SELECTED PHOTOTHERAPY RESEARCH ABSTRACTS

TABLE OF CONTENTS

General

The effects of laser therapy on tissue repair and pain control: a meta-analysis of the literature

Jason Parker, BA, MSPT, David Dowdy, BS, MSPT, Erin Harkness, BA, MSPT, Leif Sanford, BS, MSPT, Chukuka Enwemeka, PhD, FACSM; Department of Physical Therapy, University of Kansas Medical Center, Kansas City, KS, USA

Presented at WALT (World Association of Laser therapy) Annual Conference (2000) Athens, Greece.

Statement of the Problem:
Low intensity laser therapy devices were first used as a form of therapy more than thirty years ago. However, their efficacies in reducing pain and/or promoting tissue repair remain questionable.

Purpose:
We conducted a meta-analysis of the literature in order to determine the overall treatment effects of laser therapy on pain control and tissue repair.

Method:
Following a literature search, studies meeting our inclusion criteria were identified, coded, and then subjected to statistical meta-analysis procedures as detailed by Cohen. The effect size of laser therapy treatment, i.e. Cohen's d was then calculated from each study.

Results:
A total of 36 peer reviewed papers on tissue repair were coded. Thirty-four of the papers met our inclusion criteria and were used to calculate a total of 46 treatment effect sizes. Fifteen peer-reviewed papers on pain control were coded, nine met the inclusion criteria and were used to calculate nine effect sizes. Meta-analysis revealed a positive effect of laser therapy on tissue repair (d= +1.81; n=46) and pain control (d=+1.11; n=9). The positive effect of laser therapy on specific indices of tissue repair is evident in the treatment effect sizes determined as follows: collagen formation (d=+2.78), rate of healing (d=+1.57), tensile strength (d=+2.13), wound closure (d=+0.76), tensile stress (d=+2.65), mast cell numbers (d=+1.87), and flap survival (d=+2.13). Furthermore, meta-analysis revealed a positive effect of various wavelengths of laser therapy on tissue repair, including: 632.8nm (+2.11), 904nm (+1.09), 514nm (+1.89), 820nm (+1.00), 830nm (+0.61), 780nm (+0.60), and cluster diode (+1.95). The overall treatment effect for pain control was positive as well (d=+1.11). Further analysis revealed a Fail safe N (Na) of 370 for tissue repair and 41 for pain control; indicating that of 370 and 41 peer-reviewed publications with negative or no effect of laser therapy would be needed to negate the positive effect sizes calculated for tissue repair and pain control respectively.

Conclusion:
Our findings indicate that laser therapy has a positive treatment effect on tissue repair processes and also, on pain control.

A comparison of efficacy of low energy photon therapy (LEPT) vs. ultrasound for pain relief.

A randomized, placebo, controlled, double blind study

Salansky N

Submitted to PAIN in 2001, pending publication.

Objectives:
The objectives of this comparison study are to compare Low Energy Photon Therapy and Ultrasound with respect to relief of pain in the treatment of chronic and sub-acute conditions.

Methods:
This placebo, controlled, randomized, double blind study involved 72 subjects (41 females and 31 males with a mean age of 47.5 years, ranging from 18-78). The mean duration of symptoms was 7 months (ranging from .5-48 months). Twenty-eight subjects (39%) had chronic pain (6 months of longer in duration). Subjects admitted were random allocated to one of three groups: Group I – Real LEPT (26 patients), Group II – Placebo LEPT/sham device (23 patients), Group III – Ultrasound (23 patients).
All subjects in each Group received two treatments on the 1st and 3rd days of consecutive days of their prescribed program for that particular Group. LEPT incorporated both LED and low level laser therapy. Neither analgesics nor anti-inflammatory medication was allowed during the study. Both real and placebo devices appeared identical.
Two pain measurements were completed both prior to and 20 minutes after each treatment, including: 1) Pain Level Rating ("PLR") using a vertical visual analog Scale ("VAS"); 2) Pain Pressure Threshold ("PPT") at the most tender point of the affected area, measured using a dolorimeter.

Neither the patients nor the physiotherapist administering LEPT were aware which treatment modality (i.e. real or placebo) was used until after the study was completed. A different evaluator in a separate room away from the treatment area completed assessments.

Results:
One-way analysis of variance (ANOVA) revealed no statistically significant differences in mean age, symptom duration, initial pain level rating or PPT among Groups. Chi square analysis revealed no statistically significant differences among the Groups in gender, chronicity or the relative size of each Group. These results indicate that the randomization process was effective and not biased.

ANOVA revealed a statistically significant difference in the mean change in VAS measured PLR from pre to post treatment between Groups ($F=7.78$; df 2.71; $p=0.0009$).

Bonferroni post-hoc analysis revealed significant differences in the mean changes in the VAS measured PLR (from pre to post treatment) between Real LEPT and Placebo LEPT ($p=0.005$) and between Real LEPT and Ultrasound Groups ($p=0.002$). The difference between the Placebo LEPT and Ultrasound was not statistically significant.

Mean VAS measured PLR declined by 40% (from 4.26 to 2.52) after two LEPT treatments in Group I (real therapy). Whereas, these pain measurements indicated, on average, only 14% decline (from 3.72 to 3.22) in the Placebo LEPT Group and only 10% in the Ultrasound Group (from 4.48-4.02).

The statistically significant outcomes suggest the following conclusions with respect to the relieving of pain in patients with sub-acute and chronic symptoms:

1. that only 2 sessions of Low Level Photon Therapy can provide clinically significant pain relief;
2. the LEPT delivers real pain relief; and
3. the LEPT is significantly more effective than ultrasound (4.0 times more effective, on average, in this study).

Pain scores and side effects in response to Low Level Laser Therapy (LLLT) for myofascial trigger points

Laakso EL, Richardson C, Cramond T

Laser Therapy (1997) 9(2);67-72.

Clinically, Low Level Laser Therapy – LLLT has been used successfully in the treatment of chronic pain but many have questioned the scientific basis for its use. Many studies have been poorly designed or poorly controlled. A double blind, placebo-controlled, random-allocation study was designed to analyze the effect of second daily infrared 9IR) laser (820 nm, 25 mW) and visible red laser (670 nm, 10 mW) at 1 J/cm^2 and 5 J/cm^2 on chronic pain.

Forty-one consenting subjects with chronic pain conditions exhibiting myofascial trigger points in the neck and upper trunk region underwent five treatment sessions over a two-week period. To assess progress, pain scores were measured using visual analogue scales before and after each treatment. The incidence of side effects was recorded.

All groups demonstrated significant reductions in pain over the duration of the study with those groups, which received infrared (820 nm) laser at 1 J/cm^2 and 5 J/cm^2, demonstrating the most significant effects ($p<0.001$). Only those subjects who had active laser treatment experienced side effects.

Results indicated that responses to LLLT at the parameters used in this study are subject to placebo and may be dependant on power output, dose and/or wavelength.

LLLT with trigger points technique: a clinical study on 243 patients

Simunovic Z

Journal of Clinical Laser Medicine and Surgery (Aug. 1996) 14(4):163-167.

Among the various methods of application techniques in LLLT (He-Ne 632.8 nm visible red or infrared 820-830 nm continuous wave and 904 nm pulsed emission) there are very promising "trigger points" (TPs), i.e., myofascial zones of particular sensibility and of highest projection of focal pain points, due to ischemic conditions. The effect of LLLT and the results obtained after clinical treatment of >200 patients (headaches and facial pain, skeletomuscular ailments, myogenic neck pain, shoulder and arm pain, epicondylitis, tenosynovitis, low back and radicular pain, Achilles tendonitis) to whom the "trigger points" were applied were better than we had ever expected. According to clinical parameters, it has been observed that the rigidity decreases, the mobility is restored (functional recovery), and the spontaneous or induced pain decreases or even disappears, by movement, too.

LLLT improves local microcirculation and it can also improve oxygen supply to hypoxic cells in the TP areas and at the same time, it can remove the collected waste products. The normalization of the microcirculation, obtained due to laser applications, interrupts the "circulus vitiosus" of the origin of the pain and its development (Melzak: muscular tension → pain → increased tension → increased pain, etc.).

Results measured according to VAS/VRS/PTM: in acute pain, diminished >70%; in chronic pain >60%. Clinical effectiveness (success or failure) depends on the correctly applied energy dose - over/under dosage produces opposite, negative effects on cellular metabolism.

We noted no negative effects and the use of analgesic drugs could be reduced or completely excluded. LLLT can be used as monotherapy or as a supplementary treatment to other therapeutic procedures for pain treatment.

A double-blind trial of low reactive-level laser therapy in the treatment of chronic pain

Fukuuchi A, Suzuki H, and Inoue K

Laser Therapy (1998) 10: 59-64

The utility of low reactive-level GaAIAs semiconductor laser therapy for chronic pain was evaluated in a double blind clinical trial in 82 patients. Results obtained were also compared to those reported in 8 other double blind studies found in the literature.

Subjective symptoms were improved in 38 of 51 patients (efficacy rate: 75%) in whom a semiconductor laser system (output 100 mW, wavelength 810 nm) was used, while the improvement was noticed in only 4 of 31 patients (efficacy rate: 13%) in whom a sham laser system was employed. The difference in the efficacy rate between the two groups was significant. Skin temperature increased significantly in the laser treatment group.

No significant differences were found among the efficacy rates of other low-level laser therapy systems reported on in the literature despite differences in out put and wavelength used.

Thermographic study of Low Level Laser Therapy (LLLT) for acute-phase injury

Asagai Y, Imakiire A, Ohshiro T

Presented at the WALT (World Association of Laser Therapy) Annual Conference (2000) Athens, Greece.

Acute-phase injury is generally treated by localized cooling of the region, and rarely by the active use of low level laser therapy (LLLT) in Japan. Thermographic studies of acute-phase injury revealed that circulatory disturbances at the site of trauma occurred due to swelling and edema on the day following the injury, and that skin temperature was high at the site of the trauma and low at the periphery. Following LLLT, circulatory disturbances rapidly improved, while temperature in the high temperature zone around the site of trauma fell by 3 degrees on the average, but at the periphery the low temperature rose by 3 degrees on the average to nearly normal skin temperature. Clinically, swelling and edema improved. LLLT was also useful in treating necrosis of the skin in the wound area and in accelerating healing of surgical wounds of paralytic feet, which are prone to delayed, wound healing and injury.

LLLT is useful in treating swelling and edema in acute-phase injury and in accelerating healing of surgical wounds.

A randomized, controlled study of Low Energy Photon Therapy (LEPT) for whiplash injury,

Salansky N

The 8th *International Symposium of Physical Medicine Research Foundation*, Banff, Canada, October 13-15, 1995.

Purpose:
The purpose of this study was to test the efficacy of Low Level Energy Photon Therapy for extensor neck muscle recovery and a consequent improvement of nighttime sleep in comparison with results achieved through chiropractic manipulation and exercise. Based on evidence of over 10,000 scientific papers published around the world, it is commonly understood that most, if not all, traumas arising from motor vehicle accidents ("MVA") have a whiplash component.

Results:
The randomized, controlled study involved 54 subjects (29 females and 25 males, ranging in age from 23-64 years), each of whom had suffered whiplash injury after a motor vehicle accident. The subjects were randomly allocated to three treatment groups,

Group I - 17 – chiropractic manipulation therapy ("CMT"),

Group II - 18 – CMT + Exercise ("Ex"), and Group III - 19 – CMT + Ex and LEPT.
The statistical analysis of results indicated that Group III subjects achieved a greater improvement in neck extension muscle strength, at a much more rapid rate compared to both Groups I & II (p=.01). This indicates that LEPT assisted in reducing recovery time.

In whiplash injury, a patient can lose 20% of muscle strength in the neck extensor muscle. Neck extensor muscle strength improved by 9% after CMT only (not significant) and by 15% after a program of CMT + Ex. However, with the addition of LEPT, the extensor muscle strength was statistically significant at 24%.

Furthermore, a statistically significant difference in the rate of recovery was noted between the groups. The LEPT group demonstrated recovery (to the higher level) after only 4 weeks of therapy, compared to 8 weeks for the CMT + Ex Group.

Additionally, LEPT also helped to extend the patient's uninterrupted sleep after injury in comparison with the two other Groups.

The use of NASA Light-Emitting Diode Near-Infrared (IR) technology for biostimulation

Whelan HT, M.D.

North American Association of Laser Therapy (NALT) Annual Conference (2002) Atlanta, Georgia.

This work is supported and managed through the NASA Marshall Space Flight Center - SBIR Program. Studies on cells exposed to microgravity and hypergravity indicate that human cells need gravity to stimulate growth. As the gravitational force increases or decreases, the cell function responds in a linear fashion. This poses significant health risks for astronauts in long-term space flight. The application of light therapy with the use of NASA LEDs will significantly improve the medical care that is available to astronauts on long-term space missions. NASA LEDs stimulate the basic energy processes in the mitochondria (energy compartments) of each cell, particularly when near-infrared light is set to activate the color sensitive chemicals (chromophores, cytochrome systems) inside. Optimal LED wavelengths include 680, 730 and 880 nm and our laboratory has improved the healing of wounds in laboratory animals by using both NASA LED light and hyperbaric oxygen. Furthermore, DNA synthesis in fibroblasts and muscle cells has been quintupled using NASA LED light alone, in a single application combining 680, 730 and 880 nm each at 4 Joules per centimeter squared. Muscle and bone atrophy are well documented in astronauts, and various minor injuries occurring in space have been reported not to heal until landing on Earth. An LED blanket device may be used for the prevention of bone and muscle atrophy in astronauts. The depth of near-infrared light penetration into human tissue has been measured spectroscopically. Spectra taken from the wrist flexor muscles in the forearm and muscles in the calf of the leg demonstrate that most of the **light photons at wavelengths between 630-800 nm travel 23 cm through the surface tissue and muscle between input and exit at the photon detector**. The light is absorbed by mitochondria where it stimulates energy metabolism in muscle and bone, as well as skin and subcutaneous tissue. Long term space flight, with its many inherent risks, also raises the possibility of astronauts being injured performing their required tasks. The fact that the normal healing process is negatively affected by microgravity requires novel approaches to improve wound healing and tissue growth in space. NASA LED arrays have already flown on Space Shuttle missions for studies of plant growth and the U.S. Food and Drug Administration (FDA) has approved human trials. The use of light therapy with LEDs can help prevent bone and muscle atrophy as well as increase the rate of wound healing in a microgravity environment, thus reducing the risk of treatable injuries becoming mission catastrophes. Space flight has provided a laboratory for studying wound healing problems due to microgravity, which mimic traumatic wound healing problems here on earth. Improved wound healing may have multiple applications that benefit civilian medical care, military situations and long-term space flight. Enhancing the soldier's tissue responses to injury may lead to battlefield resilience and medical independence. Counter-measures to chemical, biological and radioactive weapons exposures which are based on biostimulation of natural tissue regeneration mechanisms could be more universally safe and effective than conventional drugs and surgical modalities. Regeneration of wounded organs and limbs may also be possible if biostimulation could re-awaken molecular events leading to regrowth of tissue.

