LLLT using Light Emitting Diodes research list

Relevant points in the following study:

1. Increase the cell's production of the body's fuel source, ATP (adenosine triphosphate) for optimal cellular function and communication

- (pg. 2, para.1) Results indicated that LED treatments twice a day significantly increased cellular adenosine triphosphate content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP(+)- exposed neurons as compared with untreated ones. These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson’s disease by energizing cells and increasing their viability.
- (pg. 23, para.1) NIR-LED light treatment prevents the development of oral mucositis in pediatric bone marrow transplant patients. The experimental results demonstrate that NIR-LED light treatment stimulates mitochondrial oxidative metabolism in vitro, and accelerates cell and tissue repair in vivo. NIR-LED light represents a novel, noninvasive, therapeutic intervention for the treatment of numerous diseases linked to mitochondrial dysfunction.
- (pg. 30, para.1) The results are consistent with our hypothesis that the mechanism oh photobiomodulation involves the up-regulation of cytochrome c oxidase, leading to increased energy metabolism in neurons functionally inactivated by toxins.
- (pg. 35, para.1) Based on these findings and the strong evidence that mitochondrial dysfunction is involved in the pathogenesis of numerous disease processes, we propose that NIR-LED photobiomodulation represents an innovative and non-invasive therapeutic approach for the treatment of tissue injury and disease processes in which mitochondrial dysfunction is postulated to play a role including diabetic retinopathy, age-related macular degeneration, Leber’s hereditary optic neuropathy and Parkinson’s disease.
- (pg. 36, para.1) They also suggest that photobiomodulation may enhance recovery from retinal injury and other ocular diseases in which mitochondrial dysfunction is postulated to play a role.
- (pg. 42, para.1) Thus, the results are consistent with our hypothesis that LED has a stimulating effect on cytochrome oxidase in neurons, even when they have been functionally silenced by TTX.
- (pg. 45, para.1) Results: LED produced in vitro increases of cell growth of 140-200% in mouse-derived fibroblasts, rat-derived osteoblasts, and rat-derived skeletal muscles cells, and increases in growth of 155-171% of normal epithelial cells. Would 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 DEAL 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, 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.

4. Promote cell proliferation

- (pg. 2, para.1) Results indicated that LED treatments twice a day significantly increased cellular adenosine triphosphate content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP(+)- exposed neurons as compared with untreated ones. These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson’s disease by energizing cells and increasing their viability.
- (pg. 45, para.1) Results: LED produced in vitro increases of cell growth of 140-200% in mouse-derived fibroblasts, rat-derived osteoblasts, and rat-derived skeletal muscles cells, and increases in growth of 155-171% of normal epithelial cells. Would 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 DEAL 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, 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.

5. Accelerate tissue regeneration and wound healing, reduce bruising, erythema and edema

- (pg. 4, para.1) Results: Mean erythema scores on the first visit were significantly higher (P=0.0054) on the side not treated with LED (52.7+/- 24.6) than on the LED-treated side (43.3 +/- 21.9). Visit 2 data showed a similar trend (p=0.0281). The subjects reported similar fidnings with mean erythema scores on the first visit on the LED –treated side (46.7+/- 25.3) compared with the untreated side (60.0 +/- 23.3); the difference was significant (P=0.0382)
- (pg. 4, para.1) Four patients commented that post-treatment discomfort was considerably less on the LED-treated side immediately after treatment. Conclusion: LED photomodulation treatment may accelerate the resolution of erythema and reduce posttreatment discomfort in IPL-treated patients with photodamage.
- (pg. 5, para.1) I used a light-emitting diode (LED) and superluminous Diode (SLD) to deliver low-intensity laser light as an adjunctive treatment to a patient with a chronic diabetic foot ulcer.
- (pg. 5, para.1) This combination of therapies resulted in closure of the neuropathic plantar ulcer within 8 weeks.
- (pg. 6, para.1) Conclusion: LLLT stimulates wound contraction in susceptible mouse strains but the mechanism remains uncertain.
- (pg. 10, para.1) Conclusion: Red LLLT and LED demonstrated expressive results in angiogenesis. Light coherence was shown not to be essential to angiogenesis.
- (pg. 18, para.1) Conclusion: The effect of polychromatic LED therapy in oval full-thickness would-healing in the diabetic model with the use of 5 and 10 J/cm(2) is promising.
- (pg. 22, para.1) Results: In all instances, the LED therapy-treated side was statistically superior to the unirradiated control by a factor of two or three. Conclusions: In this small series of 10 patients, red LED phototherapy after blepharoplasty and laser ablative resurfacing cut the time to resolution of side effects and the healing time by one-half one-third compared with contralateral unirradiated controls. Further studies are warranted with larger populations to confirm these findings.
- (pg. 23, para.1) NIR-LED light treatment prevents the development of oral mucositis in pediatric bone marrow transplant patients. The experimental results demonstrate that NIR-LED light treatment stimulates mitochondrial oxidative metabolism in vitro, and accelerates cell and tissue repair in vivo. NIR-LED light represents a novel, noninvasive, therapeutic intervention for the treatment of numerous diseases linked to mitochondrial dysfunction.
- (pg. 38, para.1) 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.
- (pg. 39, para.2) 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.
- (pg. 45, para.1) Results: LED produced in vitro increases of cell growth of 140-200% in mouse-derived fibroblasts, rat-derived osteoblasts, and rat-derived skeletal muscles cells, and increases in growth of 155-171% of normal epithelial cells. Would 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 DEAL 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, 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.
- (pg. 46, para.1) Conclusion: In this placebo-controlled, double blind study LEPT was an effective modality for the treatment of venous leg ulcers.

7. Reduce the effects of oxidative stress

- (pg. 2, para.1) Results indicated that LED treatments twice a day significantly increased cellular adenosine triphosphate content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP(+)- exposed neurons as compared with untreated ones. These results strongly

suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson's disease by energizing cells and increasing their viability.

12. Increase cerebral blood flow, improve memory and cognition.

- (pg. 3, para.1) Exposure to IR…elicited significant effects on working memory…overall improved cognitive performance.

LLLT using Light Emitting Diodes research list

Posted on 20 July 2008 by James Carroll

Yet another NASA NIR LED therapy paper was published recently showing that LED treatment may be therapeutic to damaged neurons, this time in a Parkinson's disease model. I thought some of you may not appreciate quite how much research has been conducted with LED's so here is a list of 43 that I found on PubMed.

Near-infrared light via light-emitting diode treatment is therapeutic against rotenone- and 1-methyl-4-phenylpyridinium ion-induced neurotoxicity.

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Parkinson's disease is a common progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Mitochondrial dysfunction has been strongly implicated in the pathogenesis of Parkinson's disease. Thus, therapeutic approaches that improve mitochondrial function may prove to be beneficial. Previously, we have documented that near-infrared light via light-emitting diode (LED) treatment was therapeutic to neurons functionally inactivated by tetrodotoxin, potassium cyanide (KCN), or methanol intoxication, and LED pretreatment rescued neurons from KCN-induced apoptotic cell death. The

current study tested our hypothesis that LED treatment can protect neurons from both rotenone- and MPP(+)-induced neurotoxicity. Primary cultures of postnatal rat striatal and cortical neurons served as models, and the optimal frequency of LED treatment per day was also determined. Results indicated that LED treatments twice a day significantly increased cellular adenosine triphosphate content, decreased the number of neurons undergoing cell death, and significantly reduced the expressions of reactive oxygen species and reactive nitrogen species in rotenone- or MPP(+)-exposed neurons as compared with untreated ones. These results strongly suggest that LED treatment may be therapeutic to neurons damaged by neurotoxins linked to Parkinson's disease by energizing the cells and increasing their viability.

Neuroscience 2008 Jun 2 153(4) 963-74

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18440709

Emotional responses and memory performance of middle-aged CD1 mice in a 3D maze: effects of low infrared light.

