-2008

Lam L K, Cheing G L. **Effects of 904-nm low-level laser therapy in the management of lateral epicondylitis: a randomized controlled trial.** Photomed Laser Surg. 2007; 25 (2): 65-67.

The aim of this study was to evaluate the effectiveness of 904-nm low-level laser therapy (LLLT) in the management of lateral epicondylitis. Background Data: Lateral epicondylitis is characterized by pain and tenderness over the lateral elbow, which may also result in reduction in grip strength and impairment in physical function. LLLT has been shown effective in its therapeutic effects in tissue healing and pain control. Methods: Thirty-nine patients with lateral epicondylitis were randomly assigned to receive either active laser with an energy dose of 0.275 J per tender point (laser group) or sham irradiation (placebo group) for a total of nine sessions. The outcome measures were mechanical pain threshold, maximum grip strength, level of pain at maximum grip strength as measured by the Visual Analogue Scale (VAS) and the subjective rating of physical function with Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire. Results: Significantly greater improvements were shown in all outcome measures with the laser group than with the placebo group ($p < 0.0125$), except in the two subsections of DASH. Conclusion: This study revealed that LLLT in addition to exercise is effective in relieving pain, and in improving the grip strength and subjective rating of physical function of patients with lateral epicondylitis.

Gungor A, Dogru S, Cincik H, Erkul E, Poyrazoglu E. **Effectiveness of transmeatal low power laser irradiation for chronic tinnitus.** Laryngol Otol. 2008; 122 (5): 447-451.

The objective in a study by Gungor was to evaluate effectiveness of 5 mW laser irradiation in the treatment of chronic tinnitus in a prospective, randomised, double-blind study. This investigation included 66 ears in 45 patients with chronic unilateral or bilateral tinnitus. A 5 mW laser with a wavelength of 650 nm, or placebo laser, was applied transmeatally for 15 minutes, once daily for a week. A questionnaire was administered which asked patients to score their symptoms on a five-point scale, before and two weeks after laser irradiation. A decrease of one scale point, regarding the loudness, duration and degree of annoyance of tinnitus, was accepted to represent an improvement. The loudness, duration and degree of annoyance of tinnitus were improved, respectively, in up to 48.8, 57.7 and 55.5 per cent of the patients in the active laser group. No significant improvement was observed in the placebo laser group.

Farouk A. H. Al-Watban, Xing Yang Zhang, Bernard L. Andres. **Low-Level Laser Therapy Enhances Wound Healing in Diabetic Rats: A Comparison of Different Lasers.** Photomed Laser Surg. 2007, 25 (2): 72-77.

The effects of wound healing acceleration on diabetic rats were determined and compared using different laser wavelengths and incident doses. Background Data: Many studies have demonstrated that low-level laser therapy (LLLT) can promote the wound healing on non-diabetic animals. Methods: Male Sprague-Dawley rats were used. Streptozotocin (70 mg/kg) was applied for diabetes induction. An oval full-thickness skin wound was created aseptically with a scalpel in 51 diabetic rats and six non-diabetic rats on the shaved back of the animals. The study was performed using 532, 633, 810, and 980 nm diode lasers. Incident doses of 5, 10, 20, and 30 J/cm² and treatment schedule of 3 times/week were used in the experiments. The area of wound on all rats was measured and plotted on a slope chart. The slope values (mm²/day), the percentage of relative wound healing, and the percentage of wound healing acceleration were

computed in the study. Results: Mean slope values were 6.0871 in non-diabetic control and 3.636 in diabetic control rats ($p > 0.005$). The percentages of wound healing acceleration were 15.23, 18.06, 19.54, and 20.39 with 532-nm laser, 33.53, 38.44, 32.05, and 16.45 with 633-nm laser, 15.72, 14.94, 9.62, and 7.76 with 810-nm laser, and 12.80, 16.32, 13.79, and 7.74 with 980-nm laser, using incident doses of 5, 10, 20, and 30 J/cm², respectively. There were significant differences ($p > 0.001$) in the mean slope value of wound healing on diabetic rats between control groups and treatment groups in 532, 633, 810, and 980 nm lasers. Conclusion: The wound healing on control rats with diabetes was slower than on control rats without diabetes. LLLT at appropriate treatment parameters can enhance the wound healing on diabetic rats. The optimum wavelength was 633 nm, and the optimum incident dose was 10 J/cm² in our study.

N. Houreld, H. Abrahamse. Photomed **In Vitro Exposure of Wounded Diabetic Fibroblast Cells to a Helium-Neon Laser at 5 and 16 J/cm²**. Photomed Laser Surg. 2007. 25(2): 78-84.

Objective: The aim of the present investigation was to assess morphological, cellular, and molecular effects of exposing wounded diabetic fibroblast cells to He-Ne (632.8 nm) laser irradiation at two different doses. Background Data: An alternative treatment modality for diabetic wound healing includes low-level laser therapy (LLLT). Although it's used in many countries and for many medical conditions, too many health care workers are unaware of this therapy, and there is still controversy surrounding its effectiveness. Methods: Normal human skin fibroblast cells (WS1) were used to simulate a wounded diabetic model. The effect of LLLT (632.8 nm, 5 and 16 J/cm² once a day on two non-consecutive days) was determined by analysis of cell morphology, cytotoxicity, apoptosis, and DNA damage. Results: Cells exposed to 5 J/cm² showed a higher rate of migration than cells exposed to 16 J/cm², and there was complete wound closure by day 4. Exposure of WS1 cells to 5 J/cm² on two non-consecutive days did not induce additional cytotoxicity or genetic damage, whereas exposure to 16 J/cm² did. There was a significant increase in apoptosis in exposed cells as compared to unexposed cells. Conclusion: Based on cellular morphology, exposure to 5 J/cm² was stimulatory to cellular migration, whereas exposure to 16 J/cm² was inhibitory. Exposure to 16 J/cm² induced genetic damage on WS1 cells when exposed to a He-Ne laser in vitro, whereas exposure to 5 J/cm² did not induce any additional damage.

Infrared Laser Photobiomodulation (λ 830 nm) on Bone Tissue Around Dental Implants: A Raman Spectroscopy and Scanning Electronic Microscopy Study in Rabbits. Cibelle B. Lopes, Antonio L.B. Pinheiro, Sokki Sathaiah, Newton Soares Da Silva, Miguel.A.C. Salgado. Photomed Laser Surg. 2007; 25 (2): 96-101.

Objective: The aim of this study was to assess, through Raman spectroscopy, the incorporation of calcium hydroxyapatite (CHA; 960 cm⁻¹), and scanning electron microscopy (SEM), the bone quality on the healing bone around dental implants after laser photobiomodulation (λ 830 nm). Background Data: Laser photobiomodulation has been successfully used to improve bone quality around dental implants, allowing early wearing of prostheses. Methods: Fourteen rabbits received a titanium implant on the tibia; eight of them were irradiated with λ 830 nm laser (seven sessions at 48-h intervals, 21.5 J/cm² per point, 10 mW, 0.0028 cm², 86 J per session), and six acted as control. The animals were sacrificed 15, 30, and 45 days after surgery. Specimens were routinely prepared for Raman spectroscopy and SEM. Eight readings were taken on the bone around the implant. Results: The results showed significant differences on the concentration of CHA on irradiated and control specimens at both 30 and 45 days after surgery ($p < 0.001$). Conclusion: It is concluded that infrared laser photobiomodulation does improve bone healing,

and this may be safely assessed by Raman spectroscopy or SEM.

Photobiomodulation on the Angiogenesis of Skin Wounds in Rats Using Different Light Sources. Adalberto Vieira Corazza, Jacks Jorge, Cristina Kurachi, Vanderlei Salvador Bagnato. *Photomed Laser Surg.*, 2007, 25 (2): 102-106.

The aim of this study was to compare the angiogenic effects of laser and light-emitting diode (LED) illumination on wounds induced in rats, with varied fluence. Background Data: The LED is an alternative light source that accelerates wound healing, and its efficiency concerning the angiogenic effect was compared to low-level laser therapy (LLLT). Methods: The experimental model consisted of a circular wound inflicted on the quadriceps of 120 rats, using a 15-mm-diameter "punch." Animals were divided randomly into five groups: two groups of laser, with dosages of 5 and 20 J/cm², respectively, two groups of LED, also with dosages of 5 and 20 J/cm², and a control group. Six hours after wound infliction, the treated groups received the diverse applications accordingly and were irradiated every 24 h. Angiogenesis was studied through histomorphometry on days 3, 7, 14, and 21 after the wounds were inflicted. Results: On days 3, 7, and 14, the proliferation of blood vessels in all irradiated groups was superior in comparison to those of the control group ($p < 0.05$). Treatment with fluence of 5 J/cm² was better than the laser group with 20 J/cm² on day 21. Conclusion: **Red LLLT and LED demonstrated expressive results in angiogenesis. Light coherence was shown not to be essential to angiogenesis.** However, further studies are needed in order to investigate the photobiomodulatory effects of LED in relation to LLLT in various biological tissues.

Ihsan F R, Al-Mustawfi N, Kaka L N. **Promotion of Regenerative Processes in Injured Peripheral Nerve Induced by Low-Level Laser Therapy.** *Photomed Laser Surg*, 2007, 25 (2): 107-111.