Near infrared (IR) light has documented benefits promoting wound healing in human and animal studies. Our **preliminary results** have also **demonstrated two to five-fold increases in growth-phase-specific DNA synthesis in normal fibroblasts, muscle cells, osteoblasts, and mucosal epithelial cells in tissue cultures treated with near-IR light**. Our animal models treated with near-IR have included wound healing in diabetic mice and ischemic bipedal skin flap in rats. **Near-IR induced a thirty percent increase in**

the rate of wound closure in these animal models. Dose- and time-dependent increases in vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF-2) occurred in animals treated with near-IR. Human studies have included the use of near-IR to prevent ulcerative mucositis resulting from high doses of chemotherapy and radiation. **Widely published reports, including those from our laboratory, described accelerated recovery from musculoskeletal injuries, hypoxic-ischemic wounds, burns, lacerations, radiation necrosis, and diabetic ulcers with the use of near-IR**. Lasers have some inherent characteristics, which make their use in a clinical setting problematic, including limitations in wavelength capabilities and beam width. The combined wavelengths of light optimal for wound healing cannot be efficiently produced, and the size of wounds that, may be treated by lasers is limited. Light-emitting diodes (LEDs) developed for NASA manned space flight experiments offer an effective alternative to lasers. These diodes can be made to produce multiple wavelengths, and can be arranged in large, flat arrays allowing treatment of large wounds. We are now investigating new collaborations with the Defense Advanced Research Projects Agency (DARPA) for military applications of LED wound healing technology in military medicine. Several uniquely military situations and indications could be addressed, optimizing near-IR parameters for wound healing via LEDs during extended missions under conditions separated from medical personnel. These include burns, chemical agents, radiation, biological agents and highly infected flesh-eating wounds (with and without extended burns) typical for the hygienic conditions occurring in battle fields, also infectious diseases and external wounds occurring in environments with no solar irradiation, low oxygen and high carbon dioxide (submarines). The dramatic results with use of near-IR LED light to prevent digestive mucosal lesions (mucositis) and pain in cancer patients, after high-dose chemotherapy and radiation, suggest the potential for military use of near-IR light to treat U.S. troops exposed to chemical and radioactive warfare agents in the field. These examples illustrate the many possible military uses for this technology. These life-saving applications require especially accelerated wound healing, rapid reduction of infections and pain modulation. Regeneration of muscles in amphibians has also been produced by near-IR therapy. The potential for regeneration of human tissue also deserves study. Central nervous system regeneration would be of particular benefit. Thus far, we have demonstrated that the best results for wound healing occur at wavelengths of 670 nm and 880 nm using 4 to 8 joules/cm2, applied at power densities of approximately 50 mW/cm2. However, studies to determine molecular mechanisms could lead to the optimization for current uses, as well as open up new applications. Despite numerous reports on the benefits of near-IR on wound healing and rehabilitation over the last decade, the basic mechanisms of its action remain poorly understood. Britton Chance's group has reported that about 50% of near-IR light is absorbed by mitochondrial chromophores, such as cytochrome oxidase. However, the underlying cellular and molecular events are still unknown.

Low Level Laser Therapy – Is there documentation?

Contributed by J. Tuner, DDS,

Swedish Laser-Medical Society, 2002

Low level laser therapy (LLLT) has been practiced for more than 30 years but there are still many skeptics, claiming that there is no scientific documentation for this kind of treatment. While this was partly true in the 80's and early 90's, it is no longer the case and critics ought to familiarize themselves with modern research.

Since the first paper was published in 1967, some 2,500 reports have been published worldwide. More than 100 positive double blind studies are there for those who want to learn about LLLT. In dentistry alone some 275 papers have been published. Eighty five institutions in thirty seven countries are represented, which illustrates the world-wide interest in LLLT. Of these 275 papers more than 90% report positive effects of LLLT.

Critics often refer to studies with a negative outcome. This is a fair point, but a large part of these studies contain flaws, and after serious scrutiny it is obvious that they cannot be used. Typical flaws are extremely low dose, ineffective treatment technique, miscalculation of the dose, unsuitable inclusion criteria or low power density. A combined knowledge about laser physics, medicine and low level laser therapy clinic seems to be necessary to carry out a proper study. Some negative studies are impeccable and should be taken quite seriously. All parameters cannot be effective and we learn from the failures.

The positive double blind studies are unfortunately, not too easy to find. Among the 100 selected for evaluation, only 28 could be found on Medline. Many of them have been published in regional or national publications, not indexed on Medline. Only 57 had been published in journals, 33 were abstracts and 10 could only be found as references. An overall rating on a scale of 0-5 was 3.6 for the published papers and 3.0 for the 33 abstracts and the 57 published papers together. No less than 19 indications are found in these papers; pain, arthritis and wound healing being the most prominent ones. It is difficult to accept that one kind of therapy can influence so many conditions. However, if the general influence of light on biological systems is considered, it is more understandable.

Several meta analysis of the available literature have been published. Some of these have not been accounted for the flaws in the studies, only the study design. More recent US University meta analyses on wound healing, tissue regeneration and pain have a very significant outcome.

It is reasonable to say that LLLT is well documented, certainly better documented than the uncontroversial ultra sound therapy. So why the controversy? There are several reasons. To begin with, industry supplied inferior lasers in the eighties. While LLLT pioneer Endre Master recommended 1.5 J/cm^2 as a suitable dose for wound healing, the industry produced lasers in the range of fractions of a mW to a couple of mW. Even researchers tried to use those midget lasers and often failed. The advent of stronger lasers at reasonable prices has improved the situation considerably. It is now well accepted that doses around 2-4 J/cm^2 are a good standard for wound healing and that pain treatment requires higher doses. These doses were not practically reachable with the lasers of the 80's. It is also logical that the enthusiastic reports from clinicians differed from those of some researchers. To simplify things it can be said that therapists treated sick people and researchers treated experimental conditions in

healthy individuals. Further, the sensitivity for LLLT differs a lot from individual to individual and certainly many therapists met patients who were responding even to rather low doses of laser light and wee surprised at what they saw.

In conclusion it can safely be stated that low level laser therapy is much better documented than many persons tend to believe and that the scientific background is sound enough to say that it is a safe and effective treatment modality. However, the biological effects of laser light on various conditions are very complex and more research is needed to find out the optimal parameters.

Arthritis

Laser better than NSAIDs?

From the WALT (World Association of Laser Therapy) News letter – Issue 1 2005

In the Dec 4th paper issue of the British Medical Journal, a new meta analysis on the effect of NSAIDs on knee osteoarthritis pain appears, that may become important to the recognition and future development of laser therapy. A research group from Norway, headed by Dr. Jan M. Bjordal summaries that non-steroidal anti-inflammatory drugs (NSAIDs), including cyclo-oxygenase-2 inhibitors (coxibs), reduce short-term pain associated with knee osteoarthritis only slightly better than placebo, and long-term use of these agents should be avoided. Up for analysis were 23 placebo-controlled trials involving 10,845 patients, 7767 of whom received NSAID therapy and 3078 placebo therapy.

21 of the NSAID-studies were funded by the pharmaceutical industry, and the results of 13 of these studies were inflated by patient selection bias as previous NSAID-users were excluded if they had not previously responded favourably to NSAID. Such an exclusion criterion for non-responders has never been seen in any controlled trial of laser therapy or other non-pharmacological therapies of osteoarthritis. In the remaining 10 unbiased NSAID-trials, the difference from placebo was only 5.9 mm on a 100mm pain scale. This is far less than established data on differences that are considered minimally perceptible (9 mm) or clinically relevant (12 mm) for knee osteoarthritis patients. In addition, none of the trials found any effects beyond 13 weeks.

Adverse events of long term medication with NSAIDs and particularly coxibs, has recently received much attention in the Vioxx-scandal. Consequently, coxibs like Vioxx has been withdrawn and Prexige has been withheld from the market, and the whole group of coxibs, are now under special observation by drug agencies in both Europe and the United States. In contrast to the virtually non-existent side-effects of laser therapy, NSAID side-effects cause an estimated number of 2000 deaths annually in Great Britain alone, because half of the 8.5 million osteoarthritis patients there take these drugs on a regular basis. The considerable international interest for the findings of the Norwegian research group has been highlighted by articles in several major newspapers across Europe and North America and more than 60 unique website-listings within two weeks after publication. The recent development is further moving the balance in disfavour of NSAIDs and coxibs, and may well be the end of the era where they served as reference treatment for osteoarthritis.

Osteoarthritis

The Effect of Low Power Laser Therapy On Osteoarthritis of the Knee

Basirnia A., Sadeghipoor G., Esmaeeli Djavid G. et al.

Radiol Med (Torino). 1998 Apr; 95(4):303-9.

Treatment was performed on 20 patients, aging from 42 to 60 years. All patients had received conservative treatment with poor results. Laser device used for this treatment was pulsed IR diode laser; 810 nm wave length once per day for 5 consecutive days, followed by a 2-day interval .The total number of applications was 12 sessions. Irradiation was performed on 5 periarticular tender points, each for 2 min.

The treatment outcome (pain relief and functional ability) was observed and measured according to the following methods: 1) Numerical rating scales (NRS), 2) Self assessment by the patient, 3) Index of severity for osteoarthritis of the knee (ISK), 4) Analgesic requirements.

We achieved significant improvement in pain relief and quality of life in 70% of patients, comparing to their previous status ($p<0.05$). There was no significant change in range of motion of the knee.

The clinical efficacy of low-power laser therapy on pain and function in cervical osteoarthritis

Oezdemir F, Birtane M, Kokino S

Clinical Rheumatology (2001) 20(3): 181-184.

Pain is a major symptom in cervical osteoarthritis (COA). Low-power laser (LPL) therapy has been claimed to reduce pain in musculoskeletal pathologies, but there have been concerns about this point. The aim of this study was to evaluate the analgesic efficacy of LPL therapy and related functional changes in COA. Sixty patients between 20 and 65 years of age with clinically and radiologically diagnosed COA were included in the study. They were randomized into two equal groups according to the therapies applied, either with LPL or placebo laser. Patients in each group were investigated blindly in terms of pain and pain-related physical findings, such as increased paravertebral muscle spasm, loss of lordosis and range of neck motion restriction before and after therapy. Functional improvements were also evaluated. Pain, paravertebral muscle spasm, lordosis angle, the range of neck motion and function were observed to improve significantly in the LPL group, but no improvement was found in the placebo group. LPL seems to be successful in relieving pain and improving function in osteoarthritic diseases.

Infrared diode laser in low reactive-level laser therapy (LLLT) for knee osteoarthrosis

M. A. Trelles, J. Rigau, P. Sala, G. Calderhead, T. Ohshiro

Laser Therapy, (1991); 3(4): 149-153.

Degenerative joint disease (DJD), in particular in the knee, is difficult to cure successfully at present, often requiring surgical intervention. In addition, the chronic DJD patient often exhibits symptoms of both a physiological and psychological nature. A study is presented using low reactive-laser therapy (LLLT) with an 830 nm infrared continuous wave gallium aluminum arsenide (GaAIAs) diode laser, with an output power of 60 mW, in light contact laser therapy for a population of 40 patients (power density of 18 J/cm^2 per session) two sessions per week for eight weeks. Radiological pain score and joint mobility assessments were made before the first session, immediately after, and at 4 months after the final LLLT session. All other medication and physical therapy was discontinued at least 15 days prior to the first treatment session. Thirty-three patients (82%) reported significant removal of pain and recovery of articular joint mobility. The remaining seven patients felt there was no significant effect following LLLT, and returned to their original pre-therapy medication. The side effects were minimal. LLLT is concluded to be a safe effective and noninvasive alternative to conventional surgical and medical treatment modalities for DJD patients.

Improvement of pain and disability in elderly patients with degenerative osteoarthritis of the knee treated with narrow-band light therapy

Stelian J, Gil I, Beni-Habot, Rosenthal M, Abramovici I, Kutok N, Khahil A

Journal American Geriatric Society (January 1992) 40(1); 23-26

Objective:
To evaluate the effects of low-power light therapy on pain and disability in elderly patients with degenerative osteoarthritis of the knee.

Design:
Partially double-blinded, fully randomized trial comparing red, infrared, and placebo light emitters.

Patients:
Fifty patients with degenerative osteoarthritis of both knees were randomly assigned to three treatment groups: red (15 patients), infrared (18 patients), and placebo (17 patients). Infrared and placebo emitters were double-blinded.

Interventions:
Self-applied treatment to both sides of the knee for 15 minutes twice a day for 10 days.

Main Outcome Measures:
Short-Form McGill Pain Questionnaire, Present Pain Intensity, and Visual Analogue Scale for pain and Disability Index Questionnaire for disability were used. We evaluated pain and disability before and on the tenth day of therapy. The period from the end of the treatment until the patient's request to be retreated was summed up 1 year after the trial.

Results:
Pain and disability before treatment did not show statistically significant differences between the three groups. Pain reduction in the red and infrared groups after the treatment was more than 50% in all scoring methods ($P<0.05$). There was no significant pain improvement in the placebo group. We observed significant functional improvement in red and infrared-treated groups ($P<0.05$), but not in the placebo group. The period from the end of treatment until the patients, required retreatment was longer for red and infrared groups than for the placebo group (4.2 ± 3.0, 6.1 ± 3.2, and 0.53 ± 0.62 months, for red, infrared and placebo, respectively).

Conclusions:
Low-power light therapy is effective in relieving pain and disability in degenerative osteoarthritis of the knee.

LLLT in osteoarticular diseases in geriatric patients –

Giavelli S, Fava G, Castronuovo G, Spinoglio L, Galanti A (1998)

Radiology Medicine (Torino) (1998) Apr; 95(4):303-309.

Laser light absorption through the skin causes tissue changes, targeting the nervous, the lymphatic, the circulatory and the immune systems with an analgesic, anti-inflammatory, anti-edematous effect and stimulating tissue repair. Therefore, LLLT is now commonly used in many rehabilitation centers, including the "Istituto Gerontologico Pio Albergo Trivulzio", Milan, Italy. However, to activate the treatment program, the basic medical research results must always be considered to choose the best optical wavelength spectrum, technique and dose, for rehabilitative laser therapy. We analyzed the therapeutic effects of different wavelengths and powers in various treatment schedules. In particular, a protocol was designed to test such physical parameters as laser type, doses and individual schedule in different pathologic conditions. We report the results obtained with LLLT in the rehabilitation of geriatric patients, considering the various physical and technical parameters used in our protocol. We used the following laser equipment: an He-Ne laser with 632.8 nm wavelength (Mectronic), a GaAs Laser with 904 nm wavelength (Mectronic) and a CO2 Laser with 10,600 nm wavelength (Etoile). To evaluate the patient clinical status, we use a different form for each involved joint; the laser beam is targeted on the region of interest and irradiation is carried out with the sweeping method or the points technique. Irradiation technique, doses and physical parameters (laser type, wavelength, session dose and number) are indicated on the form. The complete treatment cycle was 5 sessions/wk for 20 sessions in all. At the end of the treatment cycle, the results were scored on a 5-grade semi quantitative scale--excellent, good, fair, poor and no results. We examined 3 groups of patients affected with gonarthrosis (149 patients), lumbar arthrosis (117 patients), and algodystrophy (140 patients) respectively. In gonarthrosis patients, the statistical analysis of the results showed no significant differences between CO2 laser and GaAs laser treatments (p=.975), but significant differences between CO2 laser and He-Ne laser treatments (p=.02) and between GaAs laser and He-Ne laser treatments (p=.003). In lumbar arthrosis patients treated with GaAs or He-Ne laser, significant differences were found between the two laser treatments and the combined sweeping-points techniques appeared to have a positive trend relative to the sweeping method alone, especially in sciatic suffering. In the algodystrophy syndrome, in hemiplegic patients, significant differences were found between CO2 and He-Ne laser treatments (p=.026), between high and low CO2 laser doses (p=.024), and between low CO2 laser dose and high He-Ne laser dose (p=.006). LLLT can be used to treat osteoarticular pain in geriatric patients. For best results, the diagnostic picture must be correct and a treatment program defining the physical parameters used (wavelength, dose and irradiation technique) must be designed.

