**Photobiomodulation for Tissue Repair, Pain Management and Inflammation - Resources**

**Tissue Repair**

**Effect of 660/850 nm LED on the microcirculation of the foot: neurovascular biphasic reflex.**

**Abstract**

Phototherapy (LED) can be used to stimulate the healing of chronic ulcers of the lower limb, as it affects healing cells and neurons. In this way, this study has sought to know if the heat stimulus of the 660-/850-nm contact LED is sufficient to trigger the response in the peripheral sympathetic nervous system of normal volunteers. The LED was applied on the right foot of forty-two normal volunteers followed by serial infrared images. After the stimulus, a biphasic hyperthermia curve was observed synchronously in both feet, in the right and left halluxes, while hyperthermia was attributed to the redistribution of postural blood flow in the plantar region, which may indicate independent neurovascular mechanisms. Thus, periodic thermographic analysis can be used in the evolution of the LED treatment.

de Sá, C.M.D. Effect of 660/850 nm LED on the microcirculation of the foot: neurovascular biphasic reflex. *Lasers Med Sci* **36**, 1883–1889 (2021). <https://doi.org/10.1007/s10103-020-03235-4>

**Photobiomodulation using red and infrared spectrum light emitting-diode (LED) for the healing of diabetic foot ulcers: a controlled randomized clinical trial**

**Abstract**

Assessing the responses to the application of photobiomodulation using red and infrared spectrum light-emitting diodes (LED) on diabetic foot ulcers. Diabetic volunteers, of both genders, aged between 30 and 65 years, with grade I or II ulcers, were randomized into the groups: red LED, infrared LED, LED associated, and control. Home-based interventions took place on a daily basis for 12 weeks. Assessments of sample characterization were performed on day 1 and 90, and the variables wound healing index, mean skin temperature, sensitivity and pain in the wound area were measured at the pre-intervention time on days 1, 30, 60 and 90, with subsequent follow-up 30 days after the end of treatment. For statistical analysis, the software SPSS, version 17.0, intention-to-treat analysis, data normality was tested, and the linear mixed effects model, with a significance level of 5%. Magnitudes of clinical effect by Cohen’s d. At the pre vs post intervention time of 90 days, we found a large clinical effect of G-LED V (d=1.7) and G -LED IV (d=1.6) in relation to G-C, where these intervention groups showed a tendency for faster wound healing compared to G-C. We also observed small clinical effect of G-LED IV, which showed greater reduction in the area in relation to G-LED V (d=0.4) and G-LED A (d=0.3). Conclusion: The use of individually applied red and infrared LED phototherapy clinically tended to be more effective for the reduction of diabetic foot ulcer areas, and infrared LED was the most effective. Trial registration: NCT03250533 (clinicaltrials.gov).

Borges, N.C., Soares, L.R., Perissini, M.M. *et al.* Photobiomodulation using red and infrared spectrum light emitting-diode (LED) for the healing of diabetic foot ulcers: a controlled randomized clinical trial. *Lasers Med Sci* **39**, 253 (2024). <https://doi.org/10.1007/s10103-024-04199-5>

Low-level laser therapy as an adjunct to conventional therapy in the treatment of diabetic foot ulcers. Mathur RK, Sahu K, Saraf S, Patheja P, Khan F, Gupta PK Foot ulcers are serious complications of diabetes mellitus (DM) and are known to be resistant to conventional treatment. This study was conducted to evaluate the efficacy of low-level laser therapy (LLLT) for the treatment of diabetic foot ulcers in a tertiary care centre (Department of Surgery, Mahatma Gandhi Memorial Medical College and Maharaja Yashwantrao Hospital, A.B. Road, Indore). A total of 30 patients with type 2 DM having MeggittWagner grade I foot ulcers of more than 6weeks duration with negative culture were studied. Patients were randomized into two groups of 15 each. Patients in study group received LLLT (660‚ ±‚20nm, 3J/cm(2)) along with conventional therapy and those in control group were treated with conventional therapy alone. The primary outcome measure was the absolute and relative wound size reduction at 2weeks compared to the baseline parameter. Percentage ulcer area reduction was 37‚ ±‚9% in the LLLT group and 15‚ ±‚5.4% in the control group (p 15‚ ±‚5.4% in the control group (p<0.001). For‚ 75% of wounds of the treatment group, wound area reduction of 30-50% was observed. In contrast, for the control group, 80% of wounds showed a wound area reduction of <20% on day 15. Further, the wounds with the initial area 1000-2000mm2 seem to have better final outcome than the groups with larger areas. The treated groups showed higher granulation than the control group. The results suggest that LLLT is beneficial as an adjunct to conventional therapy in the treatment diabetic foot ulcers.

