

IN CELEBRATION OF THE 30-YEAR  
ANNIVERSARY OF THE WORLD ASSOCIATION  
FOR PHOTOBIO-MODULATION THERAPY



# PBM2024 LONDON

AUGUST 23rd-25th, 2024

ABSTRACTS



# CONFERENCE ABSTRACTS



**PBM2024**  
**LONDON**

AUGUST 23rd-25th, 2024

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# PBM2024 ABSTRACTS

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# FRIDAY AUGUST 23<sup>rd</sup>

## OPENING CEREMONY

### A WELCOME MESSAGE FROM PBM2024 CHAIR

PROF. REEM HANNA

CHAIR-PBM2024

#### Dear colleagues and friends

It is a great pleasure and honour for me to welcome you all to PBM2024 Conference in my beautiful city, London. It is the 14th International Congress of the World Association for Photobiomodulation Therapy (WALT) and it also marks its 30th Anniversary. We are extremely proud of the fact that more than 28 countries will be represented this year.

The Annual Meeting is the foremost international multidisciplinary and interdisciplinary conference, encompassing three days of cutting-edge research, engaging presentations and many networking activities. The scientific programme is comprehensive covering the entire photobiomodulation (PBM) spectrum. This promises to be a particularly interesting congress all round, with a range of plenary lectures, specialist presentations and contributing papers, as well as, educational courses and regular hands-on workshops. Also, a great opportunity for young investigators to share their researches, as well as, for SHARK-TANK Competition to present their PBM innovations.

Rapid advances in photobiomodulation therapy have led to numerous innovations. At PBM2024 Meeting, you would discover what's new and what's on the horizon in the diverse and exciting field of photobiomodulation. Hence, the event will feature a stellar line-up of speakers covering a breath of photobiomodulation contemporaneous research and clinical applications. The featured leading authorities in the field will address a plethora of photobiomodulation applications including: advances across all clinical categories, such as; bone and musculoskeletal; pain management and addiction; sports and rehabilitation; wound care; dermatology; dentistry and oral care, supportive care for cancer, neurorehabilitation, stem cells and regenerative medicine, photobiomodulation versus antiviral and antimicrobial applications; aesthetic medicine, acupuncture, metabolic and autoimmune disorders, and reproductive health. Also, advanced research in photobiomodulation mechanisms, treatment guidelines and position papers on the use of photobiomodulation technology will be presented.

Additionally, the "Great Debate" Plenary Session focusing on the "Pathways for PBM Mainstreams in Healthcare" will be led by an expert photobiomodulation panel. This would be a unique opportunity for clinicians, scientists, healthcare regulators, and industry to have a productive interaction and a fruitful discussion to move photobiomodulation mainstreams forward across all disciplines. Let us come together to shape the future of Photobiomodulation. PBM2024 conference is a unique opportunity to enrich your interest and expertise in field of Photobiomodulation therapy. Also, to use this conference opportunity to meet old friends and make new contacts and enjoy London sightseeing. Additionally, in keeping with the growing recognition in the field of photobiomodulation, there is a need to honour and acknowledge the leading contributors in establishing the WALT. Join us to celebrate WALT 30th Anniversary at extravagant Gala Dinner Party at Plaza Westminster Hotel on Saturday night (24th August).

No conference can be a success without the support of industry and I would like to express my sincere gratitude to all our sponsors and exhibitors for supporting PBM2024. Finally, thank you all for your valuable contributions and participations towards successful PBM2024 and wish you a productive and enjoyable conference.

With best regards,

Prof. Reem Hanna

BDS, PhD, MSc, PG DipSed, PG DipHE, PG Cert.AP, FHEA, FIADFE

Chair-PBM2024



# **A BREIF HISTORY OF THE FIRST DISCOVERY OF PHOTOBIO-MODULATION BY PROF. ENDRE MESTER - THE FATHER OF PHOTOBIO-MODULATION**

PROF. ADAM MESTER

Head of National Laser Therapy Centre, Peterfy Sandor Teaching Hospital, Budapest

## **Abstract**

Endre Mester, M.D. (1903-1984) discovered and published the Biostimulative (Photobiomodulatory) effects of low-power laser in 1967. Initially he was interested to study possible carcinogenic effects of the newly discovered laser, and therefore he applied repeated low power ruby laser irradiation on shaved mouse skin. He documented no carcinogenic effect of the laser but surprisingly, the hair started to grow faster on the irradiated skin area compared to the non-irradiated skin. When more laser irradiation was given to the skin the hair did not grow any more as opposed to the non-irradiated area where the normal hair growth has been observed. This was the first experiment documenting the Arndt-Schultz biophysical law for the laser, e.g., stimulation by the low-power and inhibition of higher power laser radiation. Since Mester was a surgeon, he was keen to help patients with non-healing or difficult healing wounds. He found that low power laser stimulated cellular repair mechanisms and wound healing of the injured skin on the back of the mouse. This experiment has been followed up in a wide variety of experimental conditions, animal models followed up with human studies resulting proper dose distribution and calculations on surface and in deeper tissues related to different wavelengths characteristics. The second surprising observation was anti-inflammatory and analgesic effects of photobiomodulation in arthritis-autoimmune diseases. Immunological experiments supported the bioregulatory effects in inflammatory mechanisms. Several experimental results and clinical evidences showed the balance of stimulative and inhibitory effects. Prof. Mester investigated separated effects of only monochromatic, and of only polarized light sources. Summared conclusion of researches based on these evidences and of other researchers concluded the expression of photobiomodulation.

# PHOTOBIMODULATION LEADERSHIP - GROUNDBREAKING RESEARCH

## THIRTY YEARS OF EXPERIENCE IN PHOTOBIMODULATION GROUNDBREAKING RESEARCH IN MITIGATING ADVERSE-EFFECTS OF ONCOLOGY THERAPIES- NEW PARADIGM OF PREVENTIVE AND THERAPEUTIC APPROACHES

RENÉ JEAN BENSADOUN

CENTRE DE HAUTE ENERGIE (CHE), NICE, FRANCE

### Abstract

The side-effects of oncology therapies are very debilitating to patients' quality of life and have a great impact on oncology course of treatments. My rigor research involvement in developing low energy lasers/LEDs and understanding dosimetry parameters has led to further appreciation of photobiomodulation (PBM) mechanistic effects, serving many clinical applications. Hence, in the last 30 years of my involvement in groundbreaking research utilising PBM, as a preventive or therapeutic approach in mitigating adverse-effects induced by anticancer treatments has led to extraordinary revolution and development of this application to be a standard supportive care for Cancer. Moreover, my extensive research work with eminent researchers in the field has extended further during my WALT presidency in the period between 2021-2024, resulted in publishing the "WALT POSITION PAPER 2022" entitled "Photobiomodulation Therapy in Management of Cancer Therapy-Induced Side Effects". During the presentation, I will pinpoint those extraordinary development and new paradigm of PBM in this application.

Let's wish a deserved success for this Anniversary Meeting in London, as well as new PBM innovative projects in the future to benefit our patients!



# THE EVOLUTION OF PHOTOBIO-MODULATION IN TREATING DIABETIC COMPLICATIONS

NICOLETTE HOURELD

LASER RESEARCH CENTRE FACULTY OF HEALTH SCIENCES, UNIVERSITY OF JOHANNESBURG,,  
JOHANNESBURG, SOUTH AFRICA

## Abstract

One of the major challenges in managing diabetes is the development of various complications that can significantly impact a patient's quality of life. Among these complications are diabetic retinopathy, neuropathy, nephropathy, and chronic ulcers, each presenting unique challenges for treatment and management. Over the years, photobiomodulation (PBM) has emerged as a promising therapeutic approach for addressing these complications, leveraging the application of light to modulate cellular functions and stimulate biological processes, and promote healing. Leadership in PBM research is characterized by pioneering investigations into the mechanisms underlying light-cell interactions, pushing boundaries in clinical applications, and driving technological innovations, all of which are instrumental in advancing PBMs integration into mainstream healthcare protocols. This talk will delve into the forefront of PBM research in treating diabetic complications, highlighting key studies and leadership trends that are shaping its future trajectory. Each one of us have a pivotal role to play in steering the course of PBM research towards greater clinical efficacy and widespread acceptance. By championing innovation, collaboration, and evidence-driven practices, PBM leaders are reshaping healthcare paradigms and unlocking new frontiers in therapeutic light-based interventions.

# **CURRENT STATE OF CLINICAL TRANSLATION OF PHOTOBIMODULATION THERAPY**

PRAVEEN ARANY

ORAL BIOLOGY, SURGERY, AND BIOMEDICAL ENGINEERING, BUFFALO UNIVERISTY, BUFFALO, USA

## **Abstract**

Significant progress has been made in the past few decades in understanding and utilizing Photobiomodulation (PBM) treatments for human health and wellness. Several tangible recent milestones include the recognition of PBM as a discrete form of light therapy by the United States Food and Drug Administration and the American Dental Association. The increasing clinical evidence has led to broader adoption of this therapy and is poised to make a major impact on supportive cancer care, rehabilitation and performance, and wound healing among others. There is several exciting new advances in overall wellness and aging that strongly support the key role of light in health, supporting newer concepts of light hygiene, light as a health supplement, and a drug (photoceutical).



# OPENING CEREMONY: FORTY YEARS OF PROGRESS IN PHOTOBIO-MODULATION

CHUKUKA ENWEMEKA

PHOTOMEDICINE RESEARCH LABORATORY, COLLEGE OF HEALTH SCIENCES, SAN DIEGO STATE UNIVERSITY, SAN DIEGO, USA

## Abstract

**Objective:** This paper summarizes forty years of advancements in photobiomodulation in the areas of pain relief, tissue repair, and photo-inactivation of bacteria and viruses. It pinpoints needed areas of research works and offers suggestions for the future, based on personal experience. **Methods:** We collated, analyzed, and synthesized our published reports and those of others since the mid-1980s, in the areas of pain relief, tissue repair, and photo-eradication of bacteria and viruses.

**Results and Discussion:** The historical review shows significant progress in our understanding of the biomedical effects of various wavelengths of light over the past four decades. It shows that some of the earliest studies were directed at improving our understanding of dose, terminology and other parameters, and the potential effects of red and infrared light in humans and animal models of pain and tissue repair. Latter studies progressively uncovered the mechanisms underlying the effects of various wavelengths in the red and near infrared ranges, and the blue and violet spectra. Further, within the last twenty years, there has been an astounding expansion of the field to include skincare, cancer therapy, treatment of various neurological disorders and injuries—including soft tissue injuries, brain injury, and spinal cord injury, and photo-inactivation of microorganisms. These developments, the current state of photobiomodulation, the positive roles played by WALT, and the future direction of the field will be discussed during the presentation.

## **OPENING CEREMONY TALK: GROUNDBREAKING RESEARCH APPLICATIONS OF PBMT FOR BRAIN DISORDERS**

MICHAEL HAMBLIN

LASER RESEARCH CENTRE HEALTH SCIENCES, UNIVERSITY OF JOHANNESBURG, JOHANNESBURG, SOUTH AFRICA

### **Abstract**

An increasing body of evidence supports the use of PBMT for treating neurodegenerative diseases (Alzheimer's and Parkinson's). PBMT has also shown good results in chronic and acute traumatic brain injury, and in various psychiatric disorders such as depression and anxiety. Here some new ground breaking applications for brain disorders will be discussed. Neurodevelopmental disorders including autism spectrum disorder, attention deficit hyperactivity disorder and Down syndrome have all been shown to benefit from PBMT. There is evidence that opioid use disorder and insomnia can respond to PBMT. More speculative applications including epilepsy and chronic stroke rehabilitation will also be discussed.

## **OPENING CEREMONY TALK: RESEARCH THAT ESTABLISHED THE USE OF PBM TO MODIFY FUNCTIONS OF THE NERVOUS SYSTEM**

JUANITA ANDRES

ANATOMY, PHYSIOLOGY AND GENETICS, SCHOOL OF MEDICINE, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES, BETHESDA, MD, USA

### **Abstract**

A number of research laboratories, including my own, have been fundamental in establishing the therapeutic effects of PBM on various aspects of injury and disease of the peripheral and central nervous systems. Research has focused on axonal regrowth, pain modification, recovery from stroke, traumatic brain injury and diseases of brain. In this presentation, I will focus on the seminal research on nerve regeneration in the central and peripheral nervous systems and pain modulation. Besides describing the major milestones in these areas, I will highlight data that also had a significant impact on the PBM treatment of other tissues and systems. These data established principles governing wavelength selection based on the target tissue location and dosing parameters as well as clarifying cellular responses.

# PHOTOBIO-MODULATION - SHARING RESEARCH EXPERIENCES

## PHOTOBIO-MODULATION IN OPHTHALMOLOGY: DEVELOPMENT OF THE MULTI-WAVELENGTH VALEDA LIGHT DELIVERY SYSTEM FOR TREATMENT OF DEGENERATIVE OCULAR DISEASE

CLARK TEDFORD

LUMITHERA INC, POULSBO, USA

### Abstract

**Learning Objectives:** To review (1) the landscape for photobiomodulation (PBM) in ophthalmology, (2) the development of a multiwavelength PBM approach for ocular disease and (3) to evaluate the safety and efficacy of multiwavelength photobiomodulation (PBM) in intermediate dry age-related macular degeneration (AMD) (LIGHTSITE Trials).

**Introduction:** Photobiomodulation (PBM) has been investigated in over 30 published reports in the ophthalmology field with positive findings in clinical, anatomical and quality of life (QoL) outcomes. Degenerative, inflammatory and other mechanistic underpinnings that underlie the development of the variety of ocular disease states may benefit from the non-invasive and targeted approach PBM therapy offers. Multiwavelength approaches offer an appealing strategy to target underlying cellular contributors of disease. The Valeda® Light Delivery System (LumiThera Inc., Poulsbo, WA, USA) was developed to address degenerative eye disease with a focus on dry age-related macular degeneration (AMD). The LIGHTSITE series of trials evaluated Valeda for dry AMD. History and current status will be discussed in detail.

**Methods:** The development of Valeda investigated three wavelengths (590, 660 and 850 nm) and underwent beam imaging and tissue penetration assessment to support development. The recent LIGHTSITE III (NCT04065490) study assessed the safety and efficacy of PBM in dry AMD. Subjects were treated with six series of PBM or Sham treatment delivered every 4 months over a 24-month period.

**Results:** 100 subjects (148 eyes) with dry AMD were randomized. LIGHTSITE III met the predetermined primary efficacy BCVA endpoint at 13 Months with a statistically significant difference between PBM and Sham ( $p = 0.02$ ) and a gain of 5.4 letters following PBM treatment. A total of 55% of PBM-treated eyes showed  $\geq 5$  letter gain (mean  $9.7 \pm 3.7$ ), 26.4% showed  $\geq 10$  letter gain (mean  $12.8 \pm 2.7$ ) and 5.5% showed  $\geq 15$  letter gain. A favorable safety profile was observed.

**Conclusions:** LIGHTSITE III, consistent with LIGHTSITE 1 and II, provides randomized controlled trial data in dry AMD showing improved clinical and anatomical outcomes following PBM treatment. Multiwavelength PBM may offer a new treatment strategy with a unique mechanism and modality for patients with dry AMD.

# PHOTOBIMODULATION THERAPY; PROVIDING HOPE IN THE MANAGEMENT OF RADIATION-INDUCED FIBROSIS

EMMA HALLAM

NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST, NOTTINGHAM, UNITED KINGDOM

## Abstract

### Learning outcomes:

1. What radiation induced fibrosis is and its physical and psychological impact
2. The importance of early identification and management
3. The use of photobiomodulation therapy for consequences of radiotherapy treatment

As ever more cancers are being cured, there is an ever-increasing need to provide support for patients living with and beyond their cancer diagnosis.

Radiation induced fibrosis a progressive, sclerotic disorder is an unintended consequence from radiotherapy treatment.

Despite advances in planning and treatment delivery, this debilitating consequence leads to a reduced quality of life with poor physical and psychological function. The Nottingham Late Effects Clinic is such a service that offers collaborative multi-disciplinary support throughout the survivorship trajectory to manage this long term condition using novel treatments such as photobiomodulation therapy (PBM).

**Methods:** 120 patients were assessed and offered holistic supportive care to manage RIF along with the use of bi weekly PBM therapy for a schedule of six weeks. Patients were offered further PBM using a combination of protocols depending on need and outcomes. Patients who had received radiotherapy for the following cancers head and neck, breast, mycosis fungoides and pelvic cancers were included. Methodologies included data collection by measuring change in range of motion, mouth opening as a result of radiation induced trismus, patient reported pain and distress scores and patient quality of life testimonials.

**Results:** Outcomes observed included changes in appearance, softening of fibrosis, reduction in lymphoedema, improved range of movement, reduction in pain and decreased psychological distress. There was a significant improvement in quality of life with many patients wanting to continue with long-term PBM therapy.

A collaborative multi-disciplinary approach is essential for offering excellent patient centred personalised self-supported care in the complex symptom management of the consequences of head and neck cancer treatment. This study highlights how PBM is the only therapy that has been shown to have such a positive impact on this cohort of patients and supports the use of PBM as a significant intervention for the effective management of RIF; however further research in assessing the quantifiable reduction is needed.

# THE EVIDENCE FOR PBM VS PHARMACOTHERAPIES

PROF. JAN BJORDAL

UNIVERSITY OF BERGEN, BERGEN, NORWAY

## Abstract

Twenty-five years ago, anti-inflammatory drugs dominated the management of musculoskeletal pain. However, the clinical effect sizes for NSAIDs were small, and their side effects began to raise concerns, creating an urgent need for more effective and safer anti-inflammatory treatments.

At the University of Bergen, Norway, we evaluated several electrophysical agents, conducted numerous clinical trials, performed many systematic reviews with meta-analyses, and identified Photobiomodulation Therapy (PBMT) as the best anti-inflammatory option.

Pharmaceutical trials use safe and well-established optimal doses, enabling precise modulation of biological reactions. In contrast, clinical PBMT lacked sufficient understanding of the biological mechanisms and appropriate dosing to reduce inflammation reliably and consistently. Consequently, only 55% of musculoskeletal clinical trials showed overall positive results with PBMT, according to our published reviews.

Through our systematic reviews and meta-analyses, we found that a small subset of trials demonstrated clinically significant effects. This led to the hypothesis that subgrouping by dose could reveal a possible dose-response pattern. The research group compared the doses from animal studies and proposed optimal dosage intervals for clinical PBMT, which have since been validated for osteoarthritis and tendinopathies.

Overall, our nine systematic reviews of randomised clinical trials on musculoskeletal pain found dozens of moderate to high-quality MSK studies involving thousands of patients, which, when treated within the effective dose range extrapolated from animal studies, consistently showed that PBMT effectively reduced MSK pain, reduced disability, with no adverse events reported and produced longer-lasting effects than widely recommended drugs.

It is our view that whilst PBMT is less convenient than taking NSAIDs, it is a safer and more effective option for treating musculoskeletal pain.

# SATURDAY, AUGUST 24<sup>th</sup>

## NEUROREHABILITATION

### HISTORY AND MECHANISMS OF PHOTOBIO-MODULATION, WITH A FOCUS ON TREATMENT OF BRAIN DISORDERS

MICHAEL HAMBLIN

LASER RESEARCH CENTRE, UNIVERSITY OF JOHANNESBURG, JOHANNESBURG, SOUTH AFRICA

#### Abstract

##### Learning objectives:

1. Understanding the history and mechanisms of PBMT
2. Appreciating how PBMT can be delivered to the head and other body sites
3. Surveying the application of PBMT in different brain disorders, traumatic, neurodegenerative, psychiatric, and neurodevelopmental.

**Abstract:** The history of the use of light to treat diseases spans >100 years. Electric light therapy, heliotherapy, and low-level laser therapy led to what we now call photobiomodulation therapy (PBMT). PBMT has traditionally been used for wound healing, pain and inflammation. However, in recent years there has been a growing interest in applying PBMT for brain disorders. PBM employs red or near-infrared (NIR) light (600-1100nm) from lasers or light emitting diodes to stimulate healing, protect tissue from dying, increase mitochondrial function, improve blood flow, tissue oxygenation, and stimulate stem cells. Progress has been made in identifying cellular chromophores and photoreceptors, including the mitochondrial respiratory chain and TRP ion channels. Results of small animal model studies as well as human studies show that PBM can also act to reduce swelling, increase antioxidants, decrease inflammation, protect against apoptosis, and modulate the microglial activation state. PBMT delivered to the head is beneficial in cases of both acute and chronic traumatic brain injury. Moreover, PBM has now been shown to be effective against neurodegenerative diseases (Alzheimer's and Parkinson's) and psychiatric disorders (depression, anxiety and opioid addiction). Neurodevelopmental disorders (autism and ADHD) and cognitive enhancement in normal individuals are other applications.



# PBM-T 1070 FOR DIABETIC HYPERGLYCAEMIC NEURO- AND RETINOPATHIES: VALIDATION FOR CLINICAL USE

PAUL CHAZOT

DURHAM UNIVERSITY, DURHAM, UNITED KINGDOM

## Abstract

Photobiomodulation therapy (PBM-T 1070) is an emerging therapeutic strategy for several neurological disorders, based on our work over the last 20 years. It utilises an infrared wavelength to target chromophores in the mitochondrial electron transport chain and water channels in the lymphatic system to elicit biological processes and exert neuroprotective, neuroplastic and neuroreparative effects (the “3Ns”). There is a growing linkage between diabetes and major neurodegenerative diseases. Diabetic hyperglycaemic neuro- and retinopathies are two common neurological disorders that display common factors, such as mitochondrial dysfunction, neuroinflammation, and disrupted neurogenesis and synaptic function and plasticity. Recently, PBMT has been implicated in modulating glucose levels. PBMT promoted glucose transporter GLUT4 translocation and glycogen synthase (GS) activation, accelerating glucose uptake and glycogen synthesis in skeletal muscle.

Recently we have conducted a study to investigate whether PBMT1070 is effective in improving the neurological dysfunction of dopaminergic neurons under hyperglycaemic conditions. Human peripheral SH-SY5Y neurons and retinal muller Mio-1 Muller glial cells were cultured with media containing 4500mg/L. Cells were exposed to PBM 1070 nm for five 6-minute intervals spread over two hours. Cell viability and pro-inflammatory cytokines released from glia, and neuronal synaptic and neurotrophic markers, calcium mobilisation and dopamine release from neurons, were measured to examine PBM1070 effects. Glucose uptake and levels were also measured under these conditions. PBM1070 improved mitochondrial function (MTT), reduced neuroinflammation (TNF $\alpha$ ), and accentuated neurogenesis (BDNF) and synaptogenesis (PSD95), increase intracellular calcium and dopamine release, in glia and neurons, respectively.

Data collected from this *in vitro* pre-clinical investigation suggests that PBM-T1070 may be an effective treatment for hyperglycaemia, and diabetic neuro- and retinopathies, and clinical studies should consider PBM-T1070 to treat these refractory chronic conditions.

# BRAIN PHOTOBIMODULATION FOR MAJOR DEPRESSIVE DISORDER: GUIDED BY NEUROPHYSIOLOGY

PAOLO CASSANO

HARVARD MEDICAL SCHOOL, BOSTON, USA

## Abstract

### Learning Objectives:

1. Understand the protocols of t-PBM used for the treatment of MDD and its clinical evidence, efficacy and safety.
2. Understand the neurobiology/neurophysiology of t-PBM when applied to patients with MDD
3. Grasp the complexity and the potential of t-PBM when applied to treat mood and anxiety disorders.

**Abstract:** Major depressive disorder (MDD) is one of the greatest factors undermining global health and is considered a financial burden for health systems. Depression is the leading cause of suicide and is associated with several medical conditions, such as diabetes, obesity, stroke, Parkinson's disease, multiple sclerosis, Alzheimer's disease, and sudden cardiac death. A plethora of factors have been implicated in the etiology of MDD, including neuroinflammation, the overdrive of the hypothalamic-pituitary-adrenal axis (HPA), the dysfunction of the neuroanatomic circuits, the imbalance of neurotransmitters, and overall abnormal neuronal activity. Moreover, MDD is heritable with a genetic predisposition accounting for about 35% of the risk and it is highly influenced by adverse life experiences. The complexity and heterogeneity of MDD might explain the inconsistent response to many existing antidepressant strategies, thus representing a challenge for patients and their families. Transcranial photobiomodulation (t-PBM) therapy utilizes near-infrared (NIR) light, delivered transcranially, to modulate the brain cortex. Preliminary evidence suggests the applicability of t-PBM for the treatment of MDD. The aim of this presentation is to revisit the antidepressant effects of t-PBM, with a special emphasis on novel findings related to neurophysiology and dose-response.

# IMPLANTABLE AND TRANSCUTANEOUS PHOTOBIMODULATION PROMOTE NEUROREGENERATION AND RECOVERY OF LOST FUNCTION AFTER SPINAL CORD INJURY

ANDREW STEVENS

NEUROSCIENCE AND OPHTHALMOLOGY, INSTITUTE OF INFLAMMATION AND AGEING, UNIVERSITY OF BIRMINGHAM, BIRMINGHAM, UNITED KINGDOM. NIHR SURGICAL RECONSTRUCTION AND MICROBIOLOGY RESEARCH CENTRE, UNIVERSITY HOSPITALS BIRMINGHAM, BIRMINGHAM, UNITED KINGDOM. PHOTOTHERAPY RESEARCH GROUP, SCHOOL OF DENTISTRY, UNIVERSITY OF BIRMINGHAM, BIRMINGHAM, UNITED KINGDOM.

## Abstract

### Three learning objectives:

1. Invasive and non-invasively applied photobiomodulation (PBM) increase axonal regeneration-associated proteins after spinal cord injury (SCI)
2. 660nm photobiomodulation (1.44J/cm<sup>2</sup>) promotes functional recovery after spinal cord injury
3. 660nm photobiomodulation (1.44J/cm<sup>2</sup>) reduces lesion size after spinal cord injury

**Brief introduction:** SCI is a cause of profound and irreversible damage, with no effective therapy which has been demonstrated to promote functional recovery. PBM may provide a viable therapeutic approach using red light to promote recovery after SCI, by mitigating neuroinflammation, preventing neuronal apoptosis and promoting neuronal morphogenesis. This study aimed to optimize PBM dose regimens and develop and validate the efficacy of an invasive PBM delivery paradigm for SCI.

**Methods:** Dose optimization studies were performed in vitro using a serum withdrawal model of injury in primary cell cultures of primary adult rat dorsal root ganglion neurons (DRGN) (applied using a BioThor device, 660nm, 4-131mW/cm<sup>2</sup>, 30-360s). Implantable and transcutaneous PBM delivery protocols were then developed using cadaveric modelling. The efficacy of PBM in promoting recovery after SCI in vivo was studied in a dorsal column crush injury model of SCI in adult rats, delivered transcutaneously (D4σ=0.4cm) or using an implanted fibre (D4σ=0.1cm), both at 24.42mW/cm<sup>2</sup> for 1min per day (1.44J/cm<sup>2</sup>).

**Results:** Optimal neuroprotection in vitro was achieved between 4-22mW/cm<sup>2</sup>. 11mW/cm<sup>2</sup> for 1min per day (0.66J/cm<sup>2</sup>) increased cell viability by 45% over five days (p<0.0001), and increased neurite outgrowth by 25% (p < 0.01). Delivery methods for PBM were developed and validated for both invasive (iPBM) and non-invasive (transcutaneous) (tcPBM) applications. iPBM and tcPBM (24 mW/cm<sup>2</sup> at spinal cord, 1 min per day (1.44J/cm<sup>2</sup>) up to 7 days) increased activation of regeneration associated protein at 3 days after SCI, increasing GAP43<sup>+</sup> axons from 18.0% (control) to 41.4%±10.5 (iPBM) and 45.8%±3.4 (tcPBM) (p<0.05). This corresponded to significant improvements at six weeks post-injury in locomotor and sensory function recovery (p<0.01), axonal regeneration (p<0.01) and reduced lesion size (p<0.01).

**Conclusions:** Our results demonstrated that PBM achieved a significant therapeutic benefit after SCI, either using iPBM or tcPBM application, and can potentially be developed for clinical use in SCI patients.

# PHOTOBIMODULATION TREATMENT OF PARKINSON'S DISEASE WITHIN AN INTERDISCIPLINARY INTEGRATIVE APPROACH: THE WAY FORWARD FOR MEANINGFUL IMPROVEMENT?

ANN LIEBERT

UNIVERSITY OF SYDNEY, SYDNEY, AUSTRALIA. SYDNEY ADVENTIST HOSPITAL, SYDNEY, AUSTRALIA.  
UNIVERSITY OF WESTERN SYDNEY, SYDNEY, AUSTRALIA.

## Abstract

### Learning Objectives

1. Understand the role of PBM in treatment of Parkinson's disease symptoms
2. Appreciate the importance of a multi-disciplinary approach to achieve the best results in the treatment of Parkinson's disease.
3. Appreciate the heterogeneity of symptoms of Parkinson's disease and the individual variation of the response to interdisciplinary therapy

**Background:** Parkinson's disease is a complex neurodegenerative disease that is highly heterogeneous in symptomology and progression. While there is no medication treatment that can slow the progression of the disease, a number of interventions such as exercise and nutrition have been shown to slow the decline in quality of life of some patients with Parkinson's disease. Photobiomodulation has recently been shown to be a promising treatment for symptoms of Parkinson's disease. Here we present a case series of patients from three different countries (Canada, Germany, Australia) at various stages of their Parkinson's disease journey who have received a multi-disciplinary approach to the treatment of their Parkinson's disease symptoms

**Methods:** All participants were treated with abdominal photobiomodulation with a class 1 laser device (2x30mW), 2 minutes per point (7.6mW), on 9 points on the abdomen and one point on the neck, with or without transcranial LED treatment using one of a variety of light helmet devices. Participants were overseen by neurologists with carefully monitoring of medication. Advice was given for dietary requirements and participants underwent high amplitude and neuroactive exercise in a social setting. Participants were assessed for outcomes by their own neurologist and physiotherapists.

**Results:** All participants showed improvement as assessed by their own (independent from treatment) neurologists, although these improvements were heterogeneous and individual to the participant. Improvements included improvements in gait, walking speed, balance, cognition, fine motor control and cognition.

**Conclusion:** An integrative approach utilising medication monitoring to increase or decrease as required with symptom changes associated with photobiomodulation and exercise appears to be best practice. The approach can result in optimal precision medicine for an increasingly prevalent disease, to slow the progression of symptoms in Parkinson's disease.

# CASE STUDIES OF A FIVE-YEAR FOLLOW-UP OF THE PHOTOBIMODULATION TREATMENT OF PARKINSON'S DISEASE SYMPTOMS

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## Abstract

### Learning Objectives:

1. Understand the role of PBM in treatment of Parkinson's disease symptoms
2. Appreciate the effects of long-term application of PBM therapy to the symptoms of Parkinson's disease
3. Appreciate the heterogeneity of symptoms of Parkinson's disease and the individual variation of the response to PBM therapy

**Background:** The progression of Parkinson's disease results in an inevitable worsening of clinical signs and symptoms. We have shown in our studies that treatment of Parkinson's disease patients with abdominal, neck and transcranial photobiomodulation can improve some symptoms for most patients and that this symptom improvement can be maintained for up to three years. Here we report on a follow-up of some participants from our original proof-of-concept clinical trial who have continued with the PBM treatment protocol for up to 5 years.

**Methods:** Participants from a previously reported trial continued to treat themselves at home for up to five years. The treatment consisted of laser (Class 1, 30mW) treatment to 9 points on the abdomen and to the C1/C2 point on the neck for 2 minutes (7.2J/point) 3 times per week. The participants also may or may not have used one of a variety of transcranial LED helmets, up to 6 or 7 days per week. Participants were assessed using MDS-UPDRS by a neurologist as well using outcome measures of cognition, balance, mobility, and fine motor control. Results were compared to the same tests measured before PBM treatment began 5 years previously.

**Results:** More than half of the participants that began the trial have continued with the treatment protocol. Participants that continued were compliant with treatment and no negative side effects were reported. There was individual variation as to the consistency of adherence to the treatment protocol over the 5-year period, as would be expected. There was a great deal of individual variation in response to the photobiomodulation treatment. There was a maintenance of the initial improvements in some participants for some of the clinical signs and symptoms of the disease.

**Conclusion:** Results of this study give a more complete indication of the long-term effects of photobiomodulation treatment for Parkinson's disease.

# STEM CELLS AND REGENERATIVE MEDICINE

## REVOLUTIONIZING REGENERATIVE MEDICINE: TRANSFORMING MESENCHYMAL STEM CELLS INTO OSTEOBLASTS THROUGH THREE-DIMENSIONAL CELL CULTURE

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### Abstract

Osteoporosis is the most common chronic metabolic bone disorder in humans resulting from a variety of reduced cellular functions in mesenchymal stem cells. Researchers have shown interest in adipose-derived stem cells (ADSCs) for cell-based tissue repair systems. However, within *in-vitro* approaches, ADSCs quickly enter replicative senescence, leading to hindered cell growth and loss of stem cell properties. Hydrogels have become promising biomaterials for tissue regeneration owing to their notable high permeability, and strong biocompatibility. While *in-vitro* research offers advantages such as a precise control over the environment, and cost-effectiveness, its' limitation lies in the inability to accurately mimic *in-vivo* conditions, reducing predictive behaviour in a clinical setting. Hydrogels address this limitation by serving as a biomechanical tool that mimics the natural extracellular matrix of *in-vivo* cells whilst in a controlled *in-vitro* setting. Notably, the differentiation of ADSCs into osteoblast cells, in addition to an increased cellular proliferation, has been successfully achieved through a combination of osteogenic differentiation inducers, hydrogel encapsulation, and PBM.

In this *in-vitro* study, osteogenic induction differentiation media incorporated dexamethasone,  $\beta$ -glycerophosphate disodium, and ascorbic acid differentiation inducers for immortalised ADSCs encapsulated within a fast-dextran hydrogel. Moreover, PBM was applied at a near-infrared (NIR) wavelength of 825 nm, a green (G) wavelength of 525 nm, and a novel combination of both wavelengths, utilising fluencies of 3 J/cm<sup>2</sup>, 5 J/cm<sup>2</sup>, and 7 J/cm<sup>2</sup> to stimulate the proliferation and differentiation effectiveness of immortalised ADSCs into early osteoblasts. Alkaline phosphatase, an early marker of cell differentiation into the osteogenic lineage, was assessed using spectrophotometry. The identification of calcium deposits within cultured cells was achieved through Alizarin red staining. Various biochemical assays, including an ATP proliferation assay, MTT viability assay, and LDH membrane permeability assay, were conducted. Real Time-PCR was employed to determine the genetic expression of transcription factors. This study's successful conclusion provides relevant scientific knowledge, a standardisation for osteogenic differentiation *in vitro* using 3D hydrogel matrices and PBM as well as bridge the gap between *in vitro* and *in vivo* investigation for the speedy implementation of clinical trials to improve osteo-degenerative disease treatment.

# UTILIZING PHOTOBIMODULATION TO ENHANCE THE NEURAL EMBRYOID BODY FORMATION OF IMMORTALIZED STEM CELLS FROM ADIPOSE TISSUE

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## Abstract

The study focused on elucidating the importance of embryoid bodies (EBs) in regenerative medicine and stem cell research, while also exploring the potential of photobiomodulation (PBM) as a non-invasive method for influencing cellular behaviors and directing stem cell differentiation. Additionally, it aimed to analyze how various PBM parameters, such as wavelength and dosage, impact transdifferentiation of adipose-derived stem cells (ADSCs) into neural embryoid bodies (NEBs), with potential implications for tissue regeneration and neural tissue engineering. Embryoid bodies (EBs) represent crucial multicellular aggregates derived from stem cells, mimicking early embryonic development stages and serving as a cornerstone in regenerative medicine. Photobiomodulation (PBM) has emerged as a non-invasive technique modulating cellular activities.

This study investigates the effects of PBM on the transdifferentiation of adipose-derived stem cells (ADSCs) into neural embryoid bodies (NEBs) using near-infrared (NIR) 825 nm, Green 525 nm (G), and a combination of NIR-G wavelengths at doses of 5 and 10 J/cm<sup>2</sup>. ADSCs were subjected to PBM using NIR (825 nm), G (525 nm), and combined NIR-G wavelengths at doses of 5 / 10 J/cm<sup>2</sup>. Cellular morphology, viability, proliferation, cytotoxicity, and gene expression were evaluated. Statistical analyses were conducted to assess the significance of the results. The study revealed significant effects of PBM on NEB health, particularly notable at the 10 J/cm<sup>2</sup> dosage, indicating substantial alterations in cellular processes. CD105 marker expression decreased over time at 5 J/cm<sup>2</sup>, suggesting differentiation towards mature neural phenotypes, while an initial increase in PAX 6 expression indicated early neural commitment. Downregulation of Nestin expression suggested neural identity establishment, notably at both 5 J/cm<sup>2</sup> and 10 J/cm<sup>2</sup>. Dynamic modulation of SOX 2 expression highlighted complex neural differentiation processes, evident at 5 J/cm<sup>2</sup>. Statistical analyses confirmed the significance of the observed results, with p-values indicating significant alterations in cellular processes and gene expression profiles. PBM demonstrates promise in modulating cellular processes, promoting tissue regeneration, and guiding stem cell differentiation into the neuronal lineage. The study provides insights into intricate mechanisms underlying PBM-induced transdifferentiation of ADSCs into NEBs, laying the groundwork for further exploration in regenerative medicine and neural tissue engineering.



# AN EVALUATION OF PHOTOBIO-MODULATION EFFECTS ON PERIODONTAL LIGAMENT MESSAGESANCHYMAL STEM CELLS TREATED WITH ZOLEDRONIC ACID

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## Abstract

### Three Learning objectives:

1. Exploring the effect of photobiomodulation on periodontal ligament mesenchymal stem cells
2. Effect of photobiomodulation on modulation of the effects of bisphosphonates
3. Comparing the efficacy of different photobiomodulation protocols.

**Introduction:** Use of bisphosphonates, is a challenge in oral and dental care. We aimed to investigate the effects of photobiomodulation (PBM) by diode lasers (red, infrared, and red-infrared combination) on periodontal ligament mesenchymal stem cells (PDLSCs) in the presence of zoledronic acid (ZA).

**Methods:** First, PDLSCs were treated with 5  $\mu$ M ZA for 48 h. Then, the cells received PBM in three consecutive day in groups 1 (660 nm, 5 J/cm<sup>2</sup>), 2 (808 nm, 3 J/cm<sup>2</sup>), and 3 (660 + 808 nm) either in normal or ZA-treated culture medium. No PBM was considered as control group. Cell viability and expression of RANKL and OPG were evaluated 24 h post- irradiation using MTT and RT- PCR tests, respectively.

**Results:** Cell viability decreased significantly in ZA-treated cells ( $p < 0.001$ ). Moreover, increase of OPG expression, and RANKL expression reduction was observed in ZA-treated groups. PBM with 808 and 660 + 808nm lasers were effective in significant increase of cell proliferation. Additionally, all PBM groups could significantly increase and decrease the RANKL and OPG, respectively, in the presence of ZA with highest effects in combination of 660 + 808 nm group (all  $p < 0.001$ ).

**Conclusions:** PBM may be effective on modulation of the effects of ZA by inducing PDLSC proliferation and increasing RANKL-to-OPG gene expression ratio.

# THE COMPARISON OF EFFECTS OF 6 DIFFERENT WAVELENGTHS OF IR AND VISIBLE PHOTOBIMODULATION THERAPY ON HUMAN MESENCHYMAL STEM CELLS

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## Abstract

**Learning Objectives:** Photobiomodulation has positive effects on stem cell therapy in case of diseases. Applying lasers with different wavelengths and the same energy density(ED) accelerates proliferation . Photobiomodulation can also affects the procedure of differentiation .

**Introduction:** The purpose of this study is to compare the effects of photobiomodulation on proliferation and differentiation of human MSCs by the Visible and Infrared laser with the same ED.

**Method:** One control and six laser irradiated groups were designated as Infrared(808 nm, 975 nm, 1064 nm), Red(660 nm), Green(522 nm) and Blue(485 nm). For the irradiation, these wavelengths with the same parameters such as ED which was 20 J/cm<sup>2</sup>, were used in continuous wave(CW) mode irradiation every 12 hours which was repeated daily for 2 days. MSCs were derived from human placenta. After 48 hours of irradiation, cell proliferation was then measured and also differentiation of MSCs to osteoblast, chondrocyte, endothelial and fibroblast cells was measured based on RT-PCR test. Biomarkers were CD44 and CD90 for mesenchymal cells, MMP1 for fibroblast cells, OC and ALP for bone, Col2 for cartilage and VEGF for vascular endothelial cells.

**Results:** The most desirable effect of PBM therapy with various wavelengths is on accelerating the differentiation rate. CD44 and CD90 were suppressed in all laser groups. MMP1 was increased in all laser groups and was highest in Red group which indicates the effect on differentiation processes. ALP expression was highest in 1064 nm laser group during immediate osseous differentiation and OC expression was highest in green laser group during secondary osseous differentiation. Green laser group also significantly effected the Col2 expression. The most significant effect on stimulating VEGF expression was found in 1064 laser group. The analysis of most of the irradiations revealed the effect on stimulating MSCs proliferation; specially after the first two irradiations.

**Conclusion:** Based on the condition of this study, Photobiomodulation therapy with different wavelengths effects stem cells which includes stimulating proliferation in most of the irradiations; moreover, differentiation rate of MSCs was significantly accelerated due to the expression of various biomarkers.

# EFFECTS OF LIGHT EMITTING DIODE AND LOW-LEVEL LASER IRRADIATION ON ANGIOGENESIS BY HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS

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## Abstract

### Learning Objectives:

1. Target molecules are sensitive to both Laser 810 and LED 850 nm and could increase angiogenesis activity
2. Laser and LED could have comparable result if calibrated properly
3. Laser may be slightly more effective than LED at peak activity

**Objectives:** This study aimed to assess the effects of 850 nm light-emitting diode (LED) and 810 nm low-level laser (LLL) on angiogenesis by human umbilical vein endothelial cells (HUVECs).

**Materials and Methods:** In this in vitro, experimental study, HUVECs were subjected to GaAlAs LLL irradiation with 810 nm wavelength for 5 and 10 seconds, and LED for 26, 52, 78, 104, 130, 156, and 182 seconds. The Abcam angiogenesis kit was used to assess tube formation and branching of endothelial cells. Photographs were also taken and assessed by the Wimasis analysis. Data were analyzed by the Mann-Whitney test and t-test ( $\alpha=0.05$ ).

Laser irradiation protocol: 810 nm wavelength, 250 mW power, 6 J/cm<sup>2</sup> energy density, and 750 mJ energy/power for 5 seconds in continuous mode. In the second laser group, laser was irradiated with the aforementioned parameters twice. The diameter of the laser hand-piece tip was 5 mm and power density is 1.2 W/cm<sup>2</sup> and Energy density (fluence)= 6 J/cm<sup>2</sup>

LED irradiation protocol: LED with 850 nm wavelength 74 mW/cm<sup>2</sup> power density, and 6 J/cm<sup>2</sup> energy density for 26, 52, **78**, 104, 156, and 182 seconds at 3 mm distance from beneath the plate. Energy Density (fluence) = 0.074 W/cm<sup>2</sup> × 78 ≈ 6 J/cm<sup>2</sup>

**Results:** Irradiation of 810 nm laser and 850 nm LED increased tube formation and branching of endothelial cells, compared with the control group. Irradiation of laser for 10 seconds had the highest efficacy, followed by LED irradiation for 156 seconds. LED irradiation for 26 seconds had the lowest effect. LED irradiation for 182 seconds decreased angiogenesis compared with 156 seconds probably because of exceeding the optimal threshold of the Arndt-Schultz curve.

**Conclusion:** According to the results, 800-850 nm wavelengths can cause significant angiogenesis changes and may be suitable for acceleration of orthodontic tooth movement (OTM). Also, the irradiation protocols of laser and LED were different.

# ZEBRAFISH TAIL REGENERATION: A NEW MODEL FOR ASSESSING PHOTOBIO-MODULATION

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## Abstract

Recently, attention of many scientists has been focused on the assessment of photobiomodulation (PBM) to increase wound healing in various cells and animal models. Photobiomodulation (PBM) can modulate cell signaling and metabolism in an injured milieu by generating reactive oxygen species while restoring energy levels by improving adenosine triphosphate (ATP) production. In cell culture experiments it was shown that PBM can contribute to dental pulp regeneration by stimulating endogenous cells to repopulate the root canals and also promote the formation tertiary dentin. In this sense, it is reasonable to presume that PBM could be used as a single strategy to promote regeneration of injured dental pulp tissue by stimulating the increase of stem cell populations. Such strategy should be validated in animal models. However, mammals animal models are expensive and ethical issues are critical [1-3] The zebrafish model have become increasingly important in scientific research as its characteristics allow for being the smart model of investigation of many human injuries. If a human tissue has any endogenous regenerative abilities, these could be enhanced through promoting regeneration. Studies for the laser regenerative improvement capacity could identify specific laser types and parameters that are capable for improving the regeneration capacity [1, 4].

Zebrafish have important and unique features that can make them one of the most informative models used for investigation of regenerative mechanisms. One of these features is their interesting capability to regenerate an amputated fin. The zebrafish model have become increasingly important in scientific research as its characteristics allow for being the smart model of investigation of many human injuries.

**Methods:** Twenty juvenile Golden Danio zebrafish (6-12 weeks post-fertilization) was housed in an aquarium with a standard heat of 24° C (75° F) and was fed with dry flake twice a day and live brine shrimp once a day. The caudal fin was amputated under anesthesia. The twenty zebrafish were randomly and equally divided into two groups including negative control group in which the caudal fin was monitored until fully regenerated, and the intervention group in which the amputated fin was irradiated with laser 810 nm. Microscopic calibration slide for measurement.

**Results:** This study showed that our experimental conditions of laser irradiation had benefits and can be considered as regenerative stimulator for the amputated zebrafish caudal fin. The results showed that regenerative stimulation of the group that received laser irradiation was significantly different when compared with the control group.

**Conclusions:** Laser can be suggested to have great regenerative capacity in the zebrafish caudal fin. Researches on zebrafish have supported in identifying multiple novel mechanisms in many tissues, and served as a guide for using different techniques to enhance several regenerative approaches in humans including photo-biomodulation in the injured human dental pulp tissues.

References 1. Chen, A., Y. Han, and K.D. Poss, Regulation of zebrafish fin regeneration by vitamin D signaling. *Developmental Dynamics*, 2021. 250(9): p. 1330-1339. 2. HIDAKA, A., et al., Conversion of provitamin D3 to vitamin D3 by monochromatic ultraviolet rays in fish dark muscle mince. *Journal of food science*, 1989. 54(4): p. 1070-1071. 3. Lock, E.J., et al., The significance of vitamin D for fish: a review. *Aquaculture nutrition*, 2010. 16(1): p. 100-116. 4. Uemoto, T., G. Abe, and K. Tamura, Regrowth of zebrafish caudal fin regeneration is determined by the amputated length. *Scientific reports*, 2020. 10(1): p. 649.

# CLINICAL AND RADIOGRAPHIC EFFICACY OF PBM, PRF, AND THEIR COMBINATION FOR SOCKET PRESERVATION

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## Abstract

### Three Learning objectives:

The combination of PRF and PBM resulted in superior socket preservation by

1. Healing enhancement
2. Pain reduction
3. Preserved KGW.

**Introduction:** This study aimed to assess the clinical and radiographic effects of photobiomodulation (PBM), platelet-rich fibrin (PRF), and their combination for socket preservation.

**Materials and Methods:** This single-blind clinical trial evaluated 72 patients who were candidates for extraction of maxillary or mandibular anterior or premolar teeth. The teeth were extracted atraumatically. The patients were randomly assigned to four groups (n=18) of laser, PRF, laser-PRF, and control (no-intervention). PRF was applied in the extraction socket and sutured in the PRF groups. The extraction socket underwent diode laser irradiation (660 nm, 100 mW, 2 J/cm<sup>2</sup>, 10 s, continuous-wave for soft tissue and 970 nm, 200 mW, 6 J/cm<sup>2</sup>, 20 s for hard tissue healing (dentsply, Germany Sirona) once every other day, starting from the day after extraction, for 2 weeks. Patients in the laser-PRF group received both interventions. Pain, soft tissue healing, keratinized gingiva width (KGW), and buccolingual ridge width and height were measured at baseline and 2 months post-extraction by cone-beam computed tomography, and compared by repeated measures ANOVA, paired t-test and regression model (alpha=0.05).

**Results:** The pain intensity was not significantly different between the laser and PRF, and PRF and the laser groups at 24, 48 or 72 hours (P>0.05) But in comparison to control groups, all three groups experienced less pain (P<0.05). The mean soft tissue healing in the laser-PRF group, the laser group, and the PRF group was significantly higher than that of the control group at 3, 7, and 14 days (P<0.001). Four groups did not show significant differences in a reduction of ridge width and ridge height within 2 months. (P>0.05). KGW was significantly higher in the laser-PRF group than the other three groups(P<0.05).

**Conclusion:** The results showed that combination of PRF and PBM resulted in superior socket preservation by healing enhancement, it also decreased pain and preserved KGW. Monotherapy with laser and PRF yielded comparable results.

# PBM VERSUS ANTIMICROBIAL AND ANTIVIRAL APPLICATIONS

## ADVANCES IN PULSED BLUE LIGHT INACTIVATION OF BACTERIA AND VIRUSES

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### Abstract

**Introduction:** Since we first showed that Pulsed Blue Light (PBL), a non-chemical and non-pharmaceutical treatment, is antibiotic and antiviral against coronaviruses, emerging reports have buttressed the view that, in general, 405 nm to 470 nm Blue Light (BL) has antimicrobial and antiviral potentials, with PBL being more effective at lower fluences than BL.

**Learning Objectives:** This invited paper, (1) presents current data on the antimicrobial and antiviral effects of BL and PBL, (2) discusses the underlying mechanisms, and (3) offers guidelines for clinical and other areas of application.

**Discussion:** The presentation will pinpoint potential areas of clinical application of PBL for bacterial and viral inactivation, as well as the antimicrobial value of light-based medical and dental technologies. Recent data from our ongoing studies will be presented showing that PBL light fixtures, designed for environmental sanitation, are antiviral and antibacterial against some of the deadliest bacteria and viruses. The potential to develop and deploy cost-effective light devices as environmental decontaminants, capable of inactivating viruses and other microorganisms safely, in clinical and non-clinical settings, will be discussed along with the implications of our findings for disease epidemics and pandemics.

# EVALUATION OF ADJUNCTIVE PHOTOBIO-MODULATION (PBMT) FOR COVID-19 PNEUMONIA VIA CLINICAL STATUS AND PULMONARY SEVERITY INDICES IN A PRELIMINARY TRIAL

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## Abstract

**Purpose:** Evidence-based and effective treatments for COVID-19 are limited, and a new wave of infections and deaths calls for novel, easily implemented treatment strategies. Photobiomodulation therapy (PBMT) is a well-known adjunctive treatment for pain management, wound healing, lymphedema, and cellulitis. PBMT uses light to start a cascade of photochemical reactions that lead to local and systemic anti-inflammatory effects at multiple levels and that stimulate healing. Numerous empirical studies of PBMT for patients with pulmonary disease such as pneumonia, COPD and asthma suggest that PBMT is a safe and effective adjunctive treatment. Recent systematic reviews suggest that PBMT may be applied to target lung tissue in COVID-19 patients. In this preliminary study, we evaluated the effect of adjunctive PBMT on COVID-19 pneumonia and patient clinical status.

**Patients and Methods:** We present a small-scale clinical trial with 10 patients randomized to standard medical care or standard medical care plus adjunctive PBMT. The PBMT group received four daily sessions of near-infrared light treatment targeting the lung tissue via a Multiwave Locked System (MLS) laser. Patient outcomes were measured via blood work, chest x-rays, pulse oximetry and validated scoring tools for pneumonia.

**Results:** PBMT patients showed improvement on pulmonary indices such as SMART-COP, BCRSS, RALE, and CAP (Community-Acquired Pneumonia questionnaire). PBMT-treated patients showed rapid recovery, did not require ICU admission or mechanical ventilation, and reported no long-term sequelae at 5 months after treatment. In the control group, 60% of patients were admitted to the ICU for mechanical ventilation. The control group had an overall mortality of 40%. At a 5-month follow-up, 40% of the control group experienced long-term sequelae.

**Conclusion:** PBMT is a safe and effective potential treatment for COVID-19 pneumonia and improves clinical status in COVID-19 pneumonia.



# PULSED BLUE LIGHT AND PHAGE THERAPY SYNERGISTIC BACTERICIDAL EFFECT OVER PSEUDOMONAS AERUGINOSA PREFORMED BIOFILM

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## Abstract

### Learning objectives:

1. To describe the danger associated with antibiotic-resistant bacteria
2. To state the pros-and-cons of bactericidal pulsed blue light (PBL).
3. To evaluate the synergistic bactericidal effect of phages and PBL

**Introduction:** Antibiotic-resistant strains and biofilms of *Pseudomonas aeruginosa* (PA) are a rising cause of morbidity and mortality. Pulsed blue light (PBL) has been shown to effectively inactivate certain bacteria in much lower doses as compared to continuous wave. Phage therapy (bacteriophages=bacteria-specific viruses), is a promising bactericidal non-antibiotic approach. This study was designed to determine if PBL combine with phage therapy culminates to a synergistic bactericidal effect against preformed biofilms.

**Methods:** Biofilms (PA14 grown for 48 hours) were irradiated with 450nm pulsed blue LEDs (33kHz, 50% duty cycle, 7.2 mW/cm<sup>2</sup>) for 1-4 ×30min sessions with 30min 'off' intervals (total dose 0-52 J/cm<sup>2</sup>). Phage 10<sup>8</sup> PFU/ml was added 24h or 10min prior to PBL or 10min after. Crystal violet stain was used to evaluate biofilm biomass. Live-dead fluorescent staining was used to measure biofilm viability. Fluorescently stained biofilms were visualized under confocal microscopy and the Z-stack maximal intensity projection of 17 sections in 12.5µm intervals was measured. n=5 biological repeats. ANOVA and Tukey as post-hoc or Kruskal-Wallis with Conover-Inman as post-hoc were used for comparisons as appropriate.

**Results:** By crystal violet stain, we found that both PBL and phage significantly reduced biofilm biomass regardless of the dose ( $p < 0.001$  across doses, presence of phage, and timing of phage addition) with the most efficient combination when adding the phage immediately before 26J/cm<sup>2</sup> PBL. By live/dead stain, the biofilm viability was significantly reduced by each of the treatments (%Live, median[IQR]: Control 80%[10]; PBL 25%[10]; Phage 40%[10]; and PBL&Phage: 15%[21],  $p < 0.001$  vs control for all). PBL with/without phage was significantly superior to phage alone ( $p = 0.012/p = 0.044$  respectively).

**Conclusions:** Phage combined with PBL was found to have a synergistic bactericidal effect in preformed biofilms of *P. aeruginosa*. Evaluating the safety and effectiveness of Phage/PBL in preclinical models is the next step toward validation of this novel approach for combating antibiotic-resistant bacteria.

# PULSED BLUE LIGHT INACTIVATES RESPIRATORY SYNCYTIAL VIRUS (RSV)

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## Abstract

**Introduction:** Respiratory syncytial virus (RSV) is a negative-sense single-stranded RNA virus that causes infections in the respiratory tract. Most infections resolve in a week or two, however infants, pregnant women and adults with chronic medical conditions and age 60 or older are more likely to develop severe RSV leading to hospitalization. In the United States, there are yearly reports of 6,000-10,000 deaths among adults 65 years and older and 100–300 deaths in children younger than 5 years old<sup>1</sup>. Even though there is a vaccine to protect susceptible individuals, antiviral regimens are in high need to inactivate the virus, and reduce the spread of RSV in the environment and hospitals.

**Learning Objective:** 1. To investigate the use of pulsed blue light (PBL) to inactivate RSV. Previously, our team reported that PBL inactivated coronaviruses, providing the background upon which the current study builds on. 2. Determine the effect of different wavelengths on RSV. 3. Utilize data obtained to advance PBL antiviral protocols.

**Methods:** Respiratory syncytial virus obtained from the American Type Culture Collection (VR-1540) was placed in six well plates and treated with 405 nm, 410 nm, 425 nm, and 450 nm PBL at an irradiance of 10 mW/cm<sup>2</sup> and fluence of 75.6 J/cm<sup>2</sup>. Viral RNA was extracted using a QIAmp viral RNA extraction kit, quantified using a Qubit fluorometer and real-time qPCR (RT-LAMP assay).

**Results:** The experiments were performed in triplicates and ANOVA was used to compare data within groups and T-test between groups with a significance level of  $p < 0.50$ . The results indicate that PBL significantly reduces RNA concentration of irradiated RSV when compared to untreated controls, with 405 nm and 410 nm yielding maximum reduction.

**Conclusion:** These findings have significant implications in the ongoing effort to mitigate RSV uprising. Our team continues to test this PBL protocol on other viruses of medical importance, with the goal of advancing the integration of this technology in the stash of clinical tools for patients with viral infections and environmental sterilization.

