

Wounds

[Cell Tissue Bank](#). 2009 Jul 11. [Epub ahead of print]

Effects of diode laser therapy on the acellular dermal matrix.

[Soares LP](#), [de Oliveira MG](#), [de Almeida Reis SR](#).

Department of Oralmaxillofacial Surgery, PUCRS School of Dentistry, Porto Alegre, Rio Grande do Sul, Brazil, liviaps@ibest.com.br.

Acellular dermal matrix (ADM) was subcutaneously implanted into calvarian skin of male Wistar rats (n = 40). Low-level laser (λ 685 nm, 4 J/cm²) was locally applied in experimental group (n = 20) above the skin flap. Grafts were harvested at 1, 3, 7 and 14 days after surgery and underwent histological analyses. In treated animals, the extent of edema and the number of inflammatory cells were reduced (P < 0.05). The amount of collagen in graft treated with low-level laser were significantly higher than those of controls (P < 0.05) and were statistically more prominent on the 14th day after surgery. The mean count of fibroblasts was significantly higher in the low-laser therapy group within the 3rd day, showing a marked influx of fibroblasts into area. In conclusion, wound healing of the ADM appear to be positively affected by laser therapy.

[Photomed Laser Surg](#). 2006 Dec;24(6):705-14

Effect of multiple exposures of low-level laser therapy on the cellular responses of wounded human skin fibroblasts.

- [Hawkins D](#),
- [Abrahamse H](#).

Laser Research Unit, Group of Health Sciences, University of Johannesburg, Doornfontein, Johannesburg, South Africa.

Objective: 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. Background Data: 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. Methods: Cellular responses to HeNe laser irradiation were evaluated by measuring changes in cell morphology, cell viability, cell

proliferation, and damage caused by multiple irradiations. Results: 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. Conclusion: 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.

Adv Skin Wound Care. 2004 Jul-Aug;17(6):295-300.

Reversal of diabetic peripheral neuropathy and new wound incidence: the role of MIRE.

Powell MW, Carnegie DE, Burke TJ.

Northwest Orthopedic Center, Springdale, AR, USA.

OBJECTIVE: To determine if improved foot sensitivity to the Semmes-Weinstein 10-g (5.07) monofilament, originally impaired because of diabetic peripheral neuropathy, might be associated with a reduced incidence of new diabetic foot wounds.

DESIGN: Retrospective cohort study using a health status questionnaire.

SUBJECTS: Sixty-eight individuals over age 64 with diabetes, diabetic peripheral neuropathy, and loss of protective sensation who had clinically demonstrable increases in foot sensation to the Semmes-Weinstein monofilament after treatment with monochromatic near infrared photo energy.

MAIN RESULTS: After reversal of diabetic peripheral neuropathy following treatment with monochromatic near infrared photo energy, only 1 of 68 patients developed a new diabetic foot wound, for an incidence of 1.5%. Comparatively, the incidence previously reported in the Medicare-aged population with diabetes was 7.3%.

CONCLUSIONS: Improved foot sensitivity to the Semmes-Weinstein monofilament in patients previously suffering from loss of protective sensation due to diabetic neuropathy appears to be associated with a lower incidence of new diabetic foot ulcers when compared with the expected incidence in the Medicare-aged population with diabetes.

CLINICAL RELEVANCE: Therapeutic interventions that effectively improve foot sensitivity that has been previously diminished due to diabetic peripheral neuropathy may substantially reduce the incidence.

J Am Podiatr Med Assoc. 2005 Mar-Apr;95(2):143-7.

Improved sensitivity in patients with peripheral neuropathy: effects of monochromatic infrared photo energy.

DeLellis SL, Carnegie DH, Burke TJ.

Gulf Coast Foot, Ankle and Wound Center, Tarpon Springs, FL, USA.

The medical records of 1,047 patients (mean age, 73 years) with established peripheral neuropathy were examined to determine whether treatment with monochromatic infrared photo energy was associated with increased foot sensitivity to the 5.07 Semmes-Weinstein monofilament. The peripheral neuropathy in 790 of these patients (75%) was due to diabetes mellitus. Before treatment with monochromatic infrared photo energy, of the ten tested sites (five on each foot), a mean \pm SD of 7.9 \pm 2.4 sites were insensitive to the 5.07 Semmes-Weinstein monofilament, and 1,033 patients exhibited loss of protective sensation. After treatment, the mean \pm SD number of insensate sites on both feet was 2.3 \pm 2.4, an improvement of 71%. Only 453 of 1,033 patients (43.9%) continued to have loss of protective sensation after treatment. Therefore, monochromatic infrared photo energy treatment seems to be associated with significant clinical improvement in foot sensation in patients, primarily Medicare aged, with peripheral neuropathy. Because insensitivity to the 5.07 Semmes-Weinstein monofilament has been reported to be a major risk factor for diabetic foot wounds, the use of monochromatic infrared photo energy may be associated with a reduced incidence of diabetic foot wounds and amputations.

Photomed Laser Surg. 2005 Feb;23(1):70-3.

Low-level laser therapy (LLLT) efficacy in post-operative wounds.

Herascu N, Velciu B, Calin M, Savastru D, Talianu C.