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Non-thermal near infra-red (IR) has been shown to have many beneficial photobiological effects on a range of cell types, including neurons. In the present study, a pretreatment with a daily 6 min exposure to IR1072 for 10 days yielded a number of significant behavioral effects on middle-aged female CD-1 mice (12-months) tested in a 3D-maze. Middle-aged mice show significant deficits in a working memory test and IR treatment reversed this deficit. Interestingly, the IR treated middle-aged group despite making less

memory errors than sham middle-aged group spent longer time in different parts of the maze than both the young group (3-months) and sham-middle-aged group (12-months). Young mice appeared more anxious than middle-aged mice in the first sessions of the test. Exposure to IR appeared to have no significant effects upon exploratory activity or anxiety responses. However, it elicited significant effects on working memory, with the IR middle-aged mice being more considerate in their decision making, which results in an overall improved cognitive performance which is comparable to that of young CD-1 mice. The present study describes a novel method for assessing emotional responses and memory performance in a 3D spatial navigation task and demonstrates the validity of our new all-in-one test and its sensitivity to ageing and non-invasive beneficial IR treatment.

Neurobiol Learn Mem 2008 May 89(4) 480-8

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17855128

Use of light-emitting diode photomodulation to reduce erythema and discomfort after intense pulsed light treatment of photodamage.

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OBJECTIVES: This study evaluates the use of light-emitting diode (LED) photomodulation therapy to accelerate resolution of post-intense pulsed light (IPL) erythema. METHODS: In this split-face study, 15 subjects were randomized to receive LED treatment to one side of the face as determined by computer-generated randomization numbers. All 15 subjects received a single IPL treatment for facial photodamage. Immediately after IPL treatment, one side of the face was treated for 35 s with the LED device. The other side

was not treated. Subjects returned 24 h later for a second LED treatment on the same side of the face. Posttreatment erythema was rated on both sides of the face by the blinded investigator and by subjects immediately after IPL treatment, 24 h later, and 1 week later on a scale of 0% (no erythema) to 100% (severe erythema). Patients commented on posttreatment discomfort immediately after IPL treatment. RESULTS: Mean erythema scores on the first visit were significantly higher (P = 0.0054) on the side not treated with LED (52.7 +/- 24.6) than on the LED-treated side (43.3 +/- 21.9). Visit 2 data showed a similar trend (P = 0.0281). The subjects reported similar findings with mean erythema scores on the first visit on the LED-treated side (46.7 +/- 25.3) compared with the untreated side (60.0 +/- 23.3); the difference was significant (P = 0.0382). On the second visit, the mean erythema scores trended lower on the LED-treated side (24.3 +/- 22.1) than on the untreated side (27.9 +/- 25.8), but the difference did not reach statistical significance (P = 0.1365). Erythema scores on both facial sides were 0 for all subjects 1 week after IPL treatment. Four patients commented that posttreatment discomfort was considerably less on the LED-treated side immediately after treatment. CONCLUSION: LED photomodulation treatment may accelerate the resolution of erythema and reduce posttreatment discomfort in IPL-treated patients with photodamage.

J Cosmet Dermatol 2008 Mar 7(1) 30-4

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18254808

Light therapy and advanced wound care for a neuropathic plantar ulcer on a Charcot foot.

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Light therapy is a relatively novel modality in wound care. I used a light-emitting diode (LED) and superluminous diode (SLD) to deliver low-intensity laser light as an adjunctive treatment to a patient with a chronic diabetic foot ulcer. Standard treatment of conservative sharp debridement, off-loading, bioburden management, and advanced dressings was delivered in a WOC clinic setting. This combination of therapies resulted in closure of the neuropathic plantar ulcer within 8 weeks.

J Wound Ostomy Continence Nurs 2008 Jan-Feb 35(1) 113-5; discussion 116-7

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18199948

Low-level light stimulates excisional wound healing in mice.

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BACKGROUND: Low levels of laser or non-coherent light, termed low-level light therapy (LLLT) have been reported to accelerate some phases of wound healing, but its clinical use remains controversial. METHODS: A full thickness dorsal excisional wound in mice was treated with a single exposure to light of various wavelengths and fluences 30 minutes after wounding. Wound areas were measured until complete healing and immunofluorescence staining of tissue samples was carried out. RESULTS: Wound healing was significantly stimulated in BALB/c and SKH1 hairless mice but not in C57BL/6 mice. Illuminated wounds started to contract while control wounds initially expanded for the first 24 hours. We found a biphasic dose-response curve for fluence of 635-nm light with a maximum positive effect at 2 J/cm(2).

Eight hundred twenty nanometer was found to be the best wavelength tested compared to 635, 670, and 720 nm. We found no difference between non-coherent 635+/-15-nm light from a lamp and coherent 633-nm light from a He/Ne laser. LLLT increased the number of alpha-smooth muscle actin (SMA)-positive cells at the wound edge. CONCLUSION: LLLT stimulates wound contraction in susceptible mouse strains but the mechanism remains uncertain.

Lasers Surg Med 2007 Oct 39(9) 706-15

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17960752

Histologic comparison of light emitting diode phototherapy-treated hydroxyapatite-grafted extraction sockets: a same-mouth case study.

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BACKGROUND: The stimulating effect of red and near-infrared (NIR) laser phototherapy on bone regeneration and growth has been shown in a number of in vitro and animal studies. However, the effect of NIR phototherapy on the bone regeneration of hydroxyapatite (HA) -treated extraction sockets has not been previously demonstrated. MATERIALS AND METHODS: An investigational Biolux extraoral light emitting diode phototherapy device was used daily for 21 days postextraction and socket grafting with HA (Osteograf LD300) unilaterally. Bone regeneration of the phototherapy-treated and nontreated side was compared in same-mouth extraction sockets. RESULTS: Histologic evaluations showed enhanced bone formation and faster particle resorption associated with the phototherapy-treated socket graft compared with the

non-phototherapy-treated socket. CONCLUSIONS: The accelerated bone healing in the phototherapy-treated HA socket graft may provide faster implant placement compared to non-phototherapy-treated socket grafts.

Implant Dent 2007 Jun 16(2) 204-11

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17563511

In vitro observations on the influence of copper peptide aids for the LED photoirradiation of fibroblast collagen synthesis.

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OBJECTIVE: The purpose of this study was to evaluate the influence of Cu-GHK aids for the LED-PI on fibroblast proliferation and collagen production in vitro. BACKGROUND DATA: Light-emitting diode photoirradiation (LED-PI) and copper-glycyl-L-histidyl-L-lysine complex (Cu-GHK) treatment may be useful in accelerating the rate of wound healing. Red LED (625-635 nm) was used as a light source for LED-PI. In the process of wound healing, Cu-GHK was shown to be an activator of remodeling. LED-PI would maintain fibroblast activity and viability, and there would be a positive effect on type I collagen (COL1) and basic fibroblast growth factor (bFGF) production from the combination of LED-PI and Cu-GHK incorporation. METHODS: Cell activity/viability, procollagen type I C-peptide (P1CP), and bFGF were evaluated in vitro with human fibroblasts (HS68). The effects of single factors (LED-PI using 0, 1, and 2 J energy doses) or a combination of factors (LED-PI and Cu-GHK) on fibroblast viability (i.e., alamarBlue reduction), collagen

production (i.e., P1CP production and COL1 mRNA expression), and bFGF secretion were also evaluated. RESULTS: Reduction in cell viability was significantly suppressed with LED-PI (1 J) and Cu-GHK-supplied incubation. Cell viability was increased 12.5-fold compared with the non-irradiated group (0 J). Collagen production was also increased significantly with LED-PI and Cu-GHK incorporation (197.6 ng/mL). A dose-response effect was observed for LED-PI combined with Cu-GHK. The combinative effects of LED-PI and Cu-GHK led to an increase not only in bFGF secretion (approximately 230%) but also in P1CP production (approximately 30%) and COL1 mRNA expression (approximately 70%) compared with LED-PI alone. CONCLUSION: LED-PI maintained human fibroblast (HS68) viability and increased collagen synthesis when applied by itself. In the combinative stimulation for in vitro collagen production (when LED-PI was followed by Cu-GHK-supplied incubation), stimulated cells showed increased bFGF secretion, P1CP production, and COL1 expression, compared to the LED-PI treatment alone.

Photomed Laser Surg 2007 Jun 25(3) 183-90

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17603859

The anti-inflammatory mechanism of 635 nm light-emitting-diode irradiation compared with existing COX inhibitors.