In a study by Ihsan 24 adult male rabbits were randomly assigned to two equal groups (control and laser-treated). General anesthesia was administered intramuscularly, and exploration of the peroneal nerve was done in the lateral aspect of the left leg. Complete section of the nerve was performed, which was followed by suturing of the neural sheath (epineurium). Irradiation was carried out directly after the operation and for 10 consecutive days. The laser used was diode with a wavelength of 901 nm (pulsed) and a power of 10 mW. It was a square-shaped window type (16 cm²), and its energy was applied by direct contact of the instrument's window to the site of the operation. Three rabbits from each group were sacrificed at the end of weeks 2, 4, 6, and 8, and specimens were collected from the site of nerve suturing and sent for histopathological examination. Two important factors were examined via histopathology: diameter of the nerve fibers and individual internodal length. Compared to the control group, significant variations in regeneration were observed, including thicker nerve fibers, more regular myelin layers, and clearer nodes of Ranvier with absence of short nodes in the treated group. Variations between the two groups for diameter were significant for the 2nd week, highly significant for the 4th and 6th weeks, respectively and very highly significant for the 8th week. Variations between the two groups for internodal length were highly significant for the 2nd and 4th weeks and very highly significant for the 6th and 8th weeks.

Effect of Low-Level Laser Therapy on Hemorrhagic Lesions Induced by Immune Complex in Rat Lungs. F. Aimbire, R.A.B. Lopes-Martins, R. Albertini, M.T.T. Pacheco, H.C. Castro-Faria-Neto, P.S.L.L. Martins, J.M. Bjordal. *Photomed Laser Surg*. April 1, 2007, 25(2): 112-117.

The aim of this study was to investigate if low-level laser therapy (LLLT) can modulate

formation of hemorrhagic lesions induced by immune complex. Background Data: There is a lack of information on LLLT effects in hemorrhagic injuries of high perfusion organs, and the relative efficacy of LLLT compared to anti-inflammatory drugs. Methods: A controlled animal study was undertaken with 49 male Wistar rats randomly divided into seven groups. Bovine serum albumin (BSA) i.v. was injected through the trachea to induce an immune complex lung injury. The study compared the effect of irradiation by a 650-nm Ga-Al-As laser with LLLT doses of 2.6 Joules/cm² to celecoxib, dexamethasone, and control groups for hemorrhagic index (HI) and myeloperoxidase activity (MPO) at 24 h after injury. Results: The HI for the control group was 4.0 (95% CI, 3.7–4.3). Celecoxib, LLLT, and dexamethasone all induced significantly ($p < 0.01$) lower HI than control animals at 2.5 (95% CI, 1.9–3.1), 1.8 (95% CI, 1.2–2.4), and 1.5 (95% CI, 0.9–2.1), respectively, for all comparisons to control. Dexamethasone, but not celecoxib, induced a slightly, but significantly lower HI than LLLT ($p = 0.04$). MPO activity was significantly decreased in groups receiving celecoxib at 0.87 (95% CI, 0.63–1.11), dexamethasone at 0.50 (95% CI, 0.24–0.76), and LLLT at 0.7 (95% CI, 0.44–0.96) when compared to the control group, at 1.6 (95% CI, 1.34–1.96; $p < 0.01$), but there were no significant differences between any of the active treatments. Conclusion: LLLT at a dose of 2.6 Joules/cm² induces a reduction of HI levels and MPO activity in hemorrhagic injury that is not significantly different from celecoxib. Dexamethasone is slightly more effective than LLLT in reducing HI, but not MPO activity.

Rochkind S, Leider-Trejo L, Nissan M, Shamir M H, Kharenko O, Alon M. **Efficacy of 780-nm Laser Phototherapy on Peripheral Nerve Regeneration after Neurotube Reconstruction Procedure (Double-Blind Randomized Study)**. *Photomed Laser Surg.* 2007; 25 (3): 137-143.

A pilot double-blind randomized study by Rochkind [1867] evaluated the efficacy of 780 nm laser phototherapy on the acceleration of axonal growth and regeneration after peripheral nerve reconstruction by polyglycolic acid (PGA) neurotube. The right sciatic nerve was transected, and a 0.5 cm nerve segment was removed in 20 rats. A neurotube was placed between the proximal and the distal parts of the nerve for reconnection of nerve defect. Ten of 20 rats received post-operative, transcutaneous, 200 mW, 780 nm laser irradiation for 14 consecutive days to the corresponding segments of the spinal cord (15 min) and to the reconstructed nerve (15 min). At 3 months after surgery, positive somato-sensory evoked responses were found in 70% of the irradiated rats, compared to 30% of the non-irradiated rats. The Sciatic Functional Index in the irradiated group was higher than in the non-irradiated group. Morphologically, the nerves were completely reconnected in both groups, but the laser-treated group showed an increased total number of myelinated axons.

Melanin Density Affects Photobiomodulation Outcomes in Cell Culture. Philip Brondon, Istvan Stadler, Raymond J. Lanzafame. *Photomed Laser Surg.* June 1, 2007, 25(3): 144-149.

This study investigated the influence of melanin on the outcome of photoradiation at 670 nm in a cell culture model. Background Data: Melanins are naturally occurring cutaneous pigments. Human skin is classified into six skin types based on melanin content. Methods: Gelatin photo filters were fabricated with varying melanin contents. Human HEP-2 and murine L929 cell lines were cultured in complete Dulbecco's Modified Eagle's Medium (DMEM) media. Photoradiation at 670 nm delivering 5.0 J/cm² per treatment/24 h (50 J/cm² total fluence) was carried out with melanin filters placed between the light source and the wells using a light-emitting diode (LED) device. Five groups based on percent melanin were treated: group 1, no filter; group 2, gelatin alone; group 3, 0.0125%; group 4, 0.025%; and group 5, 0.050%. Cell proliferation was measured using CyQuant and 3-(4,5-dimethylthiazol-2-yl)-2,5-disphenyl tetrasodiumbromide

(MTT) assays for 240 h post-photoradiation. Results: The Proliferation Index (PI) as measured by CyQuant assay was not statistically different amongst the groups in either cell line. MTT assay results demonstrated a significant dose response effect ($p \leq 0.05$) in both cell lines with activity inversely proportional to melanin concentration. The relative PI values by MTT assay at 144 h for groups 1, 2, 3, and 4, respectively, were 1.44 ± 0.06 , 1.28 ± 0.05 , 1.20 ± 0.07 , and 1.06 ± 0.04 for the L-929 cells, and 1.61 ± 0.03 , 1.47 ± 0.06 , 1.35 ± 0.03 , and 1.19 ± 0.06 for the HEP-2 cells ($n = 4$; $p < 0.05$). These results demonstrate that cutaneous melanin content should be taken into consideration in photobiomodulation paradigms. Further studies to quantify these effects are warranted.

Antiinfectives and Low-Level Light: A New Chapter in Photomedicine. Andrei P. Sommer. *Photomed Laser Surg.* June 1, 2007, 25(3): 150-158.

The purpose of this study was to identify synergistic effects in the interaction of light with biosystems in the presence of chemical agents. Their systematic analysis promises therapeutic strategies. Background Data: Light intensities around 1000 Wm^2 potentially induce density variations in nanoscopic water layers adhering to surfaces in air or subaquatically. In permeable nanoscopic compartments in the interior of biosystems, this could result in powerful flow processes and bidirectional flows for repetitive applications of light. Consequently, external stimulation with light will force microorganisms and cells to incorporate a suitable antiinfective. Nanoscale biosystems, which respond to both light stimulation and antibiotics, are nanobacteria. Responses include growth, inhibition, and slime secretion. Slime secretion was provoked in vitro by gentamycin, an agent proposed for in vivo eradication, and blocked by light. Depending on the field of action, co-operative effects between light and an antiinfective can be exploited by considering two properties of the drug: transmission of light and resorption by the tissue. Antiinfectives can be administered in an active form or via drug delivery systems. In the latter case, a double action of the light could be exploited: stimulated release from the carrier and subsequent uptake by the targeted biosystem. Methods: The attenuation of laser light (670 nm) by antiinfectives was measured in films of different thickness of a vaginal suppository. The effect of 670-nm laser light—not absorbed by water—on nanoscopic water layers was examined by comparing the evaporation time of irradiated drops of water-based nanosuspensions with non-irradiated controls. Results: The 6- μm -thick suppository films were virtually transparent to the laser light, and the 1-mm-thick films totally attenuated it. Nanosuspension drops irradiated with 670-nm light needed more time to evaporate than controls. Conclusion: Low-level light (LLL) therapy is compatible with antiinfectives, and even capable of boosting effects of superficially applied and/or absorbed antiinfectives. Temporal coordination between light treatment and drug administration maximizes drug effects and minimizes possible adverse effects. Irradiation should start when the drug concentration has reached its maximum in the desired field of action. Light-induced flow in nanoscale cavities could represent one mechanism of LLL therapy.

Influence of Broad-Spectrum and Infrared Light in Combination with Laser Irradiation on the Proliferation of Wounded Skin Fibroblasts. Denise Hawkins, Heidi Abrahamse. *Photomed Laser Surg.* June 1, 2007, 25(3): 159-

This study aimed to establish if broad-spectrum or infrared (IR) light in combination with laser therapy can assist phototherapy and accelerate cell proliferation to improve the rate of wound healing. Background Data: The effect of laser light may be partly or completely reduced by broad-spectrum light. There are few studies that investigate the benefit or detriment of combining laser irradiation with broad-spectrum or IR light. Methods: Wounded human skin fibroblasts were irradiated with a dose of 5 J/cm^2 using a heliumneon laser, a diode laser, or a

Nd:YAG laser in the dark, in the light, or in IR. Changes in cell proliferation were evaluated using optical density at 540 nm, alkaline phosphatase (ALP) enzyme activity, cytokine expression, and basic fibroblast growth factor (bFGF) expression. Results: The optical density and ALP enzyme activity indicate that 5 J/cm² using 1064 nm in the light is more effective in increasing cell proliferation or cell growth than 830 nm in the light, but not as effective as 632.8 nm in the light. bFGF expression shows that the response of wounded cells exposed to 5 J/cm² in IR light is far less than the biological response of wounded cells exposed to 5 J/cm² in the dark or light. The results indicate that wounded cells exposed to 5 J/cm² using 632.8 nm in the dark results in a greater increase in IL-6 when compared to cells exposed to 5 J/cm² in the light or in IR. Conclusion: Results indicate that 5 J/cm² (using 632.8 nm in the dark or 830 nm in the light) is the most effective dose to stimulate cell proliferation, which may ultimately accelerate or improve the rate of wound healing.