National Institute of Research and Development for Optoelectronics INOE 2000, 1 Atomistilor St., PO Box MG5, 077125, Magurele-Bucharest, Romania.
herescu@inoe.inoe.ro

OBJECTIVE: The aim of this paper was to investigate the efficacy of low-level laser radiation (LLLR) with wavelength of 904 nm on the stimulation of the healing process of postoperative aseptic wounds (early scar). **BACKGROUND DATA:** Low-level laser therapy (LLLT) has been increasingly used to treat many disorders, including wounds. However, despite such increased clinical usage, there is still controversy regarding the efficacy of this wound treatment in current clinical practice. **METHODS:** LLLT has been

used to treat cutting plague in the right instep and on the left foot. Both resulted from sutured wounds. The clinical evaluation by semiquantitative methods is presented. RESULTS: Clinical evaluation showed that the healing process of these postoperatively treated wounds has occurred and that the functional recovery of the patients (i.e., return to their ordinary life) was faster than without treatment. CONCLUSION: LLLR with wavelength of 904 nm to stimulate postoperative aseptic wounds (early scar) is efficient in both cases of cutting plague.

J Clin Laser Med Surg. 2004 Feb;22(1):19-25.

Dose and wavelength of laser light have influence on the repair of cutaneous wounds.

Mendez TM, Pinheiro AL, Pacheco MT, Nascimento PM, Ramalho LM.

IP&D, Univap & School of Dentistry, Universidade do Vale do Paraiba, Sao Jose dos Campos, Sao Paulo, Brazil.

OBJECTIVE: The objective of the present study was to compare histologically the effect of GaAlAs (λ 830 nm, ϕ approximately 2 mm², 35 mW) and InGaAlP (λ 685 nm, ϕ approximately 2 mm², 35 mW) lasers, alone or in association with doses of 20 or 50 J/cm² on cutaneous wounds in the dorsum of the Wistar rat. Background Data: The healing time of surgical wounds is of extreme importance and it is usually associated with a post-operative period free of infection and with less pain and inflammation. MATERIALS AND METHODS: Sixty Wistar rats were divided into seven groups: Group I - control (non-irradiated); Group II - λ 685 nm, 20 J/cm²; Group III - λ 830 nm, 20 J/cm²; Group IV - λ 685 nm and λ 830 nm, 20 J/cm²; Group V - λ 685 nm, 50 J/cm²; Group VI - λ 830 nm, 50 J/cm²; and Group VII - λ 685 nm and 830 nm, 50 J/cm². The animals were sacrificed 3, 5, and 7 days after surgery. RESULTS: Light microscopic analysis using H&E and Picrosirius stains showed that, at the end of the experimental period, irradiated subjects showed increased collagen production and organization when compared to non-irradiated controls. Inflammation was still present in all groups at this time. CONCLUSION: Group IV (λ 830 nm and λ 685 nm, 20 J/cm²) presented better results at the end of the experimental period. It is concluded that low-level light therapy (LLLT) can have a positive biomodulatory effect on the repair of cutaneous wounds.

J Clin Laser Med Surg. 2004 Feb;22(1):15-8.

The comparison of effects between pulsed and CW lasers on wound healing.

Al-Watban FA, Zhang XY.

Laser Medicine Research Section, Biological and Medical Research Department, King

Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia.
watban@kfshrc.edu.sa

OBJECTIVE: In order to evaluate the effects of pulsed continuous wave (CW) laser and detect the role of wound healing in rats using both pulsed and CW 635-nm low-level laser therapy (LLLT), a pilot study was undertaken. **Background Data:** Some acceleration effects of wound healing on animals were found after treatment using various lasers with CW. There are other reports, however, using pulsed CW laser to evaluate the effects of wound healing in rats. **MATERIALS AND METHODS:** An elliptic wound was created aseptically with a scalpel on the shaved back of the rats after anesthesia. The rats treated were restrained in a Plexiglas cage without anesthesia during the laser irradiation period. An Erchonia pulse laser (635 nm) was used in the experiment. The laser beam was delivered through an expander. The percentage of relative wound healing was calculated. **RESULTS:** The percentage of relative wound healing was 4.32 in 100 Hz, 3.21 in 200 Hz, 3.83 in 300 Hz, 2.22 in 400 Hz, 1.73 in 500 Hz and 4.81 in CW. **CONCLUSION:** LLLT using pulsed, CW laser at the appropriate dosimetry and frequency can provide acceleration in wound healing in rats. The 100-Hz frequency had a better effect than other pulse frequencies used in the study. The effects of treatment using CW laser was higher than pulse frequency. The frequency of pulsed CW laser was not found to increase wound healing in rats compared with normal CW laser, as reported in our previous studies.

[J Clin Laser Med Surg.](#) 2004 Feb;22(1):59-66.

Effects of low-intensity polarized visible laser radiation on skin burns: a light microscopy study.

[Ribeiro MS](#), [Da Silva Dde F](#), [De Araújo CE](#), [De Oliveira SF](#), [Pelegriani CM](#), [Zorn TM](#), [Zezell DM](#).

Center for Lasers and Applications, IPEN-CNEN/SP, Cidade Universitária, São Paulo, Brazil. mribeiro@ipen.br

OBJECTIVE: This study was carried out to investigate the influence of low-intensity polarized visible laser radiation on the acceleration of skin wound healing. **Background Data:** Low-level laser therapy (LLLT) at adequate wavelength, intensity, and dose can accelerate tissue repair. However, there is still unclear information about light characteristics, such as coherence and polarization. Some studies indicate that linearly polarized light can survive through long propagation distance in biological tissue. **MATERIALS AND METHODS:** Three burns about 6 mm in diameter were created on the back of rats with liquid N₂. Lesion "L(//)" was irradiated by He-Ne laser ($\lambda = 632.8$ nm), $D = 1.0$ J/cm², with linear polarization parallel to the spinal column of the rat. Lesion "L(inverted v)" was irradiated using the same laser and dose, but the light

polarization was aligned perpendicularly to the relative orientation. Lesion "C" was not irradiated in order to be considered as control. The animals were sacrificed at day 3-17 after lesion creation. Samples were collected and prepared for histological analysis.