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BACKGROUND AND OBJECTIVES: Inhibition of cyclooxygenase (COX) and prostaglandin E(2) (PGE(2)) protects cells against cell injury in specific

pathophysiological situations: inflammation and oxidative stress. Although the anti-inflammatory effects have been reported in clinical fields for specific wavelength irradiation during wound healing, the physiological mechanism has not been clarified yet. The aim of the present study is to investigate the anti-inflammatory mechanism of 635 nm light-emitting-diode (LED) irradiation compared with existing COX inhibitors. STUDY DESIGN/MATERIALS AND METHODS: The present study investigated anti-inflammatory effects of 635 nm irradiation on PGE(2) release, COX and phospholipase A(2) (PLA(2)) expression, and reactive oxygen species (ROS) dissociation in arachidonic acid (AA)-treated human gingival fibroblast (hGF). These results were compared with their existing COX inhibitors: indomethacin and ibuprofen. The PGE(2) release was measured by enzyme immunoassay, the COX expression was measured by western blot and reverse transcriptase polymerase chain reaction (RT-PCR), and ROS level was measured by flow cytometry, laser scanning confocal microscope and RT-PCR. RESULTS: Results showed that 635 nm irradiation and existing COX inhibitors inhibit expression of COX and PGE(2) release. Unlike indomethacin and ibuprofen, 635 nm irradiation leads to a decrease of ROS levels and mRNA expression of cytosolic phospholipase A(2) (cPLA(2)) and secretary phospholipase A(2) (sPLA(2)). CONCLUSION: Taken together, 635 nm irradiation, unlike indomethacin and ibuprofen, can directly dissociate the ROS. This inhibits cPLA(2), sPLA(2), and COX expression, and results in the inhibition of PGE(2) release. Thus, we suggest that 635 nm irradiation inhibits PGE(2) synthesis like COX inhibitor and appears to be useful as an anti-inflammatory tool.

Lasers Surg Med 2007 Aug 39(7) 614-21

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17868110

Photobiomodulation on the angiogenesis of skin wounds in rats using different light sources.

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Department of Bioengineering, Sao Carlos Engineering School, University of Sao Paulo (USP), Sao Carlos; and School of Physiotherapy, Americana School, Americana, Brazil.

OBJECTIVE: The aim of this study was to compare the angiogenic effects of laser and light-emitting diode (LED) illumination on wounds induced in rats, with varied fluence. BACKGROUND DATA: The LED is an alternative light source that accelerates wound healing, and its efficiency concerning the angiogenic effect was compared to low-level laser therapy (LLLT). METHODS: The experimental model consisted of a circular wound inflicted on the quadriceps of 120 rats, using a 15-mm-diameter "punch." Animals were divided randomly into five groups: two groups of laser, with dosages of 5 and 20 J/cm(2), respectively, two groups of LED, also with dosages of 5 and 20 J/cm(2), and a control group. Six hours after wound infliction, the treated groups received the diverse applications accordingly and were irradiated every 24 h. Angiogenesis was studied through histomorphometry on days 3, 7, 14, and 21 after the wounds were inflicted. RESULTS: On days 3, 7, and 14, the proliferation of blood vessels in all irradiated groups was superior in comparison to those of the control group ($p < 0.05$). Treatment with fluence of 5 J/cm(2) was better than the laser group with 20 J/cm(2) on day 21. CONCLUSION: Red LLLT and LED demonstrated expressive results in angiogenesis. Light coherence was shown not to be essential to angiogenesis. However, further studies are needed in order to investigate the photobiomodulatory effects of LED in relation to LLLT in various biological tissues.

Photomed Laser Surg 2007 Apr 25(2) 102-6

[Action of the red and infrared electromagnetic waves of light-emitting diodes on the behavioral manifestation of somatic pain]

Sushko BS, Lymans'kyi IuP, Huliar SO

Research of analgesic action of electromagnetic waves (EMWs) of red (1 = 640 +/- 30 nm) and infra-red (1 = 880 +/- 30 nm) light-emitting diodes of device "MEDOLIGHT" on a tonic and acute pain of white outbreed male mice is carried out. The tonic pain was caused by hypodermic injection of 20 ml of 5% formalin solution in a back surface pad of a hinder leg. Acupuncture point (AP) E-36 or the center of pain were exposed to the action of red or infrared light-emitting diodes in cumulative density of steam radiation capacity during 10 min by 26 mWt/ cm2 in continuous or pulse regimen for frequencies 10, 600, 8000 Hz. Quantitative intensity of a painful syndrome was estimated by average group duration or quantity of painful (licking of the center of a pain, twitching of a hinder leg) and non-painful (dream, grooming, eating) behaviour manifistation of animals for the certain intervals of observation. Sensitivity of animals to acute pain-"a painful threshold"-was deter- mined in experiences with "an electric floor" on size of the electric voltage caused vocalization. The analgesic action both continuous, and pulse light-emitting diode EMWs, features of their action in relation to the place of the application and modes of influence were shown. Thus, the continuous stimulation of AP E-36 only by red EMW decreased the duration of pain paw licking on 33% and quantities of twitching of animals paw on 37% while the duration of grooming, dream, and consumption of feed raised. Such changes of painful and nonpainful behaviour unequivocally specify reduction of a tonic pain. Combined action of red and infrared EMWs caused diverse changes of painful reactions of animals and increase of extremity hyperemia. Thus at summary action of EMWs on AP E-36 of mice the long increase of painful sensitivity was observed. Exposure of EMWs to the center of a pain reduced the intensity of painful reactions of mice on 30% in average, time of

their movings in a cage increased twice and duration of dream increased by 39%. Thus, summary action of red and infrared EMWs on AP E-36 promoted only to improvement of a blood circulation and increase painful sensitivity. In experiments with a tonic pain the summary pulse action on AP E-36 of the red and infrared EMWs with frequencies 10, 600, 8000 Hz reduced twice quantity of paw twitchings of animals with pain. The greatest efficiency in suppression of tonic pain syndrome observed for frequencies of 10 and 8000 Hz. The data received testify that the hypoanalgesic effect of light-emitting diode EMWs depends on area of influence, lengths of wave and the modes of an irradiation chosen in view of intensity and duration of stimulation.

Fiziol Zh 2007 53(3) 51-60

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17725044

A randomised double-blind study comparing the effect of 1072-nm light against placebo for the treatment of herpes labialis.

Hargate G

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BACKGROUND: Previous research demonstrated that 1072-nm narrowband laser light is effective in the treatment of cold sores. AIM: To evaluate the efficacy of an over-the-counter cold-sore treatment device (Virulite CS) incorporating 1072-nm light-emitting diodes. METHODS: A randomised, prospective, double-blind, self-reported study was performed to compare the efficacy of at least six 3-min treatments of 1072-nm narrowband light against placebo, in the treatment of herpes labialis. RESULTS: The 1072-nm light-emitting diode device reduced cold-sore healing time to 6.3 days

compared with 9.4 days for placebo (P=0.048). The time the cold sore took to form a crust was also reduced from 2.00 days for those treated with 1072-nm light, compared with 2.88 days for placebo (P=0.059) CONCLUSIONS: The significant difference between the mean healing times in the two groups demonstrates that the Virulite CS device is an effective means of treating herpes labialis.

Clin Exp Dermatol 2006 Sep 31(5) 638-41

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16780494

Photobiomodulation partially rescues visual cortical neurons from cyanide-induced apoptosis.

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Near-infrared light via light-emitting diode treatment has documented therapeutic effects on neurons functionally inactivated by tetrodotoxin or methanol intoxication. Light-emitting diode pretreatment also reduced potassium cyanide-induced cell death, but the mode of death via the apoptotic or necrotic pathway was unclear. The current study tested our hypothesis that light-emitting diode rescues neurons from apoptotic cell death. Primary neuronal cultures from postnatal rat visual cortex were pretreated with light-emitting diode for 10 min at a total energy density of 30 J/cm2 before exposing to potassium cyanide for 28 h. With 100 or 300 microM potassium cyanide, neurons died mainly via the apoptotic pathway, as confirmed by electron microscopy, Hoechst 33258, single-stranded DNA,

Bax, and active caspase-3. In the presence of caspase inhibitor I, the percentage of apoptotic cells in 300microM potassium cyanide was significantly decreased. Light-emitting diode pretreatment reduced apoptosis from 36% to 17.9% (100 microM potassium cyanide) and from 58.9% to 39.6% (300 microM potassium cyanide), representing a 50.3% and 32.8% reduction, respectively. Light-emitting diode pretreatment significantly decreased the expression of caspase-3 elicited by potassium cyanide. It also reversed the potassium cyanide-induced increased expression of Bax and decreased expression of Bcl-2 to control levels. Moreover, light-emitting diode decreased the intensity of 5-(and -6) chloromethy-2′, 7-dichlorodihydrofluorescein diacetate acetyl ester, a marker of reactive oxygen species, in neurons exposed to 300 microM potassium cyanide. These results indicate that light-emitting diode pretreatment partially protects neurons against cyanide-induced caspase-mediated apoptosis, most likely by decreasing reactive oxygen species production, down-regulating pro-apoptotic proteins and activating anti-apoptotic proteins, as well as increasing energy metabolism in neurons as reported previously.

