Orthodontics

Lasers Med Sci. 2007 Mar 3; [Epub ahead of print] Effects of two types of low-level laser wave lengths (850 and 630 nm) on the orthodontic tooth movements in rabbits. Seifi M, Shafeei HA, Daneshdoost S, Mir M. Faculty of Dentistry, Orthodontics Department, Shaheed Beheshti University of Medical Science, Evin, Tehran, Iran, seifimassoud@gmail.com. The effects of low-level lasers on bone cellular activity, bone structures, bone healing, fibroblasts activity and inflammation process have already been investigated. Considering orthodontic tooth movement, which is a complicated inflammatory process involving simultaneous bone apposition and resorption, the aim of this controlled study is to investigate the quantitative effects of a pulsed 850 nm laser (Optodan) and a continuous 630 nm laser (KLO3) on the orthodontic tooth movement in rabbits. This experimental study was conducted on 18 male albino rabbits divided into three equal groups of control, Optodan and KLO3. In all the groups, NiTi-closed coil springs were used on the first mandibular molars with 4-oz tension. The control group was not irradiated by laser, but the teeth in the laser groups were irradiated 9 days according to the periodontal therapeutic protocols. After 16 days, samples were sacrificed. The distance between the distal surface of the first molar and the mesial surface of the second molar was measured with 0.05-mm accuracy. The data were subjected to the statistical tests of Kolmogrov Smirnov and variance analysis. The mean orthodontic tooth movements of the first mandibular molars were 1.7 +/- 0.16 mm in control group, 0.69 +/- 0.16 mm in Optodan group and 0.86 +/- 0.13 mm in KLO3 group. There were statistically significant difference between the control and the two other laser-irradiated groups (P < 0.001). The findings of the present study imply that the amounts of orthodontic tooth movement, after low-level laser therapy, are diminished. It could not be concluded that any low-level laser will reduce the speed of teeth movement in orthodontic treatments, and further studies with less or more energies may show different results.

Hua Xi Kou Qiang Yi Xue Za Zhi. 2001 Oct;19(5):290-3. [Effects of low energy laser on tooth movement and remodeling of alveolar bone in rabbits] [Article in Chinese] Sun X, Zhu X, Xu C, Ye N, Zhu H. School of Stomatolog, Jilin University. OBJECTIVE: The aim of this study was to investigate effects of low energy laser on the experimental tooth movement and the remodeling of alveolar bone in rabbits. METHODS: A total of 42 white rabbits were chosen and randomized into one control group and six experimental groups, with 6 rabbits in each group. After anesthesia with 2% pentobaritone sodium, orthodontic appliances consisting of a coil spring connected bilaterally the upper first molar with the upper incisor by using a ligature wire. The force exerted at the time of insertion was approximately 80 g. The left side served as the control side, and the right side was the experimental side treated by receiving irradiation of low energy laser. The treatment periods of different groups lasted separately for 1, 3, 5, 7, 14, 21 days respectively. The displacement extent of teeth was measured by employing the computer image analyzing system. The results were analyzed statistically. Through HE staining, the histomorphological character of teeth was measured. The results showed statistically significant differences between the control and the laser-irradiated groups (P < 0.001). The findings of the present study imply that the amounts of orthodontic tooth movement, after low-level laser therapy, are diminished. It could not be concluded that any low-level laser will reduce the speed of teeth movement in orthodontic treatments, and further studies with less or more energies may show different results.
tissue around first molar was also investigated, and numbers of osteoclasts were counted. RESULTS: The displacement extent of teeth on the experimental side, which was irradiated by low energy laser, was more obvious than that of the normal control side. The difference was statistically significant 1, 3, 14, 21 days after the beginning of the treatment. Through histological observation under a light microscope, the osteoclasts and osteoblasts on the experimental side remained more active than those of the control side. There is significant difference in amount of osteoclasts between the experimental and the control sides, 3, 5 or 7 days after the treatment (P < 0.01, P < 0.05). CONCLUSION: The irradiation of low energy laser promote tooth movement and remodeling of alveolar bone.

Lasers Surg Med. 2004;35(2):117-20. Effects of low-intensity laser therapy on the orthodontic movement velocity of human teeth: a preliminary study. Cruz DR, Kohara EK, Ribeiro MS, Wetter NU. Centro de Lasers e Aplicacoes, Instituto de Pesquisas Energeticas e Nucleares--IPEN, Sao Paulo, Brazil. BACKGROUND AND OBJECTIVES: Low-intensity laser therapy (LILT) has been studied in many fields of dentistry, but to our knowledge, this is the first time that its effects on orthodontic movement velocity in humans are investigated. STUDY DESIGN/PATIENTS AND METHODS: Eleven patients were recruited for this 2-month study. One half of the upper arcade was considered control group (CG) and received mechanical activation of the canine teeth every 30 days. The opposite half received the same mechanical activation and was also irradiated with a diode laser emitting light at 780 nm, during 10 seconds at 20 mW, 5 J/cm2, on 4 days of each month. Data of the biometrical progress of both groups were statistically compared. RESULTS: All patients showed significant higher acceleration of the retraction of canines on the side treated with LILT when compared to the control. CONCLUSIONS: Our findings suggest that LILT does accelerate human teeth movement and could therefore considerably shorten the whole treatment duration.

Orthod Craniofac Res. 2006 Feb;9(1):38-43. Effects of low-level laser therapy on the rate of orthodontic tooth movement. Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Morthai Dental Clinic, Hatyai, Songkhla, Thailand. iwanwisa@yahoo.com OBJECTIVES: To test the hypothesis that mechanical forces combined with low-level laser therapy stimulate the rate of orthodontic tooth movement. STUDY DESIGN: This study was a double blind, randomized placebo/control matched pairs clinical trial to test the efficacy of GaAlAs low-level laser therapy (LLLT) on 12 young adult patients who required retraction of maxillary canines into first premolar extraction spaces using tension coil springs with fixed edgewise appliance. LLLT was applied on the mucosa buccally, distally and palatally to the canine on the test side and using a pseudo-application on the placebo side. Dental impressions and casts were made at the commencement of the trial and at the end of the first, second and third months after starting the trial. Measurement of tooth movements was made on each stage model using a stereo microscope. RESULTS: There was no significant difference of means of the canine distal movement between the LLLT side and the placebo side for any time periods (p-value = 0.77). CONCLUSION: The energy density of LLLT (GaAlAs) at the surface level in this
study (25 J/cm(2)) was probably too low to express either stimulatory effect or inhibitory effect on the rate of orthodontic tooth movement.