RESULTS: Histological analysis showed that the healing of irradiated wounds was faster than that of non-irradiated wounds. Moreover, it was observed that skin wound repair is dependent on polarization orientation with respect to a referential axis as the animal's spinal column. Consequently, "L(//)" was completely healed after 17 days, whereas "L (perpendicular) " showed a moderate degree of healing after the same period.

CONCLUSIONS: These results indicate that the relative direction of the laser polarization plays an important role in the wound healing process when highly coherent He-Ne laser is used.

LASER THERAPY IN WOUND MANAGEMENT

Mary Dyson, PhD FCSP FAIUM LHD(Hon) Centre for Cardiovascular Research and Biology, GKT Medical School, KCL, Guy's Hospital Campus, London SE1 9RT, UK.

The end product of wound management should be a healed wound. To appreciate how low intensity laser therapy (LILT) can assist in achieving this it is necessary first to be familiar with

- the normal structure of the tissues involved in the injury
- the stages involved in the repair of these tissues.

Following a brief description of the above as they apply to skin, the effects of LILT on the cellular events which occur during the healing of acute wounds of skin will be examined. Used correctly these effects can lead to an acceleration of the healing process in wounds healing suboptimally. This acceleration is due, at least in part, to reduction in the duration of acute inflammation resulting in a more rapid entry into the proliferative stage of repair when granulation tissue is produced. Methods of converting chronic wounds into acute wounds in which healing can be accelerated will be suggested. The cellular mechanisms that cause this acceleration will be described. Reversible membrane permeability changes, for example to calcium ions, occur. These stimulate cell activity leading to a range of events including enhanced

- growth factor release by macrophages
- keratinocyte proliferation
- mast cell recruitment and degranulation
- angiogenesis.

The urgent need for controlled, double blind clinical studies of wound healing in volunteers and patients using calibrated LILT devices whose output is known and fully reported will be emphasised. Ideally wound healing should be monitored objectively and noninvasively throughout the healing process to provide the data needed for evidence

based clinical LILT practice. The potential role of high resolution (20 MHz) digitised ultrasound B-scans of wounds in providing this data will be described.

OPEN WOUND HEALING (BED SORES, ULCUS CRURIS, BURNS) WITH SYSTEMIC EFFECTS OF LILT

Adam Mester Semmelweis University, Budapest, Hungary

I. The wound healing phases and laser effects: 1) subcellular, 2) cellular effects: leukocytes and mediators, fibroblast proliferation, lymphocyte activation and mediators, endothelial capillaries regeneration/ revascularisation, epithelial cell regeneration, mucosal regeneration.

II. Anti-inflammatory laser effects in wound healing: Prostaglandin synthesis, Immunological reactions, Helper and suppressor T-cell effects. B-cell effects. IgM/IgG/complement, skin transplantation.

III. Pain relief effect of laser irradiation: direct neurone effects, neurotransmitter effects, indirect effects. Prostaglandin synthesis related chemical effects. Oedema reduction and vascular effects. Perfusion and endothel reactions.

IV. Radiation sensitivity influencing laser effects: Dose dependent stimulation and inhibition. Cell type and status dependent reactions. T-cells: CD8/CD4 cells, C and A neurons, epithel cells/cuboid mucosal cells. Human skin types dependent reactions.

V. Side effects of laser irradiation: Carcinogenesis, co-carcinogenesis, de novo tumour provocation. Effects on growth of already existing tumours.

VI. Methods of laser irradiation: Laser specific light effects: Monochromatic High photon density Coherent Linear Polarisation Divergence Wave length Penetration Absorption Energy density, power density. Superficial dosis / effective dosis / target volume. Spot irradiation / moving irradiation forms. Frequency of sessions. Cumulative effects, synergistic effects, antagonistic effects. Non- thermal application modalities of high power lasers.

VII. Role of laser and other photostimulative therapies in the complex wound management. Acknowledgement: The Central Research Institute of the Hungarian Academy of Sciences and LASOTRONIC AG (Switzerland) was helping the research.

Adv Wound Care. 1999 Jan-Feb;12(1):35-40.

Augmentation of wound healing using monochromatic infrared energy. Exploration of a new technology for wound management.

Horwitz LR, Burke TJ, Carnegie D.

Department of Surgery, Denver Veterans Affairs Medical Center, CO, USA.

The results presented in this paper document healing of different types of extremity wounds with 890 nanometer (nm) monochromatic infrared energy. Recalcitrant dermal lesions, including venous ulcers, diabetic ulcers, and a wound related to scleroderma, were treated with a Food and Drug Administration-cleared infrared device. The infrared

protocol was instituted after conventional management protocols were shown to be ineffective. The rate and quality of healing of these previously refractory wounds, following use of monochromatic infrared energy, may be related to local increases in nitric oxide concentration. Increases in nitric oxide previously have been demonstrated to correlate with vasodilatory and anabolic responses. Further research is needed to confirm the results found in these patients.

