



Laser and photobiomodulation

Shaghayegh fouladvandi



V. Laser therapy: **Photobiomodulation**

Laser therapy is a medical treatment that uses laser light to stimulate a process called **photobiomodulation (PBM)**

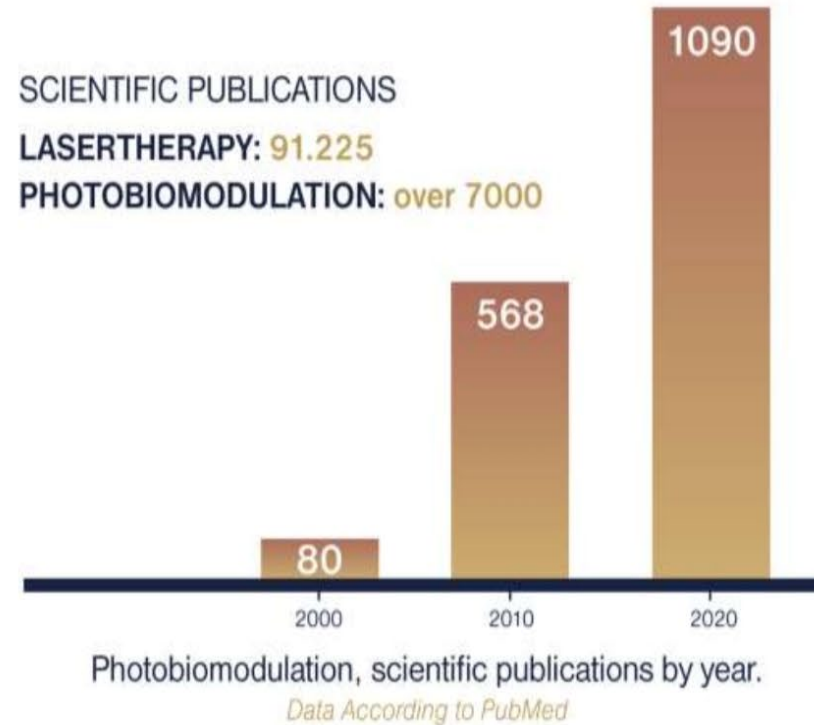
V. Laser therapy: **Photobiomodulation**

Photobiomodulation is defined as a form of light therapy that uses visible and near infrared laser sources.

It is a non-thermal or moderately thermal process that involves endogenous chromophores that cause photophysical and photochemical events at various **biological scales**. This process results in therapeutic outcomes not only aimed at reducing pain and inflammation, but also at promoting immunomodulation, wound healing and tissue regeneration.

V. Laser therapy: **Photobiomodulation**

There are over 90.000 scientific publications dedicated to laser therapy and over 7.000 dedicated to Photobiomodulation. In recent years, **Photobiomodulation is increasingly the subject of study and attention**, with an exponential increase in scientific publications produced annually. In fact, in the last 20 years we have gone from 80 researches published in 2000 to 1090 in 2020.



VI. Laser therapy: The effects of therapeutic laser light

The effects of therapeutic laser light on the tissue are three:

- **Photochemical**
- **Photothermal**
- **Photomechanical**

IV. Laser therapy: The importance of average power

Comparison of Light Penetration of Continuous Wave 810 nm and Superpulsed 904 nm Wavelength Light in Anesthetized Rats. Anders JJ¹, Wu X¹ - 2016 Sep;34(9):418-24. doi: 10.1089/pho.2016.4137. Epub 2016 Aug 8.

OBJECTIVE:

The purpose of this study was to investigate light transmission of continuous wave (CW) 810 nm wavelength light and 904 nm wavelength superpulsed light through skin and gastrocnemius muscle and skin only using an anesthetized Sprague-Dawley rat model.

RESULTS: The percentages of light transmission (fluence rate) through muscle and skin were

7.42% (810 nm wavelength)

4.01% (904 nm wavelength)

and through skin were

24.63% (810 nm wavelength)

19.94% (904 nm wavelength)

These data prove that transmission of CW 810 nm wavelength light through muscle and skin and skin alone is greater than transmission of superpulsed 904 nm wavelength light.