Photomed Laser Surg. 2006 Apr;24(2):192-6. **Photoradiation and orthodontic movement: experimental study with canines.** Goullart CS, Nour PR, Mouramartins L, Garbin IU, de Fatima Zanirato Lizarelli R. University of the South of Santa Catarina (UNISUL), Tubarao, Brazil. OBJECTIVE: 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. METHODS: 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/cm(2) 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/cm(2). 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/cm(2) dosage accelerated orthodontic movement during the first observation period, from 0 to 21 days (p < 0.05), whereas the 35.0 J/cm(2) 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). CONCLUSION: The results suggests that photoradiation may accelerate orthodontic movement at a dosage of 5.25 J/cm(2), whereas a higher dosage, 35.0 J/cm(2), may retard it.

Shanghai Kou Qiang Yi Xue. 2006 Feb;15(1):52-7. **[Effects of He-Ne laser irradiation on the expression of transforming growth factor beta1 during experimental tooth movement in rabbits]** [Article in Chinese] Sun XH, Wang R, Zhang XY. Department of Orthodontics, School of Stomatology, Jilin University, Changchun 130041, Jilin Province, China. xinhuasun8@163.com PURPOSE: The purpose of this study is to investigate the effect of He-Ne laser irradiation on the expression of transforming growth factor beta1 (TGF-beta1) during experimental tooth movement in rabbits. METHODS: Thirty-five rabbits were used in this study. The animals were randomly divided into 7 groups equally: normal group and experimental (1, 3, 5, 7, 14, 21 days) groups, 5 rabbits in each group. An orthodontic appliance, consisting of a coil spring was ligated to the bilateral first maxillary molar and connected to an orthodontic wire ligated onto the incisors, and exerting a force of approximately 80 g. The left side was used as control, and the right side was designed as irradiated side. The animals from each group were sacrificed at the time discontinued. The histological sections were proceeded with immunohistochemical staining of TGF-beta1. Then it was analyzed by Computer Image Analyzing System and statistically processed with SPSS10.0 software package for the paired Student's t test. RESULTS: The expression of TGF-beta1 was demonstrated in the area of tension and pressure of periodontium tissue in both of the irradiated and control sides. The TGF-beta1 staining in the pressure area of the irradiated side decreased significantly at 1 day (P<0.05) compared with the control side. TGF-beta1 staining increased significantly at 3 to 5 days in the pressure area (P<0.05). But in the tension area of the irradiated side, TGF-beta1 staining were significantly increased at 3 to 7 days (P<0.05). The peak value of the area of tension and pressure both appeared at the same time of the 5th day. CONCLUSION: It is concluded that He-Ne laser irradiation
can effectively accelerate the expression of TGF-beta1 in periodontal tissue of rabbits during experimental tooth movement.

**Mucositis**


INTRODUCTION: Oral mucositis (OM) is a significant early complication of hematopoietic cell transplantation (HCT). This phase III randomized double-blind placebo-controlled study was designed to compare the ability of 2 different low level GaAlAs diode lasers (650 nm and 780 nm) to prevent oral mucositis in HCT patients conditioned with chemotherapy or chemoradiotherapy. MATERIALS AND METHODS: Seventy patients were enrolled and randomized into 1 of 3 treatment groups: 650 nm laser, 780 nm laser or placebo. All active laser treatment patients received daily direct laser treatment to the lower labial mucosa, right and left buccal mucosa, lateral and ventral surfaces of the tongue, and floor of mouth with energy densities of 2 J/cm(2). Study treatment began on the first day of conditioning and continued through day +2 post HCT. Mucositis and oral pain was measured on days 0, 4, 7, 11, 14, 18, and 21 post HCT. RESULTS: The 650 nm wavelength reduced the severity of oral mucositis and pain scores. Low level laser therapy was well-tolerated and no adverse events were noted. DISCUSSION: While these results are encouraging, further study is needed to truly establish the efficacy of this mucositis prevention strategy. Future research needs to determine the effects of modification of laser parameters (e.g., wavelength, fluence, repetition rate of energy delivery, etc.) on the effectiveness of LLE laser to prevent OM.

Blood. 2007 Mar 1;109(5):2250-5. Epub 2006 Oct 19. Low-power laser in the prevention of induced oral mucositis in bone marrow transplantation patients: a randomized trial. Antunes HS, de Azevedo AM, da Silva Bouzas LF, Adao CA, Pinheiro CT, Maybe R, Pinheiro LH, Azevedo R, D’Aiuto de Matos V, Rodrigues PC, Small IA, Zangaro RA, Ferreira CG. Section of Dentistry, Instituto Nacional de Cancer (INCA), Rio de Janeiro, Brazil. hspindola@inca.gov.br We investigated the clinical effects of low-power laser therapy (LPLT) on prevention and reduction of severity of conditioning-induced oral mucositis (OM) for hematopoietic stem cell transplantation (HSCT). We randomized 38 patients who underwent autologous (AT) or allogeneic (AL) HSCT. A diode InGaAlP was used, emitting light at 660 nm, 50 mW, and 4 J/cm², measured at the fiberoptic end with 0.196 cm² of section area. The evaluation of OM was done using the Oral Mucositis Assessment Scale (OMAS) and the World Health Organization (WHO) scale. In the LPLT group, 94.7% of patients had an OM grade (WHO) lower than or equal to grade 2, including 63.2% with grade 0 and 1, whereas in the controls group, 31.5% of patients had an OM grade lower than or equal to grade 2 (P < .001). Remarkably, the hazard ratio (HR) for grades 2, 3, and 4 OM was 0.41 (range, 0.22-0.75; P = .002) and for grades 3 and 4 it was 0.07 (range,
0.11-0.53; P < .001). Using OMAS by the calculation of ulcerous area, 5.3% of the laser group presented with ulcers of 9.1 cm² to 18 cm², whereas 73.6% of the control group presented with ulcers from 9.1 cm² to 18 cm² (P = .003). Our results indicate that the use of upfront LPLT in patients who have undergone HSCT is a powerful instrument in reducing the incidence of OM and is now standard in our center.