NO-SURGICAL LASER TREATMENT IN PHLEBOLOGY

L. Longo, MD General Surgery Institute & Phlebology Center Siena University - Italy

Many Lasers have been used in the treatment of phlebologic diseases, with wavelengths of 488- 511- 532- 577 - 585 - 595 - 600 - 632 - 810 - 950 - 1064 - 1320 nm. To summarize, Laser therapy could be the elective treatment for the wound healing, while edema, haematoma, ulcers are treatable with lasers only after an accurate diagnosis. The purpose of our study is to review the different types of laser beams used in these pathologies, underlining their respective advantages and drawbacks. We can offer some options on the choice of no-surgical lasers in phlebology, based our 25 years of personal experience and the data reported in the literature. The treatment procedure is always important, and we must remember that laser beams can be used also synergistically in association with other treatments. In conclusion, laser therapy has a positive and specific role in the treatment of various phlebologic diseases, but it must be used after an exact diagnosis and according to an appropriate procedure.

WOUND HEALING PROCESS: INFLUENCE OF LLLT ON THE PROLIFERATION OF FIBROBLASTS AND ON THE LYMPHATIC REGENERATION

Lievens P, van der Veen Ph Department of Rehabilitation Research Vrije Universiteit Brussel, Brussels, Belgium

In order to fully understand the positive influence of LLLT on wound healing, we investigated the influence that laser has on proliferation of fibroblasts, one of the basic elements in the wound healing process, and on the regeneration of the lymphatic system, which is important for the evacuation of fluids and waste products out of the wound area.

Material and Method: 1) To do so we cultivated cells coming from 2 different mice (type NMRI) and divided 4 groups per mouse. Two were irradiated, two not using a IR (904nm, 3,7mW) laser. Then we did a BrdU labeling with 4 flasks (2 were irradiated, 2 control) 2) To investigate the regeneration of the lymphatic system, we made a standardized incision on the ventrolateral side of 600 mice. In the control group (n=500) as well as the experimental group the evolution of 4 parameters was studied (adhesion, local oedema, regeneration of the vein and regeneration of the lymph vessel) by means of transillumination microscopy. The wounds in the test group were irradiated twice a day with a combined HeNe (632nm, 5mW)-IR (904nm 68.8mW)

laser.

Results: 1) The results show a significant increase ($p < 0.05$) of fibroblast proliferation. The BrdU labeling showed an increased DNA activity. There is also a perfect match between number of fibroblasts and DNA activity. 2) The adhesion of the scar with the underlying tissues disappeared after 10 days in the control group and after 4 days in the experimental group. The local oedema disappeared in the test group after 8 days, while in the control group it lasted until 10 days. A considerable acceleration of the regeneration of both vein and lymph vessel was seen in the test group

**Effect of helium-neon laser on wound healing. Indian journal of experimental biology. 1999; 37(2): 187-189
Bisht D, Mehrotra R, Singh P A et al.**

Two linear skin wounds were produced on either side of dorsal midline in rats and immediately sutured. Wounds on the left side were irradiated daily with helium neon laser at 4 J/cm² for 5 min., while those on right side were not exposed and served as controls. The mean time required for complete closure in control group was 7 days while irradiated test wounds took only 5 days to heal. The mean breaking strength, as measured by the ability of the wound to resist rupture against force, was found to be significantly increased in the test group. Early epithelization, increased fibroblastic reaction, leucocytic infiltration and neovascularization were seen in the laser irradiated wounds.

Wound healing on animal and human body with use of low level laser therapy - treatment of operated sport and traffic accident injuries: a randomized clinical study on 74 patients with control group.

Simunovic Z, Ivankovich A D, Depolo A.

A wound healing study on rabbits suggested that 4 J/cm² was the optimal dose. A clinical study was performed on 74 patients suffering from injuries of soft tissue upon traffic accidents and sport activities. Two types of lasers were used: 830 nm for Trigger point treatment and a combined 633/904 for scanning, both applied in monotherapy. Clinical parameters studied were redness, heat, pain, swelling, itching and loss of function. Wound healing was accelerated 25-35% in the laser group compared to the control group. Pain relief and functional recovery was significantly improved in the laser group as well.

Wound healing; US Food & Drug Administration: results from a preliminary wound healing trial.

Waynant R,

Notes from a presentation at The 2nd Congress of The world Assoc. for Laser Therapy, Kansas, MO, USA, Sept. 2.5 1998.

A pilot study used six Sprague-Dawley rats - three controls with no treatment and three that were irradiated for 250 seconds with 630 nm. All rats were wounded on both hips - an 8mm circular full thickness hole. The irradiated rats received the 630nm 5 J/cm² dose on only the left hip. The animals were irradiated one hour after the wounds were given and then one dose per day for four days. The results are: ten days after wounding the closure on the control rats averaged 26%, but irradiated rats averaged a closure of 65% on both left (irradiated) and right hips - a systemic effect on the right, as it received no irradiation.

Schindl treated a chronic radiation ulcer with HeNe laser, 30 J/cm².

A video measuring system was used to determine the number of dermal vessels in the ulcer before and after the laser treatment. After 7 irradiations the ulcer had healed completely. Light microscopy in combination with the video measuring system showed a significant increase in the number of capillaries after laser treatment. Schindl A et al. Increased dermal neovascularization after low dose laser therapy of chronic radiation ulcer determined by a video measuring system. Proc. 2nd Congress World Assn for Laser Therapy, Kansas City, September 1998; p. 34

55 patients with long lasting chronic venous ulcers, suffering for more than 6 months without improvement, were treated with LLLT by Lichtenstein.

42 patients were treated with HeNe, 13 with 780 nm GaAlAs. The follow-up ranged from 6 months to 6 years. Wound closure was achieved after 7 to 40 treatments in most of the patients. Complete healing was achieved in 47 patients and moderate improvement in 4 patients. LLLT was used in parallel Lichtenstein D., Morga B. Laser therapy in ambulatory patients with venous stasis ulcers. Proc. 2nd Congress World Assn for Laser Therapy, Kansas City, September 1998; p. 31-32.