Red Light-Induced Redox Reactions in Cells Observed with TEMPO. Maor Eichler, Ronit Lavi, Harry Friedmann, Asher Shainberg, Rachel Lubart. *Photomed Laser Surg.* June 1, 2007, 25(3): 170-174.

The aim of this study was to determine the wavelength dependence of light-induced redox reactions in cells, particularly whether there is any contribution by red wavelengths. An additional aim was to assess the potential of 2,2,6,6-tetramethyl piperidine-N-oxyl (TEMPO) as a tool for measuring these redox reactions. Background Data: Visible light has been shown to affect cells, and redox reactions, which have been detected previously using spin traps, have been proposed as a mechanism. However, there is little evidence that red light, which is used in most such experiments, is redox active in cells. Methods: Redox activity was observed by measuring the decay of the electron paramagnetic resonance signal of TEMPO that occurs in the presence of illuminated cells. Color filters were used to generate blue, green, and red light, and the decay resulting from these wavelengths was compared to the decay caused by white light. Results: Shorter wavelengths have a considerably stronger effect than longer wavelengths, although red light has some effect. Creation of reactive oxygen species by red light was confirmed with the spin trap 5,5-dimethyl-1-pyrroline-N-oxide (DMPO). Conclusion: Red light can induce redox reactions in illuminated cells. However, shorter wavelengths are more efficient in this regard. In addition, TEMPO was found to be a more sensitive probe than DMPO for detecting light-induced cellular redox reactions.

Oron U, Ilic S, De Taboada L, Streeter J. **Ga-As (808 nm) Laser Irradiation Enhances ATP Production in Human Neuronal Cells in Culture.** *Photomed Laser Surg.* 2007; 25 (3): 180-182.

The aim of a study by Oron was to investigate whether GaAs laser irradiation can enhance adenosine triphosphate (ATP) production in normal human neural progenitor (NHNP) cells in culture. NHNP were grown in tissue culture and were treated by GaAs laser (808 nm, 50 mW/cm², 0.05 J/cm²), and ATP was determined at 10 min after laser application. The quantity of ATP in laser-treated cells was 7513 ± 970 units, which was significantly higher than the non-treated cells, which comprised 3808 ± 539 ATP units. Laser application to NHNP cells significantly increases ATP production in these cells.

Delbari A, Bayat M, Bayat M. **Effect of Low-Level Laser Therapy on Healing of Medial Collateral Ligament Injuries in Rats: An Ultrastructural Study.** *Photomed Laser Surg.* 2007; 25 (3): 191-196.

A study by Delbari sought to investigate whether or not LLLT with a helium-neon laser would increase fibril diameter of transected medial collateral ligament (MCL) in rats. 30 rats received surgical transect to their right MCL, and five were assigned as the control group. After surgery, the rats were divided into three groups: group 1 (n= 0) received LLLT with HeNe laser and 0.01 J/cm² fluence per day, group 2 (n=10) received LLLT with 1.2 J/cm² fluence per day and group 3 (sham-exposed group; n=10) received daily placebo laser with shut-down laser equipment, while control group received neither surgery nor LLLT. Transmission electron microscope (TEM) examination was performed on days 12 and 21 after surgery and dimension and density of ligament fibrils were measured. On day 12, the fibril dimension of group 2 and their density were higher than of groups 1 and 3.

Stergioulas A. Effects of Low-Level Laser and Plyometric Exercises in the Treatment of Lateral Epicondylitis. Photomed Laser Surg. 2007; 25 (3): 205-213.

A study by Stergioulas was undertaken to compare the effectiveness of a protocol of combination of laser with plyometric exercises and a protocol of placebo laser with the same program, in the treatment of tennis elbow. Fifty patients who had tennis elbow participated in the study and were randomised into two groups. Group A (n=25) was treated with a 904 nm GaAs laser, pulse repetition rate of 50 Hz, average power 40 mW and energy density 2.4 J/cm², plus plyometric exercises and group B (n=25) that received placebo laser plus the same plyometric exercises. During eight weeks of treatment, the patients of the two groups received 12 sessions of laser or placebo, two sessions per week (weeks 1–4) and one session per week (weeks 5–8). Pain at rest, at palpation on the lateral epicondyle, during resisted wrist extension, middle finger test, and strength testing was evaluated using Visual Analogue Scales. Also it was evaluated the grip strength, the range of motion and weight test. Parameters were determined before the treatment, at the end of the eighth week course of treatment (week 8), and eighth (week 8) after the end of treatment. Relative to the group B, the group A had (1) a significant decrease of pain at rest at the end of 8 weeks of the treatment and at the end of following up period (2) a significant decrease in pain at palpation and pain on isometric testing at 8 weeks of treatment and at 8 weeks follow-up (3) a significant decrease in pain during middle finger test at the end of 8 weeks of treatment and at the end of the follow-up period (4) a significant decrease of pain during grip strength testing at 8 weeks of treatment and at 8 weeks follow-up (5) a significant increase in the wrist range of motion at 8 weeks follow-up, (6) an increase in grip strength at 8 weeks of treatment and at 8 weeks follow-up, and (7) a significant increase in weight-test at 8 weeks of treatment and at 8 weeks follow-up The results suggested that the combination of laser with plyometric exercises was more effective treatment than placebo laser with the same plyometric exercises at the end of the treatment as well as at the follow-up.

Correa F, Lopes Martins R A, Correa J C, Iversen V V, Joenson J, Bjordal J M. Low-Level Laser Therapy (GaAs $\lambda = 904$ nm) Reduces Inflammatory Cell Migration in Mice with Lipopolysaccharide-Induced Peritonitis. Photomed Laser Surg. 2007; (4): 245-249.

A study by Correa was designed to study the effect of an infrared GaAs $\lambda = 904$ nm, 4 mW on inflammatory cell migration in lipopolysaccharide (LPS)-induced peritonitis in mice. Sixty male mice were randomly divided into five groups, and one group was given an intraperitoneal sterile saline injection. In the remaining four groups, peritonitis was induced by an intraperitoneal LPS injection. Animals in three of the LPS groups were irradiated at a single point over the peritoneum with doses of 3 J/cm², 7.5 J/cm², and 15 J/cm², respectively.

The fourth group injected with LPS was an LPS-control group. At 6 hours after injection the groups irradiated with doses of 3 J/cm² and 7.5 J/cm² had a reduced number of neutrophil cells in the peritoneal cavity compared with the LPS-control group, and there were significant differences between the number of neutrophils in the peritoneal cavity between the LPS-control group and groups irradiated with doses of 3 J/cm² (-42%) and 7.5 J/cm² (-70%). In the group irradiated with 15 J/cm², neutrophil cell counts were lower than, but not significantly different from, LPS controls (-38%). At 24 hours after injection, both neutrophil and total leukocyte cell counts were lower in all the irradiated groups than in the LPS controls. The 3J/cm² exposure group showed the best results at 24 hours, with reductions of 77% in neutrophil and 49% in leukocyte counts.

Renno A C, McDonnell P A, Parizotto N A, Laakso E L. **The Effects of Laser Irradiation on Osteoblast and Osteosarcoma Cell Proliferation and Differentiation in Vitro.** Photomed Laser Surg. 2007; 25 (4): 275-280.

The aim of a study by Renno was to investigate the effects of 670, 780 and 830 nm laser irradiation on cell proliferation of normal primary osteoblast (MC3T3) and malignant osteosarcoma (MG63) cell lines in vitro. 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/cm². 24 hours after laser irradiation, cell proliferation and alkaline phosphatase assays were assessed. Osteoblast proliferation increased significantly after 830 nm laser irradiation (at 10 J/cm²) but decreased after 780 nm laser irradiation (at 1, 5, and 10 J/cm²). Osteosarcoma cell proliferation increased significantly after 670 nm (at 5 J/cm²) and 780 nm laser irradiation (at 1, 5, and 10 J/cm²), 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/cm², whereas ALP activity in the osteosarcoma line was not altered, regardless of laser wavelength or intensity. Based on the conditions of this study, we conclude that each cell line responds differently to specific wavelength and dose combinations.

Fikackova H, Dostalova T, Navratil L, Klaschka J. **Effectiveness of Low-Level Laser Therapy in Temporomandibular Joint Disorders: A Placebo-Controlled Study.** Photomed Laser Surg. 2007; 25 (4): 297-303.

In a study by Fikackova the active group of 61 patients was treated with 10 J/cm² or 15 J/cm², and the control group of 19 patients was treated with 0.1 J/cm². LLLT was performed by a 830 nm laser with output of 400 mW, in 10 sessions. The probe with an aperture of 0.2 cm² was placed over the painful muscle spots in the patients with myofascial pain. In patients with TMD arthralgia the probe was placed behind, in front of, and above the mandibular condyle, and into the meatus acusticus externus. Changes in pain were evaluated by self-administered questionnaire. Application of 10 J/cm² or 15 J/cm² was significantly more effective in reducing pain compared to placebo, but there were no significant differences between the energy densities used in the study group and between patients with myofascial pain and temporomandibular joint arthralgia. Results were marked in those with chronic pain.

Rochkind S, Drory V, Alon M, Nissan M, Ouaknine G E. **Laser Phototherapy (780 nm), a New Modality in Treatment of Long-Term Incomplete Peripheral Nerve Injury: A Randomized Double-Blind Placebo-Controlled Study.** Photomed Laser Surg. 2007; 25 (5): 436-442.