Oral Health Prev Dent. 2007;5(1):63-71. Macroscopic and microscopic effects of GaAlAs diode laser and dexamethasone therapies on oral mucositis induced by fluorouracil in rats. Lara RN, da Guerra EN, de Melo NS. Oral Medicine, Department of Dentistry, School of Health Science, University of Brasilia, Brasilia, Brazil. nemetala@unb.br PURPOSE: To present an animal model for mucositis induced by fluorouracil in rats, and test two therapeutic options, the GaAlAs laser and topical dexamethasone, analysing them with regard to the quality and quantity of tissue alterations and comparing them with the phases of mucositis. MATERIALS AND METHODS: Forty-five Wistar rats (250 g) were treated with fluorouracil (60 mg/kg) and, in order to mimic the clinical effect of chronic irritation, the palatal mucosa was irritated by superficial scratching with an 18-gauge needle. When all of the rats presented oral ulcers of mucositis, they were randomly allocated to one of three groups: group I was treated with laser (GaAlAs); group II was treated with topical dexamethasone, and group III was not treated. Excisional biopsies of the palatal mucosa were then performed, and the rats were killed. Tissue sections were stained with haematoxylin and eosin for morphological analyses, and with toluidine blue for mast-cell counts. RESULTS: Group I specimens showed higher prevalence of ulcers, bacterial biofilm, necrosis and vascularisation, while group II specimens showed higher prevalence of granulation tissue formation. There were no significant statistical differences in the numbers of mast cells and epithelial thickness between groups. CONCLUSION: For the present model of mucositis, rats with palatal mucositis treated with laser (GaAlAs) showed characteristics compatible with the ulcerative phase of oral mucositis, and rats treated with topical dexamethasone showed characteristics compatible with the healing phase of mucositis. Topical dexamethasone was more efficient in the treatment of rats' oral mucositis than the laser.

Indian J Med Res. 2006 Oct;124(4):399-402. Comment in: Indian J Med Res. 2006 Oct;124(4):375-8. Effect of low level helium-neon (He-Ne) laser therapy in the prevention & treatment of radiation induced mucositis in head & neck cancer patients. Arun Maiya G, Sagar MS, Fernandes D. Departments of Physiotherapy, Manipal College of Allied Health Sciences, Kasturba Medical College, MAHE University, Manipal, India. ajmaiya@yahoo.com BACKGROUND & OBJECTIVES: Oral mucositis is a common debilitating complication of radiotherapy occurring in about 60 per cent of cancer patients. Considerable buccal toxicity of radiotherapy or chemotherapy in cancer patients to become discouraged and can affect their quality of life. In addition, such toxicity can alter the treatment plan. At present, there is no clinically appropriate prophylaxis efficacious antidote for mucositis. The low level laser (LEL) appears to be a simple, non-traumatic technique for the prevention and treatment of radiation induced mucositis. Therefore the present study was carried out to find out the effect of low-level helium-neon (He-Ne) laser in the prevention and treatment of radiation induced mucositis in head and neck cancer patients. METHODS: The patients with carcinoma of oral cavity with stages II-IV a being
uniformly treated with curative total tumour dose of 66 Gy in 33 fractions over 6 wk were selected for the study. The patients were divided based on computer generated randomization into laser (study group) and control groups with 25 patients in each group. Both study and control groups were comparable in terms of site of the lesion, stage of the cancer and histology. The study group patients were treated with He-Ne laser (wavelength 632.8 nm and output of 10 mW) and control group patients were given oral analgesics, local application of anaesthetics, 0.9 per cent saline and povidine wash during the course of radiotherapy. RESULTS: All patients tolerated the laser treatment without any adverse effect or reactions. The result showed a significant difference in pain and mucositis (P<0.001) between the two groups. At the end of radiotherapy (after 6 wk) mean pain score and mucositis grade were significantly lower (P<0.001) in the study group compared to control. INTERPRETATION & CONCLUSION: The low-level He-Ne laser therapy during the radiotherapy treatment was found to be effective in preventing and treating the mucositis in head and neck cancer patients. Further studies need to be done on a larger sample to find the mechanism.

Cancer J. 2002 May-Jun;8(3):247-54. Comment in: Cancer J. 2002 May-Jun;8(3):236-8. Pilot study of laser effects on oral mucositis in patients receiving chemotherapy. Wong SF, Wilder-Smith P. Western University of Health Sciences, College of Pharmacy, Division of Hematology/Oncology, Pomona, California 91766, USA. PURPOSE: The purpose of this study was to examine the effectiveness of laser therapy in the prevention and/or healing of chemotherapy-induced oral mucositis lesions. This study also evaluated the ease and feasibility of the laser therapy and the impact of the treatment on improving the patient's quality of life. PATIENTS AND METHODS: Fifteen patients with an episode of prior chemotherapy-induced grade 3 or 4 mucositis with 5-fluorouracil continuous infusion consented to participate in this study. All patients were provided with standardized mouth care instructions at the initiation of chemotherapy treatments. Enrolled patients received laser therapy treatments 24 hours before the chemotherapy and then recommenced weekly with evenly distributed exposure to the standardized designated areas by one operator during the entire cycle of chemotherapy at the same doses until the mucositis resolved or the chemotherapy cycle was completed. Introral perfusion was measured by laser Doppler technology. Patients were assessed for response to laser therapy according to standardized mucositis grading criteria by evaluating development of lesions, extent and duration of lesions, and time to healing. The effect of laser therapy on ability to continue planned chemotherapy, the reduction in dose, delays, and ability to maintain planned dose intensity were assessed. The impact of laser therapy on pain control was evaluated using the visual analogue score. A quality-of-life survey was completed by each patient at the initiation of chemotherapy and then weekly throughout the chemotherapy. RESULTS: Eleven of 15 patients experienced grade 0 mucositis, three patients experienced grade 1 to 2 mucositis, and one patient experienced grade 3 to 4 mucositis. Fourteen patients completed the laser therapy as planned, and none of the patients withdrew from the laser therapy treatments because of noncompliance. One patient continued to experience grade 4 mucositis that necessitated an interruption in the planned chemotherapy regimen and, consequently, the laser treatment. Patients tolerated the laser therapy very well and did not report any increased discomfort. No significant changes in perfusion were observed as a result of laser therapy. DISCUSSION: In this pilot study, laser therapy significantly reduced the incidence
and the severity of mucositis in chemotherapy patients. The laser therapy does not appear to promote wound healing by affecting the intraoral perfusion, as assessed by Doppler measurements. The mechanisms involved in the mediating of the observed effects remain unknown at this time. Continued research is warranted to determine the optimal laser wavelength and parameters.