In a study extended over 6 years Soriano treated 231 patients with venous leg ulcers.

The exclusion criterias were diabetes, arterial disease, vasculitis, congestive heart failure and loss of follow up at 6 months. 122 of 154 patients in the laser group fulfilled the study. In the control group (traditional treatment only) 46 of 77 patients fulfilled. Wounds were all of Size Rate 4 or larger (diameter major + diameter minor). A 40 mW GaAs laser at 10.000 Hz was used, The laser was applied in the point technique with a dose of 3 J/cm² per point around the border and onto the bed of the ulcer in non contact. Three sessions a week were performed for 4 months, or until the ulcer was completely healed. The results were evaluated as complete healing, partial healing (more than 50%) or non healing (less than 50%). In the laser group there was a 70% healing rate and a 14% rate of partial healing. In the control group 26% of the patients had a complete healing and 22% a partial healing. In the laser group, only 19% of the ulcers of great size (>16) healed completely and if the wound was more than one year old, the percentage of complete healing was 40%. Wounds with an oedema failed to heal with the parameters

used. Soriano F. GaAs laser treatment of venous ulcers. Proc. 2nd Congress World Assn for Laser Therapy, Kansas City, September 1998; p. 128-130.

Physical and Occupational Therapy in Geriatrics.

2000. 18 (2): 1-19. Verdote Robertson R, Munchua M M, Reddon J R.

The effect of low intensity laser therapy (LILT) biostimulation on wound healing in a largely psychogeriatric population was assessed over a period of 6 years (1991-1996). In total, 84 psychiatric patients were referred for the treatment of open wounds of varying severity and etiology. The wound status, nutritional status, walking status, and psychiatric condition of each patient were assessed prior to the administration of laser therapy treatment. Traditional wound care management was also used in addition to laser therapy. According to laser therapy treatment protocol for open wounds, a single diode laser probe was used for biostimulation of the wound bed and the wound periphery. Pre- and post-treatment measurements of wound size were obtained periodically for a total of 188 open wounds. 84% of these wounds completely healed, 11.2% partially healed, 2.1% did not change, and 2.7% got worse. The number of treatments for the 158 completely healed wounds ranged from 3 to 133 (mean 18.5) and the treatment period ranged from 5 to 383 days (mean 47.7). Wound healing was found to be related to nutritional status but neither walking status nor wound size. Results indicate that LILT is effective in the treatment of open wounds when it is used as a component of a total wound management program. Implications and directions for future research are discussed.

J Clin Laser Med Surg. 2003 Apr;21(2):67-74.

Effect of NASA light-emitting diode irradiation on molecular changes for wound healing in diabetic mice.

Whelan HT, Buchmann EV, Dhokalia A, Kane MP, Whelan NT, Wong-Riley MT, Eells JT, Gould LJ, Hammamieh R, Das R, Jett M.

Department of Neurology, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA. hwhelan@mcw.edu

OBJECTIVE: The purpose of this study was to assess the changes in gene expression of near-infrared light therapy in a model of impaired wound healing. **Background Data:** Light-Emitting Diodes (LED), originally developed for NASA plant growth experiments in space, show promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. In this paper we present the effects of LED treatment on wounds in a genetically diabetic mouse model. **MATERIALS AND METHODS:** Polyvinyl acetal (PVA) sponges were subcutaneously implanted in the dorsum of BKS.Cg-m ^{+/+} Lepr(db) mice. LED treatments were given once daily, and at the sacrifice day, the sponges, incision line and skin over the sponges were harvested and used for RNA extraction. The RNA was subsequently analyzed by cDNA array. **RESULTS:** Our studies have revealed certain tissue regenerating genes that were significantly upregulated upon LED treatment when compared to the untreated sample. Integrins, laminin, gap junction proteins, and kinesin superfamily motor proteins are some of the genes involved during regeneration process. These are some of the genes that were identified upon gene array experiments with RNA isolated from sponges from the

wound site in mouse with LED treatment. **CONCLUSION:** We believe that the use of NASA light-emitting diodes (LED) for light therapy will greatly enhance the natural wound healing process, and more quickly return the patient to a preinjury/illness level of activity. This work is supported and managed through the Defense Advanced Research Projects Agency (DARPA) and NASA Marshall Space Flight Center-SBIR Program.

J Clin Laser Med Surg. 2002 Dec;20(6):325-33.

Effects of 630-, 660-, 810-, and 905-nm laser irradiation delivering radiant exposure of 1-50 J/cm² on three species of bacteria in vitro.

Nussbaum EL, Lilge L, Mazzulli T.

Rehabilitation Services, Mount Sinai Hospital and Department of Physical Therapy, University of Toronto, Toronto, Ontario, Canada. e.nussbaum@utoronto.ca