Rochkind conducted clinical pilot study to prospectively investigate the effectiveness of laser irradiation (780 nm) in the treatment of patients suffering from incomplete peripheral nerve and brachial plexus injuries for 6 months up to several years. Injury of a major nerve trunk frequently results in considerable disability associated with loss of sensory and motor functions. Spontaneous recovery of long-term severe incomplete peripheral nerve injury is often unsatisfactory. A randomized, double-blind, placebo-controlled trial was performed on 18 patients who were randomly assigned placebo (non-active light: diffused LED lamp) or low-level laser irradiation (wavelength, 780 nm; power, 250 mW). Twenty-one consecutive daily sessions of laser or placebo irradiation were applied transcutaneously for 3 h to the injured peripheral nerve (energy density 450 J/mm²) and for 2 h to the corresponding segments of the spinal cord (energy density 300 J/mm²). Clinical and electrophysiological assessments were done at baseline, at the end of the 21 days of treatment, and 3 and 6 months thereafter. The laser-irradiated and placebo groups were in clinically similar conditions at baseline. The analysis of motor function during the 6-month follow-up period compared to baseline showed statistically significant improvement in the laser-treated group compared to the placebo group. No statistically significant difference was found in sensory function. Electrophysiological analysis also showed statistically significant improvement in recruitment of voluntary muscle activity in the laser-irradiated group compared to the placebo group.

Viegas V N, Marcelo Abreu E R, Viezzer C, Cantarelli Machado D, Sant'Anna Filho M et al. **Effect of Low-Level Laser Therapy on Inflammatory Reactions during Wound Healing: Comparison with Meloxicam.** Photomed Laser Surg. 2007; 25 (6): 467-473.

A study by Viegas evaluated the action of LLLT on the modulation of inflammatory reactions during wound healing in comparison with Meloxicam. Standardized circular wounds were made on the backs of 64 Wistar rats. The animals were divided into four groups according to the selected postoperative therapy: group A control; group B administration of Meloxicam; and groups C and D irradiation with red (685 nm) and infrared (830 nm) laser energy, respectively. The animals were killed at 12, 36, and 72 h and 7 days after the procedure. Microscopic analysis revealed significant vascular activation of irradiated sites in the first 36 h. Only group B showed decreases in the intensity of polymorphonuclear infiltrates and edema. Group D showed a higher degree of organization and maturation of collagen fibers than the other groups at 72 h. The animals in group C showed the best healing pattern at 7 days. The anti-inflammatory action of Meloxicam was confirmed by the results obtained in this research. The quantification of interleukin-1 β mRNA by real-time polymerase chain reaction (PCR) did not show any reduction in the inflammatory process in the irradiated groups when compared to the other groups.

Hourelid N, Abrahamse H. **Effectiveness of Helium-Neon Laser Irradiation on Viability and Cytotoxicity of Diabetic-Wounded Fibroblast Cells.** Photomed Laser Surg. 2007; 25 (6): 474-481.

A study by Hourelid investigated the effectiveness of helium-neon laser irradiation at increasing intervals on diabetic-induced wounded human skin fibroblast cells (WS1) at a morphological, cellular, and molecular level. The controversies over light therapy can be explained by the differing exposure regimens and models used. No therapeutic window for dosimetry and mechanism of action has been determined at the level of individual cell types, particularly in diabetic cells in vitro. WS1 cells were used to simulate an in vitro wounded diabetic model. The effect of the frequency of He-Ne irradiation at a fluence of 5 J/cm² was determined by analysis of cell morphology, viability, cytotoxicity, and DNA damage. Cells

were irradiated using three different protocols: they were irradiated at 30 min only; irradiated twice, at 30 min and at 24 h; or irradiated twice, at 30 min and at 72 h post-wound induction. A single exposure to 5 J/cm² 30 min post-wound induction increased cellular damage. Irradiation of cells at 30 min and at 24 h post-wound induction decreased cellular viability, cytotoxicity, and DNA damage. However, complete wound closure as well as an increase in viability and a decrease in cytotoxicity and DNA damage occurs when cells were irradiated at 30 min and at 72 h post-wound induction. Thus, wounded diabetic WS1 cells irradiated to 5 J/cm² showed increased cellular repair when irradiated with adequate time between irradiations, allowing time for cellular response mechanisms to take effect. Therefore, the irradiation interval was shown to play an important role in wound healing in vitro and should be taken into account.

Liu X, Lyon R, Meier H T, Thometz J, Haworth S T. **Effect of Lower-Level Laser Therapy on Rabbit Tibial Fracture.** *Photomed Laser Surg.* 2007; 25 (6): 487-494.

The purpose of a study by Liu [1876] was to demonstrate the biological effects of LLLT on tibial fractures, using radiographic, histological, and bone density examinations. 14 white rabbits with surgically induced mid-tibial osteotomies were included in the study. 7 were assigned to a group receiving LLLT (LLLT-A) and the remaining seven served as a sham-treated control group (LLLT-C). A 830 nm laser and a sham laser (a similar design without laser diodes) were used for the study. Continuous irradiation with a total energy density of 40 J/cm² and a power of 200 mW/cm² 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. Radiographic findings revealed no statistically significant fracture callus thickness difference between the LLLT-A and LLLT-C groups. 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). 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.

Mirzaei M, Bayat M, Mosafa N, Mohsenifar Z et al. **Effect of Low-Level Laser Therapy on Skin Fibroblasts of Streptozotocin-Diabetic Rats.** *Photomed Laser Surg.* 2007; 25 (6): 519-525.

In a study by Mirzaei diabetes was induced in rats by streptozotocin 30 days after its injection. Two sets of skin samples were extracted from skin under sterile conditions. Fibroblasts that were extruded from the samples were proliferated in vitro, and another set of samples were cultured as organ culture. A 24-well culture medium containing Dulbecco's modified minimum essential medium was supplemented by 12% fetal bovine serum. There were five laser-treated and five sham-exposed groups. A HeNe laser was used, and 0.9–4 J/cm² energy densities were applied four times to each organ culture and cell culture. The organ cultures were analyzed by light microscopy and transmission electron microscopy examinations. Statistical analysis revealed that 4J/cm² irradiation significantly increased the fibroblast numbers compared to the sham-exposed cultures.

Elementary Processes in Cells after Light Absorption Do Not Depend on the Degree of Polarization: Implications for the Mechanisms of Laser Phototherapy. Tiina I. Karu, Ludmila V. Pyatibrat, Sergei V. Moskvina, Sergei Andreev, Vladilen S. Letokhov. *Photomed Laser Surg.* April 1, 2008, 26(2): 77-82.

The objective of this work was to evaluate the importance of the degree of light polarization in stimulation of cellular metabolism. Background Data: Although the possible role of polarization's effects on the mechanisms of laser phototherapy is sometimes discussed in the literature, there are still no clear answers. Material and Methods: A model system (HeLa cell suspension) was used in which the lengths of light scattering (l_{sc}) and absorption (l_a) were much larger than the thickness of the irradiated layer ($L = 3$ mm). The cell suspension (1×10^6 cells/cm³) was irradiated with a diode laser ($\lambda = 637$ nm, $D = 65.7$ J/m², $\tau = 10$ sec, $I = 6.57$ W/m²). The polarization degree (99.4%, 60.9%, and 34.2%) of the beam was changed by means of optical fibers of different lengths. The irradiated suspension was incubated at 37°C for 30 min, and the attached cells were counted afterwards. Results: The cell fraction stimulated to adhere by red light at 637 nm was nearly the same in all three experimental groups ($58.1\% \pm 2.5\%$, $57.6\% \pm 3.5\%$, and $62.5\% \pm 3.2\%$ for degree of beam polarization of 99.4%, 66.9%, and 34.2%, respectively). There was no statistically significant difference in these results ($p < 0.8$, < 0.6 , and < 0.7 , respectively). At the same time, all three groups had statistically significant differences ($p < 0.01$) in adherence from the sham-irradiated control group ($39.1\% \pm 2.2\%$). Conclusion: The biological effect (stimulation of cell attachment) of light with $\lambda = 637$ nm on cells in our model system was pronounced, but did not depend on the degree of light polarization. Elementary processes in cells (light absorption and photochemistry) do not appear to depend on the degree of light polarization.

Stergioulas A. Low-Power Laser Treatment in Patients with Frozen Shoulder: Preliminary Results. *Photomed Laser Surg.* 2008; 26 (2): 99-105.

In a study by Stergioulas 63 patients with frozen shoulder were randomly assigned into one of two groups. In the active laser group ($n=31$), patients were treated with a 810 nm laser with a continuous output of 60 mW, applied to eight points on the shoulder for 30 sec each, for a total dose of 1.8 J per point and 14.4 J per session. In the placebo group ($n=32$), patients received placebo laser treatment. During 8 wk of treatment, the patients in each group received 12 sessions of laser or placebo, two sessions per week (for weeks 1–4), and one session per week (for weeks 5–8). Relative to the placebo group, the active laser group had: (1) a significant decrease in overall, night, and activity pain scores at the end of 4 wk and 8 wk of treatment, and at the end of 8 wk additional follow-up (16 wk post-randomization); (2) a significant decrease in shoulder pain and disability index (SPADI) scores and Croft shoulder disability questionnaire scores at those same intervals; (3) a significant decrease in disability of arm, shoulder, and hand questionnaire (DASH) scores at the end of 8 wk of treatment, and at 16 wk posttreatment; and (4) a significant decrease in health-assessment questionnaire (HAQ) scores at the end of 4 wk and 8 wk of treatment. There was some improvement in range of motion, but this did not reach statistical significance.