**Dentistry**

Arch Oral Biol. 2007 May 5; [Epub ahead of print] **Effects of low-power red laser on dentine-pulp interface after cavity preparation. An ultrastructural study.** Godoy BM, Arana-Chavez VE, Nunez SC, Ribeiro MS. Professional Master Lasers in Dentistry, IPEN-CNEN/SP, Sao Paulo, Brazil. OBJECTIVE: Studies on the influence of low-power red laser on the repair of dental structures are very scarce. This study investigated the effects of the laser therapy on the ultrastructure of the dentine-pulp interface after conservative class I cavity preparation. DESIGN: Two female volunteers with 8 premolars indicated for extraction for orthodontic reasons were recruited. Class I cavities were prepared and the teeth were randomly divided into two groups. The first group received treatment with a GaAlAs laser, lambda=660nm, power of 30mW and energy dose of 2J/cm², directly and perpendicularly into the cavity in a single visit. After the irradiation, the cavities were filled with composite resin. The second group received the same treatment, except by the laser therapy. RESULTS: Twenty-eight days post-preparation, the teeth were extracted and processed for transmission electron microscopy analysis. Two sound teeth, without cavity preparation, were also studied. The irradiated group presented odontoblast process and all posterior occurrences of odontoblastic to odontoblast in higher contact with the extracellular matrix and the collagen fibrils and all posterior occurrences of fibres to fibrils appeared more aggregated and organised than those of control group. These results were also observed in the healthy teeth. CONCLUSION: These findings suggest that laser irradiation accelerates the recovery of the dental structures involved in the cavity preparation at the predentine region.

Lasers Med Sci. 2007 Mar 3; [Epub ahead of print] **The importance of coherence length in laser phototherapy of gingival inflammation—a pilot study.** Qadri T, Bohdanecka P, Tuner J, Miranda L, Altamash M, Gustafsson A. Department of Periodontology, Institute of Odontology, Karolinska Institutet, Huddinge, Sweden. The aim of this study was to investigate if coherence length is of importance in laser phototherapy. Twenty patients with moderate periodontitis were selected. After oral hygiene instructions, scaling and root planing (SRP), one side of the upper jaw was randomly selected for HeNe (632.8 nm, 3 mW) or InGaAlP (650 nm, 3 mW) laser irradiation. One week after SRP, the following parameters were measured: pocket depth, gingival index, plaque index, gingival crevicular fluid volume, matrix metalloproteinase (MMP-8), interleukin (IL-8) and subgingival microflora. The irradiation (180 s per point, energy 0.54 J) was then performed once a week for 6 weeks. At the follow up examination, all clinical parameters had improved significantly in both groups. A more pronounced decrease of clinical inflammation was observed after HeNe treatment. MMP-8 levels were considerably reduced on the HeNe side, while there was no difference for IL-8 or microflora. Coherence length appears to be an important factor in laser phototherapy.

Purpose: Low level laser therapy (LLLT) has been shown to modulate acute inflammatory processes in animal studies. The purpose of this study is to investigate if these findings can be translated into clinical situations like the classical model of third molar extraction.

Materials and Methods: Systematic review of randomized controlled trials (RCT) with meta-analysis of pain (continuous data) within 0-24 hours after surgery. Methodological assessments of trials were made according to Jadad’s scale. Subgroup analyses were planned for wavelength, irradiance and energy dose.

Results: The literature search yielded 9 RCTs, of which 8 RCTs with acceptable quality and a total of 658 patients reported pain data within 0-24 hours after surgery. There was a significant pain reduction from all 8 RCTs combined at 7.8 [95% CI: 4.7 to 11.0] mm measured on a 100 mm VAS. Subgroup analysis revealed no significant interaction between effect and wavelength (red/infrared) or irradiance. But in 3 trials administering low energy doses (0.37-0.96 Joules), the overall effect was not significantly different from placebo at 1.2 [95% CI: -5.6 to 8.0] mm on VAS, while high energy doses (6 - 7.5 Joules) in 5 RCTs induced significant pain relief at 9.6 [95% CI: 6.5 to 13.1] mm on VAS. In one RCT, there was no significant difference between high dose LLLT and the anti-inflammatory drug diclofenac.

Conclusion: LLLT with red/infrared wavelengths and energy doses of 6 -7.5 Joules, is effective in reducing acute inflammatory pain. Future research should focus on determining optimal doses.


Experimental data are presented, validating the use of low-intensity laser irradiation at a wavelength of 633 nm for the treatment of chronic recurrent herpetic stomatitis. Clinical trials were carried out in 167 children. Laser exposure with the optimal stimulating parameters was found to be an effective means for the treatment of children suffering from this condition.

Lasers Surg Med. 2007 Apr;39(4):365-72. Cultured epithelial cells response to phototherapy with low intensity laser. Eduardo FP, Mehnert DU, Monezi TA, Zezell DM, Schubert MM, Eduardo CP, Marques MM. BACKGROUND AND OBJECTIVES: Little is known about the intracellular response of epithelial cells to phototherapy. The aim of this in vitro study was to analyze the effect of phototherapy with low-energy lasers with different wavelengths and powers on cultured epithelial cell growth under different nutritional conditions. STUDY DESIGN/MATERIALS AND METHODS: Epithelial cell cultures (Vero cell line) grown in nutritional deficit in culture medium supplemented with 2% fetal bovine serum (FBS) were irradiated
with low-energy laser from one to three times with a GaAlAs laser (660 nm) and InGaAlP (780 nm), 40 and 70 mW, respectively, with 3 or 5 J/cm(2). Cell growth was indirectly assessed by measuring the cell mitochondrial activity. RESULTS: Nonirradiated cell cultures grown in nutritional regular medium supplemented with 10% FBS produced higher cell growth than all cultures grown in nutritional deficit irradiated or not. The overall cell growth of cultures grown under nutritionally deficit conditions was significantly improved especially when irradiated with 780 nm for three times. CONCLUSIONS: Phototherapy with the laser parameters tested increases epithelial cell growth rate for cells stressed by growth under nutritionally deficient states. This cell growth improvement is directly proportional to the number of irradiations; however, was not enough to reach the full cell growth potential rate of Vero epithelial cell line observed when growing under nutritional regular condition.