<sup>1</sup>Hansen, C. L. et al. Mortality associated with influenza and respiratory syncytial virus in the US, 1999-2018. JAMA Network Open. 2022, 5(2):e220527. doi:10.1001/jamanetworkopen.2022.0527

# DIFFERENT MODALITIES OF PHOTOBIO-MODULATION IN THE RECOVERY OF TASTE AND SMELL AFTER COVID

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## Abstract

**Learning objectives:** understand if PBM works, what is the best way to apply it and if there is a way to make a prognosis

Changes in taste and smell after Covid infection caused eating, emotional and social disorders, making the search for recovery extremely important. Photobiomodulation (PBM) has been used for years to treat dysgeusia and recover nervous tissue, and is therefore a potential treatment. Furthermore, in addition to the local application of light, transdermal blood photobiomodulation (BPBM) has shown clinical improvement of patients with various pathologies. This work aims to evaluate the benefits of both modalities of PBM in the recovery of taste and smell post covid. 67 patients were randomly divided into 2 groups, Local PBM (L-PBM): PBM in the upper airways, tongue, salivary glands and limbic system, with Diode laser, simultaneous irradiation of 810nm and 660nm, 0,1W each, from 1 to 9 J (according to the site) spot area 0,03cm<sup>2</sup>; and group Local plus BPBM (LB-PBM): L-PBM plus B-PBM applied transdermally over the radial artery in the wrist (660nm, 0,1W, 180J, 30min, 0,03cm<sup>2</sup>). 12 weekly sessions were held, on average 4 months of treatment per patient. The gustatory and olfactory perception was evaluated per session through questionnaires on olfactory function in everyday situations and products including water, coffee, perfumes, cleaning products and other substances present in their daily lives and gustatory tests with different concentrations of Glucose, Urea, Sodium chloride and Citric acid. The results showed that there was an improvement in the taste and smell recovered in both treatment groups. In L-PBM 34.5% had taste and smell recover above 80% and 17.2% had total recovery. In the LB-PBM 65.8% had recovery above 80% and 34.2% had total recovery. There was no significant association between the groups and the patient's sex, covid symptoms, disease severity and hospitalization, age, taste and smell change time, time between the disease and the start of treatment, number of sessions and treatment time ( $p>0.05$ ). Regardless of the patient's covid history, photobiomodulation proved to be effective in recovering smell and taste, presenting better results when the local treatment modality is associated with blood photobiomodulation.

# DIODE LASER IN MANAGEMENT OF LOSS OF TASTE SENSATION IN PATIENTS WITH POST-COVID SYNDROME: A RANDOMIZED CLINICAL TRIAL

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## Abstract

**Objective:** Loss of taste (ageusia) is a symptom observed following recovery from COVID-19 infection. The loss of taste and smell sensation may negatively affect patients' quality of life (QoL). The present study aimed to evaluate the effectiveness of the Diode Laser in managing loss of taste sensation in patients with post-COVID syndrome versus the placebo.

**Material and method:** The study sample was 36 patients who complained of persistent loss of taste sensation following COVID-19. The patients were randomly assigned to one of the two groups according to the received treatment: Group I (laser treatment) and Group II (light treatment), with each patient receiving a diode laser treatment or placebo from the same operator. Taste sensation was subjectively measured after treatment for four weeks.

**Results:** The results demonstrated a significant difference between both groups regarding taste restoration after one month ( $p = 0.041$ ), with Group II having a significantly higher percentage of cases 7 (38.9%) with partial taste restoration. In contrast, a significantly higher proportion of Group I 17 cases (94.4%) had complete taste restoration ( $p < 0.001$ ).

**Conclusion:** The present study concluded that using a Diode laser 810 nm aided in a more rapid recovery from loss of taste dysfunction.

**Keywords:** Ageusia; COVID-19; Diode laser; Laser therapy; Low-level; Quality of life; Recovery of function; Taste disorder.

# BACTERIAL SENSITIVITY TO ANTIBIOTICS AFTER IRRADIATION WITH LED (LIGHT EMITTING DIODE): IN VITRO

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## Abstract

Photobiomodulation (PBM) has been investigated in microbiology using laser and LED. In this context, research on bacterial inhibition has been explored to elucidate the effects on infections since the recommended treatment is antibiotics. Antibiotic resistance is a global problem, and FBM has been widely applied to skin lesions; however, little has been investigated about the interaction of LED with antibiotics. The objective was to verify the bacterial inhibition and antibiotic sensitivity profile of bacteria irradiated with LED. Wavelengths 465 nm (4, 5 and 6 J) and 630 nm (3, 4 and 5 J) were used in the bacteria *Staphylococcus aureus* (ATCC® BAA-977), *Pseudomonas aeruginosa* (ATCC 27853) and *Escherichia coli* (ATCC 25922) and bacteria collected from burn patients. 300µl of saline solution with a suspension concentrated between 0.5-0.63 (McFarland Scale), five serial dilutions, were irradiated with LED and distributed in transparent microtubes, with pH and temperature control before and after irradiation. The cultures were stored in an oven at 37°C for 24 hours for subsequent counting of colony-forming units. Two methods were used for sensitivity profiling, one quantitative (VITEK®2 Compact) and one qualitative (Disc-diffusion). All data were subjected to the Shapiro-Wilk normality test and comparisons between groups using the single-factor ANOVA test, with Tukey's *post hoc* test ( $p < 0.05$ ). The sensitivity of antibiotics showed a change - changing from resistant to sensitive, for the ATCC bacteria *Staphylococcus aureus* and *Escherichia coli* and the bacteria *Staphylococcus aureus* and *Pseudomonas aeruginosa* collected from burn patients, in both evaluation methods. However, there was no conformity in the findings when comparing the methods. All groups showed bacterial inhibition, with greater prevalence at 465 nm, with an increase and decrease in pH for some species. It is concluded that there are changes generated in the sensitivity profile to antibiotics but that these changes need to be better investigated for clinical practice regarding possible damage to the membrane, production of reactive oxygen species or enzymatic reactions to gain greater knowledge about the mechanisms that may generate such changes.

## YOUNG INVESTIGATOR - BASIC SCIENCES

### EFFECTS OF PHOTOBIMODULATION BY MLS-MiS LASER ON MODELS OF FIBROBLAST ACTIVATION: IMPLICATIONS FOR WOUND HEALING

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#### Abstract

Inflammation is a physiological process that plays a crucial role in initiating and regulating wound healing. The inflammatory response induces a cascade of events that involves the recruitment of different cell populations, mainly immune and stromal cells. Stimulated by the release of cytokines, vasoactive factors and growth factors, immune cells contribute to the normal progression of inflammation and, subsequently, stromal cells start a process of repair/regeneration to restore a tissue structure similar for morphology and function to the original tissue. A proper regulation of the inflammatory response is crucial for optimal wound healing: an excessive or prolonged inflammatory phase can result in scar formation or healing delay. Since several years, photobiomodulation therapy (PBMT) is applied to manage many different diseases characterized by acute or chronic inflammation and to promote healing. However, cellular and molecular mechanisms underlying the effects of laser therapy are still not well understood. The aim of this study was to investigate the effect of the MLS-MiS laser, a dual-wavelengths NIR source, on *in vitro* models of activated fibroblasts. In detail, human dermal fibroblasts were stimulated with a mix of IL-1 $\beta$  and TNF- $\alpha$  or TGF- $\beta$  alone, to induce two different pro-inflammatory phenotypes, involved in early and late inflammation, respectively. Then, the samples were irradiated (wavelengths 808 nm and 905 nm; frequency 10 Hz; fluence 5 J/cm<sup>2</sup>) once a day for three consecutive days. Morphological, metabolic and functional alterations were investigated. The results showed that MLS-MiS emission is effective in reverting fibroblast activation induced by the pro-inflammatory cytokines. Metabolic analysis, carried out by Seahorse technology, revealed that MLS-MiS laser enhances mitochondrial respiratory activity in unstimulated fibroblasts while do not induce alterations in cells previously stimulated with IL-1 $\beta$  and TNF- $\alpha$ , thus avoiding to increase further their metabolic activity, already enhanced by cytokines. In addition, cell migration capability, assessed by a scratch assay, was promoted in the early inflammation model following MLS-MiS. In conclusion, the results demonstrated that PBMT by MLS-MiS is effective in controlling fibroblasts activation induced by IL-1 $\beta$  and TNF- $\alpha$  or TGF- $\beta$ , thus damping excessive inflammatory response.

# INFLUENCE OF PHOTOBIMODULATION ON THE VIABILITY OF MULTIPOTENT MESENCHYMAL STEM CELLS FROM ADIPOSE TISSUE IN VITRO.

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## Abstract

**Learning objectives:** Evaluate the responses with different physical parameters of photobiomodulation with Laser and LED on the viability of mesenchymal stem cells.

**Introduction:** Skin wounds are a public health problem that affects patients' quality of life. Photobiomodulation triggers cellular responses that can assist in healing, depending on the physical parameters used. Mesenchymal stem cells are present in the physiological healing process and, when stimulated, can enhance tissue repair. The study's objective is to investigate the effect of different photobiomodulation parameters on the cell viability of mesenchymal stem cells.

**Methods:** Mesenchymal cells derived from adipose tissue were subjected to photobiomodulation with Laser and LED with red wavelength (660 nm and 630 nm respectively), power of 100 mW and energy of 0.5 J, 2 J and 4 J. Cells were stained with Hoechst and Propidium Iodide and analyzed with MetaXpress<sup>®</sup> software 24, 48 and 72 hours after irradiation. Statistical analyses were performed using GraphPad Prisma<sup>®</sup> 7.0 software.

**Results:** The results obtained in the experiments showed that irradiation with red light increased cell viability with the Laser and LED. Within 24 hours, laser irradiation with all applied energies and LED with only 2 J showed a significant increase. Within 48 hours, the Laser with 2 J and 4 J and the LED with 2 J showed effective results compared to the control group. In 72 hours, the LED showed better results than those in the group irradiated with Laser.

**Conclusion:** Photobiomodulation can stimulate cell viability with different physical parameters and periods after stimulation.



# THE OPTIMAL WAVELENGTH AND ENERGY DENSITY OF LIGHT EMITTING DIODE (LED) FOR INFLAMMATION AND REGENERATION IN OSTEOARTHRITIS-ASSOCIATED CELLS

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## Abstract

### Three learning objectives:

To explore the optimal LED wavelength and energy density anti-inflammatory responses in synoviocytes; To investigate the optimal LED wavelength and energy density in enhancing chondrocyte extracellular matrix (ECM) formation.

**Brief introduction:** Osteoarthritis (OA) is a joint disease marked by synovial inflammation and cartilage degradation. Photobiomodulation (PBM) using LED may provide therapeutic benefits by regulating inflammatory factors and ECM metabolism in osteoarthritic cells. However, the optimal PBM parameters for the amelioration of synoviocytes and chondrocytes remain unclear.

**Methods:** Synoviocytes derived from knee joints of Sprague-Dawley rat synovial membrane and RCJ 3.1 C5. 18 chondrocyte cell line were stimulated with recombinant rat TNF- $\alpha$  to induce an inflammatory response. Various wavelengths (625nm, 810nm, 940nm, 1050nm) with different energy densities (13-78 J/cm<sup>2</sup>) of LED irradiation were applied to the cells, maintaining a constant power density of 44 mW/cm<sup>2</sup>. RT-qPCR analysis was performed to measure mRNA levels of inflammatory and chondrocyte ECM factors.

**Results:** Synoviocytes exposed to 810nm LED presented a biphasic dose response at 39 J/cm<sup>2</sup>, revealing significant reductions in IL-1 $\beta$ , iNOS, COX-2, and IL-6 expression when compared with other wavelengths (625nm, 940nm, 1050nm). At 39 J/cm<sup>2</sup>, 940nm LED significantly decreased the IL-1 $\beta$  and IL-6 expression, while 39 J/cm<sup>2</sup> of 625nm LED only lowered IL-1 $\beta$  compared to other energy densities. In chondrocytes, 52 J/cm<sup>2</sup> of 940nm LED significantly decreased mmp3 and mmp13 mRNA levels and enhanced col2a1 and ACAN expression, while 39 J/cm<sup>2</sup> of 810nm LED only lowered mmp3 and mmp13. 1050nm LED showing no significant effect on anti-inflammation in synoviocytes and preventing chondrocyte ECM degradation.

**Conclusions:** This study revealed that 810nm LED at 39 J/cm<sup>2</sup> showed the most effective anti-inflammatory effect in synoviocytes. On the other hand, 940nm LED at 52 J/cm<sup>2</sup> showed the most protective effect on chondrocytes by promoting a healthier ECM metabolism. These findings suggest the optimal parameters for LED-PBM for OA by modulating inflammation and chondrocyte degeneration.

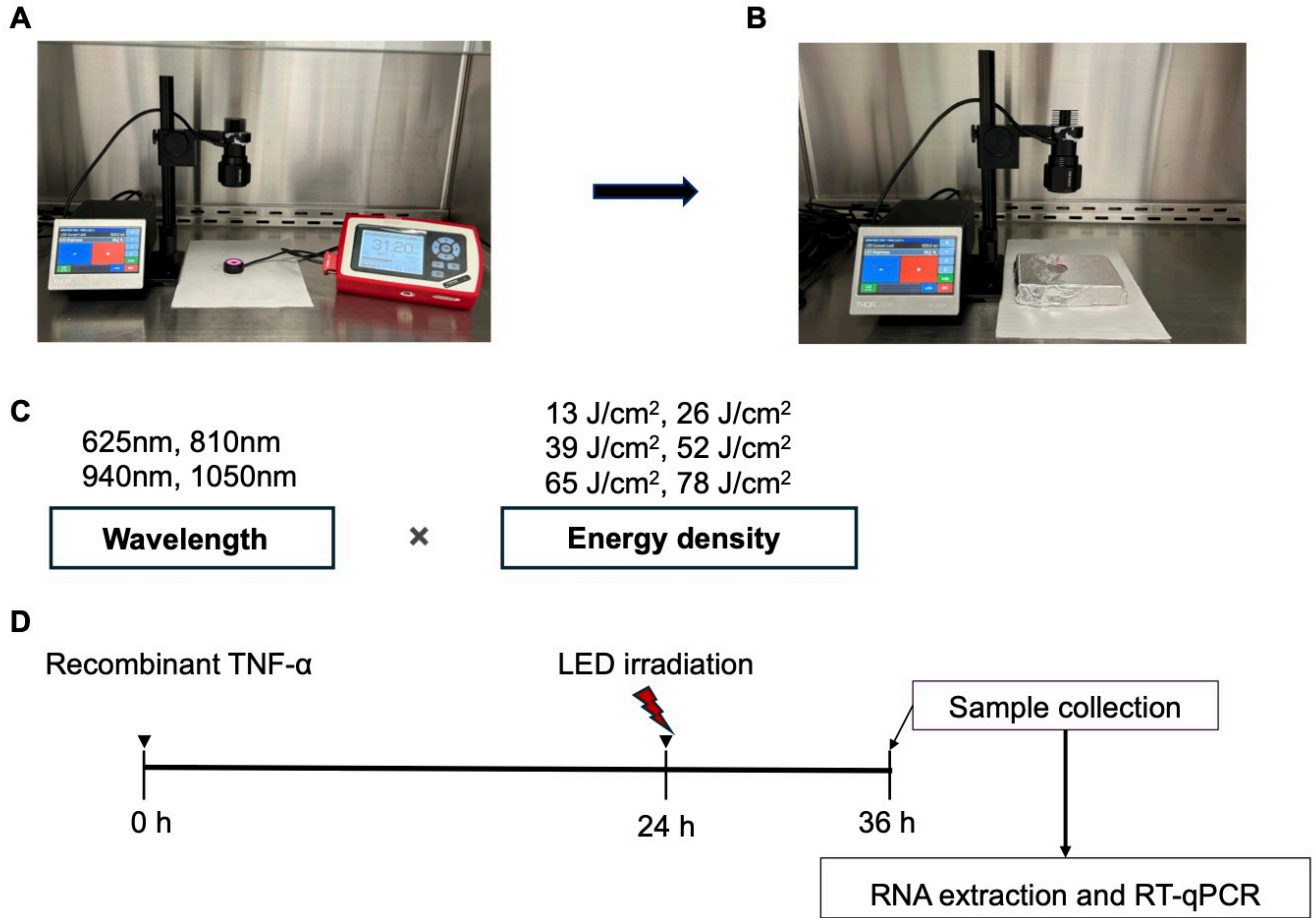


Figure 1. LED irradiation process.

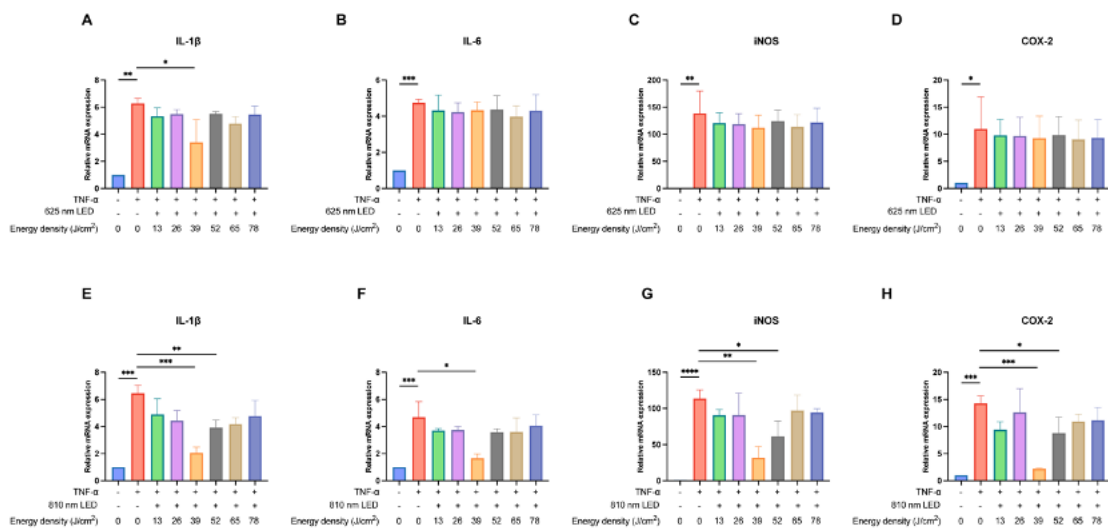


Figure 2. Effects of 625 nm and 810 nm LED irradiation on TNF- $\alpha$  stimulated rat synoviocytes

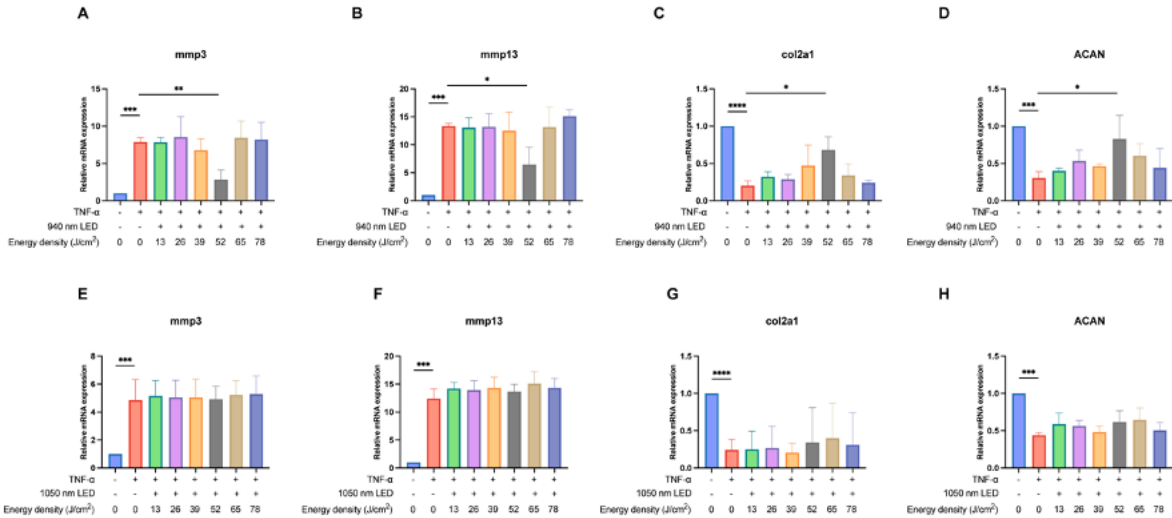


Figure 3. Effects of 940 nm and 1050 nm LED irradiation on TNF- $\alpha$  stimulated rat chondrocyte cell line C.518.

# PBM EFFECTIVENESS ON BIOFILM OF CANDIDA SPP AND STREPTOCOCCUS MUTANS - AN IN VITRO STUDY.

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## Abstract

### Learning Objectives:

1. Application of neodymium laser with parameters that are used in photobiomodulation is capable of inhibiting growth *Candida* spp.
2. Administration of low level laser parameters with neodymium laser can immediately after irradiation reduced number of *Streptococcus mutans* strains.
3. The use of flat-top handpiece with homogenous light distribution is more effective than fiber with Gaussian profile against oral microbes.

**Background:** Oral microbiota comprises a variety of different species of microorganisms. The purpose of this study was to evaluate the effects of PBM with a 1064 nm Nd:YAG laser using flat-top handpieces on the in vitro growth of clinical strains: *Candida albicans*, *Candida glabrata*, *Streptococcus mutans*, and their biofilm, and compare it with a fiber.

**Material and methods:** One- and two-species planktonic cultures of *Streptococcus mutans*, *Candida albicans*, and *Candida glabrata* were irradiated after 24 hours with a Nd:YAG laser (LightWalker, Fotona) using two flat-top handpieces: Genova and MarcoM or a glass fiber, with the following parameters: A: G1 group (Genova): G1a: irradiance 0.5 W/cm<sup>2</sup>, 10Hz, spot diameter 10mm, dose 29J; G1b: irradiance 1.75W/cm<sup>2</sup>, 30Hz, spot diameter 10mm, dose 105J; B: G2 group (MarcoM): G2a: irradiance 0.2 W/cm<sup>2</sup>, 10Hz, spot diameter 24mm, dose 64J; G2b: irradiance 0.6 W/cm<sup>2</sup>, 30Hz, spot diameter 24 mm, dose 196J; C: G3 group (fiber 300um): G3a: irradiance 0.5 W/cm<sup>2</sup>, 10Hz; G3b: irradiance 2 W/cm<sup>2</sup>, 10Hz; D: Control group: non-irradiated clinical cultures of *S. mutans* and *C. albicans*, *C. glabrata* single- and double-species. All laser groups in this study were irradiated for 60 seconds with a 100s pulse width (MSP mode), using non-contact mode. The effect of the laser was assessed immediately and 24 hours after irradiation of the plankton suspension using a quantitative method (estimation of colony-forming units in 1ml of suspension, CFU/ml) and compared with a control group in which no laser was used. The impact of PBM on biofilm biomass (single and multi-species) was assessed using the crystal violet method.

**Results:** PBM using both applicators (Genova, MarcoM) and glass fiber significantly reduced the number of *Candida albicans*, *Candida glabrata*, and *Streptococcus mutans* directly after laser application ( $p < 0.05$ ). Additionally, the reduction of CFU/ml level for *Streptococcus mutans* was significantly higher than that found for *Candida* spp. for both applicators (Genova and Marco M) and glass fiber ( $p < 0.05$ ). A greater reduction in *Candida albicans* ( $p = 0.030$ ) and *Streptococcus mutans* ( $p = 0.029$ ) CFU/ml level 24 hours after application of PBM using the Marco M applicator was found in contrast with the Genova handpiece. In the case of *Candida glabrata*, the reduction of single-species biofilm biomass when using the Nd:YAG laser with crystal violet and the Genova handpiece was significantly greater compared to the Marco Mhandpiece ( $p < 0.05$ ). Nd:YAG laser with MarcoM handpiece reduces *S. mutans* more strongly than other handpieces (Genova or fiber) ( $p < 0.05$ ). The use of an Nd:YAG laser with a fiber (300um) in the case of single-species as well as two-species biofilm and *S. mutans* gives significantly worse results compared to Genova and Marco M handpieces ( $p < 0.05$ ).

**Conclusion:** PBM allowed for the reduction of *Candida albicans*, *Candida glabrata*, and *Streptococcus mutans*. Wider laser applicators seem to be promising in effectively reducing these strains compared to glass fiber.

# EFFECT OF VISIBLE SPECTRUM LIGHT ON ADIPOSE-DERIVED STEM CELLS (ADSCs)

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## Abstract

**Introduction:** Although UV radiation is the primary carcinogenic agent in solar radiation, green and blue light appear to have the capacity to cause DNA damage through mechanisms such as the production of dark-CPDs. Visible light can reach the hypodermis of areas of the body where the skin is thinner, damaging adipose tissue stem cells (ADSCs) that play a fundamental role in skin repair.

**Objective:** To analyze the effects of visible light ADSC.

**Methods:** ADSCs were exposed to blue (448 nm), green (530 nm), and red (655 nm) light at different doses (Blue: 78, 60, 40, 30, 20, or 12 J/cm<sup>2</sup>; Green: 60, 30, or 20 J/cm<sup>2</sup>; Red: 60, 40, 30, 20, or 12 J/cm<sup>2</sup>). ADSCs under the same culture conditions maintained in darkness were used as controls. The effect of these radiations on proliferation (XTT assay) and the production of reactive oxygen species (ROS) was analyzed. Additionally, the combined effect of blue light and two compounds used in clinical practice, N-acetylcysteine (NAC; 1 μM) and hydroxychloroquine (HCQ; 1 μM), has been studied.

**Results:** Blue light at doses ranging from 20 to 78 J/cm<sup>2</sup> significantly decreased the viability of the culture compared to the control. Green light slightly decreased viability for the lowest dose used (20 J/cm<sup>2</sup>), while red light significantly increased viability after exposures of 60 and 40 J/cm<sup>2</sup>. Blue light at doses ranging from 20 to 78 J/cm<sup>2</sup> significantly increased radicals compared to the control. Treatment with NAC significantly decreased ROS production both in the presence and absence of blue light. HCQ showed no antioxidant effect in the absence of blue light; however, in cultures exposed to blue light, it reduced ROS production, although the difference was not statistically significant. One-way-ANOVA with Turkey post-test t-test was applied using GraphPad Prism 6.01 software.

**Conclusion and learning objectives:** Blue light reduces the viability of hypodermal ADSCs and increases ROS production. When stem cell cultures are exposed to blue light along with ROS production inhibitors such as NAC and HCQ, both compounds are capable of attenuating ROS production. These results indicate that both compounds may be potential antioxidants and photoprotectors against blue light.

# THE REAL-TIME EEG RESPONSE OF TRANSCRANIAL PHOTOBIMODULATION AND THE EFFECT OF LIGHT PULSATION FREQUENCY

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## Abstract

### Three Learning Objectives:

1. Effect of transcranial photobiomodulation (tPBM) on EEG power
2. EEG temporal response following the onset of tPBM
3. Effect of tPBM pulsation frequency on EEG power

**Introduction:** Transcranial photobiomodulation (tPBM) involves the application of near-infrared (NIR) light to stimulate neural tissues [1]. EEG has been used to show an increase in alpha ( $\alpha$ ), beta ( $\beta$ ) and gamma ( $\gamma$ ) power as well as a decrease in gamma ( $\gamma$ ) power post-tPBM [2],[3],[4],[5]. In this study, we demonstrate the real-time human EEG response in the  $\gamma$  band based on pulsed tPBM at two frequencies.

**Methods:** EEG data from five healthy subjects (4F/1M, age 19-25) were recorded during tPBM stimulation using a 256-channel system (Magstim). tPBM was applied using a 1064nm pulsed NIR laser with an optical power density of 150 mW/cm<sup>2</sup>. The frequency of the pulsation was alternated between 10Hz and 40Hz (50% duty cycle). The stimulation paradigm was [4-min off; 6-min on; 4-min off]. EEGLab was used for data resampling, artifact removal, ICA, and channel rejection. A custom MATLAB script was used to divide the EEG signal into frequency bands and epochs (4.5 sec) and compute dynamic power spectra. Cluster-based permutation thresholding was used to determine significant electrodes.

**Results:** Figure 1 shows both positive and negative responses of  $\gamma$  power to tPBM at both 10Hz and 40Hz pulsation frequency. Figure 2 shows the average %change in  $\gamma$  power, across all subjects at all significantly responding electrodes, also summarized as bar graphs. The 40Hz frequency elicits a larger positive response across positively significant electrodes, and the 10Hz frequency elicits a larger negative response across negatively significant electrodes. In both cases, a time lag of approximately 90 seconds after the onset of photobiomodulation is observed (Fig. 2a).

**Conclusion:** This study demonstrates for the first time the real-time EEG-power response to pulsed tPBM. Our work shows an important relationship between light pulsation frequency and different neuronal rhythms, highlighting the importance of systematically evaluating these interactions in understanding the tPBM neural response.

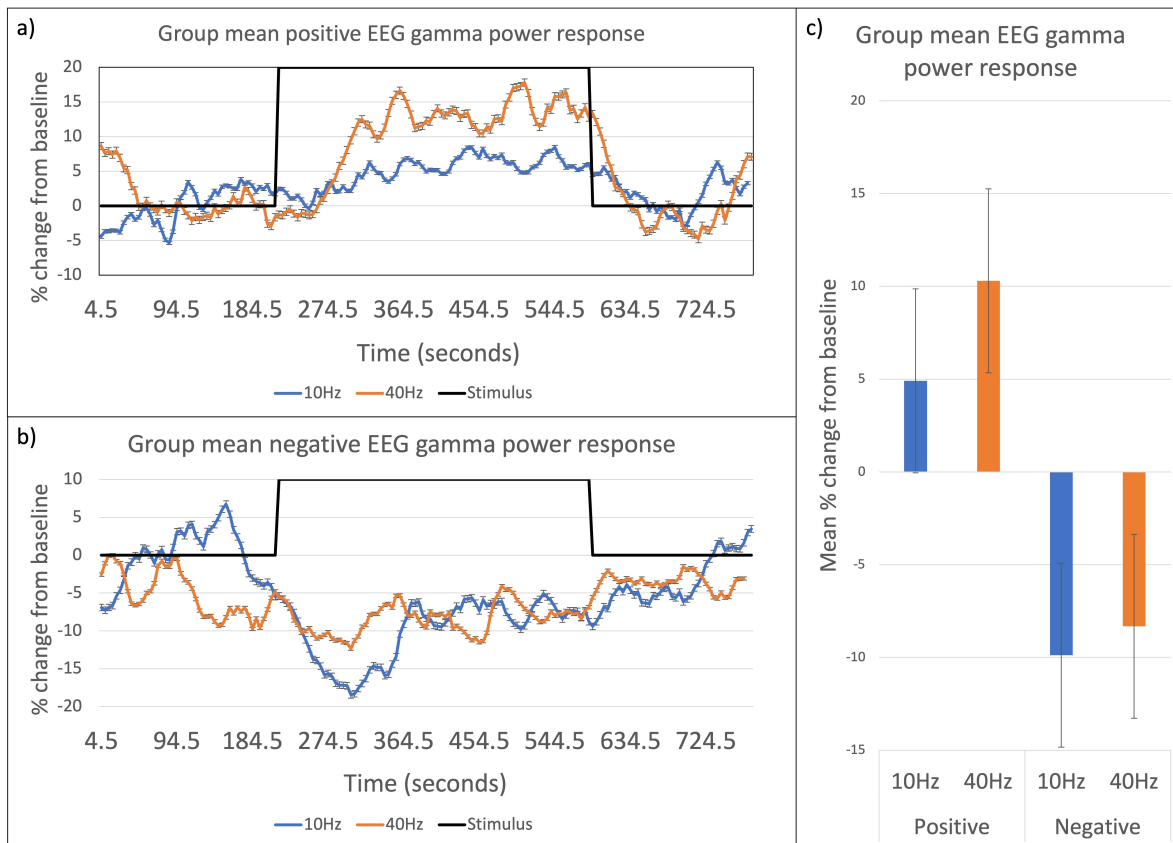
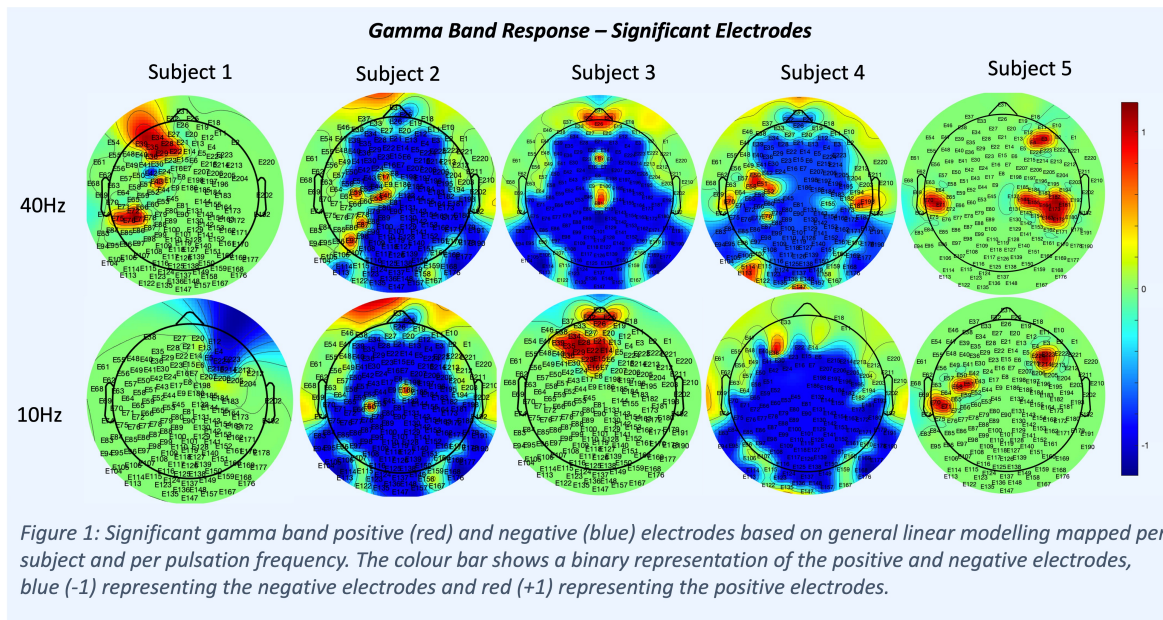


Figure 2: Group mean EEG gamma power response time course, averaged across all five subjects, for significant electrodes that have a positive (a) response to the stimulus as well as a negative (b) response to the stimulus. The mean percent change during the stimulus block is noted in (c), showing that the 40Hz pulsation frequency had a significantly larger positive response than the 10Hz.



# THE EFFECT OF PULSED BLUE LIGHT ON COMMENSAL MICROFLORA

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## Abstract

**Introduction:** Pulsed blue light (PBL) inactivates pathogenic bacteria, however its effect on innocuous commensals is not clear. Commensal bacteria can switch between commensalism and pathogenicity. This study examined: (1) the effect of PBL on three commensals, *Streptococcus salivarius* of the oral cavity, *Staphylococcus lugdunensis* of the lower abdomen, and *Staphylococcus epidermidis* found on the skin, and (2) the degree of inactivation of these commensals compared to their pathogenic counterparts.

**Learning Objective:** 1. Data obtained will shed light on PBL inactivation of commensals. 2. The significance of such inactivation will guide future development of antimicrobial PBL treatments. 3. Determine if inactivation of commensal flora is affected by commensalism or pathogenicity characteristic.

**Methods:** Commensal bacteria were obtained from the American Type Tissue Collection (ATCC), grown in their respective media and  $1 \times 10^6$  –  $1 \times 10^8$  CFU/mL plated. Each plate was irradiated thrice at 30-minute intervals with either 405, 410, 425, or 450 nm PBL at an irradiance of 10 mW/cm<sup>2</sup> and a total fluence of 75.6 J/cm<sup>2</sup>. In our previous experiments, the same protocol was used to treat pathogenic bacteria. Treated plates were incubated for 24 hours and bacterial colonies enumerated. Statistically, data were analyzed with ANOVA followed by *post-hoc* t-tests ( $p \leq 0.05$ ).

**Results:** PBL inactivated each bacterium, regardless of species or strain. *Staphylococcus* strains were more susceptible than *Streptococcus*. PBL at 405, 410 or 425 nm produced 100 % inactivation of each *Staphylococcus* strain, while treatment with 450 nm light produced 33% inactivation. In *S. salivarius*, irradiation with 405, 410, 425 or 450 wavelength resulted in 96%, 68%, 52% and 52% percent inactivation, respectively.

**Conclusion:** (1) These findings are consistent with previous reports showing the effect of these wavelengths on pathogenic bacteria, such as MRSA, *Streptococcus pyogenes* and *Streptococcus agalactiae*. Further, the effect of PBL is bacterial species-dependent, not bacterial characteristic, such as commensalism or pathogenicity. (2) While commensals are susceptible to photo-inactivation, the benefits of inactivating pathogenic bacteria, and the capacity of commensals to repopulate without provoking infection, underlie the value of PBL. Further studies are ongoing to explore the effects of other treatment protocols.



# 1068 NM PBM-T FOR THE TREATMENT OF NEUROLOGICAL COMPLICATIONS OF COVID-19: AN IN VITRO STUDY

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## Abstract

COVID-19 has several neurological manifestations, with up to 1/3 of people receiving a neurological or psychiatric diagnosis in the 6-months following infection. This may result from systemic inflammation (cytokine storm) and/or the direct binding of SARS-CoV-2 to ACE2 in the brain. Transcranial application of 1068 nm PBM-T could promote synaptic plasticity, reduce inflammation, and modulate oxidative stress to combat this.

### Aims:

1. Analyse functional responses of neurons, quantifying intracellular calcium concentrations in response to SARS-CoV-2 spike-protein-induced stress and PBM-T.
2. Evaluate the impact of PBM-T on reactive oxygen species (ROS) levels and pre-conditioning in COVID-19.
3. Investigate how PBM-T alters expression of the transcription factor NF- $\kappa$ B, and entry factors ACE2, TMPRSS2 and CD147.

**Methods:** Human SH-SY5Y and rat C6 cells were employed as neuronal and glial in vitro models respectively. Following exogenous SARS-CoV-2 spike protein (S-protein) stress for 24-hours, cells were irradiated with 1068 nm (5 irradiations of 6-minutes, 10 mW / cm<sup>2</sup>). Live single-cell imaging quantified intracellular calcium and ROS, and immunofluorescence techniques revealed relative expression and localisation of NF- $\kappa$ B and SARS-CoV-2 entry factors.

### Results:

1. Exogenous S-protein increased SH-SY5Y baseline calcium levels ( $p < 0.001$ ), which was reversed by PBM-T ( $p < 0.0001$ ). Neuronal response to KCl-induced depolarisation was lowered following S-protein exposure, but returned to control levels following PBM-T.
2. ROS increased in both cell types treated with PBM-T ( $p < 0.0001$ ). In C6 cells, this response was insult-dependent, with PBM-T decreasing ROS ( $p < 0.0001$ ) in cells pre-exposed to S-protein.
3. PBM-T increased NF- $\kappa$ B in unstressed C6 cells but decreased NF- $\kappa$ B in S-protein-stressed C6s ( $p < 0.0001$ ). Expression of 3 proteins involved in SARS-CoV-2 binding most notably showed that PBM-T reversed the S-peptide-induced redistribution of the receptor ACE2 to the C6 cell membrane.

**Conclusions:** This research provides pre-clinical evidence that 1068 nm PBM-T is suitable for combatting the neurological symptoms of COVID-19. PBM-T restores normal excitatory neurotransmitter release and synaptic communication through calcium signalling, induces insult-dependent anti-inflammatory responses, and prevents S-protein-induced localisation of ACE2 in glia (which would reduce viral binding, preventing further damage). These data are consistent with the recent validation of PBM-T 1070 nm for treating COVID-induced brain fog.

# AN IN VITRO INVESTIGATION OF THE EFFECT OF LOW-POWER LASER THERAPY AND STRONTIUM RANELATE ON THE DIFFERENTIATION OF MESENCHYMAL STEM CELLS

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## Abstract

**Learning objectives:** Following tooth replantation, serious complications may occur due to the inability of periodontium cells to proliferate and differentiate. This investigation aimed to evaluate the influence of strontium ranelate (Str) and photobiomodulation (PBM) on proliferation, osteogenic differentiation, and cementogenic differentiation of mesenchymal stem cells. If successful, PBM therapy and Strontium could be applied in treating avulsed teeth.

**Introduction:** Managing dislodged teeth is complicated and necessitates a collaborative approach. The primary therapeutic strategy for dislodged teeth is replantation. The advent of regenerative and photo medicine has provided new avenues for reducing complications following replantation.

**Methods:** In this in vitro experiment, stem cells derived from the buccal fat pad were exposed to two different laser types with wavelengths of 808 nm (250 mW, 0.4 W/cm<sup>2</sup>, 10 s, 4 J/cm<sup>2</sup>, spot area of 0.5 cm<sup>2</sup>) and 660 nm (150 mW, 0.25 W/cm<sup>2</sup>, 16 s, 4 J/cm<sup>2</sup>, spot area of 0.5 cm<sup>2</sup>) or not, with or without the addition of Str. Two or one-way ANOVA and Tukey's post hoc test were performed, and a p-value less than 0.05 was considered statistically significant.

**Results:** All experimental groups demonstrated significantly enhanced osteogenic differentiation compared to the control group ( $p < 0.05$ ), with no significant disparity between the 660 nm and 808 nm groups ( $p = 0.97$ ). In comparison to the Str group, the samples from the 660 nm and 808 nm groups exhibited significantly reduced osteogenic differentiation ( $p < 0.0001$ ), while the other groups did not show a significant difference. In terms of cementogenic differentiation, the 660 nm group demonstrated higher values than the 808 nm group ( $p < 0.01$ ). When compared to the Str group, the 660 nm, 660 nm + Str, and 808 nm + Str groups exhibited significantly increased gene expression ( $p < 0.05$ ).

**Conclusion:** Regarding osteogenic differentiation, although photobiomodulation alone had a lesser inducing effect than strontium ranelate, the combination of 808 nm diode lasers and Str may yield optimal results. Furthermore, the most effective method to induce cementogenic differentiation may be to expose stem cells to Str and use a 660 nm diode laser. Adding strontium ranelate can improve the function of both 660 nm and 808 nm diode lasers.

## DIAMOND SPONSOR'S SESSION(S)

### UNLOCKING BRAIN POTENTIAL THROUGH PHOTOBIMODULATION

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#### **Abstract**

The quest to optimize human brain function has long motivated advancements in non-invasive brain stimulation methods. While traditional techniques like electrical and magnetic stimulation have historically led interest, the spotlight in the 21st century could be progressively shifting towards Photobiomodulation (PBM), presenting a pivotal inquiry: How can PBM surpass established methodologies in efficiency, safety, and cost-effectiveness, thus redefining the forefront of brain optimization?

This presentation will offer a critical comparison between conventional brain stimulation paradigms and PBM, highlighting the latter's extensive applicability and foundational mechanisms. These mechanisms, which include the photostimulation of cellular processes, position PBM as a method that combines efficacy with minimal adverse effects. Investigating PBM's parameters—such as wavelengths, power density, placement of light sources, treatment duration, and pulse frequencies—is essential for unleashing the brain's full potential.

At the heart of this exploration is the theoretical advancement of advanced PBM devices, alongside artificial intelligence (AI), to navigate the brain's complexity. This approach promises a pathway towards personalized brain optimization, underscoring the importance of AI in personalizing treatments to individual neurophysiological profiles.

Through collaborative research, the impact of these parameters on cognitive enhancement and the management of neurodegenerative conditions, like Alzheimer's disease, is being rigorously explored. This collective endeavor not only highlights the transformative potential of transcranial PBM but also sets the stage for a broad spectrum of applications in brain function advancement. The author will demonstrate with a device, how the end goal of unlocking the brain potential is achievable.

Attendees will leave with a deeper understanding of the future landscape of brain health and cognitive enhancement, focusing on the promising role of PBM. This insight may spark new ideas for enhancing personal brain function, improving clinical outcomes, or pursuing novel research projects to advance brain functions.

# HOW PHOTOBIMODULATION MIGHT HELP DELAY THE FOUR LEADING CHRONIC NONCOMMUNICABLE CAUSES OF DEATH

JAMES CARROLL

CEO THOR PHOTOMEDICINE, UNITED KINGDOM

## **Abstract**

The four Chronic Noncommunicable Causes of Death (Atherosclerotic Cardiovascular Disease, Cancer, Neurodegenerative Diseases, and Type 2 Diabetes and related metabolic dysfunction) pose significant personal and expensive public health challenges. Preventative strategies typically emphasise diet, exercise, and sleep. This presentation reviews the potential role of photobiomodulation (PBM) in augmenting these lifestyle interventions.

PBM has been clinically proven to enhance exercise performance, improve sleep quality, reduce hypertension, and mitigate oxidative damage. These benefits are critical in delaying the onset and progression of the aforementioned chronic diseases. Additionally, PBM improves heart rate variability (HRV) and resting heart rate and increases VO2 Max, all of which are associated with a reduced risk of all-cause mortality.

Photobiomodulation could play a role in helping to delay the four leading Chronic Noncommunicable Causes of Death when used in conjunction with a suite of validated healthy lifestyle choices.

# TECHNOLOGY AND PBM DELIVERY DEVICES

## BEST PRACTICES FOR ASSESSING AND VALIDATING PHOTOBIO-MODULATION THERAPY DEVICES

JUANITA ANDERS

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### Abstract

**Introduction:** Photobiomodulation Therapy (PBMT) is a noninvasive technique employing light sources such as LEDs to enhance performance and recovery. Despite widespread use, there is a crucial gap in understanding practical outputs of PBMT devices. Specifically, there is little guidance on best practices for obtaining spectral and irradiance measurements from commercial devices. This study aims to address this gap by focusing on the methodology for collecting measurements, laying the groundwork for future PBMT investigations and applications.

**Methods:** This study focused on elucidating methodologies for obtaining spectral and irradiance measurements from three categories of PBM devices— panel-based, wearable technology, and full-body light beds. Utilizing a spectrometer, silicon photodiode power meter, bandpass filters, integrating spheres, and spectroradiometer the study team investigated ideal measurement systems for assessing PBMT device wavelengths and irradiances.

**Results:** Spectral measurements for each device's wavelength ranges were equal to or within 10 nm of wavelengths reported by the manufacturers. Reliability measurements of respective measurement devices showed variations of up to 5mW/cm<sup>2</sup> using repeated parameters. Measurements investigating various parameters (filters, apertures, software settings, etc.) found differences of up to 763mW/cm<sup>2</sup>, highlighting the importance of understanding valid measurement parameters. Similarly large differences were observed when considering means to mitigate device angle dependence. Aside from validation methodology, this research describes how to capture variability across illuminated surfaces and at various treatment distances. Utilizing these guidelines, the study determined that the NovoTHOR full-body PBM device exhibits an average irradiance of 48 mW/cm<sup>2</sup> (commercially reported irradiance: 30 mW/cm<sup>2</sup>) and the ARRCLED exhibits an average irradiance of 62 mW/cm<sup>2</sup> (reported: 75 mW/cm<sup>2</sup>).

**Conclusions:** The methodologies presented provide valuable insights into obtaining accurate spectral and irradiance measurements from PBMT technologies. In combination with showcasing the need for validated methodology, these determinations help elucidate which measurements devices should be used and how to best collect these data. Best practices for collecting preliminary validation data are outlined in order to facilitate investigations into the efficacy of PBMT.

### Objectives:

1. Discuss methodologies for assessing various categories of PBM devices.
2. Describe best practices when measuring spectral outputs of PBM devices.
3. Describe best practices when measuring irradiance outputs of PBM devices.

# OPTIMIZING INFRARED (808 nm) PHOTOBIMODULATION THERAPY BY OPTICAL CLEARING AGENT (OCA) WITH CHEMICAL PENETRATION ENHANCERS (CPEs)

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## Abstract

### Learning Objectives:

- Understand the optical clearing agents (OCAs) with chemical penetration enhancers (CPEs) effects on backscattered light;
- Identify how different phototypes respond to OCAs-CPEs;
- Thoughts about how to optimize photobiomodulation therapy (PBMT).

**Introduction:** PBMT is widely applied for several therapeutic aims. However, its efficacy depends on the light penetration through human skin. OCAs with CPEs have the purpose to increase light penetration depth by mitigating light reflection and scattering in biological tissues. However, there are no studies in humans that have combined these approaches, especially considering skin color (phototype) influence on light penetration through the skin.

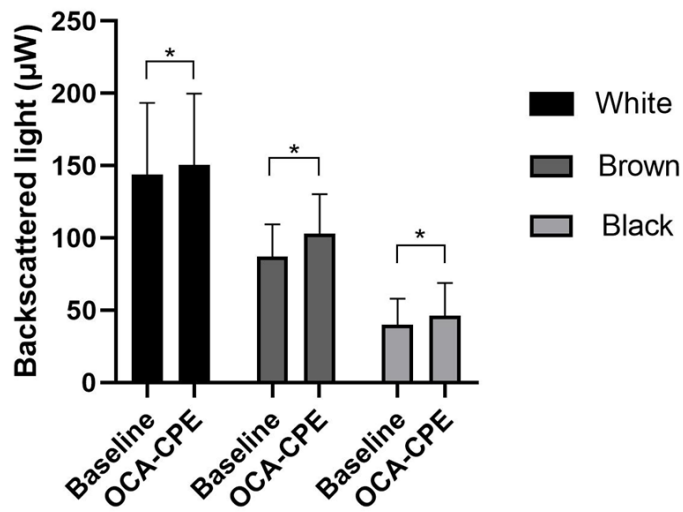
**Objective:** To verify whether the application of an OCA-CPE mixture improves the light penetration of PBMT through human skin inferred by backscattered light.

**Methods:** This consists in a clinical trial with 24 male volunteers (18-39 years old), allocated equally into 3 groups based on the skin phototypes (Fitzpatrick scale: white – phototypes I and II; brown – phototypes III and IV; black – phototypes V and VI). First, the volunteers were submitted to PBMT without intervention (BASELINE) at infrared wavelength (808nm, 1.66W/cm<sup>2</sup>, 30s, 1.5J; 50J/cm<sup>2</sup>) at the vastus medialis region of the dominant thigh. Backscattered light was measured with a PowerMeter PM100D (Thorlabs®) equipped with a S130C sensor, and its center positioned 2 cm from the irradiated area. The intervention was then carried out applying 1 mL of OCA-CPE to the vastus medialis, with an action time of 10 minutes, followed immediately by new irradiation and measurement of the backscattered light.

**Results:** 24 volunteers were included in the study (8 white, 8 brown and 8 black). The average age was 22.2 years. There was a significant increase in backscattered light in white (BASELINE = 143.92  $\mu$ W; OCA-CPE = 150.66  $\mu$ W; p = 0,009), brown (BASELINE = 87.11  $\mu$ W; OCA-CPE = 103.02  $\mu$ W; p = 0,001) and black individuals (BASELINE = 39.92  $\mu$ W; OCA-CPE = 46.08  $\mu$ W; p = 0,033).

**Conclusion:** Our results suggest that the application of OCA-CPE before PBMT with infrared light can discreetly improve light penetration inferred by backscattered light, possibly optimizing physiotherapy treatments in all skin phototypes.

**Keywords:** Photobiomodulation; Optical Clearing Agent; Skin Phototype.



**Figure 1.** Infrared (808 nm) backscattered light, in  $\mu\text{W}$ , on baseline and after Optical Clearing Agent with Chemical Penetration Enhancers (OCA-CPE) application in white (phototypes I and II), brown (phototypes III and IV) and black (phototypes V and VI) individuals. \* =  $p < 0.05$

# EFFECT OF OPERATING PARAMETERS AND APPLICATION TECHNIQUE ON OUTCOME OF ORAL PBM THERAPY. A 5-YEAR SYSTEMATIC REVIEW.

STEVEN PARKER

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## Abstract

### Three areas of inquiry:

1. Does PBM positively affect and augment the successful outcome of treatment, commensurate with a statistically significant comparison when compared to a control?
2. Where inconsistency exists between the three groups, is the outcome of PBM therapy predictability affected according to the underlying status of the treatment area in terms of inflammation or pathology?
3. Where inconsistency exists between the groups, is the effectiveness of PBM affected by disparity in light-dose, irradiation spot size or other laser operating parameters?

**Introduction:** This study provided an opportunity to evaluate PBM in relation to differing types of tissue and inflammation. Three clinical entities chosen to evaluate the influence of PBM through a 5-year systematic review of human RCT studies. Method: The initial number of 14,932 articles delivered 19, 15 and 20 articles to identify adjunctive PBM therapy in third molar surgery, orthodontic, and TMJ treatments respectively. Each paper was scrutinized to identify visible red – NIR laser wavelength PBM application, relative to dosimetry and outcome.

**Results:** Data set analysis was employed using *post hoc* ANOVA with a Bonferroni correction (threshold significance level  $\alpha = 0.05$ ); all publication data points were weighted according to the total number of participants recruited to the study. Outcome of articles related to oral surgery biostimulation and pain, revealed a statistically significant relation between PBMT and positive adjunct ( $p= 0.00625$ ), whereas biofunction stimulation across all other groupings failed to establish a positive association for PBMT.

**Conclusion:** The lack of significance is suggested to be due to a lack of operational detail relating to laser operating parameters, together with variation in a consistent clinical technique. As such, the outcome of this extensive study may expose a continued lack of accepted protocols when applying laser PBM. Adoption of consistent parameter recording and possible inclusion of laser data within ethical approval applications, may help to address the shortcomings in the objective benefits of laser PBM.



# A PILOT STUDY OF LED HOME USE PBMT DEVICES: DESIGN, FUNCTION AND POTENTIAL

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## Abstract

### Learning Objectives:

1. What potential role may home use PBMT devices have in dentistry?
2. To develop an appreciation of critical aspects of design in relation to proposed function
3. To assist clinicians in advising patients of the merits or limits of this type of appliance

In response to the benefits of PBMT many commercial LED devices are becoming available for home consumer usage. The logistics of therapy and economics are a challenge to the provision of PBMT and there are aspects of home delivery devices which may be beneficial. The performance characteristics in respect of dosimetry of many of the devices currently on direct sale to the public have not been subject to formal appraisal. PBMT may fall into disrepute with consumers should the claims of clinical gain not match the desired outcome. As an initial effort to bridge the gap between the evidence based PBMT community and clinicians as well as other interested parties an evaluation is made of a selection of LED PBMT products currently available for home use.

As a pilot study five randomly chosen LED PBMT devices were selected. The optical delivery parameters of the devices were measured using 5 sets of readings including beam divergence angle, surface area exposure as well as the output power at the level of the LED's as well as at a standardised distance of 1cm away from the surface of the LEDs using a Thor PM 160 calibrated meter. The manufacturers patient instructions were correlated to the measured optical parameters. Calculations were made of irradiance and surface radiant exposure and a statistical analysis conducted.

The results were heterogeneous with a wide range of applied wavelengths, output power and irradiance. The range of clinical applications proposed by the manufactures included dentine sensitivity, dental trauma, oral candidiasis, elimination of infection, the relief of pain as well as tooth whitening. The proposed dosimetry fail to consider tissue attenuation or the need for standardisation of dosimetry.

In conclusion, the concept of home PBMT is interesting. However the devices assessed require added design features and a mature appreciation of dosimetry parameters.

# MONTE CARLO SIMULATION OF THE LIGHT PROPAGATION IN THE SKIN DURING PBM BASED ON THE USE OF THE ATP38®.

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## Abstract

Since a precise control of the light dosimetry and spectroscopy is crucial in PBM [Joniova, 2021], we have characterized the radiometric and spectral features of the ATP38® light source produced by Swiss Bio Inov, Moudon, Switzerland. In addition, since the ATP38® is designed to treat various conditions, including certain types of inflammations and wounds, through an illumination of the skin, we have simulated the propagation of light in this organ for different illumination geometries at the wavelengths (in the visible and near-infrared) emitted by the ATP38®. As the skin is a multi-layered organ composed of many elements capable of absorbing or scattering light, the fluence rate vary significantly from place to place. In addition, these variations are strongly wavelength-dependent. Importantly, the values of the fluence rate are significantly different compared to the irradiance measured on the skin surface. Our simulations of the light propagation in the skin have been performed using a Monte Carlo-based algorithm. The absorption  $\mu_a$  and reduced scattering  $\mu_s'$  optical coefficients used for these simulations were derived from the literature for skin phototype III. These simulations were validated with calibrated (i.e. with known optical coefficients) optical phantoms in which the fluence rate was directly measured with a "microscopic" (diameter: 850  $\mu\text{m}$ ) interstitial isotropic probe [Pitzschke, 2015]. This probe, as well as flat power meters, were also used to measure the fluence rate and the irradiance at the surface of the skin for different illumination protocols delivered by the ATP38®.

Our results, which are in agreement with the literature, illustrate the strong wavelength dependence of the spatial distribution of the fluence rate in different layers of the skin. These results also illustrate the impact of the illumination geometry, particularly the ATP38®-skin surface distance, on the fluence rate within the skin.

## Reference:

Joniova J. et al., J. Photochem.&Photobiol. B : Biology, 225, pp 1-14, 2021.