Ng G Y F, Fung D T C. The Combined Treatment Effects of Therapeutic Laser and Exercise on Tendon Repair. *Photomed Laser Surg.* 2008; 26 (2): 137-141.

Ng investigated the effects of different intensities of therapeutic laser and running exercise, and their combined effects on the repair of Achilles tendons in rats. 36 Sprague-Dawley rats that received surgical hemi-transection of their right Achilles tendon were tested. Three laser dosages (4 J/cm², 1 J/cm² and 0 J/cm²) and three running periods (30 min, 15 min, and 0

min) resulting in nine different dosage and time groups were studied with four rats in each group. The treatments were given on alternate days starting on day 5 post-injury. On day 22, the tendons were tested for load-relaxation, stiffness, and ultimate strength. There was a significant effect of laser on normalized load-relaxation, the rats receiving 4 J/cm² had less load-relaxation than those receiving no laser treatment. Results of stiffness testing revealed a significant effect, and rats that ran for 30 min had more stiffness than those that did not run. For ultimate strength, due to a significant interaction, the two factors were analyzed separately, and the results showed that for rats receiving no laser therapy, those that had run for 15 min and 30 min had more strength than those that did not run. In conclusions, both laser therapy and running were found to hasten Achilles tendon repair. In general, the rats that received higher dosages of laser energy (4 J/cm²) and ran for longer periods (30 min) performed better than those that received lower dosages of laser energy and ran for shorter periods.

Meirelles G C S, Santos J N, Chagas P O, Moura A P, Pinheiro A L B. **A Comparative Study of the Effects of Laser Photobiomodulation on the Healing of Third-Degree Burns: A Histological Study in Rats.** Photomed Laser Surg. 2008; 26 (2): 159-166.

The aim of an investigation by Meirelles was to compare by light microscopy the effects of laser at wavelengths of 660 and 780 nm on third-degree burns in Wistar rats. 55 animals were used in this study. A third-degree burn measuring 1.5 × 1.5 cm was created on the dorsum of each animal. The animals were divided into three subgroups according to the type of laser they received (wavelength of 660 or 780 nm, 35 mW, $\theta = 2$ mm, and 20 J/cm²). In the animals receiving treatment, it was begun immediately post-burn at four points around the burn (5 J/cm²) and repeated at 24-h intervals for 21 d. The animals were humanely killed after 3, 5, 7, 14, and 21 d by an intraperitoneal overdose of general anesthetic. The specimens were routinely cut and stained, and then were analyzed by light microscopy. The results showed more deposition of collagen fibers, larger amounts of granulation tissue, less edema, a more vigorous inflammatory reaction, and increased revascularization on all laser-treated animals. These features were more evident at early stages when the 660 nm laser was used, and were more evident throughout the experimental period for the animals receiving 780 nm laser therapy.

Pinheiro A L B, Gerbi M E M, Ponzi E A C, Ramalho L M P, Marques A M C et al. **Infrared Laser Light Further Improves Bone Healing When Associated with Bone Morphogenetic Proteins and Guided Bone Regeneration: An in Vivo Study in a Rodent Model.** Photomed Laser Surg. 2008; 26 (2): 167-174.

A study by Pinheiro assessed histologically the effect of laser on the repair of surgical defects created in the femurs of Wistar rats treated or not treated with bone morphogenetic proteins (BMPs) and organic bovine bone graft. 48 adult male Wistar rats were divided into four randomized groups: group 1 (controls, n=12); group 2 (laser, n=12); group 3 (BMPs + organic bovine bone graft + GBR, n=12); and group 4 (BMPs + organic bovine bone graft + GBR + laser, n=12). The irradiated groups received seven irradiations every 48 h, the first immediately after the surgical procedure. Laser (830 nm, 40 mW, CW, 0.6 mm) consisted of a total of 16 J/cm² per session at four points (4 J/cm² each) equally spaced around the periphery of the defect. The animals were sacrificed after 15, 21, and 30 d, and the specimens were routinely embedded in wax and stained with hematoxylin and eosin and Sirius red stains and analyzed under light microscopy. The results showed histological evidence of increased deposition of collagen fibers (at 15 and 21 d), as well as an increased amount of well-

organized bone trabeculi at the end of the experimental period (30 d) in irradiated animals compared to non-irradiated controls.

F. Aimbire, R. Albertini, M.T.T. Pacheco, H.C. Castro-Faria-Neto, P.S.L.M. Leonardo, V.V. Iversen, R.A.B. Lopes-Martins, J.M. Bjordal. **Low-Level Laser Therapy Induces Dose-Dependent Reduction of TNF α Levels in Acute Inflammation.** Photomed Laser Surg. 2006; 24 (1): 33-37.

The aim of this study was to investigate if low-level laser therapy (LLLT) can modulate acute inflammation and tumor necrosis factor (TNF α) levels. Background Data: Drug therapy with TNF α -inhibitors has become standard treatment for rheumatoid arthritis, but it is unknown if LLLT can reduce or modulate TNF α levels in inflammatory disorders. Methods: Two controlled animal studies were undertaken, with 35 male Wistar rats randomly divided into five groups each. Rabbit antiserum to ovalbumin was instilled intrabronchially in one of the lobes, followed by the intravenous injection of 10 mg of ovalbumin in 0.5 mL to induce acute lung injury. The first study served to define the time profile of TNF α activity for the first 4 h, while the second study compared three different LLLT doses to a control group and a chlorpromazine group at a timepoint where TNF α activity was increased. The rats in LLLT groups were irradiated within 5 min at the site of injury by a 650-nm Ga-Al-As laser. Results: There was a time-lag before TNF α activity increased after BSA injection. TNF α levels increased from ≤ 6.9 (95% confidence interval [CI], 5.6–8.2) units/mL in the first 3 h to 62.1 (95% CI, 60.8–63.4) units/mL ($p < 0.001$) at 4 h. An LLLT dose of 0.11 Joules administered with a power density of 31.3 mW/cm² in 42 sec significantly reduced TNF α level to 50.2 (95% CI, 49.4–51.0), $p < 0.01$ units/mL versus control. Chlorpromazine reduced TNF α level to 45.3 (95% CI, 44.0–46.6) units/mL, $p < 0.001$ versus control. Conclusion: LLLT can reduce TNF α expression after acute immunocomplex lung injury in rats, but LLLT dose appears to be critical for reducing TNF α release.

Weber J B B, Pinheiro A L B, de Oliveira M G, Oliveira A M, Ramalho L M P. **Laser Therapy Improves Healing of Bone Defects Submitted to Autologous Bone Graft.** Photomed Laser Surg. 2006; 24 (1): 38-44.

The aim of the study by Weber was to assess histologically the effect of LLLT, 830 nm, on the healing of bone defects associated with autologous bone graft. 60 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/cm², 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 (830 nm, area = 0.5 cm², 50 mW, 10 J/cm²). The dose was fractioned in four points. The animals were sacrificed 15, 21, and 30 days after surgery; specimens were taken and routinely processed. Light microscopic analysis was performed by a pathologist. 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.

Silvia Cristina Nunez, Aguinaldo Silva Garcez, Selly Sayuri Suzuki, Martha Simoes Ribeiro. **Management of Mouth Opening in Patients with Temporomandibular Disorders through Low-Level Laser Therapy and Transcutaneous Electrical Neural Stimulation.** Photomed Laser Surg. February 1, 2006; 24(1): 45-49.

The aim of this study was to evaluate the effectiveness of low-level laser therapy (LLLT) and transcutaneous electrical neural stimulation (TENS) on the improvement of mouth opening in patients with temporomandibular disorder (TMD). TMDs are conditions that affect the form and/or function of the temporomandibular joint (TMJ), masticatory muscles, and dental apparatus. Often TMD is associated with pain localized in the TMJ and/or in the muscles of the face and neck. Methods: This clinical trial was performed in 10 patients, 18–56 years old, diagnosed with TMD of multiple causes. All patients received both methods of treatment in two consecutive weeks. LLLT was delivered via a 670-nm diode laser, output power 50 mW, fluence 3 J per site/4 sites (masseter muscle, temporal muscle, mandibular condyle, and intraauricular). TENS therapy was applied with a two-electrode machine at 20 W, maximum frequency of 60 Hz, adjusted by the patient according to their sensitivity. The amplitude of mouth opening was recorded before treatment and immediately after using a millimeter rule; the measurements were performed from the incisal of the upper incisors to the incisal of the lower incisors. A paired t-test was applied to verify the significance of the results. A significant improvement in the range of motion for both therapies was observed immediately after treatment. Comparing the two methods, the values obtained after LLLT were significantly higher than those obtained after TENS ($p < 0.01$). Both methods are effective to improve mouth opening. Comparing the two methods, LLLT was more effective than TENS applications.

F. Soriano, V. Campana, M. Moya, A. Gavotto, J. Simes, M. Soriano, R. Soriano, L. Spitale, J. Palma. **Photobiomodulation of Pain and Inflammation in Microcrystalline Arthropathies: Experimental and Clinical Results.** Photomed Laser Surg. 2006; 24(2): 140-150.