OBJECTIVE: To examine the effects of low-intensity laser therapy (LILT) on bacterial growth in vitro. **BACKGROUND DATA:** LILT is undergoing investigation as a treatment for accelerating healing of open wounds. The potential of coincident effects on wound bacteria has received little attention. Increased bacterial proliferation could further delay recovery; conversely inhibition could be beneficial. **MATERIALS AND METHODS:** *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus* were plated on agar and then irradiated with wavelengths of 630, 660, 810, and 905 nm (0.015 W/cm²) and radiant exposures of 1-50 J/cm². In addition, *E. coli* was irradiated with 810 nm at an irradiance of 0.03 W/cm² (1-50 J/cm²). Cells were counted after 20 h of incubation post LILT. Repeated measures ANOVA and Tukey adjusted post hoc tests were used for analysis. **RESULTS:** There were interactions between wavelength and species ($p = 0.0001$) and between wavelength and radiant exposure ($p = 0.007$) in the overall effects on bacterial growth; therefore, individual wavelengths were analyzed. Over all types of bacteria, there were overall growth effects using 810- and 630-nm lasers, with species differences at 630 nm. Effects occurred at low radiant exposures (1-20 J/cm²). Overall effects were marginal using 660 nm and negative at 905 nm. Inhibition of *P. aeruginosa* followed irradiation using 810 nm at 5 J/cm² (-23%; $p = 0.02$). Irradiation using 630 nm at 1 J/cm² inhibited *P. aeruginosa* and *E. coli* (-27%). Irradiation using 810 nm (0.015 W/cm²) increased *E. coli* growth, but with increased irradiance (0.03 W/cm²) the growth was significant ($p = 0.04$), reaching 30% at 20 J/cm² ($p = 0.01$). *S. aureus* growth increased 27% following 905-nm irradiation at 50 J/cm². **CONCLUSION:** LILT applied to wounds, delivering commonly used wavelengths and radiant exposures in the range of 1-20 J/cm², could produce changes in bacterial growth of considerable importance for wound healing. A wavelength of 630 nm appeared to be most commonly associated with bacterial inhibition. The findings of this study might be useful as a basis for selecting LILT for infected wounds.

J Clin Laser Med Surg. 2000 Oct;18(5):235-40.

Low-level laser therapy for wound healing: feasibility of wound dressing transillumination.

Lilge L, Tierney K, Nussbaum E.

Photonics Research Ontario, Toronto, Canada. Llilge@ociautoronto.ca

OBJECTIVE: The purpose of this study was to assess the feasibility of exposing wounds during low-level laser therapy (LLLT) by transillumination of the wound dressings. **BACKGROUND DATA:** LLLT has been associated with accelerated wound healing in chronic ulcers. The usual approach is to remove wound dressings prior to exposure and to treat three to five times weekly. Frequent change of wound dressings is time consuming and costly; it disrupts the healing process, increases the risk of wound infection, and may be traumatic for the patient. **METHODS:** A double integrating sphere setup was employed to quantify the diffuse transmittance and reflectance of various wound dressings. Differences in transmittance for large area sources and point sources were demonstrated through the use of a diode laser and an incoherent light source. **RESULTS:** There were a number of gels and membrane style wound dressings with diffuse transmittance of more than 50%. Hence, for these dressings the prescribed radiant exposure to the wound surface could be achieved by increasing the exposure duration, while maintaining reasonable overall treatment times. **CONCLUSIONS:** Although LLLT by transillumination of wound dressings is feasible for a variety of wound dressings without significant commitments in additional treatment time, the specific transmission of products not included in this study needs to be determined at the intended treatment wavelength. A transillumination approach may facilitate a faster rate of wound healing than LLLT applied to exposed wounds by reducing trauma and the risk of infection.

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

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

[Article in Russian]

Tarasenko SV, Agapov VS, Trukhina GM, Techiev SK, Artsibushev VI.

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

Vet Surg. 1997 Mar-Apr;26(2):114-20.

Evaluation of low level laser therapy on primary healing of experimentally induced full thickness teat wounds in dairy cattle.

Ghamsari SM, Taguchi K, Abe N, Acorda JA, Sato M, Yamada H.

Department of Veterinary Surgery, School of Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine, Hokkaido, Japan.

OBJECTIVE: The purpose of this study was to evaluate the effect of low-level laser therapy (LLLT) on sutured wounds of the teat in dairy cattle. **STUDY DESIGN:** By using the Latin square design, the effect of LLLT was evaluated by radiography, measurement of microcirculation flow, histopathology, tensiometry, and hydroxyproline

analysis. ANIMALS OR SAMPLE POPULATION: Sixteen teats of four dairy cattle. METHODS: Full thickness wounds were made on the cranial surface of the teats. Teats were distributed into four groups; group A and B wounds were closed with a Gambee pattern, group C and D wounds were closed with three-layers of continuous suture pattern. Group B and D wounds were treated with 3.64 J/cm² of LLLT using a helium-neon system continuous wave (632.8 nm) output of 8.5 nW. RESULTS: The teat wall in non-LLLT groups was significantly thicker than in LLLT groups on day 7, 14 and 21. The mean blood flow differences between control and sutured sites in LLLT groups were significantly lower than those in non-LLLT groups. The morphology of the epidermis in LLLT groups more closely resembled the normal epidermis than that of non-LLLT groups. Collagen fibers in LLLT groups were denser, thicker, better arranged and more continuous with existing collagen fibers than those in non-LLLT groups. The mean tensile strength was significantly greater in LLLT groups than in non-LLLT groups. CONCLUSION: The LLLT affects various aspects of the healing process, including minimizing inflammation, formation of edema, improvement of skin regeneration and enhancement of collagen synthesis. CLINICAL RELEVANCE: The LLLT could accelerate healing of sutured wounds of the teat in dairy cattle.

Br Vet J. 1996 Sep;152(5):583-92.

Evaluation of wound healing of the teat with and without low level laser therapy in dairy cattle by laser Doppler flowmetry in comparison with histopathology, tensiometry and hydroxyproline analysis.

Ghamsari SM, Acorda JA, Taguchi K, Abe N, Yamada H.

Department of Veterinary Surgery, School of Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine, Hokkaido, Japan.