Pitzschke A. et al., Proc. SPIE-OSA, 954207, pp 1 – 14, 2015.

## REPRODUCTIVE HEALTH

### PHOTOBIMODULATION THERAPY AT 632 NM WAVELENGTH AMELIORATES INTRAUTERINE ADHESION VIA ACTIVATION OF CAMP/ PKA/CREB PATHWAY

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#### Abstract

##### Three Learning objectives:

1. Understanding the Pathophysiology of Intrauterine Adhesion (IUA).
2. Evaluating the therapeutic efficacy of photobiomodulation (PBM) therapy on IUA.
3. Exploring the molecular mechanisms of PBM Therapy.

**Introduction:** Intrauterine adhesion (IUA) is a major cause of uterine infertility, which is pathologically characterized by endometrial fibrosis. The current treatments for IUA have poor efficacy and are associated with high recurrence rate due to insufficient recovery of uterine structure and function. The study aimed to investigate the therapeutic effect of photobiomodulation (PBM) therapy on IUA and its underlying mechanisms.

**Methods:** A rat IUA model was established by mechanical injury and PBM at 632 nm wavelength was applied intrauterinely. Improvement of uterine morphology was examined by histological analysis and ultrasonography measurement. The recovery of uterine function was evaluated by fertility test. *In vitro*, TGF- $\beta$ 1-induced endometrial stromal cells (ESCs) were established as a cell model of endometrial fibrosis and then treated with/without PBM. Cytoskeleton and extracellular matrix (ECM) expressions at mRNA and protein levels were detected. cAMP signaling inhibitors were used to explore the potential mechanisms.

**Results:** *In vivo*, PBM treatment increased the thickness of endometrium and reduced the endometrial fibrosis. Furthermore, the endometrial receptivity and reproductive function of IUA rats were partly recovered after PBM treatment. In TGF- $\beta$ 1-induced ESCs, PBM decreased the mRNA and protein expressions of fibrosis-related molecules. cAMP/PKA/CREB pathway was activated by PBM intervention. Pretreatment with cAMP signaling inhibitors weakened the protective effect of PBM on TGF- $\beta$ 1-induced ESCs and IUA rats.

**Conclusion:** Our results demonstrated that PBM at 632 nm wavelength promotes the restoration of endometrial morphology and function through cAMP signaling pathway, suggesting a promising therapy for IUA.

# LASER BABIES: SHAPING THE FUTURE OF PBM IN REPRODUCTIVE CARE

LORNE BROWN

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## Abstract

1. Brief history of PBM for fertility & reproductive health
2. Mechanism of PBM that hold promise for improved fertility outcomes
3. Treatment strategies
4. Future of PBM research for Reproductive Care

This talk will examine the present landscape and scrutinize the mechanisms underlying PBM's potential in improving reproductive outcomes. Its ability to modulate cellular activity and influence hormonal balance, inflammation, blood flow and the gut microbiome presents compelling prospects for clinical applications.

Looking forward, the future of PBM in reproductive health research appears dynamic and promising. Through rigorous scientific inquiry and collaborative efforts, we aim to uncover its full potential and how to integrate it into clinical practice.

In this gathering of scientific minds, let us explore the cutting-edge advancements and challenges ahead, as we collectively shape the trajectory of PBM in the realm of reproductive health.

# PILOT STUDY: IMPROVED REPRODUCTIVE HEALTH AND FERTILITY OUTCOMES AFTER PHOTOBIMODULATION THERAPY (PBM).

RUTH PHYPERS

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## Abstract

**Learning Objectives:** By the end of this presentation the following learning objectives will be achieved:

1. Basic introduction to conditions relating to unexplained age-related infertility.
2. Overview of previous clinical studies that explore the potential efficacy of PBM to improve fertility outcomes.
3. Discovery of 2024 pilot study from clinical work carried out in a London PBM clinic which demonstrate how PBM may be effective in the improvement of five unexplained infertility case studies.

**Introduction:** PBM is observed as an effective therapy for unexplained age-related infertility, due to a biological chain of events that regenerate tissue and increase mitochondrial energy. The human oocyte contains more mitochondria than any other cell in the body, therefore it is logical to think that PBM could help increase the production of adenosine triphosphate in the ovarian mitochondria, improve oocyte function and support the production of a viable embryo. Furthermore, application of PBM to the entire female reproductive system could improve tissue integrity and oxygenated blood flow, and further contribute to the potential of a full-term pregnancy and healthy birth.

**Methods and results:** This pilot study shares observations from five in-vivo case study patients with unexplained infertility, which included failure to conceive naturally beyond 2 years, multiple miscarriages, a molar pregnancy, non-viable embryos produced from IVF cycles, and failure to complete successful implantation from viable pre-implantation genetic tested embryos. In each case previous conditions were recorded and then compared after the patient received a course of PBM treatments. PBM treatments were given at weekly and / or fortnightly intervals using IR and NIR wavelengths between 600nm-1,000nm, in the lead up to natural conception, IVF oocyte retrieval and blastocyst / embryo implantation and / or the production of genetically tested euploid embryos.

**Conclusion:** In each case, fertility outcomes improved. Four cases resulted in a full-term pregnancy and the birth of healthy baby. A fifth case showed a significant increase in the number of genetically tested euploid embryos retrieved after a course of PBM treatments. Improvements in reproductive health outcomes in each case give reason to suggest that PBM may help to improve unexplained infertility.

# CLINICAL CASE-REPORT OF THE EFFECTS OF RED LIGHT IN A GYNAECOLOGIC ONCOLOGY PATIENT

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## Abstract

A 79-year-old female patient diagnosed in 2018 with epidermoid carcinoma of the anal margin T2Nx Mx in the TNM Staging System, was treated by surgical excision on September 11<sup>th</sup>, 2018, concomitant radio and chemotherapy at initial doses of 45Gy in 25 fractions IMRT to the pelvis, and boost to the anal channel from November 19<sup>th</sup> 2018 to December 21<sup>st</sup> 2018 in 9 fractions in VMAT and IGRT (Saint Louis radiotherapy centre, Toulon, France).

During the radiations, the patient developed an advanced radio-epithelitis grade 2 addressed with sitz baths and topical treatments (Cicalfat, Ialuset). Patient was also affected with diarrheic episode treated with Smecta, Imodium and Turfan. At this stage, the patient suffered from intense, constant pain, had difficulties to walk, to sleep and was affected by reactional depression. Prescribed topical ointments were neither effective on her wounds nor pain and she was asking for a solution.

Photobiomodulation sessions were initiated as a supportive care applied on December 25<sup>th</sup>, 2018, December 28<sup>th</sup> 2018, January 5<sup>th</sup> 2019 and January 19<sup>th</sup> 2019 with red light (RL) 632nm, settings of 100mw/cm<sup>2</sup>, total 60 Joules for 15 minutes at each session. After 1<sup>st</sup> PBMT session, patient reported pain improvement, then gradually improvement of her wounds and mobility.

Two other PBMT sessions were scheduled in February 2019 before a new cycle of radiotherapy. What was observed in this clinical case is the total absence of burns during this second cycle of irradiations, suggesting that RL can be significantly beneficial in pre-conditioning oncologic patients prior to radiotherapy for preventing its side-effects.

The protective role of RLT may reside in reducing oxidative stress caused by either UV or radiotherapy-radiation, regulating dysfunctions at the mitochondrial level, reducing inflammation and enhancing cellular metabolism and resilience

Based on our clinical observations and published literature, RLT shows promising indications in clinical practice as an efficient, safe and cost-effective supportive care, easily accessible for patients treated with radiotherapy or chemoradiotherapy, which may significantly reduce epithelitis rate and grade, but also prevent collateral damages and complications of these oncologic therapies. Further clinical trials may fully elucidate its mechanisms of action and optimize RLT applications in oncologic care, improving patients' quality of life during treatment.

# SHARK TANK COMPETITION

## IF PBM WORKS BY INCREASING MITOCHONDRIAL ACTIVITY, WILL IT WORK IN MITOCHONDRIAL DISEASES?

LIISA LAAKSO

MATER RESEARCH INSTITUTE - UNIVERSITY OF QUEENSLAND, BRISBANE, AUSTRALIA. MENZIES HEALTH INSTITUTE QUEENSLAND, GOLD COAST, AUSTRALIA

### Abstract

#### Learn:

- 1) about mitochondrial disease (MD)
- 2) rationale for using PBM
- 3) how we will investigate PBM in MD

**Introduction:** There is no cure for mitochondrial diseases. MELAS is one form of rare mitochondrial disease: a multisystem neurodegenerative disorder affecting any organ or tissue, and affecting people in numerous ways including fatigue, muscle weakness and incoordination. Photobiomodulation (PBM) activates mitochondria. We will test if people with MELAS report improvement in symptoms and signs after PBM. We will assess mitochondrial activity using magnetic resonance spectroscopy ( $^1\text{H}$  MRS).

**Methods:** Due to mitochondrial disease rarity, fluctuating symptomology, and heterogeneity in its clinical presentation, this exploratory study will be a prospective case series following single case experimental design methods. We will intensively test the efficacy of a multiwavelength PBM belt (BeniLight iLED-Pro ExB Multi-Wave Multi-Pulse; 465nm, 660nm, 850nm; Ave Irradiance: 5.23mW/cm<sup>2</sup>, and Total Joules: 770.1 / treatment, all sites; 5KHz; 20% duty ratio) with sequential application and withdrawal of sham and intervention. Chosen wavelengths are based on published cell culture studies of light on mitochondrial activity. Participants will self-apply PBM at home to anterior thigh and posterior calf muscles and abdomen for 10 minutes to each site, on 3 days/week for 8 weeks.

**Results:** At each assessment stage, we aim to: (1) measure blood lactate and pyruvate as indirect indicators of mitochondrial activity and muscle performance; (2) conduct hydrogen (proton) MRS to analyse lactate, glutamine, creatine, phosphocreatine, glucose, metabolite diffusion, and  $p\text{O}_2$  under normoxic conditions in target calf muscle; and (3) evaluate participant exercise tolerance, fatigue, motivation, and activity using validated measures. Descriptive statistics and parametric and non-parametric tests will be applied as relevant to variables collected.

**Conclusions:** Our innovative work will open the door to identifying a non-drug treatment for a life-limiting disorder with no known cure. If found to be effective, we will extend our work into a RCT. We expect to elucidate if mitochondrial activity in response to PBM can be measured clinically. The findings would have a profound impact on the PBM field potentially confirming the mitochondrial mechanism in a clinical model thus far established mainly at the bench top.

# REVOLUTIONISING GUT-BRAIN CONNECTION AND MENTAL HEALTH THROUGH PBM

SARAH TURNER

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## Abstract

To explore the efficacy of the CERA System, a novel PBM therapy device targeting the gut-brain axis, in improving mental well-being.

To examine the use of a mobile app for real-time monitoring of mood and mental state via HRV analysis as a complementary assessment tool.

To understand the potential of integrating digital health technologies with PBM therapy for personalized mental health interventions.

### Introduction:

Photobiomodulation (PBM) therapy presents a promising non-invasive approach to health care, with potential benefits spanning from physical to mental well-being. This study introduces the CERA System, an innovative dual-device PBM therapy aimed at enhancing the gut-brain connection. Additionally, it incorporates a novel monitoring technique using a mobile app to assess mood and mental state through Heart Rate Variability (HRV), offering a comprehensive evaluation of therapy impact.

### Methods:

A randomized controlled trial was conducted with participants divided into two groups: one receiving the CERA System therapy and the other a placebo. The CERA System delivers four wavelengths of red and near-infrared light via a headband and body panel. HRV data were collected using a mobile app to assess participants' mood and mental state throughout the intervention. PBM parameters included wavelength (660nm for red and 850nm for NIR), power density (50mW/cm<sup>2</sup>), and exposure time (10 minutes per session, three times a week for six weeks).

### Results:

Statistical analysis indicated significant improvements in HRV metrics and self-reported mood scores in the intervention group compared to the placebo ( $p < 0.05$ ). Correlation analysis further revealed a positive association between HRV improvements and enhanced mood states.

### Conclusions:

The integration of the CERA System with HRV-based mood assessment via a mobile app demonstrates a significant advancement in personalized PBM therapy, showing promising results for improving mental well-being. This study highlights the potential of combining innovative PBM devices with digital health technologies for a holistic approach to mental health care, paving the way for future research and applications in integrated health solutions.

The research to be carried out at Durham University under the supervision of Prof Paul Chazot: FBPhS Chair in Pharmacology, Department of BioSciences Past President, European Histamine Research Society (EHRS), WRIHW Pain Challenge Academy.



# PHOTOBIMODULATION TREATMENT OF INHERITED RETINAL DISEASES

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## Abstract

Retinitis pigmentosa (RP), the most common cause of inherited blindness in the developed world, cannot be prevented or treated. Mitochondrial dysfunction and oxidative damage play key roles in the pathogenesis of photoreceptor cell death in RP. Importantly, RP is an excellent model in which to study neurodegenerative disease because the pathogenic process of rod photoreceptor degeneration leading to secondary, cone degeneration, is generalizable to other forms of retinal disease, including age-related macular degeneration and normal aging.

**Approach:** We will investigate the therapeutic potential and mechanisms by which PBM modifies the disease course of retinitis pigmentosa. Studies in three mutationally distinct murine models of RP will test the hypothesis that PBM will act in the retina to restore mitochondrial function, prevent photoreceptor cell death, and preserve retinal function. We will replicate the multiwavelength treatment parameters of the clinically established LumiThera instrument and investigate both disease prevention and treatment. Retinal degeneration will be characterized over a 12-month period in each murine model by Near-infrared spectroscopy (NIRS), Optomotor Response (OMR), Electroretinogram (ERG), and Spectral Domain-Optical Coherence Tomography (SD-OCT). Biomarkers of inflammation and oxidative damage will be measured by immunohistochemistry. We will integrate and compare our findings with other investigators and determine if PBM can prolong photoreceptor survival and retinal function regardless of the genetic defect.

**Impact:** The economic and individual costs associated with retinal degenerative disease are enormous and include hospital costs, disability, decreased productivity, and loss of independence. The development and application of this non-invasive, and inexpensive therapeutic modality would have tremendous benefit to both individual patients and society.

**Innovation:** The molecular and functional insights from this research will provide crucial information for FDA approval to use PBM to treat inherited retinal diseases. They will investigate the therapeutic potential of PBM in established rodent models of RP, establishing a basis for clinical trials. They will also improve our understanding of the molecular mechanisms by which PBM exerts its retinoprotective actions and improve our understanding of the pathogenesis of retinal degenerative diseases. By harnessing the cell's cytoprotective signaling pathways, PBM provides an innovative and non-invasive therapeutic approach for preventing and treating retinal disease.

# EVALUATION OF DIFFERENT PHOTOBIMODULATION PROTOCOLS ON Wnt/ $\beta$ -CATENIN SIGNALING PATHWAY IN STEM CELL-BASED BONE REGENERATION

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## Abstract

### Three Learning objectives:

1. Exploring the efficacy of different photobiomodulation protocols in stem cell-based bone regeneration.
2. Investigating photobiomodulation effects on key signaling pathways in stem cell-based bone regeneration.
3. Suggest the best photobiomodulation protocols based on the findings.

**Introduction:** There is a significant demand for tissue-engineered bone due to the high prevalence of large segmental bone defects. Despite advances in tissue regenerative modalities, it still remains a challenging topic. In recent years, photobiomodulation has been proposed as the fourth side of tissue engineering. However, there is a lack of sufficient evidence on the effect of different PBM protocols on the bone regeneration process. This project aims to investigate the effect of different PBM protocols on one of the main signaling pathways involved in stem cell-based bone regeneration.

**Proposed method:** This study aims to investigate the effects of various PBM protocols using infrared, red, and red-infrared diode lasers on periodontal ligament stem cells and buccal fat pad stem cells – based bone regeneration. In this study, the effect of PBM will be evaluated on the Wnt/ $\beta$ -catenin signaling pathway, which is referred to as the canonical pathway in bone repair and regeneration. Furthermore, bone differentiation will be evaluated in each stem cell using various PBM protocols. Osteogenic markers, such as Runx2, osteocalcin, collagen type 1, alkaline phosphatase activity, and Alizarin red staining, are additional factors that will be evaluated in this project. After collecting data, we will analyze it to draw conclusions and present our findings in a statement. An animal study will be conducted on critical size bone defects using best results according to the stem cell type and PBM protocols

# LIGHTING UP NEW NEURONS: EXPLORING PHOTOBIMODULATION FOR NEUROGENESIS ENHANCEMENT

NATALIA ARIAS

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## Abstract

**Introduction:** The hippocampus contains neural stem cells (NSCs) crucial for adult hippocampal neurogenesis (AHN), vital for hippocampal plasticity, which declines with age. Boosting adult neurogenesis is a potential therapy. Photobiomodulation therapy (PBMT) applies low-intensity light, impacting mitochondrial activity and intracellular signaling, holding potential in regenerative medicine. Yet, its effect on NSC proliferation and differentiation is uncertain.

**Methods:** We aim: (i) to explore the differential effect of 5 Hz versus 40 Hz on AHN in adult rats and (ii) to investigate the critical time window (48 hours versus 96 hours) during which AHN is stimulated in adult rat brains. The PBM was delivered using an 810 nm LED array (Quantum Devices Warp 10) at 40 mW for 40 seconds, followed by a 10-second off period, in cycles lasting 50 seconds. 36 cycles were administered over 12 minutes, total dose of 46.50 J/cm<sup>2</sup>, with a beam size of 0.0495 cm<sup>2</sup>, was positioned along the midline of the dorsal surface of the shaven head. The protein expression levels of Ki67, DCX, Tuj-1, and Nestin in the prefrontal cortex, hippocampus, cerebellum, and hippocampus were assessed by Western blotting.

**Results:** Increased Ki67 expression, a marker of neuronal proliferation, in the 40 Hz group ( $F_{2,21}=24,13$ ;  $p<0.001$ ). Also, increased hippocampal ( $F_{2,11}=6.947$ ;  $p=0.0112$ ) and cerebral cortex ( $F_{2,11}=5.397$ ;  $p=0.0233$ ) doublecortin (DCX) expression, a marker of neuronal migration, in the 96-hour group was found. Furthermore, decreased Nestin expression, an intermediate filament involved in the structural maintenance of neurons, in both 5 Hz and 40 Hz groups ( $F_{2,20}=14.88$ ;  $p=0.0001$ ). No changes were observed in Tuj-1 expression, a marker of neuronal migration.

**Conclusion:** PBMT appears to be a promising tool for modulating neurogenesis at specific frequencies within a defined time window. Further research should focus on the integration of newborn neurons into preexisting neural networks and its significance as a therapeutic approach in neurodegenerative disorders

- Understand the role of NSCs in AHN and its significance for hippocampal plasticity.
- Assess the potential of PBMT in stimulating neurogenesis by influencing NSC proliferation and differentiation.
- Evaluate PBMT parameters' impact on neurogenic outcomes in adult rats, informing future neurodegenerative disorder therapies.

# METABOLIC AND AUTOIMMUNE DISORDERS

## EFFICACY OF COMBINED PHOTOBIO-MODULATION THERAPY WITH SUPPLEMENTS VERSUS SUPPLEMENTS ALONE IN RESTORING THYROID GLAND HOMEOSTASIS

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### Abstract

#### Learning objectives:

1. Outline the current conventional treatment of Hashimoto thyroiditis (HT)
2. Understand the efficacy of photobiomodulation (PBM) with or without supplements in restoring thyroid gland homeostasis.
3. Be familiar with the future perspective in utilising PBM therapy in thyroid diseases.

**Introduction:** Hashimoto thyroiditis (HT) is a thyroid-specific autoimmune disorder, triggering hypothyroidism in a population with an adequate dietary intake. Despite the current conventional treatment focuses on the permanent replacement of levothyroxine (LT4) deficiency, it appears that thyroid autoimmunity remains the cause of persistent symptoms in patients with HT, even when they achieve to be euthyroid from a biochemical standpoint. Photobiomodulation (PBM) showed to be an effective therapy in autoimmune diseases, but with limited evidence. Hence, our study was conducted to appraise the efficacy of PBM therapy in restoring thyroid gland homeostasis.

### Methods

Seventy-four female subjects aged between 20-50 years old were recruited and divided equally into two groups: PBM and supplements group (group 1); and supplements alone group (group 2). The PBM dosimetry and treatment protocols were as follows: wavelength, 820 nm; power output, 200 mW; continuous emission mode; irradiating time, 20 s per point; fluence, 32 J/cm<sup>2</sup> per point; treatment frequency, twice a week (excluding weekends); and treatment duration, three consecutive weeks. Whereas, the supplements protocol for both groups was the same, as follows: subjects with a serum level of vitamin D3 <40 ng/dL, who received replacement according to their serum levels, and all the subjects had a daily intake of 100 µg of oral selenium. The biochemical (FT3, FT4, antiTPO and antiTG) and anthropometric measurements were evaluated.

**Results:** Our findings showed significant improvement in group 1 parameters (PBM+ supplements) compared with group 2 (supplements only) in terms of weight loss and reduction in parameters: BMI, hip and waist circumference, waist/hip ratio, TSH, antiTPO, antiTG and treatment dose of LT4 ( $p < 0.05$ ).

**Conclusion:** Our results, for the first time, demonstrated an efficacy of PBM delivered at a lower fluence with supplements in restoring thyroid function, anthropometric parameters and lifestyle factors in patients with HT. Hence, extensive studies with a longer follow-up period are warranted.

# PHOTOBIMODULATION AT 904NM REDUCES SYMPTOMS OF INFLAMMATORY BOWEL DISEASE: EARLY RESULTS FROM A PILOT SINGLE ARM FEASIBILITY STUDY

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## Abstract

**Learning objectives:** Audience will

1. Learn about common symptoms of inflammatory bowel disease.
2. Observe PBM study application methods to reduce fatigue in IBD.
3. View the results of PBM in young people with IBD who express symptoms of fatigue.

**Brief Introduction:** Fatigue is the key contributor to functional impairment and poor quality of life in inflammatory bowel disease (IBD) and many other chronic diseases while remaining a challenge to treat. We investigate if photobiomodulation (PBM) improves fatigue in youth with IBD.

**Methods:** The methods of our world-first pilot clinical study have been published (<https://doi.org/10.3390/biomedicines11082179>). Ethics approval no.: HREC/MML/62140. We apply weekly 904nm PBM (700Hz; 720mW total) to the large thigh muscles (total energy/application: 129.6J) and abdomen (total energy/application: 861.3 J). We recruit young adults (18 to 35 years old) diagnosed with IBD with significant fatigue (<30 on FACIT-Fatigue scale). Participants act as their own controls. Fatigue is the primary outcome measure and is evaluated using the FACIT-Fatigue scale where the maximum score is 56, and lower scores indicate worse fatigue. Depression is a secondary outcome. The published minimal important difference for improvement in FACIT-Fatigue scores varies from 2.8 to 6.8 points (DOI 10.1186/s12874-016-0167-6). In our study, fatigue is assessed at baseline (entry to the study), after a non-intervention observational period of 10 weeks, after a 10-week period of weekly PBM treatment, and at exit from the study after a further 10-week non-intervention observational period. We calculate change in fatigue (and depression), the effect size and report it descriptively (mean and SD).

**Results:** Interim results (N=8) demonstrate a large effect size for improvement in fatigue scores. The mean pre-intervention fatigue score is 21.7 / 56 (SD+/-3.5) and mean post-intervention score is 31.9/56 (SD+/-3.4). The mean pre-post intervention difference is 10.1 points (SD+/-4.1) and post-intervention values are 67% higher on average than the pre-intervention scores.

**Conclusions:** Participant-reported interim fatigue scores are improved after 10 weeks of once weekly PBM to the large leg muscles and abdomen. We continue to recruit to the study.

# IMAGING GUIDED LASER APPLICATION IN PHOTOBIMODULATION THERAPY OF AUTOIMMUNE AND METABOLIC DISEASES

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## Abstract

**Learning objective:** Optimal PBM therapy effects require prproper dose planning. Imaging guided estimation of light distribution can optimize biological effects in target volume of autoimmune and metabolic diseases. Introduction: Endre Mester started PMD research in 1965 in Budapest. First observation of “biostimulation” effect was published in 1966. Reduction in Inflammation effects was observed later, based on the observations of the clinical experimental research led to an evidence of immune-modulation effect.

**Methods:** Ruby laser was the first equipment used in Budapest with 1 J/pulse in 1cm<sup>2</sup> surface of depilated mouse skin. Later,he laser devices were HeNe between 5-50 mW. After many years of clinical research, using HeNe laser and Argon ion laser of 500 mW were used. While diode lasers appeared, visible and near infra-red lasers were used. The first non-laser PBM equipment was a narrow-collimated interference-filtered narrow bandwidth red light used with and without highly polarised light. Immune modulating effects were studied with leukocyte and lymphocyte experiments. Imaging modalities were radiography, ultrasonography, MRI, CT and DECT.

**Results:** Experimental cellular, skin and mucosal surface doses showed optimal effects by minimal fluency between 1-4 J/cm<sup>2</sup>, if higher, than 5 mW. After wound healing stimulation anti-inflammatory effects appeared if higher, than 10 mW surface doses were used. The higher output infra-red doses were available, the deeper anti-inflammatory and pain relief biomodulation results were detected in range of 50 - 500 mW. Radiography gave optimal estimation of overlaying tissue thickness for estimating 4 J/cm<sup>2</sup> arriving dose in the depth of target volume (autoimmine inflammation of synovium, of enthesis, of tendon and of muscle), where the biological effect was needed. Ultrasonography has additional advantage of joint effusion thickness measurements, differentiation of actual effusion versus synovial thickenings, differentiation of actual inflammatory enthesitis versus fibrotic residual reactions. Power Doppler ultrasonography shows the level of actual inflammation related blood flow, promoting pretreatment planning of non-healing skin ulcers of diabetes mellitus patients. Elastosonography is a new tool to measure the interstitial oedema level. Dual Electron CT gives colour coded semiquantitative distribution map of uric acid deposition, helping optimal dose distribution.

**Conclusion:** Early decades of pioneer studies of Endre Mester stimulated researchers and clinicians to develop multiple wide indications and therapy modalities for optimal effects of PBM therapy. Imaging guided therapy planning offers optimal dose distribution, optimal laser effects in autoimmune and in metabolic diseases.

# PHOTO BIOMODULATION TREATMENT IN PATIENTS WITH ULCERATIVE COLITIS

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## Abstract

Current UC treatment options still fall short in effectiveness and safety. Rectal inflammation may be particularly difficult to treat. PBM has demonstrated efficacy in various mucosal inflammatory conditions. These observations combined with ex-vivo mucosal healing studies suggest a potential efficacy of this therapy in inflammatory bowel diseases. Therefore, we aimed to assess the safety and efficacy of PBM treatment in UC patients with significant rectal inflammation.

The PhotoPill-ProctCare system comprises a rectal tube that delivers therapeutic 850nm CW, illumination to the rectal mucosa, averaged 1 J/cm<sup>2</sup>. UC patients with clinical and endoscopic evidence of rectal inflammation were enrolled to the study. The rectal device was inserted and activated for 4 minutes. The study included two parts. Part 1 involved 6 treatment sessions over 14 days (n=5). Part 2 included up to 6 additional treatments over 6 weeks (n=6). Primary endpoint was treatment safety. Secondary endpoints were clinical, biochemical, endoscopic, histologic, and microbiome composition parameters during and following the intervention.

All patients tolerated the treatment well. Two patients reported adverse events related to intervention; these were mild in severity and spontaneously resolved (mild abdominal discomfort up to 2 hours post-treatment). Two unrelated events included COVID infection and URTI. In part 2, two patients dropped out after 6 sessions.

Overall, 4/11 patients (36%) achieved clinical remission. Response was observed in 7/11 patients (63%). Mayo score decreased from 7.82±1.4 at baseline, to 4.91±1.93 post treatment ( $p<0.01$ ). Rectal bleeding sub-score decreased from 1.91±0.61 to 1.09±0.67 ( $p=0.03$ ), and stool frequency sub-score decreased from 2.09±1 to 1±0.74 ( $p<0.01$ ) respectively. Mean Ulcerative Colitis Endoscopic Index of Severity decreased from 6.75±1.33 to 5.9±1.5 ( $p=0.02$ ). The number of host (human genome) reads within microbiome samples (likely indicative of shedding of epithelial cells) decreased post-treatment significantly in 4 patients and did not increase significantly in any of the patients. Moreover, several gut bacteria species (e.g. Bacteroides species) and bacterial pathways that are known to be associated with IBD activity, decreased significantly post-treatment.

This pilot study demonstrated the safety and efficacy of rectal Photo-Biomodulation for induction of response and remission in UC patients.

# PHOTOBIMODULATION IMPROVES VISCERAL HYPERALGESIA IN A RAT MODEL OF IRRITABLE BOWEL SYNDROME

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## Abstract

### Three Learning Objectives:

1. To evaluate the impact of Photobiomodulation (PBM) on a rat model of irritable bowel syndrome (IBS).
2. To evaluate the power dependence of the effect of PBM.
3. To assess the potential applicability of PBM for treating IBS symptoms.

**Introduction:** IBS is a chronic gastrointestinal disorder marked by abdominal pain, bloating, and discomfort associated with a change in bowel habits. The pathophysiology of IBS is complex and various treatments have been proposed. However, current treatments are insufficient, and a new treatment approach is desired. This study examined the effects of PBM on visceral hyperalgesia in IBS model rats.

**Methods:** Rats were exposed to restraint stress for 1 hour in a restraint stress cage (4.5 × 4.5 × 18.0 cm) to induce visceral hypersensitivity. After restraint stress, the rats were subjected to PBM or sham irradiation. A barostat catheter was inserted into the colorectum and the rats were habituated for 30 minutes. The catheter was inflated to a pressure of 60 mmHg, and the number of abdominal muscle contractions was measured for 5 minutes. The experiment was divided into two trials. In the first trial, rats were exposed to PBM with average power settings of 1 W, 70 mW, and 18 mW. In the second trial, average power levels were set at 460 mW and 3.5 mW. PBM was percutaneously irradiated on each side of the L6 dorsal root ganglion. The other PBM parameters were set as follows: 808 nm wavelength, 2.79 cm<sup>2</sup> beam area, 300 seconds per side duration, 10% pulse duty cycle, 20 ms pulse width, and 5 Hz frequency.

**Results:** The results from the first trial showed a significant reduction in abdominal muscle contractions with 70 mW and 18 mW, but not with 1 W. In the second trial, the 460 mW setting significantly suppressed abdominal muscle contractions, whereas the 3.5 mW setting did not.

**Conclusions:** The study concludes that PBM can alleviate visceral hyperalgesia induced by restraint stress, suggesting its potential as a new treatment for IBS. It also highlights the importance of optimizing PBM parameters to balance safety and efficacy for potential human applications.



## BONE AND MUSCULOSKELETAL

### EFFECTS OF WHOLE-BODY PHOTOBIO-MODULATION ON PAIN, QUALITY OF LIFE, LEISURE ACTIVITY AND PSYCHOLOGICAL FACTORS IN FIBROMYALGIA SUBJECTS: A 6-MONTH TRIAL

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#### Abstract

**Background:** Managing fibromyalgia (FM) symptoms globally remains challenging. This study aims to evaluate the impact of whole-body photobiomodulation (PBM) compared to placebo PBM on pain, functionality, and psychological symptoms in FM patients.

**Objectives:** This research aims to compare the effects of whole-body PBM and placebo PBM on pain, functionality, and psychological symptoms in FM patients.

**Methods:** 42 subjects were recruited from a private care practice for this triple-blinded, placebo-controlled, randomized clinical trial. Participants received 12 treatment sessions, with assessments conducted at baseline (T0), midway (T1), session completion (T2), and follow-ups at 2 weeks (T3), 3 months (T4), and 6 months (T5).

**Results:** Significant pain reduction was observed at T2, T3, and T5. Quality of life improved significantly at T1, T2, T3, T4, and T5. Leisure activity improved significantly at T2, T3, T4, and T5. Kinesiophobia showed significant differences between groups at T2, T3, T4, and T5. Self-efficacy showed significant differences at T3, T4, and T5. Pain catastrophizing exhibited significant differences only at T5.

**Conclusion:** Whole-body PBM treatment for 4 weeks significantly reduced pain and improved quality of life in FM patients. Improvements in kinesiophobia and self-efficacy were observed in short-term and long-term assessments, while pain catastrophizing improved at the 6-month follow-up. Whole-body PBM emerges as a promising multifactorial treatment option for FM patients, but further studies are needed to validate these results.

# EMPOWERING AND INSPIRING THE PBMT CLINICIAN: BRIDGING BENCH-SIDE TO BEDSIDE

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## Abstract

Chronic musculoskeletal (MSK) conditions affect a significant portion of the population, imposing a substantial healthcare burden globally. Over the last five decades photobiomodulation therapy (PBMT) has been offering a proven solution for chronic pain in the MSK sphere where other treatments have significant limitations. PBM2024 aims to delve into the scientific foundations, explore emerging research, and examine clinical trials to enhance our understanding of PBMT and broaden its applications. Yet despite its efficacy, the PBMT community faces two key challenges: disseminating knowledge to the wider medical community, and effectively implementing PBMT for tangible healthcare benefits.

In this presentation, I share insights from my clinical team's experience in addressing the latter challenge, drawing from over 12 years of clinical immersion in PBMT. I discuss the broader impact of MSK disorders on individuals, families, workplaces, and communities, as well as on other healthcare providers, highlighting the efficacy of PBMT within this context. We have developed and utilised a model that bridges the gap between bench-side and bedside, turning scientific research into practical therapeutic interventions, which I share. My presentation, grounded in clinical practice rather than academia, reflects thousands of patient encounters where scientific knowledge is translated into tangible improvements in patient morbidity.

Our therapeutic approach aligns with the biopsychosocial model of patient care, considering factors such as comorbidities, lifestyle, patient expectations, and the nuanced pathway of tissue healing. Of some significance is that we focus on treating patients rather than depending on their imaging results, acknowledging the frequent disparity between the two. I address the typical hurdles encountered during the patient's treatment journey and how we manage these challenges while aligning with patient expectations.

I educate on navigating all these complexities as we harness PBMT's full potential in a holistic treatment approach which consistently results in positive clinical outcomes.

My presentation explores how to effectively apply PBMT in clinical practice, empowering clinicians to deliver successful, compassionate care to patients suffering from chronic MSK conditions, aiming to inspire, change, and advance the field of PBMT for the betterment of patient outcomes.

# RECENT PHOTOBIMODULATION RESEARCH FOR TREATING OSTEOARTHRITIS AND DEGENERATIVE MYELOPATHY IN THE CANINE PATIENT

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## Abstract

In the past few years, there have been several new studies published examining the use of photobiomodulation (PBM) alone or as part of a multimodal approach for treating various musculoskeletal and neurological conditions including osteoarthritis and degenerative myelopathy in the canine patient. This recent research combined with modeling studies for light tissue interactions have contributed to the understanding of effective dosimetry for deep tissue conditions in the veterinary patient.

In three recent publications, including two randomized placebo controlled clinical trials for treating moderate to severe naturally occurring osteoarthritis in dogs as well as a retrospective study on the use of PBM combined with rehabilitation therapy for the treatment of Canine Degenerative Myelopathy (CDM), patients received on-contact treatments utilizing 980nm laser light to the affected area(s) ranging from 10-20 J/cm<sup>2</sup> (and 1-4 W/cm<sup>2</sup>). In the osteoarthritis studies, PBM treatment resulted in statistically significant reductions in clinician assessed lameness scores of patients, pet owner/handler pain scoring via validated clinical metrology instruments, and either the ability to reduce NSAID consumption in treated patients (in one study) or better and longer lasting results vs. NSAID administration (in the second study). In the retrospective study for CDM, the application of higher dose PBM combined with rehabilitation therapy resulted in significantly delayed progression of clinical signs related to the course of the disease, and increased survival compared to a lower dose PBM group and with historical controls reported in the veterinary literature.

Dosimetry for these studies will be discussed as well as findings related to potential for reducing or delaying the need for concomitant use of medications including non-steroidal anti-inflammatories as part of the multimodal management of chronically painful canine patients.

# EFFECTIVENESS OF PHOTOBIMODULATION AND REHABILITATION ON PAIN AND FUNCTIONAL RECOVERY IN PATIENTS WITH ROTATOR CUFF PATHOLOGY

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## Abstract

**Background:** Rotator cuff (RC) disorders encompass a wide range of pathological conditions, which include bursitis, tendinitis, tendinosis, partial thickness tears, and full-thickness tears. To treat painful musculoskeletal problems, photobiomodulation (PBM) has been employed as a non-pharmacological alternative PBM, which uses light-emitting diodes (LEDs) and other photo-emitting devices, is a minimally invasive approach used to treat a wide range of conditions.

**Purpose:** The purpose of this study is to evaluate the effectiveness of PBM and rehabilitation on pain and functional recovery in patients with rotator cuff pathology.

**Method:** In this intervention study, measurements were taken before and after treatment. 37 patients with shoulder injuries were screened, out of which 20 patients with rotator cuff injuries were included in the study. Patients were assessed for pain levels using the NPRS at baseline and after 6 weeks.

**Results:** The pain score at pre-intervention was  $7.33 \pm 0.79$ , which decreased to  $2.50 \pm 0.69$  following 10 days of PBM and the pain score was maintained at  $2.50 \pm 0.69$  after 6 weeks structured exercise rehabilitation.

**Discussion:** Using infrared LEDs for PBM modifies cellular and molecular metabolism, resulting in a reduction of pro-inflammatory cytokine levels (mRNA COX-2 and mRNA) and neutrophil and histiocytic counts in the treated area. Therefore, PBM and exercise therapy shows promising results in the reduction of pain and improves functional activity in clinical practice.

Key words: Rotator Cuff pathology, Photo Biomodulation, Pain, Functional Recovery

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# PHOTOBIO-MODULATION FOR THE TREATMENT OF KNEE OSTEOARTHRITIS: THERAPEUTIC EFFECTS AND POSSIBLE MECHANISM

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## **Abstract**

Knee osteoarthritis (KOA) is a common chronic and degenerative disease in clinical practice. During the development of KOA, its pathological features are articular cartilage degeneration, osteophyte formation, subchondral bone changes, and synovial hyperplasia of the joint. At present, the main treatment methods of KOA include conservative treatment and surgical treatment. Conservative treatment mainly consists of health education, weight loss, medication and physical therapy. Photobiomodulation(PBM) therapy is a type of physical therapy and utilizes non-ionizing light sources including laser and light emitting diodes(LED) in the visible and near-infrared spectrum. It is confirmed that PBM therapy produces stimulatory effect on healing and has the ability of modulating the inflammatory process in different tissues, including synovium and cartilage of KOA. Although the effects of PBM in KOA patients has been studied for many years, but the effects is controversial due to differences in study design and execution among these studies. In addition, there is no unified standards for the optimal treatment strategies, parameters and course, which hamper the application of PBM in KOA. Moreover, the mechanism of PBM in the treatment of KOA remains unclear because the current studies are all phenotypic studies on cartilage matrix metabolism, inflammatory factors, central sensitization, oxidative stress, etc. In this review, we have reviewed the progress in research on the therapeutic effects of PBM for KOA and discussed the underlying mechanism. This will contribute to the further study and application of PBM in KOA patients.

# LASER THERAPY AS AN ALTERNATIVE TREATMENT FOR MAXILLARY OSTEONECROSIS

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## Abstract

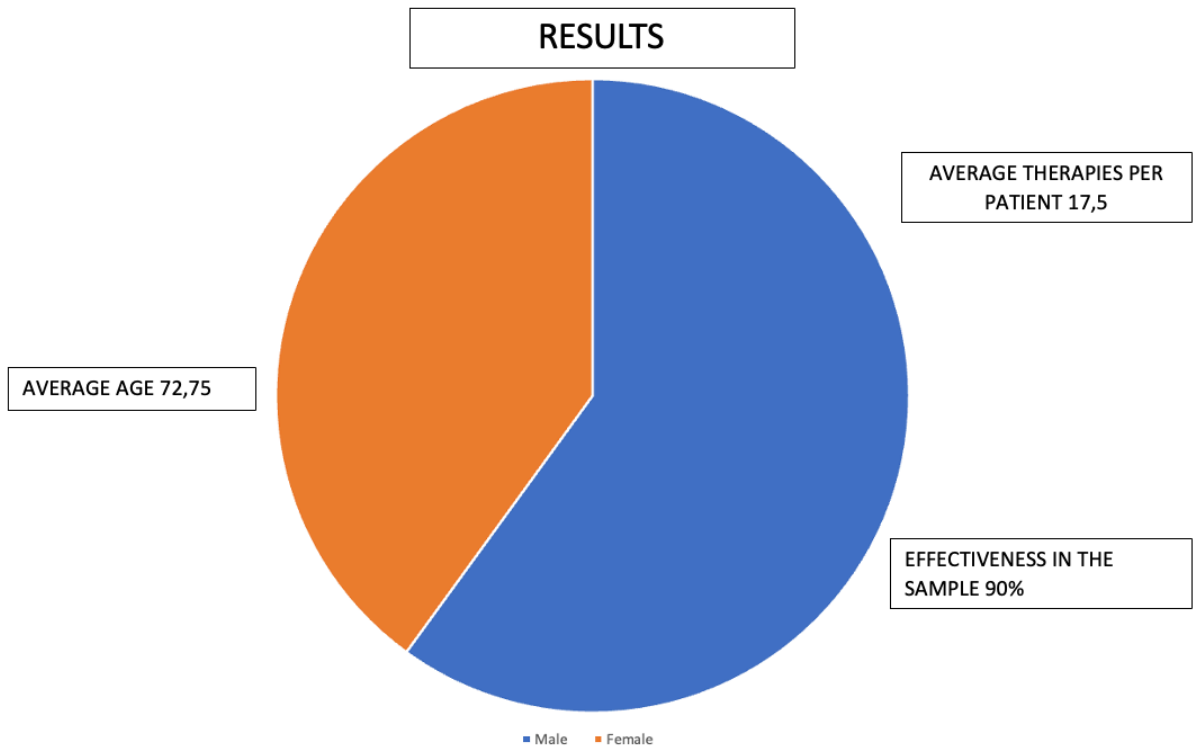
### Three Learning objectives:

1. Describe the treatment of maxillary osteonecrosis performed with Er,Cr laser: 2780nm, 650nm diode laser, 808nm diode laser (ILIB).
2. Explain the bases of photodynamic therapy and ILIB therapy used in the treatment of osteonecrosis of the jaw.
3. Cite parameters, techniques and protocols used in the treatment of osteonecrosis of the jaw. with different laser wavelengths.

**Brief Introduction:** Osteonecrosis of the jaw is the exposure of necrotic bone in the jaws due to poor vascularization. In most cases it is associated with the consumption of antiresorptive drugs (Bisphosphonates) in patients receiving treatment for pathologies such as osteoporosis or oncological patients with local and systemic involvement. The therapeutic objectives for the management of osteonecrosis related to bisphosphonates are aimed at improving the quality of life of patients; in this case, laser therapy is presented as an alternative treatment.

**Method:** Debridement and resection of the necrotic tissue was performed, profusely washing with erbium laser, using the protocol (see figure 3). Subsequently, photodynamic therapy with 0.001% methylene blue and extraoral lymphatic drainage with a 650 nm diode laser were performed, according to the protocol (see figure 3). To conclude the treatment, ILIB therapy was performed with an 808 nm diode laser on the radial artery in the left hand for 20 consecutive daily sections.

### Results including statistical analysis:



**Conclusions:** The use of laser technology can be considered a useful and predictable tool in the management of maxillary osteonecrosis since its various applications allow us complete control of the bacterial population in addition to stimulating tissue healing.

# ACUPUNCTURE

## PHOTOACUPUNCTURE AND ITS EFFECT ON TMJ

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### Abstract

#### Learning Objectives:

1. Learn integrative treatment approaches, including PBM therapy and acupuncture
2. Review the functional mechanisms of PhotoAcupuncture
3. Reveal the physiological effect of photoacupuncture on TMJ

**Introduction:** This PBM – RoM (range of motion) Study seeks to better understand PBM light energy's effect on masseter (jaw) muscle range of motion, using PBM Light. This handheld photobiomodulation device emitting red and near-infrared light energy to applied on meridian points of the masseter muscle. The integrative photoacupuncture demonstrate the positive physiological effect on the range of motion of the jaw muscle which essential for dentistry. This group project's purpose is to promote integrative treatment modalities with photoacupuncture.

**Methods:** ROM measure on four sites of each subject, bilateral meridian points ST6 (stomach 6) and ST 7 (stomach 7), located on the masseter muscles. Render PBM Light 2.5 mins per site. The participant will measure pre and post ROM of TMJ. This is a multicenter (N= 317) that was conducted from April-August 2023 using a handheld red and infrared PBM unit device with 630nm, 660nm, and 850 nm wavelength LED. After verbal consent is reviewed, locate the 4 targeted sites. Proceed to assess if any tender spot is present, palpate masseter muscle and log it on a data sheet. Begin with the pre-tx ROM measurement. All measurements are to be done in millimeters, with the zero-line aligned with the incisal edge of the lower central incisors. With the subject's mouth comfortably, fully open, take measurements against the subject's incisal edge of the upper central incisors. Begin ST6 treatment with PBM Light by using a 2.5 minute timer in contact mode (tissue seal) in circular, sweeping motion. Then move up to ST7 and repeat. Proceed to do the same on the opposite side; ST6 and ST7 -total of 10 minutes PBM Light treatment. Measure post ROM.

**Results & Conclusions:** Jaw muscle range of motion in participants increased by 3.48 mm or 12.47%. When the activation of ST6 and ST7 meridian points, we'll have positive physiological change of the masseter muscle by increasing the range of motion of the jaw movement.



# PHOTOBIMODULATION THERAPY IN KNEE OSTEOARTHRITIS - THE IMPORTANCE OF TREATMENT LOCATION, INCLUDING ACUPUNCTURE POINTS: A NARRATIVE REVIEW

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## Abstract

**Introduction:** More than 30 placebo-controlled, randomized clinical trials of photobiomodulation (PBM) in knee osteoarthritis (KOA) have been published, some of which have focused on targeting acupuncture points. Systematic reviews have confirmed its potential in reducing KOA-related pain and disability. Local inflammation is a key driver of KOA, and it may be reduced by applying PBM to the synovial region. Thus far, the optimal PBM wavelength-dependent energy density per treatment spot in the synovial region has been approximated. A next logical step is to identify the optimal sites for irradiation. It is unclear whether targeting acupuncture points with PBM, i.e., laser acupuncture (LA), in and outside this region brings additional effects.

**Methods:** We analyzed the reports of placebo-controlled, randomized clinical trials with explicit site-specific treatment locations included in the most recent systematic reviews of PBM and LA in KOA (Stausholm et al 2019 and Chen et al 2019, respectively). The anatomical locations of the treatment sites were compared.

**Results:** Twenty-three trials were analyzed for the anatomical sites of laser application. The medial, lateral and posterior aspects of the knee were predominantly irradiated. Comparison of treatment sites around the knee joint showed points common to both PBM and LA. In some LA trials, acupuncture points overlying muscles, nerves and blood vessels distant from the knee joint were additionally irradiated.

**Conclusion:** Co-location of PBM and LA treatment sites was identified at the medial, lateral and posterior aspects of knee joint covering the area of the synovium. In some LA trials, acupuncture points beyond the knee joint which target different anatomical structures, were also treated. We hypothesize that irradiation beyond the synovium may add additional benefit through effects on the vascular supply, nerves and lymphatics. Laser irradiation at anatomically selected sites in PBM and acupuncture points around the knee joint as well as acupuncture points beyond the joint can modify the pathophysiology of knee osteoarthritis.

## 3 Learning Objectives:

1. Understand the anatomical targets of PBM and Laser Acupuncture points.
2. Compare the differences between Traditional Chinese Medicine and Western Medical Acupuncture concepts.
3. Identify mechanisms relevant to PBM and LA.

# THE EFFECTIVENESS OF LASER ACUPUNCTURE AND INTENSIVE SHORT- TERM DYNAMIC PSYCHOTHERAPY IN TREATING MAJOR DEPRESSION. (A RANDOMIZED CLINICAL TRIAL)

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## Abstract

**Background:** While major depression has been treated with Laser Acupuncture (LA) and Intensive Short-Term Dynamic Psychotherapy (ISTDP), the relative efficacy of these two methods and the combination of the two is uncertain. ISTDP is a form of dynamic psychotherapy focused on enabling the experience and processing of blocked complex feelings, while LA is centered on opening blocked energy meridians.

**Objectives:** The aim of the current study was to compare the effectiveness of LA and ISTDP, as well as the combination of both, in the treatment of major depression.

**Methods:** A randomized controlled trial was conducted with 45 depressed patients divided into three equal groups (15 patients per group): Group I) LA, Group II) ISTDP, and Group III) LA and ISTDP combined.

Intervention Protocol; Laser Acupuncture:

Over 8 weeks, 12 interventions

- First 4 weeks: 2 sessions per week

- Next 4 weeks: 1 session per week

Comprised the stimulation of Body Acupuncture Points , and Ear Acuouncture Points , identified based on TCM diagnostics, using continuous contact Gallium-Aluminum-Arsenide Laser (GaAlAs), with an average output power of 200 mv , wavelength of 980 nm, and a dosage of 4 J/point for body APs and 1J/point for ear APs .

The participants were assessed at six different time points using the Hamilton Rating Depression Scale ( HDRS ) , Structured Clinical Interview for DSM Disorder ( SCID ) and Symptom Checklist-90 ( SCL-90 ) , at baseline, session 8, session 12, 1-month follow-up, 2-month follow-up, and 3-month follow-up.

Results indicated that over time, scores for HDRS, SCID, and SCL-90 decreased significantly within the laser acupuncture, laser acupuncture with ISTDP, and ISTDP groups. In the laser acupuncture with ISTDP group, HDRS scores were lower than the laser group at the eighth session and second follow-up.

However, the reduction in SCID score was not notable across the three groups. SCL-90 scores in the laser acupuncture with ISTDP group were consistently the lowest at various time points compared to the other two groups.

**Conclusions:** ISTDP and LA could be beneficial therapies for treating Major depression, potentially showing improved results in Depression symptoms when used in conjunction.

# CURRENT STATUS OF INTERNATIONAL STANDARDS IN PBM LASER ACUPUNCTURE DEVICES

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## Abstract

International standards (IS) are established to facilitate the exchange of materials or services between countries and to promote international cooperation in intellectual, scientific, technical, and economic activities. The International Organization for Standardization (ISO) is an international standardization organization consisting of representatives of standards-setting organizations from member countries. International Electrotechnical Commission (IEC) adjusts standards in the fields of electricity, electronics, telecommunications, and nuclear power. Each government establishes policies to promote the development and utilization of national standards for the harmonization of IS and national standards. Manufacturers of PBM devices are required to comply with these standards to obtain marketing permits from domestic and/or foreign regulators. In a competing market, compliance with standards acts as a guarantee of safety and performance that becomes a factor trusted by consumers.

All electrical equipments are required to comply with IEC 60601-1 (Medical Electrical Equipment - Part 1: General Requirements for Basic Safety and Essential Performance) and IEC 60601-2-22 for professional laser light source devices and IEC 60601-2-57 for home phototherapy devices.

Laser acupuncture (LA) is a kind of PBM treatment combined with traditional medicine acupuncture technique. ISO technical committee 249 established ISO 22466 (Traditional Chinese medicine - Laser acupoint devices) in 2021. It specifies requirements and test methods for laser acupoint devices. It covers certain LA devices using wavelength range of 400 nm to 1400 nm. Any carbon dioxide type lasers and invasive stimulations are out of scope. For safety issues, it requires maximum output power of a single beam shall not exceed 200 mW and maximum energy density under 10 J/cm<sup>2</sup>. ISO 22466 is expected to provide safety recommendations to manufacturers and users whereas it might lead to a technical limitation in regulatory fields.

# COMPARISON BETWEEN THE EFFECTS OF DIETARY THERAPY AND EXERCISE, LASER ACUPUNCTURE AND ACUPUNCTURE IN WEIGHT LOSS OF OBESE AND OVERWEIGHT WOMEN.

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## Abstract

Overweight and obesity are chronic health conditions defined as an increase in the size and amount of fat cells in the body. It should be considered as a disease and proper intervention should be done with timely diagnosis.

Laser acupuncture and acupuncture are two different methods used in weight loss through different mechanisms that occur through the secretion of chemical substances such as endorphins, and ACTH serotonin and decreases proinflammatory cytokines such as interleukin 6, and tumor necrosis factor- $\alpha$ .

This trial used a randomized; four-arms group design to compare the efficacy of Dietary Therapy and exercise, Laser Acupuncture and Acupuncture therapy in weight loss of obese and overweight women. Hundred overweight and obese women with a BMI between 25 to 39.9 were included in the study.

The patients were divided into four equal arms (each group: 25 patients): Group 1) group of diet therapy and exercise, group 2) acupuncture group with diet therapy and exercise, group 3) laser acupuncture therapy group with diet therapy and exercise group 4) The combination group of acupuncture and laser acupuncture along with diet therapy and exercise

In the laser acupuncture intervention group, a trained therapist in this field and according to standard protocols applied 1 Joule of Gallium-Aluminum-Arsenide Laser (GaAlAs) with a wavelength of 980 nanometers and a device power of 200 milliwatts for each of the selected ear acupuncture points. Additionally, for the body acupuncture points a dose of 4 Joules with a wavelength of 980 nm and a device power of 200 milliwatts was applied for each point. The treatment was administered in 12 laser acupuncture sessions, twice weekly (with two days between sessions).

The mean fat mass reduces about 2.8 unit after intervention compare to baseline in the diet group. In addition, the only significant p-value for the interaction variable belong to mixed treatment group, this means that patients in mixed treatment group experienced about -2.76 unit lower mean fat mass than those in the diet group during the study (p-value<0.0001).

The study suggests that the various treatments had diverse effects on BMI, fat mass, and free fat mass, with some groups exhibiting more significant changes than others.

# HYPOTHESIZING A CENTRAL THALAMIC CONTRIBUTION IN A COHORT OF CRPS PATIENTS DEVELOPING TOTAL UNILATERAL ANS DYSFUNCTION: WITH PBM TREATMENT PROTOCOL

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## Abstract

### Learning Objectives:

1. Clinical examination to elicit symptoms and signs to show a degree of ANS dysfunction extending totally unilaterally, patients generally unaware of this unilateral nature apart from the localised original presenting area with obvious CRPS symptoms and signs .
2. Dampening of the CNS and treatment of PTSD with PBM
3. PBM protocol to produce sympathectomy effect + response similar to LA lumbar sympathectomies Titration of treatments according to response to PBM

**Brief Introduction:** CRPS is a clinical diagnosis of signs and symptoms. Swelling, colour, sensitivity/ allodynia, 'electric shot' pain, patients with chronic pain and CRPS have central sensitivity and a heightened nervous system and often associated PTSD. Aetiology is unknown but there is thought to be a genetic and epigenetic predisposition

Patients can occasionally develop CRPS on both sides of the body and upper and lower limbs .

In this study patients who are unaware of showed unilateral changes that extended up one whole side of the body

**Method:** Clinical Assessment and diagnosis of a unilateral involvement which dictates treatment protocol.

Treatment must be totally contralateral

PBM CONTRALATERAL lymphatic treatment with PBM laser acupuncture, and THOR LED lymphatic protocol

PBM laser acupuncture points - including tranquillising, sedative, analgesic and ear stress points (shenmen )

Treatment frequency and dose titrated according to response and sympathectomy effect observed.

**Results:** Collection of Clinical case studies.

Symptoms and signs of CRPS collated at pre and post each consultation and treatment.

eg Swelling, colour, sensitivity/ allodynia, 'electric shot' pain ,movement, resting sleep,

Area of involvement and intensity of sensitivity changes are documented and over course of treatment showing affected side becoming more normal and similar to the non affected side,

**Conclusions:** Patients with CRPS can have a more extensive area affected and can extend the whole one side of the body

PBM is a simple, noninvasive treatment and with its sympathectomy like changes it is safe and can significantly help reduce patients CRPS symptoms and signs.

The contralateral treatment seems to help switch off the Glitch in the nervous system (ANS)

The PBM laser acupuncture treatment is important to help the central and thalamic involvement

## YOUNG INVESTIGATOR- CLINICAL STUDIES

### NOVEL THERAPEUTIC PBM APPROACH WITH FLATTOP BEAM PROFILE IN PAEDIATRIC RECURRENT APHTHOUS STOMATITIS. CASE SERIES WITH 3-MONTHS FOLLOW-UP

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#### Abstract

##### Learning objectives:

1. Efficacy of therapeutic  $\lambda 980$  nm PBM delivered with flattop beam profile in all recurrent aphthous stomatitis (RAS) subtypes.
2. PBM therapy can offer an immediate pain relief and rapid wound healing in all RAS subtypes.
3. Study's PBM dosimetry and treatment protocols can be reproduced in future RCTs

**Introduction:** RAS are one of the most common oral mucosal lesions and very debilitating, especially in paediatrics. The current pharmacotherapy offers pain relief, but not without side-effects and therefore, PBM can be an alternative therapy. To the best knowledge of the authors, there is no published study explored the efficacy of  $\lambda 980$  nm PBM in management of all RAS subtype in paediatrics, and therefore our study was conducted to bridge this scientific literature gap.

