

Non Invasive Physical Regenerative Therapies: Laser therapy, Mechanism of Action and Results

W. Leonardo Guiloff¹, Ondrej Prouza², Dragana Žarković²

Abstract

Low-level laser therapy (LLLT) and high-intensity laser therapy (HILT) have emerged as a therapeutic alternative suitable for a wide range of medical conditions. The main advantage of high-intensity laser over LLLT is its ability to deliver a much higher dose in a shorter time while achieving deeper penetration into the affected tissue and producing a thermal effect. Although HILT, provides very satisfactory clinical results, more clinical research is require to justify its massive use.

Keywords: Low-level laser therapy, High-level laser therapy, Biostimulation, Phototherapy

Introduction

Mechanotherapy [1] by means of pressure waves, such as focused shockwaves and radial waves, has provided a therapeutic tool capable of giving solutions in chronic musculoskeletal conditions in which previously the only alternative was surgery [2]. Focused shockwaves trigger a biological response that includes angiogenesis and vasculogenesis, in addition to lymphangiogenesis [3]. However, in cases of acute inflammation with bursitis or synovitis, the application of this type of physical energy can increase pain. Low-level laser therapy (LLLT) and high-intensity laser therapy (HILT) have emerged as an alternative in these cases.

Laser light is characterized by being coherent, polarized, and monochromatic electromagnetic waves [4, 5] that can be used in medicine for both invasive and non-invasive purposes. The efficacy of laser therapy is strongly related to photon propagation and distribution speed in irradiated tissues affected by their wavelength. The healing effects of laser light therapy on the human body have been known since the 60's, producing biostimulation and pain relief. Since then, laser therapy has

gained popularity as it is a painless and non invasive modality suitable for a wide range of medical conditions [6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34].

The purpose of this review is to provide an overview about the history, mechanism of action, and indications of laser in the skin and musculoskeletal pathology.

History and Development of Laser Technology

Although Albert Einstein predicted stimulated electromagnetic radiation in 1917 in his article

“Zur Quantentheorie der Strahlung” [35], it took more than four decades for different scientists to come up with theories on how to intensify light in the visible spectrum and in the adjacent infrared wavelength areas using stimulated emission.

The theoretical principles to develop laser devices were defined by Nikolaj G. Basov and Alexandra M. Prokhorov in the Soviet Union in 1955 [36], followed by Charles Townes [37] and Arthur Schawlow [38] in the USA, in 1957. Both American researchers received the Nobel Prize for their studies in quantum physics in 1964.

After many patent disputes between various researchers, Gordon Gould is considered the official inventor and author of the acronym LASER which stands for Light Amplification by Stimulated Emission of Radiation, introduced in 1959 [4].

Despite the official story, many authors consider Theodore Maiman the true inventor of laser. He was the first to create a functional ruby laser in 1960 [1, 5, 39]. Later, laser devices were built using various active agents that generate coherent electromagnetic radiation. The most frequently used are alkali metal vapors and other gases such as He, Ne, Ar, CO₂. These active agents have been successfully adapted to surgery, dermatology, and ophthalmology. New technological solutions allowed the development of significantly cheaper and smaller semiconductor diode lasers, with a wider spectrum of wavelengths, that gave way to a wider clinical use in different medical areas, including physical medicine and rehabilitation (PMR).

In the late 90's, high-intensity laser, or class 4 laser, expanded into the field of PMR and sports medicine. Such technology allowed to generate energy levels of 10W and more, achieving a stronger biostimulation [40].

