Journal of Research in Clinical Medicine
J Res Clin Med 2026;14:35591
doi:10.34172/jrcm.35591
https://jrcm.tbzmed.ac.ir
TUOMS PRESS

Case Report

Photobiomodulation in a Patient With Phantom Limb Pain and Depression Following Arm Amputation: A Case Report

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Article info

Article History:
Received: September 26, 2025
Revised: July 14, 2026
Accepted: July 15, 2026
ePublished: September 19, 2026

Keywords:
Laser, Low-level light therapy, Major depression, Phantom limb pain

Abstract

Chronic post-amputation pain is associated with significant psychological distress, reduced quality of life, and depressive symptoms. Photobiomodulation (PBM) therapy relieves pain and reduces inflammation. We report a 49-year-old male with chronic post-amputation pain who presented with depressive mood, suicidal ideation, and functional disability despite prior pharmacological treatment and electroconvulsive therapy. PBM was applied using an 810 nm laser (1 W, 200 mW/cm^2) once daily for five days. Each session combined transcranial PBM, targeting the left and right dorsolateral prefrontal cortex, and proximal PBM applied sequentially to nine anatomical sites, including the residual limb, brachial plexus, stellate ganglia, and cervical spine. Pain, measured by the Visual Analog Scale, decreased by 50% after the fifth session and by 63% at four-week follow-up, with complete resolution at six months. Burning sensation scores decreased by 44%, 67%, and 80% across follow-up assessments, and the patient reported improvement in mood to a euthymic state at six months.

Introduction

Photobiomodulation (PBM) therapy is a noninvasive technique that uses non-thermal red to near-infrared (NIR) light (wavelengths from 600 nm to 1100 nm) and regulate metabolism, increase ATP and reduce inflammation in biological tissue.[1] PBM works on mitochondria, specifically cytochrome *c* oxidase (CCO), the terminal enzyme of the mitochondrial electron transport chain, which is considered one of the primary photon acceptors of red and NIR light. The U.S. Food and Drug Administration (FDA) has recently approved PBM for age-related dry macular degeneration[2] and cleared multiple PBM devices for the treatment of musculoskeletal pain, highlighting its growing recognition as a neuromodulation technique.[3-5] In Europe, PBM has been approved for oral mucositis, back pain, neck pain, joint pain, and tendinopathies.

PBM applied to the prefrontal cortex (PFC) has been shown to photo-oxidize neuronal CCO, increasing adenosine triphosphate (ATP) synthesis and prefrontal oxygenation in healthy individuals.[6] Bilateral transcranial PBM (t-PBM) targeting the PFC has also been shown to improve cerebral metabolism and enhance hemodynamic activity in individuals with major depression[7] and bipolar disorder.[8] The mechanisms of action of t-PBM in major depression have been explored in animal models, demonstrating that its antidepressant effects are associated with improvements in mitochondrial function, such as increased mitochondrial CCO expression and activity, as well as enhanced ATP biosynthesis in the PFC,[9] along with increased hippocampal neurogenesis.[10] Moreover, in a human trial, 823 nm t-PBM applied bilaterally to the forehead twice weekly for 8 weeks improved depressive symptoms in patients with major depression, as evidenced by a mean reduction in HAM-D17 scores, with a medium to large effect size.[11] Recent research has also suggested that t-PBM-induced improvements in cerebral blood flow may be a key neurobiological mechanism underlying its antidepressant effects.[12]

Phantom limb pain is a neuropathic pain condition following amputation that involves both peripheral and central nervous system mechanisms, including abnormal nerve signaling and cortical reorganization.[13] Persistent phantom limb pain is commonly associated with psychological distress, reduced quality of life, and depressive symptoms.[14] Although studies specifically investigating PBM for phantom limb pain are limited, PBM has demonstrated analgesic and anti-inflammatory effects in neuropathic pain conditions and has been shown to reduce acute and chronic pain through

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neuromodulatory and anti-inflammatory mechanisms.[15] PBM applied to the dorsal root ganglia has been shown to significantly increase pain thresholds in mice, with this analgesic effect associated with modulation of pain-related neural biomarkers, such as reduced mGluR1 expression and increased levels of prostatic acid phosphatase.[16] Additionally, in a triple-blinded randomized clinical trial, PBM significantly reduced pain and improved quality of life and psychological factors in individuals with fibromyalgia.[3]

This case study aims to present improvements in depressive symptoms and pain levels following t-PBM and proximal PBM (p-PBM) in a patient experiencing chronic post-amputation pain. In the present case, t-PBM targeting the dorsolateral prefrontal cortex (dl PFC) was combined with p-PBM, defined here as PBM applied to peripheral and sympathetic anatomical targets proximal to the amputated limb, based on the possibility that simultaneous modulation of central and peripheral mechanisms may be beneficial in patients experiencing concurrent phantom limb pain and depression.