Mathur RK, Sahu K, Saraf S, Patheja P, Khan F, Gupta PK. Low-level laser therapy as an adjunct to conventional therapy in the treatment of diabetic foot ulcers. *Lasers Med Sci* 2016 Nov 29 <https://pubmed.ncbi.nlm.nih.gov/27896528>

**Photobiomodulation: systematic review and meta-analysis of the most used parameters in the resolution diabetic foot ulcers**

**Abstract**

The most common photobiomodulation parameters used to aid in the treatment of diabetic foot ulcers were investigated in this paper. The databases MEDLINE, LILACS, MEDCARIB, PAHO-IRIS, and WHOLIS were searched with the following descriptors: diabetic foot ulcers AND low-level laser therapy OR low-level therapy AND wound healing; this search was conducted from January of 2014 to December of 2019. Inclusion criteria were randomized clinical trials on humans. Exclusion criteria were systematic reviews, literature reviews, studies with animals, studies lacking photobiomodulation parameters, and studies with non-diabetic individuals. The Jadad scale was used in order to analyze the methodological quality of the matching papers. There were seventeen studies found on PubMed and four on LILACS. Among these, seven were selected, according to the inclusion and exclusion criteria. Two out of the seven matching studies obtained a high score, and five obtained a low score, on the Jadad scale. The studies settled on the use of 600-nm and 800-nm wavelength spectrum. Most of the analyzed papers on photobiomodulation on diabetic foot ulcers did not describe the detailed parameters in their methodology. None of the studies featured the maximum score with regard to the Jadad scale for methodological quality. The relations of energy versus wavelength and power versus wavelength were divergent among the parameters on the papers. Therefore, it is necessary to analyze the parameters for an optimized power value in order to improve the results of the treatment.

dos Santos Mendes-Costa, L., de Lima, V.G., Barbosa, M.P.R. *et al.* Photobiomodulation: systematic review and meta-analysis of the most used parameters in the resolution diabetic foot ulcers. *Lasers Med Sci* **36**, 1129–1138 (2021). <https://doi.org/10.1007/s10103-020-03192-y>

**Low-laser light therapy in venous ulcer healing: a randomized clinical trial**.

**Abstract**

Objectives: to compare the effect of adjuvant low-laser light therapy versus conventional treatment alone on venous ulcer healing.

Methods: this is a randomized clinical trial with 40 patients randomized equally to a control group (topical and compressive treatment) and intervention group (adjuvant low-laser light therapy).

Outcomes: of interest were Wound Healing: Secondary Intention and Tissue Integrity: Skin & Mucous Membranes, as described in the Classification of Nursing Outcomes/NOC. Results: groups with similar sociodemographic and clinical characteristics. Eighty-two ulcers were assessed, with an average duration of 1 to 5 years, in 1,066 nursing consultations, with a statistically significant difference in the time and number of healed ulcers (intervention group). There was a significant improvement in the nursing outcomes under study and in eight clinical indicators.

Conclusions: low-laser light therapy improves and reduces tissue regeneration time, contributing to advances in wound treatment.

Bavaresco T, Lucena AF**.** Low-laser light therapy in venous ulcer healing: a randomized clinical trial*Rev Bras Enferm,* 2021 11 75(3) E20210396 <https://pubmed.ncbi.nlm.nih.gov/34787240>

**Photobiomodulation in Promoting Wound Healing: A Review**

**Abstract**

Despite diverse methods being applied to induce wound healing, many wounds remain recalcitrant to all treatments. Photobiomodulation involves inducing wound healing by illuminating wounds with light emitting diodes or lasers. While used on different animal models, *in vitro*, and clinically, wound healing is induced by many different wavelengths and powers with no optimal set of parameters yet being identified. While data suggest that simultaneous multiple wavelength illumination is more efficacious than single wavelengths, the optimal single and multiple wavelengths must be better defined to induce more reliable and extensive healing of different wound types. This review focuses on studies in which specific wavelengths induce wound healing and on their mechanisms of action.