Rheumatoid Arthritis

Beneficial effects of laser therapy in the early stages of rheumatoid arthritis onset

Ailioaie C, Lupusoru-Ailioaie LM

Laser Therapy (1991) 11(2); 79-87.

The purpose of this study was to determine the effects of laser therapy in pain reduction and/or recovery of patients at the onset of Rheumatoid Arthritis (RA), comparatively with the traditional non-steroidal anti-inflammatory drugs (NSAIDs). Fifty-nine patients with RA of 6-12 months duration were included in the study. The patients were divided into 3 groups: Group 1 (21 patients) received laser therapy; Group 2 (18 patients) was submitted to placebo laser therapy and NSAIDs medication; Group 3 (20 patients) was treated only with NSAIDs. Physical therapy was instituted in all three groups. GaAIAs diode laser of 830 nm wavelength and 200mW maximum output power was used. Group 1 received laser therapy once each day, eight days per month, for a total of 32 treatments during a four-month period. The parameters used were 2-4 J/cm^2 energy density, and a frequency of 5 Hz or 10 Hz depending on the number and severity of pain in the affected joints. Placebo laser treatment was given to Group 2. The functional activity score, the acute pain phase reactants (ESR and C – reactive protein), T-lymphocytes and NK (natural killer) – cells were estimated. Synovial biopsies and Magnetic Resonance Imaging (MRI) of the synovial membrane were performed as well. The analysis of the clinical and biological parameters at the end of treatment showed a statistically significant decrease of duration of morning stiffness, of pain at rest and during movements, and improved acute phase reactants. The overall efficacy rate in these studies was 86% in the first group, 50% in laser placebo group and 40% in the NSAIDs-treated third group. After four months of treatment, our investigations showed that 830 nm infrared laser therapy promoted the restoration of function, relieved pain and limited the complications of RA.

Low Powered Laser Therapy for Rheumatoid Arthritis

Lindsay Agambar, KE Herbert, DL Scott

Inflammation and Arthritis Group, Department of Rheumatology, St. Bartholomew's Hospital, London.

British Society for Rheumatology IXth Annual General Meeting, 1998

There are very few prospective controlled randomized trials of physiotherapy methods of treatment in arthritis. When new modalities of physical therapy become available it is especially important they are evaluated in this way. Low powered laser treatment is a novel form of local treatment which can be used in rheumatoid arthritis (RA). Placebo therapy can be given with specially adapted equipment. We used such an approach to examine the efficacy of laser therapy for RA knee joints using a double blind trial design.

A multi-head laser was used with optical light for direction finding and laser light (at 820nm) for therapy. Two leads were used for the study (coded A and B) but apparently identical to the operator, one was fully operational; the other gave optical light only. We studied 40 RA patients randomized to receive active or placebo low powered laser treatment. Where possible both knees were treated. Patients were assessed initially, at 3 and 6 weeks of therapy, and after treatment had been completed. Six variables were measured: flexion, extension, strength, stiffness, pain and overall grading of knee arthritis. Active therapy led to significant improvements in strength ($p=0.003$, unpaired t-test) and decreased pain ($p=.058$) compared to placebo treatment. Active treatment also led to fewer persistently flexed knees (22%) compared to controls (62%) and a greater number of normally graded knees (97.5%) compared to controls (73%); but were significant by Chi-squared testing ($p<0.025$ and <0.005 respectively).

This study shows randomized controlled studies of physiotherapy are possible; using such an approach low powered laser therapy appears to be an effective treatment for RA knees.

Carpal Tunnel Syndrome

Carpal tunnel syndrome: clinical outcome after LLLT-acupuncture, microamps TENS, and other alternative therapies: an open protocol study.

Branco K, Naeser MA,

Journal of Alternative Complementary Medicine (1999) 1:5-26.

Acupuncture Healthcare Services, Westport, Massachusetts, USA. They measured outcome for carpal tunnel syndrome (CTS) patients (who previously failed standard medical/surgical treatments) treated primarily with a red-beam, LLLT-AP and microamps TENS on the affected hand; secondarily, with other alternative therapies. Design: Open treatment protocol, patients diagnosed with CTS by their physicians. Treatment was given by licensed acupuncturist in a private practice office. 36 hands were treated (from 22 women, 9 men), ages 24-84 yr, median pain duration, 24 mo. Fourteen hands had failed 1-2 surgical release procedures. Primary treatment: red-beam, 670 nm, continuous wave, 5 mW, diode LLLT pointer (1-7 J per point), and microamps TENS (<900 uA) on affected hands. Secondary treatment: infrared LLLT (904 nm, pulsed, 10 W) and/or needle AP on deeper acupoints; Chinese herbal medicine and supplements, on a case-by-case basis (3 treatments/wk for 4-5 wk). Pre- and post treatment Melzack pain scores and profession and employment status were recorded. Post treatment, pain significantly reduced ($p<.0001$), and 33/36 hands (91.6%) had no pain, or pain reduced by >50%. Fourteen hands that failed surgical release were successfully treated. Patients remained employed, if not retired. Follow-up after 1-2 yr with cases aged <60, only 2/23 hands (8.3%) had return of pain, but were successfully re-treated within a few weeks. Possible mechanisms for effectiveness include increased adenosine triphosphate (ATP) on cellular level, decreased inflammation, temporary increase in serotonin. Combined treatment with LLLT-AP + microamp TENS + Chinese herbs has potential cost-savings (current estimated cost per case, $12,000; this treatment, $1,000). It is safe when applied by a licensed acupuncturist trained in laser-AP; supplemental home treatments may be performed by patient under supervision of acupuncturist.

A pilot study to determine effectiveness of low level photon therapy for chronic Carpal Tunnel Syndrome "CTS"

Salansky N

Presented at the Lasers in Surgery and Medicine conference (1994) Vol. 16.

Objective:
The purpose of this study was to determine the potential effectiveness of LEPT for the treatment of chronic CTS.

Methods:
Twenty-one patients (aged 28-66 years) with chronic CTS were admitted for the study and provided treatments 3 times per week with 15 treatments as one course.

Results:
a) 15 (71.4%) patients obtained complete symptom relief and returned to their regular work; b) 2 (9.5%) patients obtained partial symptom relief (at least one evaluation criteria was negative on final measurement); c) 4 (19.1%) patients did not respond.
The 15 cured patients remained symptom free with follow-up interviews ranging from 3 –18 months after therapy. Overall, this study was considered successful related to using LEPT to resolve symptoms of chronic CTS.

Future of laser biostimulation in America today: microlight 830

Smith CF & Vangsness CT

Proceedings SPIE (1992) 1643; 275-276.

For the last 2 years, we have been investigating the use of an 830 nm laser for LLLT in chronic pain syndromes. The laser output does not exceed 100 mW. This wave length has been carefully selected to be in the 'window' of wavelengths between 650 and 900 nm. At this level, the laser energy will penetrate the epidermis, the dermis and the subcutaneous layers to the deep tissue. The tissue effect of this laser energy is not thermal but rather a stimulation of micro-circulation with a secondary effect of blocking pain enzymes and activation of the synthesis of endorphin enzymes. We have experience with approximately 75 patients who have been treated with LLLT. We used a double-blind study at several General Motors facilities in Michigan to determine the effectiveness of LLLT in inflammatory conditions. Repetitive injuries in the work place have moved from 18% of industrial accidents in 1981 to 52% in 1989. Carpal Tunnel Syndrome is the number one economic problem in occupational medicine; 15% of employees of American automotive plants have Carpal Tunnel Syndrome. This large number of patients have been treated in the past by standard physiotherapy treatment modalities and ultimately by surgery for failure of conservative therapy. Incidence of 'return to work activities' has been low. LLLT affords a positive solution to this problem not only therapeutically but prophylactically. Indications for treatment are Chronic Pain Syndrome and Carpal Tunnel Syndrome of mild to moderate degree.

Treatment of repetitive use carpal tunnel syndrome

Smith CF, Vangsness CT, Anderson T & Good W (1995)

Proceedings SPIE (1995) 2395; 658-661.

In 1990, a randomized, double-blind study was initiated to evaluate the use of an eight-point conservative treatment program in carpal tunnel syndrome. A total of 160 patients were delineated with symptoms of carpal tunnel syndrome. These patients were then divided into two groups. Both groups were subjected to an ergonomically correct eight-point work modification program. A counterfeit LLLT unit was used in Group A, while an actual LLLT unit was used in Group B. Groups A and B were statistically significantly different in terms of return to work, conduction study improvement, and certain range of motion and strength studies.

Noninvasive laser neurolysis in carpal tunnel syndrome

Weintraub MI, MD, FACP

Muscle Nerve (1997) 20:1029-1031.

The peripheral nervous system is photosensitive providing the scientific rationale for this study, which determines the efficacy and safety of laser light exposure in 30 cases with CTS. Nine joules of energy over 5 points (7-15 treatments) reversed the signs and symptoms of CTS in 77% of cases with three-fold normalization of CMAP. A photobiologic response was seen in 80% of nerves. This unique and novel approach is cost-effective and will play a role in future management of CTS.

The effectiveness of Low Level Laser Therapy on Carpal Tunnel Syndrome

Steven Balmes, Yolanda Cooper, Olabisi Jarrett, Bobby Kennedy, Jr

Presented at WALT (World Association of Laser therapy) Annual Conference (2000) Athens, Greece.

Carpal Tunnel Syndrome (CTS) is a debilitating musculoskeletal disorder, decreasing hand function and quality of life. Patients with CTS often complain of numbness and tingling during the day, waking at night, weakness and pain in hands and wrist. There are numerous treatment options available, including surgery, splinting, and steroid injections. However, no single treatment is consistently effective. The use o Low Level laser Therapy (LLLT) as a noninvasive, painless, and cost effective treatment technique for CTS is becoming popular in physical therapy worldwide. However, compelling evidence to support its efficacy does not exist yet. The purpose of this study is to assess the physiological effects of LLLT (MEDX^{TM}) in reducing any or all the signs and symptoms of CTS under placebo controlled, double-blind conditions.

Twenty participants (33 hands) were randomly assigned to one of two groups: LLLT for 4 min/day (dosage=5.184 J/cm^2) or a placebo for 4 min/day (dosage=0 J/cm^2), for an average of 15 (range 11 to 18) weekday treatments. Each participant was assessed standardized CTS questionnaire, 2) grip strength, 3) pinch strength, 4) median nerve sensory and motor distal latencies, prior to treatment, reassessed after the final treatment, and at the one month follow-up. Sensory and motor median nerve distal latencies were measured weekly, in addition to the above mentioned. Eighteen participants (30 hands) completed the study, and 11 participants (23 hands) made it to the one-month follow-up.

Data analysis was conducted using repeated measures ANOVA and a Kruskal-Wallis Test. The results indicated that there was a statistically significant decrease in median nerve sensory distal latency in the laser group compared to a placebo from pre-test to post-test; however, no statistically significance was found for the other five variables measured. There was a decrease in symptoms and an increase in functional status in both groups. Analysis of grip strength showed no statistical significance, although a slight decrease in placebo group and a slight increase in the laser group was observed. There was no difference within or between groups for pinch strength.

The results of this study suggest that LLLT may effectively decrease sensory distal latency of the median nerve and improve nerve function. The five remaining variables were not found to show statistically significant changes between groups. Verbal reports of improvement from the participants differed from the results of the CTS questionnaire. The researchers believe that LLLT is a beneficial alternative treatment for CTS when considering the participant's verbal reports and improvement in nerve function.

Epicondylitis

Treatment of medial and lateral epicondylitis - tennis and golfer's elbow - with LLLT: a multicenter double blind, placebo-controlled clinical study on 324 patients.

Simunovic Z, Trobonjaca T, Trobonjaca Z

Journal of Clinical Laser Medicine and Surgery (Jun 1998) 16(3):145-151.

Among the other treatment modalities of medial and lateral epicondylitis, LLLT has been promoted as a highly successful method. The aim of this clinical study was to assess the efficacy of LLLT using trigger points (TPs) and scanner application techniques under placebo-controlled conditions. The current clinical study was completed at two Laser Centers (Locarno, Switzerland and Opatija, Croatia) as a double-blind, placebo controlled, crossover clinical study. The patient population (n=324), with either medial epicondylitis (Golfer's elbow; n=50) or lateral epicondylitis (Tennis elbow; n=274), was recruited. Unilateral cases of either type of epicondylitis (n=283) were randomly allocated to one of three treatment groups according to the LLLT technique applied: (1) Trigger points; (2) Scanner; (3) Combination Treatment (i.e., TPs and scanner technique). Bilateral cases of either type of epicondylitis (n=41) were subject to crossover, placebo-controlled conditions. Laser devices used to perform these treatments were infrared (IR) diode laser (GaAlAs) 830 nm continuous wave for treatment of TPs and He-Ne 632.8 nm combined with IR diode laser 904 nm, pulsed wave for scanner technique. Energy doses were equally controlled and measured in Joules/cm2 either during TPs or scanner technique sessions in all groups of patients. The treatment outcome (pain relief and functional ability) was observed and measured according to the following methods: (1) short form of McGill's Pain Questionnaire (SF-MPQ); (2) visual analogue scales (VAS); (3) verbal rating scales (VRS); (4) patient's pain diary; and (5) hand dynamometer. Total relief of the pain with consequently improved functional ability was achieved in 82% of acute and 66% of chronic cases, all of which were treated by combination of TPs and scanner technique. The best results were obtained using combination treatment (i.e., TPs and scanner technique). Good results are obtained from adequate treatment technique correctly applied, individual energy doses, adequate medical education, clinical experience, and correct approach of laser therapists. Under- and over irradiation dosage can result in the absence of positive therapy effects or even opposite, negative (e.g., inhibitory) effects. The data gave further evidence of the efficacy of LLLT in the management of lateral and medial epicondylitis.

Comparison between low level laser therapy, transcutaneous electro-neural stimulation, visible incoherent polarised light and placebo in the treatment of lateral epicondylitis: A pilot clinical study on 120 patients

Simunovic Z and Trobonjaca T

Lasers in Surgery and Medicine (2002) Supplement 14, Atlanta, Georgia

The aim of this pilot study was to compare the efficacy of Low Level Laser therapy (LLLT), Transcutaneous Electro-Neural Stimulation (TENS), visible incoherent polarized (VIP) light and placebo in the treatment of lateral epicondylitis-tennis elbow. The patient population (n=120) was randomly allocated into four groups according to treatment applied. The therapy lasted three weeks per each treatment modality, where total number of treatments per patient was twelve (5 + 4 + 3 per three weeks). LLLT was applied as trigger points technique in all patients, using an infrared diode laser in a dosage of 4 J/point. TENS was applied using gummy plates in the same sizes and by exactly measuring the amount of mA, mV and Hertz in all patients. VIP light was applied in a dosage of 4/J.cm^2. Placebo was applied by using a laser device with no active laser emission. All patients suffered from chronic form of lateral epicondylitis, with x-ray proved no changes on the cervical spine. The outcome measurement was focused on the level of pain relief, estimated according to the Visual Analogue Scale (VAS). The results have demonstrated that the highest percentage of pain relief was achieved in patients treated with LLLT (over 45% of lased patients reported 90-100% pain relief). The second best pain relief was reported in the group of patients treated with TENS. None of the patients treated with VIP light reported 90-100% pain relief. The worst results were reported in placebo group (<20% of average pain relief). This pilot study indicates epicondylitis compared to other treatments modalities and placebo. Carefully conducted multicenter, randomized, placebo controlled clinical studies are recommended for assessing the efficacy of LLLT, TENS and VIP light in the treatment of chronic form of lateral epicondylitis.