Case report

This case report was prepared in accordance with the CARE case reporting guidelines.[17] Written informed consent was obtained from the patient for publication of this case report and accompanying clinical details. This case involves the third hospitalization of a 49-year-old male at Razi Education and Research Mental Hospital in Tabriz, Iran, who presented with persistent pain and psychological distress following a right arm amputation. The amputation occurred in 2018 as a result of a workplace accident. Since the incident, the patient has been unable to return to work, leading to significant functional disability and contributing to a depressed mood accompanied by frequent suicidal ideation. Despite receiving multiple therapeutic interventions aimed at managing both chronic pain and depressive symptoms, the outcomes were inconsistent and generally unsatisfactory.

At the time of presentation, the patient was taking the following prescribed medications: Lacosamide 100 mg twice daily, Nortriptyline 10 mg three times daily, Clonazepam 1 mg every night, Citalopram 20 mg twice daily, Magniforte 150 mg once daily, Celecoxib 200 mg once daily, and Propranolol (Inderal) 10 mg three times daily. No changes were made to the patient's pharmacological regimen during the PBM intervention period or throughout follow-up assessments. Additionally, the patient had undergone a single session of electroconvulsive therapy during a previous hospitalization. However, the procedure was discontinued due to a worsening of pain symptoms and the development of ecchymosis on the amputated limb following the seizure.

PBM therapy was administered using a 1 W, 810 nm laser cluster (5 × 200 mW) with a beam area of 5 cm^2, resulting in an irradiance of 200 mW/cm^2 (THOR Photomedicine Ltd., Amersham, UK). Each PBM session included both t-PBM and p-PBM approaches. For t-PBM, the laser probe was directed bilaterally to the F3 (left) and F4 (right) positions, based on the international 10–20 EEG system, to target the dlPFC. Each t-PBM session consisted of eight one-minute intervals, alternating between the right dlPFC for the first 4 minutes and the left dlPFC for the remaining 4 minutes, with a side switch every minute. A fluence of 48 J/cm^2 (200 mW/cm^2 × 240 seconds) was delivered to each site per session. For proximal-PBM (p-PBM), the laser probe was directed to multiple anatomical regions, including the residual nerve pathways of the amputated limb, the cervical region along the brachial plexus, the contralateral upper limb, bilaterally over the stellate ganglia, and the cervical spine (midline and paravertebrally on both sides). Each region was irradiated for 30 seconds, and the probe was immediately moved to the next site sequentially. In total, each p-PBM session included 9 treatment sites. A fluence of 6 J/cm^2 (200 mW/cm^2 × 30 seconds) was delivered to each site per session. Protective eyewear was worn by both the experimenter and the patient at all times. Additionally, the patient was instructed to keep his eyes closed during laser operation. PBM therapy was administered over five consecutive daily sessions.

Results

The patient was assessed using the Beck Depression Inventory-II (BDI-II), and received a total score of 18 at baseline, indicating mild to moderate clinical depressive symptoms. Domain-specific analysis revealed that emotional symptoms accounted for 25%, suggesting a low affect component; somatic symptoms comprised 47.7%, indicating a moderate level of physical symptom expression (e.g., fatigue, sleep disturbance, appetite changes, and low libido); and cognitive symptoms accounted for 20.8%, representing a low degree of dysfunctional thoughts or pessimism. These findings highlighted a predominantly somatic presentation of depressive symptoms, with relatively low emotional and cognitive involvement. Additionally, the patient's baseline pain score before the first PBM session was 8 out of 10, and the burning sensation was rated as 9 out of 10, on the Visual Analog Scale (VAS). VAS ratings reflected the patient's self-reported severity of pain and burning sensation at each assessment time point.

After the fifth PBM session, the patient's BDI-II score remained at 18, showing no change from baseline. However, at the 4-week follow-up, the patient subjectively reported improvement in mood to a euthymic state, although the BDI-II was not re-administered during follow-up assessments. As he reported a euthymic mood at follow-up, the BDI-II was not re-administered. Additionally, following the fifth PBM session, the patient's pain score decreased to 4 out of 10, and the burning sensation was reduced to 5 out of 10. At the 4-week follow-up, further improvements were observed, with both the pain and burning sensation scores reduced to 3 out of 10.