IV. Laser therapy: **The importance of average power**

The ability of a laser to penetrate into biological tissues depends **solely on the wavelength**



The peak power does not increase the ability of the laser light to penetrate inside biological tissues!

VI. Laser therapy: **The effects of therapeutic laser light**

Interaction with mechanoreceptors



Analgesic effect



Mechanical stress of tissues



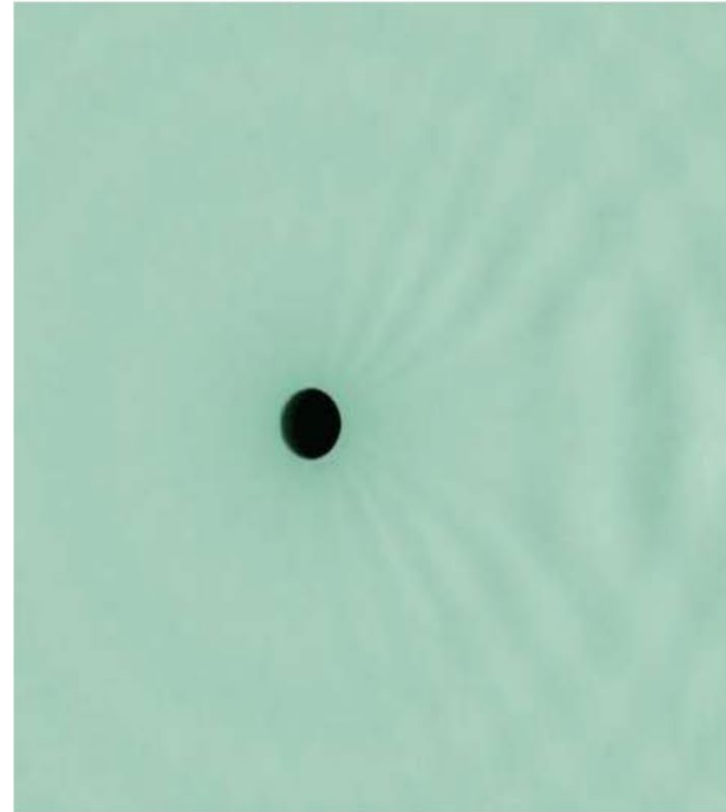
Supports tissue regeneration

Anti-inflammatory action



VI. Laser therapy: **The effects of therapeutic laser light**

Laser light interacts with the tissue transforming the light energy in an acoustic / mechanical impulse.



PHOTOMECHANICAL EFFECT

59/189



VI. Laser therapy: The effects of therapeutic laser light



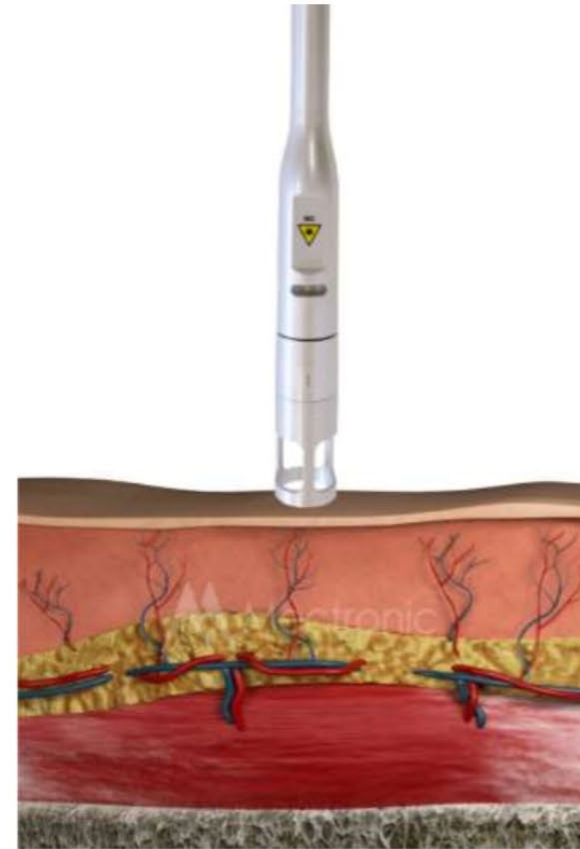
VI. Laser therapy: The effects of therapeutic laser light

980 nm and 1064 nm

Due to these peculiarities, these two wavelengths trigger further metabolic pathways that may act in some cases at the same time as those triggered by photobiomodulation.