Neuroscience 2006 May 12 139(2) 639-49

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16464535

Combination blue (415 nm) and red (633 nm) LED phototherapy in the treatment of mild to severe acne vulgaris.

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BACKGROUND AND OBJECTIVE: Acne vulgaris represents both a challenge to the treating dermatologist and a major concern for the patient. Conventional treatments have proved inconsistent with often unacceptable side effects and high rates of recurrence. Non-thermal, non-laser, phototherapy for acne with a combination of blue and red light has recently attracted attention. The present study was designed to assess the efficacy of this combination phototherapy. METHODS: Twenty-four subjects, Fitzpatrick skin types II-V, with mild to severe symmetric facial acne vulgaris were recruited for the study. Subjects were well matched at baseline in terms of both age and duration of acne. Subjects were treated over eight sessions, two per week 3 days apart, alternating between 415 nm blue light (20 minutes/session, 48 J/cm2) and 633 nm red light (20 minutes/session, 96 J/cm2) from a light-emitting diode (LED)-based therapy system. Patients received a mild microdermabrasion before each session. Acne was assessed at baseline and at weeks 2, 4, 8 and 12. RESULTS: Twenty-two patients completed the trial. A mean reduction in lesion count was observed at all follow-up points. At the 4-week follow-up, the mean lesion count reduction was significant at 46% (p=0.001). At the 12-week follow-up, the mean lesion count reduction was also significant at 81% (p=0.001). Patient and dermatologist assessments were similar. Severe acne showed a marginally better response than mild acne. Side effects were minimal and transitory. Comedones did not respond as well as inflammatory lesions. CONCLUSIONS: Combination blue and red LED therapy appears to have excellent potential in the treatment of mild to severe acne. Treatment appears to be both pain- and side effect-free.

J Cosmet Laser Ther 2006 Jun 8(2) 71-5

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16766484

Brief report: embryonic growth and hatching implications of developmental 670-nm phototherapy and dioxin co-exposure.

Yeager RL, Franzosa JA, Millsap DS, Lim J, Hansen CM, Jasevicius AV, Heise SS, Wakhungu P, Whelan HT, Eells JT, Henshel DS

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OBJECTIVE: We assessed the effect of 670-nm light therapy on growth and hatching kinetics in chickens (Gallus gallus) exposed to dioxin. BACKGROUND DATA: Photobiomodulation has been shown to stimulate signaling pathways resulting in improved energy metabolism, antioxidant production, and cell survival. In ovo treatment with 670-nm light-emitting diode (LED) arrays improves hatching success and increases hatchling size in control chickens. Under conditions where developmental dioxin exposure is above the lethality threshold (100 ppt), phototherapy attenuates dioxin-induced early embryonic death. We hypothesized that 670-nm LED therapy would attenuate dioxin-induced developmental anomalies and increase hatching success. METHODS: Fertile chicken eggs were injected with control oil, 2, 20, or 200 ppt dioxin, or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) prior to the start of incubation. Half of the eggs in each dose group were treated once per day from embryonic days 0-20 with 670-nm LED light at a fluence of 4 J/cm2. Hatchling size, organ weights, and energy parameters were compared between dose groups and LED treatment. RESULTS: LED therapy resulted in earlier pip times (small hole created 12-24 h prior to hatch), and increased hatchling size and weight in the 200 ppt dose groups. However, there appears to be an LED-oil interaction within the oil-treated controls that results in longer hatch times and decreased liver weight within the LED control dose groups in comparison to the non-LED control dose groups. CONCLUSION: Size and hatching times suggest that the hatching success and preparedness of chicks developmentally exposed to dioxin concentrations above the lethality threshold is improved by 670-nm LED treatment administered throughout the gestation period, but the relationship may be

complicated by an LED-oil interaction.

Photomed Laser Surg 2006 Jun 24(3) 410-3

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16875452

[A comparison of the effects of laser and light-emitting diodes on superoxide dismutase activity and nitric oxide production in rat wound fluid]

Klebanov GI, Shuraeva NIu, Chichuk TV, Osipov AN, Vladimirov IuA

The action of laser and light-emitting diode radiation in the visible region on the content of reactive nitrogen species and activity of superoxide dismutase in rat wound fluid was studied, and efficiency of action of coherent laser and incoherent light emitting diode radiations in the red region of the spectrum on the parameters under study was compared. A model of incised aseptic wounds in rats proposed by L.I. Slutskiy was used. A He-Ne laser (632 nm) and a Y-332B light emitting diode served as radiation sources. It was shown that (1) exposure of wounds to the visible light of both laser and light-emitting diodes causes dose-dependent changes in superoxide dismutase activity and production of nitrites and (2) the radiation coherence does not play any significant role in the changes of superoxide dismutase activity or nitrogen oxide formation by wound fluid phagocytes.

Biofizika 2006 Jan-Feb 51(1) 116-22

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16521561

Polychromatic LED in oval full-thickness wound healing in non-diabetic and diabetic rats.

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OBJECTIVE: Our goal was to determine the efficacy of polychromatic light-emitting diode (LED) in the enhancement of wound healing in non-diabetic and diabetic rats. BACKGROUND DATA: LEDs are increasingly used as an alternative light source for phototherapy. METHODS: A cluster of 25 LED photons at 510-543, 594-599, 626-639, 640-670, and 842-872 nm wavelengths with 272-mW output power was used. Male Sprague-Dawley rats (n = 61) were randomly assigned into non-diabetic and diabetic groups and into light treatment groups, that is, control, 5, 10, 20, and 30 J/cm(2). Streptozotocin was used for diabetes induction. Wounds were created using a scalpel after 1 week of wounding. Wounds were measured daily and plotted in time, and the trendline was fitted to obtain slope values. Relative wound healing percentage was computed as follows: RWH% = [(Slope treated – Slope control)/(Slope control)] x 100. The t-test (alpha = 0.05) was used for analysis. RESULTS: The RWH% in the non-diabetic rats was insignificant (p > 0.05) at 5, 10, 20, and 30 J/cm(2) treatments, giving 4.3 +/- 1.97%, 5.4 +/- 1.94%, 4.5 +/- 1.96%, and 1.2 +/- 2.03%, respectively. The healing of diabetic rats was significantly impaired by -11.7 +/- 3.25% (p = 0.02), which was mitigated by 5 J/cm(2) treatment (2.4 +/- 3.02%, (p) = 0.40) and 10 J/cm(2) treatment (-5.5 +/- 3.28%, p = 0.11). Diabetic wound healing using 20 J/cm(2) (-8.7 +/- 3.39%, p = 0.03) and 30 J/cm(2) (-10.90 +/- 1.97%, p = 0.01) affected significant inhibition. CONCLUSION: The effect of polychromatic LED therapy in oval full-thickness wound-healing in the diabetic model with the use of 5 and 10 J/cm(2) is promising. Further studies to determine optimum dosimetry and efficacy of LEDs are recommended.

Photomed Laser Surg 2006 Feb 24(1) 10-6

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16503782

Survivorship and mortality implications of developmental 670-nm phototherapy: dioxin co-exposure.

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OBJECTIVE: We assessed the effect of 670-nm light therapy on dioxin-induced embryonic mortality in chickens (Gallus gallus). BACKGROUND DATA: Developmental photobiomodulation using 670-nm light-emitting diode (LED) arrays improves hatching success and increases body size in hatchling chickens. Photobiomodulation also stimulates signaling pathways resulting in improved energy metabolism, antioxidant production and cell survival. Dioxin causes embryonic mortality, including increases in the frequency of chicken embryos that pip but can't go to hatch. We hypothesized that 670-nm LED therapy would attenuate dioxin-induced embryo mortality. METHODS: Fertile chicken eggs were injected with control or 2, 20, or 200 ppt 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD; dioxin) prior to the start of incubation. Half of the eggs in each dose group 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 hatching success were compared between dose groups and LED treatment. RESULTS: LED therapy decreased the embryonic mortality rate by 41%, resulting in increased embryonic survival and improved hatching success in eggs exposed to 200 ppt dioxin. However, at sub-lethal dioxin

concentrations and in oil-treated controls, LED therapy slightly increased mortality. CONCLUSION: Overall survivorship and hatching success of chicks developmentally exposed to dioxin concentrations above the lethality threshold (>100 ppt TCDD) is improved by 670-nm LED treatment administered throughout the gestation period, but the relationship may be complicated by an LED-oil interaction.