Kuffler, D. P. (2015). Photobiomodulation in Promoting Wound Healing: A Review. *Regenerative Medicine*, *11*(1), 107–122. <https://doi.org/10.2217/rme.15.82>

**Photobiomodulation Therapy for Wound Care: A Potent, Noninvasive, Photoceutical Approach**

**Abstract**

To provide background and examine evidence for the therapeutic application of light energy treatments for wound healing.

A search was performed in PubMed for peer-reviewed scientific articles published in the last 5 years using the search terms “photobiomodulation therapy” and “low-level laser therapy,” and these terms combined with “wound,” using a “human species” filter. This search yielded 218 articles on photobiomodulation therapy or low-level laser therapy and wounds. Of these, only articles on in vivo wound care using light treatments were specifically included in this review (n = 11).

The wound healing effects of low-dose laser treatments were first described over 50 years ago. Various doses ranging from 0.1 to 10 J/cm2 and wavelengths ranging from 405 to 1,000 nm appear to provide therapeutic benefits for a broad range of chronic wounds. A range of light energy sources from LEDs to lasers have been used and have specific advantages and limitations. There is a lack of consensus on standardized treatment parameters such as wavelengths, dose, and therapeutic outcomes in the reviewed studies, preventing direct comparison and clinical protocol recommendation. An expert opinion based on ongoing research studies and reported literature is offered.

Noninvasive, economical, and multipurpose light devices are an attractive tool for wound management. However, there is an urgent need in the wound care community to develop optimal clinical protocols for use based on well-designed, rigorous clinical research studies.

Mosca, Rodrigo Crespo PhD, DDS, MSc; Ong, Adrian A. MD; Albasha, Omar; Bass, Kathryn MD, MBA; Arany, Praveen PhD, BDS, MDS, MMSc. Photobiomodulation Therapy for Wound Care: A Potent, Noninvasive, Photoceutical Approach. *Advances in Skin & Wound Care* 32(4):p 157-167, April 2019. | DOI: 10.1097/01.ASW.0000553600.97572.d2 <https://journals.lww.com/aswcjournal/fulltext/2019/04000/photobiomodulation_therapy_for_wound_care__a.3.aspx>

**Blue light photobiomodulation: a therapy to reactivate the healing process of stagnant wounds of different aetiologies**

**Abstract**

Stagnant wounds are wounds that don’t progress in the healing process, despite adequate therapy. Blue light photobiomodulation is a novel therapy that has been demonstrated to positively influence wound healing by stimulating the resolution of the inflammatory response and promoting tissue repair. This case series evaluated the effect of photobiomodulation on five patients with silent wounds of various aetiologies who were treated with blue light for four weeks. At the end of the observation period, five patients had a significant reduction in lesion area, an improvement in wound bed score and a reduction in pain.

Conti A, Brilli M, Norgini E, Falini S, De Fina L, Spargi G and Gasperini S**.** Blue light photobiomodulation: a therapy to reactivate the healing process of stagnant wounds of different aetiologies.*Wounds International* 2023 | Vol 14 Issue 2, 41-45. <https://woundsinternational.com/wp-content/uploads/2023/05/WINT-14-2_41-45_gasperini-PRINT-NEW.pdf> <https://woundsinternational.com/journal-articles/blue-light-photobiomodulation-a-therapy-to-reactivate-the-healing-process-of-stagnant-wounds-of-different-aetiologies/#:~:text=Stagnant%20wounds%20are,reduction%20in%20pain>