**Methods:** Prospective observational clinical study aimed to evaluate  $\lambda 980$  nm PBM efficacy in symptomatic RAS management in paediatrics. Pain intensity and wound healing were evaluated at following timepoints: T0: pre-treatment; T1: immediately after 1<sup>st</sup> PBM session; T2: 5 h post-1<sup>st</sup> PBM session (via telephone call); T3: immediately after 2<sup>nd</sup> PBM session (three-days post 1<sup>st</sup> PBM session); T4: three-day follow-up (after complete PBM treatments); T5: two-week follow-up; T6: three-month follow-up. PBM dosimetry and treatment protocols:  $\lambda 980$  nm; 300mW; 60 s; 18 J; CW; flattop beam profile; 1 cm<sup>2</sup>; 18 J/cm<sup>2</sup>; twice a week irradiation.

**Results:** At T1, significant immediate pain intensity relief was reported. 33.33% recorded "4" and 66.67% reported "5" on quantitative numeric pain intensity scale (NPIS), and this continued to improve significantly (83.33%) at T2. All the subjects reported "0" on NPIS at T3, T4, T5 and T6. Significant reduction of lesion surface area (> 50%) at T3 compared to T0. At T4, T5 and T6, complete healing (100%) with no evidence of lesion recurrence.

**Conclusions:** This is the first report demonstrating  $\lambda 980$  nm efficacy in RAS subtype management in paediatrics and adolescents based on 3-month follow-up whereby its dosimetry and treatment protocols were effective from scientific and practical standpoints. Hence multicenter RCTs with large data are warranted to validate its reproducibility and to enrich our knowledge in PBM application in all RAS subtypes.

# NEAR-INFRARED LOW POWER LASER PHOTOBIMODULATION THERAPY FOR BURNING MOUTH SYNDROME: A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL

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## Abstract

This project had as learning objectives: efficacy assessment, safety/tolerability and long-term treatment effects of the near-infrared low-power laser photobiomodulation therapy (PBMT) in relation to the standard therapy with topical clonazepam in Burning Mouth Syndrome (BMS) management. BMS is characterized by a burning sensation of the oral mucosa despite the absence of local or systemic signs. Different therapies have been studied, with limited level of evidence. Topical clonazepam is considered an effective treatment, but the potential risk of side effects must be considered. PBMT have emerged as an option since low power laser act an inhibitor of pain mediators without side effects. Thus, this randomized double-blind controlled clinical trial aimed to compare the effects of both therapies for BMS management. The intervention group (n = 11) underwent 6 sessions (twice a week for 3 weeks) of PBMT with near-infrared low power laser (880nm, 100mW, 6J/cm<sup>2</sup> at the symptomatic area) and rinsed a placebo solution. The control group (n = 10) rinsed 5 ml of 0.5mg/mL clonazepam solution, 3 times a day for 3 weeks, and received sham PBMT. The evaluations were carried out by a blinded research, at the baseline, end of treatment, 30 and 60 days of follow-up, according the patient-reported outcome measures recommended by the IMMPACT-II. The mixed effect models analysis, associated with the Dunnett post-hoc test, showed pain reduction (numerical rating scale) and improvement in oral health related quality of life assessment at the end of the treatment in both groups (p < 0,05), without difference between them. Interestingly, only in PBMT group was observed a significant improvement at psychological domain evaluation (Beck's Depression Inventory) the maintenance of the positive result at the follow-up evaluation. All patients concluded the protocol and none of them used analgesics or other drugs not prescribed in this trial. None reported any adverse effects and evaluated both treatments positively (patient global impression of change). These results indicate that both therapies are efficient in controlling the BMS symptoms and improving the quality of life of these patients. However, PBMT positive effects were maintained after the end of the treatment.

# PHOTOBIMODULATION THERAPY WITH 445 NM DIODE LASER FOR PERI-IMPLANT SOFT TISSUE HEALING: A TRIPLE-BLIND, SPLIT-MOUTH, RANDOMIZED CONTROLLED TRIAL

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## Abstract

**Introduction:** Low-power laser treatment is a non-invasive method to stimulate fibroblastic function and tissue repair, which leads to regulation of cell reactions such as increase in protein production, cell proliferation and migration, anti-inflammatory signaling, immune regulation, pain reduction and tissue repair.

In implant-based reconstruction, attention should be paid to the state of health, the quality of the soft tissue around the implant, and the speed of restoration. The quality and speed of restoration plays an important role in determining the success of the treatment. So far, no study has been conducted to investigate the effect of low-power laser with a wavelength of 445 nm on the soft tissue repair around the implant after the second stage surgery.

**Materials and methods:** This split-mouth, triple-blind, randomized controlled clinical trial study was conducted for patients to receive dental implants bilaterally, after performing the second stage surgery. After performing the process of uncovering and healing abutment placement, using a simple randomization method, on the intervention side, the soft tissue surrounding the implant was irradiated by diode laser for 15 seconds in the buccal and lingual areas of each tooth on days 0, 3, 7 and 14 after surgery. On the control side, the probe of the laser device was used in the off-mode state. The outcome of the study is the early wound healing score, which was measured on days 3, 7, 14, and 21 after surgery by observing the photos of the patients in these sessions.

**Results:** The wound healing score on days 3 and 7 was significantly higher on the intervention side than on the control side ( $p=0.04$  and  $p=0.01$ , respectively). However, on days 14 and 21, no statistically significant difference was observed between the two sides in terms of wound healing score ( $p=0.20$  and  $p=0.17$ ).

**Conclusion:** Based on the results, diode laser photobiomodulation with a wavelength of 445 nm was able to bring the surgical tissue to ideal repair in a shorter period of time, for one week.



# EFFECT OF PHOTOBIMODULATION THERAPY ON NEUROSENSORY RECOVERY OF PATIENTS WITH MANDIBULAR NERVE INJURY: A RANDOMIZED TRIPLE-BLINDED CLINICAL TRIAL

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## Abstract

**Introduction and aims:** There is a possibility of neurotmesis of the inferior alveolar nerve (IAN) in mandibular fractures, which leads to neurosensory impairment. In this study, we aimed to investigate the efficacy of photobiomodulation therapy (PBMT) in patients with neurotmesis of of IAN following trauma and mandibular fracture.

**Methods:** This study was carried out on patients who suffered from neurotmesis of IAN at least for 6 months. In the intervention group, laser irradiation was applied with a low-level GaAlAs diode laser (continuous wave of 810 nm wavelength, power of 200 mW, and energy density of 12–14 J/cm<sup>2</sup>). In the control group, the laser probe was turned off and placed on the affected area. LLLT was done for 12 sessions. Light touch sensations, two-point discrimination, thermal discrimination (cold and warm stimulus), electric pulp test (EPT), and oral health impact profile (OHIP)-14 questionnaire were performed before the intervention, immediately after each PBMT session, and after 3, 6, 9 and 12 months.

**Results:** In both groups, 3 and 23 patients were female and male, respectively. The results showed significantly improved light (cotton swab), light (wooden cotton swab), and sharp (dental needle) touch sensations, and two-point discrimination test in the PBMT group after the 10th, 11th, 10th, and 10th session, respectively. Two-way repeated measure ANOVA revealed that the trend of light touch sensation with cotton swab and two-point discrimination test was statistically significant ( $p$ -value = 0.002 and 0.001, respectively). The results of OHIP- 14 test showed a significantly higher mean in the PBMT group 3 months after PBMT.

**Conclusion:** PBMT could be an effective treatment for late post-traumatic nerve neurotmesis following a traumatic mandibular fracture.

# PHOTOBIMODULATION THERAPY WITH 810 NM DIODE LASER FOR RECOVERY OF MID-FACE SENSATION AFTER LE FORT 1 SURGERY: SPLIT-FACE, RANDOMIZED CONTROLLED TRIAL

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## Abstract

**Introduction:** Many facial skeletal deformities treated with orthognathic surgeries and Le Forte 1 osteotomy is one of the most frequent orthognathic surgeries. This technique has post-surgical consequences like neurosensory changes in face. The aim of this study was determining the effect of photobiomodulation treatment with 810 nm diode laser on the restoration of sensation in the mid-face area after Le Fort 1 maxillary surgery.

**Materials and methods:** In this split-face randomized controlled clinical trial study, 15 patients were subjected to Le Fort 1 maxillary osteotomy surgery, on the intervention side, GaAlAs diode laser radiation with a wavelength of 810 nm and a power of 250 mW at 13 points for 24 seconds, from the vermilion of the upper lip to the zygoma. Sensory evaluations on the day before surgery and on days 1, 3, 7, 14, 21, 28 and 35 after surgery using four tests, as well as patient satisfaction with the VAS index were measured.

**Results:** Two-point discrimination score changes on day 7 compared to day 1 between intervention and control sides in upper lip ( $p=0.07$ ) and nasolabial fold ( $p=0.08$ ). The changes in Brush stroke directional score was the same between the two sides in the upper lip ( $p=0.33$ ). This parameter in the nasolabial fold on day 7 compared to day 1 did not differ between the two sides ( $p=0.40$ ). The thermal discrimination score changes in the upper lip on day 7 compared to day 1 did not differ between the two sides ( $p=0.53$ ). The trend of changes in the Sharp and blunt discrimination score in the upper lip on the 7th day increased compared to 1 in the intervention side and decreased in the control side ( $p=0.01$ ). However, no difference was observed in the nasolabial fold in this interval ( $p=0.31$ ). The changes in the VAS index on the intervention side on day 7 compared to day 1 had a statistically significant increase ( $P<0.0001$ ).

**Conclusion:** Considering that photobiomodulation is a non-invasive treatment, it can be used to speed up the recovery of sensation in the mid-face area after Le Fort 1 maxilla surgery.

# EFFECT OF PHOTOBIMODULATION THERAPY ON THE MANAGEMENT OF DENTAL TRAUMA IN ANTERIOR PERMANENT TEETH: RANDOMIZED, DOUBLE-BLIND, CONTROLLED CLINICAL TRIAL

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## Abstract

Childhood and adolescence are periods of high risk for traumatic dental injuries (TLDs), which occur by impact on teeth, surrounding hard and soft tissues. In general, dislocations have an unfavorable prognosis, due to the frequent presence of root resorption, which can lead to loss of the dental element. Photobiomodulation therapy (PBM) can improve cell proliferation, migration, differentiation, growth factor secretion, among other cellular biological activities. The aim of this randomized, double-blind, controlled clinical trial was to evaluate the effect of low level laser (660nm and 808nm) on analgesia and pulp tissue response in traumatized anterior permanent teeth.

**Materials and Methods:** This study was carried out with 41 participants, totaling 60 teeth that were randomly divided into 3 groups: Group1: retainer + placebo PBM; Group2: containment + infrared PBM (880nm); Group3: containment + red PBM (660nm). Participants underwent 4 sessions of PBM (1x/week) and were evaluated immediately before and after each intervention, at the initial times, 7, 14, 21 and 28 days after the intervention, through pain level measurements (VAS) and pulp necrosis (pulp sensitivity test and radiographic examination). For data analysis, the Kruskal Wallis test was used, with a significance level of 5%.

**Results:** The median difference in pain from the final minus initial assessment was -1 point in group1, -7 in group2 and -4 in group3, with a statistically significant difference when the three groups were compared with each other ( $p < 0.001$ ), the comparison between groups for the difference in final less initial pain (two by two) was performed only between group2 and 3, ( $p = 0.062$ , Mann-Whitney test). Regarding pulp necrosis, there was no change in group1. Considering only the 22 teeth of groups G2 and G3 with negative results for pulp necrosis at the beginning of treatment, it appears that there was no statistically significant difference between them in relation to the test result at the end ( $p = 0.282$ , Fisher's exact test), with 13 (81.3%) teeth from the G2 group and 3 (50.0%) from the G3 group with a positive result at the end of the study.

**Conclusion:** TFBM with low power laser with emission in the infrared (808nm) and red (660nm) spectrum showed a favorable result evaluating pulp tissue remodeling in relation to placebo.

# PHOTOBIMODULATION THERAPY IN THE PREVENTION AND MANAGEMENT OF RADIOTHERAPY-INDUCED VAGINAL TOXICITY

MARITHÉ CLAES

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## Abstract

### Learning Objectives

1. Investigate the efficacy of vaginal photobiomodulation (PBM) in gynaecological cancer patients
2. Assess the effect of PBM on the quality of life (QoL) of gynaecological cancer patients
3. Define the optimal PBM parameters for vaginal PBM treatment

**Introduction:** The global cancer burden keeps growing, as 1.4 million patients were diagnosed with gynaecological cancers in 2020. While medical progress has led to a rise in long-term cancer survivors, the management of treatment-related complications remains a challenge. Among these complications, radiotherapy-induced vaginal toxicity (RIVT) stands out, adversely affecting patients' quality of life (QoL) and sexual functioning. Unfortunately, symptom-based treatment for RIVT is often insufficient. Research suggests that PBM could be efficient in improving vaginal health and pain, but robust clinical evidence is lacking. Therefore, this trial aims to investigate whether PBM can be used to prevent and manage RIVT.

**Methods :** A prospective, multi-centric, site-randomized, controlled trial was set up at the Jessa Hospital (Hasselt, Belgium) and Ziekenhuis-Oost Limburg (Genk, Belgium) with patients diagnosed with endometrial or cervical cancer undergoing radiotherapy (RT). Participants (n=62) are randomized into the treatment group (PBM and standard vaginal care) or the control group (standard vaginal care). PBM was applied twice weekly during RT and two weeks post-RT using the INTIMLEDs®-device (MostLeds, France). The device has two modes with a wavelength of 639 and 855 nm, a power of 1.8 and 1.3 W, and a fluence of 8.53 and 6.12 J/cm<sup>2</sup>. The patient-reported outcomes consist of questionnaires assessing the patient's symptoms, QoL, sexual health, and satisfaction. The physician reports the vaginal health using validated criteria. Data is collected at the first RT-session, last RT-session, two weeks, three months, and one-year post-RT.

**Results:** Of the 29 eligible patients identified thus far (January 2024), 10 have been enrolled, evenly distributed between the treatment and control arms. Given the limited sample size, a preliminary analysis was deemed unfeasible at this stage.

**Conclusion:** This pioneering multi-centre clinical trial aims to establish the efficacy of vaginal PBM as a supportive intervention in cancer care. Anticipated outcomes include enhanced QoL and sexual well-being among gynaecological cancer patients during and post-RT.

# SUNDAY, AUGUST 25<sup>th</sup>

## SUPPORTIVE CARE FOR CANCER

### PHOTOBIO-MODULATION IN THE MANAGEMENT OF CANCER THERAPY-INDUCED SIDE EFFECTS: WALT POSITION PAPER.

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#### Abstract

##### Learning objectives:

- Highlighting the main indications of PBM in Supportive Care in Cancer.
- Appreciating the levels of PBM evidence in these Cancer Supportive Care indications
- Sharing experts' proposal for PBM parameters in Cancer Supportive Care indications.

**Objective:** This position paper reviews the potential prophylactic and therapeutic effects of photobiomodulation (PBM) on side-effects of cancer therapy, including chemotherapy (CT), radiation therapy (RT), and hematopoietic stem cell transplantation (HSCT).

**Background:** There is a considerable body of evidence supporting PBM efficacy in preventing oral mucositis (OM) in patients undergoing RT for head and neck cancer (HNC), CT, or HSCT. This could enhance patients' quality of life, adherence to the prescribed cancer therapy, and treatment outcomes while reducing the cost of cancer care.

**Methods:** A literature review on PBM effectiveness and dosimetry considerations for managing certain complications of cancer therapy were conducted. A systematic review was conducted when numerous randomized controlled trials were available. Results were presented and discussed at the international consensus meeting at the WALT, by the world expert oncologists, radiation oncologists, oral oncologists, oral medicine professionals, physicists, engineers, and oncology researchers. The potential PBM mechanism of action and evidence of its efficacy through reported outcomes for individual indications were assessed.

**Results:** There is a large body of evidence demonstrating PBM efficacy in preventing OM in certain cancer patient populations, as recently outlined by the Multinational Association for Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). Building on these, the WALT group outlines evidence and prescribed PBM treatment parameters for prophylactic and therapeutic use in supportive care for radiodermatitis, dysphagia, xerostomia, dysgeusia, trismus, mucosal and bone necrosis, lymphedema, hand-foot syndrome, alopecia, oral and dermatologic chronic graft-versus host disease, voice/speech alterations, peripheral neuropathy, and late fibrosis amongst cancer survivors.

**Conclusions:** There is robust evidence for using PBM to prevent and treat a broad range of complications in cancer care. Specific clinical practice guidelines or evidence-based expert consensus recommendations are provided. These recommendations are aimed to improve the clinical utilization of PBM therapy in supportive cancer care and promote research in this field. It's anticipated these guidelines will be revised periodically.

# INCORPORATING PHOTO BIO MODULATION THERAPY IN EARLY INTEGRATION OF SUPPORTIVE CARE, A LOW COST MODULE FOR DEVELOPING COUNTRIES

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## Abstract

**Objectives:** (i) To assess the effectiveness of PBMT in supportive care of oral cancer patients during combined radiation and chemotherapy treatment, (ii) to evaluate its impact on treatment compliance and (iii) to analyse the cost effectiveness of PBMT as a low cost supportive care modality for early integration of supportive care in developing countries.

1. Given the scenario of late stage diagnosis, radiotherapy and chemotherapy are frequently employed as combined modality of treatment causing significant side effects that impair quality of life, occasionally impacting on the continuity of treatment, the outcome of treatment and thereby the overall prognosis.

The Indian Institute of Head and Neck Oncology a charitable cancer center in Indore, began early integration of supportive care

(EISC) since 2022. Photo modulation therapy was later incorporated into the early integration of supportive care for symptoms relief of subgroup of patient of oral cancers undergoing radiation and chemotherapy for better loco-regional control.

For PBMT in our institute we are using Novoduolase & 16 Array cluster model. In Novoduolase there are two wavelengths 660nm & 810nm. 16 Array cluster has 4 electrodes of 660nm and 12 electrodes of 810nm wavelength. The 660nm wavelength is used for healing & regeneration while 810nm wavelength is used for pain & edema. PBMT is given 2 to 3 times in a week during the period of RT and CT

**Methodology:** A prospective nonrandomized clinical observational study was started since 2022. Every cancer patient registered was subjected to series of processes under EISC.

**Conclusion:** Supportive and Curative approaches are layered on one another, depending on the needs of the patient at any given point in time. Our patients were supported throughout the treatment period.

Early integration of nutritional support, multidisciplinary supportive interventions such as speech and swallow therapist interface along with oral care and rehabilitation lead to: improved quality of life, reduced treatment interruptions and improved treatment adherence. PBM therapy could significantly prevent or reduce the severity of many side effects related to cancer therapies. In future it will become an effective as well as cost effective tool for symptoms control and better treatment compliance. Cost benefit results will be shared.

# RADIATION-INDUCED CHRONIC ULCERATIONS AND FISTULAE SUCCESSFULLY TREATED WITH PHOTOBIMODULATION

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## Abstract

About half of cancer patients benefit from radiotherapy, of which over 90% experience skin toxicity. Chronic radiation dermatitis results from direct radiation-induced injuries and can manifest months to years after treatment. Once ulcerations develop in areas affected by chronic radiation dermatitis, therapeutic options are limited and often unsatisfactory. We report the case of a 79-year-old patient who had been dependent on a nasogastric tube for nutrition for the past eight years due to two ulcers and deep fistulae in the frontal and lateral neck. He had undergone surgery and radiotherapy for laryngeal cancer 25 years prior. Given that photobiomodulation has not only shown to stimulate stem cells and induce angiogenesis, but also to reduce radiation-induced tissue inflammation and prevent severe acute radiation dermatitis, we proposed treating this patient with photobiomodulation using deep-penetrating near-infrared light at 830 nm. After 69 irradiation sessions over 10 months, we observed complete remission. Interestingly, the fistulae in the frontal and lateral neck healed consecutively after we adjusted the irradiation angle to ensure sufficient dosimetry reached each ulceration.

# NOVEL IMPLEMENTATION OF PHOTOBIMODULATION THERAPY DECREASES ORAL MUCOSITIS SEVERITY IN PEDIATRIC STEM CELL TRANSPLANT (SCT) PATIENTS

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## Abstract

### Objectives

1. Describe the pathophysiology of photobiomodulation ( PBM).
2. Identify supportive care interventions used for mucositis.
3. Evaluate effectiveness of photobiomodulation.

**Introduction:** Oral mucositis (OM) is a common stem cell transplant (SCT) complication of approximately 90% of pediatric patients undergoing SCT. OM consists of painful ulcerations in the oral cavity that interfere with dietary intake and oral care. Patients with high-grade OM require patient-controlled analgesia (PCA), total parenteral nutrition (TPN) and intravenous (IV) medications thus increasing length of stay (LOS) and hospital costs.

**Methods:** An analysis between a retrospective and an intervention group was completed. Eighty three patients transplanted from January to December 2021 were reviewed. Sixty- two received an allogeneic SCT for a variety of diagnosis and 21 autologous for neuroblastoma. An intervention group consisting of fifty-eight patients received PBM from January to September 2023 while undergoing an allogeneic SCT (55) and auto (3) SCT for neuroblastoma. The analysis looked at OM pain scores, mucositis days, PCA and TPN days, oral care adherence, TPN at discharge, cost analysis of OM and length of stay.

**Results:** PBM was administered to 88% of eligible patients (66). PBM therapy contributed to a 20% reduction in PCA usage (63% vs. 50%). TPN use decreased from a baseline of 91% of patients with an average of 22 days to 83% of patients with an average of 16 days. OM-associated costs decreased on average \$33, 306 per patient and 55% fewer patients were discharged home on TPN. This reduction in TPN was most striking in our leukemia cohort showing a baseline 41% of patients requiring TPN at discharge and in our intervention cohort 6% of patients requiring TPN at discharge. Specifically in our leukemia cohort we demonstrated a LOS reduction from 44 days (n=27) to 40 days (n=17).

**Conclusions:** PBM was implemented as standard of care in our BMT unit with the goal of preventing and treating OM. We sought to determine its effect in OM severity, need for PCA, TPN and hospital costs when compared to routine oral care. Our project demonstrated how PBM could lead to decreased PCA and TPN use, decreased LOS, and minimized hospital costs.



# PHOTOBIO-MODULATION AND SUPPORTIVE CARE IN CANCER: HOW TO CREATE AN OPTIMAL ECOSYSTEM IN THE HOSPITAL SETTING?

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## Abstract

### Three learning objectives:

- Know the medical indications of photobiomodulation in supportive care in cancer.
- Understand the qualitative challenges of a rigorous implementation of photobiomodulation in supportive care in cancer.
- Know how to build an efficient, ergonomic, and financially balanced ecosystem.

**Introduction:** Photobiomodulation is the subject of numerous international recommendations in several indications in supportive oncological care, including those of WALT, including the treatment of mucositis or radiodermatitis. At the same time, many emerging indications are already relevant in daily clinical practice to literally "support" the adverse effects of cancer treatments, such as xerostomia, chemo-induced neuropathy, dysgeusia, dysphonia, dysphagia, trismus, palmar-plantar erythrodysesthesia, osteonecrosis and mucosal necrosis, radiation fibrosis, alopecia, or graft-versus-host disease.

Other medical indications, such as chemobrain or complex pain syndromes treatment, are rich in prospects. Photobiomodulation is currently one of the most relevant non-invasive techniques in supportive care, alongside drug, interventional, or complementary reference approaches.

**Methods:** Cross-referencing between feedback from the largest hospital photobiomodulation center in France and analysis of the literature

**Results:** Nevertheless, to be able to implement photobiomodulation in daily clinical practice in an efficient way, it is essential to define a real ecosystem that integrates several dimensions including the quality of photobiomodulation equipment, the training of nursing staff, the medical filter to retain the relevant indications, the objective evaluation of sessions with the patient, the creation of an information technology tool for prescription and follow-up, but also the organization of the sessions, the ergonomics of the caregivers and finally the medico-economic aspects. By integrating all these dimensions, photobiomodulation can then become a supportive care technique to be offered throughout the care pathway, including in prevention, during cancer treatments, in the event of sequelae symptoms after recovery, or even in complex palliative situations.

# PHOTOBIMODULATION THERAPY FOR POST-RADIATION FIBROSIS IN HEAD AND NECK CANCER: A SERIES OF CASE REPORTS

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## Abstract

### Learning Objectives:

1. Understand the Mechanistic Basis of Photobiomodulation in Treating Post-Radiation Fibrosis in patients with head and neck cancer.
2. Critically Evaluate the Therapeutic Outcomes of PBM Using MLS Laser Devices in Case Reports.
3. Explore the broader implications of MLS Laser Therapy as a non-invasive treatment modality for Oncological Rehabilitation.

**Background:** Post-radiation fibrosis (PRF) remains a challenging consequence for survivors of head and neck cancer (HNC), often leading to a decline in functional abilities and life quality.

Multiwave Locked System (MLS) Laser Therapy has recently been investigated as a therapeutic intervention for PRF with potential benefits. This series of case reports examines the clinical outcomes of HNC patients treated with MLS Laser Therapy for PRF.

**Methods:** Case reports for 10 patients with a history of HNC who developed PRF following radiation therapy and received MLS Laser Therapy are presented. Detailed case descriptions, including treatment parameters, frequency, and duration, were documented. Outcomes were assessed through clinical measures of fibrosis severity, range of motion, pain levels, and functional status involving speech and swallowing. Quality-of-life changes were evaluated.

The PBM parameters were as follows: wavelength (808nm and 905nm), power (1.5W), frequency (1000Hz), with an energy dose of 3.99 Joules/cm<sup>2</sup> per session, administered over the wound area.

**Results:** All patients demonstrated varying degrees of improvement in fibrosis and associated symptoms, including reduced Lymphoedema symptoms. Results showed a significant improvement in fibrosis symptoms, including reduced stiffness, increased range of motion, and decreased pain. Statistical analysis was conducted to evaluate the treatment outcomes, using pre- and post-treatment assessments of fibrosis symptoms and quality of life measures. The therapy was well-tolerated, with no adverse effects recorded. Most patients reported a subjective improvement in quality of life.

**Conclusion:** These case reports contribute to the emerging evidence that MLS Laser Therapy may be a safe and effective treatment for PRF in HNC patients, offering pain relief and functional improvements.

While these reports highlight the therapeutic potential, they also underscore the need for further research through larger-scale studies to establish standardized treatment protocols and long-term efficacy of MLS Laser Therapy for PRF.

# WOUND CARE

## LIGHT-BASED APPROACHES IN WOUND CARE: EMPHASIS ON PHOTOBIO-MODULATION THERAPY

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### Abstract

#### Learning Objectives

1. To learn about the foundational light-tissue responses in wound care;
2. To appreciate the progress in discrete forms of light treatments for wound management;
3. To assess the evidence for current forms of light therapies for tissue healing.

Wound healing is an extraordinarily dynamic and complex process. Several light-based treatments can modulate the wound microenvironment, including ablative (surgical) and non-ablative (non-surgical) techniques. The incident light energy must be transferred (biochemical) and transformed (biological) to generate a therapeutic clinical response. This presentation will outline our current understanding of electromagnetic energy transfer, especially with low-dose laser energy. It will highlight the utility and differences between high-power ablative Photothermal Therapy (PTT) and non-ablative PTT (hyperthermia), as well as contrast the other destructive, low-power, non-thermal photochemical responses termed Photodynamic therapy (PDT) from Photobiomodulation (PBM) treatments in wound care. Improved wound healing was among the very first clinical observations with PBM treatments. A key PBM mechanism mediating this response is its ability to directly activate a potent pro-healing latent growth factor complex, TGF- $\beta$ 1. Other studies have outlined the role of Cytochrome C oxidase and non-visual opsins in PBM responses. Further, the role of ATF-4 in the phototoxicity pathway enables the determination of maximal dosing. These advances in recent PBM mechanisms and dosimetry are allowing the use of optimal PBM treatments in wound care safely and effectively.

# MOLECULAR AND CLINICAL EVIDENCE FOR PHOTOBIMODULATION IN DIABETIC WOUND HEALING

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## Abstract

Wound healing is a dynamic process aimed at replacing damaged tissue and is hampered by underlying pathological conditions like Diabetes Mellitus. Chronic wounds do not heal according to a regular, timely sequence, and their anatomical and functional integrity is frequently not restored. At a cellular and molecular level, chronic wounds are characterised by alterations in signal transduction pathways, Photobiomodulation (PBM) is a non-invasive approach that harnesses the therapeutic properties of light to promote healing, reduce inflammation, and relieve pain for the benefit of patients. Despite the medical advancement and increasing acceptance of PBM, the full underlying cellular and molecular mechanisms are not fully uncovered and understood. PBM has been shown to accelerate wound healing through activation of various cellular signalling pathways, increased growth factor and extracellular matrix production, and transcription of genes essential to healing. PBM has shown significant potential to become a portable, minimally invasive, easy-to-use, and cost-effective treatment modality for wound healing of various aetiologies. This lecture will focus on *in vitro* cellular and molecular evidence of PBM at 660 and 830 nm at 5 J/cm<sup>2</sup> on signal transduction in human skin fibroblast cells (WS1), and clinical evidence of daily, at home-use PBM (808 nm) on non-healing-diabetic foot ulcers in individuals with a darker skin tone.

# ACCELERATING WOUND HEALING IN OLDER PATIENTS: A FOUR-CASE ANALYSIS OF PHOTOBIO-MODULATION THERAPY

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## Abstract

### Three Learning Objectives:

1. Understand the Mechanisms and Efficacy of Photobiomodulation in Wound Healing.
2. Evaluate the effectiveness of Multiwave Locked System (MLS) Laser Therapy in enhancing wound healing processes.
3. Apply Knowledge of PBM Therapy to Clinical Decision-Making in Geriatric Care

**Brief Introduction:** Wound healing in older patients presents a significant clinical challenge, particularly in cases of venous ulcers and traumatic wounds. MLS Laser Therapy, a form of Photobiomodulation, has emerged as a potential therapeutic approach to accelerate wound healing. This abstract summarises the outcomes of MLS Laser Therapy in four older patients, including two with venous ulcers and two with non-healing wounds.

**Methods:** Four patients (two with venous ulcers and two with non-healing wounds) underwent MLS Laser Therapy. The PBM parameters were as follows: wavelength (808nm and 905nm), power (1.5W), frequency (1000Hz), with an energy dose of 3.99 Joules/cm<sup>2</sup> per session, administered over the wound area.

Treatment was provided three times a week for a period of four weeks. Efficacy was evaluated through wound surface area measurement, pain assessment using the Visual Analogue Scale (VAS), and photographic documentation before and after the treatment period.

**Results:** Statistical analysis demonstrated significant wound size reduction in all patients. The venous ulcer patients exhibited a 95-100% reduction in wound surface area, while the patients with accidental wounds showed a 100% reduction.

Pain levels also decreased across all cases, with an average drop in VAS scores from 8 to 2. All patients reported improved quality of life. Photographic evidence supported these findings, showing notable improvement in wound appearance.

**Conclusions:** The case studies indicate that MLS Laser Therapy can significantly enhance wound healing in elderly patients, regardless of the wound etiology. The therapy was effective in accelerating healing rates, reducing wound size, and alleviating pain in both venous ulcers and traumatic wounds.

These findings suggest that MLS Laser Therapy could be a valuable adjunctive treatment in the management of wound healing in the elderly, encouraging further research in this area to optimise treatment protocols.

# LASER PHOTOBIMODULATION ON PRESSURE ULCER CATEGORY FOUR IN FRAIL ELDERLY WITH MUNICIPALITY HOME HEALTHCARE

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## Abstract

**Learning objectives:** A combination of laser photobiomodulation (PBM) 904nm and 635nm is effective on pressure ulcers category 4, despite ulcer severity and patient frailty.

**Introduction:** Frail elderly are a high-risk population for developing pressure ulcer (PU). Patients treated in municipality home healthcare living in nursing homes or in their home residence are the frailest. Home healthcare include palliative care. Laser PBM has shown to have effect on wound and tissue healing [1-3]. In the municipality there is an ongoing scientific study of PBM in addition to dressing of PU4. The Swedish registry RiksSar for ulcer treatment present national data from municipality primary home healthcare, primary healthcare and specialist hospital care, general PU data from the registry are presented as one PU group with the categories PU2, PU3 and PU4 together [4].

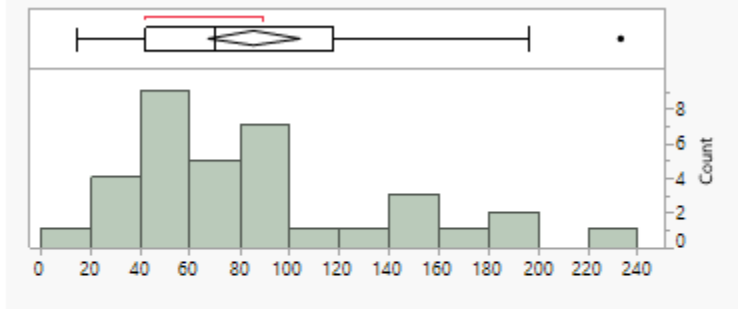
**Method:** Home healthcare patients with 35 PU4 were in addition to dressing, treated two times per week until healing, with PBM. GaAs, 904nm, 60mW, 700Hz, dose 2.4J/cm<sup>2</sup> targeting lymphatic area and ulcer area. PBM GaAlInp, 635nm, 75mW, 250Hz, dose 3.1J/cm<sup>2</sup> targeting ulcer area.

Controls from RiksSars general PU group.

**Results:** Median ulcer duration before PBM and median PBM treatment time to heal the PU4 was 133 days.

(Charts and Conclusions on next page)

## Treatment time with PBM



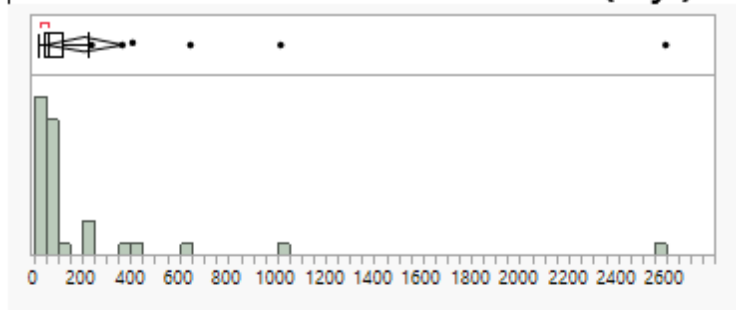
## Quantiles

100.0%	maximum	233
99.5%		233
97.5%		233
90.0%		172,2
75.0%	quartile	117
50.0%	median	70
25.0%	quartile	42
10.0%		28
2.5%		15
0.5%		15
0.0%	minimum	15

## Summary Statistics

Mean	85,6
Std Dev	53,44
Std Err Mean	9,03
Upper 95% Mean	104,0
Lower 95% Mean	67,3
N	35

## Duration of the PU4 when PBM started (days)



## Quantiles

100.0%	maximum	2597
99.5%		2597
97.5%		2597
90.0%		501,2
75.0%	quartile	119
50.0%	median	63
25.0%	quartile	42
10.0%		28
2.5%		21
0.5%		21
0.0%	minimum	21

## Summary Statistics

Mean	206,6
Std Dev	461,78
Std Err Mean	78,06
Upper 95% Mean	365,2
Lower 95% Mean	48,0
N	35

**Conclusions:** Median total healing time data 2020 from the registry RiksSar was 167 days for the total group of PU [4]. Median healing time of the 35 PU4 in the PBM group was faster despite the homogeneous severity category 4. This indicates that PBM may be an effective treatment of PU4.

## References:

1. Degerman M, Öhman M, Bertilson BC (2022) Photobiomodulation, as additional treatment to traditional dressing of hard-to-heal venous leg ulcers, in frail elderly with municipality home healthcare. PLoS ONE 17(9): e0274023. <https://doi.org/10.1371/journal.pone.0274023>
2. Taradaj J, Shay B, Dymarek R, Sopol M, Walewicz K, Beeckman D, et al. Effect of laser therapy on expression of angio- and fibrogenic factors, and cytokine concentrations during the healing process of human pressure ulcers. Int. J Med. Sci. 2018;15(11):1105-1112.
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4. RiksSår, the Swedish national quality Registry for Ulcer Treatment ([rikssar.se](http://rikssar.se))



# QUANTITATIVE IDENTIFICATION OF THE OPTIMAL RADIOMETRIC PHOTOBIMODULATION CONDITIONS TO ENHANCE ANGIOGENESIS IN VITRO AND IN VIVO

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## Abstract

Photobiomodulation therapy (PBM) is a non-invasive approach that utilizes the therapeutic properties of sub-thermal irradiances applied at specific wavelengths in the red or near infra-red to stimulate cellular metabolism. One of the mechanisms through which PBM exerts its beneficial effects *in vivo* is promoting angiogenesis, forming new blood vessels from existing ones. In this study, we have explored and optimized different precisely controlled PBM irradiation conditions (ranging between 1.5 to 25 mW/cm<sup>2</sup>) *in vitro* on human umbilical vein endothelial cells and vascular smooth muscle cells and *in vivo* on the chicken embryo chorioallantoic membrane model (CAM). We have compared *in vitro* the PBM effects on cell migration, proliferation, endogenous protoporphyrin IX production, mitochondrial potential, oxygen consumption rate, and changes in the Rhodamine 123 fluorescence lifetimes. The observed effects have also been compared to those observed during angiogenesis of the vascular network induced in the CAM. These results illustrate the importance of precise control of the light dosimetry to induce optimal PBM effects. Importantly, our results quantitatively demonstrated the potential of PBM to promote angiogenesis. Our study also evidences the important potential role of PBM not only for angiogenesis, but also for tissue repair and wound healing. These effects are playing a key role in regenerative medicine and vascular surgery. Altogether, our results strongly suggest that the PBM effects have a common “fundamental” origin.

# INFLUENCE OF DIFFERENT PARAMETERS OF LASER PHOTOBIMODULATION ON IN VITRO WOUND CLOSURE

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## Abstract

**Learning objectives:** Evaluate the influence of different physical parameters of laser photobiomodulation on mesenchymal stem cells on wound closure.

**Introduction:** Photobiomodulation stimulates cell viability and assists in tissue repair; however, using other physical parameters can trigger different cellular responses. The *in vitro* wound healing assay helps evaluate an artificial wound's reactions to the various photobiomodulation parameters. The study's objective was to evaluate the effects of lasers with red and infrared wavelengths and different energies on mesenchymal stem cells *in vitro*.

**Methods:** Mesenchymal stem cells derived from human adipose tissue were irradiated with a laser of wavelengths of 660 nm and 830 nm, power of 100 mW, and energy of 2 J and 4 J. Wound closure was evaluated with the *in vitro* wound closure (Scratch Assay) with monitoring of the reduction in the lesion area through images acquired with the confocal microscope over time.

**Results:** After six hours, the area reduction showed no significant difference compared to the initial time. In 24 hours, the area of the lesion decreased. Comparing the groups that received irradiation with the control group, only the infrared Laser with 4 J energy did not show a significant difference.

**Conclusion:** Different physical parameters of the Laser can mediate cellular responses related to wound closure.

# REVERSING THE TRAJECTORY OF COMPLEX NON-HEALING WOUNDS THROUGH PHOTOBIMODULATION: A NOVEL APPROACH AVERTING MAJOR LIMB AMPUTATIONS

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## Abstract

### Learning Objectives:

1. To elucidate the application of PBM in the treatment of difficult-to-heal wounds.
2. To introduce a predictive model for assessing wound healing trajectories.
3. To highlight the significance of integrating best medical practices in wound management.

**Introduction:** Complex non-healing wounds significantly burden both healthcare resources and patient quality of life. PBM has emerged as a promising intervention. Yet, its efficacy in cases where major amputation appears to be the inevitable course, has remained unexplored. This study investigates the efficacy of PBM particularly in severe cases where amputation has been considered the only solution.

**Methods:** We conducted a study on five clinical cases, each earmarked for major limb amputation, who then underwent a rigorous treatment regimen after full informed consent. Our protocol involved applying PBM using ThorLaser(TM) with/without Keresis xenografts adjunct. Wavelengths of 810nm and 660nm targeted the wound base, surrounding surface, and draining lymph nodes. Treatment specifics included six sessions targeting the groin with a 69 LED cluster probe (1420 mW), delivering 26.76 Joules per 6 cm<sup>2</sup> per minute, at 1-min intervals, using pulse rates of 20Hz and continuous beam. Similar protocols were applied to popliteal area and along primary lymphatic channels of the lower limb.

**Results:** Remarkably, all participants achieved complete wound healing within a 4-12 week period post-enrollment in the PBM program, negating the need for any planned amputations. Significant improvements in mobility, pain cessation, and opioid discontinuation were observed, with minor side effects reported in two cases. Our predictive model, using regression analysis derived from comparing observed healing to established mathematical models, indicated a direct correlation between early neovascularization and a six-week healing period, challenging the conventional trajectory towards amputation.

**Conclusion:** PBM, utilizing specific wavelengths and energy parameters, has emerged as a transformative approach in managing complex wounds, averting the need for major amputations. This study not only reaffirms the efficacy of PBM in accelerating wound healing but also emphasizes the importance of integrating it with best medical practices to enhance patient outcomes. Further exploration into PBM's clinical applications promises to broaden its therapeutic scope, offering new avenues in complex wound management.

# DENTISTRY AND ORAL CARE

## CLINICAL IMPROVEMENT AND P63-DEFICIENCY CORRECTION IN OLP PATIENTS AFTER PBM

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### Abstract

**Learning objectives:** Oral lichen planus, PBM, p63 levels

**Introduction:** Oral lichen planus (OLP) is a chronic inflammatory disease often presented with symptomatic mucosal lesions and worsening the patient's quality of life. The standard immunosuppressive therapy often demonstrates unsatisfactory results and side effects in contrast to PBM. To be effective the therapy should not only improve the symptoms but also to be able to affect the pathological changes in the cells. Recently, it has been speculated that p63 deficiency may have an important role in the pathogenesis of the disease. P63 is required for epidermal development and regeneration since it regulates the proliferation and differentiation of the keratinocytes. In our previous study, we found the level of p63 to be significantly reduced in OLP patients.

**Aim:** The aim of this study is both to assess the clinical effectiveness of PBM in OLP patients and to evaluate the ability of PBM to restore the molecular disturbances associated with OLP.

**Materials and Methods:** Twenty patients with histologically proven OLP underwent PBM with a diode laser (810nm), (0,50W, 30s, 1,2J/cm<sup>2</sup>), 3 times weekly for a month. The size and clinical scores of the lesions and pain level were recorded before and after therapy, using Thongprasom sign scoring and VAS respectively.

Biopsies were taken before and after therapy and analyzed immunohistochemically for expression of p63. To assess p63-related process of proliferation, the immunoreactivity for Ki-67 in the specimens was also examined.

**Results:** After a month of treatment with diode laser the pain level, the size and clinical scores of the lesions decreased significantly. The percentage of p63-positive cases increased from 65% to 85%. The intensity of expression of this marker was also found to be enhanced and almost comparable with this in normal mucosa. All cases of elevated p63 were also accompanied by increased Ki-67 levels.

**Conclusion:** Even though not statistically significant, PBM corrected the reported p63-deficiency in OLP patients. One of the effects of this molecular change is activated proliferation. This could explain the better improvement of the atrophic-erosive forms of OLP as compared to the keratotic ones.

# PBM IN CONTEMPORARY PAEDIATRIC DENTAL PRACTICE : FROM MINIMALLY INVASIVE PULPOTOMY TO PAIN-FREE & ACCELERATED ORTHODONTICS IN CHILDREN

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## Abstract

Laser PBM's ability to enhance tissue repair, reduce inflammation, and manage pain without the need for invasive procedures or pharmaceuticals makes it an innovative and patient-friendly tool in the paediatric dental arsenal. Two of the most notable applications of PBM in Children are Paediatric Endodontics & Orthodontics. PBM's ability to reduce pulpal inflammation whilst preserving the vitality of the radicular pulp calls for a paradigm shift from 'Pharmaceutical' to 'Photochemical' / 'Drug Free' Pulpotomy. Similarly, for Orthodontics, the focus lies on its capability to alleviate pain and expedite tooth movement.

## Objectives:

1. To compare and assess the clinical and radiographic outcomes of Laser PBM Pulpotomy (LPBM) vs Conventional Pharmaceutical agents in human primary molars.
2. To evaluate the efficacy of PBM therapy on alleviation of pain and acceleration of orthodontic tooth movement in human subjects.

## Methods:

*A. Randomised Clinical Trial for Paediatric Pulpotomy* split-mouth design was employed and a computer-generated random sequence allocated subjects to either Group I (Pharmaceutical Pulpotomy) or Group II (Laser PBM Pulpotomy). Under local anesthesia, coronal pulp was amputated using a sharp spoon excavator, followed by irrigation with saline. In the PBM group complete hemostasis was achieved by exposing canal orifices to 660 nm diode laser (100 mW output in non contact mode for 2 mins =12 J/cm<sup>2</sup>). Conventional Pharmaceutical pulpotomy agents were used in the control group.

*B. Systematic review & Meta-analysis for Paediatric Orthodontics* The protocol has been published in the PROSPERO database.

## Results:

*Randomised Clinical Trial* - There was no statistically significant difference in the clinical success rates between the pharmaceutical group (97.05%) and the PBM group (94.1%) ( $\chi^2 = 0.34, P = 0.55$ ); however, the radiographic success rate was significantly better in the PBM group (94.1%) vs (58.82%) ( $\chi^2 = 11.76, P = 0.001$ )

*Systematic review & Meta-analysis:* Overall, the literature states that PBM positively affects bone metabolism and Orthodontic Tooth movement at the cellular, animal, and human levels without any harmful effects. It also significantly alleviates Pain and discomfort.

**Conclusions:** As the field of paediatric dentistry continues to evolve, Laser PBM stands out as a promising technology that prioritises the well-being and comfort of young dental patients.

# THE SUCCESS OF PHOTOBIMODULATION ON INCIDENCE OF ALVEOLAR OSTEITIS AND POSTOPERATIVE PAIN FOLLOWING MANDIBULAR WISDOM TOOTH SURGERY: A CLINICAL TRIAL

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## Abstract

**Introduction:** Surgical extraction of impacted wisdom tooth tends to be considered as one of the most frequent types of oral surgery that is often associated with postoperative complications. One of the most common postoperative complications following tooth extraction is Alveolar Osteitis (AO) or dry socket that is highly prevalent after surgical removal of impacted mandibular third molar.

**Objectives:** the current study aimed to assess the effectiveness of Photobiomodulation therapy (PBMT) for the prevention or reduction of incidence of alveolar osteitis (AO) and postoperative pain following mandibular wisdom tooth surgery.

**Methods:** the study design was based on a double-blind randomized clinical trial and patients with bilateral impacted mandibular third molars were selected for surgical extraction; after surgery, one socket was randomly assigned to receive PBMT and the other received sham treatment. The PBMT was accomplished by a laser irradiation with 660 nm, 200 mW, CW, at a distance of ~1cm to 4 points on the occlusal area of extraction socket (beam area at the tissue ~0.64 cm<sup>2</sup>, 312.5 mW cm<sup>-2</sup>, 1J, 1.6 J cm<sup>-2</sup>). Also, supplementary irradiation with 810 nm, 200 mW, CW was applied at tissue surface at three points on the buccal and three points on the lingual gingiva, for 15 s (400 mW cm<sup>-2</sup>, 3 J, 6 J cm<sup>-2</sup>).

**Results:** a statistically meaningful difference was found in AO frequency between the two groups, and PBMT group illustrated lower AO frequency compared with the sham PBMT (P-value = 0.035).

**Conclusions:** the results of the study showed that PBMT reduced the incidence of AO following surgical extraction of impacted mandibular wisdom teeth. The incidence of AO typically occurs 3–7 days post-extraction, and our findings suggest that PBMT within the 7 days could help reduce the risk of AO development.

# THE EFFICACY OF 940 NM LOW-LEVEL LASER THERAPY ON TREATMENT OF PATIENTS WITH MYOGENIC TEMPROMANDIBULAR JOINT DISORDERS

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## Abstract

**Introduction:** Temporomandibular disorders lead to masticatory muscle pain, jaw movement disability and limitations in mouth opening. Usually these disorders involve masseteric muscles which result Myofascial Pain Dysfunction Syndrome (MPDS). This study aims to determine the analgesic effects of low level laser therapy in patients with MPDS.

**Materials and methods:** In this double-blind experimental clinical trial, 26 patients with painful masticatory dysfunction syndrome were randomly divided into 2 groups. The laser treatment group was subjected to low-power diode laser radiation with a wavelength of 940 nm for 4 weeks and a total of 8 sessions. The control group is exposed to placebo radiation (device off) with similar conditions. A digital ruler is used to quantify variations in pain intensity of visual analog scale and the maximal mouth opening with assistant and without help.

**Results:** 25 patients were female and one was male. The largest number of patients (84.6%) reported pain in the master muscle, 65.4% pain in the temporalis muscle, 30.8% pain in the internal pterygoid muscle, and 15.4% of the patients in the external pterygoid muscle. Descriptive findings showed that the average pain intensity before the start of the intervention, in the laser and in the placebo group were 6.63 and 5.31, respectively. This value gradually decreased in the other measurement times to 6.00 in the second, 3.54 in the third, and 2.26 in the fourth. These results were confirmed by multivariate analysis of variance with repeated measurements of patient's pain intensity score at four times ( $\eta^2=0.705$ ) with  $P<0.001$  and  $F(3,22)=17.532$ ). With the passage of time and use of laser, there is an interaction both within and between groups ( $\eta^2=0.625$  and  $P<0.001$ ,  $F(3) ,22)=12.199$ ). Significant difference was shown between the mean scores of mouth opening with and without the help of an assistant in the laser and placebo groups ( $F=8.606$ ;  $p=0.001<0.05$ ).

**Conclusion:** Low power lasers can be considered as an alternative treatment method or a complementary treatment method for patients with temporomandibular joint disorders of muscular origin which result significant improvement in mouth opening with or without an assistant and hence increase the level of patients satisfaction.

# THE EFFECT OF PHOTOBIMODULATION THERAPY WITH TWO WAVELENGTHS ON THE VIABILITY AND MIGRATION OF NICOTINIZED HUMAN GINGIVAL FIBROBLASTS (HGF)

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## Abstract

**Learning objectives:** Nicotine induces cell apoptosis and is one of the main causes of periodontal diseases. This *in vitro* study aimed to assess the effect of photobiomodulation (PBM) therapy with different wavelengths on the viability and migration of nicotine-treated human gingival fibroblasts (HGF). If effective, PBM could be used in the treatment of gingivitis and periodontitis in smoking patients.

**Introduction:** PBM therapy influences the proliferation, differentiation, migration, and adhesion of cells. However, the effects of PBM on cells exposed to nicotine, a cytotoxic agent simulating smoking at the cellular level, have not been previously explored.

**Methods:** HGF cells were divided into eight groups according to nicotine and LASER application. Twenty-four hours after the initial seeding of cells, in nicotine groups, a concentration of 3 mM of nicotine was added to the culture, and in PBM groups, LASER irradiation (for MTT assay:  $\lambda 660\text{nm}$ , CW, 150mW,  $0.4\text{W}/\text{cm}^2$ ,  $4\text{J}/\text{cm}^2$ ,  $0.5\text{cm}^2$ , 60s or  $\lambda 808\text{nm}$ , CW, 250mW,  $0.24\text{W}/\text{cm}^2$ ,  $4\text{J}/\text{cm}^2$ ,  $0.5\text{cm}^2$ , 16s; for scratch assay:  $\lambda 660\text{nm}$ , CW, 150mW,  $0.02\text{W}/\text{cm}^2$ ,  $4\text{J}/\text{cm}^2$ ,  $3\text{cm}^2$ , 200s or  $\lambda 808\text{nm}$ , CW, 250mW,  $0.035\text{W}/\text{cm}^2$ ,  $4\text{J}/\text{cm}^2$ ,  $3\text{cm}^2$ , 114s) was executed. Twenty-four hours after the first session, LASER groups were irradiated again. Twenty-four and 48 hours after the second LASER irradiation, the methyl-thiazole-tetrazolium (MTT) assay was performed to evaluate the viability of cells. Also, scratch assay was performed to assess the migration of cells. The data were analyzed using one-way ANOVA, Tukey's post-hoc test, and pair-wise t-test at the significance level of 0.05.

**Results:** Twenty-four and 48 hours after the second irradiation, reduced viability was observed in all cells exposed to nicotine ( $P < 0.05$ ), and PBM therapy did not influence the viability of nicotine-treated cells ( $P > 0.05$ ). Twenty-four hours after the second irradiation, PBM therapy did not affect the viability of cells not exposed to nicotine. However, 48 hours after the second irradiation, decreased viability was seen in cells irradiated with both 660 and 808 nm LASERS ( $P < 0.05$ ). Twenty-four hours after the scratch assay, decreased migration was observed in nicotine groups ( $P < 0.05$ ). Forty-eight hours after the scratch assay, all groups had 100% migration.

**Conclusion:** Neither cell migration nor viability of nicotine-treated HGF was improved by LASER irradiation.



# COMPARING CIRCUMFERENTIAL SUPRACRESTAL FIBERTOMY WITH SURGICAL SCALPEL VERSUS PHOTOBIMODULATION IN ORTHODONTIC RELAPSE REDUCTION: A CLINICAL TRIAL

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## Abstract

### Three Learning objectives:

1. Photobiomodulation (PBM) plus laser supracrestal fibertomy (CSF) and PBM plus conventional CSF had significantly different results from the other groups.
2. The six groups had no significant difference in gingival recession
3. The six groups had no significant difference in pain score

**Brief Introduction:** Relapse is the tendency of teeth to move back to their preoperative position after removal of orthodontic appliances. This investigation aimed to compare the efficacy of circumferential CSF with surgical scalpel, laser CSF, and PBM for reduction of relapse after orthodontic tooth rotation.

**Methods:** This randomized controlled clinical trial was conducted on 90 rotated teeth at the final stages of fixed orthodontic treatment. The teeth were randomly divided into six groups ( $n = 15$ ) of (1) control (no intervention), (2) PBM alone (wavelength of 940 nm, 0.2 W, and 4 J/cm<sup>2</sup>), (3) conventional CSF, (4) laser CSF (wavelength of 940 nm, 1.5 W, and 4 J/cm<sup>2</sup>, and power density of 160 mW/cm<sup>2</sup>), (5) conventional CSF plus PBM, and (6) laser CSF plus PBM. Measurements were made on clinical photographs and dental casts using the AutoCAD software. Level of pain of patients was measured within the first 24 h after CSF using a visual analog scale. Data were analyzed by ANOVA and Kruskal–Wallis test ( $\alpha = 0.05$ ).

**Results:** The magnitude ( $p = 0.014$ ) and percentage ( $p = 0.035$ ) of relapse were significantly different among the six groups, and they were the highest in the control group followed by PBM alone, laser CSF, conventional CSF, conventional CSF plus PBM, and finally, laser CSF plus PBM. Moreover, PBM plus laser CSF and PBM plus conventional CSF had significantly different results from the other groups. The six groups had no significant difference in sulcus depth changes, gingival recession (difference in primary and secondary crown height), or pain score ( $p > 0.05$ ).

**Conclusions:** This study suggests that utilizing PBM combined with laser CSF or conventional CSF can be effective in reducing relapse. However, further clinical trials are required to support this idea.

# PHOTOBIMODULATION IN ACCELERATING ORTHODONTIC TOOTH MOVEMENT: A RANDOMIZED CLINICAL TRIAL

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## Abstract

**Aims:** Present study was designed to determine if intraoral 850 nm LED irradiation could reduce the duration of lower anterior crowding alignment and also could relief the orthodontic pain .

**Introduction:** Long duration of orthodontic treatment is often associated with patient discomfort , and increased the risk of some complications. Surgical interventions, vibrations, and photobiomodulations (PBM) are evaluated in this era. Several systematic reviews are available regarding effect of low-level laser therapy (LLL) on accelerated orthodontic tooth movement (OTM). In a few trials with limitations, it was shown that LEDs can decrease treatment time of teeth crowding but there is no systematic review regarding LED.

**Methods:** In a parallel designed, randomized controlled clinical trial 60 patients with 2 to 6 mm of lower incisor crowding who needs non-extraction treatment, were randomly assigned to the intervention and control groups by block randomization (36 females, 24 males, mean age:  $19.93 \pm 3.05$ ). MBT brackets (0.022 x 0.28-inch) were bonded for both groups and the NiTi wires in sequences put in place until correction of crowding. The intraoral LED device with wavelength of 850 nm and power density of 70 mW/cm<sup>2</sup> was used for 5 minutes per day in intervention group. The control group did not receive any light. Primary outcome was the duration of crowding correction. The patient's pain according to modified McGill pain questionnaire was secondary outcome. Cox regression model had been used to compare groups. Mann-Whitney test was used for pain analyzing.