Photomed Laser Surg 2006 Feb 24(1) 29-32

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16503785

Er:YAG laser ablation of plantar verrucae with red LED therapy-assisted healing.

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OBJECTIVE: The aim of this study was to evaluate Er:YAG ablation of plantar verrucae with red light-emitting diode (LED) therapy to assist healing. BACKGROUND DATA: Successful removal of troublesome plantar verrucae still presents problems, particularly regarding complete removal and pain both postoperatively and during healing. A further problem is a high recurrence rate due to the aggressive viral dissemination associated with this kind of wart. METHODS: Over 2 years, the author treated 121 plantar warts under local anesthesia in 58 patients with Er:YAG laser ablation followed by red LED therapy to assist wound healing. The Er:YAG laser (96 J/cm2, 2.0 J/pulse, 350 microsec pulsewidth, 2-mm collimated handpiece) is used first to ablate precisely the verrucous tissue until normal architecture is seen. Immediately after treatment, a red LED therapy system is applied (633 nm, 20 min, 96

J/cm2) to the wound and surrounding area. LED therapy at the same parameters is repeated on postoperative days 2, 6, and 10. A representative plantar verruca case is presented. RESULTS: The Er:YAG laser precisely and cleanly ablates the plantar verrucae with clear margins into normal skin architecture, exhibiting minimal secondary thermal damage. After the first treatment session, patients are usually able to walk normally without any pain, even those who have bilateral verrucae, and no exudate is usually seen from postoperative day 2 on. By postoperative day 6, the wounds have shrunk noticeably and are filled with healthy granulation tissue, and by day 15 they are usually completely healed, with minimal scarring. At the 12-month follow-up, recurrence rates have been less than 6% (3/58 patients). CONCLUSION: From the author's experience in 121 cases, the Er:YAG laser is ideally suited for precise and speedy ablation of plantar verrucae with minimal thermal damage to surrounding tissue, which, when coupled with visible red LED therapy, has given excellent, accelerated, and pain-free healing in these difficult-to-treat and slow-to-heal lesions with very low recurrence rates.

Photomed Laser Surg 2006 Aug 24(4) 494-8

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Red light-emitting diode (LED) therapy accelerates wound healing post-blepharoplasty and periocular laser ablative resurfacing.

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BACKGROUND AND AIMS: Blepharoplasties can be associated with sequelae-

related patient downtime, often extended or reinforced by periocular laser ablative resurfacing. The present controlled study examined the effects of a new-generation LED phototherapy system on enhancing wound healing following such combination surgery. METHODS: Two males and eight females participated in the trial, with ages ranging from 44 to 59 years (average 52.3 years). Following blepharoplasty and Er:YAG/CO2 laser ablative resurfacing, one-half of each subject's face was treated with the red LED therapy (20 min, 96 J/cm2, 633 nm), the contralateral half being the unirradiated control. Patients reported subjectively on pain levels and resolution. Resolution of erythema, edema, bruising and days to healing were independently evaluated from the clinical photography. All findings were compared between the treated and untreated sides. RESULTS: In all instances, the LED therapy-treated side was statistically significantly superior to the unirradiated control by a factor of two to three. CONCLUSIONS: In this small series of 10 patients, red LED phototherapy after blepharoplasty and laser ablative resurfacing cut the time to resolution of side effects and the healing time by one-half to one-third compared with contralateral unirradiated controls. Further studies are warranted with larger populations to confirm these findings.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16581685

Clinical and experimental applications of NIR-LED photobiomodulation.

Desmet KD, Paz DA, Corry JJ, Eells JT, Wong-Riley MT, Henry MM, Buchmann EV, Connelly MP, Dovi JV, Liang HL, Henshel DS, Yeager RL, Millsap DS, Lim J, Gould LJ, Das R, Jett M, Hodgson BD, Margolis D, Whelan HT

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This review presents current research on the use of far-red to near-infrared (NIR) light treatment in various in vitro and in vivo models. Low-intensity light therapy, commonly referred to as “photobiomodulation,” uses light in the far-red to near-infrared region of the spectrum (630-1000 nm) and modulates numerous cellular functions. Positive effects of NIR-light-emitting diode (LED) light treatment include acceleration of wound healing, improved recovery from ischemic injury of the heart, and attenuated degeneration of injured optic nerves by improving mitochondrial energy metabolism and production. Various in vitro and in vivo models of mitochondrial dysfunction were treated with a variety of wavelengths of NIR-LED light. These studies were performed to determine the effect of NIR-LED light treatment on physiologic and pathologic processes. NIRLED light treatment stimulates the photoacceptor cytochrome c oxidase, resulting in increased energy metabolism and production. NIR-LED light treatment accelerates wound healing in ischemic rat and murine diabetic wound healing models, attenuates the retinotoxic effects of methanol-derived formic acid in rat models, and attenuates the developmental toxicity of dioxin in chicken embryos. Furthermore, NIR-LED light treatment prevents the development of oral mucositis in pediatric bone marrow transplant patients. The experimental results demonstrate that NIR-LED light treatment stimulates mitochondrial oxidative metabolism in vitro, and accelerates cell and tissue repair in vivo. NIR-LED light represents a novel, noninvasive, therapeutic intervention for the treatment of numerous diseases linked to mitochondrial dysfunction.

Photomed Laser Surg 2006 Apr 24(2) 121-8

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16706690

Treatment of chemotherapy-induced oral mucositis with light-emitting diode.

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OBJECTIVE: The aim of this study was to assess the clinical effectiveness of phototherapy with noncoherent light in the alleviation of chemotherapy-induced mucositis in patients with metastatic cancer. BACKGROUND DATA: Mucositis occurs in more than 40% of chemotherapy-treated patients, significantly reducing the quality of their lives. Many different interventions have been evaluated to reduce oral mucositis. Recently, good results have been achieved by phototherapy with photoradiation, a technique which has virtually no side effects. Some clinical results seem to indicate that also phototherapy through noncoherent light emissions which can be produced by less expensive light sources such as light-emitting diodes (LEDs) may be effective. However, until now, no studies have been available on this subject. METHODS: Twelve patients, aged from 34 to 82, selected on the basis of a diagnosis of chemotherapy-induced oral mucositis, were treated intra-orally through a noncoherent LED emission, wavelength 645 +/- 15 nm, 7.8 mW, fluence 0.99 J/cm(2), three times a day for 1 week. Mucositis was scored daily using the Daily Mucositis Index (DMI), a scale that evaluates the disease evolution through 16 different items. The primary end-point assessed was the time to recovery, from the start of LED treatment, compared to a nonrandomized control group of 12 patients with comparable stomatitis. RESULTS: The median healing time, expressed as the DMI decrease, was 1.7 (range 1-2.8) and, in seven LED-treated patients, was shorter than in the control group. The healing rate (measured as the ratio of the DMIs) increased from 117% to 164%. CONCLUSION: This pilot study shows that LED treatment is safe and capable of reducing the duration of chemotherapy-induced mucositis. This result needs to be confirmed in an adequate phase III study.

Photomed Laser Surg 2006 Apr 24(2) 207-13

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16706701

670 nanometer light treatment attenuates dioxin toxicity in the developing chick embryo.

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2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is an acutely toxic anthropogenic chemical. Treatment with a red to near-infrared (630-1000 nm) light-emitting diode (LED) attenuates the toxicant-induced oxidative stress and energy deficit in neuronal cell culture. For this study, fertile chicken (Gallus gallus) eggs were injected once at the start of incubation with sunflower oil vehicle or 200 pg TCDD/g egg (200 parts per trillion), an environmentally relevant dose. Daily LED treatment after TCDD exposure reduced embryonic mortality by 47%. LED treatment of TCDD-exposed eggs also decreased the hepatic oxidized-to-reduced glutathione ratio by 88%. Activities of other hepatic indicators of oxidative stress, such as glutathione reductase and catalase, were increased after LED treatment of TCDD-exposed eggs. Our study demonstrates that 670 nm phototherapy can mitigate the oxidative stress and energy deficit resulting from developmental exposure to TCDD while reducing TCDD-induced embryo mortality. Moreover, LED treatment restores hepatic enzyme activities to control levels in TCDD-exposed embryos. The effective attenuation of TCDD-induced embryo toxicity by LED treatment could extend to mitigating the effects of other teratogens that induce oxidative and energy stress.