VI. Laser therapy: The effects of therapeutic laser light

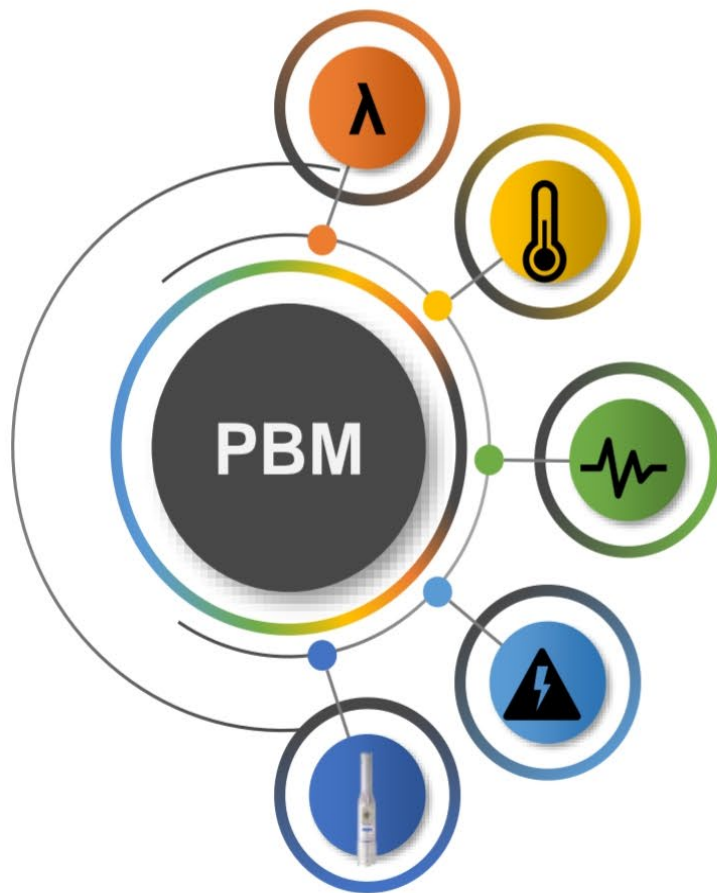
The thermal gradient created increases the blood flow at the local level.



VI. Laser therapy: **The effects of therapeutic laser light**



The laser light interacts with the tissue transforming the light energy in heat.



● Wavelengths

● Thermal control

● Emission mode

● High Average Power

● Correct transfer method

VI. Laser therapy: **The effects of therapeutic laser light**

The effects of therapeutic laser light on the tissue are three:

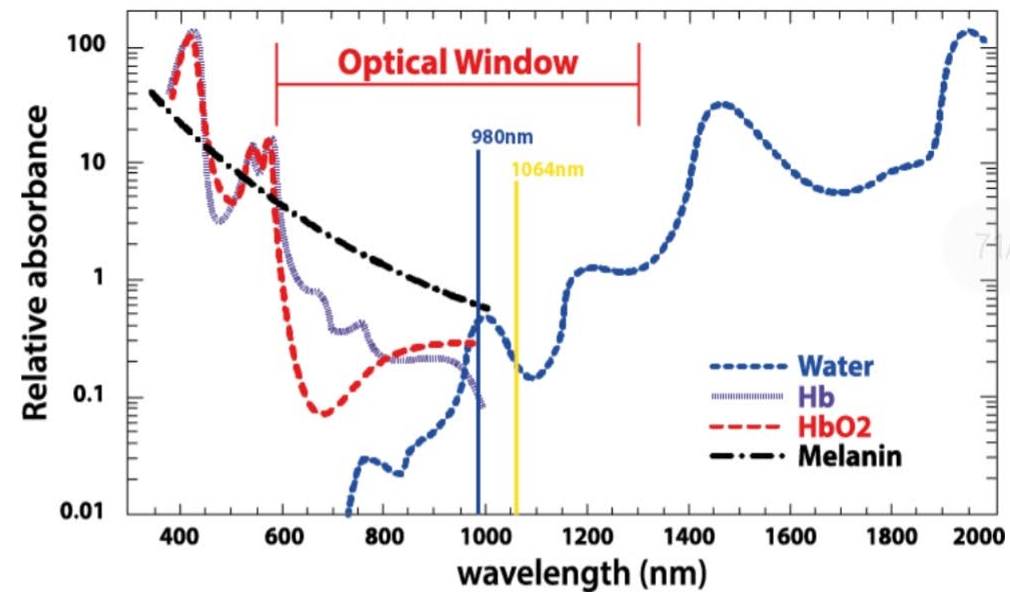
- **Photochemical**
- **Photothermal**
- **Photomechanical**

PHOTOTHERMAL EFFECT

VI. Laser therapy: The effects of therapeutic laser light

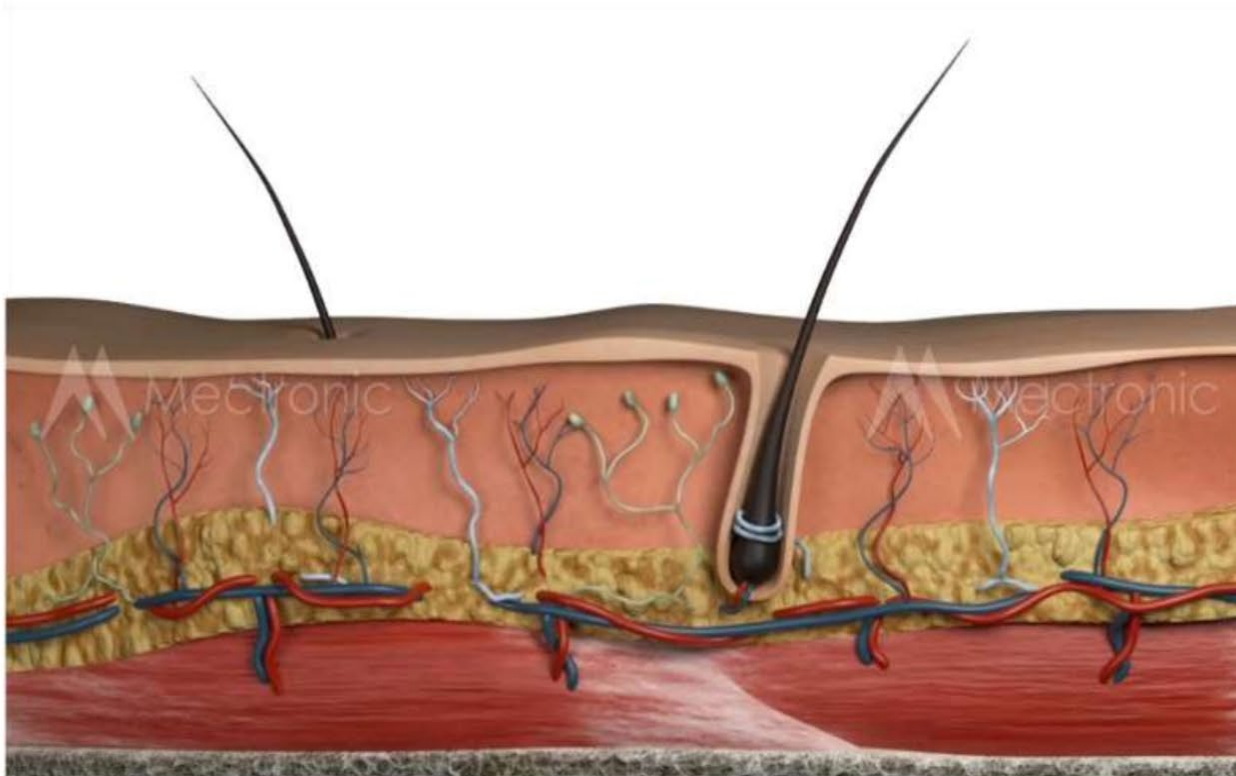
All the wavelengths of the therapeutic window applied with a sufficiently high-power density allow to obtain a photothermal effect.