This article presents the results of laser therapy in crystal (hydroxyapatite, calcium pyrophosphate, and urates) deposition–induced arthritis in rats and the clinical applications in humans. Background Data: Microcrystalline arthropathies are prevalent among geriatric patients, who are more vulnerable to the side effects of drugs. The effectiveness of laser therapy for pain relief, free of side effects, has been reported in painful conditions. Two milligrams of each of the above-mentioned crystals was injected in both joints of the back limbs in three groups of rats; these groups were then treated with laser irradiation. Three other groups received no treatment after the injections. We determined the plasmatic levels of inflammatory markers (fibrinogen, prostaglandin E2, and TNF), tissues (prostaglandin E2) and conducted anatomopathological studies. Twenty-five patients with acute gout arthritis were randomized into two groups and treated over 5 days: group A, diclofenac 75 mg orally, twice a day; and group B, laser irradiation once a day. Forty-nine patients with knee chronic pyrophosphate arthropathy were randomized into two groups and treated over 21 days; group A, diclofenac 50 mg orally, twice a day; and group B, laser irradiation once a day. Thirty patients with shoulder chronic hydroxyapatite arthropathy were randomized into two groups and treated over 21 days; group A, diclofenac 50 mg orally, twice a day; and group B, laser irradiation once a day. Results: Fibrinogen, prostaglandin E2, and TNF concentrations in the rats injected with crystals and treated with laser decreased significantly as compared with the groups injected with crystals without treatment. Both laser therapy and diclofenac achieved rapid pain relief in patients with acute gouty arthritis without significant differences in efficacy. Laser therapy was more effective than diclofenac in patients with chronic pyrophosphate arthropathy and in patients with chronic apatite deposition disease. Laser therapy represents an effective treatment in the therapeutic arsenal of microcrystalline arthropathies.

Jan Magnus Bjordal, Mark I. Johnson, Vegard Iversen, Flavio Aimbire, Rodrigo Alvaro Brandao Lopes-Martins. **Low-Level Laser Therapy in Acute Pain: A Systematic Review of Possible Mechanisms of Action and Clinical Effects in Randomized Placebo-Controlled Trials.** *Photomed Laser Surg* 2006; 24(2): 158-168.

The aim of this study was to review the biological and clinical short-term effects of low-level laser therapy (LLLT) in acute pain from soft-tissue injury. Background Data: It is unclear if and how LLLT can reduce acute pain. Methods: Literature search of (i) controlled laboratory trials investigating potential biological mechanisms for pain relief and (ii) randomized placebo-controlled clinical trials which measure outcomes within the first 7 days after acute soft-tissue injury. Results: There is strong evidence from 19 out of 22 controlled laboratory studies that LLLT can modulate inflammatory pain by reducing levels of biochemical markers (PGE₂, mRNA Cox 2, IL-1 β , TNF α), neutrophil cell influx, oxidative stress, and formation of edema and hemorrhage in a dose-dependent manner (median dose 7.5 J/cm², range 0.3–19 J/cm²). Four comparisons with non-steroidal anti-inflammatory drugs (NSAIDs) in animal studies found optimal doses of LLLT and NSAIDs to be equally effective. Seven randomized placebo-controlled trials found no significant results after irradiating only a single point on the skin overlying the site of injury, or after using a total energy dose below 5 Joules. Nine randomized placebo-controlled trials (n = 609) were of acceptable methodological quality, and irradiated three or more points and/or more than 2.5 cm² at site of injury or surgical incision, with a total energy of 5.0–19.5 Joules. Results in these nine trials were significantly in favor of LLLT groups over placebo groups in 15 out of 18 outcome comparisons. Poor and heterogeneous data presentation hampered statistical pooling of continuous data. Categorical data of subjective improvement were homogeneous (Q-value = 7.1) and could be calculated from four trials (n = 379) giving a significant relative risk for improvement of 2.7 (95% confidence interval [CI], 1.8–3.9) in a fixed effects model. LLLT can modulate inflammatory processes in a dose-dependent manner and can be titrated to significantly reduce acute inflammatory pain in clinical settings. Further clinical trials with adequate LLLT doses are needed to precisely estimate the effect size for LLLT in acute pain.

Antonio Luiz B. Pinheiro, Marleny Elizabeth M.M. Gerbi. **Photoengineering of Bone Repair Processes.** *Photomed Laser Surg.* 2006; 24(2): 169-178.

This paper aims to report the state of the art with respect to photoengineering of bone repair using laser therapy. 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. 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 neof ormation 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. 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.

Carlos Sechi Goulart, Paulo Roberto Aranha Nouer, Laura Mouramartins, Ivana Uglík Garbin, Rosane de Fatima Zanirato Lizarelli. **Photoradiation and Orthodontic Movement: Experimental Study with Canines.** *Photomed Laser Surg.* 2006; 24 (2): 192-196.

The aim of this study was to evaluate, through a double-blind study, the effect of gallium-aluminium-arsenic (GaAlAs) laser irradiation on the speed of orthodontic movement in canine premolars. Eighteen dogs were divided into two groups, and their third molars were extracted. An orthodontic device was placed between the first molar and the second premolar for stabilization purpose. Group I was irradiated with a dosage of 5.25 J/cm² on the right side, whereas the left side was used as the control group. Group II was submitted to the same procedure, but was irradiated with a dosage of 35.0 J/cm². Irradiations were done every 7 days, for a total of nine irradiations. The orthodontic space was measured every 21 days. Results: The 5.25 J/cm² dosage accelerated orthodontic movement during the first observation period, from 0 to 21 days ($p < 0.05$), whereas the 35.0 J/cm² dosage retarded the orthodontic movement in the treated group when compared with the control group, during both the first and second observation periods, from 0 to 42 days ($p < 0.05$). The results suggest that photoradiation may accelerate orthodontic movement at a dosage of 5.25 J/cm², whereas a higher dosage, 35.0 J/cm², may retard it.

Rodrigo Alvaro Brandao Lopes-Martins, Regiane Albertini, Patricia Sardinha Leonardo Lopes-Martins, Flavio Aimbire Soares de Carvalho, Hugo Caire Castro Faria Neto, Vegard Vereide Iversen, Jan Magnus Bjordal. **Steroid Receptor Antagonist Mifepristone Inhibits the Anti-inflammatory Effects of Photoradiation.** *Photomed Laser Surg.* 2006; 24 (2): 197-201.

The authors designed an animal pleurisy study to assess if the anti-inflammatory effect of photoradiation could be affected by concomitant use of the cortisol antagonist mifepristone. Background Data: Although interactions between photoradiation and pharmacological agents are largely unknown, parallel use of steroids and photoradiation is common in the treatment of inflammatory disorders such as arthritis and tendinitis. Forty BALB/c male mice were randomly divided in five groups. Inflammation was induced by carrageenan administered by intrathoracic injections. Four groups received carrageenan, and one control group received injections of sterile saline solution. At 1, 2, and 3 h after injections, photoradiation irradiation was performed with a dose of 7.5 J/cm². Two of the carrageenan-injected groups were pre-treated with orally administered mifepristone. Results: Total leukocyte cell counts revealed that in carrageenan-induced pleurisy, photoradiation significantly reduced the number of leukocyte cells ($p < 0.0001$, mean 34.5 [95% CI: 32.8–36.2] versus 87.7 [95% CI: 81.0–94.4]), and that the effect of photoradiation could be totally blocked by adding the cortisol antagonist mifepristone ($p < 0.0001$, mean 34.5 [95% CI: 32.1–36.9] versus 82.9 [95% CI: 70.5–95.3]). The steroid receptor antagonist mifepristone significantly inhibited the anti-inflammatory effect of photoradiation. Commonly used glucocorticoids are also known to down-regulate steroid receptors, and further clinical studies are necessary to elucidate how this interaction may decrease the effect size of photoradiation over time. For this reason, we also suggest that, until further clinical data can be provided, clinical photoradiation trials should exclude patients who have received steroid therapy within 6 months before recruitment.

Ana Claudia Muniz Renno, Fernanda Mendes de Moura, Nadia Slemmer Andrade Dos Santos, Renata Passarelli Tirico, Paulo Sergio Bossini, Nivaldo Antonio Parizotto. **Effects of 830-nm Laser, Used in Two Doses, on Biomechanical Properties of Osteopenic Rat Femora.** Photomed Laser Surg. 2006; 24 (2): 202-206.

The aim of this study was to investigate the effects of photoradiation—infrared at 830 nm—used in two doses, on femora of osteopenic rats. Osteoporosis has recently been recognized as a major public health problem. Based on stimulatory effects of photoradiation on the proliferation of bone cells, we hypothesized that photoradiation would be efficient in improving bone mass in osteopenic rats. Sixty female animals, divided into six groups, were used: sham-operated control (SC), osteopenic control (OC), sham-operated irradiated with the dose of 120 J/cm² (I120), osteopenic irradiated with the dose of 120 J/cm² (O120), sham-operated irradiated with the dose of 60 J/cm² (I60), and osteopenic irradiated with the dose of 60 J/cm² (O60) Animals were 90 days old when operated. Laser irradiation was initiated 8 weeks after operation, and it was performed 3 times a week for 2 months. Femora were submitted to a biomechanical test and to a physical properties evaluation. Maximal load of O120 did not show any difference when compared with SC and I120, but it was higher than the O60 group. Wet weight, dry weight, and bone volume of O60 and O120 did not show any difference when compared with SC. The results of the present study indicate that photoradiation had stimulatory effects on femora of osteopenic rats, mainly at the dose of 120 J/cm². However, further studies are needed to investigate the effects of different parameters, wavelengths, and sessions of applications on ovariectomized rats.

Ferreira A N S, Silveira L, Genovese W J, Cavalcante de Araujo V, Frigo L et al. **Effect of GaAlAs Laser on Reactional Dentinogenesis Induction in Human Teeth.** Photomed Laser Surg. 2006; 24 (3): 358-365.