J Biochem Mol Toxicol 2006 20(6) 271-8

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17163486

Clinical experience with light-emitting diode (LED) photomodulation.

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BACKGROUND: Light-emitting diode (LED) photomodulation is a novel nonthermal technology used to modulate cellular activity with light. OBJECTIVE: We describe our experience over the last 2 years using 590 nm LED photomodulation within a dermatologic surgery environment. METHODS: Practical use of nonthermal light energy and emerging applications in 3,500 treatments delivered to 900 patients is detailed. RESULTS: LED photomodulation has been used alone for skin rejuvenation in over 300 patients but has been effective in augmentation of results in 600 patients receiving concomitant nonablative thermal and vascular treatments such as intense pulsed light, pulsed dye laser, KTP and infrared lasers, radiofrequency energy, and ablative lasers. CONCLUSION: LED photomodulation reverses signs of photoaging using a new nonthermal mechanism. The anti-inflammatory component of LED in combination with the cell regulatory component helps improve the outcome of other thermal-based rejuvenation treatments.

Dermatol Surg 2005 Sep 31(9 Pt 2) 1199-205

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?

cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16176771

Probing the differential effects of infrared light sources IR1072 and IR880 on human lymphocytes: evidence of selective cytoprotection by IR1072.

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Light therapy, both laser and LED, have been shown to provide clinical benefit in many therapeutic arenas. The effects of IR1072 and IR880 were investigated, using a range of single and multiple irradiation protocols, for their effect on freshly prepared human lymphocytes stimulated with phytohemagglutinin. Viable cell numbers remained significantly higher after irradiation with IR1072 and were significantly lower after IR880 irradiation compared to untreated controls, following a daily single irradiation over a 5-day period. Cell numbers were significantly higher after pre-treatment with IR1072 and exposure to UVA, compared to cells treated with UVA only. Cells irradiated twice on Day 3 post-harvest with various wavebands confirm on Day 5, an increase in % cell viability after IR1072, and IR1072 alternating with IR1268 irradiation, and a decrease in % cell viability after IR880 irradiation alone. Further, wavebands tested displayed no significant differences compared to the control. Cells were collected after exposure on Days 3 and 5 with IR1072 and IR880 treatments and protein levels were compared using quantitative immunoblotting probed with an anti-iNOS antibody. Following IR1072, but not IR880, treatment there was a 4.9+/-2.1-fold higher iNOS protein expression in treated cells compared to the control on Day 5 post-treatment.

J Photochem Photobiol B 2005 Oct 3 81(1) 9-14

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16046143

[A comparative study of the effects of laser and light-emitting diode irradiation on the wound healing and functional activity of wound exudate leukocytes]

Klebanov GI, Shuraeva NIu, Chichuk TV, Osipov AN, Rudenko TG, Shekhter AB, Vladimirov IuA

The effects of coherent He-Ne laser and non-coherent light-emitting diode radiation on rat skin wound healing and functional activity of wound exudate leukocytes were compared. A comparative pathomorphological analysis showed that the He-Ne laser and light-emitting diode irradiation stimulated the transition of the inflammatory phase of the wound healing into the reparative (proliferative) and scarring phases sequentially. It was also detected that the functional activity of leucocytes changed in a dose-dependent manner. The leukocyte activity was found to be similar in the groups with laser and light-emitting diode irradiation. Thus, we can conclude that coherent laser and non-coherent light-emitting diode radiation have very close effects on wound healing and activity of wound exudate leukocytes, and coherence is not required for this activity.

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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

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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/cm2. 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.

Photomed Laser Surg 2005 Jun 23(3) 268-72

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15954813

Photobiomodulation directly benefits primary neurons functionally

inactivated by toxins: role of cytochrome c oxidase.

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Far red and near infrared (NIR) light promotes wound healing, but the mechanism is poorly understood. Our previous studies using 670 nm light-emitting diode (LED) arrays suggest that cytochrome c oxidase, a photoacceptor in the NIR range, plays an important role in therapeutic photobiomodulation. If this is true, then an irreversible inhibitor of cytochrome c oxidase, potassium cyanide (KCN), should compete with LED and reduce its beneficial effects. This hypothesis was tested on primary cultured neurons. LED treatment partially restored enzyme activity blocked by 10-100 microm KCN. It significantly reduced neuronal cell death induced by 300 microm KCN from 83.6 to 43.5%. However, at 1-100 mm KCN, the protective effects of LED decreased, and neuronal deaths increased. LED significantly restored neuronal ATP content only at 10 microm KCN but not at higher concentrations of KCN tested. Pretreatment with LED enhanced efficacy of LED during exposure to 10 or 100 microm KCN but did not restore enzyme activity to control levels. In contrast, LED was able to completely reverse the detrimental effect of tetrodotoxin, which only indirectly down-regulated enzyme levels. Among the wavelengths tested (670, 728, 770, 830, and 880 nm), the most effective ones (830 nm, 670 nm) paralleled the NIR absorption spectrum of oxidized cytochrome c oxidase, whereas the least effective wavelength, 728 nm, did not. The results are consistent with our hypothesis that the mechanism of photobiomodulation involves the up-regulation of cytochrome c oxidase, leading to increased energy metabolism in neurons functionally inactivated by toxins.

J Biol Chem 2005 Feb 11 280(6) 4761-71

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15557336

Clinical trial of a novel non-thermal LED array for reversal of photoaging: clinical, histologic, and surface profilometric results.

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BACKGROUND AND OBJECTIVES: Photomodulation has been described as a process which modifies cell activity using light sources without thermal effect. The objective of this study was to investigate the use of a non-thermal low dose light emitting diode (LED) array for improving the appearance of photoaged subjects. STUDY DESIGN/MATERIALS AND METHODS: This prospective study investigated a random cohort of patients (N = 90) with a wide range of photoaged skin treated by LED photomodulation using a full panel 590 nm non-thermal full face LED array delivering 0.1 J/cm(2) with a specific sequence of pulsing. Subjects were evaluated at 4, 8, 12, 18 weeks and 6 and 12 months after a series of 8 treatments delivered over 4 weeks. Data collected included stereotactic digital imaging, computerized optical digital profilometry, and peri-ocular biopsy histologic evaluations for standard stains and well as collagen synthetic and degradative pathway immunofluorescent staining. RESULTS: Digital imaging data showed a reduction of signs of photoaging in 90% of subjects with smoother texture, reduction of peri-orbital rhytids, and reduction of erythema and pigmentation. Optical profilometry showed a 10% improvement by surface topographical measurements. Histologic data showed markedly increased collagen in the papillary dermis of 100% of post-treatment specimens (N =

10). Staining with anti-collagen I antibodies demonstrated a 28% (range: 10%-70%) average increase in density while staining with anti-matrixmetalloproteinase (MMP)-1 showed an average reduction of 4% (range: 2%-40%). No side effects or pain were noted. CONCLUSIONS: Photomodulation to reverse photoaging is possible with a specific array of LEDs with a specific fluence using a precise pulsing or "code" sequence. Skin textural improvement by digital imaging and surface profilometry is accompanied by increased collagen I deposition with reduced MMP-1 (collagenase) activity in the papillary dermis. This technique is a safe and effective non-painful non-ablative modality for improvement of photoaging.

Lasers Surg Med 2005 Feb 36(2) 85-91

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15654716

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

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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.

Photomed Laser Surg 2005 Apr 23(2) 167-71

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15910180

Evidence of changes in sural nerve conduction mediated by light emitting diode irradiation.