Fibromyalgia

Efficacy of low power laser therapy in fibromyalgia: a single-blind, placebo-controlled trial

Gur A, Karakoc M, Nas K, Cevik R, Sarac J, Demir E.

Lasers in Medical Science (2002) 17(1):57-61.

Low energy lasers are widely used to treat a variety of musculoskeletal conditions including fibromyalgia, despite the lack of scientific evidence to support its efficacy. A randomised, single-blind, placebo-controlled study was conducted to evaluate the efficacy of low-energy laser therapy in 40 female patients with fibromyalgia. Patients with fibromyalgia were randomly allocated to active (GaAs) laser or placebo laser treatment daily for two weeks except weekends. Both the laser and placebo laser groups were evaluated for the improvement in pain, number of tender points, skinfold tenderness, stiffness, sleep disturbance, fatigue, and muscular spasm. In both groups, significant improvements were achieved in all parameters ($p<0.05$) except sleep disturbance, fatigue and skinfold tenderness in the placebo laser group ($p>0.05$). It was found that there was no significant difference between the two groups with respect to all parameters before therapy whereas a significant difference was observed in parameters as pain, muscle spasm, morning stiffness and tender point numbers in favour of laser group after therapy ($p<0.05$). None of the participants reported any side effects. Our study suggests that laser therapy is effective on pain, muscle spasm, morning stiffness, and total tender point number in fibromyalgia and suggests that this therapy method is a safe and effective way of treatment in the cases with fibromyalgia.

Light-Emitting Diode

Effect of NASA Light-Emitting Diode Irradiation on Wound Healing

Whelan, H.T., Smits R.L., Buchman, E.V., Whelan, N.T., Turner, S.G., Margolis, D.A., Cevenini, V., Stinson, H., Ignatius, R., Martin, T., Cwiklinski, J., Philippi, A.F., Graf, W.R., Hodgson, B., Gould, L., Kane, M., Chen, G., Caviness, J.

Journal of Clinical Laser Medicine & Surgery (2001) 19(6): 305-314

***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.

Effect of NASA Light-Emitting Diode Irradiation on Molecular Changes for Wound Healing in Diabetic Mice

Source: Journal of Clinical Laser Medicine & Surgery Volume: 21 Number: 2 Page: 67 -- 74
DOI: 10.1089/104454703765035484
Author(s): Harry T. Whelan MD ; Ellen V. Buchmann BS ; Apsara Dhokalia PhD ; Mary P. Kane BS ; Noel T. Whelan BS ; Margaret T.T. Wong-Riley PhD ; Janis T. Eells PhD ; Lisa J. Gould MD, PhD ; Rasha Hammamieh PhD ; Rina Das PhD ; Marti Jett PhD

Abstract. 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 +/+ Leprdb 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.

The NASA Light-Emitting Diode Medical Program –Progress in Space Flight and Terrestrial Applications

Whelan, H.T., Houle, J.M., Whelan, N.T., Donohoe, D.L., Cwiklinski, J., Schmidt, M.H., Gould, L., Larson, D., Meyer, G.A., Cevenini, V., and Stinson, H.

Abstract. This work is supported and managed through the NASA Marshall Space Flight Center – SBIR Program. Studies on cells exposed to microgravity and hypergravity indicate that human cells need gravity to stimulate cell growth. As the gravitational force increases or decreases, the cell function responds in a linear fashion. This poses significant health risks for astronauts in long term space flight. LED-technology developed for NASA plant grown experiments in space shows promise for delivering light deep into tissues of the body to promote wound healing and human tissue growth. This LED-technology is also biologically optimal for photodynamic therapy of cancer.

LED-ENHANCEMENT OF CELL GROWTH

The application of light therapy with the use of NASA LED's will significantly improve the medical care that is available to astronauts on long-term space missions. NASA LED's stimulate the basic energy processes in the mitochondria (energy compartments) of each cell, particularly when near-infrared light is used to activate the color sensitive chemicals

(chromophores, cytochrome systems) inside. **Optimal LED wavelengths include 680, 730 and 880 nm**. The depth of near-infrared light penetration into human tissue has been measured spectroscopically (Chance, et al 1988). Spectra taken from the wrist flexor muscles in the forearm and muscles in the calf of the leg demonstrate that most of the light photons at wavelengths between 630-800 nm travel 23 cm through the surface tissue and muscle between input and exit at the photon detector. Our laboratory has improved the healing of wounds in laboratory animals by using NASA LED light and hyperbaric oxygen. **Furthermore, DNA synthesis in fibroblasts and muscle cells has been quintupled using NASA LED light alone, in a single application combining 680, 730, and 880 nm each at 4 Joules per centimeter squared.**

Muscle and bone atrophy are well documented in astronauts, and various minor injuries occurring in space have been reported not to heal until landing on Earth. Long term space flight, with its many inherent risks, also raises the possibility of astronauts being injured performing their required tasks. The fact that the normal healing process is negatively affected by microgravity requires novel approaches to improve wound healing and tissue growth in space. NASA LED arrays have already flown on Space Shuttle missions for studies of plant growth. The U.S. Food and Drug Administration (FDA) has approved human trials. The use of light therapy with LED's is an approach to help increase the rate of wound healing in the microgravity environment, reducing the risk of treatable injuries becoming mission catastrophes.

Wounds heal less effectively in space than here on Earth. Improved wound healing may have multiple applications which benefit civilian medical care, military situations and long-term space flight. Laser light and hyperbaric oxygen have been widely acclaimed to speed wound healing in ischemic, hypoxic wounds. An excellent review of recent human experience with near-infrared light therapy for wound healing was published by Conlan, et al in 1996. Lasers provide low energy stimulation of tissues which results in increased cellular activity during wound healing (Beauvoit, 1989, 1995; Eggert, 1993; Karu, 1989; Lubart, 1992, 1997; Salansky, 1998; Whelan, 1999; Yu, 1997). **Some of these activities include increased fibroblast proliferation, growth factor syntheses, collagen production and angiogenesis.**

Lasers, however, have some inherent characteristics, which make their use in a clinical setting problematic, including limitations in wavelengths and beam width. The combined wavelengths of light optimal for wound healing cannot be efficiently produced, and the size of wounds which may be treated by lasers is limited. **Light-emitting diodes (LED's) offer an effective alternative to lasers.** These diodes can be made to produce multiple wavelengths, and can be arranged in large, flat arrays allowing treatment of large wounds. Our experiments suggest potential for using LED light therapy at 680, 730 and 880 nm simultaneously, alone and in combination with hyperbaric oxygen therapy, both alone and in combination, to accelerate the healing process in Space Station Missions, where prolonged exposure to microgravity may otherwise retard healing. NASA LED's have proven to stimulate wound healing at near-infrared wavelengths of 680, 730 and 880 nm in laboratory animals, and have been approved by the U.S. Food and Drug Administration (FDA) for human trials. Furthermore, near-infrared LED light has quintupled the growth of fibroblasts and muscle cells in tissue culture. The NASA LED arrays are light enough and mobile enough to have already flown on the Space Shuttle numerous times. LED arrays may prove to be useful for improving wound healing and treating problem wounds, as well as speeding the return of deconditioned personnel to full duty performance. Potential benefits to NASA, military, and civilian populations include treatment of serious burns, crush injuries, non-healing fractures, muscle and bone atrophy, traumatic ischemic wounds, radiation tissue damage, compromised skin grafts, and tissue regeneration.

The use of NASA Light-Emitting Diode Near-Infrared (IR) technology for biostimulation

Whelan HT, M.D.

North American Association of Laser Therapy (NALT) Annual Conference (2002) Atlanta, Georgia.

This work is supported and managed through the NASA Marshall Space Flight Center - SBIR Program. Studies on cells exposed to microgravity and hypergravity indicate that human cells need gravity to stimulate growth. As the gravitational force increases or decreases, the cell function responds in a linear fashion. This poses significant health risks for astronauts in long-term space flight. The application of light therapy with the use of NASA LEDs will significantly improve the medical care that is available to astronauts on long-term space missions. NASA LEDs stimulate the basic energy processes in the mitochondria (energy compartments) of each cell, particularly when near-infrared light is set to activate the color sensitive chemicals (chromophores, cytochrome systems) inside. Optimal LED wavelengths include 680, 730 and 880 nm and our laboratory has improved the healing of wounds in laboratory animals by using both NASA LED light and hyperbaric oxygen. Furthermore, DNA synthesis in fibroblasts and muscle cells has been quintupled using NASA LED light alone, in a single application combining 680, 730 and 880 nm each at 4 Joules per centimeter squared. Muscle and bone atrophy are well documented in astronauts, and various minor injuries occurring in space have been reported not to heal until landing on Earth. An LED blanket device may be used for the prevention of bone and muscle atrophy in astronauts. The depth of near-infrared light penetration into human tissue has been measured spectroscopically. Spectra taken from the wrist flexor muscles in the forearm and muscles in the calf of the leg demonstrate that most of the light photons at wavelengths between 630-800 nm travel 23 cm through the surface tissue and muscle between input and exit at the photon detector. The light is absorbed by mitochondria where it stimulates energy metabolism in muscle and bone, as well as skin and subcutaneous tissue. Long term space flight, with its many inherent risks, also raises the possibility of astronauts being injured performing their required tasks. The fact that the normal healing process is negatively affected by microgravity requires novel approaches to improve wound healing and tissue growth in space. NASA LED arrays have already flown on Space Shuttle missions for studies of plant growth and the U.S. Food and Drug Administration (FDA) has approved human trials. The use of light therapy with LEDs can help prevent bone and muscle atrophy as well as increase the rate of wound healing in a microgravity environment, thus reducing the risk of treatable injuries becoming mission catastrophes. Space flight has provided a laboratory for studying wound healing problems due to microgravity, which mimic traumatic wound healing problems here on earth. Improved wound healing may have multiple applications that benefit civilian medical care, military situations and long-term space flight. Enhancing the soldier's tissue responses to injury may lead to battlefield resilience and medical independence. Counter-measures to chemical, biological and radioactive weapons exposures which are based on biostimulation of natural tissue regeneration mechanisms could be more universally safe and effective than conventional drugs and surgical modalities. Regeneration of wounded organs and limbs may also be possible if biostimulation could re-awaken molecular events leading to re-growth of tissue. Near infrared (IR) light has documented benefits promoting wound healing in human and animal studies. Our preliminary results have also demonstrated two to five-fold increases in growth-phase-specific DNA synthesis in normal fibroblasts, muscle cells, osteoblasts, and mucosal epithelial cells in tissue cultures treated with near-IR light. Our animal models treated with near-IR have included wound healing in diabetic mice and ischemic bipedal skin flap in rats. Near-IR induced a thirty percent increase in the rate of wound closure in these animal models. Dose- and time-dependent increases in vascular endothelial growth factor

(VEGF) and fibroblast growth factor (FGF-2) occurred in animals treated with near-IR. Human studies have included the use of near-IR to prevent ulcerative mucositis resulting from high doses of chemotherapy and radiation. Widely published reports, including those from our laboratory, described accelerated recovery from musculoskeletal injuries, hypoxic-ischemic wounds, burns, lacerations, radiation necrosis, and diabetic ulcers with the use of near-IR. Lasers have some inherent characteristics, which, make their use in a clinical setting problematic, including limitations in wavelength capabilities and beam width. The combined wavelengths of light optimal for wound healing cannot be efficiently produced, and the size of wounds that, may be treated by lasers is limited. Light-emitting diodes (LEDs) developed for NASA manned space flight experiments offer an effective alternative to lasers. These diodes can be made to produce multiple wavelengths, and can be arranged in large, flat arrays allowing treatment of large wounds. We are now investigating new collaborations with the Defense Advanced Research Projects Agency (DARPA) for military applications of LED wound healing technology in military medicine. Several uniquely military situations and indications could be addressed, optimizing near-IR parameters for wound healing via LEDs during extended missions under conditions separated from medical personnel. These include burns, chemical agents, radiation, biological agents and highly infected flesh-eating wounds (with and without extended burns) typical for the hygienic conditions occurring in battle fields, also infectious diseases and external wounds occurring in environments with no solar irradiation, low oxygen and high carbon dioxide (submarines). The dramatic results with use of near-IR LED light to prevent digestive mucosal lesions (mucositis) and pain in cancer patients, after high-dose chemotherapy and radiation, suggest the potential for military use of near-IR light to treat U.S. troops exposed to chemical and radioactive warfare agents in the field. These examples illustrate the many possible military uses for this technology. These life-saving applications require especially accelerated wound healing, rapid reduction of infections and pain modulation. Regeneration of muscles in amphibians has also been produced by near-IR therapy. The potential for regeneration of human tissue also deserves study. Central nervous system regeneration would be of particular benefit. Thus far, we have demonstrated that the best results for wound healing occur at wavelengths of 670 nm and 880 nm using 4 to 8 joules/cm2, applied at power densities of approximately 50 mW/cm2. However, studies to determine molecular mechanisms could lead to the optimization for current uses, as well as open up new applications. Despite numerous reports on the benefits of near-IR on wound healing and rehabilitation over the last decade, the basic mechanisms of its action remain poorly understood. Britton Chance's group has reported that about 50% of near-IR light is absorbed by mitochondrial chromophores, such as cytochrome oxidase. However, the underlying cellular and molecular events are still unknown.

Effects of 670-nm Phototherapy on Development

Yeager RL, Franzosa JA, Millsap DS, Angell-Yeager JL, Heise SS, Wakhungu P, Lim J, Whelan HT, Eells JT, Henshel DS

Photomed Laser Surgury (2005) 23(3): 268-72.

School of Public and Environmental Affairs, Indiana University, Bloomington, Indiana.

Objective: The objective of the present study was to assess the survival and hatching success of chickens (Gallus gallus) exposed in ovo to far-red (670-nm) LED therapy.

Background Data: Photobiomodulation by light in the red to near-infrared range (630-1000 nm) using low-energy lasers or light-emitting diode (LED) arrays has been shown to accelerate wound healing and improve recovery from ischemic injury. The mechanism of photobiomodulation at the cellular level has been ascribed to the activation of mitochondrial respiratory chain components resulting in initiation of a signaling cascade that promotes cellular proliferation and cytoprotecton.

Materials and Methods: Fertile chicken eggs were treated once per day from embryonic days 0-20 with 670-nm LED light at a fluence of 4 J/cm(2). In ovo survival and death were monitored by daily candling (after Day 4).

Results: We observed a substantial decrease in overall and third-week mortality rates in the light-treated chickens. Overall, there was approximately a 41.5% decrease in mortality rate in the light-treated chickens (NL: 20%; L: 11.8%). During the third week of development, there was a 68.8% decrease in the mortality rate in light-treated chickens (NL: 20%; L: 6.25%). In addition, body weight, crown-rump length, and liver weight increased as a result of the 670-nm phototherapy. Light-treated chickens pipped (broke shell) earlier and had a shorter duration between pip and hatch.