**Pain Management of the Lower Limb and Foot**

**Low Level Laser Therapy in patients with chronic foot and ankle joint pain.**

**Abstract**

BACKGROUND AND AIMS: Chronic foot and ankle joint pain is one of the most frequent complaints which is regularly seen in the out-patient clinic of our medical institute. In previous studies we have reported on the benefits of low level laser therapy (LLLT) for chronic pain in the elbow, hand, finger and the lower back. The present study examined the effects of LLLT on chronic foot and ankle joint pain. MATERIALS AND METHODS: Over the past 5 years, 17 subjects visited the out-patient clinic with complaints of chronic foot and ankle joint pain of a variety of aetiologies. The patients received LLLT using a 1000 mW semi-conductor laser device, delivering 20.1 J/cm(2) per point at 830 nm in continuous wave. Each patient was given four shots per session per foot twice a week for 4 weeks. RESULTS: A visual analogue scale (VAS) was used to determine the effects of LLLT for the chronic pain and after the end of the treatment regimen a significant improvement was observed (p < 0.01). All but 2 of the patients showed improvement: excellent (2) and good (13). After treatment, no significant differences were observed in the ankle joint range of motion, however. Discussions with the patients revealed that it was important for them to learn how to avoid overuse of the ankle when walking, poor walking posture and a poor pacing technique that would caused them foot and ankle pain in everyday life. Following these postural guidelines could ensure continuous benefits from the treatment. CONCLUSION: The present study demonstrated that LLLT was an effective form of treatment for chronic foot and ankle joint pain, in conjunction with postural education during all activities of daily living.

Izukura H, Miyagi M, Harada T, Ohshiro T, Ebihara S. Low Level Laser Therapy in patients with chronic foot and ankle joint pain. *Laser Ther* 2017 26(1) 19-24 <https://pubmed.ncbi.nlm.nih.gov/28740325>

**Efficacy of low-level laser therapy on pain and disability in knee osteoarthritis: systematic review and meta-analysis of randomised placebo-controlled trials.**

**Abstract**

OBJECTIVES: Low-level laser therapy (LLLT) is not recommended in major knee osteoarthritis (KOA) treatment guidelines. We investigated whether a LLLT dose-response relationship exists in KOA. DESIGN: Systematic review and meta-analysis.

DATA SOURCES: Eligible articles were identified through PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, Physiotherapy Evidence Database and Cochrane Central Register of Controlled Trials on 18 February 2019, reference lists, a book, citations and experts in the field.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES: We solely included randomised placebo-controlled trials involving participants with KOA according to the American College of Rheumatology and/or Kellgren/Lawrence criteria, in which LLLT was applied to participants' knee(s). There were no language restrictions.

DATA EXTRACTION AND SYNTHESIS: The included trials were synthesised with random effects meta-analyses and subgrouped by dose using the World Association for Laser Therapy treatment recommendations. Cochrane's risk-of-bias tool was used.

RESULTS: 22 trials (n=1063) were meta-analysed. Risk of bias was insignificant. Overall, pain was significantly reduced by LLLT compared with placebo at the end of therapy (14.23 mm Visual Analogue Scale (VAS; 95% CI 7.31 to 21.14)) and during follow-ups 1-12 weeks later (15.92 mm VAS (95% CI 6.47 to 25.37)). The subgroup analysis revealed that pain was significantly reduced by the recommended LLLT doses compared with placebo at the end of therapy (18.71 mm (95% CI 9.42 to 27.99)) and during follow-ups 2-12 weeks after the end of therapy (23.23 mm VAS (95% CI 10.60 to 35.86)). The pain reduction from the recommended LLLT doses peaked during follow-ups 2-4 weeks after the end of therapy (31.87 mm VAS significantly beyond placebo (95% CI 18.18 to 45.56)). Disability was also statistically significantly reduced by LLLT. No adverse events were reported.

CONCLUSION: LLLT reduces pain and disability in KOA at 4-8 J with 785-860 nm wavelength and at 1-3 J with 904 nm wavelength per treatment spot. PROSPERO REGISTRATION NUMBER: CRD42016035587.

Stausholm MB, Naterstad IF, Joensen J, Lopes-Martins RÁB, Sæbø H, Lund H, Fersum KV, Bjordal JM. Efficacy of low-level laser therapy on pain and disability in knee osteoarthritis: systematic review and meta-analysis of randomised placebo-controlled trials. *BMJ* Open 2019 Oct 28 <https://pubmed.ncbi.nlm.nih.gov/31662383>

Jang, H, Lee H. **Meta-Analysis of Pain Relief Effects by Laser Irradiation on Joint Areas.**

**Abstract**

Background: Laser therapy has been proposed as a physical therapy for musculoskeletal disorders and has attained popularity because no side effects have been reported after treatment. However, its true effectiveness is still controversial because several clinical trials have reported the ineffectiveness of lasers in treating pain.