Lasers Med Sci. 2006 Jul;21(2):86-9. Epub 2006 May 13. **Influence of different power densities of LILT on cultured human fibroblast growth : a pilot study.** Azevedo LH, de Paula Eduardo F, Moreira MS, de Paula Eduardo C, Marques MM. Department of Stomatology, School of Dentistry, University of Sao Paulo, Sao Paulo, Brazil. The aim of this in vitro study was to analyze the influence of different power densities of low-intensity laser therapy (LILT) on the biomodulation of human gingival fibroblasts. The cells were cultured in nutritional deficit. Laser irradiation was carried out with a GaAlAs diode laser (lambda-660 nm, 2 J/cm2). The irradiation was done twice with 12-h interval using the punctual technique, at continuous mode and in contact. The experimental groups were: I, control, nonirradiated; II, power of 10 mW and intensity approximately or equal to 142.85 mW/cm2; III, 29 mW and 428.57 mW/cm2. Growth curves were obtained by using the trypan blue dye exclusion assay. The cell growth of the irradiated groups was significantly higher than control group (P<or=0.05). The cultures of Group II presented cell growth superior to that of Group III. Based on the conditions of this study, we concluded that the power density influences cell growth in an inversely proportional manner.

**Nerve recovery**

Lasers Med Sci. 2004;19(1):57-65. Epub 2004 Jul 30. **Low-power laser biostimulation enhances nerve repair after end-to-side neurorrhaphy: a double-blind randomized study in the rat median nerve model.** Gigo-Benato D, Geuna S, de Castro Rodrigues A, Tos P, Fornaro M, Boux E, Battiston B, Giacobini-Robecchi MG. Previous studies have shown that low-power laser biostimulation (lasertherapy) promotes posttraumatic nerve regeneration. The objective of the present study was to investigate the effects of postoperative lasertherapy on nerve regeneration after end-to-side neurorrhaphy, an innovative technique for peripheral nerve repair. After complete transection, the left median nerve was repaired by end-to-side neurorrhaphy on the ulnar "donor" nerve. The animals were then divided into four groups: one placebo group, and three laser-treated groups that received lasertherapy three times a week for 3 weeks starting from postoperative day 1. Three different types of laser emission were used: continuous (808 nm), pulsed (905 nm), and a combination of the two. Functional testing was carried out every 2 weeks after surgery by means of the grasping test. At the time of withdrawal 16 weeks postoperatively, muscle mass
recovery was assessed by weighing the muscles innervated by the median nerve. Finally, the repaired nerves were withdrawn, embedded in resin and analyzed by light and electron microscopy. Results showed that laser biostimulation induces: (1) a statistically significant faster recovery of the lesioned function; (2) a statistically significant faster recovery of muscle mass; (3) a statistically significant faster myelination of the regenerated nerve fibers. From comparison of the three different types of laser emissions, it turned out that the best functional outcome was obtained by means of pulsed-continuous-combined laser biostimulation. Taken together, the results of the present study confirm previous experimental data on the effectiveness of lasertherapy for the promotion of peripheral nerve regeneration and suggest that early postoperative lasertherapy should be considered as a very promising physiotherapeutic tool for rehabilitation after end-to-side neurorrhaphy.

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The purpose of this study was to determine whether low-power pulsed laser irradiation could affect the regeneration of a 10-mm gap of rat sciatic nerve created between the proximal and distal nerve stumps, which were sutured into silicone rubber tubes. After 8 weeks of recovery, pulsed laser-irradiated groups at frequencies of 5 kHz and 20 kHz both had significantly lower success percentages of regeneration (50% and 44%, respectively) compared to sham-irradiated controls (100%). In addition, qualitative and quantitative histology of the regenerated nerves revealed a less mature ultrastructural organization with a smaller cross-sectional area and a lower number of myelinated axons in both pulsed laser-irradiated groups than in controls. These results suggest that pulsed laser irradiation could elicit suppressing effects on regenerating nerves.

Wound healing

BACKGROUND AND OBJECTIVES: In this study, the ability of photostimulation to promote healing of impaired wounds was investigated using a Ga-As laser in rats with experimental diabetes and the results were compared with previously reported findings of the effects of a He-Ne laser on the repair of healing-impaired diabetic rat wounds 1. STUDY DESIGN/MATERIALS AND METHODS: Diabetes was induced in male rats by streptozotocin injection following which two full thickness punch wounds of 6-mm diameter were created in the skin, one on either side of the spine of each animal. The left wound of each animal was treated with infrared radiation at 904 nm produced by a Ga-As laser at an energy density of 1.0 J/cm(2). The right wound of each animal served as the control. The wounds were treated with a laser 5 days a week for 3 weeks. Following animal sacrifice, the strips of skin containing the wound sites were collected and analyzed. RESULTS: The results from the biomechanical analysis indicated that the Ga-As laser used in this study significantly increased wound tensile strain and toughness compared to the control wounds. Marginal increases in wound tensile strength (9%) and stress (7%) were observed in the Ga-As
laser-treated wounds compared to the controls. No significant changes were found in Young's modulus and energy absorption capacity between the control and laser-treated wounds. Analysis of wound collagen revealed a significant increase in total collagen (14%), salt soluble collagen (31%), acid soluble (14%), and insoluble collagen (50%) with simultaneous decrease in pepsin soluble collagen (19%) in the Ga-As laser-treated wounds compared to controls. Comparisons of these results with the earlier findings revealed that the He-Ne laser appears to be superior to the Ga-As laser, at the parameters of treatment tested, in promoting the wound healing in diabetic rats. CONCLUSIONS: The differences in stimulatory effects noted between the He-Ne and Ga-As lasers suggest that the photochemical response the cells for each laser may depend on the wavelength and coherent properties of the electromagnetic radiation.