**Results:** The crowding at baseline was the same between the two groups ( $P > 0.05$ ). Duration of treatment in the intervention group was 104.7 days (95% CI: 95.6 -113.8) and significantly shorter than 161.9 days (95% CI: 151.5 - 171.2) in the control group. The control group experienced significantly higher pain score 6.8 (95% CI: 6.1-7.5) immediately after arch wire placement than intervention group 5.4 (95% CI: 4.6-6.3).

**Conclusions:** Intraoral LED 850 nm significantly decreased the duration of correction of crowded lower incisors up to 36% and reduced pain experience.

# INNOVATIVE PBM RESEARCH

## UNCOVERING THE OPTIMAL WAVELENGTH FOR TRANSCRANIAL PHOTOBIO-MODULATION AFTER MILD TRAUMATIC BRAIN INJURY

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### Abstract

#### Three learning objectives:

1. 660 and 810nm photobiomodulation (PBM) improve cognitive, behavioural and balance function after mild traumatic brain injury (mTBI)
2. Combined administration of 660/810nm PBM does not confer an advantage over either wavelength alone
3. 810nm PBM demonstrates greatest efficacy and reduces astrocyte and microglial activation in the acute phase after mTBI

**Brief introduction:** mTBI is a common consequence of head injury, and over 50% of those injured report ongoing symptoms persisting for more than six months after injury, including headaches, depression, cognitive symptoms and balance problems. Despite this, there is no recognised intervention to promote metabolic recovery of the brain. Transcranial PBM presents a potential therapy, yet the optimal parameters for improving recovery are yet to be established.

**Methods:** Cadaveric studies were performed to calibrate 660 and 810nm MDL-III 800mW lasers for transcutaneous delivery of 20mW/cm<sup>2</sup> PBM to the cortical surface. A weight drop mTBI model was used in adult Wistar rats and 20mW/cm<sup>2</sup> PBM was applied for 120s per day for the first three days post-injury (2.4J/cm<sup>2</sup>), with either 660nm (D4σ=0.7cm), 810nm (D4σ=0.7cm), or 660/810nm (60s (1.2J/cm<sup>2</sup>) each). Functional outcomes were assessed using novel object recognition (NOR) and beam balance testing for four weeks post-injury. Histology was used to assess TBI neuropathology whilst molecular markers were assessed using immunofluorescence.

**Results:** No discernible structural injury was observed in injured or PBM-treated groups. Four weeks post-injury, 810nm treated subjects improved NOR performance by 100.5% (p<0.0001), 660nm improved by 46.2% (p<0.01), and 660/810nm by 61.5% (p<0.001). Beam walk performance improved by 65.8% (810nm, p<0.001), 63.8% (660nm, p<0.05) and 42.3% (660/810nm, p=0.08). Using 810nm PBM, at 3 days post-injury, expression of microglial activation marker CD11b was reduced by 53.8% compared to untreated subjects, and expression of astrocytic marker GFAP was reduced by 24.8%. Cortical expression of cleaved caspase-3 reduced by 27.6%. Reductions in extracellular matrix deposition were modest with PBM and limited to choroid plexus and periventricular areas.

**Conclusions:** Our results demonstrate that 810nm PBM alone was the optimum PBM therapy for improving functional outcomes after mTBI, coinciding with a reduction in markers associated with apoptosis and astrocyte/microglial activation.

# THE FMRI RESPONSE TO TRANSCRANIAL PHOTOBIO-MODULATION: THE DEPENDENCE OF BLOOD-OXYGENATION AND CEREBRAL BLOOD FLOW RESPONSES ON STIMULATION PARAMETERS

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## Abstract

### Three Learning Objectives:

1. The effect of transcranial photobiomodulation (tPBM) on the BOLD fMRI response
2. The effect of tPBM on the cerebral blood flow (CBF) response
3. tPBM stimulation parameters and their effect on BOLD and CBF responses

**Introduction:** Transcranial photobiomodulation (tPBM) is the process of delivering light photons through the skull [1]. We use blood-oxygen-level dependent (BOLD) and cerebral blood flow (CBF) fMRI techniques to study the real-time functional brain response to pulsed tPBM.

**Methods:** 4 healthy participants (2F/2M, aged 20-27) were scanned using a Siemens Prisma 3 T scanner with dual-echo pseudo-continuous arterial-spin labeling (ASL), (TR=4500ms, TE1=9.4ms, TE2 = 30ms) to measure the BOLD and CBF responses while undergoing laser stimulation to the right frontal cortex. Two lasers were used to stimulate at two wavelengths (808 and 1064nm), pulsed at two frequencies (10 and 40Hz) and at the optical power density of 200mW/cm<sup>2</sup>. The stimulation paradigm was [4-min off; 4-min on; 4-min off]. The irradiated surface area and application technique remained the same for all subjects and scans.

FSL was used for brain extraction, motion correction, distortion correction, slice timing, and FSL FEAT was used to implement a general-linear model to assess the block wise tPBM-evoked BOLD and CBF responses.

**Results:** The BOLD and CBF response amplitudes, averaged across subjects, are summarized in bar graphs Figure 1. The BOLD response exhibits noticeable distinctions among pulsation frequencies. In comparison to 40 Hz, the 10 Hz frequency elicited a more significant BOLD response at both wavelengths.

Figures 2 and 3 show the BOLD and CBF spatial responses ( $p < 0.05$ ), averaged across subjects, which are highly consistent. Similar to the bar graphs, the spatial response maps show the global BOLD response at 10Hz, compared to the smaller and more spatially localized response of the 40Hz.

**Conclusion:** This study presents initial evidence of wavelength and pulsation frequency dependences of the real-time BOLD and CBF responses to tPBM. Our ongoing work investigates additional power densities and combinations of dose parameters. This work pioneers imaging-based optimization of tPBM protocols.

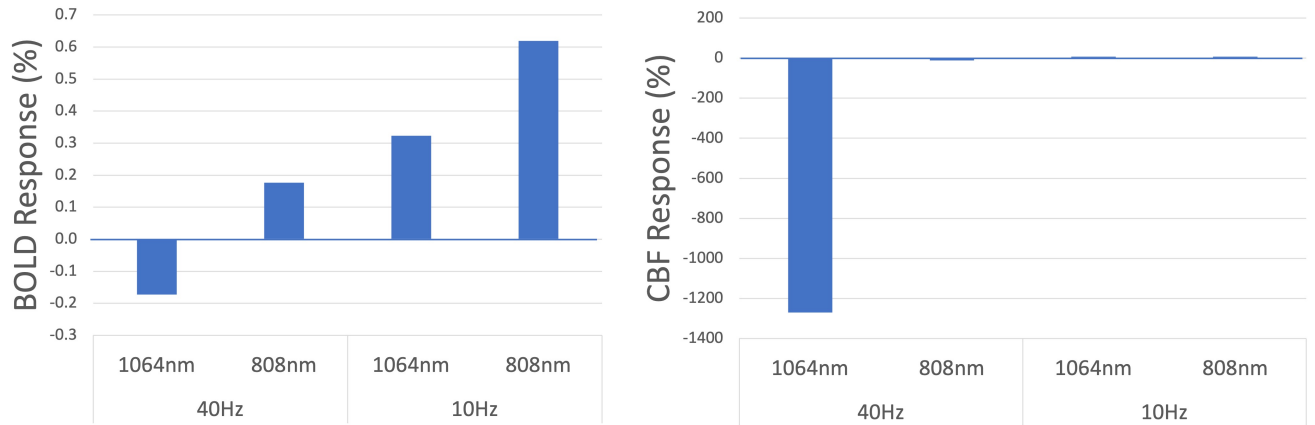


Figure 1: The BOLD and CBF signal average response to transcranial photobiomodulation with an optical power density of 200mW/cm<sup>2</sup>, and varied wavelength (1064nm and 808nm) and frequency (10Hz and 40Hz).

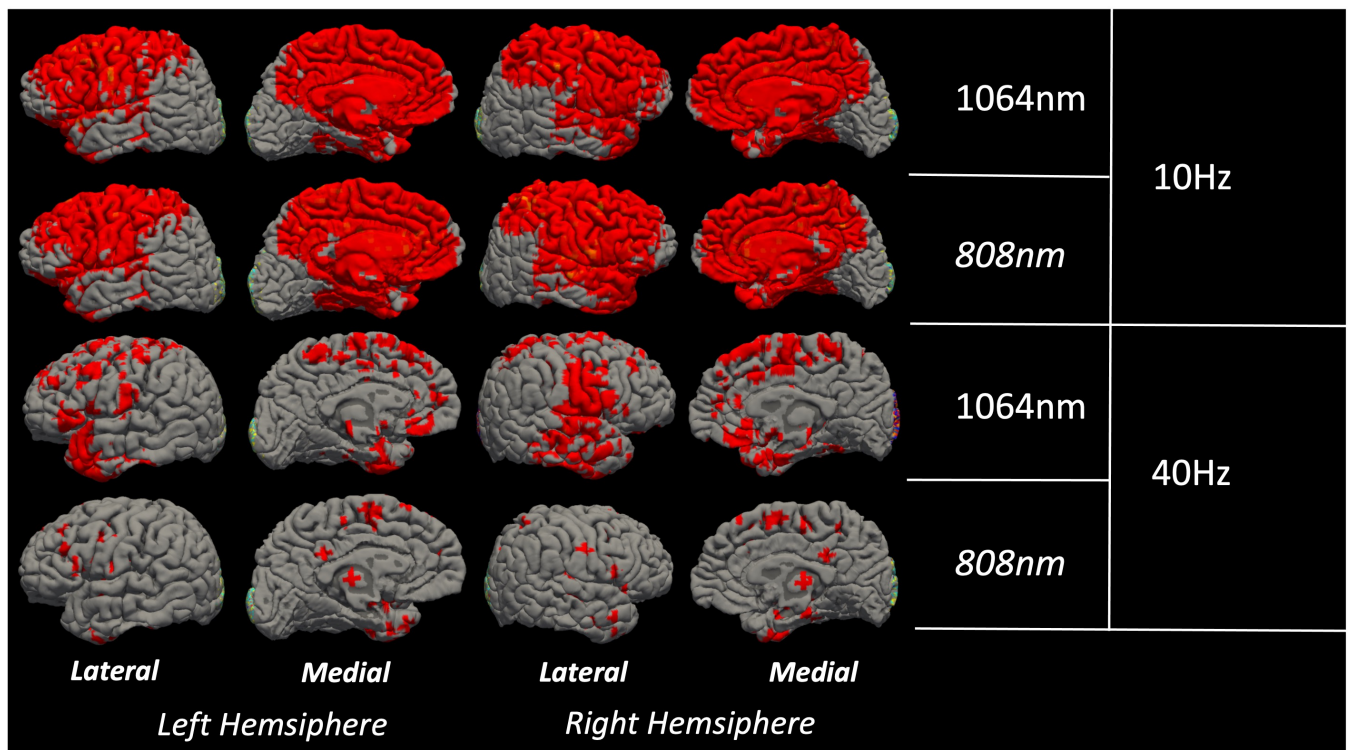


Figure 2: Spatial BOLD response to 200mW/cm<sup>2</sup> tPBM at varied wavelengths (1064nm and 808nm) and varied frequencies (10Hz and 40Hz).

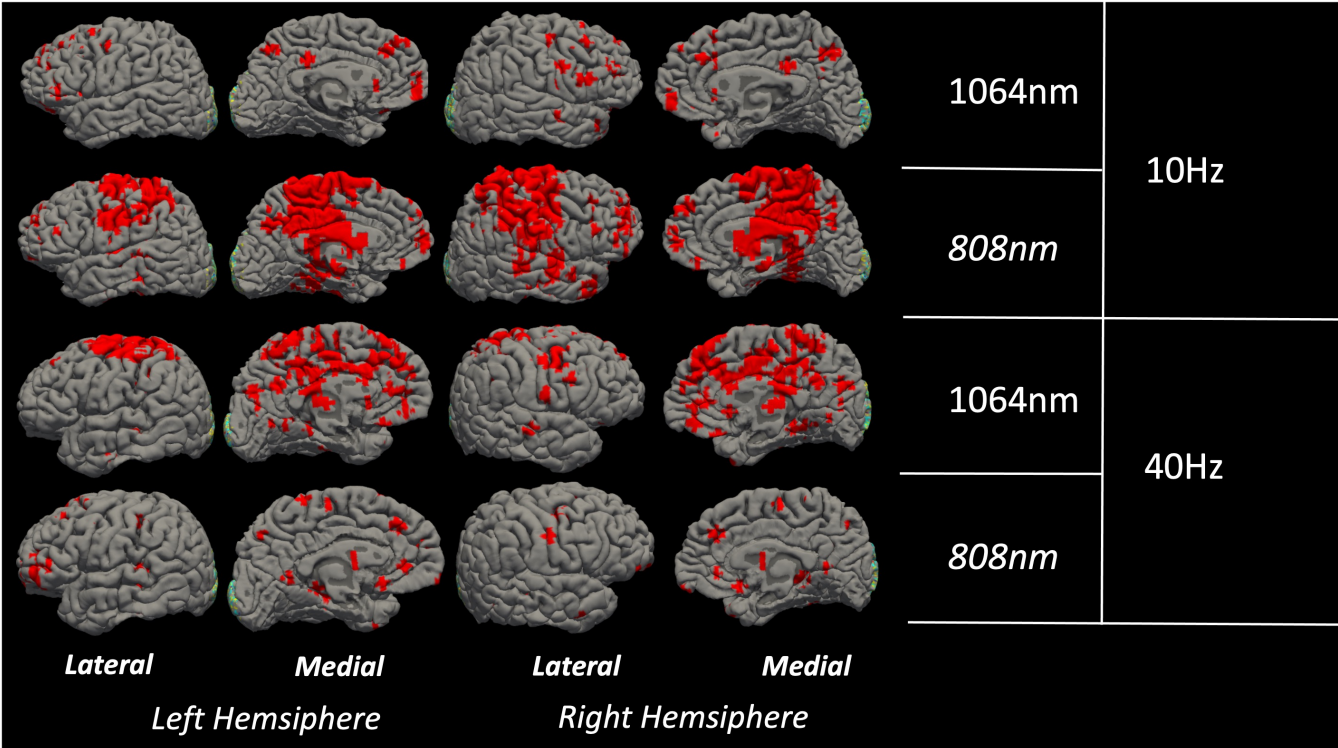


Figure 3: Spatial CBF response to 200mW/cm<sup>2</sup> tPBM at varied wavelengths (1064nm and 808nm) and varied frequency (10Hz and 40Hz).

# DEVELOPMENT AND OPTICAL REFLECTANCE CHARACTERIZATION OF PHANTOMS MIMICKING BIOLOGICAL TISSUES FOR STUDIES OF LIGHT PENETRATION IN THE BRAIN

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## Abstract

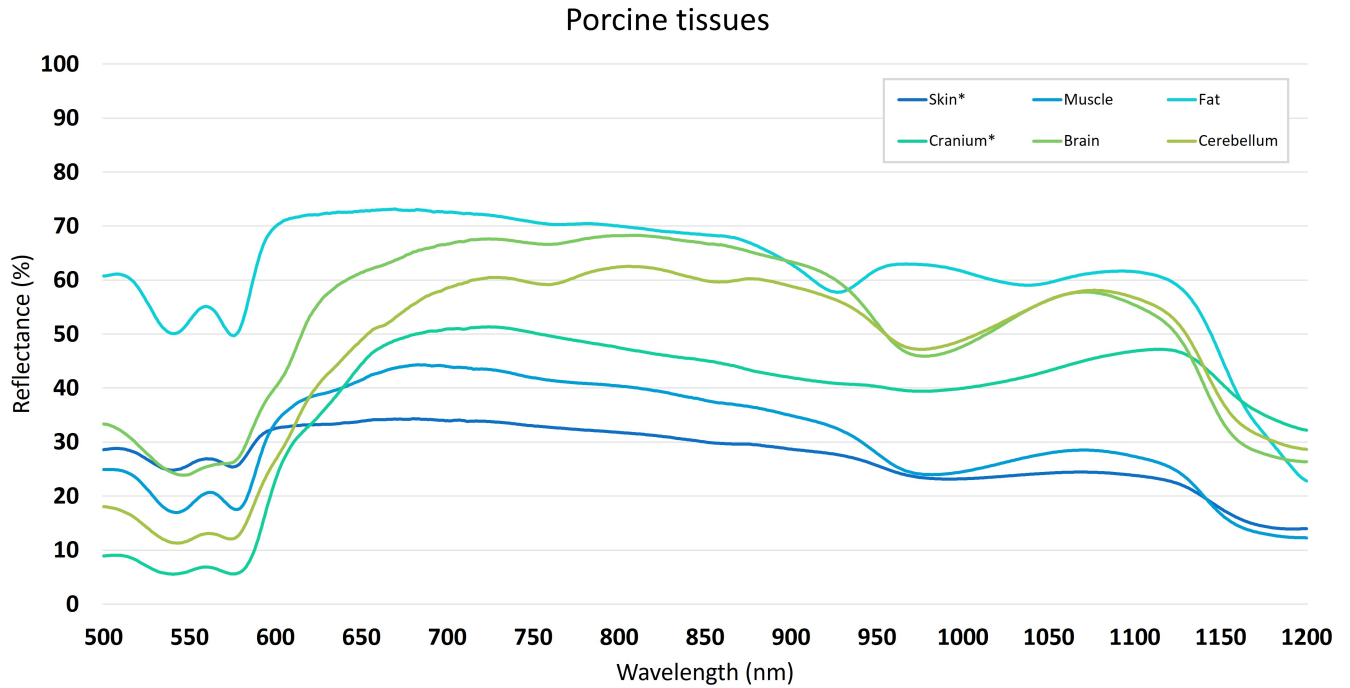
The search for materials that accurately mimic the optical properties of biological tissues is essential, particularly for research in transcranial photobiomodulation, where it is necessary to comprehend how light propagates through the head tissues. There is a lack of information in literature on the reflectance spectra of these materials, which is a relevant property when determining how light interacts with tissues. Thus, the first objective of this study was to characterize the reflectance spectra of different porcine tissues, which show similar properties to those of human tissues, to serve as reference. The second objective was to understand and evaluate if it is possible to mimic the reflectance spectra of those tissues. Finally, the third objective was to determine the best materials and concentrations for future studies with multilayer phantoms, that accurately mimic the reflection of light in the head, up to the brain.

In this research, we characterized, in the 500-1200-nm range, the reflectance spectra of porcine tissues (skin, fat, cranium, muscle, brain, cerebellum) and different agarose-based phantoms. These phantoms were developed using different combinations of titanium dioxide (TiO<sub>2</sub>), India ink, organometallic compounds and laser-sintered gold and zinc oxide nanoparticles. The reflectance measurements were performed using an integrating sphere (1-nm sampling interval, 20-nm slit, at a medium scan speed).

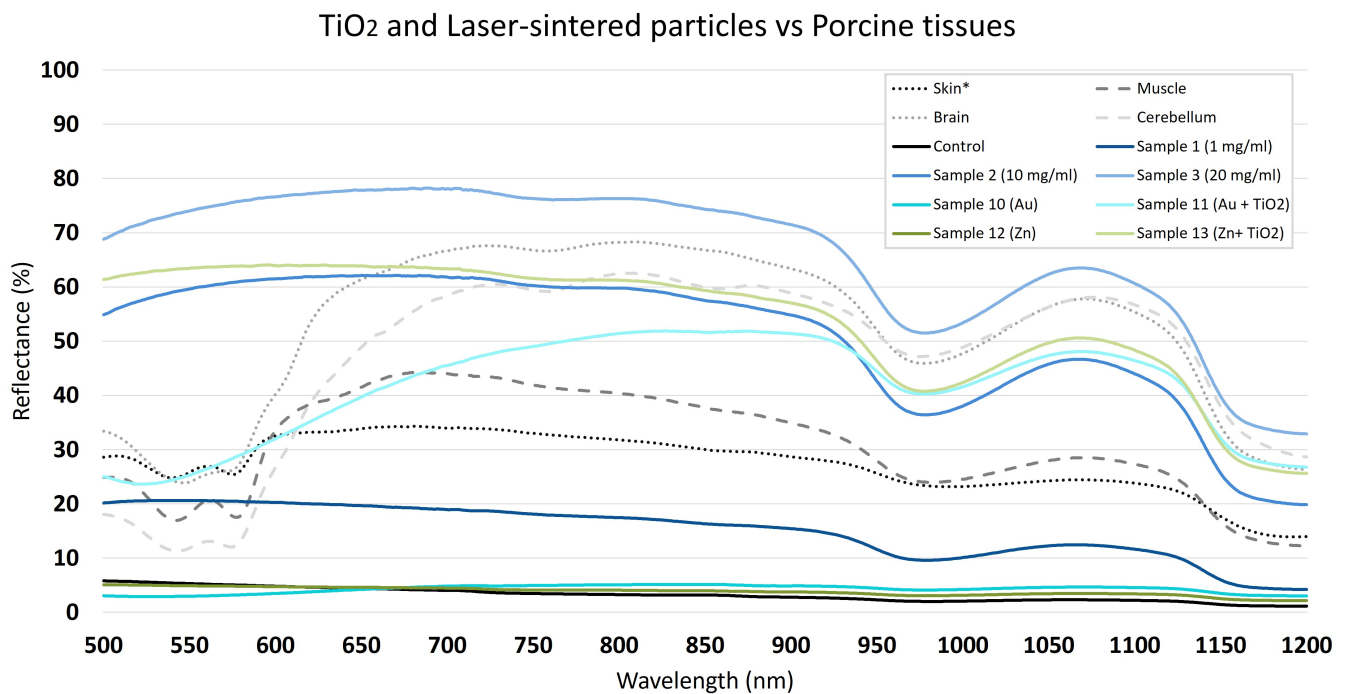
The results showed that increasing TiO<sub>2</sub> concentration increased the optical reflectance of the phantoms. Additionally, when TiO<sub>2</sub> was added to the India ink and laser-sintered nanoparticles' phantoms, not only it increased reflectance amplitude, but it also accentuated the fluctuations in the spectral curves. Comparing the phantoms and biological tissues' results, the spectral profiles of TiO<sub>2</sub> samples appeared similar to that of muscle, skin and brain/cerebellum; organometallic compounds replicated the skin and muscle curves; India Ink emulated the skin; while laser-sintered nanoparticles with the addition of TiO<sub>2</sub> showed similarities to the spectra of muscle and brain/cerebellum, but only after 750-nm.

Although it was possible to establish qualitative similarities between the phantoms and the biological tissues' optical reflectance spectra, there is a need for further studies with different components' combinations, to ascertain curves that more closely mimic the biological tissues spectra.





**Figure 1** – Reflectance spectra (%) of the porcine tissues, in the 500 – 1200 nm optical range. \*Skin (2.5 mm) and cranium (4 mm) samples have different thickness from the other samples (5.5 mm).



**Figure 2** - Reflectance spectra (%) of the TiO<sub>2</sub> (samples 1, 2 and 3) and Laser-sintered particles (samples 10, 11, 12 and 13) the 500 – 1200 nm optical range. The dashed lines represent some of the biological porcine tissues and how they are portrayed close to the phantoms' spectral curves.



### Organometallic compounds and India Ink vs Porcine tissues

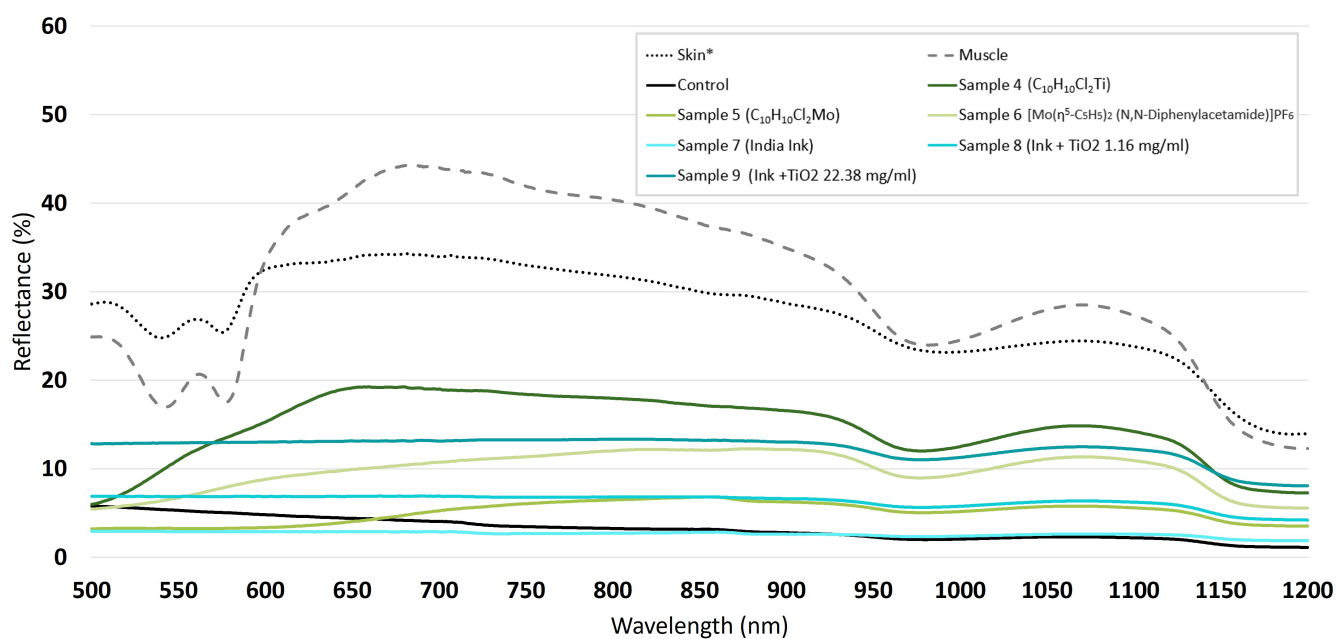


Figure 3 - Reflectance spectra (%) of the organometallic compounds (samples 4, 5 and 6) and India Ink (samples 7, 8 and 9) in the 500 – 1200 nm optical range. The dashed lines represent some of the biological porcine tissues and how they are portrayed close to the phantoms' spectral curves.

# EFFICACY OF RED AND NEAR-INFRARED PBM IN DENTAL EXTRACTIONS: INTEGRATING SYSTEMATIC REVIEW AND PRE-CLINICAL LIGHT TRANSMISSION STUDIES

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## Abstract

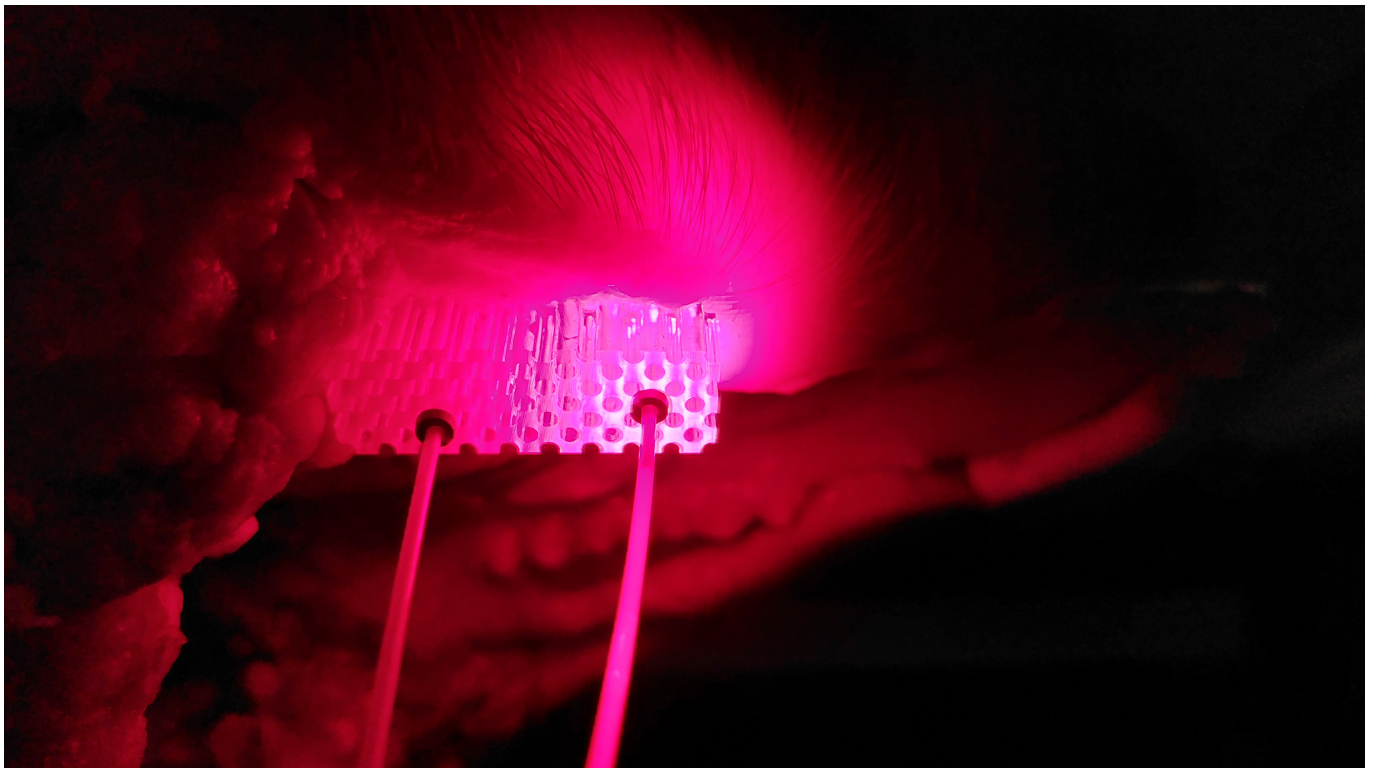
1. Understand the efficacy of PBM in dental extractions as highlighted in existing literature and porcine model studies for both red and near-infrared wavelengths.
2. Identify the differential effects of 661nm and 810nm PBM light transmission across various soft tissues of the dental oral craniofacial region.
3. Explore the optimization of PBM parameters for enhanced clinical application in dentistry for wound healing and postoperative pain reduction.

**Introduction:** PBM using red and near-infrared wavelengths is known to improve wound healing and reduce pain after dental extraction. This study aims to better understand the delivery of PBM light for intra-oral applications by correlating findings from a comprehensive systematic review with pre-clinical data from a 661nm & 810nm light-transmission study.

**Methods:** A two-phase approach was taken, which analyzed the clinical application and efficacy of a systematic review of PBM in dental extractions. This was followed by a comprehensive assessment of light transmission ( $\text{mW}/\text{cm}^2$ ) of a novel porcine model ( $n=2,100$  data points) that mirrors human head and neck anatomy. PBM light transmission was examined across six soft tissues: genioglossus, masseter, sternohyoid, buccinator muscles, cutaneous fascia, and vestibular tissue. The porcine modeling parameters documented included light wavelength, power density, and distance. Histological analysis was conducted for tissue-specific response evaluation.

**Results:** The systematic review demonstrated PBM's efficacy in improving post-extraction healing and pain reduction. The porcine model study revealed significant variations ( $p<.001$ ) in light transmission for both the 661nm & 810nm. Histologic assessment identified regions comprised of higher muscle tissue ratios were correlated with lower transmission values, whereas those with higher adipose tissue ratios exhibited the highest transmission values. Pearson's correlation indicated a negative correlation (-0.552) between distance and light transmission and a positive correlation (0.75) for anatomical region. These statistical findings emphasize the impact of tissue type, proximity to the light source, and site of clinical application on PBM effectiveness.

**Conclusions:** This integrative analysis provides a detailed understanding to enhance PBM light delivery protocols. The study emphasizes the importance of adapting PBM parameters to specific tissue characteristics. These findings demonstrate the potential of a personalized approach in PBM application, leading to more effective therapy protocols and improved patient outcomes.



# MATRIX MECHANICS DICTATE ODONTOBLAST RESPONSIVENESS TO PHOTOBIMODULATION TREATMENTS

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## Abstract

**Objectives:** Regenerative dentistry promotes the directed differentiation of stem cells. While the predominant focus of these efforts has been genetic manipulations, the critical epigenetic role of extracellular matrix (ECM) mechanics has been poorly investigated. This project aims to dissect the cellular responses of odontoblasts to matrix mechanics by replicating a wound-like environment

**Methods:** Polydimethylsiloxane matrices were poured into 12-well plates. The polydimethylsiloxane (PDMS) plates were degassed and cured in a 95°C oven. Mechanical stiffness was then assessed using a Shore A Durometer (Insize). Following sterilization with 70% ethanol, UV treatments, and serum coating, odontoblasts (MDPC-23) were seeded in hypoxic (1µg/mL ) and serum starvation (0.2% FBS DMEM) to simulate a wound-like environment. Alamar blue assay was performed at 24 hours to assess cell viability. Photobiomodulation (PBM) treatments were performed with a near-infrared (810 nm) laser at 10 mW/cm<sup>2</sup>, 5 min, 3 J/cm<sup>2</sup>, 4.5 p.J/cm<sup>2</sup> or 1 Einstein.

**Results:** The shore stiffness assessment noted the ratio 10:1 had a stiffness of 1.14 ± 1.65 MPa, 2:1 of 1.16 ± 0.48 MPa, and 40:1 of 0.57 ± 0.27 MPa. These stiffnesses were significantly (n = 3, p < 0.05) lower compared to the polystyrene culture dish control of 5.41 ± 0.96 MPa. No differences were observed in cell adhesion assays in any of the conditions. Significant (n = 3, p < 0.05) changes were observed in cell proliferation with varying matrix stiffness. TGF-β1 and FAK1 signaling was noted to modulate these responses.

**Conclusion:** The results from this study suggest that precision engineering of biomaterial mechanical properties and PBM treatments can synergistically promote directed differentiation for optimal dentin regeneration. These findings will be extended to in vivo animal models for human clinical translation as a novel Endodontic Regenerative Therapy.

# OSTEOBLAST DIFFERENTIATION AND CHANGES IN THE REDOX STATE IN PULP STEM CELLS BY LASER TREATMENT

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## Abstract

**Introduction:** Previous studies have demonstrated that photobiomodulation (PBM) may promote proliferation, survival, and differentiation in various cell types, under appropriate application parameters, which makes it a useful tool for achieving the objectives of tissue engineering, such as reconstructing or regenerating deteriorated or damaged tissues. Tissue reconstruction is achieved by the combination of scaffolds, stem cells, and inducing factors that act together to regenerate injured or missing tissues. Stem cells are capable of self-renewal, and because of their undifferentiated nature, they can be stimulated to perform specific biological tasks and differentiate into several cell types.

**Objectives:** The aim of this study was to determine the effect of low-level laser therapy (LLLT) on cell proliferation, mitochondrial membrane potential changes ( $\Delta\Psi_m$ ), reactive oxygen species (ROS), and osteoblast differentiation of human dental pulp stem cells (hDPSCs).

**Methods:** These cells were irradiated with 660- and 940-nm lasers, 0.1 W for 5 s, 50 s, and 180 s. Cell proliferation was assessed using the resazurin assay, cell differentiation by RUNX2 and BMP2 expression, and the presence of calcification nodules using alizarin-red S staining. ROS was determined by the dichlorofluorescein-diacetate technique and changes in  $\Delta\Psi_m$  by the tetramethylrhodamine-ester assay. Data were analyzed by a Student's t-test and Mann–Whitney U test.

**Results:** The 940-nm wavelength for 5 and 50 s increased proliferation at 4 days postirradiation. After 8 days, a significant decrease in proliferation was observed in all groups. Calcification nodules were evident in all groups, with a greater staining intensity in cells treated with a 940-nm laser for 50 s, an effect that correlated with increased RUNX2 and BMP2 expression. ROS production and  $\Delta\Psi_m$  increased independently of irradiation time.

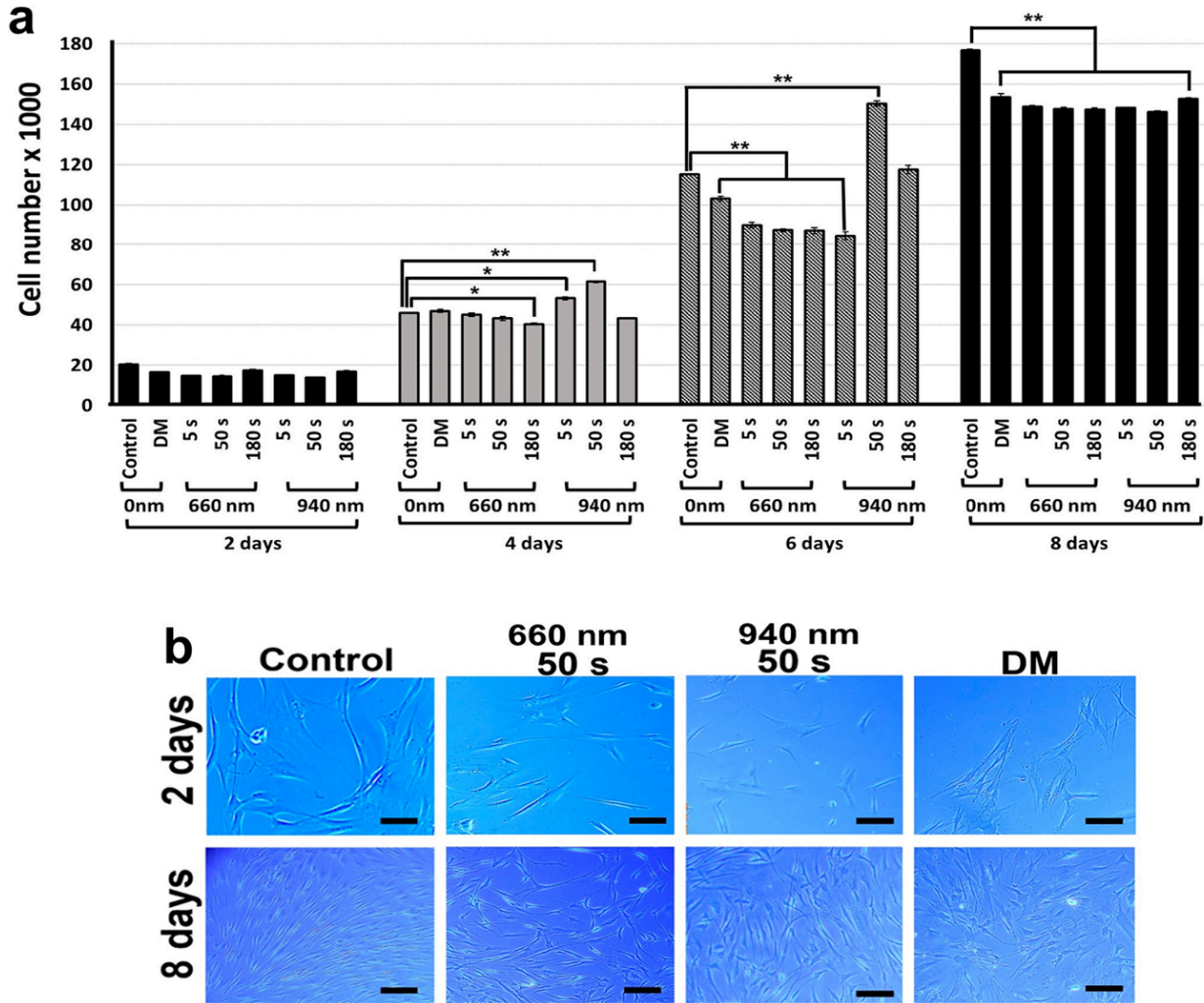
**Conclusions:** PBM with LLLT induced morphological changes and reduced cell proliferation rate, which was associated with osteoblastic differentiation and increased ROS and  $\Delta\Psi_m$ , regardless of wavelength and time.

**Table 1. Application parameters of the study**

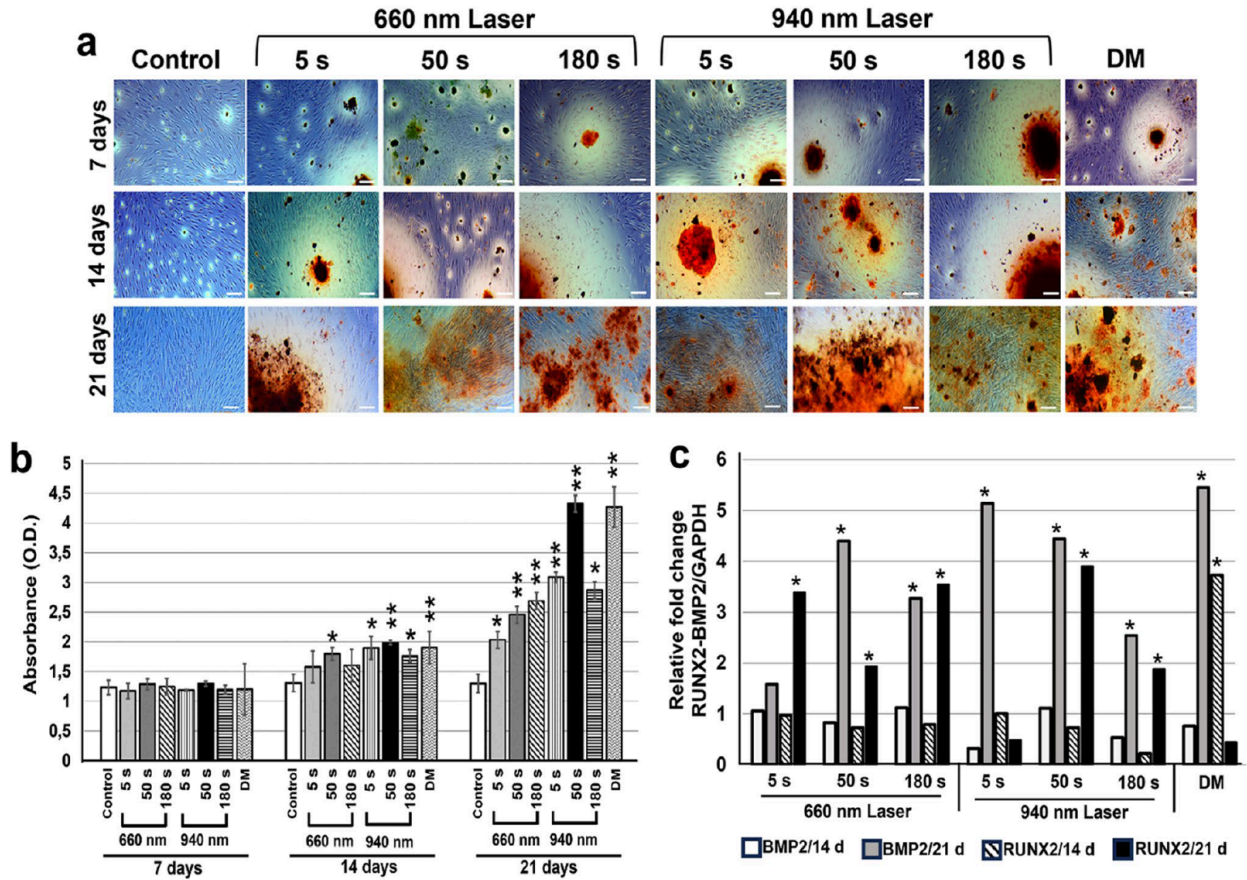
<b>Wavelength</b>	<b>660 nm</b>	<b>940 nm</b>
<b>Beam spot size (cm<sup>2</sup>)</b>	0.2	0.78
<b>Area irradiated per application (cm<sup>2</sup>)</b>	1	1
<b>Area per well (96/ 12)* (cm<sup>2</sup>)</b>	0.32/ 4	0.32/ 4
<b>Power density (W/cm<sup>2</sup>)</b>	0.5	0.13
<b>Power output (W)</b>	0.1	0.1
<b>Exposure time (s)</b>	5, 50, 180	5, 50, 180
<b>Energy density (J/cm<sup>2</sup>)</b>	2.5, 25, 90	0.64, 6.4, 23.1
<b>Energy per point (J)</b>	0.5, 5, 18	0.5, 5, 18
<b>Total energy per well (96)* (J)</b>	0.5, 5, 18	0.5, 5, 18
<b>Total energy per well (12)* (J)</b>	2, 20, 72	2, 20, 72
<b>Application points per well (96)*</b>	1	1
<b>Application points per well (12)*</b>	4	4
<b>Application technique</b>	Fixed-point with support	Fixed-point with support
<b>Distance from laser spot (96/ 12*) (cm)</b>	1.1/ 1.9	1.1/ 1.7
<b>Number of applications</b>	<u>Single-dose</u>	<u>Single-dose</u>

\* calculations performed for 96-well and 12-well cell culture plates, respectively.





**Fig. 1** Changes in cell number and morphological analysis of hDPSCs cultures treated with LLLT. **a** Irradiation with a 660-nm laser for 5, 50, and 180 s caused a significant reduction in cell number at 6 days postirradiation. The 940-nm laser initially produced an increase in cell number when irradiating these cells for 5 and 50 s at 4 days postirradiation. At 8 days, all experimental groups exhibited a significant reduction in cell number compared with the control group.  $p < 0.05$  (\*),  $p < 0.01$  (\*\*). Data are expressed as averages  $\pm$  SD. **b** To determine morphologic changes, cells were treated with 660 nm and 940 nm LLLT for 5, 50, and 180 s and maintained in culture for 8 days postirradiation. The control group corresponded to hDPSCs without irradiation. Differentiation medium (DM). Magnification bar 200  $\mu$ m.



**Fig. 2** Mineralization of the extracellular matrix. **a** Alizarin red staining. The strong intensity of the staining indicated the formation of calcification nodules. **b** Measured absorbance of alizarin red staining extracted from LLLT-treated cells at different wavelengths (660 nm and 940 nm) and times (5, 50, and 180 s) at 7-, 14-, and 21-days postirradiation. **c** Quantification of RUNX2 and BMP2 expression in 660-nm and 940-nm laser-treated hDPSCs for 14 and 21 days. Data are expressed relative to GAPDH gene expression levels and cells treated with osteogenic differentiation medium (DM) without laser irradiation were analyzed as a positive differentiation control. Cells without LLLT (control), differentiation medium (DM).  $p < 0.05$  (\*);  $p < 0.01$  (\*\*). Data are shown as the mean  $\pm$  SD



# TRANSCRANIAL PHOTOBIMODULATION IMPROVES PERFORMANCE ON A MOTOR TASK IN HEALTHY ADULTS: THE EFFECT IS GREATER ON NON-MUSICIANS

MARJORIE DOLE

FONDS CLIMATEC, GRENOBLE, FRANCE

## Abstract

We present preliminary behavioural results of the effects of transcranial photobiomodulation (tPBM) on a motor task performed whilst subjects were in a MRI scanner; it was part of a larger study evaluating tPBM effects on brain activity. We analysed differences between tPBM and sham in a group of healthy adults (n=20). We further divided this group into two sub-groups, based on age (young (n= 15) vs older (n=5)) and in a second analysis on music training (musicians (n=9) vs non-musicians (n=11)).

Each subject received both active and sham treatments across two different, randomised, visits. The active treatment consisted of a LED-lined helmet delivering light at wavelengths of 670nm (12mins) followed by 810nm (12mins) (wellred.com.au). The sham was the same device, but had masked LEDs. The motor task involved sequential finger tapping, where subjects performed randomly presented 5-digit sequences, over sixteen 20s blocks, with sequences changing between each block. We had three main measures; correct sequences, tap number and inter-tap interval. Each measure was compared pre- and post-stimulation for each group and both treatments.

For the **correct sequences**, subjects that received tPBM performed better than sham ( $p < 0.05$ ). When analysing the different sub-groups, we found that this effect was present whatever the age or music training. For the **number of taps**, there were no differences between tPBM and sham, although there was a tendency for tPBM to perform better ( $p = 0.09$ ). When comparing the sub-groups, tap number was higher with tPBM than sham whatever the age or music training. Finally, for the **inter-tap interval**, we found no major differences between tPBM and sham ( $p = 0.19$ ). However, tPBM improved the performance of non-musicians (Post-Pre difference tPBM:  $p < 0.001$ ) but not in musicians (Post-Pre difference tPBM:  $p = 0.11$ ). In addition, tPBM was more effective in young subjects ( $p < 0.001$ ) than in older ones ( $p = 0.52$ ).

In summary, our preliminary results suggest that tPBM improves motor task performance. The effect appeared more salient in non-musicians compared to musicians, and in younger compared to older individuals. Our early results are encouraging and we are in process of increasing our sample size for all groups.

# PAIN MANAGEMENT AND ADDICTION

## DIRECT HIGH IRRADIANCE PHOTOBIO-MODULATION (DIRECT PBM) THERAPY FOR PAIN MODULATION

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### Abstract

**Introduction:** Transcutaneous delivery of near infra-red light to peripheral nerves has established photobiomodulation (PBM) as an effective modulator of pain, selectively blocking pain transmission in small-diameter nerve fibers which transmit nociception and thermal sensation. High irradiance PBM of nerves cannot readily be achieved transcutaneously in humans, so Direct PBM (irradiation at the neural target) must be considered for clinical translation. State-of-the-art research on Direct PBM will be presented.

**Methods:** We utilized the rat spared nerve injury (SNI) model of chronic pain for transcutaneous and Direct PBM studies, measuring small-fiber (thermal) functional sensitivity changes for 14 days after a single laser irradiation. For transcutaneous PBM, a single treatment (810 nm; 2 min; in contact with shaved skin; dorsal root ganglion 10W or sciatic notch 5W) was applied on day 7 post SNI. Direct PBM involved reopening the initial surgical incision on day 7, and positioning a fiber (1mm diameter) 1.0 mm away from the sural nerve. Irradiances at the emitter of 7.64W/cm<sup>2</sup> and 2.55W/cm<sup>2</sup> for two durations, corresponding to either 4.8J or 14.4J total energy were delivered at 808 nm.

**Results:** Transcutaneous PBM: there was a reduction in thermal hypersensitivity (70%) beginning at 1 hour post-irradiation and peaking between days 3 and 5. Direct PBM: The irradiance and total emitted energy tested (7.64 W/cm<sup>2</sup>, 14.4 J; 2.55 W/cm<sup>2</sup>, 14.4 J; and 7.64 W/cm<sup>2</sup>, 4.8 J, significantly reduced the withdrawal latency ratio by 37%, 26%, and 28%, at 24 hours post-PBM. All three treatments reduced the hypersensitivity over the 14-day experimental period (mixed-design ANOVA, p < 0.05). 2.55 W/cm<sup>2</sup>, 4.8 J did not change observed thermal hypersensitivities.

**Conclusions:** These data support the use of Direct PBM to reduce pain associated with small-fiber activity. Our research is focusing on different methods to deliver Direct PBM to nerves and determining the duration and pain reduction as a function of laser irradiation parameters in large and small preclinical animal models.

### Learning Objectives:

1. To gain a working knowledge of Direct PBM
2. To understand the data supporting Direct PBM for clinical pain modulation
3. To learn methods to clinically deliver Direct PBM.

### Disclaimer:

*This project is sponsored by the Transforming Technology for the Warfighter Program, USUHS, Project Number: VPR12802, NIH PAR-19-158, Project Number:1R01NS121372-01, and NIH Institutional Training Grant: T32EB004314. The information or content and conclusions do not necessarily represent the official position or policy of, nor should any official endorsement be inferred on the part of, USU, the Department of Defense, or the U.S. Government.*

# OUTPATIENT ORAL NEUROPATHIC PAIN MANAGEMENT WITH PHOTOBIMODULATION THERAPY. A PROSPECTIVE ANALGESIC PHARMACOTHERAPY-PARALLELED FEASIBILITY TRIAL

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## Abstract

### Learning Objectives:

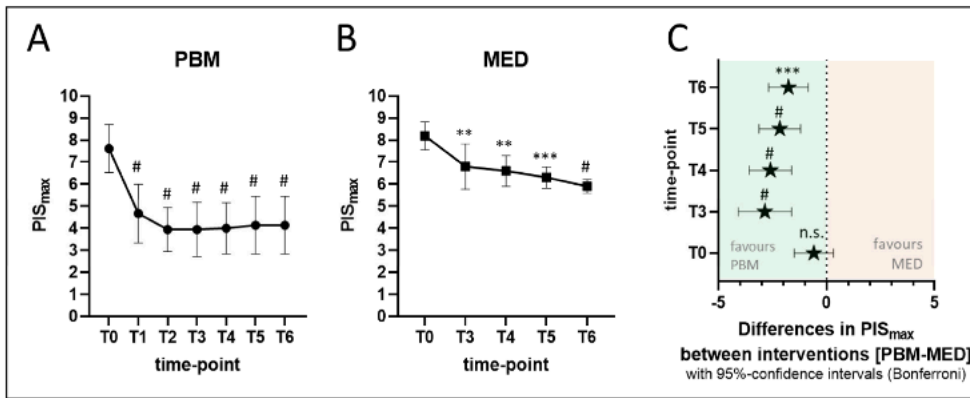
1. Efficacy of  $\lambda 810\text{nm}$  photobiomodulation (PBM) in modulating neuropathic pain (NP).
2. PBM modulates NP pathology in a pro-regenerative manner, presumably via oxidant mechanisms.
3. The study's PBM dosimetry and treatment protocols prove to be valid and reproducible for future RCTs.

**Introduction:** NP can be challenging to treat effectively as analgesic pharmacotherapy (MED). It reduces pain, but without complete relief. Our pilot approach is to assess the feasibility and efficacy of an evidence-based PBM intervention protocol, as an alternative to paralleled MED for modulating NP in a mixed neurological burning mouth syndrome (BMS) and oral iatrogenic neuropathy (OIN) study population ( $n=28$ ). Our prospective parallel study aimed to evaluate pre/post-benefit of PBM and to allow for the first qualitative comparison with MED:

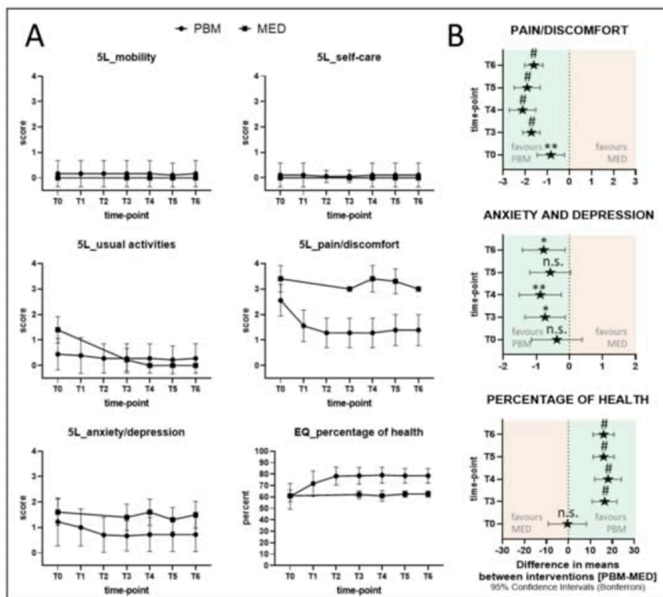
**Methods:** Pain intensity, functionality and QoL variables were assessed with VAS, functional problems-15 indices scale and EQ-5D 5L respectively at T0 (baseline); T1 (mid-treatment); T2 (end-treatment); T3 (one-month); T4 (3-month); T5 (6-months); T6 (9-month). The PBM protocol is as follows:  $\lambda 810\text{nm}$ ; 200mW,  $0.088\text{cm}^2$ ; 30s/point; 9-points; twice a week for five consecutive weeks. whereas, MED protocol followed NICE Guidelines.

**Results:** Despite the severe and persistent nature of symptoms of  $57.50 \pm 47.93$  months at T0 in PBM group, a notably rapid reduction in PISmax on VAS from 7.6 at T0 to 3.9 at T3. Whereas, the mean PISmax was only reduced from 8.2 at T0 to 6.8 at T3 in MED group (**Figure 1**). Our positive PBM findings furthermore support more patients' benefits in improving QoL and functional activities, which were considerably impaired by NP such as: eating, drinking, tasting, whereas MED regimes did not. QoL and functionality findings are shown in Figures 2,3.