Methods: In this systematic review, we investigate the clinical effectiveness of low-level laser therapy (LLLT) on joint pain. Clinical trials on joint pain satisfying the following conditions are included: the laser is irradiated on the joint area, the PEDro scale score is at least 5, and the effectiveness of the trial is measured using a visual analogue scale (VAS). To estimate the overall effectiveness of all included clinical trials, a mean weighted difference in change of pain on VAS was used.

Results: MEDLINE is the main source of the literature search. After the literature search, 22 trials related to joint pain were selected. The average methodological quality score of the 22 trials consisting of 1014 patients was 7.96 on the PEDro scale; 11 trials reported positive effects and 11 trials reported negative effects. The mean weighted difference in change of pain on VAS was 13.96 mm (95% CI, 7.24-20.69) in favor of the active LLLT groups. When we only considered the clinical trials in which the energy dose was within the dose range suggested in the review by Bjordal et al. in 2003 and in World Association for Laser Therapy (WALT) dose recommendation, the mean effect sizes were 19.88 and 21.05 mm in favor of the true LLLT groups, respectively.

Conclusions: The review shows that laser therapy on the joint reduces pain in patients. Moreover, when we restrict the energy doses of the laser therapy into the dose window suggested in the previous study, we can expect more reliable pain relief treatments.

Jang, H, Lee H.Meta-Analysis of Pain Relief Effects by Laser Irradiation on Joint Areas. *Photomed Laser Surg* 2012 Jun 29 <https://pubmed.ncbi.nlm.nih.gov/22747309>

**Achilles Pain, Stiffness, and Muscle Power Deficits: Achilles Tendinitis**

**Abstract**

The Orthopaedic Section of the American Physical Therapy Association presents this sixth set of clinical practice guidelines on Achilles pain, stiffness, and muscle power deficits that are characteristic of Achilles Tendinitis. These clinical practice guidelines are linked to the International Classification of Functioning, Disability, and Health (ICF). The purpose of these practice guidelines is to describe evidence-based orthopaedic physical therapy clinical practice and provide recommendations for (1) examination and diagnostic classification based on body functions and body structures, activity limitations, and participation restrictions, (2) interventions provided by physical therapists, (3) and assessment of outcome for common musculoskeletal disorders.

**Note:** Not all Recommendations are included[\*](https://www.jospt.org/doi/10.2519/jospt.2010.0305#fn1)

**INTERVENTIONS — ECCENTRIC LOADING:** Clinicians should consider implementing an eccentric loading program to decrease pain and improve function in patients with midportion Achilles tendinopathy. (Recommendation based on strong evidence.)

**INTERVENTIONS — LOW-LEVEL LASER THERAPY:** Clinicians should consider the use of low-level laser therapy to decrease pain and stiffness in patients with Achilles tendinopathy. (Recommendation based on moderate evidence.)

**INTERVENTIONS — STRETCHING:** Stretching exercises can be used to reduce pain and improve function in patients who exhibit limited dorsiflexion range of motion with Achilles tendinopathy. (Recommendation based on weak evidence).

**INTERVENTIONS — FOOT ORTHOSES:** A foot orthosis can be used to reduce pain and alter ankle and foot kinematics while running in patients with Achilles tendinopathy. (Recommendation based on weak evidence.)

**INTERVENTIONS — MANUAL THERAPY:** Soft tissue mobilization can be used to reduce pain and improve mobility and function in patients with Achilles tendinopathy. (Recommendation based on expert opinion.)

**INTERVENTIONS — HEEL LIFT:** Contradictory evidence exists for the use of heel lifts in patients with Achilles tendinopathy. (Recommendation based on conflicting evidence.)

**INTERVENTIONS — NIGHT SPLINT:** Night splints are not beneficial in reducing pain when compared to eccentric exercise for patients with Achilles tendinopathy. (Recommendation based on weak evidence.)