A study by Ferreira investigated the biomodulatory effect of the 670 nm laser in pulp cells on reactional dentinogenesis, and on the expression of collagen type III (Col III), tenascin (TN), and fibronectin (FN) in irradiated dental tissues and controls (not irradiated). Sixteen human premolar teeth were selected (after extraction due to orthodontal reasons) and divided into irradiated and control groups. Black class V cavity preparations were accomplished in both groups. For the irradiated group, laser (670 nm, 50 mW) with an energy density of 4 J/cm² was used. Soon after, the cavities were restored with a glass ionomer and the extractions made after 14 and 42 days. Histological changes were observed by light microscopy; less intense inflammatory reaction in the irradiated group was found when compared to the controls. Only the irradiated group of 42 days exhibited an area associated with reactional dentinogenesis. After immunohistochemical analysis, the expression of Col III, TN, and FN was greater in the irradiated groups. Conclusion: These results suggest that a laser with energy density of 4 J/cm² and wavelength of 670 nm causes biomodulation in pulp cells and expression of collagen, but not collagen of the extracellular matrix, after preparation of a cavity.

Effect of Phototherapy on Delayed Onset Muscle Soreness. Peter Douris, Veronica Southard, Richard Ferrigi, Joshua Grauer, Dina Katz, Christine Nascimento, Peter Podbielski. Photomed Laser Surg. 2006; 24 (3): 377-382.

The purpose of this study was to investigate the effects of phototherapy on delayed onset muscle soreness (DOMS) as measured using the Visual Analog Scale (VAS), McGill Pain Questionnaire, Resting Angle (RANG), and girth measurements. Background Data: Previous research has failed to prove the beneficial effects of phototherapy on DOMS. Methods: This was a randomized double-blind controlled study with 27 subjects (18–35 years) assigned to one of three groups. The experimental group received 8 J/cm² of phototherapy each day for five consecutive days using **super luminous diodes** with wavelengths of 880 and visible diodes of 660 nm at three standardized sites over the musculotendinous junction of the bicep. The sham group received identical treatment from a dummy cluster. The controls did not receive treatment. The study was completed over five consecutive days: on day one baseline measurements of RANG and upper arm girths were recorded prior to DOMS induction. On days 2–5, RANG, girth, and pain were assessed using VAS and the McGill Pain Questionnaire. Results: The experimental group exhibited a significant decrease in pain associated with DOMS compared to the control ($p = 0.01$) and sham groups ($p = 0.03$) based upon the VAS at the 48-h period. The McGill Pain Questionnaire showed a significant difference in pain scores at the 48-h period between the experimental and the sham groups ($p = 0.01$). There were no significant differences day to day and between the groups with respect to girth and RANG. The results of this study provide scientific evidence that phototherapy as used in this study provides a beneficial effect to patients who may experience DOMS after a novel exercise session.

Effects of Power Densities, Continuous and Pulse Frequencies, and Number of Sessions of Low-Level Laser Therapy on Intact Rat Brain. Sanja Ilic, Sandra Leichliter, Jackson Streeter, Amir Oron, Luis DeTaboada, Uri Oron. *Photomed Laser Surg.* 2006; 24 (4): 458-466.

The aim of the present study was to investigate the possible short- and long-term adverse neurological effects of low-level laser therapy (LLLT) given at different power densities, frequencies, and modalities on the intact rat brain. LLLT has been shown to modulate biological processes depending on power density, wavelength, and frequency. To date, few well-controlled safety studies on LLLT are available. One hundred and eighteen rats were used in the study. Diode laser (808 nm, wavelength) was used to deliver power densities of 7.5, 75, and 750 mW/cm² transcranially to the brain cortex of mature rats, in either continuous wave (CW) or pulse (Pu) modes. Multiple doses of 7.5 mW/cm² were also applied. Standard neurological examination of the rats was performed during the follow-up periods after laser irradiation. Histology was performed at light and electron microscopy levels. Both the scores from standard neurological tests and the histopathological examination indicated that there was no long-term difference between lasertreated and control groups up to 70 days post-treatment. The only rats showing an adverse neurological effect were those in the 750 mW/cm² (about 100-fold optimal dose), CW mode group. In Pu mode, there was much less heating, and no tissue damage was noted. Long-term safety tests lasting 30 and 70 days at optimal 10× and 100× doses, as well as at multiple doses at the same power densities, indicate that the tested laser energy doses are safe under this treatment regime. Neurological deficits and histopathological damage to 750 mW/cm² CW laser irradiation are attributed to thermal damage and not due to tissue–photon interactions.

Comparison between Wound Healing in Induced Diabetic and Nondiabetic Rats after Low-Level Laser Therapy. Sylvia Bicalho Rabelo, Antonio Balbin Villaverde, Renata

Amadei Nicolau, Miguel A. Castillo Salgado, Milene Da Silva Melo, Marcos Tadeu T. Pacheco. *Photomed Laser Surg.* 2006; 24 (4): 474-479.

The aim of this work was to compare the effect of low-level laser therapy (LLLT) on the wound healing process in nondiabetic and diabetic rats. Background Data: Among the clinical symptoms caused by diabetes mellitus, a delay in wound healing is a potential risk for patients. It is suggested that LLLT can improve wound healing. The tissue used for this study was extracted from animals suffering from diabetes, which was induced by Streptozotocin®, and from nondiabetic rats. Animals were assembled into two groups of 25 rats each (treated and control) and further subdivided into two groups: diabetic (n = 15) and nondiabetic (n = 10). A full-thickness skin wound was made on the dorsum area, with a round 8-mm holepunch. The treated group was irradiated by a HeNe laser at 632.8 nm, with the following parameters: 15 mW, exposition time of 17 sec, 0.025 cm² irradiated area, and energy density of 10 J/cm². Square full-thickness skin samples (18 mm each side, including both injured and noninjured tissues) were obtained at 4, 7, and 15 days after surgery and analyzed by qualitative and quantitative histological methods. Quantitative histopathological analysis confirmed the results of the qualitative analysis through histological microscope slides. When comparing tissue components (inflammatory cells, vessels and fibroblast/area), we found that treated animals had a less intense inflammatory process than controls. Results obtained by both qualitative and quantitative analyses suggested that irradiation of rats with HeNe (632.8 nm), at the tested dose, promoted efficient wound healing in both nondiabetic and diabetic rats as, compared to the control group.

Arthralgia of the Temporomandibular Joint and Low-Level Laser Therapy. H. Fikackova, T. Dostalova, R. Vosicka, V. Peterova, L. Navratil, J. Lesak. *Photomed Laser Surg.* 2006; 24 (4): 522-527.

This case report describes the treatment of a patient with arthralgia of the temporomandibular joint (TMJ) caused by disc displacement. The goal of the treatment of TMJ arthralgia is to decrease pain by promotion of the musculoskeletal system's natural healing ability. Methods: This report describes the complex treatment of TMJ arthralgia. Low-level laser therapy (LLLT) was chosen for its antiinflammatory and analgesic effects. Laser therapy was carried out using the GaAlAs diode laser with an output power of 400 mW, emitting radiation with a wavelength of 830 nm, and having energy density of 15 J/cm²; the laser radiation was applied by contact mode on four targeted spots in 10 sessions. Physiotherapy was recommended to this patient to prevent the injury of intraarticular tissue caused by incorrect movement during opening of the mouth. Splint stabilization and prosthetic treatment were used to reduce overloading of the TMJ, resulting from unstable occlusion and to help repositioning of the dislocated disc. Results: Five applications of LLLT led to decrease of pain in the area of the TMJ on the Visual Analog Scale, from 20 to 5 mm. The anti-inflammatory effect of the laser was confirmed by thermographic examination. Before treatment, the temperature differences between the areas of the normal TMJ and TMJ with arthralgia was higher than 0.5°C. However, at the conclusion of LLLT, temperatures in the areas surrounding the TMJ were equalized. This study showed the effectiveness of complex non-invasive treatment in patients with arthralgia of the TMJ. The analgesic and anti-inflammatory effects of LLLT were confirmed by infrared thermography.

Low-Level Laser Therapy at Different Energy Densities (0.1–2.0 J/cm²) and Its Effects on the Capacity of Human Long-Term Cryopreserved Peripheral Blood Progenitor

Cells for the Growth of Colony-Forming Units. Rogerio Xavier Do Nascimento, Fernando Callera. *Photomed Laser Surg.* 2006; 24 (5): 601-604.

The aim of this research was to investigate the effects of low-level laser therapy (LLLT) at different energy densities (0.1–2.0 J/cm²) on the capacity of long-term cryopreserved peripheral blood progenitor cell (PBPC) for growth of colony-forming units (CFU) in vitro. There are no data concerning the effects of LLLT on human cryopreserved PBPC. Methods: Cryopreserved PBPC samples were thawed after 3 years in order to demonstrate the positive effect of LLLT and after 5 years in order to confirm the LLLT's proliferative effect. Cultures were plated in quadruplicate 35-mm-diameter Petri dishes in methylcellulose medium (2 × 10⁵/mL final concentration) and incubated for 14 days at 37°C with 5% CO₂. A 685-nm diode laser with 25-mW optical power was used as the source of irradiation. Cultures were exposed to energy densities of 0.1, 0.5, 1.0, 1.5, and 2.0 J/cm² before incubation (10 irradiated and 10 controls at each energy density group). Results: A higher number of CFU was observed at the dose of 1.0 J/cm² (control 21.3 ± 8.5 × 10⁵ cells, irradiated 40.1 ± 10.5 × 10⁵ cells, *p* < 0.001). No differences were observed in cultures exposed to doses of 0.1, 0.5, and 1.5 J/cm². A decreased number of CFU was demonstrated in samples exposed to the dose of 2.0 J/cm² (control 21.4 ± 11.9 × 10⁵ cells, *p* = 0.013). PBPC samples cryopreserved for 5 years were thawed for CFU assays and exposed to a single dose of 1.0 J/cm²; once again the exposed group showed a higher number of CFU (control 8.8 ± 7.8 × 10⁵ cells, irradiated 18.1 ± 13.1 × 10⁵ cells, *p* = 0.026). Dependent upon the energy density, LLLT elevates (1.0 J/cm²) or decreases (2.0 J/cm²) the potential of long-term cryopreserved PBPC for growth of CFU in vitro.