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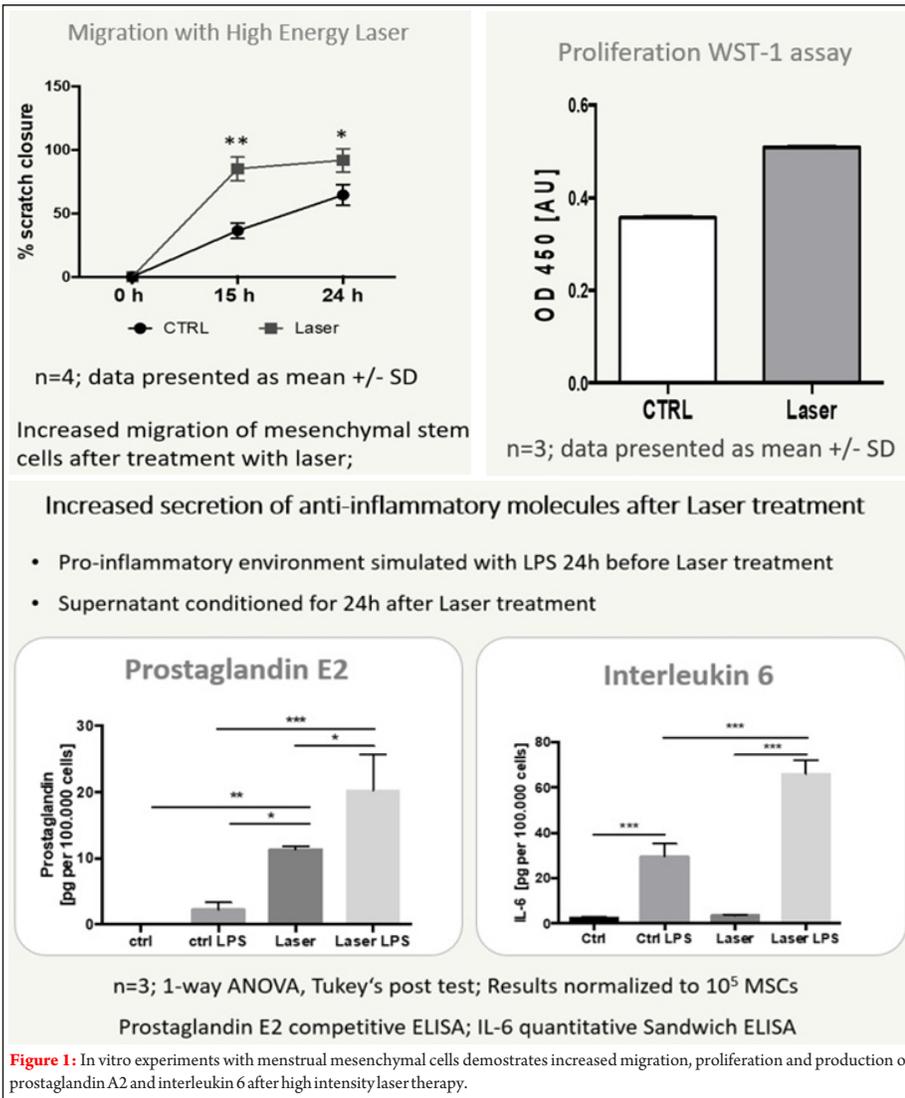
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Submitted Date: 7 August 2021, Review Date: 9 October 2021, Accepted Date: 12 November 2021 & Published: 31 December 2021

© 2021 by Journal of Regenerative Science | Available on www.jrsonweb.com | DOI:10.13107/jrs.2021.v01.i01.013

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The main advantage of high-intensity lasers over lower intensity lasers is its ability to deliver high therapeutic doses (J/cm^2) in a significantly shorter period of time due to its high power (W). The maximum therapeutic dose in LLLT is still debated, however, it generally does not exceed $16 J/cm^2$, but in high-intensity laser the common dose is generally around $80-120 J/cm^2$, which determines higher clinical effectiveness. Other advantages of HILT over LLLT, is that at wavelengths above 1000 nm, it can penetrate deeper improving clinical effects. LLLT is unable to penetrate deep into the joints and large muscle groups and to release enough energy to achieve a therapeutic effect. HILT generates immediate analgesic and muscle relaxant effects on pulsed emissions and has thermal effect when applied in continuous emission. This is valuable for treating acne [41], scars [42, 43, 44, 45, 46] and superficial muscles [47]. There are two

useful basic high-intensity laser technologies in the fields of PMR and sports medicine: modified invasive NdYAG laser and high-intensity diode laser. NdYAG lasers emit very high power in kilowatts but only in extremely short pulses. It is impossible to generate a continuous emission and achieve thermal effect. Other than that, these devices are quite robust and have high operating costs. On the other hand, iode lasers can generate both continuous and pulsed emissions and can offer more wavelength combinations. Such devices usually have smaller dimensions or they are even portable, having low operating costs. The inability to reach extremely high peak values in pulsed emissions can only be considered a relative disadvantage [29, 39, 47]. In the last decade, the laser industry has explored innovations, time savings, and technical solutions that emphasize ergonomics for the operator without

compromising clinical efficacy. Laser therapy, for years, was carried out and controlled in a conventional way, that is, the applicator was handled by an operator on the site to be treated. Despite all preventive and safety measures, a human operator will never be able to constantly perform the same movement over the affected area, therefore, the power distribution could differ. For this reason, automated laser applicators were designed, they can perform replicable movements on the affected area to guarantee a homogeneous distribution of laser energy, as shown by Baack [48,49].

Laser Radiation Absorption

Human skin represents a biological, mechanical, and chemical barrier. It also gives optical protection to laser light. The reflection of the laser light represents the loss of electromagnetic radiation caused by the difference in refraction. Previous research confirms that wavelengths in the near-infrared (NIR) regions (above 1000 nm) lead to less energy loss. Absorption means transferring energy to the target tissue and results in an energy loss defined by the absorption coefficient. The main laser light absorbers in human tissues are melanin, water, and hemoglobin.

The absorption of light increases with the concentration of melanin in the skin. The peak of melanin absorption is between 300 and 400 nm in NIR regions and decreases with longer wavelengths. At wavelengths >1100 nm, melanin absorption is almost negligible [48]. Water is a weak absorption chromophore in the visible wavelength spectrum increasing absorption within the NIR and infrared regions. Studies showed that there is almost no absorption below 800 nm, while the highest absorption was shown at wavelengths within the range of 900/1150 nm [50].