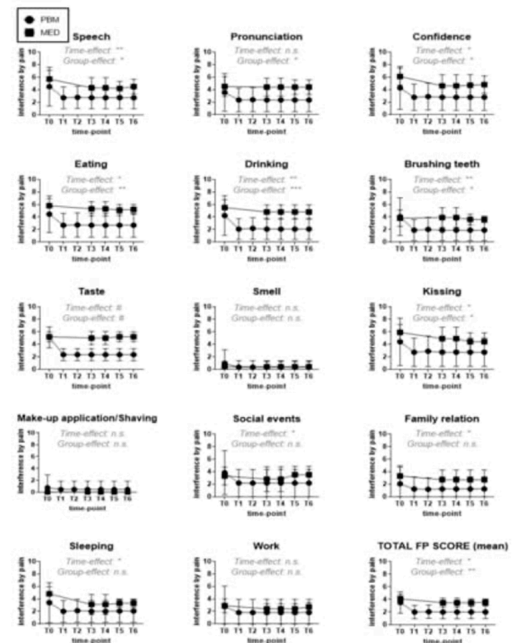
**Conclusions:** Our study, for the first time, proves PBM efficacy and safety, as a potent analgesic in oral NP and, as a valid alternative to MED



**Figure 1.** (A–C) Shows self-reported highest pain intensity score (PIS<sub>max</sub>). (A) PIS<sub>max</sub> (mean ± SD) over time in the PBM group (circles) and (B) PIS<sub>max</sub> (mean ± SD) over time for the parallel MED group (squares) on a visual analogue scale from zero to ten cm. (C) mean differences in PIS<sub>max</sub> between both interventions and the 95%-confidence intervals as the result of a full mixed-effects two-way ANOVA analysis, demonstrating analgesic efficacy in favour of the PBM-treatment throughout the study period. Bonferroni's multiple comparison statistics: *p*-value indications: n.s. = not significant; \*\* < 0.01; \*\*\* < 0.001; # < 0.0001. In (A, B) (means ± SD); *p*-value indications show the significance level of pairwise differences between means of the respective time points



**Figure 2.** Shows results of EQ-5D-5L indices for PBM and MED for the different assessment time points. (A) Self-reported EQ-5D-5L indices as mean (± SD) and aligned for parallelled intervention groups PBM (circles) and MED (squares). (B) Depicts mean differences between the interventions (±95%-confidence intervals) at different time points of selected EQ-5D-5L indices-significant group and time dependency, along with *p*-value indications for Bonferroni's multiple comparison statistics of the full mixed-effects model: n.s.: not significant; \* < 0.05; \*\* < 0.01; # < 0.0001.



**Figure 3.** Pain interference with 14 functional indices: The functional parameters assessed, relating to QoL, as well as the significance level of the main effects by ANOVA analysis (Group-effect = intervention dependency, Time-effect = time-point dependency) for the respective functional parameter in the study (n.s. = not significant; \* < 0.05; \*\* < 0.01; \*\*\* < 0.001; # < 0.0001).

# PHOTOBIMODULATION AS AN ALTERNATIVE PAIN MANAGEMENT SOLUTION IN THE EVOLUTION OF THE OPIOID CRISIS

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## **Abstract**

The opioid crisis in America has reached unprecedented levels, posing significant challenges to public health and healthcare systems. Traditional approaches to pain management, often reliant on opioid medications, have contributed to the escalation of this crisis. Amidst this backdrop, there is a growing interest in exploring alternative solutions that are effective, safe, and devoid of the risks associated with opioids.

This talk will discuss the evolution of the opioid epidemic that was started by large pharmaceutical companies and medical societies, as well as the struggle to identify alternative pain management strategies.

By highlighting the latest research findings, clinical outcomes, and practical considerations related to PBM, this discussion aims to catalyze positive change in pain management practices and contribute to the broader effort to mitigate the impact of the opioid crisis on individuals, communities, and society as a whole.

# A PERSPECTIVE ON THE ROLE OF CYTOSKELETON IN THE NERVOUS SYSTEM AND ITS MODULATION BY PBM: IMPLICATIONS FOR PAIN AND NEUROLOGICAL DISEASES

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## Abstract

### Learning Objectives:

1. Understand the history of the cytoskeleton in the cell
2. Appreciate the effect of photobiomodulation on the cytoskeleton in the PNS and CNS
3. Apply knowledge of the photobiomodulation influenced changes on the cytoskeleton to neurological diseases

**Background:** While there has been a number of studies that show the effect of photobiomodulation on the cytoskeleton in the peripheral nervous system, there are few studies that address the interaction of PBM and the cytoskeleton of the central nervous system.

**Method:** The literature of experimental findings relating to the effects of photobiomodulation on the cytoskeleton of neurons and other cell types to be reviewed. The aim was to synthesise the photobiomodulation response and to determine the implications for the treatment of injury, epilepsy and chronic neurogenic pain. Many neurological and neurodegenerative diseases are reviewed as a function of a neuronal cytoskeleton structural change.

**Results:** A cytoskeleton photobiomodulation therapeutic effect in the central nervous system was developed. Literature on the role of the cytoskeleton and the potential interaction with PBM was shown to be associated with transcranial photobiomodulation and other photobiomodulation applications directed to the central nervous system. The photobiomodulation interactions with cytoskeleton is recognized to be associated with the action of light on photoacceptors such as ion channels, with cytoskeletal modulations affecting downstream signalling, resulting in changes in the integrity of cell membrane and overall sub-cellular and cellular structural changes.

### Conclusion:

We propose that conformational changes to the cytoskeleton is a plausible mechanism of photobiomodulation that is additional to its other known therapeutic targets. The reversible changes to the cytoskeleton in peripheral and central nerve cells may be one mechanism underlying pain relief by photobiomodulation intervention. These conformational changes may lead to secondary effects within nerve cells, such as such changes in membranes and lipid rafts, the slowing of conduction velocity and changes in mitochondrial membrane potentials, all being amenable to modulation by photobiomodulation. This proposed mechanism has potential implications for pathologies involving cytoskeletal dysfunctions, such as chronic pain, and neurological diseases such as traumatic brain injury, epilepsy and Parkinson's disease.

# TRANSCRANIAL PHOTOBIMODULATION AND COGNITIVE REHABILITATION IN OPIOID DRUG ADDICTION

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## Abstract

**Introduction:** Drug addiction refers to a maladaptive pattern of drug use that frequently leads to substance abuse problems and accompanying cognitive and behavioral symptoms. Among the crucial criteria of drug addiction, craving stands out as a potent factor contributing to ongoing drug abuse and relapse following period of abstinence. This study aimed to assess and compare the efficacy of cognitive rehabilitation and photobiomodulation in alleviating drug cravings among individuals undergoing addiction treatment in clinical settings.

**Method:** The research employed a randomized clinical trial as the chosen research method. The statistical population encompassed all clients receiving treatment for addiction at clinics, selected through the convenience sampling method, with  $\alpha = 0.05$  significance level and an effect size of 85%. Gpower software was utilized to determine three equal groups. Sixty-three participants, each having a mean total score higher than 3 out of 5 on the Desire for Drug Questionnaire (DDQ), were randomly assigned to two experimental groups (n=21 each) and a control group (n=21). For the assessment of immediate and periodic opioid craving, the Desires for Drug Questionnaire (DDQ) and the Obsessive Compulsive Drug Use Scale (OCDUS) were employed. In the low-level laser group, a 810 nm wavelength with continuous irradiation was applied twice a week at a distance of 1 cm by 1 cm to the prefrontal part of the brain for duration of 6 weeks (12 sessions). In the brain rehabilitation group, the Stop Signal and N-Back tasks software were used twice a week for period of 6 weeks (comprising 12 sessions, each lasting 30 minutes).

**Results:** The results demonstrated that each intervention significantly reduced drug craving in both the post-test and follow-up phases compared to the control group. The Bonferroni post-hoc test indicated that photobiomodulation was more effective than cognitive rehabilitation in terms of working memory and inhibitory control for reducing drug craving ( $P < 0.05$ ).

**Conclusion:** While both photobiomodulation and cognitive rehabilitation targeting working memory and inhibitory control effectively reduced opioid drug craving, low-level laser therapy proved to be more effective than cognitive rehabilitation in this regard.

# WHOLE-BODY PHOTOBIMODULATION THERAPY FOR FIBROMYALGIA: A FEASIBILITY TRIAL

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## Abstract

1. Learn the challenges faced by patients with fibromyalgia and the difficulties the NHS encounters in managing this condition
2. Assess the viability of integrating a whole-body photobiomodulation service into the NHS framework.
3. Understand the benefits of whole-body Photobiomodulation as a non-invasive treatment for an FM population

Effective treatment for fibromyalgia (FM) is lacking and further treatment options are needed. Photobiomodulation therapy (PBMT) represents one potential treatment option. Whilst favourable findings have been reported using localised PBMT, no investigations have established the value of whole-body PBMT for the complete set of symptom domains in FM. A single-arm feasibility study was conducted in accordance to CONSORT guidelines. A non-probability sampling method was used to access individuals with FM. The primary outcome measure was identified as the Revised Fibromyalgia Impact Questionnaire (FIQR). Forty-nine participants were screened and 21 trial participants entered the trial. Nineteen participants completed the intervention (18 whole-body PBMT sessions over approximately six weeks). The whole-body PBMT device was a NovoTHOR, the treatment parameters were; 660 & 850 nm LED, 30 mW/cm<sup>2</sup>, 20 mins per session, 36 J/cm<sup>2</sup>. Descriptive statistics and qualitative analysis was undertaken to represent feasibility outcomes. Acceptability of the trial device and processes were established. Outcome measures towards efficacy data were guided by core and peripheral OMERACT domains, utilising a combination of participant-reported and performance-based outcome measures. Positive changes were observed for FM-specific quality of life, pain, tenderness, stiffness, fatigue, sleep disturbance, anxiety, depression and cognitive impairment. Patient global assessment revealed improvements at 6 weeks, with continued effect at 24 weeks. FM- specific quality of life at 24 weeks remained improved compared with baseline scores. Data for the embedded qualitative component of the trial were captured by participant-reported experience measures and audio-recorded semi-structured interviews. Findings provide evidence to support a full-scale trial and shows promise regarding potential efficacy of this novel non-invasive treatment in an FM population.



## PBM MECHANISM – ADVANCED RESEARCH

### PHOTOBIMODULATION: & NBSP; THERAPEUTIC POTENTIAL IN CARDIOVASCULAR PATHOLOGY

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#### **Abstract**

Dysfunction of endothelial cells and mitochondria have been implicated as major pathogenetic features of a variety of cardiovascular diseases. It has been shown that photobiomodulation (PBM) increases nitric oxide secretion derived from endothelium and stimulates angiogenesis. PBM also increases mitochondrial membrane potential and subsequent production of ATP. In this lecture we will provide an overview of the preclinical and clinical studies in which PBM was tested for relevance to cardiovascular diseases, including from our laboratory, and discuss the underlying cellular and physiological mechanisms. Novel therapeutic methods of PBM application for cardiovascular pathologies also will be discussed.

# TRAUMATIC BRAIN INJURY RECOVERY WITH PHOTOBIO-MODULATION: PATHOPHYSIOLOGICAL ASPECTS, CLINICAL EVIDENCE AND POTENTIAL

LEW LIM

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## Abstract

### Learning Objectives:

1. Understand the cellular mechanisms of Transcranial Photobiomodulation (PBM) in Traumatic Brain Injury (TBI) recovery.
2. Analyze how TBI's pathophysiological aspects are addressed through PBM, correlating literature with these aspects.
3. Explore the optimization of PBM parameters for enhanced neurorestorative outcomes in TBI treatment.

**Introduction:** Traumatic Brain Injury (TBI) remains a significant global health challenge with limited effective pharmacological treatments due to its complex pathophysiology, including axonal damage, mitochondrial dysfunction, oxidative stress, and neuroinflammation. Transcranial PBM is emerging as a promising intervention. Literature reveals that PBM interventions have helpfully addressed various pathophysiological aspects of TBI.

**Methods:** This study conducts a comprehensive analysis correlating the pathophysiological aspects of TBI with PBM's therapeutic impacts. Cellular mechanisms are scrutinized to understand these correlations better. An extensive review of human clinical studies evaluates the safety and effectiveness of PBM, providing guidance for future research aimed at optimizing real-life applications. Key parameters studied include wavelength, power density, dose, light source positioning, and pulsing frequencies, all of which could influence treatment outcomes significantly. See Figure 1.

**Results:** The pathophysiological aspects can be matched with related PBM mechanisms, suggesting that PBM can unlock the complex TBI pathology. See Table 1.

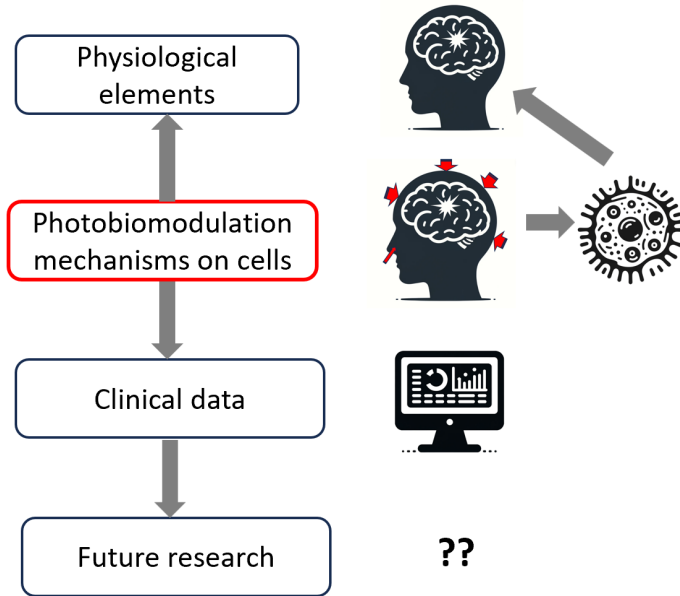
Variations in PBM parameters are found to significantly affect treatment outcomes, emphasizing the importance of careful parameter selection. Emerging evidence indicates that specific pulse frequencies, power density, wavelength, and LED location significantly influence outcomes. These findings reflect the complexity of brain functions and the potential for numerous parameter combinations. Advances in artificial intelligence are poised to significantly enhance outcome optimization.

Additionally, new insights into the electrical properties and polymerization dynamics of neuronal microstructures, like microtubules and tubulins, contribute to further improving PBM parameters for better outcomes.

**Conclusion:** Transcranial PBM stands out as a multifaceted, versatile therapeutic approach for TBI, underlining the critical need for parameter optimization to boost treatment efficacy. The study advocates for more research, including the integration of artificial intelligence, to establish optimal PBM protocols. This strategy holds the promise of more personalized and effective TBI treatment modalities, potentially revolutionizing the therapeutic paradigm in TBI recovery by using PBM.

**Figure 1**

**Schematic of Study Content**



**Table 1****Summary of pathophysiological aspects and related photobiomodulation research**

<b>Pathophysiological aspects</b>	<b>Description of the PBM Research</b>
Axonal Injury	PBM may aid axonal recovery through improved ATP generation and modulation of secondary mediators. It activates the PI3K/Akt signaling pathway.
Mitochondrial Dysfunction	The effects of PBM on mitochondria, particularly cytochrome c oxidase, can restore electron transport and increase mitochondrial membrane potential, aiding axonal regeneration.
Excitotoxicity	PBM was found to increase ATP content, Ca <sup>2+</sup> levels, and mitochondrial membrane potential, counteracting excitotoxicity.
Reactive oxygen species (ROS)	PBM reduces ROS levels and oxidative stress, promoting antioxidant capacity and reducing damage. It can modulate exercise-induced oxidative stress.
Neuroinflammation	PBM can reduce pro-inflammatory cytokines, activate anti-inflammatory responses, and downregulate neurotoxic microglia and astrocytes.
Axonal Degeneration	PBM increases axonal regeneration and counters growth inhibitors, potentially preventing axonal damage and degeneration.
Apoptotic cell death	PBM activates anti-apoptotic mechanisms, potentially preventing cell death and promoting neurogenesis.
Autophagy and Lysosomal Dysfunction	PBM can restore mitochondrial function and improve mitophagy by regulating autophagy and lysosomal activity.
Additional Systemic Mechanisms	PBM enhances cellular energy production, improves blood flow, and modulates synaptic plasticity.

# MULTIMODAL PHOTOBIMODULATION (PBM): TRANSCRANIAL, BLOOD AND ABDOMINAL, IN CHILDREN WITH AUTISM SPECTRUM DISORDER - PILOT STUDY

DAIANE MENEGUZZO

ALLASER, CAMPINAS, BRAZIL. SÃO LEOPOLDO MANDIC, CAMPINAS, BRAZIL.

## Abstract

Autistic Spectrum Disorder (ASD) symptoms cause significant impairment in personal, social or professional functioning. The increase in incidence brings the need for new treatments, and PBM has shown many benefits in neuromodulation, reducing brain inflammation, neuronal apoptosis and oxidative stress, alteration of neuronal mitochondrial function, immune and hormonal deregulation and reduction on alteration in the composition of the microbiome. The objective of this pilot study was to evaluate the effects of PBM on the clinical signs of ASD looking for multimodal PBM (transcranial, blood and abdominal) effectiveness and how plausible the application of PBM is for ASD children. The study was approved by the ethics committee, and it was carried out in a social institution in Campinas, SP, Brazil. 4 children under 8 were selected, 1 control and 3 for PBM, and all received standard multidisciplinary treatment. The PBM protocol had two phases: 1: Blood PBM for 10 days on the wrist (100mW, 660nm, 15min, 90J total); phase 2: Transcranial PBM in 6 cortical regions with 810nm, 3W, 40Hz, 30s per region, and 540J total; and abdominal PBM, 810nm, 3W, 40Hz, 120s, 360 J total. The whole protocol was applied twice a week totaling 12 sessions. The effectiveness of the treatment was measured using the Childhood Autism Rating Scale (CARS) before, after phase 1 and 8 and 12 sessions of phase 2. The results showed an important reduction in ASD symptoms according to the CARS scoring and the mean score of the 3 children who received PBM was: 36 at baseline, 30.17 after phase 1 (16% reduction), 24.83 after 8 sessions (31%) and 23 after 12 sessions (36%). Comparing the CARS score before and after full treatment the reduction was 13 points (mean), while in the control child was an increase of 5.5 points. Furthermore, in this pilot study, blood PBM alone and the complete protocol proved to be effective in reducing ASD symptoms. These results indicate that PBM may be an effective and plausible clinical tool to help ASD patients. Further studies in a larger population are needed.

# EMERGING NEW PARADIGMS PROVIDE GUIDEPOSTS TO A COMPELLING FUTURE IN BRAIN PHOTOBIO-MODULATION

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## Abstract

### Learning Objectives:

1. Explore emerging paradigms guiding brain photobiomodulation (PBM) evolution for enhanced applications.
2. Examine new research evidence supporting these guideposts.
3. Appreciate the potential compelling future of brain PBM with continued research.

**Introduction:** This presentation delves into the untapped potential of brain PBM in treating neurological conditions. It emphasizes the need for in-depth exploration of various parameters like wavelength, power, light source positioning, pulse frequency, and treatment duration, with a particular focus on how pulse frequency affects brain functions. These insights create new paradigms that are pivotal in refining PBM applications.

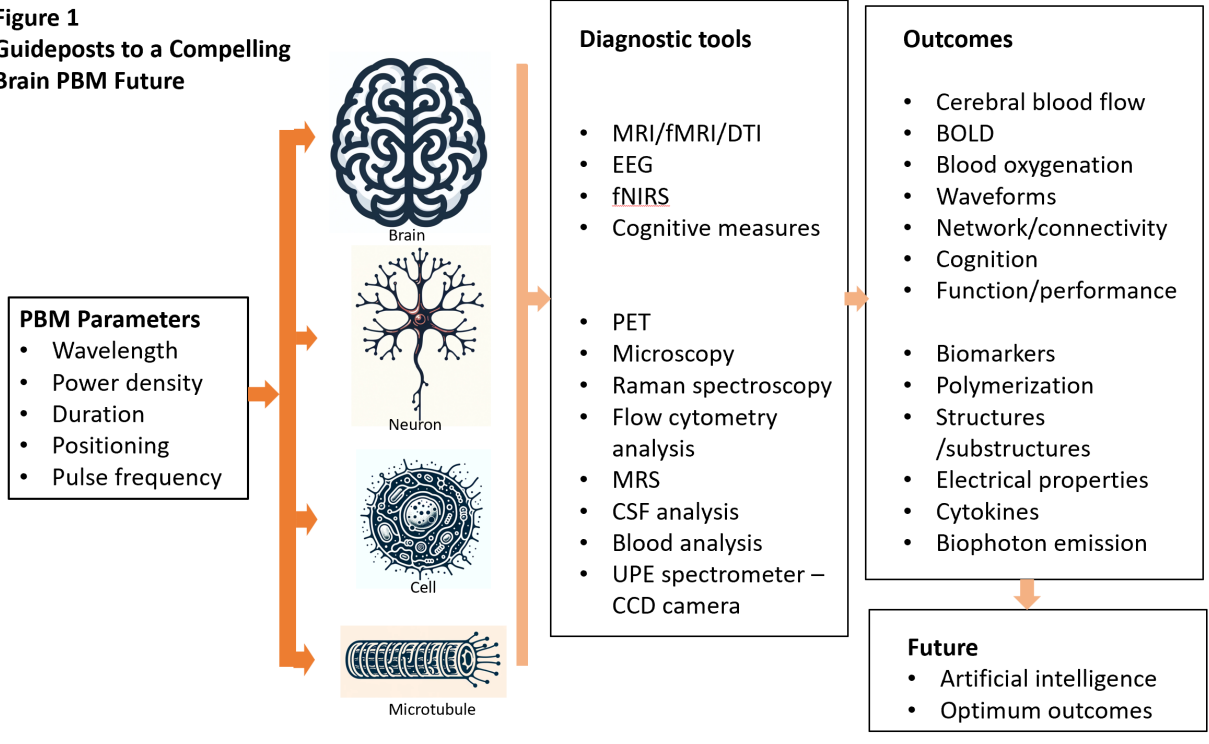
**Methods:** A comprehensive literature review spanning in vitro, animal, and human studies reflect PBM's positive impact on brain conditions. Yet, the variability in results across human studies, attributed to diverse and unclear parameter utilization, necessitates deeper investigation into parameter effects. The results covered in this presentation were revealed through EEG, fMRI, MRI, DTI, cognitive measures, microscopy, and Raman spectroscopy, blood analysis among other techniques, to analyze brain responses to pulse frequencies and other parameters. The aim is to understand their effects on electrophysiological signals, connectivity, blood flow, cognitive assessment, polymerization, molecular structures, and biophoton emission. Unpublished preliminary data provide additional support for the results. See Figure 1.

**Results:** Key findings highlight:

- PBM's significant influence on brain function.
- The differential effects of wavelengths (1064 nm and 810 nm) on blood flow and physiological aspects.
- Inhibitory effects of pulse frequencies above 40 Hz.
- Individual variability in response to pulse frequencies affecting brain waveforms.
- The role of LED positioning and pulse frequencies in modulating network connectivity.
- The substantial effects of low-power intranasal irradiance.
- Rapid EEG and fMRI responses to PBM.
- NIR irradiation at 10 Hz improving cellular electrical flow, resilience, and influencing microtubular structures. These findings emphasize the importance of pulse frequency.

**Conclusion:** Recent findings on parameter effects reflect emerging paradigms that set the course for a compelling future for brain PBM. However, further study on the diverse parameters is needed to further fine-tune their effects on cellular, brain network and other physiological characteristics. Artificial intelligence would be integral in the process, and in the final solution.

**Figure 1**  
**Guideposts to a Compelling**  
**Brain PBM Future**



# PHOTOBIO-MODULATION IN NEUROSCIENCE: A SUMMARY OF 30 YEARS OF PERSONAL EXPERIENCE

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## Abstract

**Learning Objective:** To summarize personal experience with laser photobiomodulation and its potentials for the treatment of peripheral and central nerve system injuries.

**Methods and Results:** Studies investigating effects of laser photobiomodulation on injured peripheral nerves in rats reported immediate protective effects which increase the functional activity of the nerve, decrease or prevent scar tissue formation at the injured site and degeneration in corresponding motor neurons of the spinal cord, and significantly increase axonal growth and myelination.

A direct application of laser on spinal cord had a positive impact on the corresponding injured peripheral nerve and promoted recovery. A 780-nm laser phototherapy was applied following peripheral nerve reconstruction using a guiding nerve tube. Results showed myelinated axons crossing through the nerve tube and continuation of axonal sprouting through the tube toward distal part of the nerve. In a double-blind, placebo-controlled randomized pilot clinical trial in patients with incomplete stable long-term peripheral nerve injury (PNI), 780-nm laser irradiation progressively improved peripheral nerve function and led to substantial functional recovery.

Muscle atrophy represents a major challenge in restorative medicine. Laser phototherapy was shown to increase biochemical activity and improve morphological recovery in muscle and, thus, could have a direct therapeutic application, especially during progressive muscle atrophy resulting from PNI. The effectiveness of composite implants of cultured embryonal nerve cells and the role of laser irradiation on regeneration and repair of rats' injured spinal cord were examined. Results suggested that laser photobiomodulation treatment accelerates the axonal growth at injury site.

**Conclusions:** The significance of performed experimental and clinical studies is in the provision of new laser technology and its therapeutic value for peripheral nerve and muscle preservation.



# DIFFERENTIAL EFFECT OF PHOTOBIMODULATION ON BIOPHOTON ACTIVITY IN CULTURED BRAIN CELLS

JAIMIE HOH KAM

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## Abstract

**Introduction:** Biophotons, also called ultra-weak photon emissions, refers to the release of light by the metabolic reactions of all living cells. Here, we detected biophotons from both cultured Neuro-2a cells and astrocytes under different conditions; at rest, after application of a stressor and after photobiomodulation treatment. In essence, we tested the idea that biophoton activity can reflect different states of stress and whether photobiomodulation can influence these activities.

**Methods:** Biophotons from cultured Neuro-2a (CCL-131) cells and C8-D1A astrocytes were analysed at ambient temperature in complete darkness. Biophotons were measured using a photomultiplier for 10 mins. The cells were treated with an LEDs emitting 670nm and 810nm for 2 mins at either 50mW/cm<sup>2</sup> (810nm) and 70mW/cm<sup>2</sup> (670nm)- low dose or 96mW/cm<sup>2</sup> (810nm) and 134.6mw/cm<sup>2</sup> (670nm) – high dose equating to a dose of 6J/cm<sup>2</sup> /8.4J/cm<sup>2</sup> and 11.5J/cm<sup>2</sup> /16.2J/cm<sup>2</sup> respectively. After treatment, biophotons were measured for another 10 mins. Cells were then treated with sodium troclosesene as a stressor and the number of biophotons were measured for 10 mins.

**Results and Conclusions:** We found that both the Neuro-2a cells and astrocytes emitted a small number of biophotons at rest (n=14.5 and 12.4 respectively). This number increased substantially for both Neuro-2a cells (n=28.4), and the astrocytes (n=29), when stressed with sodium troclosesene. When treated with 670nm/810nm light, biophoton emission was reduced in the Neuro-2a cells compared to the control (p<0.0001 for both energy intensities), but hardly in the astrocytes (p= 0.0171 for low dose and p=0.0532 for high dose). In conclusion, our results indicated key differences in biophoton activity under states of health and that photobiomodulation has a differential effect on this activity on the different types of brain cells.

# A REVIEW ON THE EFFECTS OF PHOTOBIOMODULATION ON HYPERTENSION IN EXPERIMENTAL STUDY.

INSOO JANG

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## Abstract

**Objective:** We investigate experimental studies through literature review to confirm the effect of photobiomodulation (PBM) on high blood pressure.

**Materials and methods:** Related search terms related to hypertension and PBM were searched in PubMed and SCOPUS. Primary analysis was conducted on the papers searched the titles and abstracts, and papers unrelated to the subject were excluded. In addition, studies used in combination with other interventions or used together for various indications were excluded.

**Results:** As a result of analyzing four experimental research papers, four used an experimentally induced high blood pressure in animal model, and one used spontaneous hypertension rats. All light sources used in the study were lasers, and their wavelengths were mainly 660 nm and 780 nm, and the laser irradiation method was percutaneous irradiation on the abdomen or tail of the experimental animals. In the results, it was reported that all five papers showed a decrease in blood pressure.

**Conclusion:** This review suggests that there is a limited possibility for the blood pressure-lowering effect of PBM. However, the limitations of experimental studies are remained, so more scientific experimental studies and additional clinical studies should be warranted. (KHIDI grant number HF23C0031)

## PBM-WHAT REACHES THE TARGET TISSUE

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### Abstract

#### Learning Objectives:

1. Learn effect of skin on bone on light penetration
2. Does increasing power increase light reaching target tissue
3. Does tip size affect penetration

**Introduction:** As a clinician we have dose recommendations for clinical treatment; however this is the dose that comes out of the machine and not what reaches the target tissue. Study tries to quantify those numbers.

**Study:** In the study I used several different lasers and LED devices:

Konf: 808nm 250mW laser (Konf Taiwan) and 660nm 150mW Laser with an 8mm diameter Tip. Powers were fixed with these devices. Zolar photon laser 810nm 3W (Zolar lasers Canada) with a 3 mm tip diameter Power on this unit Canada be adjusted by 10mW. Readings were taken with a Coherent Field Max 2 TO power Meter (Coherent USA). Power in Watts to 2 decimal places so 10mW. First the actual power coming out the end of the tip were taken. The readings were taken by shining the device through the web of the skin between the then thumb and first finger or through the bone of the fingers. Thickness were measured using a digital caliper.

Results using different tip thicknesses and powers. All measurements were taken at 1cm skin thickness

Konf 250mW 808 nm

Power

300 mW power at 1cm 70mW = 23.3%

Zolar 810 mw

Power

100mw power at 1cm 20mW=20%

200mW 40mW=20%

300mW 70mW =23.13%

1W 220mW=22%

In this part of the study the penetration depth was consistent throughout the various power outputs.

Also at 300mW the power output was identical with both an 8mm and 3mm tip diameters.

Power through various tissue with Konf 808nm, 250mw and 150mW 660 nm

Results different tissues and thicknesses

Power at tip 808nm 300mW 660nm 130mW

Skin 5mm 808nm 120=40% 660nm 20mW=15.3%

Skin 1cm 808nm .7 =23.13% 660nm 10mW=7.17%

Finger 5mm 808nm 50mW=16.7% 660nm 20mW=15.4%

Finger 1cm 808nm 20mW=6.7% 660nm 0 reading=<5mw

**Conclusion:** Power and tip size had no effect on depth of penetration. Infrared wavelengths had a greater percentage of power at the target compared to red.

Clinical consideration of these results will be discussed.

# DERMATOLOGY

## PHOTOBIO-MODULATION AND PHOTODYNAMIC THERAPY IN DERMATOLOGY: MECHANISMS, APPLICATIONS, AND FUTURE PERSPECTIVES

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### Abstract

#### Learning objectives:

1. Photo biomodulation have metabolic and anti-inflammatory effects in dermatology.
2. PBMT can be useful in management of acne vulgaris, psoriasis and alopecia.
3. Low Dose Photodynamic Therapy can accelerate skin wound healing.

Photobiomodulation therapy (PBMT), has emerged as a promising modality in dermatology, offering non-invasive and effective treatment options for various cutaneous conditions. PBMT stimulate cellular processes and promote tissue repair and regeneration. In dermatology, PBMT has shown efficacy in the treatment of wound healing, inflammatory skin disorders, and aesthetic dermatology. PBMT enhances cellular metabolism, reduces inflammation, and promotes collagen synthesis, leading to accelerated wound healing and tissue remodeling.

Current applications of PBMT in dermatology include the management of chronic wounds, acne vulgaris, psoriasis, and alopecia. PBMT has also gained popularity in aesthetic dermatology for its ability to improve skin texture, tone, and elasticity, with minimal side effects and downtime.

Future perspectives in PBMT research focus on optimizing treatment parameters, elucidating molecular mechanisms of action, and exploring novel applications. Despite its promising potential, PBMT faces challenges such as standardization of treatment protocols and variability in treatment response among patients.

On the other hand, Photodynamic therapy (PDT) has become a cornerstone in dermatological practice, offering an effective treatment modality for various cutaneous conditions. PDT involves the administration of a photosensitizing agent, such as aminolaevulinic acid (ALA) or methyl aminolevulinate (MAL) and etc. followed by exposure to light of a specific wavelength. Upon light activation, the photosensitizer generates reactive oxygen species, leading to localized tissue destruction and therapeutic effects.

In dermatology, PDT is widely utilized in the treatment of actinic keratoses (AKs), basal cell carcinoma (BCC), and acne vulgaris. PDT offers several advantages, including targeted therapy, minimal scarring, and excellent cosmetic outcomes. Additionally, PDT has shown efficacy in the management of photodamaged skin, inflammatory dermatoses, and vascular lesions.

In conclusion, PBMT and PDT represent a valuable therapeutic approach in dermatology, offering safe, effective, and non-invasive treatment options for a wide range of cutaneous conditions. Continued research and innovation in PBMT and PDT hold promise for further expanding its applications and improving patient outcomes in dermatological practice.

# SYNERGISTIC EFFECT OF BLUE LIGHT AND TERBINAFINE ON THE PRODUCTION OF REACTIVE OXYGEN SPECIES: A POTENTIAL TREATMENT FOR RESISTANT CUTANEOUS MYCOSES

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## Abstract

**Introduction:** Terbinafine is one of the most commonly used antifungals in the treatment of cutaneous mycoses. It acts by inhibiting the enzyme squalene epoxidase in the fungal cell membrane, although it also increases the production of reactive oxygen species (ROS), contributing to its antifungal effect. The increasing therapeutic failures in cutaneous mycoses due to the growing resistance have led to the search for new therapeutic options such as photodynamic therapy or laser treatment.

**Objective:** To study the combined effect of high doses of blue light and terbinafine on the production of reactive oxygen species.

**Methods:** Cultures of human keratinocytes (HaCaT) were divided into 4 groups: treated with blue light (78 J/cm<sup>2</sup>, 2 exposures of 20 min separated by 24 hours with blue light of 448 nm), treated with terbinafine (concentration of 10 microM for 48 hours), treated with both light and terbinafine, and controls without light or terbinafine. Cell viability studies (XTT assay) and quantification of reactive oxygen species (quantitative immunofluorescence for ROS) were performed.

**Results:** Terbinafine reduced cell viability by 44%, while blue light decreased it by 31%, compared to controls ( $p < 0.001$ ). The combination of both treatments reduced viability by 56% ( $p < 0.001$ ). When the combined treatment was performed under nutrient restriction conditions, viability decreased by up to 80% ( $p < 0.001$ ), compared to control. Concurrently, terbinafine increased ROS production by 30% (SD 9.2%,  $p < 0.001$ ) while HEVL increased it by 23% (SD 12.5%,  $p < 0.001$ ) compared to controls. The combination of both treatments, the increase in ROS production reached 108% (SD 13.4%,  $p < 0.001$ ) compared to controls.

At least three independent replicates were conducted per experiment. One way ANOVA with Turkey post-test t-test was applied using GraphPad Prism 6.01 software (GraphPad Software, San Diego, CA, USA).

**Conclusion and learning objectives:** The study demonstrates a marked synergy of blue light and terbinafine in ROS production. The synergistic effect of the combination of these treatments, photonic and pharmacological, could be useful in clinical practice, as it could improve therapeutic response, reduce the duration of antifungal treatment, and treat mycoses resistant to conventional antifungals.

# EVALUATION OF THE EFFECTS OF PHOTOBIMODULATION BY 940NM DIODE LASER ON NASAL TIP EDEMA REDUCTION TWO MONTHS AFTER RHINOPLASTY.

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## Abstract

### Three Learning Objectives:

1. Common rhinoplasty complications
2. Anti inflammatory effect of Photobiomodulation
3. Early edema management

**Introduction:** Rhinoplasty surgery difficulties are soft tissue complications such as edema and ecchymosis in the early postoperative days. Photobiomodulation reduces inflammatory mediators and accelerates the healing process after surgery. Therefore, this study investigated the effects of Photobiomodulation on nasal tip edema after rhinoplasty.

**Methods:** This clinical trial study was conducted on 20 rhinoplasty candidates. In the intervention group, a 940 nm diode laser was irradiated in eight areas of the nose and around the nose, in the submandibular and jugular-digastric areas, and in two nostrils. The energy per area was 9 J. Power density: 44 mW/cm<sup>2</sup>; Energy density: 4 J/cm<sup>2</sup>, Output power: 0.1W, spot size: 2.27 cm<sup>2</sup> and 90 seconds of radiation was applied to each area. The first radiation was performed immediately after the operation, and afterwards every other day for a week. Then, the laser was irradiated twice a week until the end of the second month. In control group sham laser was used.

**Results:** Statistical analysis by ANOVA, kruskal-wallis and t-test showed width of the nose in the area between the tip of the nostril and the tip of the nose, width of the nose in the area of the tip of the nostrils, width of the nose in the middle area of the columella, depression of the upper area of the tip of the nose, the tip of the nose projection, the degree of visibility of the columella, and the rotation of the tip of the nose, in the intervention and control groups had no significant difference ( $P>0.05$ ).

**Conclusion:** The findings of the differences in changes in nasal projection, the indentation of the upper area of the tip of the nose, rotation of the tip of the nose, and the degree of visibility of the columella at different time intervals after the operation, indicate the positive effect of low intensity laser in reducing acute nasal edema after rhinoplasty. However, it was not statistically significantly different from the control group.

# EXPERIMENTAL STUDY OF COMBINATION THERAPY OF 980NM LOW-LEVEL LASER AND ELECTRON RADIATION THERAPY ON NON-MELANOMA HUMAN SQUAMOUS CELL CANCER (SCC)

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## Abstract

**Introduction:** In this research, we aimed to find the efficacy of combined electron-laser therapy on non-melanoma Squamous cell carcinoma (SCC) cancer cells in an in-vitro study.

**Material and methods:** The human SCC cancer line (TSCC-1) was cultured based on the standard protocol. The groups of this study were control; only electron radiation; only Low-Level Laser Therapy (LLLT); and combined laser-electron radiation. Single session LLLT was done using a 980 nm 50 mW with energy doses of 1 and 1.5 J/cm<sup>2</sup>. Electron radiation was done using a Varian accelerator with a radiation dose of 2 and 4 Gy. MTT and flow cytometry bioassays were performed and analyzed to check their effectiveness.

**Results:** The cell viability test for irradiation with 980 nm 50 mW laser irradiation time of 20 and 30 s in combination with 2 and 4 Gy electrons showed a significant difference (P-value <0.01). Flow cytometry test of the electron-radiated cell samples showed that the sum of early and late apoptosis was the highest. However, the maximum percentage of apoptosis and necrosis was obtained close to the electron alone and for the combination of electron-laser radiation of 30 s with 2 and 4 Gy electrons. Except for the control group, the quantitative interval of induced necrosis of all the groups evaluated by electron alone, laser alone, and combined electron laser was almost equivalent.

**Conclusions:** This study showed that the physical parameters of a 980 nm LLLT might not have a synergy effect on treatment response in combination with an electron ionizing beam on SCC cancer cells. In more extensive studies, it is critical to doublecheck the effect of various laser wavelengths, and powers for combination therapy with ionizing radiation.

# PHOTOBIMODULATION FOR THE VETERINARY ONCOLOGY PATIENT

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## Abstract

Historically, there has been very mixed recommendations about the use of photobiomodulation therapy (PBMT) in oncology patients. These recommendations have ranged from cautions to not use the modality at all in patients that were currently or previously being treated for neoplastic disease, or in those that could have unknown neoplasia, to using it only in patients so long as PBM was not applied directly over the area of known tumor tissue. Early recommendations were originally made out of an abundance of caution. This was largely based on a few early studies that showed PBM stimulated the growth of cancer cells in cell culture. Not all experimental studies found the same results, however, and not only does a growing body of research show that PBM can be very beneficial in mitigating numerous side effects that occur as a result of cancer therapies in humans, other research shows that there may even be some potential mechanisms by which PBM can actually be applied against cancer.

Studies that suggest that PBM can actually stimulate cancer growth in animal tumor models *in vivo* are very rare and some of these studies suffer from inherent design flaws such as failing to account for the protective role of the immune system. Other researchers have found that when PBM parameters that increased cancer cell growth *in vitro* are recapitulated *in vivo*, a lower index of tumor growth and invasiveness was seen in laser treated animals. Evidence for the use of PBM in mitigating cancer treatment side effects will be extensively discussed in this presentation, alongside the results of several studies suggesting that PBMT using wavelengths and fluences typically recommended for clinical practice in veterinary medicine is well tolerated and effective for application in cancer patients. Real world clinical cases where PBM has been used in the veterinary patient to help manage side effects of cancer treatment(s) including diarrhea, sterile hemorrhagic cystitis, and wounds from extravasation type injuries will be presented.



# EFFICACY OF ALA PHOTODYNAMIC THERAPY WITH HALF- VERSUS FULL-LIGHT DOSE IN LARGE SEVERE FIELD CANCERIZATION

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## Abstract

### Learning objectives:

1. Irradiation parameters in photodynamic therapy (PDT) play an important role in experienced pain during the procedure.
2. Halving total light dose in PDT does not seem to reduce clinical efficacy of the procedure even in severe field cancerization.
3. Reduced light dose protocol seems to offer a better tolerability profile compared to standard parameters.

**Introduction:** Conventional red-light photodynamic therapy (PDT) is an effective treatment for actinic keratoses (AKs) and field cancerization. However, reducing the pain during conventional PDT is still a pitfall in this kind of therapy. With this objective we assessed the clinical efficacy, tolerability, and safety profiles between two protocols with different light regimes for conventional red-light PDT with BF-200 ALA.

**Methods:** A prospective, randomized, clinical trial was conducted in 15 patients. One group (n=8) was treated with LED red light (635nm) full-light dose PDT (10 minutes, 77mW/cm<sup>2</sup> irradiance, 37 J/cm<sup>2</sup> light dose) and the other group was treated (n=7) with a half-light dose PDT (5 minutes, 77mW/cm<sup>2</sup> irradiance, 18.5 J/cm<sup>2</sup> light dose). The clinical response was evaluated 1.5 months after 1 PDT session with subsequent follow-up at 3 and 6 months.

**Results:** Fifteen patients with multiple AKs and severe scalp field cancerization were included in this study. The mean lesions per scalp were 37.1 (grade I and II according to Olsen) and a mean AKASI of 6.2. Efficacy of both protocols was statistically comparable (p>0,05) at all time points with initial lesion clearance rates of 87.44% (grade I) and 95.94% (grade II) for the half-light dose protocol and 85.08% (grade I) and 87.44% (grade II) for the full-light dose protocol. A reduction in VAS score was documented from 8.57 for the full-light dose protocol to 7 for the half-light dose protocol with a statistically comparable (p>0,05) AKASI, AKQoL and DLQI improvement for both treatment protocols.

**Conclusions:** The half-light dose protocol with BF-200 ALA seems to be a highly effective and safe option to maintain successful clearance rates yet reducing pain exposure during PDT illumination even in severe field cancerization. Further studies are necessary in order to confirm these promising findings and implement modifications in real clinical practice.

# THE EFFECT OF PULSED BLUE LIGHT ON FIBROBLASTS AND LUNG CELLS

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## Abstract

**Introduction:** Pulsed blue light (PBL) inactivates bacteria and viruses at low fluences, and irradiances compared to continuous wave Blue Light (BL). Previously, we showed that human fibroblasts irradiated with 100 mW/cm<sup>2</sup> irradiance and 110 J/cm<sup>2</sup> dose or higher, were impaired and had altered morphology. PBL is 50 to 100 times more efficacious than BL, therefore, we used a lower irradiance (10 mWcm<sup>-2</sup>) and dose (75.6 J/cm<sup>2</sup>) known to be antiviral to explore the effect of PBL on human dermal fibroblasts—which can harbor bacteria, and lung epithelial cells which are susceptible to viral infection.

**Learning Objective:** To determine (1) the potential cytotoxic effect of germicidal doses of PBL on normal cells, and (2) the relative effect of two PBL wavelengths. (3) To obtain data that could help refine PBL treatments.

**Methods:** Human dermal fibroblasts and BEAS-2B lung bronchus epithelial cells obtained from ATCC were irradiated thrice at 30-minute intervals with either 405 or 450 nm PBL. Following irradiation, the culture plates were incubated for 24 h, then cell viability assays were performed. Cell morphology was also studied with an inverted microscope, and data analyzed with ANOVA and *post hoc* Bonferroni test.

**Results:** Live cell concentration and viability of fibroblasts irradiated with 405 nm and 450 nm wavelengths decreased insignificantly to 80% and 90% of controls ( $p > .05$ ). Unlike the fibroblasts, under bright field microscopy, the lung epithelial cells became rounded and floated in the medium, indicating distress and cell death. This effect was wavelength dependent and more pronounced at 405 nm than 450 nm.

**Conclusion:** (1) PBL irradiation of dermal fibroblasts did not significantly affect the concentration and viability of the cells. (2) PBL irradiation of the lung epithelial cells significantly reduced the concentration and viability of the cells. (3) The cytotoxic effect of PBL was less pronounced at the longer 450 nm wavelength. (4) This suggests the use of lower doses and longer wavelengths of PBL to treat lung epithelial cells. Studies are ongoing to determine the effect of lower doses and irradiances. The implications of these findings for treatment modalities will be discussed.

# DOSE REDUCTION WITH RED LED LIGHT IN PHOTODYNAMIC THERAPY: LOOKING FOR THE BALANCE BETWEEN PHOTOBIMODULATION AND PPIX TARGET.

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## Abstract

**Introduction:** Pain represents a significant limitation in the treatment of Photodynamic Therapy (PDT) with red light (RL) for actinic keratoses (AK). Furthermore, the doses that have been applied for years at 37J/cm<sup>2</sup> seems arbitrary, and why those doses were recommended in the literature is not clear. On the other hand, with those doses, the photosensitizer, protoporphyrin IX, is mostly consumed in the first 3 minutes of treatment, although the treatment duration is 8 minutes.

**Objectives:** The aim of this study was to find optimal doses of RL parameters which produced a response in PDT of AK and reduce pain within a reasonable time of light delivery in the dermatologist's office.

**Material and methods:** A single-center, open-label, randomized clinical trial was conducted involving adult patients with more than 15 grade I and II actinic keratoses (AK) on the scalp candidates for PDT.. Patients were treated with occluded ALA for two hours. Patients were randomized to treatment with a red LED light dose of 18J/cm<sup>2</sup> administered over 15 minutes (37 mW/cm<sup>2</sup>) compared to 30 minutes (22 mW/cm<sup>2</sup>) using a RhodoLeDÒ lamp (Germany). AK counts and quality of life were assessed before treatment and at 3 months. During treatment, pain intensity was measured using the Visual Analog Scale (VAS). Patients reported side effects 48 hours post-treatment via photographs and a questionnaire. Patients were followed-up at 3 months, and statistical analysis was performed using SPSSÒ.

**Results:** A total of 15 patients were treated in each treatment group with an average of 26 actinic keratoses (AKs) on the scalp. Responses of 75% were achieved, comparable to conventional PDT doses of 37J/cm<sup>2</sup>, with a significant reduction in the pain scale.

**Conclusions:** The change from conventional PDT doses to lower doses allows the addition of photobiomodulation effects to PdT treatment by avoiding necrosis and inducing cellular activation. Additionally, the technique is optimized, resulting in better pain control and good treatment response within a reasonable timeframe during the dermatologist's consultation.

# FLASH POSTER ORAL PRESENTATION

## REDUCTION OF LARGE ODONTOGENIC CYSTS WITH SOFT LASER THERAPY

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### Abstract

In this short presentation, I would like to present cases demonstrating the cyst reduction and bone regeneration effects of soft laser therapy based on cases in a village practice of 5000 people.

- Number of cases treated: 5
- Sample composition: The age of the patients ranged from 16 to 63 years. Males and females, mixed.
- Outcome achieved: In all five cases, despite the large size, a successful cystectomy could be performed, and in 4 cases we were even able to save the compromised teeth.

In dentistry, low-power laser light therapy is mainly used for pain relief and inflammation reduction, less often for biostimulation. It is known that laser light enhances the regeneration of bone tissue. Odontogenic cysts are epithelial tubes surrounded by a connective tissue capsule, the cavities of which are filled with fluid.

They typically grow continuously, destroying the surrounding bone tissue. They do not heal without surgical treatment. Surgery for large cysts often involves the removal of the surrounding teeth. With root canal therapy and soft laser therapy, these teeth can be retained and the cysts can be significantly reduced in size before surgery.

Laser treatment was initially performed with an infrared laser of 50 mW at a wavelength of 808 nm at a dose of 4J/cm<sup>2</sup>. In later years, an infrared laser with a power of 100 mW and a wavelength of 808 nm was used, also with a dose of 4J/cm<sup>2</sup>.

The frequency of treatments was 2 times/week. The number of treatments per patient was 10-12.

The age of the patients ranged from 16 to 63 years. Males and females, mixed. One case was cysta follicularis, the other 4 cases were cysta radicularis.

**In all cases, the cysts were significantly narrowed by soft laser treatment, and by Patsch II surgery successful cystectomies were performed. All patients were cured without complications**

# PBM USE FOR NERVE REGENERATION IN DENTISTRY

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## Abstract

### Learning Objectives:

1. What wavelength and dosage is best
2. Where to apply device
3. Measuring Success

**Introduction:** The author has been using and lecturing on PBM for over 30 years. The presentation will outline the techniques to treat nerve damage in his dental practice as well as the cases that he has consulted on throughout the world.

**Abstract:** Nerve damage in the dental environment can be a parasthesia or a total severing of the nerve. The presentation will focus on damage to the Mandibular Nerve (V3) and the Maxillary Nerve (v2). The most common causes are damage during 3rd Molar extractions, Orthognathic Surgery, Implant Placement and Infection. Studies have shown near Infrared wavelengths to be best for treatment. I try to apply a dose of 4J//cm<sup>2</sup> to the nerve. It is very important that the power is at the nerve and not the power coming out of the unit. The effect of power reduction at deeper depths will be covered and illustrated. The nerve is treated from the site of the injury to the anterior end of the nerve. Near the end of the nerve there are larger areas of the chin and tongue involved and these can be treated using scanning techniques or a larger Cluster Probe. In the case of the mandibular nerve it will be shown how to mark out the are of numbness in the chin and how to use the reduction in the size of the area to give an objective measurement of the success of the treatment. I generally treat the patient 3 times a week for 3 weeks and dismiss the patient for 3 to 4 weeks and then reassess. The techniques will be illustrated by clinical cases the author has treated and will discuss what to watch for as treatment progresses and communication with the patient before and during treatment.

**Conclusion:** PBM has proven to be a very useful tool in the treatment of nerve damage in the oral cavity

# APPLICATIONS OF PHOTOBIMODULATION THERAPY IN PEDIATRIC DENTISTRY: A SYSTEMATIC REVIEW

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## Abstract

**Background:** Pediatric dentistry often necessitates non-invasive and painless treatment modalities to ensure the comfort and well-being of young patients. Photobiomodulation therapy (PBM) has emerged as a promising approach for various dental applications due to its, minimal invasiveness, and potential for cell response modulation and tissue regeneration. This systematic review aims to assess the efficacy of PBM in pediatric dentistry.

**Methods:** A comprehensive search of electronic databases was conducted to identify relevant studies published from 2018 to 2024. Inclusion criteria encompassed randomized controlled trials, clinical trials, and observational studies evaluating the use of PBM in pediatric patients. Data extraction and quality assessment were performed using predefined criteria, and findings were synthesized narratively.

**Results:** A total of 35 studies met the inclusion criteria and were included in the review. Findings indicate that PBM demonstrates promising results in pediatric dentistry, particularly in providing effective reduction of pain perception during anaesthesia injection, reversal of soft tissue local anesthesia, management of oral mucositis in pediatric oncology patients, and promoting pulp regeneration in immature permanent teeth.

**Conclusion:** Photobiomodulation therapy emerges as a promising adjunctive treatment modality in pediatric dentistry for anesthesia, oral mucositis management, and pulp regeneration. While further research is warranted to elucidate optimal protocols and long-term outcomes, the evidence suggests that PBM holds significant potential in improving clinical outcomes and enhancing the overall dental experience for pediatric patients.

**Keywords:** photodynamic therapy, pediatric dentistry, anesthesia, oral mucositis, pulp regeneration

# EFFECTIVENESS OF PHOTOBIMODULATION (PBM) FOR THE TREATMENT OF IRRITABILITY ASSOCIATED WITH AUTISM SPECTRUM DISORDER: CASE REPORT

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## Abstract

The study examined the effectiveness of photobiomodulation (PBM), also known as low-level laser therapy (LLLT) for the treatment of irritability associated with autism spectrum disorder in a 5-year-old child. With the aim of analyzing the effects of laser therapy on the irritability of children with autism, verifying the child's tolerance to therapy, and, finally, verifying the feasibility of studies with a larger number of individuals. The subject received diode low-level laser therapy irradiation, in the frontal areas of the skull, in 6 points lasting 60 seconds at each point, 6J of power were used, with infrared wavelength. Subsequently, Intravascular Laser Irradiation of Blood (ILIB) therapy was performed on the dorsal artery of the foot, for 15 minutes, at the red wavelength, the conduct was carried out for a period of 4 weeks. The subject was evaluated with the Aberrant Behavior Checklist (ABC), with the global scale and five subscales (irritability/agitation, lethargy/social withdrawal, stereotypical behavior, hyperactivity/noncompliance and inappropriate speech), Autism Treatment Evaluation Checklist (ATEC) and the Clinical Global Impression Scale (CGI).

The assessment occurred at the beginning of the study, in week 4 (endpoint), and week 8 (post-procedure) of the study. Student t-analysis concluded that this difference was statistically significant ( $p < 0.001$ ) in comparison to the baseline ABC irritability subscale score. The study found that low-level laser therapy is safe and can be an effective tool for reducing irritability and other symptoms and behaviors associated with autism spectrum disorder in children, with positive changes maintained and increased over time. However, randomized clinical trials are needed to confirm the effectiveness

# ANTIMICROBIAL PHOTODYNAMIC THERAPY OPTIMIZING THE MANAGEMENT OF ULCERATED HEMANGIOMA IN A NEWBORN: A CASE REPORT

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## Abstract

This case report has the following learning objectives: description of the clinical characteristics of ulcerated hemangioma in orofacial region of infants; evaluation of the efficacy of the antimicrobial photodynamic therapy (aPDT) in ulcerated hemangioma management; provide information to develop a treatment protocol for ulcerated hemangioma using aPDT. Infantile hemangioma is the most common vascular tumor in children, evidence of the presence of infantile hemangioma can be observed from birth, but its most classic characteristics begin to appear in the first weeks of life. Ulceration is a common complication of infantile hemangioma at an earlier stage and can cause pain, bleeding, risk of infection, scarring and functional impact. A 40-day-old white skinned male newborn went to the Oral Diagnosis Clinic due to a reddish discoloration in the upper lip, since birth, which progressed to an ulceration. The lesion consisted in a red papular proliferation with a crateriform ulcer without infiltration. These features led to the diagnosis of ulcerated hemangioma. An aPDT protocol was used to prevent ulcer progression and accelerate the repair process using red low-level laser (InGaAlP diode laser, 660nm, 100mW, 9J/cm<sup>2</sup>, 45 sec per point with a tip diameter of 0,04cm<sup>2</sup>) associated with the photosensitizer methylene blue. After five weekly aPDT sessions the ulcer healed completely, and the follow-up of 4 months showed no signs of recurrence despite the persistence of the hemangioma. Ulceration of hemangiomas is a common complication, occurring most frequently in anogenital region, followed by neck and lower lip. These ulcers use to heal slowly, causing pain and scar, due to the disruption of the regular inflammatory cascades especially caused persistent infection. Management with aPDT generates low levels of reactive oxygen species that eradicate a variety of microorganisms, conferring its safe and affordable antimicrobial effect. But also seems to play a role similar to photobiomodulation therapy, since it can mediate intracellular signaling for collagen deposition and cell proliferation, which accelerate wound healing providing comfort and better aesthetic results.



# THERAPEUTIC EFFICACY OF PHOTOBIO-MODULATION IN MANAGING CHRONIC AND RELAPSING BONE PAIN IN A VARIANT FORM OF CAMURATI-ENGELMANN DYSPLASIA: A CASE STUDY

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## Abstract

### Three Learning Objectives:

1. Understand the potential benefits of MLS Laser Therapy in the management of Camurati-Engelmann Dysplasia.
2. Learn about the specific Photobiomodulation (PBM) parameters used in treating chronic pain associated with skeletal dysplasias.
3. Analyse the impact of MLS Laser Therapy on pain relief, mobility improvement, and medication reduction in Camurati-Engelmann Disease.

**Brief Introduction:** Camurati-Engelmann Dysplasia (CED) is a rare autosomal dominant genetic disorder characterized by an increased build up of bone along the shafts of long bones (diaphyseal dysplasia), limb girdle muscle weakness, and severe chronic and relapsing pain predominantly in the lower limbs with impaired mobility issues.

Traditional treatment modalities which include life-long corticosteroid treatment, penicillamine and an Interferon Inhibitor (Infliximab infusions) have been only moderately effective in managing the symptoms. This case study explores the use of Multiwave Locked System (MLS) Laser Therapy, a form of Photobiomodulation, as a novel approach to manage chronic pain in a 40-year-old female patient diagnosed with severe variant CED.

**Methods:** The patient underwent MLS Laser Therapy sessions twice a week for six weeks. The PBM parameters were meticulously documented: wavelength (808nm and 905nm), power output (1.5W), frequency (1000Hz), and a cumulative energy dose of 2 Joules/cm<sup>2</sup> per session. Pre- and post-therapy assessments included Visual Analogue Scale (VAS) for pain, Range of Motion (ROM) measurements, and medication usage tracking.

**Results:** Statistical analysis revealed significant improvements post-therapy. The patient reported a substantial reduction in pain, evidenced by a decrease in VAS scores from 8 to 2. Improved mobility was indicated by enhanced ROM in the affected limbs. Notably, there was a 50% reduction in the patient's analgesic medication usage. These outcomes suggest a positive impact of MLS Laser Therapy on managing CED symptoms.