Perforated teat wounds in eight lactating Holstein-Friesian cows were closed by four suture patterns with or without low level laser therapy (LLLT). Wound healing was evaluated by laser Doppler flowmetry (LDF), tensiometry and hydroxyproline analysis, and compared with histopathological examination. The three-layer pattern provided the best healing of the entire teat. Mucosal hyperplasia was observed in Gambee and continuous two-layer pattern while eversion of the skin, presence of suture tracts and a greater amount of granulation tissue were observed with the continuous and interrupted two-layer patterns. The epidermis in LLLT groups more closely resembled the normal epidermis, and collagen fibres were denser, thicker and better arranged in LLLT than in non-LLLT groups. LDF, tensiometry and hydroxyproline analysis correlated well with histopathological examination. The results suggest that LDF, a more rapid, less invasive and painless procedure, can replace tensile strength measurement or hydroxyproline analysis to assess the progress of teat wound healing.

Vet Q. 1996 Mar;18(1):17-21.

Histopathological effect of low-level laser therapy on sutured wounds of the teat in dairy cattle.

Ghamsari SM, Taguchi K, Abe N, Acorda JA, Yamada H.

Department of Veterinary Surgery, Obihiro University of Agriculture and Veterinary Medicine, Hokkaido, Japan.

Perforating wounds were made on the cranial surface of 32 teats in eight dairy cattle. The teats were distributed into eight groups with four kinds of suture patterns. The used suture patterns were Gambee in Groups A and E, continuous 2-layer (Cushing for submucosal layer, continuous horizontal mattress for intermediate layer and skin) in Groups B and F, separated 2-layer (simple continuous for mucosal layer, vertical mattress for intermediate layer and skin) in Groups C and G, and 3-layer (simple continuous for mucosal and intermediate layers, simple interrupted for skin) in Groups D and H. The wounds of Groups E, F, G and H were subjected to 3.64 J/cm² dose of low-level laser, using a helium-neon system with an output of 8.5 mW, continuous wave at 632.8 nm. Histopathologically, healing was different between various suture patterns and between low level laser therapy (LLLT) and non-LLLT-groups. The results suggest that the 3-layer pattern was the best and LLLT could accelerate healing of perforating wounds of the teat in dairy cattle.

Lasers Surg Med. 1996;19(4):433-7.

Effect of laser pulse repetition rate and pulse duration on mast cell number and degranulation.

el Sayed SO, Dyson M.

Tissue Repair Research Unit, U.M.D.S., London, United Kingdom.

BACKGROUND AND OBJECTIVE: Mast cell activation by low-level laser therapy (LLLT), leading to degranulation and the release of mediators, may be one of the mechanisms by which LLLT can accelerate tissue repair in mammals. The objective of this work, part of an investigation to determine the optimum parameters for increasing mast cell number and degranulation in injured skin, was to determine the effect of different pulsing frequencies of LLLT. **STUDY DESIGN/MATERIALS AND METHODS:** Partial-thickness wounds in anaesthetized adult male Wistar rats were irradiated immediately after injury with monochromatic coherent light (wavelength 820 nm) pulsed at either 2.5, 20, 292, or 20,000 Hz at an average power density of 800 mW/cm² for 27 seconds; the energy density was 21.6 J/cm². The effects on mast cell number and degranulation were assessed 2 hours post-treatment by counting the numbers of intact and degranulated mast cells in Carnoy-fixed, toluidine blue-stained, sections of irradiated and sham-irradiated wounds. **RESULTS:** The total number of mast cells was increased significantly ($P < 0.05$) by all the frequencies when compared to the sham-irradiated group, but there was no significant difference between frequencies ($P > 0.05$). However, although the number of degranulated mast cells was higher in all laser-treated wounds, in comparison with the sham-irradiated group, only the 20 Hz (pulse duration 45 ms) and 292 Hz (pulse duration 3 ms) frequencies were significantly effective ($P < 0.05$). **CONCLUSION:** Increase in mast cell number is not pulsing frequency dependent, whereas degranulation is.

Med Pregl. 2003 Mar-Apr;56(3-4):137-41.

[Low level laser irradiation and its effect on repair processes in the skin]

[Article in Croatian]

Matic M, Lazetic B, Poljacki M, Duran V, Ivkov-Simic M.

Klinika za kozno-venericne bolesti, Medicinski fakultet Novi Sad, Klinicki centar Novi Sad. mamatic@ptt.yu

INTRODUCTION: Application of laser beams for therapeutic purposes is of relatively recent date, but today there is no field of medicine where lasers cannot be used. **PHYSICAL CHARACTERISTICS OF LASER RADIATION:** Laser radiation is a type of electromagnetic radiation with some specific characteristics such as coherence, monochromaticity and parallelity. **TYPES OF LASER DEVICES:** Nowadays, there are many laser devices on the market used in medicine and dentistry. According to the type of their active medium, lasers can be classified as solid, gas, semiconductor and liquid. **EFFECTS OF LOW LEVEL LASER THERAPY ON BIOLOGICAL SYSTEMS:** The exact mechanism of action of low level laser therapy is still not completely understood. Its basic feature is to modulate cell behaviour, without causing significant temperature increase. During irradiation of a tissue with a laser beam, an interaction between cells and photons takes place--photochemical reaction. After a cell absorbs the photon, the photon stops existing, and its energy is incorporated into the molecule which has absorbed it. Once this energy is transferred to different biomolecules, it can be transferred to other molecules as well. The energy transferred to the molecule can increase its kinetic energy, and activate or deactivate enzymes or alter physical or chemical properties of main macromolecules. **EFFECTS OF LOW LEVEL LASER THERAPY ON WOUND HEALING:** Effects of low level laser therapy on wound healing process is one of the most fully studied aspects of this type of therapy. It affects all phases of this very complex process. This paper offers a more detailed analysis of these aspects.