Conclusion: These results indicate that 670-nm phototherapy by itself does not adversely affect developing embryos and may improve the hatching survival rate.

Green light emitting diode irradiation enhances fibroblast growth impaired by high glucose level

Vinck EM, Cagnie BJ, Cornelissen MJ, Declercq HA, Cambier DC

Photomed Laser Surgury (2005) 23(2): 167-71.

Background and Objective: The chronic metabolic disorder diabetes mellitus is an important cause of morbidity and mortality due to a series of common secondary metabolic complications, such as the development of severe, often slow healing skin lesions. In view of promoting the wound-healing process in diabetic patients, this preliminary in vitro study investigated the efficacy of green light emitting diode (LED) irradiation on fibroblast proliferation and viability under hyperglycemic circumstances.

Materials and Methods: To achieve hyperglycemic circumstances, embryonic chicken fibroblasts were cultured in Hanks' culture medium supplemented with 30 g/L glucose. LED irradiation was performed on 3 consecutive days with a probe emitting green light (570 nm) and a power output of 10 mW. Each treatment lasted 3 min, resulting in a radiation exposure of 0.1 J/cm2.

Results: A Mann-Whitney U test revealed a higher proliferation rate ($p = 0.001$) in all irradiated cultures in comparison with the controls.

Conclusion: According to these results, the effectiveness of green LED irradiation on fibroblasts in hyperglycemic circumstances is established. Future in vivo investigation would be worthwhile to investigate whether there are equivalent positive results in diabetic patients.

Increased fibroblast proliferation induced by light emitting diode and low power laser irradiation

Vinck EM, Cagnie BJ, Cornelissen MJ, Declercq HA, Cambier DC

Lasers Med Science (2003) 18(2): 95-9

Background and Objective: As Light Emitting Diode (LED) devices are commercially introduced as an alternative for Low Level Laser (LLL) Therapy, the ability of LED in influencing wound healing processes at cellular level was examined.

Study Design, Materials and Methods: Cultured fibroblasts were treated in a controlled, randomized manner, during three consecutive days, either with an infrared LLL or with a LED light source emitting several wavelengths (950 nm, 660 nm and 570 nm) and respective power outputs. Treatment duration varied in relation to varying surface energy densities (radiant exposures).

Results: Statistical analysis revealed a higher rate of proliferation ($p < 0.001$) in all irradiated cultures in comparison with the controls. Green light yielded a significantly higher number of cells, than red ($p < 0.001$) and infrared LED light ($p < 0.001$) and than the cultures irradiated with the LLL ($p < 0.001$); the red probe provided a higher increase ($p < 0.001$) than the infrared LED probe and than the LLL source.

Conclusion: LED and LLL irradiation resulted in an increased fibroblast proliferation in vitro. This study therefore postulates possible stimulatory effects on wound healing in vivo at the applied dosimetric parameters.

Post-Op Rehab

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

Philip Gable, B App Sc P.T. G Dip Sc Res (LLLT) MSc, Australia
Jan Tunér, D.D.S., Sweden

Presented at the WALT annual conference, Japan.

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

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

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

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

Reports of stimulation of Rabbit radii fractures were made by Tang in 1986 and similar reports by Trelles in 1987 on mice femurs. In both situations the irradiated bones healed faster than the controls. In another study by Hernandez-Ros, in 1987, LLLT demonstrated stimulation of fresh fractures on Sprague-Dawley rats that were fractured bilaterally. The unexpected results of this study were that the contra-lateral fractured non-treated limb also healed faster than the control group. Over the following decade and a half further studies (Yamada 1991; Pyczek, Sopala et al. 1994; Ozawa 1995; Horowitz 1996; Yaakobi 1996; Saito and Shimizu 1997) have also investigated and demonstrated that LLLT is effective for promoting the stimulation of bone healing. Recently Nicolau and colleagues (2002) from Brazil demonstrated the positive effect of LLLT on the stimulation of bone in mice with latent promotion of bone remodulation at injury sites without changes in bone architecture, increased bone volume and increased osteoblast surface through increased resorption and formation of bone with higher apposition rates. A positive effect on bony implants has been demonstrated by Dörtbudak (2002) and Guzzardella (2003). The effect of laser irradiation on osteoblastic cells has been reported by Yamamoto (2001) and Guzzardella (2002).

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

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

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

If LLLT is then considered within the context of this new theory on bone circulation and the contribution of the lymphatic circulation then a further logical reasoned deduction for the action of LLLT on bone stimulation can be made. LLLT has a well documented and known effect influencing the lymphatic circulation. This has been demonstrated from the early works of Lievens, (1985) that demonstrated the influence of "Laser Irradiation" on the motricity of the lymphatic system and on the wound healing process. This is supported by several wound studies that demonstrate that the levels of protein rich exudates in non-healing wounds increase markedly from exposure to LLLT. This demonstrated action is determined to be as a result of the increase in lymphatic circulation (Robinson and Walters 1991; Gabel 1995). More recent work at the Flinders Medical Center in Adelaide South Australia has been completed and presented at the World Association of Laser Therapy conference in Tokyo Japan (Anderson, Carati et al. 2002). This study has demonstrated the positive effects of LLLT on the lymphatic circulation and its consequential benefits to the post mastectomy patient. An understanding of the existing knowledge of the effects of LLLT on the lymphatic system combined with the hypothesis of bone fluid transport provides a coupled theory that would demonstrate a positive description and explain of the predominant effects of LLLT in bone stimulation.

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

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

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

References:

Anderson, S, Carati, C et al. (2002). Low Level Laser Therapy (LLLT) as a Treatment for Post-matestectomy Lymhoedema. WALT 2002, Tokyo Japan.

Coombe, A R et al (2001). The effect of low level laser irradiation on osteoblastic cells. Clin Ort Res. 4: 3-14.

Dörtbudak, O et al (2002). Effect of low-power laser irradiation on bony implant sites. Clin Oral Implants Res 13(3):288-292.

Fenyo, M. (1990). Theoretical and Experimental Basis of Biostimulation by Bioptron, Bioptron AG, Monchaltorf, Switzerland.

Gabel, C. P. (1995). "Does Laser enhance bruising in acute sporting injuries." Aust. J. Physio. 41(4): 267-269.

Gabel, C. P. (1995). The effect of LLLT on slow healing wounds and ulcers. Health Sciences. Darwin, Northern Territory.

Guzzardella, G A et al (2002). Laser stimulation on bone defect healing: An in vitro study. Lasers Med Sci. 17(3): 216-220.

Guzzardella, G A et al (2003). Osseointegration of endosseous ceramic implants after postoperative low-power laser stimulation: an in vivo comparative study. Clin Oral Implants Res. 14: 226-232.

Horowitz, I. et al. (1996). "Infrared spectroscopy analysis of the effect of low power laser irradiation on calvarial bone defect healing in the rat (abstract)." Laser Therapy 8: 29.

Karu, T. I. (1988). "Molecular mechanism of the therapeutic effects of low intensity laser radiation." Lasers in Life Science 2: 53-74.

Karu, T. I. (1989). Photobiology of low-power laser therapy. London, Harwood Academic Publishers.
Lievens, P. (1985). The influence of "Laser Irradiation" on the motricity of the lymphatical system and on the wound healing process. International Congress on Laser in Medicine and Surgery., Bologna.

Nicolau, R A., Jorgetti, V, Rigau, J et al. "Effect of low power laser Ga-Al-As (660nm) in the bone tissue remodulation in mice"

Ozawa, Y. et al (1995). "Stimulatory effects of low-power laser irradiation on bone formation in vitro." SPIE Proc. 1995 Vol. 1984: 281-288.

Pohl, T. (1999). Bone circulation, the lymphatic system contribution. Personal Communication to C. P. Gabel. Adelaide Oct 1999.

Pouyssegur, J. (1985). "The growth factor-automatable Na+/H+ exchange system: a genetic approach. In Karu, T.I. 1988, 'Molecular mechanism of the therapeutic effects of low intensity laser radiation', Lasers in Life Science, vol.2, p.53-74." Trends in Biochemical Science 10: 453-455.

Pyczek, M., Sopala, M et al. (1994). "Effect of low-energy laser power on the bone marrow of the rat.". Folia Boil (Krakow) 42(3-4): 151-156.

Robinson, B. and Walters, J (1991). "The use of low level laser therapy in diabetic and other ulcerations." Journal of British Podiatric Medicine 46(10): 186-189.
Saito, S. and. Shimizu, N. (1997). "Stimulatory effects of low-power laser irradiation on bone regeneration in midpalatal suture during expansion in the rat." Am J Ortod Dentofac Orthop 11(5): 525-.

Smith, K. C. (1990). Light and life: The photobiological basis of the therapeutic use of radiation from lasers. International Laser Therapy Association Conference, Osaka.

Yaakobi, T. et. al. (1996). "Promotion of bone repair in the cortical bone of the tibia in rats by low energy laser (He-Ne) irradiation." Calcif Tissue Int. 59(4): 297-300.

Yamada, K. (1991). "Biological effects of low power laser irradiation on clonal osteoblastic cells (MC3T3-E1)." Nippon Seikeigeka Gakkai Zasshi 65(9): 787-799.

Yamamoto, M et al (2001). Stimulation of MCM3 gene expression in osteoblast by low level laser irradiation. Laser in Med Sci. Abstract issue. 16(3): 213-217.

The Effects of Infrared Diode Laser Irradiation on the Duration and Severity of Post Operative Pain:

A Double Blind Trial

Laser Therapy 1992, 4(4): 145 – 9.

Kevin Moore, Naru Hira, Ian J. Broome and John Cruickshank
Department of Anaesthesia and General Surgery, Royal Oldham Hospital, Oldham, U.K.
Department of Anaesthesia, The Royal Hallamshire Hospital, Sheffield, U.K.
General Practitioner, Pennymeadow Clinic, Ashton-under-Lyne, U.K.

The trial was designed to test the hypothesis that LLLT reduces the extent and duration of post operative pain. Twenty consecutive patients for elective cholecystectomy were randomly allocated for either LLLT or as control. The trial was double blind. Patients for LLLT received 6 - 8 minutes treatment (GaAlAs: 830 nm: 60 mW CW) to the wound area immediately following skin closure prior to emergence from GA. All patients were prescribed on demand post operative analgesia (IM or oral according to pain severity). Recordings of pain scores (0 - 10) and analgesics requirements were noted by an independent assessor. There was a significant difference in the number of doses of narcotic analgesics (IM) required between the two groups. Controls n = 5.5; LLT n =2.5. No patient in the LLLT group required IM analgesia after 24 hours. Similarly the requirement for oral analgesia was reduced in the LLLT group. Controls n = 9; LLLT n = 4. Control patients assessed their overall pain as moderate to severe compared with mild to moderate in the LLLT group.

The results justify further evaluation on a larger trial population.

Preoperative Low Level Laser application to reduce post-operative pain in patients receiving winograd type of partial matrixectomy surgery of hallux.

Les Jonsson B H Sc (Podiatry). Dip. Podiatry, Dip Podiatric Surgery, Dip. Soc. Sc. (Psychology). Cert. L.L.T. Mary Needham, R.G.O.N., Cert., L.L.T.

Introduction: Low level laser was introduced as a part of our surgical regime to assist with post operative healing following digital surgery. It was observed that fewer patients returned for post-operative redressings complaining of post operative pain. A pilot study has been undertaken to report the level of pain experienced by patients who received a Winograd type partial matrixectomy of the hallux. To reduce the number of extraneous variables the surgery was undertaken in the same setting with the same surgeon and staff with the same operative instructions provided. Laser Therapy was used within 30minutes of surgery.

Methodology: Each patient was placed on the operating table in the supine position. The laser probe was placed against the epidermis and applied at 1.8J/cm 2 ,5.7Hz, with wavelength 830 nm and output power 40mW. from a "Maestro", laser manufactured by Medicom, Praha , Czech Republic . The probe was applied at 2 points at each surgical site and at one point at each of the two sites for undertaking the digital anaesthetic block at the proximal aspect of the great toe. A mixture 5cc of 50/50 2% plain xylocaine and 0.5% Marcaine was injected dorsal to plantar into the proximal aspect of the great toe. The feet were prepped and draped in the normal sterile manner. A partial nail plate avulsion was achieved with removing 2-3mm of the fibular and/or tibia nail borders. A Betadine scrub was then undertaken. This was followed with an incision proximal to the proximal end of the matrix along the course of the new nail edge to the distal end of the nail. A second incision was made in a semi elliptical fashion from the proximal end of the first incision along the course of the original nail border joining with the distal end of the first incision. Both incisions were made down to bone and all tissue was removed. Matrix within the cavity was removed. Saline irrigation was applied to the cavity. The cavity was closed with Proline sutures at proximal and distal ends with steristrips across the nail section. The tourniquet was released and blood flow was observed to return to the area. A dressing of Betadine and Bactagras was applied with 4 x 4 sterile gauze, followed by gauze bandage and Coban.

Each patient was given oral and written instruction and an appointment for redressing in 5 to 7 days. Instructions included the suggestion that the patient take Panadol. Each patient appeared tolerated the procedure well and left the surgery ambulated.

One returning to the surgery after five to seven days for re-dressings, each patient scored on a 10cm Visual Analogue Scale, the level that best illustrated the highest level of pain that they experienced following the operation.

Results: Those in the Laser group (N=12) scored an average of 2.1 whereas those in the Non laser group scored an average 7.2 (N=3).

Conclusion: The level of self medication for pain relief was not monitored and no breakdown of ethnicity, age or sex was recorded for any patients. The authors note the small number of subjects in this study, in particularly the “No Laser” group. Given the low pain scores of the laser group reporting low pain scores, it is expected that these authors will afford all future eligible patients the opportunity of pre-operative laser therapy for this and other types of surgery. Other practitioners who do not use laser, who use like surgical techniques are encouraged to conduct a similar study on their patients, to make a comparison with the current study and to report their findings.

Advances in Laser Therapy for Bone Repair

A. Barber 1, JE. Luger 1, A. Karpf 1 , Kh. Salame 2 , B. Shlomi 3, G. Kogan 3, M. Nissan 4, M. Alon 5, and S. Rochkind 2,6.

1Foot & Ankle Unit, Departments of Orthopedic Surgery "B", Departments of 2Neurosurgery, 3Oral and Maxillofacial Surgery, and 5Rehabilitation, 6Division of Peripheral Nerve Reconstruction, Tel Aviv Sourasky Medical Center, Tel Aviv University; 4Ben Gurion University, Israel.

During the last decade, it was discovered that low-power laser irradiation has stimulatory effects on bone cell proliferation and gene expression. The purposes of this review are to analyze the effects of low- power laser irradiation on bone cells and bone fracture repair, to examine what has been done so far, and to explore the additional works needed in this area. The studies reviewed show how laser therapy can be used to enhance bone repair at cell and tissue levels. As noted by researchers, laser properties, the combinations of wavelength and energy dose need to be carefully chosen so as to yield bone stimulation.

Effects of Visible NIR Low Intensity Laser on Implant Osseointegration In Vivo.

Laser Med Surg Abstract issue, 2002: 11.

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

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

At 6 weeks the removal torque in the laser groups was much higher than in the control group.