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The introduction of light emitting diode (LED) devices as a novel treatment for pain relief in place of low-level laser warrants fundamental research on the effect of LED devices on one of the potential explanatory mechanisms: peripheral neurophysiology in vivo. A randomised controlled study was conducted by measuring antidromic nerve conduction on the peripheral sural nerve of healthy subjects (n=64). One baseline measurement and five post-irradiation recordings (2-min interval each) were performed of the nerve conduction velocity (NCV) and negative peak latency (NPL). Interventional set-

up was identical for all subjects, but the experimental group (=32) received an irradiation (2 min at a continuous power output of 160 mW, resulting in a radiant exposure of 1.07 J/cm(2)) with an infrared LED device (BIO-DIO preprototype; MDB-Laser, Belgium), while the placebo group was treated by sham irradiation. Statistical analysis (general regression nodel for repeated measures) of NCV and NPL difference scores, revealed a significant interactive effect for both NCV (P=0.003) and NPL (P=0.006). Further post hoc LSD analysis showed a time-related statistical significant decreased NCV and an increased NPL in the experimental group and a statistical significant difference between placebo and experimental group at various points of time. Based on these results, it can be concluded that LED irradiation, applied to intact skin at the described irradiation parameters, produces an immediate and localized effect upon conduction characteristics in underlying nerves. Therefore, the outcome of this in vivo experiment yields a potential explanation for pain relief induced by LED.

Lasers Med Sci 2005 20(1) 35-40

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15895289

Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy.

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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, improve recovery from ischemic injury in the heart and attenuate degeneration in the injured optic nerve. Recent evidence indicates that the therapeutic effects of red to near infrared light result, in part, from intracellular signaling mechanisms triggered by the interaction of NIR light with the mitochondrial photoacceptor molecule cytochrome c oxidase. We have demonstrated that NIR-LED photo-irradiation increases the production of cytochrome oxidase in cultured primary neurons and reverses the reduction of cytochrome oxidase activity produced by metabolic inhibitors. We have also shown that NIR-LED treatment prevents the development of oral mucositis in pediatric bone marrow transplant patients. Photobiomodulation improves wound healing in genetically diabetic mice by upregulating genes important in the promotion of wound healing. More recent studies have provided evidence for the therapeutic benefit of NIR-LED treatment in the survival and functional recovery of the retina and optic nerve in vivo after acute injury by the mitochondrial toxin, formic acid generated in the course of methanol intoxication. Gene discovery studies conducted using microarray technology documented a significant upregulation of gene expression in pathways involved in mitochondrial energy production and antioxidant cellular protection. These findings provide a link between the actions of red to near infrared light on mitochondrial oxidative metabolism in vitro and cell injury in vivo. Based on these findings and the strong evidence that mitochondrial dysfunction is involved in the pathogenesis of numerous diseases processes, we propose that NIR-LED photobiomodulation represents an innovative and non-invasive therapeutic approach for the treatment of tissue injury and disease processes in which mitochondrial dysfunction is postulated to play a role including diabetic retinopathy, age-related macular degeneration, Leber's hereditary optic neuropathy and Parkinson's disease.

Mitochondrion 2004 Sep 4(5-6) 559-67

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?

cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16120414

Therapeutic photobiomodulation for methanol-induced retinal toxicity.

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Methanol intoxication produces toxic injury to the retina and optic nerve, resulting in blindness. The toxic metabolite in methanol intoxication is formic acid, a mitochondrial toxin known to inhibit the essential mitochondrial enzyme, cytochrome oxidase. Photobiomodulation by red to near-IR radiation has been demonstrated to enhance mitochondrial activity and promote cell survival in vitro by stimulation of cytochrome oxidase activity. The present studies were undertaken to test the hypothesis that exposure to monochromatic red radiation from light-emitting diode (LED) arrays would protect the retina against the toxic actions of methanol-derived formic acid in a rodent model of methanol toxicity. Using the electroretinogram as a sensitive indicator of retinal function, we demonstrated that three brief (2 min, 24 s) 670-nm LED treatments (4 J/cm(2)), delivered at 5, 25, and 50 h of methanol intoxication, attenuated the retinotoxic effects of methanol-derived formate. Our studies document a significant recovery of rod- and cone-mediated function in LED-treated, methanol-intoxicated rats. We further show that LED treatment protected the retina from the histopathologic changes induced by methanol-derived formate. These findings provide a link between the actions of monochromatic red to near-IR light on mitochondrial oxidative metabolism in vitro and retinoprotection in vivo. They also suggest that photobiomodulation may enhance recovery from retinal injury and other ocular diseases in which mitochondrial dysfunction is postulated to play a role.

Proc Natl Acad Sci U S A 2003 Mar 18 100(6) 3439-44

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12626762

The use of polarised polychromatic non-coherent light alone as a therapy for venous leg ulceration.

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OBJECTIVE: This study assessed the effectiveness of polarised, polychromatic, non-coherent light therapy in the treatment of venous leg ulcers. Investigators in previous studies have advocated the use of light as an adjunct to other proven therapies or on its own. METHOD: This was a pilot prospective case-series study. We enrolled 25 patients with venous leg ulcers. All were treated with light only. Phototherapy (light therapy) treatments were given once a day over four weeks. RESULTS: All ulcers except one (99%) had a positive value for the change in healing area at the end of the four weeks. The total number of 73 leg ulcers recorded at the beginning of the study was reduced to 51 at the end of the four weeks ($p < 0.01$). The decrease in wound surface area following the treatment was statistically significant (mean: 57.15%; SD: 31.87%; $p < 0.01$). CONCLUSION: Polarised, polychromatic light therapy applied as a monotherapy was associated with positive healing rates in patients with venous leg ulcers. It is a simple and non-invasive treatment. However, a well-designed randomised controlled study is needed to confirm the efficacy of this form of phototherapy and to objectively evaluate recommendations for its routine use in clinical practice.

J Wound Care 2003 Jan 12(1) 37-40

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12572235

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

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

patient to a preinjury/illness level of activity. This work is supported and managed through the Defense Advanced Research Projects Agency (DARPA) and NASA Marshall Space Flight Center-SBIR Program.

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http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12737646

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

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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.

Lasers Med Sci 2003 18(2) 95-9

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12928819

NASA light-emitting diodes for the prevention of oral mucositis in pediatric bone marrow transplant patients.

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OBJECTIVE: The purpose of this study was to determine the effects of prophylactic near-infrared light therapy from light-emitting diodes (LEDs) in pediatric bone marrow transplant (BMT) recipients. BACKGROUND DATA: Oral mucositis (OM) is a frequent side effect of chemotherapy that leads to increased morbidity. Near-infrared light has been shown to produce biostimulatory effects in tissues, and previous results using near-infrared lasers have shown improvement in OM indices. However, LEDs may hold greater potential for clinical applications. MATERIALS AND METHODS: We recruited 32 consecutive pediatric patients undergoing myeloablative therapy in preparation for BMT. Patients were examined by two of three pediatric dentists trained in assessing the Schubert oral mucositis index (OMI) for left and right buccal and lateral tongue mucosal surfaces, while the patients were asked to rate their current left and right mouth pain, left and right xerostomia, and throat pain. LED therapy consisted of daily treatment at a fluence of 4 J/cm(2) using a 670-nm LED array held to the left extraoral

epithelium starting on the day of transplant, with a concurrent sham treatment on the right. Patients were assessed before BMT and every 2-3 days through posttransplant day 14. Outcomes included the percentage of patients with ulcerative oral mucositis (UOM) compared to historical epidemiological controls, the comparison of left and right buccal pain to throat pain, and the comparison between sides of the buccal and lateral tongue OMI and buccal pain. RESULTS: The incidence of UOM was 53%, compared to an expected rate of 70-90%. There was also a 48% and 39% reduction of treated left and right buccal pain, respectively, compared to untreated throat pain at about posttransplant day 7 ($p < 0.05$). There were no significant differences between sides in OMI or pain. CONCLUSION: Although more studies are needed, LED therapy appears useful in the prevention of OM in pediatric BMT patients.

J Clin Laser Med Surg 2002 Dec 20(6) 319-24

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12513918

Light-emitting diode treatment reverses the effect of TTX on cytochrome oxidase in neurons.

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Light close to and in the near-infrared range has documented benefits for promoting wound healing in human and animals. However, mechanisms of its action on cells are poorly understood. We hypothesized that light treatment with a light-emitting diode array at 670 nm (LED) is therapeutic in stimulating cellular events involving increases in cytochrome oxidase activity.

LED was administered to cultured primary neurons whose voltage-dependent sodium channels were blocked by tetrodotoxin. The down-regulation of cytochrome oxidase activity by TTX was reverted to control levels by LED. LED alone also up-regulated enzyme activity. Thus, the results are consistent with our hypothesis that LED has a stimulating effect on cytochrome oxidase in neurons, even when they have been functionally silenced by TTX.