J Clin Laser Med Surg. 2001 Dec;19(6):305-14.

Effect of NASA light-emitting diode irradiation on wound healing.

Whelan HT, Smits RL Jr, Buchman EV, Whelan NT, Turner SG, Margolis DA, Cevenini V, Stinson H, Ignatius R, Martin T, Cwiklinski J, Philippi AF, Graf WR, Hodgson B, Gould L, Kane M, Chen G, Caviness J.

Department of Neurology, Medical College of Wisconsin, Milwaukee 53226, USA.

OBJECTIVE: The purpose of this study was to assess the effects of hyperbaric oxygen (HBO) and near-infrared light therapy on wound healing. **BACKGROUND DATA:** Light-emitting diodes (LED), originally developed for NASA plant growth experiments in space show promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. In this paper, we review and present our new data of LED treatment on cells grown in culture, on ischemic and diabetic wounds in rat models, and on acute and chronic wounds in humans. **MATERIALS AND METHODS:** In vitro and in vivo (animal and human) studies utilized a variety of LED wavelength, power intensity, and energy density parameters to begin to identify conditions for each biological tissue that are optimal for biostimulation. **Results:** LED produced in vitro increases of cell growth of 140-200% in mouse-derived fibroblasts, rat-derived osteoblasts, and rat-derived skeletal muscle cells, and increases in growth of 155-171% of normal human epithelial cells. Wound size decreased up to 36% in conjunction with HBO in ischemic rat models. LED produced improvement of greater than 40% in musculoskeletal training injuries in Navy SEAL team members, and decreased wound

healing time in crew members aboard a U.S. Naval submarine. LED produced a 47% reduction in pain of children suffering from oral mucositis. **CONCLUSION:** We believe that the use of NASA LED for light therapy alone, and in conjunction with hyperbaric oxygen, will greatly enhance the natural wound healing process, and more quickly return the patient to a preinjury/illness level of activity. This work is supported and managed through the NASA Marshall Space Flight Center-SBIR Program.

J Clin Laser Med Surg. 2000 Apr;18(2):67-73.

Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with control group.

Simunovic Z, Ivankovich AD, Depolo A.

Department of Anesthesiology, La Carita Medical Center, Laser Center, Locarno, Switzerland. info@lasermedico.ch

BACKGROUND AND OBJECTIVE: The main objective of current animal and clinical studies was to assess the efficacy of low level laser therapy (LLLT) on wound healing in rabbits and humans. **STUDY DESIGN/MATERIALS AND METHODS:** In the initial part of our research we conducted a randomized controlled animal study, where we evaluated the effects of laser irradiation on the healing of surgical wounds on rabbits. The manner of the application of LLLT on the human body are analogous to those of similar physiologic structure in animal tissue, therefore, this study was continued on humans. Clinical study was performed on 74 patients with injuries to the following anatomic locations: ankle and knee, bilaterally, Achilles tendon; epicondylus; shoulder; wrist; interphalangeal joints of hands, unilaterally. All patients had had surgical procedure prior to LLLT. Two types of laser devices were used: infrared diode laser (GaAlAs) 830 nm continuous wave for treatment of trigger points (TPs) and HeNe 632.8 nm combined with diode laser 904-nm pulsed wave for scanning procedure. Both were applied as monotherapy during current clinical study. The results were observed and measured according to the following clinical parameters: redness, heat, pain, swelling and loss of function, and finally postponed to statistical analysis via chi2 test. **RESULTS:** After comparing the healing process between two groups of patients, we obtained the following results: wound healing was significantly accelerated (25%-35%) in the group of patients treated with LLLT. Pain relief and functional recovery of patients treated with LLLT were significantly improved comparing to untreated patients. **CONCLUSION:** In addition to accelerated wound healing, the main advantages of LLLT for postoperative sport- and traffic-related injuries include prevention of side effects of drugs, significantly accelerated functional recovery, earlier return to work, training and sport competition compared to the control group of patients, and cost benefit.

Low-level laser irradiation attenuates production of reactive oxygen species by human neutrophils.

Fujimaki Y, Shimoyama T, Liu Q, Umeda T, Nakaji S, Sugawara K.

Department of Hygiene, Hirosaki University School of Medicine, Japan.

OBJECTIVE: The aim of this study was to examine the effects of low-level laser therapy

(LLLT) on production of reactive oxygen (ROS) species by human neutrophils.
BACKGROUND DATA: LLLT is an effective therapeutic modality for inflammatory conditions. **MATERIALS AND METHODS:** The laser device used was the infrared diode laser (GaAlAs), 830-nm continuous wave (150 mW/cm²). After irradiation, ROS production by neutrophils was measured using luminol-dependent chemiluminescence (LmCL) and expression of CD11b and CD16 on neutrophil surface was measured by flow cytometry. **RESULTS:** The LmCL response of neutrophils was reduced by laser irradiation at 60 min prior to the stimulation with opsonized zymosan and calcium ionophore. The attenuating effect of LLLT was larger in neutrophils of smokers than non-smokers, while the amount of produced ROS was larger in neutrophils of smokers. Expression of CD11b and CD16 on neutrophil surface was not affected by LLLT. **CONCLUSION:** Attenuation of ROS production by neutrophils may play a role in the effects of LLLT in the treatment of inflammatory tissues. There is a possible usage of LLLT to improve wound healing in smokers.