 *J Orthop Sports Phys Ther 2010:40(9):A1–A26. doi:10.2519/jospt.2010.0305*

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<https://www.jospt.org/doi/10.2519/jospt.2010.0305>

Clinical Practice Guidelines Linked to the International Classification of Functioning, Disability, and Health from the Orthopaedic Section of the American Physical Therapy Association

**Effects of Low-Level Laser Therapy and Eccentric Exercises in the Treatment of Recreational Athletes With Chronic Achilles Tendinopathy. Tendinopathies**

**Abstract**

BACKGROUND: Eccentric exercises (EEs) are recommended for the treatment of Achilles tendinopathy, but the clinical effect from EE has a slow onset. HYPOTHESIS: The addition of lowlevel laser therapy (LLLT) to EE may cause more rapid clinical improvement.

STUDY DESIGN: Randomized controlled trial; Level of evidence, 1.

METHODS: A total of 52 recreational athletes with chronic Achilles tendinopathy symptoms were randomized to groups receiving either EE + LLLT or EE + placebo LLLT over 8 weeks in a blinded manner. Low-level laser therapy (lambda = 820 nm) was administered in 12 sessions by irradiating 6 points along the Achilles tendon with a power density of 60 mW/cm(2) and a total dose of 5.4 J per session. RESULTS: The results of the intention-to-treat analysis for the primary outcome, pain intensity during physical activity on the 100-mm visual analog scale, were significantly lower in the LLLT group than in the placebo LLLT group, with 53.6 mm versus 71.5 mm (P = .0003) at 4 weeks, 37.3 mm versus 62.8 mm (P = .0002) at 8 weeks, and 33.0 mm versus 53.0 mm (P = .007) at 12 weeks after randomization. Secondary outcomes of morning stiffness, active dorsiflexion, palpation tenderness, and crepitation showed the same pattern in favor of the LLLT group.

CONCLUSION: Low-level laser therapy, with the parameters used in this study, accelerates clinical recovery from chronic Achilles tendinopathy when added to an EE regimen. For the LLLT group, the results at 4 weeks were similar to the placebo LLLT group results after 12 weeks.

Stergioulas A, Stergioula M, Aarskog R, Lopes-Martins RA, Bjordal JM. Effects of Low-Level Laser Therapy and Eccentric Exercises in the Treatment of Recreational Athletes With Chronic Achilles Tendinopathy. Tendinopathies. *Am J Sports Med* 2008 Feb 13. <https://www.researchgate.net/publication/5578907_Effects_of_Low-Level_Laser_Therapy_and_Eccentric_Exercises_in_the_Treatment_of_Recreational_Athletes_With_Chronic_Achilles_Tendinopathy>

**Inflammation**

**Mechanisms and applications of the anti-inflammatory effects of photobiomodulation**

**Abstract**

Photobiomodulation (PBM) also known as low-level level laser therapy is the use of red and near infrared light to stimulate healing, relieve pain, and reduce inflammation. The primary chromophores have been identified as cytochrome c oxidase in mitochondria, and calcium ion channels (possibly mediated by light absorption by opsins). Secondary effects of photon absorption include increases in ATP, a brief burst of reactive oxygen species, an increase in nitric oxide, and modulation of calcium levels. Tertiary effects include activation of a wide range of transcription factors leading to improved cell survival, increased proliferation and migration, and new protein synthesis. There is a pronounced biphasic dose response whereby low levels of light have stimulating effects, while high levels of light have inhibitory effects. It has been found that PBM can produce ROS in normal cells, but when used in oxidatively stressed cells or in animal models of disease, ROS levels are lowered. PBM is able to up-regulate anti-oxidant defenses and reduce oxidative stress. It was shown that PBM can activate NF-kB in normal quiescent cells, however in activated inflammatory cells, inflammatory markers were decreased. One of the most reproducible effects of PBM is an overall reduction in inflammation, which is particularly important for disorders of the joints, traumatic injuries, lung disorders, and in the brain. PBM has been shown to reduce markers of M1 phenotype in activated macrophages. Many reports have shown reductions in reactive nitrogen species and prostaglandins in various animal models. PBM can reduce inflammation in the brain, abdominal fat, wounds, lungs, spinal cord.

Hamblin MR. Mechanisms and applications of the anti-inflammatory effects of photobiomodulation. *AIMS Biophys*. 2017;4(3):337-361. doi: 10.3934/biophy.2017.3.337. Epub 2017 May 19. PMID: 28748217; PMCID: PMC5523874. <https://pmc.ncbi.nlm.nih.gov/articles/PMC5523874/pdf/nihms879874.pdf>