Biomodulatory Effects of LLLT On Bone Regeneration

Antonio L.B. Pinheiro1, Marilia G. Oliveira2, Pedro Paulo M. Martins3, Luciana Maria Pedreira Ramalho4, Marcos A. Matos de Oliveira5, Aurelнcio Novaes Jъnior and Renata Amadei Nicolau

Tissue healing is a complex process that involves local and systemic responses. The use of Low Level Laser Therapy (LLLT) for wound healing has been shown to be effective in modulating both local and systemic response. Usually the healing process of bone is slower than that of soft tissues. The effects of LLLT on bone are still controversial as previous reports show different results. This paper reports recent observations on the effect of LLLT on bone healing. The amount of newly formed bone after 830nm laser irradiation of surgical wounds created in the femur of rats was evaluated morphometricaly. Forty Wistar rats were divided into four groups: group A (12 sessions, 4.8J/cm2 per session, 28 days); group C (three sessions, 4.8J/cm2 per session, seven days). Groups B and D acted as non-irradiated controls. Forty-eight hours after the surgery, the defects of the laser groups were irradiated transcutaneously with a CW 40mW 830nm diode laser, (f~1mm) with a total dose of 4.8J/cm2. Irradiation was performed three times a week. Computerized morphometry showed a statistically significant difference between the areas of mineralized bone in groups C and D (p=0.017). There was no significant difference between groups A and B (28 days) (p=0.383). In a second investigation, we determined the effects of LLLT on bone healing after the insertion of implants. It is known that dental implants need four and six months period for fixation on the maxillae and on the mandible before receiving loading. Ten male and female dogs were divided into two groups of five animals that received the implant. Two animals of each group acted as controls. The animals were sacrificed 45 and 60 days after surgery. The animals were irradiated three times a week for two weeks in a contact mode with a CW 40mW 830nm diode laser, (f ~1mm) with a total dose per session of 4.8J/cm2 and a dose per point of 1.2J/cm2.

The results of the SEM study showed better bone healing after irradiation with the 830nm diode laser. These findings suggest that, under the experimental conditions of the investigation, the use of LLLT at 830nm significantly improves bone healing at early stages. It is concluded that LLLT may increase bone repair at early stages of healing.

Bone Repair of Periapical Lesions Treated or Not With Low Intensity Laser (λ, =904 NM)

American Society for Laser Medicine and Surgery Abstracts
Annual Conference Dallas, Texas 2004 p. 81,303

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

Mestrado Profissionalizente Lasers em Odontologia,

The purpose of this study was to evaluate the influence of low intensity laser on the bone repair over periapical lesions of dental elements. Fifteen patients with a total of eighteen periapical lesions were selected and divided into two groups. The University of Sao Paolo, Dentistry School's Research Ethics Committee, granted ethical approval. Lesions of the control group was submitted to endodontic treatment and/or periapical surgery and the lesions of the experimental laser group, were submitted to the same procedures of the first group but also irradiated by low intensity laser. It used a 904 nm wavelength laser GaAs, employing 11 mW of power delivered by a fiber optic system, irradiation continuous and contact mode, using a fluency of 9 J/cm2. The aforementioned treatment was repeated for 10 sessions with intervals of 72 hours between each session. Bone repair was evaluated through lesion measurements, which were accessed from the X ray pictures. These were statistically analyzed.

Results showed a significant difference between the laser and control groups ($p<0,10$), emphasizing that the laser group presented a significant reduction of the lesion areas. X-ray confirmed this.

Low-level laser therapy stimulates bone-implant interaction: An experimental study in rabbits

Clin Oral Implants Res. 2004 Jun; 15 (3):325-32.

Khadra M, Ronold HJ, Lyngstadaas SP, Ellingsen JE, Haanaes HR.

Department of Oral Surgery and Oral Medicine, Faculty of Dentistry, University of Oslo, Oslo, Norway

The aim of the present study was to investigate the effect of low-level laser therapy (LLLT) with a gallium-aluminium-arsenide (GaAlAs) diode laser device on titanium implant healing and attachment in bone. This study was performed as an animal trial of 8 weeks duration with a blinded, placebo-controlled design. Two coin-shaped titanium implants with a diameter of 6.25 mm and a height of 1.95 mm were implanted into cortical bone in each proximal tibia of twelve New Zealand white female rabbits (n=48).
The animals were randomly divided into irradiated and control groups. The LLLT was used immediately after surgery and carried out daily for 10 consecutive days. The animals were killed after 8 weeks of healing. The mechanical strength of the attachment between the bone and 44 titanium implants was evaluated using a tensile pullout test.
Histomorphometrical analysis of the four implants left in place from four rabbits was then performed. Energy-dispersive X-ray microanalysis was applied for analyses of calcium and phosphorus on the implant test surface after the tensile test. The mean tensile forces, measured in Newton, of the irradiated implants and controls were 14.35 (SD+/-4.98) and 10.27 (SD+/-4.38), respectively, suggesting a gain in functional attachment at 8 weeks following LLLT (P=0.013). The histomorphometrical evaluation suggested that the irradiated group had more bone-to-implant contact than the controls. The weight percentages of calcium and phosphorus were significantly higher in the irradiated group when compared to the controls (P=0.037) and (P=0.034), respectively, suggesting that bone maturation processed faster in irradiated bone.

These findings suggest that LLLT might have a favorable effect on healing and attachment of titanium implants

Raynaud's Disease

Low Level Laser Treatment of Primary and Secondary Raynaud's Phenomenon

al-Awami M, Schillinger M, Gschwandtner ME, Maca T, Haumer M, Minar E.

VASA (2001) Nov; 30(4):281-284.

Background:
Patients who had been treated with low level laser (LLL) for their digital ulcers reported an impressive improvement of their symptoms of episodic digital ischemia. Therefore, this pilot study was performed to evaluate the efficacy of LLL as a new non-drug non-invasive treatment for patients with primary and secondary Raynaud's phenomenon (RP).

Patients and Methods:
Forty patients (29 female, 11 male, mean age 51 years) with active primary (28%) and secondary (72%) Raynaud's phenomenon received 10 sessions of LLL distant irradiation during winter months. Assessment of subjective and objective parameters was performed at baseline, one week after the last session and three months later. Variations of subjective parameters as number of daily acute episodes and severity of discomfort were assessed by a coloured visual analogue scale. A standardised cold challenge test using computed thermography of continuous temperature recordings by means of infrared telethermography was used to assess the digital blood flow.

Results:
A significant improvement was noticed clinically and thermographically after 6 weeks and 3 months, respectively ($p < 0.0001$).
Conclusions: These data suggest that LLL treatment has a good short and medium term effectiveness in patients with Raynaud's phenomenon.

Tendonopathies

Low Level Laser Therapy can be Effective for Tendonitis –A Meta Analysis

J.M. Bjordal, C. Couppe University of Bergen, Dept. Physiotherapy Science, Bergen, Norway

Purpose:
To investigate if low level laser therapy (LLLT) with previously defined optimal treatment parameters can be effective for tendonitis.

Material:
Randomized controlled trials with LLLT for tendonitis.

Method:
Literature search for trials published after 1980 using LLLT on Medline, Embassy, Cochrane Library and hand search of physiotherapy journals in English and Scandinavian languages. Only trials that compared laser exposure of the skin directly over the injured tendon with optimal treatment parameters with identical placebo treatment were included.

Results:
The literature search identified 77 randomized controlled trials with LLLT, of which 18 included tendonitis. Three trials were excluded for lack of placebo control, of which one trial was comparative; another lacked patients with tendonitis in the treatment group, while the last unwittingly gave the placebo group active treatment. Four trials used too high power density or dose, and three trials did not expose the skin directly overlying the injured tendon. The remaining eight trials were included in a statistical pooling, where the mean effect of LLLT over placebo in tendonitis was calculated to 32% [25.0-39.0, 95% CI].

Conclusion:
Low level laser therapy with optimal treatment procedure/ parameters can be effective in the treatment of tendonitis.

Level Laser Therapy In Tendon Injuries? – A Review of In Vitro and In Vivo Trials

J.M. Bjordal, C. Couppe University of Bergen, Dept. Physiotherapy Science, Bergen, Norway

Purpose:
To investigate the effect of different laser treatment parameters on fibroblast inflammation and production of collagen fibers.

Material:
Controlled in vitro or in vivo trials with low level laser therapy (LLLT)

Method:
Literature search for trials published after 1980 using LLLT on Medline, Embase, Cochrane Library and hand search of physiotherapy journals in English and Scandinavian languages. Optimal treatment parameters regarding timing, treatment frequency, dose and power density at target tissue were synthesized.

Results:
The literature search identified 31 controlled trials with LLLT on collagen tissue. Three in vitro trials were performed on stretch-induced and inflammation in fibroblast cultures and five in vitro trials were performed on collagen production. Optimal dose and power density for inhibition of prostaglandin PGE2 and interleukin 1- beta production was found to be 3.2-6.3 J/cm2 and 5.3 mW/cm2 measured at the target fibroblast cells after 5 days of irradiation. Data on upper range limits for anti-inflammatory treatment were inconclusive. Optimal dose and power density for collagen production was found to be in the range 0.2-2.0 J/cm2 and 2 –20 mW/cm2 measured at the target fibroblast cells. Daily treatment for 2 weeks with optimal parameters yielded a maximum increase in collagen production of 37%. The results from three in vivo trials showed similar increase in collagen production. Doses in excess of 4.5 J/cm2 and power densities higher than 30 mW/cm2 inhibited fibroblast metabolism and decreased collagen production.

Conclusion:
There is evidence of a dose-response pattern for LLLT in the treatment of tendon injuries during the proliferative phase of regeneration

Laser Photostimulation of Collagenous Tissues Repair Processes in Patients and Experimental Animal Models of Tendon Repair and Diabetic Skin Ulcers

Enwemeka ES, PhD, FACSM, Reddy GK, PhD, Stehno-Bittel L, PhD, Thomas J, MD

North American Association of Laser Therapy (NALT) Annual Conference (2002) Atlanta, Georgia.

Connective tissues are notorious for their slow rates of healing. As a result, they are often protected in immobilization casts for long periods of time after surgery. The long period of immobilization predisposes a multitude of complications, including muscle atrophy, osteoarthritis, skin necrosis, infection, tendo-cutaneous adhesion, re-rupture, and thrombophlebitis.

If healing can be quickened, then, the duration of cast immobilization can be reduced to minimize the deleterious effects of immobilization. In several experiments, we studied the effects of HeNe, GaAs, and GaAlAs lasers on tissue repair. Furthermore, we tested the hypothesis that early weight-bearing, ultrasound, HeNe laser, and GaAs laser, when used singly or in combination, accelerate the healing process of experimentally tenotomized and repaired rabbit Achilles tendons as evidenced by biochemical, biomechanical, and morphological indices of healing.

Our results demonstrate that:
(1) Laser therapy of appropriate intensity promotes skin and tendon tissue repair processes;
(2) Appropriate doses of each modality, i.e., early weight-bearing, ultrasound, HeNe and GaAs laser therapy augment collagen synthesis, modulate maturation of newly synthesized collagen, and overall, enhance the biomechanical characteristics of the repaired tendons;
(3) Combinations of either of the two lasers with early weight-bearing and either ultrasound or electrical stimulation further promote collagen synthesis when compared to early weight-bearing alone.

However, the biomechanical effects measured in tendons receiving the multi-modality therapy were similar, i.e., not better than the earlier single modality trials. In other experiments, we tested the hypotheses that appropriate doses of laser therapy promote tissue repair in a rat model of experimental diabetes, and also in clinical cases of healing-resistant diabetic ulcers.

Our experimental diabetic ulcers healed faster with laser therapy, as did some human cases of diabetic leg ulcers. Our recent meta-analyses of the laser therapy literature corroborate these results, and support the widely held belief that appropriate intensities of laser therapy accelerate healing of collagenous tissues, i.e., skin, bones, tendons, ligaments, and cartilage.

Low Level Laser Therapy (LLLT) of Tendonitis and Myofascial Pains – A Randomized, Double-blind, Controlled Study

Logdberg-Andersson M, Mutzell S, and Hazel A

Laser therapy (1997) 9: 79-86.

The purpose of this randomized, double-blind study was to examine the effect of GaAs laser therapy for tendonitis and myofascial pain in a sample from the general population of Akersberga in the northern part of Greater Stockholm. 176 patients (of an original group of 200) completed the scheduled course of treatment. The patients were assigned randomly to either a laser group (92 patients, of whom 74 had tendonitis, completed the study) or a placebo group (84 patients, of whom 68 had tendonitis, completed the study). All 176 patients received six treatments during a period of 3-4 weeks. Their pain was estimated objectively using a pain threshold meter, and subjectively with a visual analogue scale before, at the end of, and four weeks after the end of treatment. Laser therapy had a significant, positive effect compared with placebo measured from the first assessment to the third assessment, four weeks after the end of treatment. Laser treatment was most effective on acute tendonitis.

Low Level Laser Therapy for Tendonopathy. Evidence of a Dose-Response Pattern

Bjordal J M, Couppé C, Ljunggren E

Physical Therapy Reviews (2001) 6: 91-99.

To investigate whether low-level laser therapy can reduce pain from tendonopathy, the authors performed a review of randomized placebo-controlled trials with laser therapy for tendonopathy. Validity assessment of each trial was done acc. to predefined criteria for location-specific dosage and irradiation of the skin directly overlying the affected tendon. The literature search identified 78 randomized control trials of which 20 included tendonopathy. Seven trails were excluded for not meeting the validity criteria on treatment procedure and trial design. 12 of the remaining 13 trials investigated the effect of laser therapy for patients with subacute and chronic tendonopathy and provided a pooled mean effect of 21%. If results from only the nine trials adhering to assumed optimal treatment parameters were included, the mean effect over placebo increased to 32%. Laser therapy can reduce pain in subacute and chronic tendonopathy if a valid treatment procedure and location-specific dose is used.

Effects of Skin-Contact Monochromatic Infrared Irradiation on Tendonitis, Capsulitis, and Myofascial Pain

Thomasson TL

Journal of Neurology Orthopedic Medicine Surgery (1996) 16(4): 242-245.

Skin-contact monochromatic infrared irradiation has recently become available via adaptation of superluminous diode technology. Craniofacial and cervical myalgias, insertion tendonitis, and dysfunctions of the temporomandibular joints are addressed. This article attempts to establish protocol guidelines and reports patient responses to this very effective, noninvasive, physiotherapeutic treatment modality. Both surgical and nonsurgical cases are reported, and clinical applications as well as home unit use is evaluated. Details on technique are given, and contraindications are outlined. Particular advantages are rapid patient response, operator-friendly technique, diversity of application parameters, and the opportunity to manage both acute and chronic conditions in the absence of oral or injectable pharmacology.

Discussion:
Wavelength-dependent photobiostimulation responses are a part of our everyday life. Increased melanin production, color recognition, and synthesis of vitamin D are a few examples. In this study, the excellent results of the infrared portion of the electromagnetic spectrum on pain relief seem to be related to several factors. One of these is the opportunity to place the infrared irradiation in direct contact with the patient's skin for extended periods of time without harm to the patient. Another factor is the delivery of the irradiation perpendicular to all target areas via flexible pads containing the superluminous diodes. Consistent, homogenous dosage delivery form patient to patient and condition to condition allows ease of establishing application protocols and uniform comparison of treatment results between practitioners. The consistent results from diagnosis to diagnosis indicate commonality of effects on inflammatory processes, regardless of site or etiology.