BACKGROUND AND OBJECTIVE: This study aimed to evaluate a 815-nm diode-laser system to assist wound closure to accelerate and improve healing process.

STUDY DESIGN/MATERIALS AND METHODS: A total of 25 male hairless rats (mutant OFA Sprague-Dawley rats, IFFA-CREDO, L'Arbresle, France) with four dorsal skin incisions were used for the study. For each wound, the good apposition of the edges was obtained with buried absorbable suture. In the laser group, the laser beam was applied spot by spot through a transparent adhesive dressing along two incisions with the following parameters: 1.5 W; 3 seconds; spot diameter, 2 mm; fluence, 145 J/cm(2). Both control wounds were closed with conventional suture techniques. The duration of the closure procedure was noted for each group. Clinical examination, histologic study, and measurement of tensile strength were performed at 3, 7, 15, and 21 days after surgery. Determination of activation of heat shock protein 70 (Hsp70) through immunocytochemistry was performed at days 1 and 7.

RESULTS: LASC was 4 times faster to process than conventional suture: 1 minute 49 +/- 20.6 seconds vs. 7 minutes 26 +/- 62.2 seconds. In the laser group, healing was accelerated resulting in a more indiscernible scar than in the control groups. Histologic aspect was better with earlier continuous epidermis and dermis and a thinner resulting scar. Tensile strength was 30 to 58% greater than in control groups at 7 and 15 days (P < 0.001). Expression of Hsp70 was markedly induced in skin structures examined after laser exposure. CONCLUSIONS: This study shows the ability of the 815-nm diode-laser system to assist wound closure leading to an acceleration and an improvement of wound healing with indiscernible resulting scar. The mechanisms of this phenomenon are still unclear but further investigations are in progress to attempt to explain them.


Clinical observations have suggested that low-energy lasers might promote wound healing. Evidence suggests that He-Ne laser irradiation induces an increase in the rate of keratinocyte migration and proliferation as compared with nonirradiated controls in vitro. This study sought to determine whether He-Ne laser could induce cytokine production in cultured keratinocytes. The results revealed (i) a significant increase in interleukin-1 alpha and interleukin-8 production and their respective mRNA
expression in He-Ne laser-treated groups as compared with nonirradiated controls, and (ii) under 1.5 joules/cm² irradiation, this stimulating effect of He-Ne laser treatment is concentration-dependent. Because interleukin-1 alpha induces keratinocyte migration, this finding may partially explain the stimulatory effects on the motility of keratinocytes. As both interleukin-1 alpha and interleukin-8 provoke proliferation of keratinocytes, it is not unreasonable to propose that these two cytokines play a profound role in the enhancement of keratinocyte proliferation as a result of He-Ne laser irradiation. Our findings provide further evidence of enhanced wound healing at the cellular and molecular level as a result of the He-Ne laser.

Cytokine production after helium-neon laser irradiation in cultures of human peripheral blood mononuclear cells. Funk JO, Kruse A, Kirchner H.

The effects of laser light on the immune system have not been extensively characterized. Low-power laser sources, such as the helium-neon (He-Ne) laser with a wavelength of 632.8 nm, have been found to produce photobiological effects with evidence of interference with immunological functions. We have investigated the effects of He-Ne laser irradiation on Ficoll-Hypaque-isolated human peripheral blood mononuclear cells (PBMC). Cultured cells were irradiated for various times at two selected intensities and then stimulated with different mitogens. The rate of incorporation of 3H-thymidine into the DNA of stimulated cells decreased with increasing energy density. The levels of interleukin-1 alpha (IL-1 alpha), interleukin-2 (IL-2), tumour necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) in supernatants of the cultures were determined (irradiated either before or after stimulation). When stimulating cells after irradiation, significantly increased levels of all cytokines were detected after 30 min of irradiation (18.9 J cm⁻²), whereas after 60 min of irradiation (37.8 J cm⁻²) cytokine levels were found to be significantly decreased.

Helium-neon laser irradiation induces effects on cytokine production at the protein and the mRNA level. Funk JO, Kruse A, Neustock P, Kirchner H.

The construction of an in vitro model allowed an investigation of the basic functions of immunocompetent cells after laser irradiation. Among low-energy laser sources, the helium-neon (He-Ne) laser, with a wavelength of 632.8 nm, has often been found to produce photobiological effects including evidence of interference with immunological functions. Previous experiments revealed an influence of He-Ne laser irradiation on concentrations of interleukin-1 alpha (IL-1 alpha), tumor necrosis factor-alpha (TNF-alpha), interleukin-2 (IL-2), and interferon-gamma (IFN-gamma) in supernatants of cultures of human peripheral blood mononuclear cells (PBMC) with increased cytokine concentrations after irradiation of 18.9 J/cm² and decreased concentrations after irradiation of 37.8 J/cm². Now, the mechanisms involved were studied. Results showed that cytokine production of cells stimulated with phytohemagglutinin (PHA), concanavalin A (Con A), or bacterial lipopolysaccharide (LPS) was altered significantly after laser irradiation but not after stimulation with staphylococcus aureus enterotoxin B (SEB). In situ hybridization of IFN-gamma mRNA producing PBMC revealed that the number of positive cells was modulated similarly. The results were identical in cultures of enriched monocytes (M phi) or enriched T cells. Cells of the human monocytic cell line Mono Mac 6 were also influenced after LPS stimulation, whereas constitutively IL-2-producing Jurkat cells were not influenced by laser irradiation at any energy density. Analysis of the IL-2
receptor (IL-2R) and intercellular adhesion molecule-1 (ICAM-1) expression in PBMC showed partial down-regulation of both receptors at 37.8 J/cm², but only after stimulation with PHA. (Lasers Surg Med. 2001;29(5):433-41. Helium-Neon laser irradiation of hepatocytes can trigger increase of the mitochondrial membrane potential and can stimulate c-fos expression in a Ca²⁺-dependent manner. Greco M, Vacca RA, Moro L, Perlino E, Petragallo VA, Marra E, Passarella S.