Among these the 980nm, having a peak of absorption on the water, at the same power can create a greater thermal gradient.



"Mechanisms of low-level light therapy" (2006)
Proc. of SPIE Vol. 6140 614001-1 - M. HAMBLIN, T. DEMIDOVA

I. PBM: Which wavelengths can make it more efficient?



I. PBM: Which wavelengths can make it more efficient?

“Multiple Roles of Cytochrome c Oxidase in Mammalian Cells Under Action of Red and IR-A Radiation» (2010) IUBMB LIFE - **T. I. KARU**



There are numerous studies that explain **Photobiomodulation**. **Tina Karu** is one of the most important expert and researcher of the phenomenon of light absorption on **Cytochrome C Oxidase**.

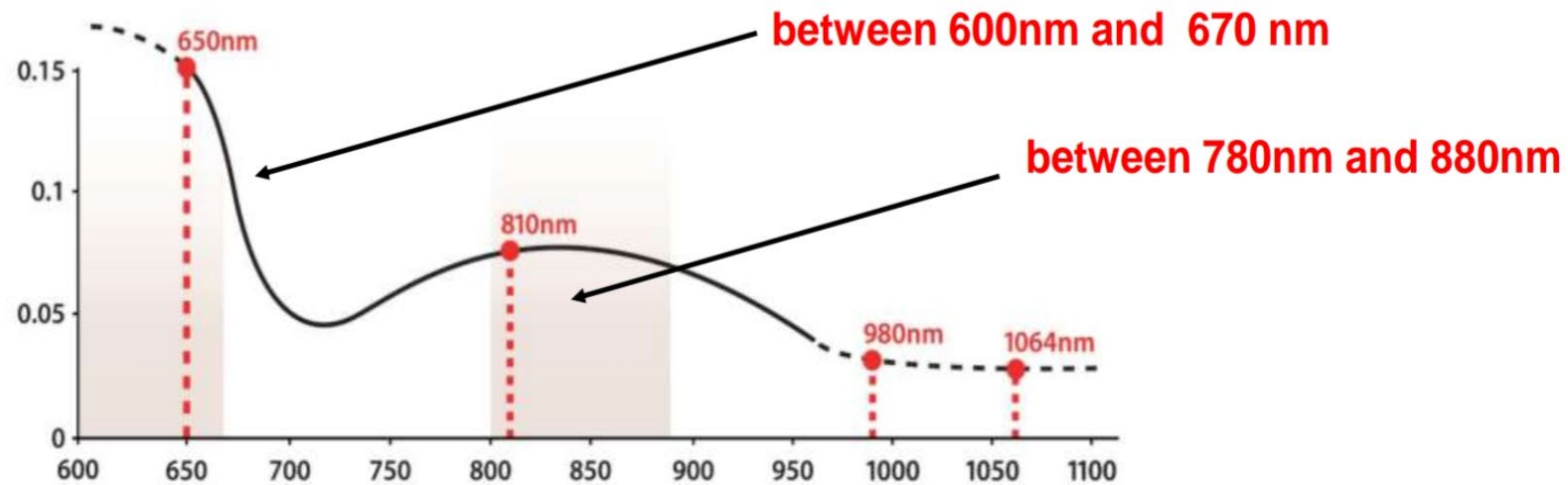
I. PBM: Which wavelengths can make it more efficient?

Other wavelengths within the therapeutic window (for example 980 nm and 1064 nm), although less absorbed by the Cytochrome C oxidase, are useful because they guarantee excellent interaction with thermo- and mechanoreceptors.