**Conclusions:** The case study indicates that MLS Laser Therapy has been significantly beneficial in managing chronic pain, improving mobility, and reducing medication usage in a patient with an autoimmune phenocopy of Camurati-Engelmann Dysplasia. These findings highlight the potential of MLS Laser Therapy as a complementary treatment modality for CED, warranting further research to validate its efficacy and establish standardized treatment protocols.

# IN VITRO INVESTIGATION OF ANTIMICROBIAL PHOTODYNAMIC THERAPY WITH METHYLENE BLUE AND INDOCYANINE GREEN ON BACTERIA ASSOCIATED WITH STAINING OF TEETH

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## Abstract

**Learning objectives:** Black stains of teeth pose great aesthetic concerns. The primary objective of our *in vitro* research was to assess the antibacterial efficacy of antimicrobial photodynamic therapy (aPDT) utilizing two photosensitizers, Indocyanine Green (ICG) and Methylene Blue (MB), on *Actinomyces naeslundii* (*A.n*) and *Aggregatibacter actinomycetemcomitans* (*A.a*). The findings of this study can pave the way for future phototherapy solutions for tooth staining.

**Introduction:** Although the etiology of black stains is not totally understood, it has been shown that chromogenic gram-negative bacteria, such as *A.n* and *A.a*, play essential roles in developing them.

**Methods:** In this experiment, two isolates of each bacterium were cultured and subjected to various treatments: no treatment (-control); CHX (+control); ICG; MB; ICG activated with an 808 nm laser (CW, 250 mW, 0.4 W/cm<sup>2</sup>, 24 J/cm<sup>2</sup>, 0.5 cm<sup>2</sup>, 60 s); and MB activated with a 660 nm laser (CW, 150 mW, 0.25 W/cm<sup>2</sup>, 15 J/cm<sup>2</sup>, 0.5 cm<sup>2</sup>, 60 s). Colony-forming units per milliliter (CFU/mL) were quantified to compare the groups. Biofilm formation was qualitatively evaluated using scanning electron microscopy on treated enamel specimens. One-way ANOVA and the Welch test were used for statistical analysis. Multiple comparisons were made using Tukey HSD and Games-Howell tests. A p-value of 0.05 and lower was deemed statistically significant.

**Results:** Using ICG alone or combined with 808 nm laser significantly lowered the colony counts of *A.a* and *A.n*. There was no significant decrease in bacterial colonies in the MB group compared to the +control. However, MB activated with 660 nm laser showed significant antibacterial activity. The density of the bacterial biofilm was significantly reduced in the groups treated with MB and ICG without laser activation compared to the control group. However, the reduction in bacterial biofilm density was more pronounced when aPDT with ICG was used.

**Conclusion:** aPDT using ICG with an 808 nm laser and MB with a 660 nm laser significantly decreased the number of chromogenic *A.n* and *A.a* bacteria. aPDT with ICG was found to be significantly more effective than MB, regardless of laser usage.

# EFFICACY OF ADJUVANT PHOTO BIOMODULATION WITH ACYCLOVIR IN HSV TYPE 1 RECURRENCE ULCERS TREATMENT, A SINGLE-BLIND RANDOMIZED CLINICAL TRIAL

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## Abstract

**Objective:** This study aimed to determine the effect of Photobiomodulation (PBM) in the treatment of recurrent herpes labialis (RHL), one of the most common herpes simplex virus type 1 infections.

**Material and Methods:** In this single-blind randomized clinical trial, Twenty-four symptomatic patients with RHL were enrolled. The patients were randomly allocated into the case (received 1% acyclovir cream 5 times a day for 5 days accomplished PBM once in the first visit and control groups who received acyclovir cream similar to the regimen of the treatment group without PBM. The size of the lesions, and pain intensity (based on a visual analogue scale) were considered as the outcome.

**Results:** Our findings suggested that, pain intensity 48 hours and 72 hours after treatment in case group were significantly  $p < 0.001$ ). The lesion's size was significantly reduced on the 7th and 10th days in the case group ( $p < 0.05$ ). Patients in the treatment group were significantly more satisfied with their treatment process group ( $p = 0.008$ ).

**Conclusion:** The results of the present study showed that LLLP in addition with acyclovir cream could be more efficient in treating pain intensity, lesion size, and recovery time in patients treated with recurrent herpes labialis infection.

# **DOSE DELIVERY PARAMETERS IN PBMT: HIGH ENERGY VS. LOW ENERGY PBM. ENERGY, POWER AND IRRADIANCE & TREATMENT OUTCOMES - A SYSTEMATIC REVIEW.**

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## **Abstract**

Learning Objectives are as follows:

1. To further develop an appreciation between the relation of overall energy delivery, surface area and optical transport to sub-surface tissues.
2. To assist in an understanding of the safety aspects of higher energy optical delivery therapies in PBMT
3. To aid researchers in design to reduce the potential for reporting errors due to placebo effects.

PBMT has achieved a high degree of acceptance as an evidenced base procedure for some superficial conditions such as oral mucositis. However due to tissue attenuation and absorption photon delivery to depth poses a challenge to optical delivery. Prior studies support usage of larger surface applicators with an overall greater energy delivery to improve the likelihood of clinical success. However this represents a new paradigm as high energy systems may be associated with an increased photothermal tissue response. Also as the inherent power distribution of the beam is predominantly Gaussian dosimetry is complicated due to the central peak in the spectral beam profile.

This study is based on a further in depth retrospective analysis of six previously published systematic reviews and meta-analyses. The tools employed include a modified Cochrane type risk of bias assessment with an added measure related to the reportage of parameters as well as use or otherwise of a placebo. The key metrics relate to the energy, power and surface area of the included dental clinical trials. statistical tools employed include ANOVA with a Bonferroni correction method. Datasets were subject to univariate data analysis & linear regression approaches for quantitative and qualitative outcome variables.

The results demonstrate the importance of the use of an additional control group employing a placebo as evident. Furthermore the clinical outcome is weighted against the total energy delivery in relation to sub-surface anatomy. The outcome is discussed in relation to the safety aspects of high surface energy systems as well as proposed surface delivery parameters for wavelengths in the red to NIR range for sub-surface targets up to 1cm in depth in dentistry. Within the context of a greater discussion proposals are made to assist clinicians in dosimetry in PBMT.

# LIGHT THERAPY ON A FUNCTIONALIZED ZIRCONIA SURFACE WITH ANTIMICROBIAL NANOPARTICLES FOR DENTAL APPLICATIONS

DANIEL COSTA

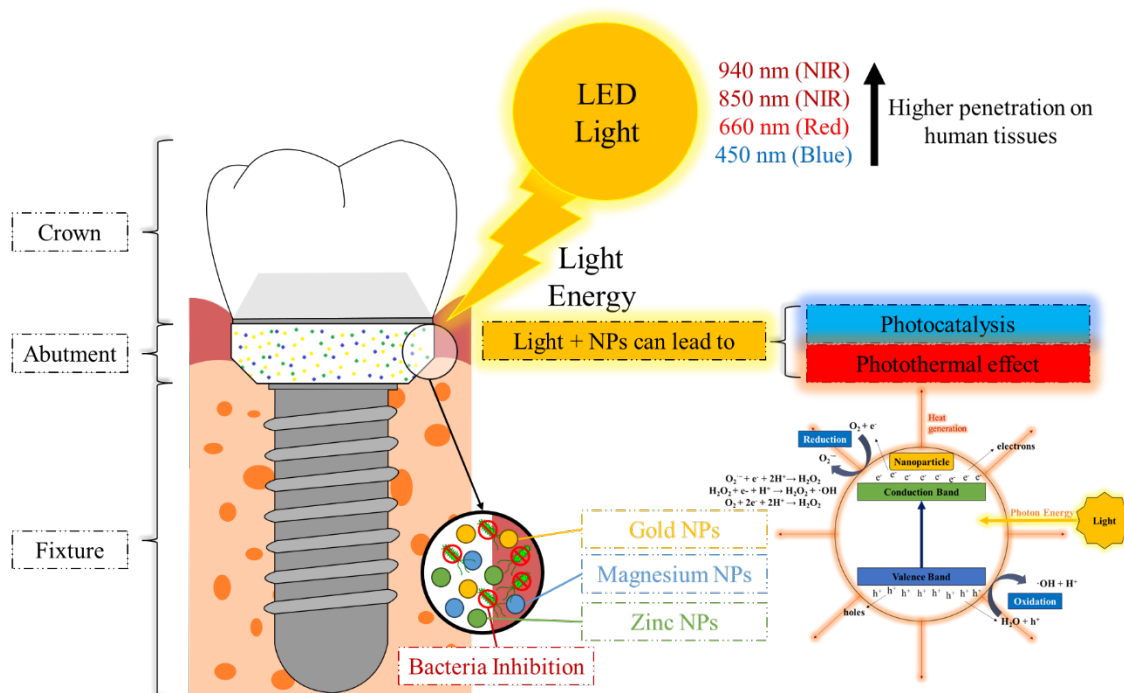
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## Abstract

Dental implants are considered the best solution for missing teeth but are sometimes associated with complications such as peri-implantitis, which is caused by bacteria and is characterized by tissue inflammation and bone loss which causes dental implants to fail over time [1].

Metal nanoparticles (NPs) can be a good antibacterial agent to be employed in dental implantology to prevent this pathology [2]. Furthermore these nanoparticles in conjunction with light energy, through a process known as photocatalysis, can produce harmful reactive oxygen species and with radiation in the red and near infrared region (660-940 nm) can also induce a localized photothermal therapy. On par with these effects, red and nir light radiation has also been shown to be positive for cell growth [3].

The present work was designed to, first, produce and characterize three different types of nanoparticles (gold, magnesium and zinc), obtained by laser ablation in distilled water and sodium dodecyl sulphate (SDS) using a Nd:YAG laser system. Secondly, validate their adhesion to zirconia surfaces. And finally, with the surfaces prepared, the antibacterial efficacy and cytotoxicity of these surfaces in conjunction with LED light radiation (with wavelengths of around 940, 850, 660 and 450 nm), were addressed, in order to confirm their potential use as an active functionalized antibacterial surface in dental implant abutments, to prevent peri-implantitis disease as shown in **Figure 1**.



**Figure 1.** Proposed antibacterial surface.

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# LED THERAPY IN THE TREATMENT OF RECURRENT BULLOUS ERYSIPELAS

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## Abstract

Erysipelas is an infection of the superficial layers of the skin, causing pain, redness, swelling, and blistering lesions. They are complex wounds that require daily care and impact the patient's quality of life. Associated with conventional treatment with antibiotics, local and postural care, photobiomodulation therapy through LED has photochemical effects that influence cellular behavior, primarily in tissue repair, anti-inflammatory, and pain relief.

Two case reports in home care, aged 45 and 58 years, male, residents in Rio de Janeiro. They present similar past pathological histories: obesity, hypertension, type 2 diabetes, under conservative renal insufficiency treatment, and sedentarism. Both developed recurrent erysipelas by *Streptococcus*, starting about 2 years ago. Due to the chronicity of the lesions, they developed lymphedema and aesthetic deformities, in addition to depressive symptoms and worsening quality of life. They had blistering and ulcerated lesions, exsudative and painful throughout, affecting from the infrapatellar region to the ankles of both lower limbs. The dimensions of the lesions were 34 cm x 54 cm. Daily dressings and cleansing with distilled water were performed, followed by alternate application of healing powder, 1% silver sulfadiazine, and 0.4% cerium nitrate, with gauze coverage and compressive bandage. After healing, 100% Rosehip oil was used. Transdermal ILIB technique (660nm, power 100 mW) was applied for 30 minutes to the radial artery. Blue LED (irradiance of 900 to 1100 mW/cm<sup>2</sup>) was irradiated twice a week, with continuous operation mode at 1J/cm<sup>2</sup>, total delivery of 1,836 Joules in direct contact with the tissue. Patient 1 (58 years) underwent 12 sessions and patient 2 (45 years) underwent 20 sessions. Healing was assessed weekly using the Pressure Ulcer Scale for Healing (PUSH) instrument.

Both patients showed complete healing of the lesions after treatment with blue LED. Additionally, a significant improvement was observed in their overall condition, pain reduction, better sleep, increased social interaction and relief from depressive symptoms.

LED therapy proved to be a complementary strategy to treatment, accelerating the healing of erysipelas lesions and improving the quality of life of the patients.





# PHOTOBIMODULATION THERAPY IN DERMATOLOGY: CLINICAL UPDATE

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## Abstract

**Background:** Photobiomodulation Therapy (PBMT) has multiple applications in Medicine. In Dermatology, PBM has indications as a therapeutic option or an adjuvant therapy in the management of several dermatological conditions, or in assisting recovery of post-procedural injuries to skin tissues. Although some mechanistic insights of PBM are understood, the evidence on PBMT effectiveness in dermatological clinical practice is more difficult to demonstrate. PBMT paradigm resides in abundance of published literature on one side, while few methodologically strong clinical trials with statistically significant evidence can be found, on the other. The heterogeneity of light parameters results in few PBM trials accepted in Cochrane databases. However, as more and more dermatologists worldwide are showing interest in PBMT, more clinical studies have emerged.

**Objective:** By conducting a systematic literature review of PBMT interest in Dermatology, specifically in acne vulgaris, eczema, atopic dermatitis, herpes simplex and zoster, psoriasis, acute and chronic wound healing and skin rejuvenation, this presentation provides an update of evidence, summary and analysis of applicability of findings of most recent trials translated into clinical context.

**Methods:** Primary data sources, principally from randomised control trials, well-conducted non-randomised clinical trials and studies on humans, published between 2007 and 2023 in English or French, evaluating the effects of PBM interventions in the pre-selected dermatological indications, with pre-defined studies'eligibility criteria, and pre-defined primary outcomes of interest enabled a search strategy applicable to PICO and PRISMA guidelines in reporting.

**Results:** This systematic search has retained thirty-three trials consisting of twenty-seven randomized control trials, two non-randomized clinical trials, one preliminary study, one observational study, one case-series and one longitudinal epidemiological study, allocated per dermatological indication: acne (n=9), psoriasis (n=4), eczema and atopic dermatitis (n=2), herpes (n=2), wound healing (n=8) and skin rejuvenation (n=8). Most of the clinical findings evidenced significant improvement of the pre-defined outcomes for each condition, some correlated to findings of anterior clinical investigations in vitro.

**Conclusion:** The assessment from retained studies of the beneficence-risks and adverse-events, suggests that PBMT is a safe and efficient non-thermal therapeutic option for the dermatological indication investigated, here demonstrated by a significant body of evidence in Dermatology.

# NON BIOMODULATORY PHOTOMEDICINE (APDT) FOR 3 DIMENSIONAL DISRUPTION OF BIOFILMS IN ENDODONTICS & ORAL CARE

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## Abstract

Non Biomodulatory, antimicrobial Photodynamic therapy (aPDT) is a groundbreaking and innovative approach that addresses the critical issue of antibiotic-induced bacterial resistance. By harnessing the power of light and a photosensitising agent, aPDT provides a non-invasive and targeted method to combat oral infections whilst minimising the reliance on antibiotics. Oral biofilm-associated infections, particularly those involving *Enterococcus faecalis*, *Streptococcus mutans*, and *Prevotella intermedia*, pose significant challenges which can be mitigated by a combination of specific dyes and wavelengths. This randomised, in vitro trial seeks to fill the research gap by systematically evaluating the antibacterial effects of dual-dye and dual-wavelength aPDT on oral biofilms.

**Objectives:** To assess and compare the antibacterial efficacy of methylene blue (MB) with red laser (660 nm) vs indocyanine green (ICG) with infrared laser (810 nm) and dual-dye (MB + ICG) with Combined Coherent light (red + infrared) on oral biofilms of *Enterococcus faecalis*, *Prevotella intermedia* & *Streptococcus mutans*.

**Methods:** Biofilms of *E. faecalis*, *S. mutans*, and *P. intermedia* were grown at 36°C and 5% CO<sub>2</sub> for 7 days in a 96-well plate in a brain heart infusion (BHI) growth medium. Before aPDT, a total of 27 inoculums were collected from culture wells and grown on culture plates to assess baseline colony forming units (CFU). The microbial wells were treated with Group I - MBaPDT (660 nm, 200 mW, for 60 seconds), Group II - ICGaPDT (810 nm, 300 mW for 60 seconds), and Group III - MBICGaPDT (660 nm, 100 mw + 810 nm, 100 mw for 120 seconds). Post-aPDT, inoculums were collected from wells to be cultured to assess CFU.

**Results:** Methylene blue antimicrobial photodynamic therapy (MBaPDT) resulted in significant reduction in *E. faecalis* counts compared to other groups ( $f = 11.15$ ,  $p = 0.01$ ). aPDT on *S. mutans* resulted in significant ( $p = 0.04$ ) reduction of counts in the ICGaPDT group. aPDT on *P. intermedia* resulted in significant reduction in counts ( $p \leq 0.05$ ) in MBaPDT and ICGaPDT groups.

**Conclusion:** aPDT may effectively reduce *E. faecalis* counts in infected root canals thus improving endodontic outcomes. Similarly, dual dye & dual wavelength strategies can mitigate the risk of antibiotic-induced bacterial resistance in mixed biofilm infections.

# THE USE OF PHOTOBIMODULATION THERAPY TO REDUCE SWELLING, PAIN AND TRISMUS AFTER DENTAL SURGERY: A CASE SERIES

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## Abstract

**Objective:** The aim of this study was to evaluate the effect of photobiomodulation therapy on postsurgical swelling, pain and trismus.

**Introduction:** Laser application has recently been established as an effective alternative to conventional procedures or as adjuvant therapy following oral surgery.

Among various types of lasers, the diode laser stands out for its application in photobiomodulation (PBM) or low-level laser therapy. Issues such as limited mouth opening, swelling, and pain can arise from procedures like mandibular third molar extraction, complex implant surgery, sinus lifting surgery, and mandibular fractures. This study aims to evaluate the efficacy of PBM in reducing postoperative side effects after different dental surgeries.

**Case Reports:** Five patients visited a private office, where thorough medical history assessments and oral examinations were conducted to establish individualized oral diagnoses and treatment plans: Case 1: A 53-year-old male with a mandibular unilateral body fracture. Case 2: A 38-year-old female who underwent sinus lifting surgery. Case 3: A 23-year-old female with impacted mandibular third molar surgery. Case 4: A 47-year-old female who received a bone block graft for reconstructing an alveolar defect. Case 5: A 35-year-old female who underwent ridge splitting surgery. The treatment plan for all the patients involved Photobiomodulation using diode laser wavelengths of 808 and 980 nm, as well as the use of 660 nm laser as a synergistic laser.

**Conclusion:** Following dental surgery, all patients experienced improvements in trismus, swelling and pain. Positive treatment results were noticeable during follow-up appointments. Low level laser therapy may be considered a safe and efficient technique for controlling pain, edema and trismus.

**Keywords:** Diode Laser, Photobiomodulation, pain, Trismus, Dental surgery, Swelling

## **PBM AT THE UNIVERSITY: NEW INSIGHTS**

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### **Abstract**

Studying photobiomodulation (PBM) at a university level, which is open to all French and foreign healthcare professionals for the past 3 years, has been enriched by specific features, in France at the University of Montpellier, on the campus of the Faculty of Medicine in Nîmes. The course has proved its worth by focusing on the explanation and rigorous learning of the physico-chemical and biological concepts involved in PBM. The most scientifically validated mechanisms are presented and discussed in depth. Autonomy is also encouraged through courses about critical reading. By alternating between individual and teamwork, a dynamic is established between the students, who progress by helping each other. Satellite modules, introduced last year, provide additional practical experience and feedback. These modules are attended by students who have passed their university exams. They focus on topical and hot issues, with the aim of offering different perspectives. Two new modules have been added to the program this year: "Pain" and "Brain". The teaching methods used in the modules are adapted to learners who are increasingly experts in their field: workshops for reflection and sharing experiences are set up, initiating avenues of research. Modules with partnerships with international universities are being created.

## SPORTS AND REHABILITATION

### PHOTOBIMODULATION EFFECTS ASSOCIATED WITH AN EXERCISE PROTOCOL IN THE TREATMENT OF NON-SPECIFIC NECK PAIN: PROPOSAL FOR A RANDOMIZED CLINICAL TRIAL

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#### Abstract

**Introduction:** Chronic neck pain is characterized by pain between the occipital region and the spinous process of the first vertebral segment of the thoracic region, which may radiate to the upper limbs and/or dorsal region, in addition to causing restriction of range of motion (ROM) and functionality. Therefore, several resources are explored in an attempt to reduce pain, many of them being associated with the practice of specific exercises.

**Objective:** To evaluate the effects of laser photobiomodulation (FBM) associated with an exercise protocol in patients with chronic nonspecific neck pain.

**Methods:** Is about a randomized clinical trial, with 36 individuals, randomly distributed into 4 groups: Exercise Control Group (ECG); Laser Group(LG); Laser Group associated with Exercises(LGE). Quality of life, functionality and pain experience assessments will be evaluated using the Analogic Visual Scale (AVS), Beck Anxiety Inventory (BDI), Item Health Survey (SF-12) and Neck Dissability before and after the interventions. A specific exercise protocol will be carried out in the (ECG) and (LGE) groups, including stretching, mobilization and cervical traction exercises. The groups treated with FBM will receive laser application with a wavelength of 808nm and maximum energy of 27J.

**Results:** The literature already highlights that laser FBM is beneficial in reducing a series of pain conditions, however, in chronic conditions; it's believed that the association with physical exercises and manual techniques tends to enhance its effects, in addition to making them longstanding. Therefore, this study aims to demonstrate that the combination of resources can provide greater effectiveness for these patients.

**Conclusion:** Although this study has not been completed yet, available evidence in the literature suggests that combining laser FBM therapy with physical exercise and manual techniques may offer significant benefits superior to isolated techniques in managing this type of pain.

**Key Words:** Photobiomodulation; Neck pain; Exercises.

# INFLUENCE OF ENERGY DENSITY ON PHOTOBIO-MODULATION THERAPY FOR MUSCLE PERFORMANCE IN HEALTHY SUBJECTS IN A STRENGTH TRAINING PROGRAM.

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## Abstract

**Introduction:** The volume of studies employing photobiomodulation (PBM) as an ergogenic modality for physical activity underscores its substantial potential in this domain. However, the diverse array of devices utilized across these studies, alongside those commercially available, engenders uncertainty regarding the optimal parameters. Consequently, this investigation endeavors to elucidate the interplay of various PBM parameters with observed outcomes after a training regimen.

**Methods:** Forty-two participants were stratified into three cohorts (Sham, Cluster, LED-Blanket), with irradiated groups receiving 300 J of energy under distinct parameters (*Cluster*: 850 nm, 4 diodes, 20 cm<sup>2</sup> emitting source area, 60 mW/cm<sup>2</sup> power density, 300 mW diode power, 1,2 W total power, 50 seconds application time by area, 500 seconds of total application time and an energy density of 3 J/cm<sup>2</sup> by area / *LED-Blanket*: 940 nm, 180 diodes, 480 cm<sup>2</sup> emitting source area, 2,25 mW/cm<sup>2</sup> power density, 6 mW diode power, 1,08 W total power, and 278 seconds of total application time and an energy density of 0,625 J/cm<sup>2</sup>. Irradiation preceded all 10 prescribed training sessions, comprising 3 sets of stiff and squat exercises. Participants underwent assessment during sessions, encompassing measurements of blood lactate and psychophysiological scales (Numerical Rating Scale for Pain and Effort Perception Scale). Additionally, pre-intervention, post-intervention, and follow-up evaluations on an isokinetic dynamometer measured peak torque. Two-way repeated measures ANOVA facilitated intra- and inter-group comparisons.

**Results:** No significant inter-group differences or group-time interactions were discerned in lactate concentration or psychophysiological indices. Solely, a difference surfaced in peak torque of the dominant limb during knee flexion, manifesting across pre, post, and follow-up intervals ( $p=0.003$  and  $p<0.001$ ) with an effect size of  $\eta^2=0.080$ .

**Conclusion:** Within the outlined methodological framework, PBM was not effective to elicit performance enhancements, with divergent parameters evincing equivocal efficacy in this regard.

# PHOTOBIMODULATION TO ENHANCE MILITARY READINESS PROGRAM

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## Abstract

**Introduction:** Photobiomodulation (PBM) involves applying non-ionizing forms of light from various sources in the visible and near infrared spectrum to biologically modulate cellular activity and improve healing. PBM can enhance repair and tissue regeneration, stimulate metabolism, and reduce inflammation and pain. We are investigating the use of PBM to address health needs of United States (US) Service Members (SMs), focusing on musculoskeletal injury, performance, recovery, self-reported behavioral health, wellness, nerve and hearing repair, and wound healing.

**Methods:** The Photomedicine to Enhance Military Readiness Program employs 16 PBM studies - 7 basic science and 9 human participant studies - to assess and analyze the capabilities of applying PBM to a variety of conditions. A total of 1047 participants are projected to be enrolled. Currently, 242 participants have enrolled, and 4 *in vitro*, 3 *ex vivo*, and 11 preclinical animal studies with approximately 2,349 animals have been completed.

**Results:** *In vitro* and *in/ex vivo*: PBM was effective in enhancing physical performance, treating tendon rupture, decreasing acute inflammation in knee osteoarthritis and post-nerve repair surgery, facilitating cartilage generation in knee surgeries, and protecting from hearing loss. A prototype low-power, portable antimicrobial blue light bandage providing microbial suppression/killing and a novel optical imaging modality to noninvasively measure mechanical properties of biological tissues/engineered biomaterials have also been developed. Irradiance verification for 4 PBM devices will be presented. Common outcomes of interests for PBM treatment of injuries/to increase performance/wellness, including return to duty, pain, inflammatory reduction, and general wellbeing will be presented. Preliminary outcomes for comparative treatment of PBM to standard of care for plantar fasciitis, and in addition to shockwave therapy and platelet-rich plasma for Achilles tendinopathy and knee osteoarthritis, respectively, also will be presented.

**Conclusions:** PBM is a unique modality that may help SMs recover from their injuries and improve their overall health.

## Objectives:

1. Name the applicability of PBM to aid in recovery and performance of SMs.
2. Discuss PBM as a treatment modality in comparison to other treatments.
3. Detail the translational approach applied to utilize from bench-side project data to inform

## Disclaimer:

*This project is sponsored by the Uniformed Services University of the Health Sciences (USU); however, the information or content and conclusions do not necessarily represent the official position or policy of, nor should any official endorsement be inferred on the part of, USU, the Department of Defense, or the U.S. Government. Award Number HU00011920056.*

# PHOTOBIMODULATION THERAPY ASSOCIATED WITH AEROBIC EXERCISE TRAINING MODULATES INFLAMMATION IN AN EXPERIMENTAL MODEL OF KNEE OSTEOARTHRITIS

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## Abstract

Knee osteoarthritis (KOA) is considered a progressive wear of the articular cartilage and is characterized as an inflammatory disease of the entire synovial joint, associated with structural and functional changes of the entire joint, including the synovium, meniscus, ligament and subchondral bone. KOA is one of the most common degenerative diseases that causes disability in the elderly. Therefore, the objective of the study was to investigate the effects of PBM and aerobic exercise (associated or not) on cartilage tissue in an experimental model of KOA of rats. Wistar rats (N=40; weigh,  $\pm$  150g) were divided into 4 groups: KOA control (KOAC), KOA and PBM (KOAP), osteoarthritis and exercise (KOA-E). and KOA and exercise and PBM (KOAEP). The exercise training (treadmill; 16m/min; 50 min/day) and the PBM (GaAlAs diode laser, Photon Laser II, DMC<sup>®</sup> equipment Ltda, SP, São Carlos, Brazil, 808 nm wavelength, 50 mW power output, 28 sec irradiation time, 0.028 cm<sup>2</sup> spot area, dose 50 J/cm<sup>2</sup>, irradiance 1.7 W/cm<sup>2</sup>, 1.4 J total energy per point/section) started 4 weeks after the surgery, 3 days/week for 8 weeks. The results showed that all treatments (KOAP, KOA-E, KOAP and KOAEP) were able to attenuate the OARSI score and the degenerative process due to OA. However, only the KOAEP group reduced COX-2 immunoexpression when compared to KOAC. These results suggest that aerobic physical training attenuated degenerative changes related to KOA progression. Furthermore, exercise associated with PBMT reduced the inflammatory process in KOA in rats.



## YOUNG INVESTIGATOR-BASIC SCIENCES

### IN VIVO ELECTROPHYSIOLOGICAL STUDY OF THE ANALGESIC EFFECTS OF PHOTOBIMODULATION IN RATS

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#### Abstract

##### Three learning objectives

1. To understand the differential effects of photobiomodulation (PBM) on neuronal firing in different regions of the spinal dorsal horn.
2. To explore the selectivity of the inhibitory effects of PBM on noxious versus innocuous stimuli.
3. To assess the potential of PBM in pain management through its targeted neural mechanisms.

**Introduction:** PBM has analgesic effects, but the underlying mechanisms remain poorly understood. The spinal dorsal horn receives different types of sensory information depending on the region, with the superficial layers (lamina I-II) processing noxious information and the deeper layers (lamina III-IV) processing innocuous information. However, few reports have investigated the effects on the spinal dorsal horn. In this study, we investigated the effects of PBM on sciatic nerves, which are conduction pathways for sensory information, on neuronal firing in lamina I-II and lamina III-IV of the rat spinal dorsal horn evoked by mechanical stimulation.

**Methods:** In anesthetized rats, electrodes were inserted into either lamina I-II or lamina III-IV of the exposed spinal dorsal horn. Mechanical stimulation was applied to the skin using 0.6-26.0 g von Frey filaments (vFFs). An 808 nm laser (continuous wave) was applied to the exposed sciatic nerves. The PBM parameters were set to 0.79 W output power, 0.79 cm<sup>2</sup> beam area, and 180 s duration.

**Results:** The 26.0 g vFF-evoked firing frequency was significantly inhibited from 5 min after PBM and persisted for 3 h in lamina I-II. At 15 min after PBM, the 15.0 g and 26.0 g vFF-evoked firing, which corresponded to noxious stimuli, were selectively inhibited significantly. PBM did not alter vFF-evoked firing frequency in lamina III-IV for any vFFs. The inhibition ratio of 26.0 g vFF-evoked firing was approximately 13% in lamina III-IV and approximately 70% in lamina I-II.

**Conclusions:** PBM did not affect neuronal firing evoked by innocuous stimuli such as tactile sensations, but selectively inhibited neuronal firing evoked by noxious stimuli such as pain, suggesting a targeted effect on Ad and/or C fibers, but not on Ab fibers. These findings contribute to understanding PBM's analgesic mechanisms and may guide its application in pain management.

# TRANSCRANIAL PHOTOBIMODULATION IN TREATMENT OF TINNITUS

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## Abstract

Tinnitus is a common cure-less disorder that has severely affected the quality of life of about 140 million people worldwide. Here, PBMT was used to improve behavioral, neurophysiological and neuroplastic changes in tinnitus.

21 rats were divided into control (normal saline injection), tinnitus and PBMT groups (sodium salicylate injection for both to induce tinnitus). Evaluating tools were: gap prepulse inhibition of acoustic startle (GPIAS) which confirms the occurrence of tinnitus with the gap-in-noise (GIN) value based on the assessment of a reflex response, auditory brainstem response (ABR) which records auditory evoked potentials from the auditory nerve to inferior colliculus, and immunohistochemistry (IHC) that investigated the expression of doublecortin (DCX) as a marker of neuroplasticity in dorsal cochlear nucleus (DCN), dentate gyrus (DG) and parafloccular lobe (PFL) of cerebellum (Fig 1).

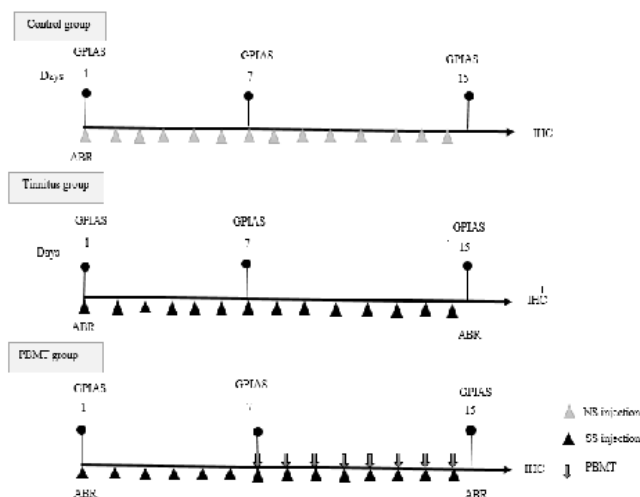


Fig. 1 Diagram of methods

Abbreviations: GPIAS (Gap Prepulse Inhibition of Acoustic Startle), ABR (auditory brainstem response), SS (sodium salicylate), Cont. (control), PBMT (photobiomodulation therapy), IHC (immunohistochemistry)

PBMT device was "MDL-LLL-808" (CNI China). WL :808 nm, PD: 165 mW/cm<sup>2</sup>, ED: 99 J/cm<sup>2</sup>, TD: 297 J/cm<sup>2</sup>, 8 sessions, 30 min/ session, non-contact mode. The brain, right and left ears were each irradiated for 10 min.

ANOVA and Scheffe were performed for between groups comparison.

In the tinnitus group, GIN was decreased significantly (indicated the occurrence of tinnitus), ABR threshold (the lowest sound pressure level at which "uniform" peaks and troughs is observed) and brainstem transmission time

(BTT) (the time between the peak of wave I and the trough of wave V) were significantly decreased. In the PBMT group, GIN was significantly increased and threshold and BTT were decreased (Fig 2).

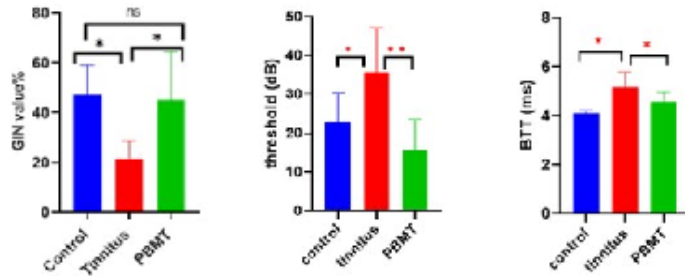


Fig. 2 Between-groups comparison of GIN value of GLIAS test and threshold and BTT parameters of ABR test in control, tinnitus and PBMT groups.

In the tinnitus group, DCX (indicator of neuroplasticity) was significantly increased in the DCN, DG and PFL compared to the control group. In the PBMT group, DCX decreased in all areas, but the decrease was significant only in DG (Figure 3).

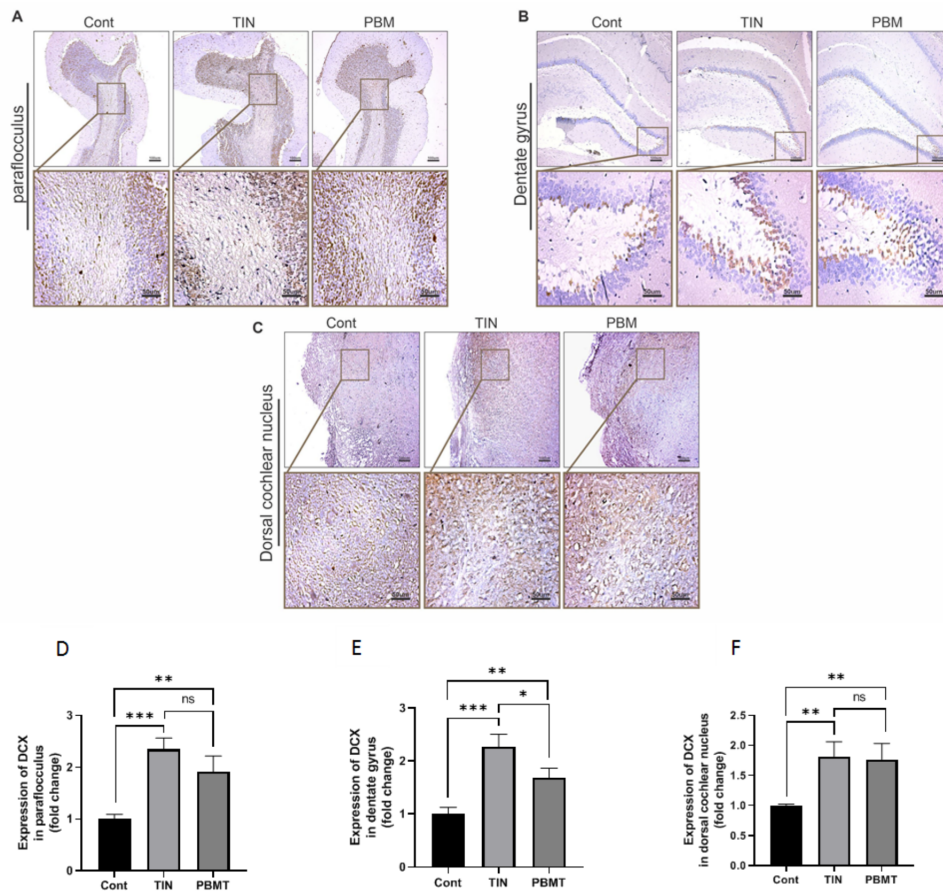


Fig 3. Doublecortin (DCX) expression and bar graphs in 3 brain regions (coronal sections) in the control (Cont), Tinnitus (TIN) and PBM (PBMT) groups. DCX expression indicated as brown infiltration. (A) DCX expression in the paraflocculus (B) DCX expression in the dentate gyrus (C) DCX expression in the dorsal cochlear (D) DCX expression in Paraflocculus (E) DCX expression in dentate gyrus (F) DCX expression in dorsal cochlear nucleus

PBMT effects in the improvement of plasticity, GIN, BTT and threshold can be explained by its effects on stimulating BDNF (brain-derived neurotrophic factor) production, nerve regeneration, improving electrophysiological function, release of growth factors and enhancing collagen vascular network.

In conclusion, PBMT has the potential to use in treatment of tinnitus. However, further animal and clinical studies are needed to optimize the PBMT parameters and confirm the results.

# SKIN WOUND HEALING IN DIABETIC RAT MODEL USING LOW-DOSE PHOTODYNAMIC THERAPY (LDPDT)

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## Abstract

### Three learning objectives:

1. LDPDT accelerate the wound-healing process.
2. LDPDT increased epithelial regeneration, collagen production and follicles formation.
3. LDPDT can decreased the side effect of chronic wounds specially in diabetics.

**Introduction:** Chronic wound is one of the major challenges in medicine and imposes a heavy financial burden on the healthcare of different countries. Diabetic foot ulcers as one of the important examples for chronic wounds can lead to lower limb amputation, disability, and death in diabetics. In this regard, novel technology with low side effects got attention in recent years. Low-dose photodynamic therapy (LDPDT) is one of the non-invasive techniques that can be considered for wound healing in diabetic wounds.

**Methods and materials:** In this experiment, we aim to study the effect of LDPDT on diabetic rats' wound healing and compare it to healthy rats. In this in vitro experimental study, 32 male rats were used. Rats in both normal and diabetic (streptozotocin injection) groups after being wounded (two wounds [0.8 × 0.8 cm]) on the back of each rat were randomly divided into four groups, including the control group (without treatment), radiation-only (WL :660 nm – ED: 1 J/cm<sup>2</sup>) group, 5-ALA-only (1 µg/mL) group, and LDPDT-recipient group. The procedure has been done for 2 days, and at the end of Days 3, 7, 14, and 21, the wound sample was sent to the histopathology laboratory, and the wound size and tissue indices in these groups were evaluated by histology and microscopy techniques.

**Result:** Based on the student t-test analysis, the impact of low concentrations of 5-ALA and low irradiation energy density in both normal and diabetic rats were positive, which accelerated the wound-healing process as seen in the histology study. In diabetic rats treated with only radiation and LDPDT, the process of epithelial regeneration, collagen production, reduction of mast cells, and production of follicles was more as compared to the normal group.

**Conclusion:** The results suggest that LDPDT can have a positive impact on the diabetic rat model wound healing.

# DISCRETE EFFECTS OF DIRECTED ENERGY THERAPEUTICS ON NORMAL AND CANCER STEM CELLS

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## Abstract

**Objectives:** Supportive cancer care is a key aspect of improving cancer morbidity and mortality. A common complication of various forms of oncotherapy is mucositis. Directed energy approaches such as Photobiomodulation (PBM) therapy and Static-Electricity Emitting Devices (SEED) are gaining popularity in managing oral mucositis. However, their effects on normal and tumor cells remain to be fully elucidated, which motivated this study.

**Methods:** Normal human keratinocytes and Oral Squamous Cell Carcinoma cells at different cell densities were subjected to PBM and SEED treatments. PBM was performed with an 810 nm laser at 10 mW/cm<sup>2</sup> while SEED treatments were performed using a high-frequency Argon probe. Cell proliferation was evaluated through colony forming units (CFU) and AlamarBlue assays at 24 and 72 hours. Key markers for the expansion of normal and cancer epithelial stem cells, namely Gli1, CD44, and NRF2, were assessed using RT-qPCR.

**Results:** PBM-treated normal keratinocytes demonstrated reduced proliferation and CFUs at low density, while increased proliferation and CFUs were observed at high density. The SEED treated normal keratinocytes noted decreased proliferation at low density, while no significant effects were observed at high cell density. There was an inverse correlation between the expression of CD44 and both proliferation and CFU responses following these treatments. PBM-treated oral squamous cell carcinoma exhibited responses similar to those demonstrated by the PBM-treated keratinocytes. Current analysis is focused on examining the effects of treatment duration on keratinocytes and cancer cells with both directed energy treatments.

**Conclusion:** These results suggest that directed energy approaches like SEED and PBM can modulate normal and transformed keratinocyte responses differentially. These effects appear to be cell density- and secreted factor-dependent. Future research will focus on exploring the role of directed energy mechanistic pathways, especially TGF- $\beta$ 1, in mediating these responses.

# OPTIMIZATION OF RED TO NEAR-INFRARED STIMULATION BY LIGHT-EMITTING DIODES TO INCREASE CELLULAR METABOLISM

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## Abstract

**Learning objectives:** Light-emitting diodes (LEDs) in near-infrared spectrum (810, 850 and 940 nm) enhanced cellular metabolism in a dose-dependent manner. Operation mode, power density, duration and periodicity must be considered in tailoring photobiomodulation (PBM) protocols for specific clinical scenarios. PBM by LEDs enhanced cells' activity with minimal temperature increase, being a feasible and safe alternative to lasers.

**Brief introduction:** Although PBM is used for tissue repair, it is not yet clinically implemented due to conflicting evidence in the literature. This may arise from the lack of studies investigating the most adequate stimulation parameters to elicit therapeutic effects at cellular level. This study aims to investigate the impact of different PBM parameters in cellular metabolism.

**Methods:** Human-derived cells were stimulated by PBM, applied by an array of LEDs, on top of each well, at: 600, 655, 810, 850 and 940 nm wavelengths; 4, 7, 10, 14 and 17 mW/cm<sup>2</sup> power densities; continuous mode for 1 min or pulsed mode for 2 min (with 1 Hz pulse frequency and 50% duty cycle); daily or every other day. Stimulation time was further increased up to 4 min to assess the PBM dose response. The applied energy density and total energy varied from 0.2 to 4.1 J/cm<sup>2</sup> and 1.2 to 20 J, respectively. Temperature increase during stimulation was measured. After three days of stimulation, cellular metabolism was assessed by metabolic activity. Significant differences were represented at p-value < 0.01.

**Results:** Cellular metabolism was significantly improved by 810 nm at 17 mW/cm<sup>2</sup> (continuous, every other day, p = 0.000); 850 nm at 4 mW/cm<sup>2</sup> (pulsed, every other day, p = 0.001), 7 mW/cm<sup>2</sup> (continuous, daily, p = 0.000); and 10 mW/cm<sup>2</sup> (continuous, daily, p = 0.000); 940 nm at 4 mW/cm<sup>2</sup> (continuous, daily, p = 0.006); 14 mW/cm<sup>2</sup> (pulsed, daily, p = 0.0003); 17 mW/cm<sup>2</sup> (continuous, daily, p = 0.000). A dose response was demonstrated, being distinct among the PBM parameters. The temperature rise during stimulation was minimal.

**Conclusions:** Stimulation with near-infrared LEDs was efficient in promoting cellular metabolism. These findings will significantly impact and improve the current knowledge of PBM effectiveness by LEDs.

# COMPARISON BETWEEN CONTACT AND NON-CONTACT MODE AND TWO HANDPIECES TO OPTIMIZE THE NON-CONTACT MODE OF PHOTOBIO-MODULATION IN THE POST-SURGICAL TREATMENT OF CRANIAL CRUCIATE LIGAMENT RUPTURE IN DOGS.

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FINA CARDONA FISIOTERAPIA Y REHABILITACIÓN VETERINARIA, IBIZA, SPAIN. COLLABORATOR  
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## Abstract

Rupture of the cranial cruciate ligament (RCCL) in dogs is one of the most common pathologies in clinical practice, requiring surgery and rehabilitation. Osteotomies (CTWO: cranial tibial wedge osteotomy) are the most used surgical techniques. Photobiomodulation (PBM) is a fundamental tool for the recovery. In veterinary medicine, more articles are appearing demonstrating the benefits of PBM<sup>1</sup>. On one hand, despite the benefits, there is a lack of consensus regarding the parameters and the mode (contact or non-contact). On the other hand, the non-contact mode sometimes becomes the only option<sup>2</sup>. Handpieces are designed according to the need to avoid reflection<sup>3</sup> and loss of energy.

**Goal:** The first comparison is between the contact and non-contact modes. The second comparison is between two handpieces, Zoom and Sweeper, in the post-surgical treatment of RCCL in dogs undergoing CTWO.

## Materials And Methods:

Dogs

The study included 28 dogs (20-30 kilograms) randomly divided into:

1. Contact (CM) and non-contact (NCM) groups.
2. Zoom and Sweeper groups.

Affected by RCCL and subjected to CTWO.

Laser

Parameters of CM and NCM groups are (Table 1):

Schedule: 3 times/week for 2 weeks.

Parameters of Zoom and Sweeper groups are (Table 2):

Schedule: 3 times/week for 1 week.

## Assessment:

Double blinded by veterinarians.

First comparison is evaluated: after surgery, the 3<sup>rd</sup> and 6<sup>th</sup> laser session.

Second comparison is evaluated: after surgery, the 7<sup>th</sup> and 14<sup>th</sup> day after surgery.

**Statistical Method:** A mean degree of lameness was determined (Table 3):

**Results:** The average in the first comparison was (Table 4) and in the second one was (Table 5).



**Conclusion:** The present study demonstrates the benefits of contact mode and Sweeper handpiece in the postsurgical treatment of RCCL in dogs.

**Table 1**

	CM	NCM
Device	Doctorvet (Class IV)	Doctorvet (Class IV)
Wavelength (nm)	660, 808, 915	660, 808, 915
Frequencies(Hz)- CW (continuous wave)	CW-5- 200-4000-10000	CW-5-200-4000-10000
Doses (J/cm <sup>2</sup> )	5	5
Average total Joules	842,85	760,71
Power (W)	6,6	6,6
Handpiece	Massager	Sweeper
Treatment technique	Scanning	Scanning

**Table 2**

	<b>Zoom</b>	<b>Sweeper</b>
Device	Doctorvet (Class IV)	Doctorvet (Class IV)
Wavelength (nm)	660, 808, 915	660, 808, 915
Frequencies(Hz)- CW (continuous wave)	CW-5- 200-4000-10000	CW-5-10-4000-10000
Doses (J/cm <sup>2</sup> )	5	5
Average total Joules	971,42	750,10
Power (W)	6,6	6,6
Treatment technique	Scanning	Scanning
Mode	Non-contact	Non-contact

**Table 3**

<b>GRADE 0</b>	No lameness
<b>GRADE 1</b>	Intermittent medium lame after rest and exercise
<b>GRADE 2</b>	Continuous medium lameness or intermittent moderate lameness after rest and exercise
<b>GRADE 3</b>	Continuous moderate lameness or no weight bearing after exercise
<b>GRADE 4</b>	There is no use of the limb maintaining the limb in flexion

**Table 4**

Patients	POSTSURGERY	3 <sup>RD</sup> SESSION		6 <sup>TH</sup> SESSION		
	CM	NCM	CM	NCM	CM	NCM
1	4/4	3/4	4/4	3/4	1/4	1/4
2	4/4	3/4	2/4	3/4	0/4	1/4
3	4/4	4/4	3/4	4/4	2/4	2/4
4	3/4	4/4	3/4	2/4	1/4	3/4
5	4/4	4/4	3/4	3/4	0/4	2/4
6	3/4	4/4	2/4	4/4	0/4	2/4
7	4/4	3/4	3/4	2/4	1/4	1/4
<b>AVERAGE</b>	<b>3,71/4</b>	<b>3,57/4</b>	<b>2,85/4</b>	<b>3/4</b>	<b>0,71/4</b>	<b>1,71/4</b>

**Table 5**

PATIENTS	ZOOM			SWEEPER		
	24H	7 DAYS	14 DAYS	24 H	7 DAYS	14 DAYS
1	4/4	3/4	2/4	4/4	4/4	2/4
2	3/4	3/4	3/4	4/4	3/4	1/4
3	4/4	3/4	2/4	4/4	3/4	1/4
4	3/4	3/4	1/4	3/4	3/4	1/4
5	3/4	2/4	1/4	4/4	4/4	2/4
6	4/4	3/4	2/4	3/4	2/4	1/4
7	3/4	2/4	2/4	3/3	2/4	0/4
<b>AVERAGE</b>	<b>3,42/4</b>	<b>3,14/4</b>	<b>1,85/4</b>	<b>3,57/4</b>	<b>3/4</b>	<b>1,14/4</b>

# PHOTOBIOSTIMULATORY EFFECTS OF LOW DOSE PHOTODYNAMIC THERAPY WITH 2 PHOTSENSITIZER DRUGS ON HUMAN MESENCHYMAL STEM CELLS

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## Abstract

**Learning Objectives:** Low doses of Photodynamic therapy have photobiomodulatory effect on human mesenchymal stem cells (MSCs).

Low doses of photosensitizer drugs can stimulate osseous differentiation of human MSCs.

All photosensitizer drugs do not have stimulatory effect on human MSCs osseous differentiation.

**Introduction:** patients' rehabilitation in minimum time is critical goal of medical team because disability and malfunction have psychological and social effect for patients.

Many lesions like metabolic, traumatic (accidents, wars, occupational etc.) and pathologic can be treated by stem cells. Lasers or photobiomodulation can accelerate this procedure more reliably.

**Methods:** human bone marrow mesenchymal stem cells was isolated and cultured in sterile medium. Two photosensitizer drugs as 5- amino levulenic acid (1mM) (5-ALA) and Methylen blue (1 $\mu$ M) (MB) were used for stem cells incubation. Photoactivation was done by 630 and 660 nm wavelength laser irradiation with 1 J/cm<sup>2</sup> energy density. MTT test was used for evaluating cell viability in before and after laser irradiation. Also Alizarin red histologic test was used for calcium nodule formation.

**Results:** 1mM concentration for 5-ALA and 1 $\mu$ M concentration for MB were optimized in order MTT test in dark situation. Unpaired Student's t test (two-tailed) was used for evaluating statistical difference between experimental and control groups. ALA group did not show any significant osseous differentiation according no calcium nodule formation after laser irradiation. On the contrary, MB group had significant calcium nodule formation compare with control group.

**Conclusion:** low doses of photodynamic therapy with lower doses of photosensitizer may have promote bone marrow-MSCs viability or their osseous differentiation.

## OPHTHALMOLOGY

### PHOTOBIMODULATION REDUCES RISK FOR VISION LOSS AND ONSET OF GEOGRAPHIC ATROPHY IN DRY AGE-RELATED MACULAR DEGENERATION

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#### Abstract

##### Learning Objectives:

- To evaluate the safety of photobiomodulation (PBM) in intermediate dry age-related macular degeneration (AMD).
- To evaluate the efficacy of PBM in intermediate dry AMD.
- To evaluate the anatomical effect of PBM in intermediate dry AMD.

**Introduction:** Dry AMD is a top contributor to vision loss across the globe. No current treatment exists in early/intermediate dry AMD.

**Methods:** LIGHTSITE III (NCT04065490) was a randomized, controlled, multicenter study to assess the efficacy and safety of PBM in dry AMD. Subjects were treated with six series of multi-wavelength PBM (590, 660 and 850 nm) or active Sham (3x per week/3-5 weeks) delivered every 4 months over a 24-month period using the Valeda® Light Delivery System. A Cox proportional hazards model was performed to evaluate the time to event hazard ratio of 1) best corrected visual acuity (BCVA) loss >5 ETDRS letters and 2) onset of geographic atrophy (GA).

**Results:** 100 subjects (148 eyes) with dry AMD were randomized. The LIGHTSITE III study demonstrated a sustained improvement in BCVA with a primary endpoint BCVA benefit at both 13 and 24 months in the PBM vs. Sham treatment group. Subjects in the Sham group showed a greater vision loss over two years and continued to progress into GA, with 18% of the sham patients losing >5 letters and 24% disease progression with evidence of new GA. The hazard ratio for BCVA with a >5 letter loss was 0.47, ( $p < 0.02$ ) which indicated a significant 53% reduction in onset of vision loss of >5 letters for subjects that received PBM vs. Sham treatment. The hazard ratio for onset of new GA was 0.27, ( $p < 0.006$ ) indicating a significant risk reduction of 73% to new GA over two years with PBM.

**Conclusions:** The current analysis supports a reduced risk of BCVA vision loss and progression to new GA. PBM therapy may offer a new treatment with a unique mitochondrial mechanism and modality for patients with dry AMD to maintain retinal health and slow AMD disease progression.

# ULTRA-LOW IRRADIATION PHOTOBIO-MODULATION WITH A NEW SELF-MEDICATION DEVICE FOR THE TREATMENT OF THE AGE-RELATED MACULAR DEGENERATION: SHORT-AND MEDIUM-TERM EFFECTS

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## Abstract

**Background:** Age-related macular degeneration (AMD) is responsible of 5% of blindness worldwide and only few treatment options are available. We designed a new wearable self-medication device that employs the same broadband red light described in literature, but with extremely low irradiance. Our aim is to assess the safety and effectiveness of low-fluence light stimulations emitted by an LED source with appropriate wavelengths through our new device, in improving short- and medium-term visual function in patients affected by severe non-neovascular AMD.

**Study design:** the study will consist of 2 phases

- Phase 1: prospective, placebo-controlled and single blind
- Phase 2: prospective, cohort study, not blinded

**Materials and methods:** we prospectively enrolled patients affected by severe non-neovascular AMD. All patients were randomly assigned in placebo or in treatment group. The treatment consisted of 10 sessions of 10-minutes each, using the new device comprised of micro-LEDs that emitted light onto an amorphous support assembled within Metallic eyeglasses. The used fluence was 15  $\mu$ W emitted through a lens not directly focused on the retina (the LEDs were offset by 2 cm from the pupil). The placebo group blindly underwent the same number sessions, but with the micro-LED turned off. Before and after each placebo/treatment session all the patients received: optical coherence tomography, best corrected visual activity, and microperimetry. Only patients in the active group were included in the second phase with 2 sessions/week and were after 90 days.

**Results:** of 50 patients (78 eyes), 31 (50 eyes) were in the treatment group. No adverse effects were observed in both groups. Subjective improving in colours and contrast perception were reported. No significant differences in the OCT parameters were observed. The microperimetry mean sensitivity and the central visual function both far and near significantly improved in the treated group (respectively  $p < 0.001$ ,  $p < 0.001$ ). 23 patients (30 eyes) were included in the phase 2 confirming the safety and efficacy of our device.

**Conclusions:** LED photobiomodulation delivered through our new device is a safe and effective tool for improving short- (10 days) and medium- term (3 months) visual function in patients affected by severe non-neovascular AMD.

# PHOTOBIMODULATION FOR THE TREATMENT OF RETINAL INJURY AND DISEASE: EXPERIMENTAL STUDIES

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## Abstract

### Learning Objectives:

- Evaluate the effect of PBM on mitochondrial integrity in retinal disease.
- Evaluate the efficacy of PBM on retinal function in retinal disease.
- Evaluate the efficacy of PBM on photoreceptor survival in retinal disease.

**Introduction:** Photobiomodulation (PBM) induced by far-red to near-infrared light restores the function of damaged mitochondria, upregulates cytoprotective factors and promotes cell survival. PBM modifies the redox state of cytochrome c oxidase (CcO) increasing the mitochondrial membrane potential and ATP synthesis. We tested the *hypothesis that PBM treatment would preserve mitochondrial integrity, protect retinal function, and attenuate photoreceptor loss in animal models of retinal injury and disease.*

**Methods:** Studies were conducted in three experimental models of mitochondrial toxicity methanol intoxication, retinitis pigmentosa [RP] (P23H rat), and age-related macular degeneration [AMD] (Nrf2 ko mouse). Animals were treated with 670 nm or 830 nm light (180s; 25mW/cm<sup>2</sup>; 4.5J/cm<sup>2</sup>) delivered by a LED array (Quantum Devices, Barneveld, WI). PBM treatment was administered once per day in each protocol as follows: Mitochondrial injury model at 5, 25 and 50 hours of intoxication; RP model from p10 to p25; AMD model 3x per week from 9-12 months of age. Sham-treated animals were restrained, but not treated with FR/NIR light. Retinal metabolic state, retinal function and retinal morphology were assessed by measurement of mitochondrial redox state, electroretinography (ERG) and spectral-domain optical coherence tomography (SD-OCT).