BACKGROUND AND OBJECTIVE: To gain some insight into the photostimulation of isolated hepatocytes irradiated with Helium-Neon (He-Ne) laser light certain biochemical events were studied with respect to two mechanisms: i) the direct light dependent activation of certain biochemical events investigated in intact cells and isolated mitochondria, ii) the indirect stimulation of processes per se light independent. STUDY DESIGNS/MATERIALS AND METHODS: Irradiation of either isolated hepatocytes or isolated rat liver mitochondria was carried out with He-Ne laser (wavelength, 632.8 nm; fluence, 0.24 J cm⁻²; fluence rate, 12 mW cm⁻²). Changes in mitochondrial membrane potential in isolated hepatocytes were monitored using the cationic probe safranine. The c-fos expression was studied by Northern blot and immunoblot analysis. RESULTS: As a result of irradiation, increase of the mitochondrial membrane potential was found to occur in irradiated hepatocytes both in the presence or in the absence of CaCl₂. The hyperpolarization of the mitochondrial membrane is assumed to cause an increase in mitochondrial Ca²⁺ uptake that was measured in isolated mitochondria. Finally, an increase in c-fos expression was found in irradiated hepatocytes when incubated in the presence of CaCl₂. CONCLUSION: This paper gives additional information on the mechanism by which He-Ne laser light, either directly or in a cascade-like effect dependent on increase in cell Ca²⁺, can cause cell stimulation.

Radioprotection

The effect of He-Ne laser (632.8 nm) pre-irradiation on UVA (343 nm)-induced DNA damage in the human B-lymphoblast cell line NC37 was investigated using the comet assay. He-Ne laser pre-irradiation was observed to result in a dose-dependent decrease in UVA-induced DNA damage. This effect was also found to be dependent on the incubation period between He-Ne laser pre-irradiation and the UVA exposure. Whereas the control cells with a higher DNA damage point to an initial ability of faster repair, both the control and the He-Ne laser pre-irradiated cells subsequently show the same rate of DNA repair. The results suggest that He-Ne laser irradiation protect the cells from UVA-induced DNA damage primarily through an influence on processes that prevent an initial DNA damage.

He-Ne laser pre-irradiation-induced protection against UVC damage was investigated in wild-type E. coli K12 strain AB1157 and its isogenic DNA repair mutant strains. At a dose of 7 kJ/m², pre-irradiation was observed to induce protection in recA
proficient strains (AB1157 and uvrA(-) AB1886) at both the irradiances investigated (2 and 100 W/m²). However, at the same dose (7 kJ/m²), while no protection was observed at 100 W/m² in the recA(-) strain, some protection appeared to be there at 2 W/m². Mechanistic studies carried out on these strains at the two irradiances suggest that, whereas the protection observed at 100 W/m² is mediated by singlet oxygen, that observed at 2 W/m² is not. Further, the fact that protection at 100 W/m² was observed only in recA proficient strains suggests that it may arise due to the induction of DNA repair processes controlled by the recA gene. The latter may arise due to the oxidative stress produced by singlet oxygen generated by He-Ne laser irradiation. In contrast, the protection observed at 2 W/m² appears to be independent of the DNA repair proficiency of the stra


We have observed that preirradiation with a helium-neon laser (632.8 nm) induces protection against UVC radiation in wild-type E. coli strain K12AB1157. The magnitude of protection was found to depend on the helium-neon laser irradiance, exposure time, and period of incubation between helium-neon laser exposure and subsequent UVC irradiation. The optimum values for dose, irradiance and interval between the two exposures were found to be 7 kJ/m², 100 W/m² and 1 h, respectively. The possible involvement of singlet oxygen in the helium-neon laser-induced protection is also discussed.


A study was made of the combined effect of laser radiation (helium-neon laser, lambda = 633 nm) and X-rays on bacteria of different genotypes. The sensitivity of cells to X-rays was decreased by pre- and post-irradiation with laser. In the latter case, the radio-modifying effect of laser was more pronounced.


The combined effect of 532 nm laser radiation and alpha-particles on survival of Escherichia coli (AB 1157) has been investigated. The sensitivity of cells to alpha-particles was decreased by pre- and post-irradiation with laser.


A monolayer of HeLa cells, at the stationary phase of growth, exposed to He-Ne laser radiation (632.8 nm; 100 J/m²) either 5 min or 60 min prior to gamma irradiation (0.1-10 Gy; 6.75 Gy/min), or 5 min after irradiation has been investigated. With a 5-min interval between irradiation sessions (both sequences) the survival curves are virtually the same as those for gamma-irradiated cells only. With He-Ne laser radiation delivered 60 min before gamma irradiation with doses exceeding 5 Gy, a fraction of radioresistant cells is identified whose D0 is almost twice as high as D0 of basic cell mass (3.6 and 1.7 Gy respectively. The survival curve becomes a two-
A hypothesis is proposed that He-Ne laser radiation activates, in some cells, the processes that promote the repair of radiation

Arthritis


OBJECTIVE: To investigate the effect of low-power laser therapy on levels of stress proteins (SPs) in experimental arthritis and their relation to the bioeffects on arthritic cartilage repair. DESIGN: A total of 42 rats with similar degrees of induced arthritis evaluated by means of bone scan were divided randomly into two groups. In the treated group, 21 rats received helium-neon laser treatment; in the control group, 21 rats received sham laser treatment. The changes in chondrocytes of SPs were measured by electrophoresis of proteins extracted from chondrocytes of arthritic cartilage at various time periods. The histopathologic changes and the presence of SP of arthritic cartilage were identified by hematoxylin and eosin stain and by immunostains of SP72 antibody individually from frozen sections of arthritic cartilage. RESULTS: SP density increased markedly in rats after laser treatment and was closely related to the repair of arthritic cartilage. Furthermore, the pathohistology of arthritic cartilage improved significantly with the decline of SP levels in the follow-up period. CONCLUSION: Helium-neon (632 nm) low-power laser can enhance SP production in arthritic chondrocytes. The extragenic production of SP is well correlated with the therapeutic effect of low-power laser in preserving chondrocytes and the repair of arthritic cartilage in rats.