- **980 nm: the most absorbed by water within the therapeutic window**
- **1064 nm: less scattering and more directional**

I. PBM: Which wavelengths can make it more efficient?

Several studies show how **Cytochrome C Oxidase** mainly absorbs laser light:



"Re-evaluation of the near infrared spectra of mitochondrial cytochrome c oxidase: Implications for non invasive in vivo monitoring of tissues"

BBA Bioenergetics - (2014) G.MASON, P. NICHOLLS, E. COOPER

I. PBM: Which wavelengths can make it more efficient?

Numerous scientific articles have shown how the wavelengths in the range **600 nm - 670 nm** and in the range **780 nm - 880 nm** are more absorbed by the main **photoacceptor** of laser therapy (Cytochrome C Oxidase) and therefore make it possible to make **photobiomodulation** (PBM) more efficient.

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- 980 nm: the most absorbed by water within the therapeutic window
- 1064 nm: less scattering and more directional

II. PBM: Which emission mode can make it more efficient?

It has been demonstrated that the optimal laser emission to trigger photobiomodulation must be continuous or pulsed with a pulse duration of at least a few milliseconds (10^{-3} seconds), as stated by Hamblin, in 2010 in the article “Effect of Pulsing in Low-Level Light Therapy”.

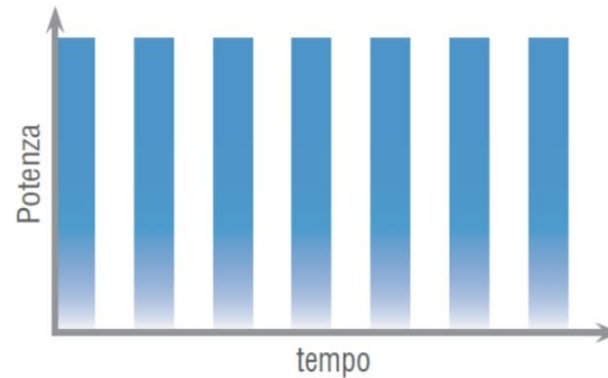
II. PBM: Which emission mode can make it more efficient?



ATTENTION !!!
SUPERPULSED LASER: pulse duration microseconds ($s \cdot 10^{-6}$)
nanoseconds ($s \cdot 10^{-9}$)



Pulse duration



II. PBM: Which emission mode can make it more efficient?

CLINICAL TEST

Key words: Hilaria; pulsed Nd:YAG laser; photomechanical effect; tissue repair; extracellular matrix

Energy for Health [85]

Relationship between cellular and systemic effects of pulsed Nd:YAG laser.

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2) ASScampus Joint Laboratory, ASA Res. Div., Dept. Clinical Physiotherapy, Torneo University, Florence, Italy.

ABSTRACT

Notwithstanding the wide diffusion of lasertherapy in clinics and numerous studies reported in literature, molecular mechanisms of interaction between laser and tissues are not well understood.

The analysis of biological effects induced by laser radiation is rather complicated due to the wide possibility of setting instruments, the variability of applied protocols and the differences in treated tissues.

In this review, we describe our studies on the cellular and molecular mechanisms at the basis of the systemic effects produced by treatment with pulsed Nd:YAG laser, that is known as Hilaria.

Starting from studies on photothermal effects, the hypothesis is that this type of laser cause an indirect photomechanical effect. The heat produced by transfer of radiation energy to the irradiated volume, diffuse into surrounding tissues, inducing temperature gradients which result in transitory modifications of mechanical-elastic properties of the extracellular microenvironment, thus changing mechanical forces acting on cells.

Considering these studies and knowing

the key role of the extracellular matrix, not only as a structural support but also in maintaining tissue homeostasis, our experiments focused on the analysis of extracellular matrix molecules and cytoskeleton behavior, responsible of contact between cell and matrix and considered the best candidate to act as a mechanotransducer.

The data obtained have shown, in laser-treated cells, an increase in production of ECM molecules, such as aggrecan, collagen I and II, and a reorganization of microtubules and actin microfilaments network. It is well known that similar effects are obtained when cells are subjected to mechanical stress. Our data on absorption of Nd:YAG pulses by matrix components (proteins and polysaccharides) suggest that Nd:YAG pulses principally interact with the extracellular matrix, whose transitory deformation applies a mechanical stress to the cells.