Neuroreport 2001 Oct 8 12(14) 3033-7

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11568632

Biostimulatory windows in low-intensity laser activation: lasers, scanners, and NASA's light-emitting diode array system.

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OBJECTIVE: The purpose of this study was to assess and to formulate physically an irreducible set of irradiation parameters that could be relevant in the achieving reproducible light-induced effects in biological systems, both in vitro and in vivo. BACKGROUND DATA: Light-tissue interaction studies focusing on the evaluation of irradiation thresholds are basic for the extensively growing applications for medical lasers and related light-emitting systems. These thresholds are of central interest in the rejuvenation of collagens, photorefractive keratectomy, and wound healing. METHODS: There is ample evidence that the action of light in biological systems depends at least on two threshold parameters: the energy density and the intensity. Depending on the particular light delivery system coupled to an irradiation source, the mean energy density and the local intensity have to be

determined separately using adequate experimental methods. RESULTS: From the observations of different research groups and our own observations, we conclude that the threshold parameters energy density and intensity are biologically independent from each other. CONCLUSIONS: This independence is of practical importance, at least for the medical application of photobiological effects achieved at low-energy density levels, accounting for the success and the failure in most of the cold laser uses since Mester's pioneering work.

J Clin Laser Med Surg 2001 Feb 19(1) 29-33

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11547815

Monochromatic infrared irradiation (890 nm): effect of a multisource array upon conduction in the human median nerve.

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OBJECTIVE: Antidromic conduction studies in the human median nerve were used to assess the neurophysiological effects of irradiation of the skin overlying the nerve using a novel treatment unit comprising a multisource monochromatic infrared diode array (Equilight, Denver, CO). MATERIALS AND METHODS: Healthy human volunteers (n = 40) were recruited and randomly allocated to one of four groups: control, placebo, or one of two treatment groups (1.7 and 4.0 J/cm2). After baseline recordings of negative peak latency (NPL) were completed on the nondominant arm, subjects were treated according to group allocation. Recordings were subsequently repeated at 5-min intervals over a 45-min period. RESULTS: Analysis of negative peak

latency difference scores (ANOVA) demonstrated significant differences in NPL between groups and over time ($p < 0.05$). While in the control and placebo groups NPL values remained relatively stable, in the two treatment groups such values decreased marginally, with the greatest effects observed in the 4.0 J/cm2 group (e.g., at 5 min, differences in NPL [mean +/- SEM]: control group, 0.02+/-0.03 msec; treatment group 2, 4 J/cm2, -0.07+/-0.03 msec). Similar significant differences were observed in skin temperature; correlation analysis indicated a weak (but expected) positive linear relationship between skin temperature and nerve conduction velocity ($r = 0.125$). CONCLUSION: These results suggest that irradiation at the parameters and under the conditions used here produce a direct neurophysiological effect. The magnitude of such effects are in keeping with previous findings using single source arrays at higher radiant exposures or thermal effects of the treatment unit.

J Clin Laser Med Surg 2001 Dec 19(6) 291-5

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11776446

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

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

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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.

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The use of low energy photon therapy (LEPT) in venous leg ulcers: a double-blind, placebo-controlled study.

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BACKGROUND: Venous ulcers are estimated to be present in 0.2 to 0.4% of the population. Although new therapies have significant promise, nonhealing ulcers still represent a significant problem. OBJECTIVE: To evaluate the efficacy of low energy photon therapy (LEPT) in the treatment of venous leg ulcers. METHODS: A placebo-controlled, double-blind study using low energy photon therapy was performed in nine patients with 12 venous ulcers. Treatment was given three times a week for 10 weeks, using two monochromatic optical sources. One source provided a wavelength (lambda) of 660 nm (red) while the second source delivered a wavelength of 880 nm (infrared). Two optical probes were used, one consisted of an array of 22 monochromatic sources, operating at a wavelength of 660 nm and covering an area 6 x 10 cm2. The second probe had seven infrared sources, operating at a wavelength of 880 nm and covering an area of 4 cm2. The above configuration of optical probes was selected to cover the majority of the ulcer area being treated. The patients who were randomized to placebo treatment received sham therapy from an identical-appearing light source from the same delivery system. RESULTS: Nine patients with 12 venous ulcers were randomized to receive LEPT or placebo therapy. At the conclusion of the study, the percentage of the initial ulcer area remaining unhealed in the LEPT and placebo groups was 24.4% and 84.7%, respectively (P = 0.0008). The decrease in ulcer area (compared to baseline) observed in the LEPT and placebo groups was 193.0 mm2 and 14.7 mm2, respectively (P = 0.0002). One patient dropped out of the study, complaining of lack of treatment efficacy; he was found to be randomized to the placebo group. There were no adverse effects. CONCLUSION: In this placebo-controlled, double-blind study LEPT was an effective modality for the treatment of venous leg ulcers.

Dermatol Surg 1998 Dec 24(12) 1383-6

cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9865208

Comparison of the effect of multi-wavelength light produced by a cluster of semiconductor diodes and of each individual diode on mast cell number and degranulation in intact and injured skin.

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Intact skin and partial thickness wounds in adult male Wistar rats were irradiated by pulsed, monochromatic light of different spectral wavelength peaks simultaneously and the effects on mast cell number and degranulation were assessed. The light was produced by a Biotherapy 3ML (Omega Universal Technologies) device utilizing a 21 semiconductor diode cluster probe emitting 6 different wavelengths in the red and near infrared part of the spectrum simultaneously, only one of the wavelengths (820 nm) being coherent. The duration of treatment was 4 minutes. The average power density, distributed over the surface area of the probe (19.62 cm2) was 45 mW/cm2. The average energy density at the wound site was 10.8 J/cm2. The effect of each of the wavelengths incorporated in the cluster probe was then examined separately. The average power density for each single probe was 120 mW/cm2, except for the 820 nm diode which was 400 mW/cm2. The average energy density was maintained at 10.8 J/cm2 as with the cluster probe. After 2 hours the rats were killed and the skin was removed, processed for light microscopy, and stained with toluidine blue to identify the mast cells. The numbers of the intact and degranulated mast cells were counted in 100 high power fields (i.e., over a total area of 20 mm2) in each irradiated specimen and compared to the sham-irradiated and untreated groups. To avoid bias, the slides examined were coded and evaluated blind. In intact skin, the cluster probe irradiation was followed by a statistically

significant increase in the total number of mast cells compared to the sham-irradiated group, but the percentage of the degranulated mast cells was not affected. In the partial thickness wound, the cluster probe irradiation was also followed by a statistically significant increase in the total number of mast cells compared to the sham-irradiated group; however, there was, in addition, a significant increase in the percentage of degranulated mast cells. Concerning the single probes, only the 660, 820, 940, and 950 nm wavelength emitters produced statistically significant increases in both mast cell number and degranulation in partial thickness wounds. However, when intact skin was irradiated with probes emitting these wavelengths, although the total number of mast cells was increased significantly, there was no change in degranulation compared with the sham-irradiated group. The effects observed were less than those of the cluster probe. No significant differences were found between the 870 and 880 nm wavelength-irradiated, sham-irradiated, and untreated groups in either intact or injured skin. (ABSTRACT TRUNCATED AT 400 WORDS)

Lasers Surg Med 1990 10(6) 559-68

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Macrophage responsiveness to light therapy.

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Macrophages are a source of many important mediators of wound repair. It was the purpose of this study to see if light could stimulate the release of these mediators. In this study an established macrophage-like cell line (U-

937) was used. The cells were exposed in culture to the following wavelengths of light: 660 nm, 820 nm, 870 nm, and 880 nm. The 820-nm source was coherent and polarised, and the others were non-coherent. Twelve hours after exposure the macrophage supernatant was removed and placed on 3T3 fibroblast cultures. Fibroblast proliferation was assessed over a 5-day period. The results showed that 660-nm, 820-nm, and 870-nm wavelengths encouraged the macrophages to release factors that stimulated fibroblast proliferation above the control levels, whereas the 880-nm wavelength either inhibited the release of these factors or encouraged the release of some inhibitory factors of fibroblast proliferation. These results suggest that light at certain wavelengths may be a useful therapeutic agent by providing a means of either stimulating or inhibiting fibroblast proliferation where necessary. At certain wavelengths coherence is not essential.

Lasers Surg Med 1989 9(5) 497-505

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2811573

About James Carroll
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