Effects of 830-nm Laser Light on Preventing Bone Loss after Ovariectomy. Ana Claudia Muniz Renno, Fernanda Mendes De Moura, Nádia Slemmer Andrade Dos Santos, Renata Passarelli Tirico, Paulo Sérgio Bossini, Nivaldo Antonio Parizotto. *Photomed Laser Surg.* 2006; 24 (5): 642-645.

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). 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/cm² (I120), and OVX irradiated at a dose of 120 J/cm² (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. 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. 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.

Evaluation of Low-Level Laser Therapy in the Treatment of Temporomandibular Disorders. Sedat Cetiner, Sevil A. Kahraman, Sule Yucetas. *Photomed Laser Surg.* 2006; 24 (5): 637-641.

The purpose of this study was to assess the effectiveness of low-level laser therapy (LLLT) in the treatment of myogenic originated temporomandibular disorders (TMD). Limited studies have demonstrated that LLLT may have a therapeutic effect on the treatment of TMD. Thirty-nine patients with myogenic TMD-associated orofacial pain, limited mandibular movements, chewing difficulties, and tender points were included in this study. Twenty-four of them were treated with LLLT for 10 sessions per day excluding weekends as test group, and 15 patients with the same protocol received placebo laser treatment as a control group. These parameters were assessed just before, just after, and 1 month after the treatment. Maximal mouth-opening improvement and reductions in pain and chewing difficulty were statistically significant in the test group when compared with the control group. Statistically significant improvements were also detected between two groups regarding reduction in the number of tender points. Based on the results of this placebo-controlled report, LLLT is an appropriate treatment for TMD and should be considered as an alternative to other methods.

Effect of Multiple Exposures of Low-Level Laser Therapy on the Cellular Responses of Wounded Human Skin Fibroblasts. Denise Hawkins, Heidi Abrahamse. *Photomed Laser Surg.* 2006; 24 (6): 705-714.

This study aimed to establish the behavior of wounded human skin fibroblasts (HSF) after heliumneon (HeNe) (632.8 nm) laser irradiation using one, two, or three exposures of different doses, namely, 2.5, 5.0, or 16.0 J/cm² on each day for 2 consecutive days. Low-level laser therapy (LLLT) is a form of phototherapy used to promote wound healing in different clinical conditions. LLLT at than adequate wavelength, intensity, and dose can accelerate tissue repair. However, there is still conflicting information about the effect of multiple irradiations on the cellular responses of wounded cells. Cellular responses to HeNe laser irradiation were evaluated by measuring changes in cell morphology, cell viability, cell proliferation, and damage caused by multiple irradiations. A single dose of 5.0 J/cm², and two or three doses of 2.5 J/cm² had a stimulatory or positive effect on wounded fibroblasts with an increase in cell migration and cell proliferation while maintaining cell viability, but without causing additional stress or damage to the cells. Multiple exposures at higher doses (16 J/cm²) caused additional stress, which reduces cell migration, cell viability, and ATP activity, and inhibits cell proliferation. The results show that the correct energy density or fluence (J/cm²) and number of exposures can stimulate cellular responses of wounded fibroblasts and promote cell migration and cell proliferation by stimulating mitochondrial activity and maintaining viability without causing additional stress or damage to the wounded cells. Results indicate that the cumulative effect of lower doses (2.5 or 5 J/cm²) determines the stimulatory effect, while multiple exposures at higher doses (16 J/cm²) result in an inhibitory effect with more damage.

Lirani-Galvao A P, Jorgetti V, Lopes Da Silva O . **Comparative Study of How Low-Level Laser Therapy and Low-Intensity Pulsed Ultrasound Affect Bone Repair in Rats.** *Photomed Laser Surg.* 2006; 24 (6): 735-740.

A study by Liriani-Galvao aimed to compare the consequences of LLLT and low-intensity pulsed ultrasound (LIPUS) on bone repair. Many studies have assessed the effects of LLLT and LIPUS on bone repair, but a comparison of them is rare. Male Wistar rats (n= 8) with tibial bone osteotomy were used. One group had the osteotomized limb treated with LLLT (GaAlAs laser, 780 nm, 30 mW, 112.5 J/cm²) and the second group with LIPUS (1.5 MHz, 30 mW/cm²), 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. In the bending test, maximum load at failure of LLLT group was significantly higher. 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. In conclusion LIPUS enhanced bone repair by promoting bone resorption in the osteotomy area, while LLLT accelerated this process through bone formation.

Comparative Study Using 685-nm and 830-nm Lasers in the Tissue Repair of Tenotomized Tendons in the Mouse. Patricia M. Carrinho, Ana Claudia Muniz Renno, Paulo Koeke, Ana Claudia Bonogne Salate, Nivaldo Antonio Parizotto, Benedito Campos Vidal. *Photomed Laser Surg.* 2006; 24 (6): 754-758.

The objective of this study was to evaluate the effects of 685- and 830-nm laser irradiations, at different fluences on the healing process of Achilles tendon (Tendon calcaneo) of mice after tenotomy. Background Data: Some authors have shown that low-level laser therapy (LLLT) is able to accelerate the healing process of tendinuos tissue after an injury, increasing fibroblast cell proliferation and collagen synthesis. However, the mechanism by which LLLT acts on healing process is not fully understood. Forty-eight male mice were divided into six experimental groups: group A, tenomized animals, treated with 685 nm laser, at the dosage of 3 J/cm²; group B, tenomized animals, treated with 685-nm laser, at the dosage of 10 J/cm²; group C, tenomized animals, treated with 830-nm laser, at dosage of 3 J/cm²; group D, tenomized animals, treated with 830-nm laser, at the dosage of 10 J/cm²; group E, injured control (placebo treatment); and group F, non-injured standard control. Animals were killed on day 13 post-tenotomy, and their tendons were surgically removed for a quantitative analysis using polarization microscopy, with the purpose of measuring collagen fibers organization through the birefringence (optical retardation [OR]). All treated groups showed higher values of OR when compared to injured control group. The best organization and aggregation of the collagen bundles were shown by the animals of group A (685 nm, 3 J/cm²), followed by the animals of group C and B, and finally, the animals of group D. All wavelengths and fluences used in this study were efficient at accelerating the healing process of Achilles tendon post-tenotomy, particularly after the 685-nm laser irradiation, at 3 J/cm². It suggests the existence of wavelength tissue specificity and dose dependency. Further studies are required to investigate the physiological mechanisms responsible for the effects of laser on tendinuos repair.

Desmettre T, Maurage C A, Mordon S. Transpupillary thermotherapy (TTT) with short duration laser exposures induce heat shock protein (HSP) hyperexpression on choroidoretinal layers. *Lasers Surg Med.* 2003; 33 (2): 102-107.

The study by Desmettre was performed to assess a choroidal heat shock protein hyperexpression after transpupillary thermotherapy (TTT) performed with exposures shorter than 60 seconds. Male pigmented rabbits were anesthetized and TTT was performed on their right eye with a 810 nm laser (spot size: 1.3 mm). Three exposure durations (60, 30, or 15 seconds) were used with three ranges of power for each duration ("high," "mild," or "low"). A

series of laser impacts was delivered to the posterior pole of the retina. Left eyes were used as controls. Twenty-four hours after laser irradiation, the animals were killed and histological study was performed on chorioretinal layers. Tissue samples were fixed in formalin and embedded in paraffin. A monoclonal antibody was used to detect Hsp70 immunoreactivity followed by a biotinylated goat anti-mouse antibody revealed by the avidin-biotin complex and the AEC chromogen. Retinal structures were further identified by HES coloration. During the experiments, the laser spots were not visible except for the strongest "high" powers for each exposure duration, where a whitening was discernable at the end of the laser exposures. A strong HSP70 immunoreactivity was detected in choroidal, non-pigmented cells for laser exposures lasting 60, 30, or 15 seconds with "mild" laser powers. On the contrary, rare HSP hyperexpression was detected with "high" or "low" laser powers lasting 60, 30, or 15 seconds. No HSP-70 immunoreactivity was detected on control eyes nor outside of the irradiated zones of treated eyes. Transpupillary laser irradiation lasting 15, 30, or 60 seconds induces an hyperexpression of HSP on choroidal layers.

Parkinson's disease:

[Kommelkova L V](#), [Vitreshchak T V](#), [Zhirnova I G](#), [Poleshchuk V V](#) et al. [**Biochemical and immunological induces of the blood in Parkinson's disease and their correction with the help of laser therapy**]. [Patol Fiziol Eksp Ter](#). 2004; (1): 15-18.

Kommelkova studied the influence of LLLT on the course of Parkinson's disease in 70 patients. This influence appeared adaptogenic both in the group with elevated and low MAO B and Cu/Zn SOD activity. LLLT resulted in reduction of the neurological deficit, normalization of the activity of MAO B, Cu/Zn-SOD and immune indices. There was a correlation between humoral immunity and activity of the antioxidant enzymes (SOD, catalase).

[Vitreshchak T V](#), [Mikhailov V V](#), [Piradov M A](#), [Poleshchuk V V](#), et al. **Laser modification of the blood in vitro and in vivo in patients with Parkinson's disease**. [Bull Exp Biol Med](#). 2003; 135 (5): 430-432.

The effect of He-Ne laser on the activity of MAO B, Cu/Zn-SOD, Mn-SOD, and catalase in blood cells from patients with Parkinson's disease was studied in vivo and in vitro by Vitreshchak. The effects of intravenous in vivo irradiation (intravenous laser therapy) were more pronounced than those observed in similar in vitro experiments.

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