We then focused on the effect of pulsed Nd:YAG on endothelial function and tissue repair processes. In treated endothelial cells and fibroblasts, key elements of angiogenesis and tissue repair, we found

overexpression of genes involved in the chemokine-mediated inflammatory pathways. Moreover, the treatment promoted the formation of ordered endothelial monolayers as well as ordered fibronectin fibril assembling. The findings indicate that treatment with Nd:YAG pulses has a stimulatory effect in the acute phase of inflammation and significant effect on the remodeling phase of tissue repair, also considering the important role that fibronectin plays in tissue structure regeneration. Therefore we can support that Hilaria can efficaciously promote tissue repair processes.

INTRODUCTION

In spite of a wide application in clinics, many studies and a great body of literature, the molecular mechanisms of the interaction between laser and tissues, and the consequent cellular response, are still not completely known. They are object of current and future research in the field of laser biomedical application. Unfortunately, not always scientifically rigorous studies, a limited knowledge of the molecular and cellular mechanisms underlying the biological effects of laser and, in turn, the systemic effects of laser therapy give rise to confusing results, unsupported hypotheses and unconvincing theories.

The studies on laser biological effects are very difficult due to the variety of biological responses that depend on laser source (wavelength, continuous/pulsed mode), operative conditions (fluence, time of exposure, etc.) and biological substrate considered (the body area, the tissue, the cell type etc.). Nevertheless, they are of critical importance for correct clinical applications, to improve instruments and protocols, to increase therapeutic effectiveness.

When the light interacts with a biological tissue a small part of radiation (~3-5%) is specular reflected, the most part propagates within the tissue and it is partially diffused (scattering) and

"Relationship between cellular and systemic effects of pulsed Nd:YAG laser."

CIALDAI F., MONICI M.

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II. PBM: Which emission mode can make it more efficient?

CLINICAL TEST

Key words: Photochemical stress, pulsed Nd:YAG laser, connective tissue, cutaneous melan, Hilterapia®

Effects of pulsed Nd: YAG laser at molecular and cellular level. A study on the basis of Hilterapia®.

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ABSTRACT

Lasers have been widely applied in many different fields of medicine, proving their effectiveness in the treatment of a wide range of diseases. In spite of the great amount of literature, it is difficult to understand the molecular and cellular mechanisms at the basis of the systemic effects induced by laser radiation because of different levels of laser used, specific conditions, variety of biological targets and responses.

The application of high power lasers in physiotherapy is quite recent. It is due to the development of instruments which allow the control of photochemical and photomechanical processes, so as to obtain therapeutic effects without tissue damage. In particular, pulsed Nd:YAG laser has proved its versatility and efficacy in the treatment of many different musculoskeletal diseases and it is believed to have anti-inflammatory, anti-edema, analgesic and also reparative effects.

The aim of the study presented was to contribute to understanding the molecular mechanisms and cellular processes at the basis of the systemic effects produced by pulsed Nd:YAG laser radiation.

Owing to the lack of chromophores efficiently absorbing Nd:YAG radiation

(wavelength 1064 nm) in cells and tissues, we hypothesized that, rather than photochemical processes, specific mechanisms probably due to combined photothermal and photomechanical interactions could be responsible for the above mentioned effects of pulsed Nd:YAG laser.

The finding suggests that cells "sense" pulsed Nd:YAG laser irradiation and respond to it through mechanotransduction machinery. We hypothesize that the interaction between tissue and laser radiation alters the mechanics of cell microenvironment, thus acting on the cells as a mechanical stress.

INTRODUCTION

Phototherapy, that is the use of light for the treatment and prevention of diseases, has been widely used from ancient times all over the world. The use of the laser, until relatively recent times the source of light was the sun.

The last century saw a rapid evolution in light sources, from incandescent arc lamps to lasers, which are the most advanced kind of light source.

The great advantage of the laser, in comparison with other sources, is the very high intensity and monochromaticity of the emitted radiation and also the

possibility to be effectively focused and coupled to optical fibers.