Hemoglobin is the main blood component responsible for absorbing and scattering radiation. The absorption spectra depend on the oxygen rich or oxygen poor hemoglobin state. The main difference between these two states occurs at wavelengths >950 nm. According to Tseng et al. [51], the absorption of deoxyhemoglobin decreases continuously from the wavelength of 900 nm. The reflection is negligible for the wavelength of 1064 nm. The absorption coefficient of melanin decreases from 690 nm to 1064 nm

and reduces energy loss in the skin [48, 52, 53].

Biological Effects of Laser Radiation

Biostimulation is considered to be the main laser biological effect. It was first described in 1967 by Endre Mester, a professor at Semmelweis University in Budapest, who used experimental radiation on a group of mice to verify whether laser radiation can produce malignant tissue [54]. However, this effect was not demonstrated, and mice that were exposed to experimental low-intensity laser radiation, within the red spectrum of light radiation, showed significantly faster regeneration of their shaved skin compared to the non-exposed group. Mester also applied laser on open skin lesions and demonstrated the healing effects of laser radiation through a series of histological and immunological tests [54]. The term laser biostimulation [54] was later generalized by some of the authors as "laser bio-modulation," for a better specification of the stimulation to which other effects such as suppression of inflammation and its powerful analgesic effect are added.

Specific parts of the cellular mitochondrial chains can absorb the specific wavelength of laser radiation and release signaling molecules (NO, cytokines, growth factors). This leads to increased adenosine triphosphate formation and cell metabolism, resulting in tissue regeneration and healing. The biostimulation effect is linked to studies indicating that laser radiation increases fibroblast activity, collagen synthesis, and angiogenesis due to the proliferation of

endothelial cells in affected tissues [52, 53, 55, 56, 57, 58, 59].

Peat et al. [60] demonstrated in the equine bone marrow that HILT has an anti-inflammatory action by inhibiting the synthesis of proinflammatory cytokines at the transcriptional level. We had a similar result in conjunction with the biomedical engineer Dr. Christina Schuh, at the Universidad del Desarrollo, Santiago de Chile. Mesenchymal cells treated with 1064 nm laser, migrated, proliferated, and produced Prostaglandin E2 and Interleukin 6 in much greater quantity than the control group (Fig. 1). The effect was greater in cells previously seeded with a cellular irritant lipopolysaccharide, equivalent to those found in the cell membrane of Gram-negative bacteria. Bjordal et al. demonstrated that LLLTs reduced microdialysis measured PGE2 levels in LLLT activated Achilles tendonitis [61]. Laser therapy can also be used to reduce edema [16].

Pain relief is achieved by stimulation of the A, δ , and C nerve fibers and the secretion of endogenous opioids alpha and beta-endorphins that bind to opiate receptors of the nociceptive system. This was demonstrated by Walker et al. [62] that described the elimination of 5 hydroxy indoleacetic acid in urine after local irradiation with LLLT in patients suffering from chronic pain. Laser therapy can directly affect the peripheral nervous system.

Due to the biological background of the aforementioned effects, laser appears clinically effective in acute and chronic neck and low back pain [11, 12, 13, 14, 15, 23, 63],

and in degenerative joint conditions such as osteoarthritis of the knee [20, 21, 25, 28, 30, 33] and rheumatoid arthritis [27, 33, 64]. A systematic review by Wyszynska and Bal-Bochenska [33], analyzed the literature on the use of high-energy laser therapy in knee osteoarthritis and concluded that HILT seems to be efficient in reducing pain and for providing functional improvements. We were able to replicate these results in a treatment protocol developed by our team [65].

Laser therapy is also useful in other disorders such as temporomandibular degenerative processes [26], shoulder impingement syndrome [32], tendinopathies [17, 18, 66], fibromyalgia [67], peripheral nerve disorders [12, 68, 69], and in the healing of wounds [24, 41, 42, 43, 44, 45, 70]. Laser therapy has promising results for the treatment of cold sores [71] and onychomycosis [72, 73].

Conclusión

Laser therapy is a clinically proven, non-invasive modality suitable for a wide range of medical conditions. LLLT has been in use for over 50 years. Despite the limits of LLLT, therapy may be suitable for superficial and dermatological problems.

The main advantage of high-intensity laser over LLLT is its ability to deliver a much higher dose in a shorter time while achieving deeper penetration into the affected tissue and producing a thermal effect. Although HILT, provides very satisfactory clinical results, more clinical research is required to justify its massive use.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Conflicts of Interest: Nil. **Source of Support:** None.

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Conflict of Interest: NIL
Source of Support: NIL

How to Cite this Article

Guiloff WL, Prouza O, Žarković D | Non Invasive Physical Regenerative Therapies: Laser therapy, Mechanism of Action and Results | *Journal of Regenerative Science* | December 2021; 1(1): 21-25.