Since nearly all patients treated (91.9%) had a history of some type of previous therapeutic intervention, the results indicate a high rate of successful conservative treatment whether or not the diagnosis were new or subjected to previous applied standard treatment parameters. This is a great benefit, as skin-contact monochromatic infrared irradiation can be considered as a first line of physiotherapeutic treatment for soft tissue disorders encountered in pain management. The absence of technique-sensitive application and lack of harmful patient side effects enables this modality to be easily delegated to auxiliary personnel or to home use, and the rapid patient response is certainly an aid in pain-patient management.

The vast majority of supportive research regarding photobiostimulation has been limited to evaluation of effects of low level laser therapy. This is primarily because, until recently, lasers were the only convenient means of delivering effective monochromatic irradiation. However, with recent developments in superluminous diodes technology, we can now deliver effective, safe, user-friendly skin-contact monochromatic infrared irradiation with energy densities previously limited to laser irradiation. This eliminates or reduces the restrictions of immobility, hand-held delivery, or high cost some laser systems impose. Basford, Smith, Karu, and Baxter have indicated that the effects are not necessarily due to the unique qualities of laser irradiation, but are primarily wavelength dependent. It has been previously reported that these excellent responses to treatment may be partially due to increase fibroblastic activity, respiratory chain photobioactivation, bioactivation of serotonin, improved lymphatic evacuation, or increased circulation. Whatever may be the mechanism(s) involved, this easy, safe, and effective modality is an extremely valuable tool for eliminating or reducing pain, inflammation, edema, and loss of range of motion.

Possibilities of the analgesic therapy of ultrasound and non-invasive laser of plantar fasciitis

Hronkova H, Navratil L, Skopek J, Kymplova J

Laser Partner Clinicexperience (2000) No. 21, 19.

Objective:
To compare the effectiveness of the two therapeutic approaches, ultrasound and low level laser used in patients suffering from calcar calcaneus-plantar fasciitis.

Methods:
171 patients with calcar calcaneus and plantar facilities diagnosed with the x-ray were divided into four groups**.**

Group A - 60 patients treated with ultrasound therapy (UST). Ultrasound with the output of 1 W per cm^2 was applied for 5 minutes in each of 10 applications and the head of device pointed to the place of maximum pain;

Group B - 61 patients were treated with low level laser therapy (LLLT) without any additional treatment including pharmacotherapy. Laser with 870 nm of wavelength, output of 200 mW, was applied on the place of maximum pain. Energy density of 9 J/cm^2 in the series of 10 laser applications every other day was used.

Group C - 8 patients where previous UST had no or minimal effect and therefore LLLT was subsequently applied the same way as in the group B. Laser was applied not earlier than 14 days after the ultrasound.

Group D (Control) - In this group of 52 patients the sham laser radiation (no laser beam) was applied whereas patient and personnel could not identify whether the laser was shamed or not. This group is used as control "placebo" group.
The effectiveness of the treatment was determined according to the evaluation of the patient using certain criteria described in the table.

Results:
The complete disappearance of pain was seen in 50% of patients, partial improvement in 16.6% and no effect in 33.3% of patients treated with US.
In *Group B*, where LLLT has been used, 64% of patients described disappearance of pain, 26% with improvement and in 10% of patients this therapy brought no effect.
In the *Group C* of previous UST and subsequent use of LLLT, 75% of patients evaluated their treatment as successful. In 25% however, laser had no effect.
In summary, 69 patients were treated with LLLT from which 67% described complete pain relief, 20% partial improvement and in 13% laser brought no effect.
In the *Group D* there were 50 patients treated with sham laser and full effect was seen in 18% of them, partially reduced pain in 42% and without any effect in 40%.

Discussion and Conclusions:
The results show that the LLLT is a good therapeutic approach in the treatment of pain in patients suffering from calcar-calcaneus – plantar faciitis. The treatment with laser was significantly more successful then the ultrasound therapy, which is currently the most common therapy used for plantar fasciitis.

Temporomandibular Disorders

Clinical evaluation of the low intensity laser antialgic action of GaAlAs (wavelength=785 nm) in the treatment of the temporomandibular disorders

Sanseverino NTM, Sanseverino CAM, Ribeiro MS et al.

Lasers in Medicine and Surgery (2002) Supplement 14, Atlanta, Georgia.

The improved outcome of laser therapy, if higher doses are given, is documented in the study by Sanseverino 10 patients with pain and limitation of movements of the jaw were treated by 785 nm GaAlAs laser, dose 45 J/cm2. The joint and tender points in the masticatory and otherwise involved muscles was applied three times per week during three weeks. A control group of 10 patients was given sham laser therapy. The evaluation was performed through subjective pain assessment and measurement of the movements of the jaw. There was a significant improvement in the laser group only.

Wound Healing

The Effects of Laser Therapy on Tissue Repair and Pain Control: A Meta-analysis of the Literature

Jason Parker, BA, MSPT, David Dowdy, BS, MSPT, Erin Harkness, BA, MSPT, Leif Sanford, BS, MSPT, Chukuka Enwemeka, PhD, FACSM; Department of Physical Therapy, University of Kansas Medical Center, Kansas City, KS, USA

Statement of the Problem:
Low intensity laser therapy devices were first used as a form of therapy more than thiry years ago. However, their efficacies in reducing pain and/or promoting tissue repair remain questionable.

Purpose:
We conducted a meta-analysis of the literature in order to determine the overall treatment effects of laser therapy on pain control and tissue repair.

Method:
Following a literature search, studies meeting our inclusion criteria were identified, coded, and then subjected to statistical meta-analysis procedures as detailed by Cohen. The effect size of laser therapy treatment, i.e. Cohen's d was then calculated from each study.

Results:
A total of 36 peer reviewed papers on tissue repair were coded. Thirty-four of the papers met our inclusion criteria and were used to calculate a total of 46 treatment effect sizes. Fifteen peer-reviewed papers on pain control were coded, nine met the inclusion criteria and were used to calculate nine effect sizes. Meta-analysis revealed a positive effect of laser therapy on tissue repair (d= +1.81; n=46) and pain control (d=+1.11; n=9). The positive effect of laser therapy on specific indices of tissue repair is evident in the treatment effect sizes determined as follows: collagen formation (d=+2.78), rate of healing (d=+1.57), tensile strength (d=+2.13), wound closure (d=+0.76), tensile stress (d=+2.65), mast cell numbers (d=+1.87), and flap survival (d=+2.13). Furthermore, meta-analysis revealed a positive effect of various wavelengths of laser therapy on tissue repair, including: 632.8nm (+2.11), 904nm (+1.09), 514nm (+1.89), 820nm (+1.00), 830nm (+0.61), 780nm (+0.60), and cluster diode (+1.95). The overall treatment effect for pain control was positive as well (d=+1.11). Further analysis revealed a Fail safe N (Na) of 370 for tissue repair and 41 for pain control; indicating that of 370 and 41 peer-reviewed publications with negative or no effect of laser therapy would be needed to negate the positive effect sizes calculated for tissue repair and pain control respectively.

Conclusion:
Our findings indicate that laser therapy has a positive treatment effect on tissue repair processes and also, on pain control.

The Efficacy of Laser Therapy in Wound Repair: A Meta-Analysis of the Literature

Photomedicine and Laser Surgery 1 June 2004, vol. 22, no. 3, pp. 241-247(7)

Lynda D. Woodruff[1]; Julie M. Bounkeo[1]; Windy M. Brannon[1]; Kenneth S. Dawes; Cameron D. Barham[1]; Donna L. Waddell[2]; Chukuka S. Enwemeka[3]

[1] Department of Physical Therapy, North Georgia College and State University, Dahlonega, Georgia. [2] Department of Nursing, North Georgia College and State University, Dahlonega, Georgia. [3] Department of Physical Therapy and Rehabilitation Sciences, University of Kansas Medical Center, Kansas City, Kansas.

Objective:
We determined the overall effects of laser therapy on tissue healing by aggregating the literature and subjecting studies meeting the inclusion and exclusion criteria to statistical meta-analysis.

Background Data:
Low-level laser therapy (LLLT) devices have been in use since the mid sixties, but their therapeutic value remains doubtful, as the literature seems replete with conflicting findings.

Materials and Methods:
Pertinent original research papers were gathered from library sources, online databases and secondary sources. The papers were screened and coded; those meeting every inclusion and exclusion criterion were subjected to meta-analysis, using Cohen's d. statistic to determine the treatment effect size of each study. Results: Twenty-four studies with 31 effect sizes met the stringent inclusion and exclusion criteria. The overall mean effect of laser therapy on wound healing was highly significant (d = +2.22). Sub-analyses of the data revealed significant positive effects on wound healing in animal experiments (d = +1.97) as well as human clinical studies (d = +0.54). The analysis further revealed significant positive effects on specific indices of healing, for example, acceleration of inflammation (d = +4.45); augmentation of collagen synthesis (d = +1.80); increased tensile strength (d = +2.37), reduced healing time (d = +3.24); and diminution of wound size (d = +0.55). The Fail-Safe number associated with the overall effect of laser therapy was 509; a high number representing the number of additional studies—in which laser therapy has negative or no effect on wound healing—required to negate the overall large effect size of +2.22. The corresponding Fail-Safe number for clinical studies was 22.

Conclusion:
We conclude that laser therapy is an effective tool for promoting wound repair.

Low-Level Laser Therapy Facilitates Superficial Wound Healing in Humans: A Triple-Blind, Sham-Controlled Study

J. Ty Hopkins*; Todd A. McLoda†; Jeff G. Seegmiller‡; G. David Baxter§

Journal of Athletic Training 2004;39(3):223–229 by the National Athletic Trainers' Association

Objective:
Low-level laser therapy (LLLT) has been promoted for its beneficial effects on tissue healing and pain relief. However, according to the results of in vivo studies, the effectiveness of this modality varies. Our purpose was to assess the putative effects of LLLT on healing using an experimental wound model.

Design and Setting:
We used a randomized, triple-blind, placebo-controlled design with 2 within-subjects factors (wound and time) and 1 between-subjects factor (group). Data were collected in the laboratory setting.

Subjects:
Twenty-two healthy subjects (age = 21 +/- 1 years, height = 175.6 +/- 9.8 cm, mass = 76.2 +/- 14.2 kg).

Measurements:
Two standardized 1.27-cm^2 abrasions were induced on the anterior forearm. After wound cleaning, standardized digital photos were recorded. Each subject then received LLLT (8 J/cm^2; treatment time = 2 minutes, 5 seconds; pulse rate = 700 Hz) to 1 of the 2 randomly chosen wounds from either a laser or a sham 46-diode cluster head. Subjects reported back to the laboratory on days 2 to 10 to be photographed and receive LLLT and on day 20 to be photographed. Data were analyzed for wound contraction (area), color changes (chromatic red), and luminance.

Results:
A group X wound X time interaction was detected for area measurements. At days 6, 8, and 10, follow-up testing revealed that the laser group had smaller wounds than the sham group for both the treated and the untreated wounds ($P < .05$). No group X wound X time differences were detected for chromatic red or luminance.

Conclusions:
The LLLT resulted in enhanced healing as measured by wound contraction. The untreated wounds in subjects treated with LLLT contracted more than the wounds in the sham group, so LLLT may produce an indirect healing effect on surrounding tissues. These data indicate that LLLT is an effective modality to facilitate wound contraction of partial-thickness wounds.

Key Words:
modalities, experimental wound model

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.

Journal of Clinical Laser Medicine and Surgery (2000) Apr; 18(2):67-73.

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; epicondylitis; 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 submitted 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.

Laser Therapy - Positive Double Blind Studies

Allergic Rhinitis Neuman I. et al. Low energy phototherapy in allergic rhinitis and nasal polyposis. Laser Therapy. 1996. 1: 37.

Arthritis

Antipa C. et al. Comparative effects of various IR low energy diodes in the treatment of the rheumatic diseases. 1997. In press (Monduzzi Editore, Bologna)

Barabas K. et al. Controlled clinical and experimental examinations on rheumatoid arthritis patients and synovial membranes performed with neodym phosphate glas laser irradiation. Proc. 7th Congr Internat Soc for Laser Surg and Med, Munich June 1987. Abstract no 216a.

Goldman J. A. et al. Laser therapy of rheumatoid arthritis. Lasers Surg Med. 1980; 1: 93 102.

Gärtte S. et al. Doppelblindstudie zur Ueberpruefung der Wirksamkeit und Vertraeglichkeit einer niederenergetischen Lasertherapie bei Patienten mit aktiver Gonarthrose. Jaros Orthopaedie. 1995. 12: 3034.

Hoteya K. et al. Effects of a 1 W GaAlAs diode laser in the field of orthopedics. In: Meeting Report: The first Congress of the International Association for Laser and Sports Medicine. Tokyo, 1997. Laser Therapy 1997; 9 (4): 185

Lonauer G. Controlled double blind study on the efficacy of He-Ne-laser beams versus He-Ne- plus Infrared-laser beams in the therapy of activated osteoarthritis of finger joints. Clin Experim Rheuma. 1987; 5 (suppl 2) : 39

Mach E. S. et al. Helium-Neon (Red Light) Therapy of Arthritis. Rheumatologia, 1983; 3: 36.

Miyagi K. Double-blind comparative study of the effect of low-energy laser irradiation to rheumatoid arthritis. Current awareness of Excerpts Medica. Amsterdam. Elsevier Science Publishers BV. 1989; 25: 315.

Molina J. J. et al. La laserterapia como coadyuvante en el tratamiento de la A.R. (Artritis Reumatoidea). Boletin C.D.L., Barcelona. 1987; 14: 4-8.

Nivbrant Bo et al. Therapeutic laser treatment in gonarthrosis. Acta Orthop Scand. 1989; 60: 231.

Ortutay J et al. Psoriatic Arthritis Treatment with low power laser irradiation. A double blind clinical study. Lasermedizin -Laser in Med Surg. 1998; 13 (3-4): 140.

Oyamada Y. et al. A double blind study of low power He-Ne laser theraphy in rheumatioid arthritis. Optoelectronics in Medicine. 1987; p 747-750. Springer Verlag, Berlin (abstract). Complete study in Boleton de CDL. 1988; 17: 8-12.

Palmgren N. et al. Low-Power Laser Therapy in Rheumatoid Arthritis. Lasers in Medical Science. 1989; 4: 193.

Willner R. et al. Low power infrared laser biostimulation of chronic osteoarthritis in hand. Lasers Surg Med. 1985; 5: 149.

Epicondylitis

Gudmundsen J. et al. Laserbehandling av epicondylitis humeri og rotatorcuff-syndrom. Dobbelt blindstudie -200 pasienter. (Laser treatment of epicondylitis humeri and rotator cuff syndrome. Double blind study -200 patients. In Norwegian) Norsk tidsskrift for idrettsmedisin. 1987; 2: 6.

Haker E. et al. Is low-energy laser treatment effective in lateral epicondylalgia? J of Pain and Symptom Management. 1991; 6(4): 241.

Hopkins G. O. et al. Double blind cross over study of laser versus placebo in the treatment of tennis elbow. Proc International. Congress on Lasers, "Laser Bologna". 1985: 210. Monduzzi Editore S.p.A., Bologna.