Lasers have been widely applied in many different fields of medicine, proving their effectiveness in the treatment of a wide range of diseases [1, 2].

In spite of the great amount of literature, the molecular and cellular mechanisms at the basis of the systemic effects induced by laser radiation are mostly unknown. The studies on this subject are very difficult because of the numerous effects and the variety of biological responses. The kind of laser used, the operative conditions, the biological targets (different areas of the body, different tissues, different cell populations, etc. ...) However, they are very important because the increase in knowledge can lead to a higher therapeutic efficacy by improvement of laser sources and treatment protocols.

Depending on interaction time and effective power density, three types of interactions between laser radiation and tissues can be distinguished: photochemical, photothermal and photomechanical [3]. The effects induced by low power lasers, the kind to be applied in physiotherapy, are mostly due to photochemical processes. These occur when endogenous or exogenous chromophores situated in the tissue absorb radiation of suitable wavelength.

A chromophore molecule which absorbs a photon is converted in an excited state and may subsequently participate in a chemical reaction that leads to the final biological effect [4].

High power lasers have been used at first for tissue ablation and surgery, because they are able to produce important photochemical and photomechanical effects (direct waves) [5]. Their application in fields different from surgery, such as physiotherapy, is quite recent and it has been possible thanks to the development of laser systems with emission modulations which allow the control of photothermal and photomechanical processes, so as to obtain therapeutic effects without tissue damage.

In particular, pulsed Nd:YAG laser has proved its versatility and efficacy in the

"Effects of pulsed Nd: YAG laser at molecular and cellular level. A study on the basis of Hilterapia®."

MONICI M., CIALDAI F., FUSI F., ROMANO G., PRATESI R.

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In conclusion, our results demonstrate that the effects of Nd:YAG pulses on culture cells are very similar to those induced by mechanical stress, thus supporting our

III. PBM: Is a temperature control system necessary?

Photobiomodulation is a **non-thermal** or **moderately thermal** process. It is essential to monitor the temperature of biological tissues during laser therapy and modulate the laser therapy according to the thermal response of biological tissues (**Vobulate Thermal Control**).

IV. PBM: The correct dose



PHOTOMEDICINE AND LASER
SURGERY

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[Photomed Laser Surg.](#) 2013 May; 31(5): 189–191.

doi: [10.1089/pho.2013.3510](https://doi.org/10.1089/pho.2013.3510)

PMCID: PMC3643261

PMID: [23600376](https://pubmed.ncbi.nlm.nih.gov/23600376/)

Is It Time to Consider Photobiomodulation As a Drug Equivalent?

[Tiina Karu](#), PhD, DrSc^{MD}

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THE QUESTION OF WHETHER photobiomodulation should be used as a drug equivalent arose in my mind after listening to presentations at the recent conference of the World Association for Laser Therapy (WALT)-2012 (Gold Coast City, Australia), and later at home when searching MEDLINE® for the years 2009–2012. Photobiomodulation (earlier terms: low level laser therapy, LLLT, laser biostimulation) has been used in clinical practice for >40 years by now, and its action mechanisms on cellular and molecular levels have been studied for >30 years. Enthusiastic medical specialists successfully used photobiomodulation in treating healing-resistant wounds and ulcers (e.g., chronic diabetic ulcers), in pain management, and in spinal cord and nervous system injuries when other methods had had limited success.¹ However, photobiomodulation is still not a part of mainstream medicine. The goal of the present Editorial is to highlight some important recent developments in clinical applications and in studies of cellular and molecular mechanisms behind the clinical findings.

Is it Time to Consider Photobiomodulation As a Drug Equivalent?

Photomedicine and Laser Surgery (2013)

T.Karu

IV. PBM: The correct dose

The **dose** is the determined quantity of a substance, in relation to an effect to be achieved directly or through the presence of other substances in reciprocal quantitative relationship.

In the rehabilitation field, we mean **the amount of energy needed to induce cellular metabolic activity.**

The energy dose can be insufficient, effective or toxic.