Discussion

In this case, five consecutive 810 nm PBM sessions coincided with improvements in mood and pain scores at the 4-week follow-up in an individual experiencing chronic post-amputation pain and depression. Our findings are consistent with those reported by Schiffer et al., who first demonstrated the antidepressant effects of 810 nm PBM in individuals with major depression. In that study, a single 8-minute bilateral t-PBM session, delivered as two 4-minute exposures to the left and right dlPFC, each delivering 60 J/cm², resulted in significant reductions in depression scores at 2- and 4-week follow-ups.[7] In the current study, we employed t-PBM parameters largely consistent with those reported by Schiffer et al. (2009), with a couple of methodological differences. Specifically, we used a laser device rather than light-emitting diodes (LEDs), and whereas their protocol involved a single t-PBM session, our protocol consisted of five consecutive daily sessions. Additionally, the fluence per site in our study was 20% lower than that reported in their study. Furthermore, 823 nm t-PBM applied bilaterally to the dlPFC twice weekly for 8 weeks has also been shown to improve depressive symptoms in patients with major depression.[11]

Nevertheless, in our case, the delayed emergence of subjective mood improvement at follow-up, despite the absence of immediate changes in BDI-II scores after the fifth session, warrants cautious interpretation. Delayed neurobiological processes, cumulative psychosocial influences, concurrent pharmacotherapy, or natural symptom variability may have contributed to the observed changes. Therefore, the temporal relationship between PBM administration and mood improvement in this case should be interpreted as exploratory rather than causal.

We also applied PBM to the residual nerve pathway proximal to the amputated limb, as well as to sympathetic targets associated with brain and upper-limb innervation. The observed reduction in phantom limb pain and burning sensations may potentially relate to several mechanisms proposed in the literature, including modulation of dorsal root ganglion signaling phosphatase activity,[16] attenuation of inflammation,[18] regulation of antioxidant systems and cytokines,[19] and local activation of opioid pathways.[20] These mechanisms may collectively contribute to decreased nociceptive transmission and peripheral sensitization in chronic neuropathic pain conditions.[21]

Research on the application of PBM therapy for pain reduction in cases with concurrent depression remains limited. In a case–control trial, p-PBM administered to the back and thighs, without any transcranial application, using 660 nm and 850 nm light significantly alleviated depressive symptoms in patients with low back pain.[22] Although most studies on PBM for neurorehabilitation have focused on the direct effects of t-PBM targeting subjacent regions of the cerebral cortex, some investigations have also suggested potential indirect effects of p-PBM.[23,24] Proximal administration of a 1064 nm laser to the forearm in healthy individuals has additionally been shown to produce local effects, including increased hemoglobin oxygenation and elevated CCO concentration.[25] It can be speculated that p-PBM targeting peripheral regions may also have indirectly contributed to the observed antidepressant effects in our case, potentially through the aforementioned mitochondrial and hemodynamic mechanisms, as well as activation of circulating immune cells or stem cells.[26,27] Randomized clinical trials are warranted to further explore the impact of p-PBM on mood and its possible synergistic effects when combined with transcranial stimulation.

The selection of the 810 nm wavelength and bilateral dlPFC stimulation parameters in the present case was based on prior clinical studies reporting antidepressant effects of t-PBM targeting prefrontal regions.[1] Additionally, p-PBM targets were selected to modulate residual peripheral nerve pathways and sympathetic regions potentially involved in phantom limb pain.[15] Five consecutive daily sessions were administered based on the possibility that repeated stimulation may provide cumulative neuromodulatory and analgesic effects.[28]

Limitations

This report describes a single uncontrolled clinical observation and therefore does not allow causal inference regarding the therapeutic effects of PBM. The observed improvements may have been influenced by placebo effects, concurrent pharmacological treatments, natural symptom fluctuation, or other psychosocial factors. Additionally, depressive symptoms were not reassessed using the BDI-II during follow-up, and pain outcomes relied on subjective single-point VAS ratings without repeated measurements or variability estimates. Therefore, the findings should be considered preliminary and hypothesis-generating, warranting further investigation in randomized sham-controlled clinical studies.

Conclusion and Future Directions

Repeated sessions of 810 nm laser PBM were associated with some improvements in depressive symptoms and phantom limb pain in this case. These observations may suggest the potential therapeutic relevance of multimodal PBM combined with concurrent pharmacotherapy in individuals experiencing chronic pain and depressive symptoms. Future studies should employ a randomized, sham-controlled clinical design that incorporates concurrent pharmacological treatments to more rigorously evaluate the efficacy of PBM.

Acknowledgments

We would like to thank the patient and his family for allowing us to share his story. This study was approved by the Research Ethics Committees of Tabriz University of Medical Sciences (ethical code: IR.TBZMED.REC.1404.204), and we gratefully acknowledge the support of the Razi Clinical Research Development Unit for their assistance in obtaining the necessary ethical approval.

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Competing Interests

Farzad Salehpour is the Research Manager, James Carroll is the Founder and CEO, and Kevin Carroll is the Clinical Advisor at THOR Photomedicine Ltd. The remaining authors declare no conflicts of interest.

Ethical Approval

A written informed consent was obtained from the patient and his family. This study was approved by Research Ethics Committees of Tabriz University of Medical Sciences (ethical code: IR.TBZMED.REC.1404.204).

Funding

None.

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