OBJECTIVE: To investigate the effects of mucopolysaccharide induction after treatment by low power laser for experimental osteoarthritis (OA). METHODS: Seventy-two rats with three different degrees of papain induced OA over right knee joints were collected for helium-neon (He-Ne) laser treatment. The severity of induced arthritis was measured by 99mTc bone scan and classified into three groups (I-III) by their radioactivity ratios (right to left knee joints). The rats in each group were further divided into study subgroups (Is, IIs, and IIIs) and control subgroups (Ic, IIc, and IIIc) randomly. The arthritic knees in study subgroups received He-Ne laser treatment, and those in controls received sham laser treatment. The changes of arthritic severity after treatment and follow-up 2 months later were measured. The histopathological changes were evaluated through light microscope after disarticulation of sections (H.E. stain), and the changes of mucopolysaccharide density in cartilage matrix were measured by Optimas scanner analyzer after Alcian blue (AB) stain. The densities of mucopolysaccharide induced after treatment in arthritic cartilage were compared and correlated with their histopathological changes. RESULTS: The density of mucopolysaccharide rose at the initial stage of induced arthritis, and decreased progressively in later stages. The densities of mucopolysaccharide in treated rats increased upon complete laser treatment more than those of the controls, which is closely related with the improvement in histopathological findings, but conversely with the changes in arthritic severity.
CONCLUSION: He-Ne laser treatment will enhance the biosynthesis of arthritic cartilage, and results in the improvement of arthritic histopathological changes.


The aim of this study was to determine whether low-level laser therapy (LLLT) aided the recovery of damaged articular cartilage in joints with artificially induced osteoarthritis (OA). OA was induced by injecting hydrogen peroxide (H2O2) into the articular spaces of both knees in rabbits, twice a week for 4 weeks. The induction of OA and the effect of LLLT were evaluated by biochemical, radiological and histopathological analysis. Superoxide dismutase (SOD) activity increased about 40% in the OA group, as compared to the controls. Although SOD activity in the OA group was not significantly different from the 2-week groups, it was significantly different from the 4-week control and treatment groups. There was also a significant difference between the 4-week control and treatment groups. Simple radiographs and three-dimensional computed tomographs (3D CT) did not show detectable arthropathy in the OA group, nor any particular changes in the 2-week groups. In contrast, distinct erosions were seen in the distal articular cartilage of the femur, with irregularity of the articular surface, in the 4-week control group, while the erosions were reduced and arthropathy improved slightly in the 4-week treatment group. Grossly, erosions formed on the articular surface in the OA group. In comparison, severe erosions damaged the articular cartilage in the 4-week control group, but not in the 2-week control and treatment groups. Regeneration of articular cartilage was seen in gross observations in the 4-week treatment group. Histopathologically, there was slight irregularity of the articular surface and necrosis in the OA group, and serious cartilage damage, despite slight chondrocyte regeneration, in the 4-week control group. Conversely, the 4-week treatment group showed chondrocyte replacement, with sometimes close to normal articular cartilage on the articular surface. These results suggest that LLLT was effective in the treatment of chemically-induced OA.

**Vitiligo**


Lan CC, Wu CS, Chiou MH, Hsieh PC, Yu HS.

Helium-neon laser (He-Ne Laser, 632.8 nm) is a low-energy laser that has therapeutic efficacy on various clinical conditions. Our previous study has demonstrated efficacy of He-Ne laser on vitiligo, a disease characterized by skin depigmentation. To regain skin tone on vitiligo lesions, the process began by the migration of the immature melanoblasts (MBs) to the epidermis, which was followed by their functional development to produce melanin. In this study, we investigated the physiologic effects of He-Ne laser irradiation on two MB cell lines: the immature NCCmelb4 and the more differentiated NCCmelan5. The intricate interactions between MBs with their innate extracellular matrix, fibronectin, were also addressed. Our results showed that He-Ne laser irradiation enhanced NCCmelb4 mobility via enhanced phosphorylated focal adhesion kinase expression and promoted melanogenesis in NCCmelan5. In addition, He-Ne laser decreased the affinity between NCCmelb4 and fibronectin, whereas the attachment of NCCmelan5 to fibronectin increased. The
alpha5beta1 integrin expression on NCCmelb4 cells was enhanced by He-Ne laser. In conclusion, we have demonstrated that He-Ne laser induced different physiologic changes on MBs at different maturation stages and recapitulated the early events during vitiligo repigmentation process brought upon by He-Ne laser in vitro.

**Irradiation of the eye**


Safe doses of low-intensive infrared laser (LIIL) exposure for the structures of the eye were searched for in rabbit experiments, and the potentials of such lasers in ophthalmology were assessed. Uzor, a therapeutic laser device with gamma = 0.89 mm, was employed. The doses varied from 0.0001 to 1.0 J/cm², this corresponding to exposure duration of 0.3 to 45 min. Experiments were carried out on 20 animals. The right eyes were exposed, and the left ones were control. An increase of intraocular pressure was recorded at a dose of 0.1 J/cm² (4.5 min) and higher; morphological study showed dilated, well-filled and newly formed vessels in the ciliary body and iris, as well as edema and destruction of the external layers of the retina. Exposure to a dose of 0.05 J/cm² and lower did not lead to destruction of ocular structures and increase of intraocular pressure. The maximal LIIL dose causing no side effects for the organ of vision was established at 0.05 J/cm², this corresponding to 2.5 min exposure.


Treatment of diseases of the lacrimal duct remains a pressing problem in ophthalmology. These diseases are responsible for 71-85.4% diseases in capable people. Sixty patients with chronic dacryocystitis with partially retained patency of the lacrimal duct were treated by He-Ne low-frequency laser ULF-01 (output power 6.10 mcWt, laser beam wave length 0.632 nm). The patients received 3-5 min sessions twice a week, 5-8 sessions per course. Positive effect was attained in 56 patients: complete cessation of excessive lacrimal discharge in 38 patients and subjective improvement in 18. He-Ne laser exposure brings about a good antiinflammatory effect; in combination with antibiotic therapy it promotes rapid sanitization of the lacrimal duct, removes edema, and rapidly normalizes lacrimal discharge.