Palmieri B. A double blind stratified cross over study of amateur tennis players suffering from tennis elbow using infrared laser therapy. Medical Laser Report. 1984; 1: 3-14

Simunovic Z., Trobonjaca T. et al. Treatment of medial and lateral epicondylitis -tennis and golfer elbow -with low level laser therapy: a multicenter double blind, placebo controlled clinical study on 324 patients. J Clin Laser Med & Surg. 1998; 16 (3): 145-151.

Vasseljen O. et al. Low level laser versus placebo in the treatment of tennis elbow. Scand Scand J Rehab Med. 1992; 24: 37. Also in Physiotherapy. 1992; 5: 329.

Fibrositis/Fibromyalgia

Scudds R. A. et al: A double-blind crossover study of the effects of low-power gallium arsenide laser on the symptoms of fibrositis. Physiotherapy Canada. 1989; 41: (suppl 3): 2.

Herpes Simplex

Volez-Gonzalez M. et al. Treatment of relapse in herpes simplex on labial and facial areas and of primary herpes simplex on genital areas and "area pudenda" with low power HeNelaser or Acyclovir administered orally. SPIE Proc. 1995; Vol. 2630: 43-50 Hypersensitive Dentine

Gelskey S. C. et al. The effectiveness of the Nd:YAG laser in the treatment of dentinal hypersensitivity. J Can Dent Assoc. 1993; 59 (4): 337-386.

Gerschman J. A. et al. Low Level Laser in dentin hypersensitivity. Australian Dent J. 1994;39:6.

Yamaguchi M. et al. Clinical study on the treatment of hypersensitive dentin by GaAlAs laser diode using the double blind test. Aichi Gakuin Daigaku Shigakkai Shi -Aichi-Gakuin Journal of Dental Science. 1990; 28(2): 703-707. (in Japanese)

Microcirculation

Schindl A. et al. Low intensity laser irradiation improves skin circulation in patients with diabetic microangiopathy. Lasers Surg Med. 1998; Suppl. 10: 7. Mucositis

Cowen D. et al. Low energy helium neon laser in the prevention of oral mucositis in patients undergoing bone marrow transplant: results of a double blind randomized trial. Int J Radiat Oncol Biol Phys. 1997; 38 (4): 697-703.

Nerve Functions

Antipa C. et al. Clinical results of the low energy laser action on distal forearm posttraumatic nerve lesions. Laser Therapy. 1996; 1: 36.

Khullar S. M. et al. Low level laser treatment improves longstanding sensory aberrations in the inferior alveolar nerve following surgical trauma. J Oral Maxillofac Surg. 1996; 54: 2-7.

Khullar S. M. et al. Effect of low-level laser treatment on neurosensory deficits subsequent to sagittal split ramus osteotomy. Oral Surgery Oral Medicine Oral Pathology. 1966; 82 (2): 1328.

Rochkind S. et al. Double-blind Randomized Study Using Neurotube and Laser Therapy in the Treatment of Complete Sciatic Nerve Injury of Rats. Proc. 2nd Congr World Assoc. for Laser Therapy, Kansas City, 1998.

Snyder-Mackler L. et al. Effect of helium-neon laser irradiation on peripheral sensory nerve latency. Physical Therapy. 1988; 68: 223.

Walker J. Temporary suppression of clonus in humans by brief photostimulation. Brain Research. 1985; 340: 109.

Walsh D. et al. The effect of low intensity laser irradiation upon conduction and skin temperature in the superficial radial nerve. Double-blind placebo controlled investigation using experimental ischaemic pain. Proc. Second Meeting of the Internat Laser Therapy Association, London, sept. 1992.

Pain

Armino L. et al. Laser therapy in post-episiotomic neuralgie. LASER. Journ Eur Med Laser Ass. 1988; 1(1):7.

Atsumi K. et al. Biostimulation effect of low-power energy diode laser for pain relief. Lasers Surg Med. 1987; 7: 77.

Carillo J. et al. A randomized double-blind clinical trial on the effectiveness of helium-neon laser in the prevention of pain, swelling and trismus after removal of impacted third molars. Int Dent Journ. 1990; 40: 31.3

Ceccherelli F. Diode laser in cervical myofascial pain. A double-blind study versus placebo. The Clin J Pain. 1989; 4: 301-304.

Cheng R. Combined treatments of electrotherapy plus soft laser therapy has synergistic effect in pain relief and disease healing. Surgical and Medical Lasers. 1990; 3 (3): 135 (abstract).
Eckerdal A., Lehmann Bastian H. Can low reactive-level laser therapy be used in the treatment of neurogenic facial pain? A double-blind, placebo controlled investigation of patients with trigeminal neuralgia. Laser Therapy. 1996; 8: 247-252.
Emmanoulidis O. et al. CW IR low-power laser application significantly accelerates chronic pain relief rehabilitation of professional athletes. A double blind study. Lasers Surg Med. 1986; 6: 173.
De Bie R. A. Effect of laser therapy on ankle sprains Ned. T. Fysiotherapie. 1988; 95: 108-112. (in Dutch)
Flöter T., Refisch H. P. Pain treatment with laser. A double blind study. Proc. of the 4th Internat Symposium.Acupunct & Electro-Therap Res. 1988; 13(4): 236-237. Also: Schmerzbehandlung mit Laser. Eine Dopppelblinde Studie. Top Medizin. 1990; 4(4): 52-56.
Gertner C. Analgesy by low power laser (LPL): a controlled double blind study in ankylosing spondarthritis (SPA). Lasers Surg Med. 1989; Suppl 1:55.
Hashimoto T. et al. Efficacy of laser irradiation on the area near the stellate ganglion is dose-dependent: a double-blind crossover placebo-controlled study. Laser Therapy. 1997; 1(9): 7-11
Kemmotsu M. D. et al. LLLT for pain attenuation -the current experience in the pain clinic. In: Progress in Laser Therapy. Eds Oshiro T, Calderhead R G. 1991: 197-200. John Wiley & Sons, Chichester, Engl. ISBN 0-471-93154-3.
Kemmotsu M. D. et al. LLLT for pain attenuation -the current experience in the pain clinic. In: Progress in Laser Therapy. Eds Oshiro T, Calderhead R G. 1991: 197-200. John Wiley & Sons, Chichester, Engl. ISBN 0-471-93154-3.
Longo L. et al. Treatment with 904 nm and 10600 nm laser of acute lumbago -double blind control. LASER. Journ Eur Med Laser Ass. 1988; 1(3):16.
Mokhtar B. et al. A double blind placebo controlled investigation of the hypoalgesic effects of low intensity laser irradiation of the cervical roots using experimental ischaemic pain. Proc. Second Meeting of the International Laser Therapy Assn., ôLondon Laserö, Sept 1992, p 61.
Moore K. et al The effect of infra-red diode laser irradiation on the duration and severity of postoperative pain. A double-blind trial. Laser Therapy. 1992; 4: 145.
Moore K. et al. LLLT treatment of post herpetic neuralgia. Laser Therapy. 1988; 1: 7.
Roumeliotis D. et al. 820nm 15mW 4J/cm2, laser diode application in sports injuries. A double blind study. Proc. Fifth Annual Congress British Medical Laser Association. 1987.
Saeki N. et al. Double blind test for biostimulation effects on pain relief by diode laser. 1989. Laser Surgery; 1066: 93-100.
Sato K. et al. A double blind assessment of low power laser therapy in the treatment of postherpetic neuralgia. Surgical and Medical Lasers. 1990; 3 (3): 134 (abstract)
Simunovic Z., Trobonjaca T. Soft tissue injury during sport activities and traffic accidents - treatment with low level laser therapy. A multicenter double blind, placebo controlled clinical study on 132 patients. Proc. IXX ASLMS Congress, Orlando, Florida, April 1999.
Soriano F. A. et al Acute cervical pain is relieved with gallium-arsenida (GaAs) laser irradiation. A double-blind preliminary study. Laser Therapy. 1996; 8: 149-154.
Soriano F. A. et al. Low level laser therapy response in patients with chronic low back pain. A double blind study. Lasers Surg Med. 1998, Suppl. 10, p. 6.
Toya S. et al. Report on a computer-randomized double blind clinical trial to determine the effectiveness of the GaAlAs (830 nm) diode laser for pain attenuation in selected pain. Laser Therapy 1994; 6:143.
Taguchi T. et al. Thermographic changes following laser irradiation for pain. Clinical Laser Med Surg. 1991; 2(9): 143.

Tsurko V. et al. Laser therapy of rheumatoid arthritis. A clinical and morphological study. Terap Arkh. 1983; 97. (Russian).
Walker J. Relief from Chronic Pain by Low Power Laser Irradiation. Neuroscience Letters. 1983; 43: 339
Wylie L. et al. The hypoalgesic effects of low intensity infrared laser therapy upon mechanical pain threshold. Lasers Surg Med. 1995; Suppl 7:9.

Sinusitis

Kaiser C. et al. Estudio en doble ciego randomizado sobre la eficacia del He-Ne en el tratamiento de la sinuitis maxilar aguda: en pacientes con exacerbacion de una infeccion sinusal cronica. (Double blind randomized study on the effect of HeNe in the treatment of acute maxillary sinusitis: in patients with exacerbation of a chronic maxillary sinusitis). Boleton CDL. 1986; 9: 15.

Sjoegren's Syndrome

Fructuoso F. J. G., Moset J. M. Estudio randomizado doble ciego sobre los efectos bioestimulantes del lßser en la irradiacion de glandula paratida en pacientes afectos de syndrome de Sjoegren. (Double blind study on the biostimulatory effects of laser irradiation on the parotid gland in patients affected by Sjoegrens syndrome). Investigacion y Clinica Laser. 1987; 4 (1): 18-25.

Tendinitis

Loegdberg-Andersson M. et al. Low level laser therapy (LLLT) of tendinitis and myofascial pains -a randomized, double-blind, controlled study. Laser Therapy. 1997; 2 (9): 79-86.
Meier J. L, Kerkour K. Traitement laser de la tendinite. Med. et Hyg. 1989; 46: 907-911.
Saunders L. The efficiacy of low-level laser therapy in supraspinatus tendinitis. Clin Rehab. 1995; 9: 126-134

Trigger Points

Airaksinen O., et al. Effects of infra-red laser irradiation at the trigger points. Scand J of Acu & El Therapy. 1988; 3: 56-61
Laakso E. L. et al. Pain scores and side effects in response to low level laser therapy (LLLT) for myofascial trigger points. Laser Therapy. 1997; 2 (9): 67-72.
Snyder-Mackler L. et al. Effect of helium-neon laser on musculoskeletal trigger points. Physical Therapy. 1986; 66: 1087.
Snyder-Mackler L. et al. Effect of helium-neon laser irradiation on skin resistance and pain in patients with trigger points in the neck or back. Physical Therapy. 1989; 69: 336.

Wound Healing

Bihari I., Mester A. The biostimulative effect of low level laser therapy of long-standing crural ulcer using Helium Neon laser, Helium Neon plus infrared lasers and non coherent light: Preliminary report of a randomized double blind comparative study. Laser Therapy. 1989; 1(2): 97.
Kim J. W., Lee J. O. Double blind cross-over clinical study of 830 nm diode laser and 5 years clinical experience of biostimulation in plastic & aesthetic surgery in Asians. Lasers Surg Med. 1998; Suppl. 10: 59.
Kinoshita F. et al. Clinical evaluation of low-energy, semi-conductor laser therapy in oral surgery -a double blind study. Josai Shika Daigaku Kiyo. 1986; 15 (3): 735-742. (in Japanese)
Lucas C. et al. Low level laser therapy bij decubitus statium III. Rapport Hoegschool van Amsterdam. 1994.

Mester A. Biostimulative effect in wound healing by continous wave 820 nm laser diode. Double-blind randomized cross-over study. Lasers in Med Science, abstract issue July 1988, No 289.
Palmgren N. et al. Low Level Laser Therapy of infected abdominal wounds after surgery. Lasers Surg Med. 1991; Suppl 3:11.
Sasaki K. et al. A double-blind controlled study on free amino acid analysis in CO2 laser burn wounds in the mouse model following doses of low incident infrared (830 nm) diode laser energy. Proc. 2nd Meeting of the Internat Laser Therapy Assn., London, 1992, p.4.
Sasaki K. et al. A preliminary double blind controlled study on free amino acid analysis in burn wounds in the mouse following 830 nm diode laser therapy. Laser Therapy. 1997; 2 (9): 59-65.

Selected Books on Low Level Laser Therapy

Wolbarsht, M.L.(1977) **Laser Applications in Medicine and Biology**; Vol 3. 4.3
ISBN 0-306-37163-4 (v.3). Plenum Press, New York, USA

Laser, (1986) **Proceedings of the International Congress on Laser in Medicine and Surgery**; Bologna June 26-28, 1985. Edited by G. Galletti. Monduzi Editore S.p.A, via Ferrarese 119/2, IT-40128 Bologna, Italy.

Ohshiro T. and Calderhead R.G. (1988) **Low Level Laser Therapy; A Practical Introduction**;
ISBN 0-471-91956-X. John Wiley & Sons, Chichester, England.

Kert J., Rose L. (1989) **Clinical Laser Therapy**;
ISBN 87-983204-1-6. Scandanavian Medical Laser Technology, Copenhagen, Denmark

Goldman L. (1991) **Laser Non-Surgical Medicine: New Challenges for an Old Application**;
ISBN 87762-792-4. Technomic Publishing Co, USA.

Wolbarsht M.L. (1991) **Laser Applications in Medicine and Biology**; Vol 5. (see espec. Chapter 1).
ISBN 0-306-43753-8 (v. 5). Plenum Press, NY, USA.

Ohshiro T. (1991) **Low Reactive-Level Laser therapy; Practical Application**;
ISBN 0-471-9845-3. John Wiley & Sons, Chichester, England.

Oshiro T. and Calderhead R.G. (1991) **Progress in Laser Therapy; Selected Papers from the October 1990 ILTA Congress**.
ISBN 0-471-93154-3. John Wiley & Sons, Chichester, England.

Galletti G. (1992) **Laser Applications in Medicine and Surgery**;
Monduzi Editore S.p.A., via Ferrarese 119/2, IT-40128 Bologna, Italy.

Pontinen P. (1992) **Low Level Laser therapy as a Medical treatment Modality**;
ISBN 951-96632-0-7. Art Urpo Ltd. Tampere, Finland.

Baxter G.D. (1994) **Therapeutic Lasers; Theory and Practice**.
ISBN 0-443-04393-0. Churchill Livingstone, England.

Hajder D. (1994) **Acupuncture and Lasers**; 2nd ed.
ISBN 86-81979-17-6. DaDa, Sredacka 11, Belgrad, Yugoslavia.

Tuner J., Hode L. (1996) **Laser Therapy in Dentistry and Medicine**;
ISBN SE 91-630-4078-6. Prima Books, Grangesburg, Sweden.

Van Brugel H. (1997) **Laser Therapy in Medical Practice**;
ISBN 90-6523-048-3. Van den Boogaard Publishing, Oisterwijk, The Netherlands.

Karu T. (1998) **The Science of Low Power laser Therapy**;
ISBN 90-5699-108-6. The Gordon and Breach Publishing Group.

Tuner J., Hode L. (1999) **Low Level Laser Therapy: Clinical Practice and Scientific Background**;
ISBN 91-630-7616-0. Prima Books, Grangesburg, Sweden.

Waynant R.W. (ed.) (2002) **Lasers in Medicine**;
CRC Press, Washington, D.C., USA

Websites

www.laser.nu