**Results:** 670 nm and 830 nm PBM treatment preserved retinal redox state, retinal function, and retinal morphology in PBM-treated animals compared to the sham-treated group. PBM protected against the disruption of the oxidation state of the mitochondrial respiratory chain observed in sham-treated animals ( $p < 0.001$ ). Scotopic ERG responses were significantly ( $p < 0.001$ ) greater in PBM-treated rats compared to sham controls. SD-OCT studies and histological assessment showed that PBM preserved the structural integrity of the retina.

**Conclusions:** These studies show that chronic proteotoxic stress disrupts retinal bioenergetics resulting in mitochondrial dysfunction, and retinal degeneration. They further demonstrate beneficial effect of PBM on retinal mitochondrial redox status in retinal injury and disease suggesting that therapies normalizing mitochondrial metabolism have potential for the treatment of retinal degenerative disease.

# IMPROVEMENT IN CENTRAL SEROUS CHORIORETINOPATHY FOLLOWING MULTIWAVELENGTH PHOTOBIMODULATION TREATMENT

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## Abstract

### Learning Objectives:

- To discuss photobiomodulation (PBM) treatment in ophthalmology
- To discuss treatment landscape for central serous chorioretinopathy
- To evaluate the utility of PBM in CSCR

**Introduction:** Central serous chorioretinopathy (CSCR) is an ocular condition in which fluid build-up accumulates underneath the retina resulting in retinal pigment epithelial detachment and vision loss. Some patients show irreversible functional and anatomical changes in the retina. Treatment approaches for CSCR are under discussion and further research into novel strategies to aid in recovery are of interest. Photobiomodulation (PBM) treatment uses light wavelengths to improve cellular function and has recently shown positive effects in several ocular conditions including those with edema.

**Methods:** This prospective case report details a 39-year old woman diagnosed with CSCR. Multiwavelength PBM treatment was initiated with the Valeda® Light Delivery System (LumiThera, Inc., Poulsbo, WA, USA). A series of treatment included 9 sessions delivered over 3-5 weeks (9 total treatments). Follow-up treatments were conducted. Optical Coherence Tomography (OCT) imaging and best-corrected visual acuity (BCVA) measures were taken. The patient has been followed for approximately one-year.

**Results:** The patient presented with blurred vision and a BCVA score of 65 letters in the left (OS) eye. After 3-weeks observation, the vision in the patient had further declined two lines on the ETDRS chart to 55 letters. Fluorescein angiography was performed, confirming CSCR diagnosis, and PBM was initiated. PBM treatment improved BCVA and fluid build-up in the RPE within one-week of treatment (3 treatment sessions). Following the full series of treatment (9 PBM treatment sessions), fluid was completely resolved and BCVA scored at 80 letters. The patient had a repeat PBM treatment ~6 months later and has shown stable vision and no fluid present on OCT scan. The patient was seen again ~ 1 year later with continued stable vision and no fluid detection.

**Conclusions:** PBM is a non-invasive treatment option that may provide benefit in CSCR to resolve fluid, macular change and vision loss. Research into PBM as an immediate treatment option for CSCR, especially those with chronic presentations or those posed to have irreversible damage, is warranted.

# PHOTOBIMODULATION; EFFECTIVE TREATMENT FOR RETINITIS PIGMENTOSA

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## Abstract

Our objectives are to study the behaviour of the retina in patients affected by this disease after treatment with photobiomodulation, to study their improvement in quality of life, visual acuity and campimetry.

We describe two cases of patients aged 39 and 27 years respectively, diagnosed with retinitis pigmentosa since the age of 20 and 14 years, who both presented a progressive decrease in acuity and visual field, until reaching respectively a visual acuity of 1/10 in both eyes in the first case and a finger count at 1 metre in the second, as well as a shotgun barrel campimetry in both cases. No side effects were reported.

The examination of visual acuity is carried out by the same examiner, under the same conditions, the Pelli-Robson contrast sensitivity chart is used to measure night vision, and the SF 36 questionnaire is used to assess the quality of life, the Oculus perimeter Easyfield c Centerfield 2, twinfield 2, the OCT is carried out with the Moptim Mocean 4000 equipment, the retinography is carried out with the Optos California equipment.

After starting a photobiomodulation treatment of 9 sessions every other day for 3 weeks, both had an improvement in visual acuity, the first one reaching a vision of 9/10 in both eyes and the second one a vision of 2/10 and being able to read the lottery numbers, as well as a significant improvement in night vision, campimetry and quality of life. Given the small sample size we did not use any statistics.

We conclude photobiomodulation could be considered as a potential treatment for retinitis pigmentosa.



# PHOTOBIMODULATION FOR THE TREATMENT OF DRY EYE DISEASE - FDA APPROVAL AND BEYOND

ROLANDO TOYOS

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## Abstract

Over 24 years ago I introduced the concept of utilizing Intense Pulse Light (IPL) and Low Level Light LLLT treatment to treat a disease that affects over 10 percent of the world population - Dry Eye Disease (DED). I was met with skepticism by my colleagues at first but providing published research eventually some eye doctors adopted my technologies and treatment protocols. My early work led to a published FDA study that helped gain a specific approval for the use of IPL to treat DED. I am going to present all relevant research concerning the use of IPL and LLLT including the results of the FDA study,

<https://pubmed.ncbi.nlm.nih.gov/35737696/>.

In my 25 years of experience treating DED patients I am convinced the photobiomodulation is the best path to controlling this disease.

## AESTHETIC MEDICINE

### LASER PHOTOBIO-MODULATION FREQUENCY IN THE VIABILITY OF THE SKIN FLAP IN RATS

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#### Abstract

Several parameters influence the success of photobiomodulation therapy (PBMT) for increasing the viability of the skin flap, however, the literature is lacking regarding treatment frequency. This study aims to evaluate the effect frequency of laser PBMT applications in skin flap viability. Thirty and two wistar rats were used for this study and divided into 4 experimental groups: sham group (GS) - submitted to PBMT simulation; group 2PBMT (2PBMT) - submitted to laser PBMT for 2 consecutives days; group 5PBMT (5PBMT) - submitted to laser PBMT for 5 days and group PBMT for 7day (7PBMT) - submitted to laser 7PBMT. The treatment adopted was started immediately after the surgery, with the following parameters: 90 J/cm<sup>2</sup> fluency, 40 mW output power, 90 seconds application time and 3.6 J energy per point. Irradiation was performed in 3 points, with a 24-hour interval between applications until completing the proposed experimental period for each group. On the 7th postoperative day, biological material was collected at the laser application site. The area of skin necrosis was analyzed, as well vessel and mast cells morphometry and immunohistochemistry of angiogenesis in the application region. 2PBMT groups presented a greater reduction of necrosis area ( $p = 0.047$ ), and greater number of markers (VEGF and HIF-1 $\alpha$ ) compared to GS ( $p = 0.013$ ;  $p = 0.048$  respectively). For blood vessel and mast cell morphometry, and the number of FGF and CD34, there was no difference between groups ( $p > 0.05$ ). It is concluded that the frequency of PBMT laser applications interferes with the viability of the skin flap, and two applications present the better viability of the skin flap in rats.

# ROLE OF PHOTOBIMODULATION IN ANTI-AGING: ENHANCING MELATONIN'S CONSERVED FUNCTIONS FOR CELLULAR REJUVENATION

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## Abstract

### Learning Objectives:

1. Examine the evolutionary conservation of light-induced melatonin and its universal role as an antioxidant across species.
2. Understand how melatonin contributes to cellular protection, rejuvenation, and anti-aging.
3. Explore the potential of Photobiomodulation (PBM) in stimulating extra-pineal melatonin synthesis for anti-aging applications.

**Brief Introduction:** Melatonin, a conserved molecule across evolution, plays a pivotal role in the biological defense system against oxidative stress, thus implicating its significance in anti-aging. This presentation explores the role of Photobiomodulation (PBM) in boosting extra-pineal melatonin production, thereby amplifying its antioxidant capabilities and presenting an innovative strategy to mitigate the effects of aging.

**Methods:** We synthesized insights from various studies on melatonin's evolutionary history, its multifaceted roles in cellular protection, and the interplay between PBM and melatonin synthesis. Special attention was given to the potential of PBM in reversing age-associated changes by stimulating melatonin production in extra-pineal sites, including the skin and gastrointestinal tract.

**Results:** Melatonin's role extends beyond sleep regulation to encompass broad-spectrum antioxidant activities, including free radical scavenging and DNA repair. Its presence in extra-pineal tissues suggests an adaptive mechanism for localized protection against oxidative damage. Preliminary research report findings indicate that PBM can stimulate extra-pineal melatonin synthesis, enhancing its anti-aging effects.

**Conclusions:** The conservation of melatonin across species highlights its fundamental role in oxidative stress management and anti-aging. PBM emerges as a promising non-invasive therapy to stimulate extra-pineal melatonin synthesis, potentially offering a holistic approach to mitigate aging processes. This underscores the need for further research into the synergistic effects of PBM and melatonin in anti-aging strategies.



Ref:

Zimmerman, S. and Reiter, R. 2019. Melatonin and the Optics of the Human Body. *Melatonin Research*. 2, 1 (Feb. 2019), 138-160. DOI:<https://doi.org/https://doi.org/10.32794/mr11250016>.

# APPLICATION OF LASER THERAPY IN ORALFACIAL HARMONIZATION

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## Abstract

**Introduction:** The Orofacial Harmonization is a specialty of Dentistry, which aims to promote the aesthetic and functional balance of the face, through surgical and minimally invasive procedures, using different materials and techniques, including biophotonics and laser therapy.

**Objective:** 1) Appreciate the effects of photobiomodulation (PBM) in adjunct to other treatment modalities in achieving orofacial harmonization. 2) Understand the benefits of the local and systematic action of laser photonic therapy in orofacial harmonisation treatments. 3) Appreciate the impact of non-invasion PBM on biological tissue in the aesthetic zone like the orofacial filed.

**Methodology:** The benefits of the practical applicability of laser therapy on the results of orofacial harmonization treatments will be demonstrated in three distinct aspects: systemic action, through intravascular blood laser irradiation (ILIB) (Live Blood Testing T™, Ulverston Natural Health Centre, 2mW, 632.8m, 30 minutes); presentation of clinical cases performed by the author for the treatment of postoperative complications through antimicrobial photodynamic therapy (a-PDT) (Therapy EC™, DMC, 100mW, 660m, 54J; Chimiolux T™, DMC, methylene blue 0.01%); and for the treatments of cutaneous integumentary tissue by the action of photobiomodulation in minimally invasive surgical and aesthetic procedures of orofacial harmonization, through biophotonics (Elite Duo™, DMC) of LEDs (blue LED - 520mW ± 20%, 450 # 10m, and amber LED - 520mW ± 20%, 590 \$ 10nm) and lasers (red laser 100mW, 660m and infrared laser 100mW, 808nm).

**Results:** Erythrocytes in rouleaux after an induced glycemic diet recovered their beta potential after the ILIB protocol in healthy patients, observed under an optical microscope. Postoperative local infection in bichectomy surgery and after injection of hyaluronic acid in the nasolabial fold with secondary infection in the nasal skin tissue, were combated with 1 or 2 sessions of a-PDT and systemic antibiotic therapy, in 100% of cases. And finally, biophotonic photobiomodulation with local application of lasers and LEDs proved to be effective and efficient in the hydration and quality of skin integumentary tissue in all patients, in the specialty of orofacial harmonization.

**Conclusion:** The beneficial effects provided by photobiomodulation in biological tissues are excellent allies for the clinical practice of the specialty of orofacial harmonization in the search for aesthetic perfection.

# FINDING MOLECULAR MECHANISMS OF LOW LEVEL LASER THERAPY IN SCAR ACNE AND REPAIR PROGRESSION

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## Abstract

### Three Learning objectives:

1. Identify and characterize differential gene expression patterns associated with scar formation using bioinformatics analysis of transcriptomic data from scar tissues and adjacent normal skin samples.
2. Analyze the effects of low-level laser therapy (LLLT) on gene expression profiles implicated in extracellular matrix remodeling, inflammation, and fibrosis during scar formation.
3. Interpret the potential synergistic effects of integrating LLLT with bioinformatics-driven approaches in modulating key molecular pathways involved in scar reduction and wound healing.

**Brief Introduction:** Cutaneous scars pose a significant challenge in clinical dermatology, often resulting in functional impairment and aesthetic concerns. While various therapeutic modalities have been explored to mitigate scar formation, the molecular mechanisms underlying scar development remain incompletely understood. This study investigates the interplay between gene expression profiles and low-level laser therapy (LLLT) in the context of skin scar formation and repair..

**Methods:** Leveraging bioinformatics analysis of transcriptomic data from scar tissues and adjacent normal skin samples, differential gene expression patterns associated with scar formation are identified. Additionally, the study explores the effects of LLLT on gene expression profiles implicated in extracellular matrix remodeling, inflammation, and fibrosis during scar formation. Integration of LLLT with bioinformatics-driven approaches elucidates potential synergistic effects in modulating key molecular pathways involved in scar reduction and wound healing

**Results:** 2750 up and downregulated genes isolated from microarray dataset. these genes involved in TGF-beta, NF-kappa B, cellular senescence, PI3K-Akt and ubiquitin mediated proteolysis. In gene ontology analysis and molecular functions, cell adhesion molecule binding, cytoskeletal protein binding and enzyme regulator activity were showed in data. In protein- protein interaction network, the RPS27A, UBA52, CDK1, SMAD3, CCNB1, TRAF6, CCNA2, MDM2 and ATM were high node degrees, betweenness and centrality in the network. These genes roles as transcription factors and kinases, also regulatory several other intermediate proteins in repair mechanisms of scar acne.

**Conclusions:** Insights gleaned from this interdisciplinary approach provide a comprehensive understanding of the molecular basis of scar formation and offer novel strategies for optimizing LLLT as an adjunctive therapy for scar management. This integrative framework holds promise for advancing personalized therapeutic interventions aimed at improving scar outcomes and restoring skin functionality and aesthetics.

# COMBINATION EFFECT OF STEM CELLS AND PBM THERAPY

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## Abstract

In this study, we reviewed the combined effect of PBM therapy and stem cells on treatment of diseases in different parts of body. This research aimed to reach a consensus on suitable parameters in PBMT regarding its application on stem cells. Study designs on PBMT and stem cell therapy are very diverse regarding light parameters, and there is lack of comprehensive clinical trials. Therefore, suggesting a guideline for clinical studies in this field would help researchers in designing their studies. Studies report the effectiveness of PBMT in conjunction with stem cell therapy in cell proliferation, differentiation, tissue regeneration, wound healing, angiogenesis, and treatment of different diseases. However, clinical studies are very few in all the reviewed fields. In each category, we attempted to recommend a PBMT protocol based on information from literature, experience, and expertise. Protocols for PBMT on stem cells were reviewed in each field of medicine, and recommendations were made for further clinical studies. The main wavelengths used in PBMT studies in relation to stem cells, were in the range of 630-660 nm, and 800-890 nm. To increase proliferation of stem cells, 0.5-2 J/cm<sup>2</sup> energy density is recommended. For future studies on wound healing, we suggest the power density of 10-50 mW/cm<sup>2</sup>. To study wound healing in diabetic animals, energy density of 0.2 J/cm<sup>2</sup> can be suggested. More well-designed clinical studies are necessary to reach a consensus on parameters in PBMT on other tissues.

# EXPLORING THE FRONTIERS OF AESTHETICS: A DETAILED ANALYSIS OF ENDOLASER AS AN INNOVATION

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## Abstract

**Introduction:** Technological advancements have propelled the development of endolaser as a promising therapeutic tool in aesthetic procedures. The diversity in parameters adopted in studies underscores the need for a systematic analysis to comprehend the effectiveness of endolaser in various aesthetic pathologies.

**Methods:** A bibliographic search was conducted up to the present, using Boolean operators AND and OR. Search terms included "endolaser", "endolift", "lipolaser", "aesthetic dermatology". Studies detailing endolaser parameters such as wavelength, power, pulse mode, fiber used, and assessment measures were included. Studies on vascular endolaser were excluded.

**Results:** Positive outcomes were observed in 16 aesthetic studies involving endolaser, covering progressive lipodystrophy (1), acne (1), rosacea (1), skin laxity (11), and localized adipose tissue (3). Different parameters were identified, including wavelengths of 1470 nm, powers of 6-9 W, and 600  $\mu\text{m}$  fibers for lipodystrophy; 1470 nm endolaser with 300  $\mu\text{m}$  fiber and 4-6 W powers for facial wrinkles; a combination of 1470 nm endolaser and non-ablative fractional laser of 1540 nm with 2 W power for acne; and 980 nm endolaser with 3 W power for rosacea.

**Conclusions:** The review highlights the diversity in endolaser parameters used for different aesthetic conditions. The lack of standardization in protocols and the absence of objective measures in some studies limit the comparison and interpretation of results. The need for randomized clinical trials and standardization in endolaser parameters is evident to ensure the validity and generalizability of results.

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## LATE SUBMISSION AND MISCELLANEOUS SESSION

### THE EFFECTS OF PHOTOBIOMODULATION ON MRONJ FORMATION IN ORAL CAVITY IN RAT MODEL

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#### Abstract

##### Three learning objectives:

1. Photobiomodulation shows promise effects in preventing of wound healing in MRONJ
2. PBMT has improving effects on wound healing in MRONJ.
3. Laser therapy has good effects on wound healing in both soft and hard tissues

**Introduction:** This study aims to explore the preventive potential of photobiomodulation (PBM) in bisphosphonate-related osteonecrosis of the jaw (BRONJ) using a rat model.

**Methods and Materials:** An experimental rat model was established, exposing rats to zoledronate (ZA), a primary risk factor for MRONJ. An 810 nm diode laser was applied with parameters of 0.33 W/cm<sup>2</sup> power density and 10 J/cm<sup>2</sup> energy density for 30 seconds. PBM was initiated one day pre-extraction and continued for two weeks. The impact of PBM on wound healing in both soft and hard tissues was evaluated post tooth extraction.

**Results:** ZA exposure hindered wound healing in both soft and hard tissues after tooth extraction. PBM intervention effectively mitigated the adverse effects of ZA, promoting healing processes in both tissue types. This suggests the potential of PBM as a preventive strategy for MRONJ in patients on long-term bisphosphonate treatment. Moreover, PBM exhibited enhanced wound healing in normal rats, indicating its broader applicability beyond MRONJ cases.

**Conclusion:** Photobiomodulation shows promise in preventing and improving wound healing in MRONJ and normal cases. These findings underscore the significance of optimizing PBM parameters and suggest its potential clinical relevance as a preventive intervention for MRONJ and a promoter of wound healing.

# PERI-OPERATIVE PBM TREATMENT FOR ANKLE / FOOT SURGERY WITH CRPS

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## Abstract

### Learning Objectives:

- 1 Dampening of the CNS with select PBM treatment including Laser Medical Acupuncture.
- 2 PBM method to produce sympathectomy effect + response similar to LA lumbar sympathectomies.
- 3 Desensitising and optimising local operation site and lymphatics.
- 4 Preop Anxiolytic, Analgesic and Antiemetic PBM treatment

### Brief Introduction:

Foot surgery and injury can be very problematic and often has varying nerve symptoms pre and /or post op that influence pain, swelling, colour, temperature, and function. These symptoms can vary in intensity and severity. CRPS is a clinical diagnosis of these signs and symptoms.

Patients with chronic pain and CRPS have central sensitivity and a heightened nervous system and often associated PTSD.

These conditions and symptoms are difficult to treat even with our pharmacopeia and anaesthetic interventions. PBM is a simple, noninvasive treatment that can significantly help reduce patients CRPS symptoms and signs and help prepare them for surgery and /or their post op recovery.

### Methods:

PBM laser acupuncture points - including tranquillising, sedative, analgesic and ear stress points (shenmen )

PBM contra lateral lymphatic treatment. THOR LED Cluster

Treatments titrated according to response weekly or fortnightly depending on severity, or surgery date,

Preop treatment of PBM preferred within 24 hours prior to surgery.

**Results - Collection of Clinical case studies:** Symptoms and signs of CRPS collated at pre and post each consultation and treatment. eg Swelling, colour, sensitivity/allodynia, 'electric shot' pain, movement, resting and walking pain, sleep,

**Conclusions:** Patients presenting for surgery with mild or severe CRPS or developed CRPS post op or injury have a hindered recovery. Swelling and pain and limited movement causes stress and anxiety and reduces rehabilitation. A non invasive and conservative PBM protocol of laser acupuncture and Lymphatic and analgesic (Thor ) treatment pre and /or post-op foot surgery can help recovery and reduce nerve pain and CRPS symptoms and signs.

This PBM treatment with its sympathectomy like changes is safe and non invasive and does not require hospital or theatre admission, anaesthesia or invasive sympathectomy blocks (associated complications)

# COMPARISON OF TWO INTERVENTION METHODS, PHOTOBIO-MODULATION AND COGNITIVE REHABILITATION, ON THE RISK-TAKING FACTOR IN OPIOID DRUG USERS

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## Abstract

**Aims:** Risk-taking is a behavior that endangers a person's health and provides the basis for a person to suffer from physical and psychological diseases. Substance dependence disorder includes cognitive, behavioral, and psychological symptoms along with a pattern of repetition and withdrawal tolerance consequences. The aim of the current research was the effectiveness of cognitive rehabilitation and phototherapy on the risk-taking of people with substance dependence disorder.

**Materials And Methods:** The current study is an experiment with a pre-test, post-test, and control group design with a 2-month follow-up level. The statistical population of this research was all the clients of opioid drug abuse treatment clinics of Nikteb, Golrizan, and Hami in Tehran in 2020. In the first level, using the available sampling method, according to  $\alpha=0.05$ , the effect size of 85%, and three equal groups, using Gpower software, 63 people were determined. These people were selected among those who had received a score higher than the cut-off line in the risk test and then were replaced by a simple random method in 2 experimental groups (21 people in the cognitive rehabilitation group and 21 people in the phototherapy group) and a control group (21 people). The first experimental group received 12 cognitive rehabilitation sessions and the second experimental group received 12 phototherapy sessions, but the people in the control group did not receive any intervention and remained on the waiting list.

**Findings:** The average age of the cognitive rehabilitation group was  $34.19 \pm 8.27$ , the phototherapy group was  $32.76 \pm 7.68$ , and the control group was  $33.33 \pm 7.73$ . The results of the mixed variance analysis test showed that both interventions in the post-test and follow-up level had a significant effect on reducing risk-taking compared to the control group ( $p < 0.05$ ). In addition, the results of the Bonferroni post hoc test showed that phototherapy was more effective in reducing risk-taking ( $p < 0.05$ ).

**Conclusion:** Cognitive rehabilitation and phototherapy can be used as treatment methods to reduce the problems caused by the riskiness of clients of drug addiction clinics.

# FROM ZERO TO HERO: DEVELOPING A HOSPITAL WIDE PHOTOBIO-MODULATION PROGRAM FOR A PEDIATRIC ONCOLOGY HOSPITAL

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## Abstract

### Learning Objectives:

1. Review the feasibility and efficacy of published PBM trial in children and adolescents undergoing hematopoietic cell transplantation.
2. Define strategies needed in development of an institutional PBM program.
3. Describe program development in wound care, neuropathy and gastrointestinal mucositis.

**Background and Aims:** Oral mucositis is a significant and common toxicity associated with high-dose chemotherapy and head/neck radiation. In a prospective clinical trial, we found photobiomodulation (PBM) to be feasible, with significant efficacy in the prevention and reduction of mucositis in children and adolescents undergoing a hematopoietic cell transplantation (HCT). Concurrently, the Children's Oncology Group recommended PBM in the supportive care guidelines for the treatment of oral mucositis in patients undergoing HCT and head/neck radiation. This translational program's purpose was to develop strategies for implementing a PBM program for all children and adolescents at risk for oral mucositis.

**Methods:** The supportive care PBM therapy team was created, with oversight by two PBM-trained nurses. Nursing policies and standard operating procedures were created. Educational sessions were conducted for physicians and advanced practice providers, detailing methods for patient referrals. Educational materials for patients and families were developed, explaining the PBM service. To facilitate the program, electronic orders were developed in Epic, a designated PBM treatment room was allocated, and additional units were purchased and housed on the outpatient/inpatient and HCT unit. For patient communication, the PBM nurse has a phone for scheduling appointments and communicating with families.

**Results:** Promotion of the PBM therapy team has led to an increase in referrals, with an average of 12 new consultations per month. Since the program's initiation in 2021, 324 patients have been treated and followed by the team. In addition to patients undergoing HCT, patients at high-risk for oral mucositis and treated with PBM include: Burkitt/B-Cell lymphoma, Rhabdomyosarcoma, Ewing sarcoma and patients receiving head/neck radiation. After the first year of program initiation, the PBM program was awarded the Clinical Care Improvement Award.

**Conclusions:** We found the utilization of PBM for the prevention and treatment of oral mucositis to be feasible with significant efficacy, leading to institutional support for a sustainable program beyond oral mucositis.

# EVALUATION OF PHOTOBIMODULATION TO REDUCE ORAL MUCOSITIS IN PATIENTS UNDERGOING RADIOTHERAPY

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## Abstract

### Objectives:

1. To establish if PBM can reduce oral mucositis (OM) during radiotherapy treatment.
2. If analgesia and supportive medications could be reduced.
3. To assess oral comfort (patient reported) and establish if oral eating can be maintained throughout treatment.

**Introduction:** Patients having radiotherapy (RT) and/ or chemotherapy to the oral cavity and surrounding structures will experience inflammation to the oral cavity. This is a debilitating, painful condition that can impact on nutritional intake, increase pain and reduce quality of life. RT causes OM in areas receiving >30gy, and OM Can increase the risk of infection, taking 2-4 weeks to heal.

**Methods:** 84 patients included in audit, prospective data collection was used during a 12 month period. PBM was used in addition to standard of care.

External probe used in 5 positions, covering all the oral mucosa, timed at 1min at 2.5Hz in each position. Lollipop probe used intra-orally 1min on top of the tongue, 1min below tongue directed at the floor of mouth. Patients had access to the device 5 days per week.

Patient-, and clinician-graded OM scores were recorded using the WHO scale, medications documented at weekly on-treatment review clinic

**Results:** 79 (86%) patients completed all planned treatment. Patient-graded OM was on the whole higher than clinician-graded which was multifactorial. At the end of treatment 20 (26%) patients had >grade 2 OM, 57 (74%) had < grade 2 OM. 66 (78.6%) had grade 2 or 3 OM. More medications were required by patients having RT alone, compared to chemo-RT/ post-op RT. All grades of OM were higher (clinician-graded) in the chemoRT group.

Patient- vs clinician-graded OM were the same in 15 cases, less in 5, and higher in 19.

**Conclusion:** OM is subjective to each patient and varied to clinician-grading. PBM is very well tolerated, easy to use, and has no side effects. Supportive medication escalation was minimised. When compared with our historical data, oral eating was maintained for longer. Post-treatment recovery back to oral eating was accelerated. Limitations include no control arm. Recommendations are to improve data collection categories weekly for more accurate conclusions.

# HARNESSING PHOTOBIOMODULATION THERAPY AND PHOTODYNAMIC THERAPY AS A POTENTIAL INTERVENTION FOR COVID-19

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## Abstract

The COVID-19 pandemic has prompted a global quest for effective therapeutic strategies to combat the virus and mitigate its devastating consequences. Photobiomodulation therapy (PBMT) emerges as a compelling candidate due to its non-invasive nature and proven ability to modulate immune responses and tissue repair processes. PBMT utilizes laser or light-emitting diode devices to deliver specific wavelengths of light to target tissues, eliciting biological responses that promote healing and immunomodulation.

The proposed mechanism involves the delivery of photonic energy to key sites of viral infection, exerting anti-inflammatory and immunomodulatory effects. PBMT has been shown to enhance cellular metabolism, improve tissue oxygenation, and modulate cytokine production, all of which are pertinent factors in COVID-19 pathogenesis.

Preclinical studies investigating the use of PBMT against respiratory viruses, including coronaviruses, have yielded promising results, demonstrating its ability to reduce inflammation, improve pulmonary function, and enhance viral clearance. Furthermore, PBMT's favorable safety profile and ease of administration make it an attractive adjunctive therapy for COVID-19 management.

However, further research is warranted to optimize PBMT parameters, including wavelength, dose, and treatment regimen, to maximize therapeutic efficacy and ensure reproducibility of results. Clinical trials assessing the efficacy of PBMT in COVID-19 patients are underway, aiming to elucidate its potential role in improving clinical outcomes and reducing disease severity.

Alternatively, there is potential application of Photodynamic therapy (PDT) in managing COVID-19. The proposed mechanism involves the administration of a PS, which selectively accumulates in viral-infected cells. Upon exposure to specific wavelengths, the PS generates ROS, leading to viral inactivation and destruction of infected cells. Moreover, PDT's immunomodulatory effects assist in alleviating cytokine storm associated with COVID-19, thereby reducing disease severity and improving patient outcomes.

In conclusion, PBM and PDT hold promise as an adjunctive treatment for COVID-19, offering a novel approach to combatting the virus and its associated complications. Further studies are warranted.

# USE OF LOW LEVEL LASER THERAPY IN THE TREATMENT OF NECROTIZING FASCIITIS: AN EXPERIENCE REPORT

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## Abstract

**Introduction:** Fournier Syndrome, also defined as Necrotizing Fasciitis, is characterized by an acute and severe infectious process of the affected subcutaneous tissue and superficial fascia. It has high morbidity and mortality rates. Anaerobic germs or gram-negative bacilli are responsible for Necrotizing Fasciitis.

**Objective:** To present a technique to reduce the healing time of this pathology in a diabetic patient by more than 60%, reducing the chance of mortality, which is common in the presence of diabetes. To use photobiomodulation as a tool to reduce costs and promote a significant improvement in the patient's quality of life. To present a care treatment option for patients with infected wounds that is effective, low cost, painless, non-surgical, quick and scientifically proven technique.

**Method:** This is a descriptive study, developed at the Arantes Ferreira Institute from 1st April, 2023 to 15th May, 2023. Patient R.P.M., male, 46 years old, sought the service after hospital treatment with antibiotic therapy and surgical debridement in the genital area (scrotal pouch). After R.P.M.'s evaluation, a treatment plan was developed with appointments three times a week with prescription of antimicrobial dressing with ionic silver, gauze impregnated with biguanide polyhexamethylene and association of Low Intensity Photobiomodulation Therapy (ALGaAs diode device with power of 100mW; wavelength of 660nm and 880nm; spot 0,028 cm<sup>2</sup>). Protocol used: 1J Infrared, with point technique on edges with a distance of 2 cm between each point in a total of 8 irradiated areas. 10J of red laser in divided in two areas of 5J each, using scanning technique.

**Results:** The treatment time was 45 days. The evolution of the wound healing process was observed at each appointment to change the dressing, as shown in the following images:





01/April/2023

10/April/2023

15/May/2023

Source: Photographic records taken during the patient's treatment.

**Conclusion:** The use of low-intensity laser therapy associated with a dressing with interactive coverage and antimicrobial gauze has been shown to be capable of accelerating the healing process of Fournier's Ulcer, reducing treatment time, assistance costs and the significant impact on the patient's quality of life.



# **PBM THERAPY IN A TYPICAL AUSTRALIAN PODIATRY PRACTICE : CASE EXAMPLES ACROSS MULTIPLE PATHOLOGIES**

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## **Abstract**

Modern podiatry practice, like general medical and therapy practices, encompasses treatment of an array of clinical conditions, across skin, infection, rheumatology, endocrinology, oncology, sports injuries and the like. The advent of modern, high power laser units has resulted in significant improvement in service delivery of PBM therapy.

This presentation will provide the audience with an appreciation -

1. of the wide ranging clinical conditions that PBMt can dramatically improve
2. that a change in pain and function is possible from the application of the first dose of a course of treatment
3. of the time and cost effective outcomes that PBMt can provide for many chronic and intractable conditions.

Photographs of conditions, pre and post treatment, including an avulsed Quadriceps muscle at insertion, ankylosing spondylitis, cellulitis, haematoma, midfoot arthrosis, neuropathy, Parkinson's Disease and post surgical repair of ruptured Tendo Achilles will be included in these cases.

This presentation serves as a timely reminder to all clinicians the importance of the collection of documentary evidence of patients improvement and can be useful to help improve awareness of PBMt with other clinicians involved in these patients care. The author has been doing this for some 8 years now.

All PBM treatments were carried out using a 25W MLS laser, with dual wavelengths of 905nm pulsed emissions combined with 808nm continuous emissions. Applications were either using a hand held single diode and/or a hands free triple diode unit. Dosage was based on the manufacturers specifications and/or WALT guidelines, combined with some variations for individual cases. The treatments were carried out in a private practice clinical setting.

## LATE SUBMISSION AND MISCELLANEOUS SESSION 2

### EFFECTIVENESS OF PHOTOBIMODULATION WITH LOW-LEVEL LASERS ON THE ACCELERATION OF ORTHODONTIC TOOTH MOVEMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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#### Abstract

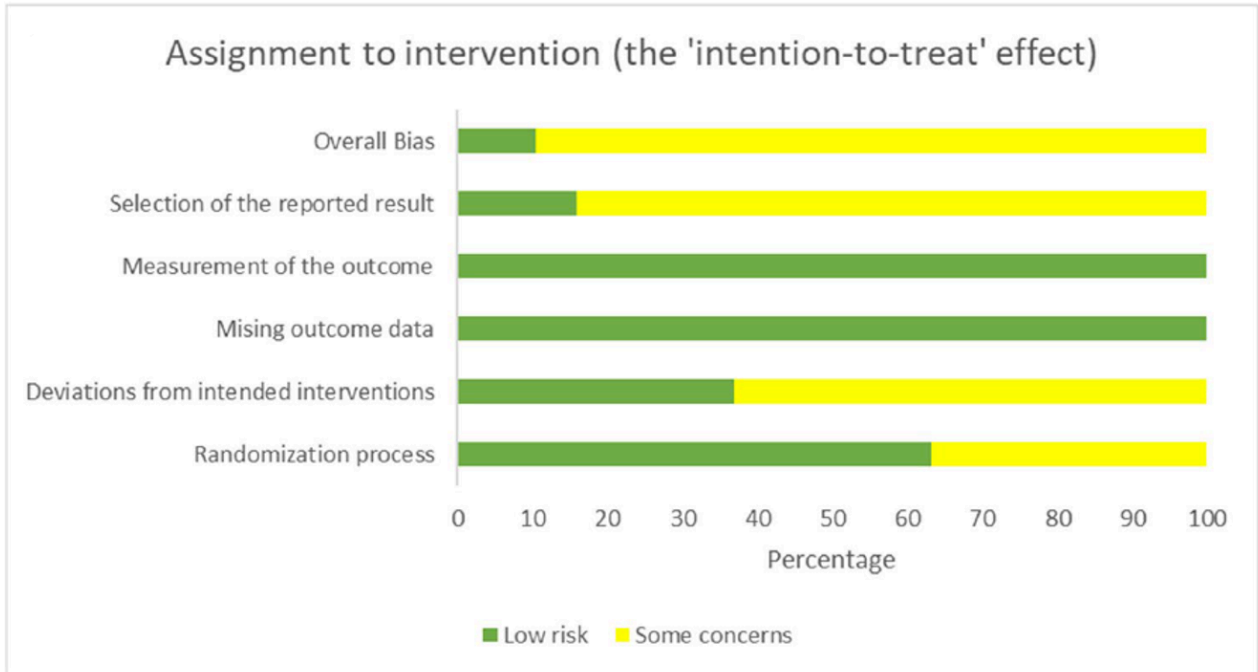
**Introduction:** Although several studies have evaluated the effect of low-level laser therapy (LLLT) on orthodontic movement acceleration, results are still inconsistent. Such inconsistencies may be attributed to the differences in the LLLT application protocols, especially in terms of wavelength ranges.

**Objective:** (i) to assess the clinical effects of LLLT on the acceleration of orthodontic movement, (ii) to establish the most effective LLLT wavelength and (iii) to estimate the most effective energy density to accelerate tooth movement during orthodontic treatments.

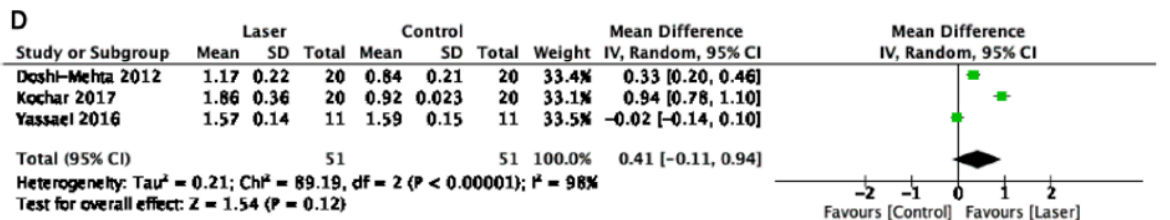
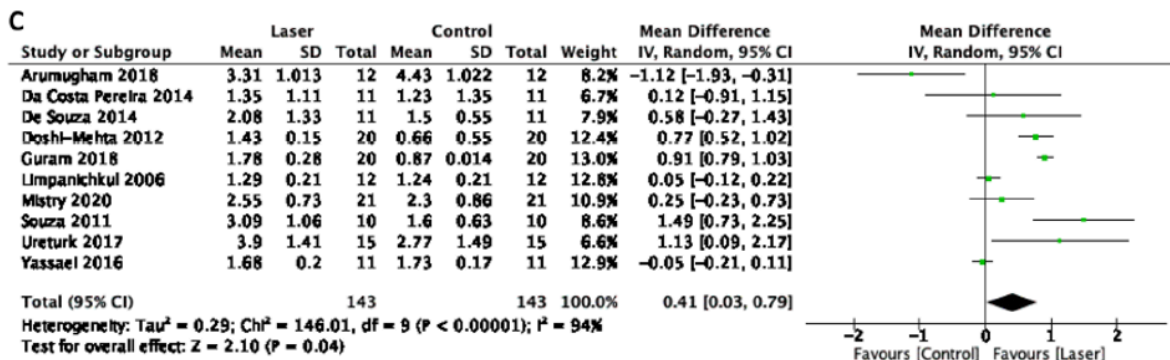
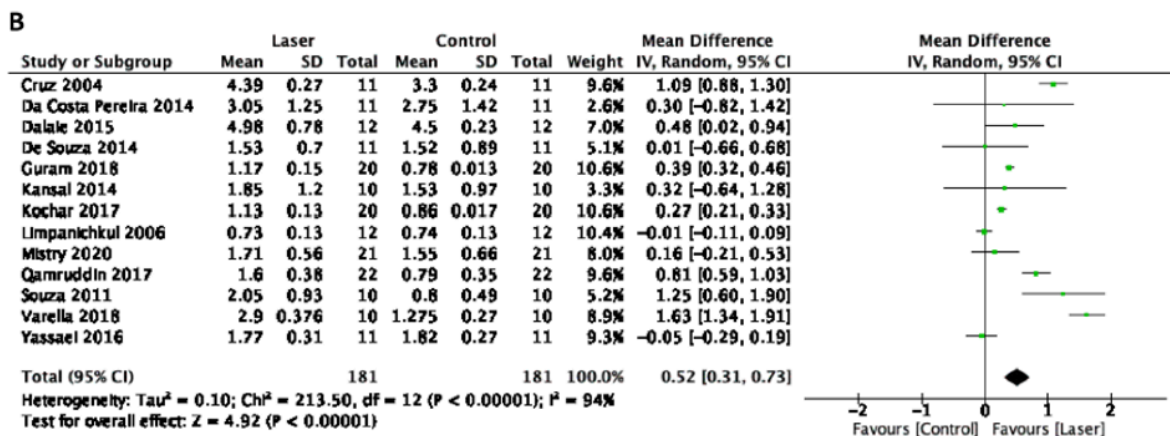
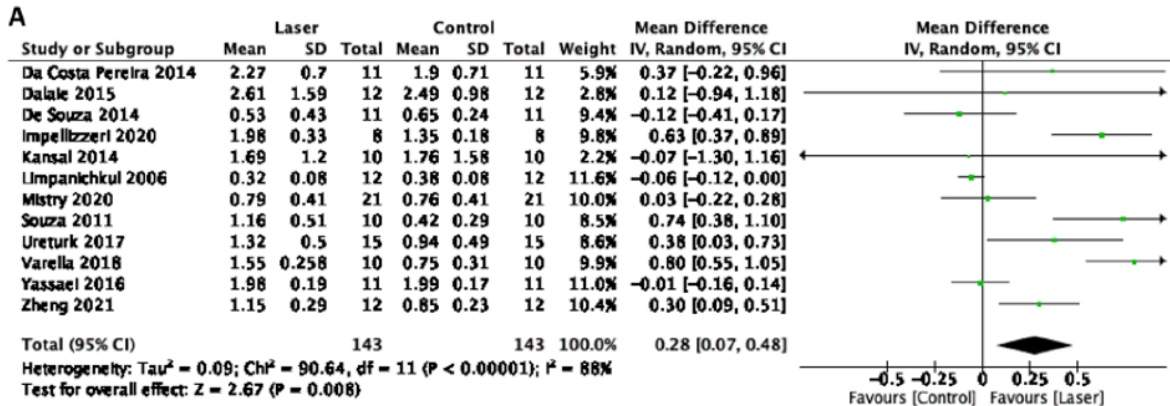
**Methods:** PROSPERO registration CRD42022332585. MEDLINE (PubMed), Scopus, ScienceDirect, and LILACS were searched from inception to October 2022. Inclusion criteria: Split-mouth randomised clinical trials (RCTs) on systemically healthy patients reporting the effect of LLLT in accelerating orthodontic movements, specifically retraction of canines. The risk of bias was assessed using RoB-2. A random effect model was applied.

**Results:** Nineteen RCTs met the inclusion criteria for qualitative synthesis, and eighteen RCTs were included in the quantitative synthesis. Seventeen studies were rated as at some concerns of bias and two studies were classified as having a low risk of bias. This systematic review and meta-analysis presents a moderate risk of bias and findings pointing to a tendency for faster orthodontic dental movement in the groups receiving LLLT during the first (OR of 0.28 95% CI (0.07 to 0.48)), second (OR of 0.52 95% CI (0.31 to 0.73)), and third (OR of 0.41 95% CI (0.03 to 0.79)) month follow-up. Wavelengths  $\leq 810$  nm and energy density values  $\leq 5.3$  J/cm<sup>2</sup> were associated with faster orthodontic tooth movement.

**Conclusions:** Photobiomodulation with LLLT tends to be effective in accelerating canine retraction during orthodontic treatment. Wavelengths  $\leq 810$  nm and energy density values  $\leq 5.3$  J/cm<sup>2</sup> are associated with an increase in the acceleration of orthodontic tooth movement. Nonetheless, the selected studies for meta-analysis have substantial heterogeneity due to sample sizes, the age range of participating patients, and varied irradiation settings that prevent the extrapolation of these results. Future research on the influence of LLLT on orthodontic movement acceleration should focus on improving study methodological quality to reduce the risk of bias and improve the strength of the results.



**Fig. 1** Collective data for risk of bias, according to RoB-2 domains



**Fig. 2 A-D** Forest plot of the comparison between the LLLT and control groups at months 1, 2, 3, and 4, respectively. OR, odds ratio; CI, confidence interval

# ANTIMICROBIAL PHOTODYNAMIC THERAPY (A-PDT) APPLIED TO CANINE PAW WOUNDS

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## Abstract

**Background:** a-PDT is the treatment of infections caused by microorganisms, which can be viruses, fungi and bacteria, through the association of a light source, a photosensitizer compatible with the wavelength of this light, and the presence of oxygen, leading to apoptosis microbial.

**Objectives:** 1) To appreciate the effects of a-PDT in the treatment of infections caused by microorganisms. 2) To understand the benefits of the local action of a-PDT in surgical interventions for chronic wounds. 3) To evaluate the positive impact of a-PDT on the speed of tissue repair.

**Methodology:** The benefits of the practical applicability of a-PDT in the treatment of dog paw wounds will be demonstrated through the presentation of a clinical case performed by the author for the treatment of postoperative complications, culminating in the indication for amputation of the left front paw, which was preserved after the implementation of surgical treatment. combined with antimicrobial photodynamic therapy (Therapy EC™, DMC, 100mW, 660nm, 54J; Chimiolux™, DMC, methylene blue 0.01%), and lasers (red laser 100mW, 660nm and infrared laser 100mW, 808nm).

**Results:** Postoperative local infection after surgical treatment combined with a-PDT was combated after 3 months of treatment without the prescription of systemic antibiotic therapy, proving to be effective and efficient for the repair of persistent chronic wounds in the canine paw.

**Conclusion:** The beneficial effects provided by a-PDT on biological tissues are excellent allies for clinical practice in the treatment of chronic wounds in veterinary medicine.

# EFFICACY OF NON-PHARMACEUTICAL TREATMENTS OF XEROSTOMIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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## Abstract

**Objective:** The aim of this literature review and meta-analysis was to evaluate the impact of non-pharmaceutical treatments for xerostomia on salivary flow rate and examine differences in group allocation.

**Methods:** This systematic review and meta-analysis examined five published articles between 2000 and 2022. 4 articles assessed the effect of photobiomodulation and one was regarding electrostimulation effects on xerostomia. The search was conducted in 3 databases including PubMed (MEDLINE), Scopus, and Web of Science (ISI). The articles were all in English. The included studies were analyzed using a systematic review protocol and were combined using random-effects model for meta-analysis. index was used to assess heterogeneity among studies. Meta-regression was used to investigate the relationship between unstimulated salivary flow rate and group allocation (treatment or control). STATA.MP software 17 was used to analyze data. Laser parameters are as follows: Ferrandez Pujante employed a diode laser (810 nm, 6 J/cm<sup>2</sup>, 1 W); Terlevic Dabic utilized a GaAlAs laser (830 nm, 0.1–100 J/cm<sup>2</sup>, 35 mW); Fidelix employed an aluminum-gallium-arsenide laser diode (808 nm, 100 mW, 4.0 J/cm<sup>2</sup> per irradiation point per session); and Cafaro used a pointer pulse (650 nm, 19.2 J/cm<sup>2</sup>, 5 mW).

**Results:** In the five studies, the mean unstimulated salivary flow rate for the treatment group before intervention was 0.098 ml/min (0.044-0.153 CI 95%). After the intervention the salivary flow rate increased to the estimated amount of 0.166 (0.096-0.236 CI 95%). In the control group before the intervention, the unstimulated salivary flow rate was estimated to be 0.096 (0.062-0.131 CI 95%). After the intervention, the salivary flow rate increased to 0.122 (0.074-0.169 CI 95%). The increase in salivary flow rate was more significant in the treatment group compared to the control group, where also an increase was observed.

**Conclusion:** Non-pharmaceutical treatments, such as photobiomodulation, Electrostimulation, and acupuncture demonstrate a significant increase in salivary flow rate among patients in the treatment groups, surpassing the changes observed in the control groups. The need for additional studies is emphasized to further validate the effectiveness of these treatments.

# PBM AND SPORT: CAN WE DETERMINE AN OPTIMAL PROTOCOL TO OBTAIN THE BEST EFFECTS TO REDUCE MUSCLE DAMAGE AND IMPROVE PERFORMANCE?

## NARRATIVE REVIEW

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### Abstract

**Learning objectives:** Confirm the usefulness of PBM in sport, determine the best optical characteristics and practical PBM protocols to optimize its efficacy.

**Introduction:** PBM has demonstrated physiological effects very interesting in sport management, reducing muscle damage and improving performance. Despite a wide range of evidence, the use of PBM in sport still remains very limited, due to the lack of a clear efficient protocol. The aim of this review is to determine whether the current scientific literature allows to determine an optimal protocol for using PBM in sport.

**Method and results:** Among the 348 studies found with a PubMed query, we selected 45 articles reporting properly-designed clinical trials using PBM in sport. Primary endpoint (PE) was a significant effect on reducing muscle damage and/or improving performance, we studied the influence on PE of optical characteristics and PBM protocols.

1059 patients were studied, median age 24.8 years, mainly men, 30.4% were athletes. PBM was delivered with local illumination device in 93.1%, mainly before sport sessions (64,7%). Median follow-up duration was 2 days.

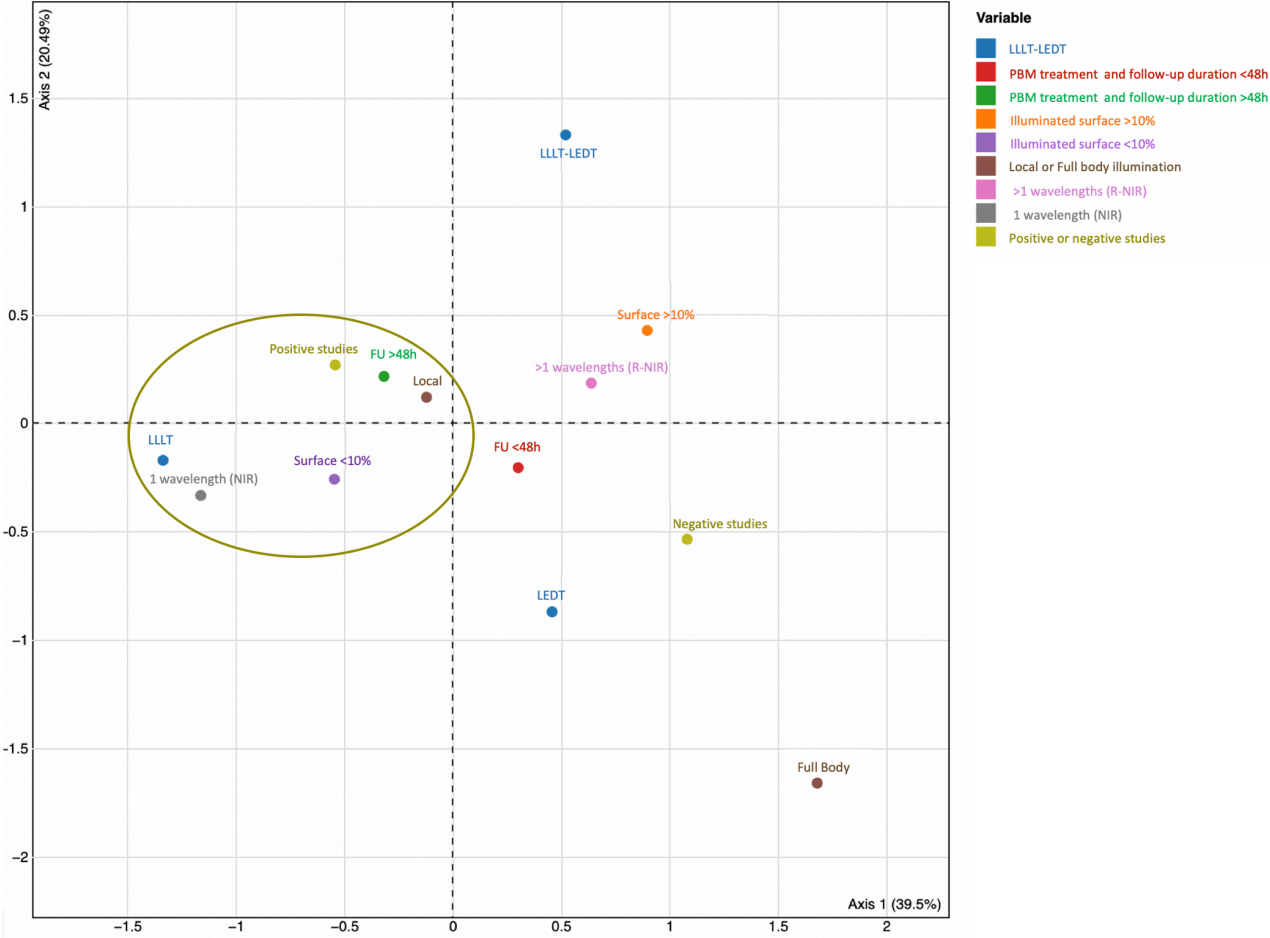
A significant effect on PE was found in 30/45 studies (66.7%), with reduction of muscle damage in 15/18 (83.3%), improvement of performance in 26/43 studies (60.5%). In univariate analysis as well as using a *Multiple Correspondence Analysis*, the use of LLLT and single wavelength (NIR light) were associated with a significantly improved efficacy, illuminated surface  $\geq 10\%$  of target muscle, local illumination and treatment  $>2$  days were over-represented in positive studies. Delivering PBM with an energy in accordance with expert recommendations, as other studied criteria, had no significant influence on PE.

A work has to be done first to optimize optical protocols to deliver the right dose to the target, second to build protocols compatible with the constraints of sports practice.

**Conclusions:** PBM is efficient in reducing muscle damage and improving performance in sport. LLLT and single wavelength increase its efficacy. Further studies, with specific optical protocol and precise determination of the energy delivered in the target muscles, are needed to optimize the use of PBM in sports.



FIGURE 1 : Multiple Correspondence Analysis





**TABLE 1** Influence of optical protocol on endpoints

	Patients (n)	Performance and/or Muscle protection effect	Muscle damage reduced	Performance improved
<b>All Studies</b> (n=45)	1059	30/45 (66,7%)	15/18 (83,3%)	26/43 (60,5%)
<b>Optical characteristics</b>				
<u>LLLT/LEDT</u>				
<b>LLLT only</b> (n=12)	315	<b>12/12 (100%)</b>	5/6 (83,3%)	<b>11/12 (91,7%)</b>
LEDT only (n=19)	320	8/19 (42,1%)	6/8 (75%)	5/17 (29,4%)
LLLT/LEDT combined (n=14)	424	10/14 (71,4%)	4/4 (100%)	10/14 (71,4%)
<i>p value (univariate analysis)</i>		<b>0,003</b>	0,8 (NS)	<b>0,002</b>
<u>One/multiple wavelength(s)</u>				
<b>1 wavelength (NIR)</b> (n=16)	350	<b>16/16 (100%)</b>	7/8 (87,5%)	<b>15/16 (93,7%)</b>
>1 wavelengths (R/NIR) (n=29)	709	14/29 (48,3%)	8/10 (80%)	11/27 (40,7%)
<i>p value (univariate analysis)</i>		<b>&lt;0,001</b>	>0,9 (NS)	<b>&lt;0,001</b>
<u>Continuous/Pulsed current</u>				
<b>Continuous</b> (n=31)	628	<b>21/31 (67,7%)</b>	11/14 (78,6%)	<b>17/29 (58,6%)</b>
<b>Pulsed</b> (n=11)	388	<b>9/11 (81,8%)</b>	4/4 (100%)	<b>9/11 (81,8%)</b>
Continuous/Pulsed combined (n=3)	43	0/3 (0%)	/	0/3 (0%)
<i>p value (univariate analysis)</i>		0,025	>0,9 (NS)	0,04
<u>Energy delivered in accordance with recommendations [8]</u>				
Yes (n=28)	733	20/28 (71,4%)	9/10 (90%)	19/27 (70,4%)
No (n=17)	326	10/17 (58,8%)	6/8 (75%)	7/16 (43,8%)
<i>p value (univariate analysis)</i>		0,4 (NS)	0,6 (NS)	0,08 (NS)

**TABLE 2** Influence of practical organization of PBM sessions on endpoints

	Patients (n)	Performance and/or Muscle protection effect	Muscle damage reduced	Performance improved
<b>All Studies</b> (n=45)	1059	30/45 (66,7%)	15/18 (83,3%)	26/43 (60,5%)
<b>Practical organization of PBM sessions</b>				
<u>Illuminated surface (% of target muscle)</u>				
Surface ≤10% (n=28)	613	23/28 (82,1%)	14/14 (100%)	19/27 (70,4%)
Surface >10% (n=17)	446	7/17 (41,2%)	1/4 (25%)	7/16 (43,7%)
<i>p value (univariate analysis)</i>		0,05	0,05	0,08 (NS)
<u>Local/Whole-body illumination</u>				
Local (n=42)	986	30/42 (71,4%)	15/16 (93,8%)	26/41 (63,4%)
Whole-body (n=3)	73	0/3 (0%)	0/2 (0%)	0/2 (0%)
<i>p value (univariate analysis)</i>		0,032	0,02	0,2 (NS)
<u>Timing to sport session</u>				
Before sport session (n=33)	685	20/33 (60,6%)	10/12 (83,3%)	18/32 (56,2%)
After sport session (n=7)	174	6/7 (85,7%)	4/4 (100%)	4/7 (57,1%)
Both (n=5)	200	4/5 (80%)	1/2 (50%)	4/4 (100%)
<i>p value (univariate analysis)</i>		0,4 (NS)	0,3 (NS)	0,3 (NS)
<u>Follow-up duration</u>				
≤2 days (n=23)	414	12/23 (52,2%)	7/7 (100%)	11/23 (47,8%)
>2 days (n=22)	645	18/22 (81,8%)	8/11 (72,7%)	15/20 (75%)
<i>p value (univariate analysis)</i>		0,035	0,2 (NS)	0,07 (NS)