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Photobiomodulation Therapy in Systemic Healing and Wound Repair – Mechanisms, Evidence, and Safety

Overview of Photobiomodulation (PBM)

Photobiomodulation (PBM), also known as low-level laser (or light) therapy (LLLT), is a nonionizing light treatment typically using red to near-infrared (NIR) wavelengths to stimulate healing, relieve pain, and reduce inflammation [1]. Unlike surgical or ablative lasers, PBM operates at low power densities that **do not induce tissue burning**. Instead, PBM light photons are absorbed by cellular photoreceptors – most notably **cytochrome c oxidase** in mitochondria – initiating a cascade of biological effects [1]. Through these photochemical reactions, PBM aims to **boost cellular metabolism and tissue repair** without causing thermal damage.

How PBM Works – Molecular to Systemic Effects: At the molecular level, absorption of PBM light leads to increased production of cellular energy (ATP), a brief burst of reactive oxygen species (ROS), release of nitric oxide (NO), and modulation of calcium ion flux [1]. These **primary and secondary photobiological effects** activate various transcription factors that promote cell survival, proliferation, migration, and new protein synthesis [1]. As multiple cells respond, tissue-level outcomes become evident. PBM's **cellular effects translate into broader systemic benefits**, including modulation of inflammation, accelerated tissue repair, enhanced wound healing, reduced edema, and pain relief [2]. Notably, PBM exhibits a **biphasic dose-response**: lower light doses tend to **stimulate** beneficial activity, whereas higher doses (or excessively long exposures) can **inhibit** cellular responses [3]. For example, in vitro wound-healing studies found that low energy density (<20 J/cm^2) **stimulated** cell proliferation and migration, while higher energy (~20–50 J/cm^2) **significantly reduced** cell growth and metabolic activity [4]. This underscores the importance of proper dosimetry in PBM treatments.

Systemic and Immune-Modulatory Effects of PBM

One of the most widely reported systemic effects of PBM is its **anti-inflammatory action**. PBM has been shown to upregulate anti-oxidant defenses and **reduce markers of inflammation** in various contexts [5]. In both laboratory models and clinical settings, PBM consistently shifts the immune response away from a pro-inflammatory state. For instance, PBM can suppress the production of inflammatory cytokines and prostaglandins, and it reduces the classically activated M1 macrophage phenotype associated with inflammation [6]. **Overall, a reduction in inflammation is one of PBM's most reproducible effects**, observed in diverse tissues such as joints (arthritis models), lungs, spinal cord, brain, adipose tissue, and healing wounds [6]. This systemic anti-inflammatory effect underpins many of PBM's therapeutic benefits, as excessive inflammation often impedes healing in both acute injuries and chronic diseases.

Clinical studies in humans further demonstrate PBM's systemic benefits. In a representative example, **patients with community-acquired pneumonia** received adjunct PBM via an array of NIR LEDs over the chest in addition to standard care. Compared to controls, the PBM-treated group showed faster recovery of blood parameters: **white blood cell counts dropped** more rapidly (reflecting resolution of infection/ inflammation) and **red blood cell/hemoglobin levels rose** more markedly (indicating improved systemic status) [7]. Specifically, after one week of daily PBM, the treated patients had significantly greater normalization in **leukocyte counts and neutrophil levels**, and an ~86% increase in erythrocyte count (versus ~35% in controls) [7]. These results suggest that PBM can broadly **support the body's recovery processes** during systemic illness – likely by mitigating excessive inflammation and improving microcirculation in affected tissues. Beyond infections, researchers are exploring whole-body or **"systemic" PBM techniques** (such as intravascular blood illumination or full-body light beds) for conditions like sepsis, metabolic syndrome, and athletic recovery, capitalizing on PBM's ability to influence circulating immune cells and cytokines [6]. While more studies are needed, early data indicate PBM's systemic effects can translate into **faster healing and improved clinical outcomes** in certain medical conditions when used alongside standard therapies.

PBM in Wound Healing Applications

Wound healing is one of the cornerstone applications of photobiomodulation, with a strong evidence base spanning laboratory research to clinical trials. PBM's pro-healing reputation dates back to the 1960s when Endre Mester first noted that low-powered ruby laser light accelerated hair regrowth and wound closure in animal models [8]. Clinically, **PBM was soon applied to aid surgical wound healing**, where it was observed to promote faster incision closure [9]. Since then, a wide range of wound types have been investigated. Randomized trials and case series have reported PBM benefits in **chronic skin ulcers** (such as diabetic foot ulcers, venous stasis ulcers, and pressure sores) as well as **acute injuries** like burns [9].

Aggregated data support these findings. For example, a systematic review and meta-analysis of 13 randomized controlled trials (361 patients) assessed PBM for **diabetic foot ulcers**, a common and stubborn chronic wound. The meta-analysis found that PBM-treated patients had significantly greater ulcer size reduction and faster healing compared to standard care alone [10]. In quantitative terms, PBM led to roughly a **23% additional decrease in ulcer area** versus controls ($p < 0.0001$), confirming a measurable enhancement in wound closure rate [10]. The trials achieving the best outcomes typically used red-spectrum lasers or LEDs (wavelengths ~630–685 nm) at doses on the order of 3–6 J/cm^2 per session, applied several times per week [11]. These parameters fall in the stimulatory range of the biphasic dose response and align with empirical guidelines for wound healing. Such evidence has led experts to conclude that **PBM is effective and safe as an adjunct therapy for chronic foot ulcers** and potentially other non-healing wounds [12].

Beyond human trials, **preclinical studies** have helped elucidate *how* PBM improves wound healing. PBM appears to act on multiple phases of the repair process – from modulating initial inflammation to stimulating new tissue formation. In animal models, PBM increases the activity of fibroblasts (which produce collagen and extracellular matrix), promotes angiogenesis (growth of new blood vessels), and encourages re-epithelialization (migration of skin cells to cover the wound) [13] [14]. A notable mechanism involves **transforming growth factor beta-1 (TGF-β1)**, a cytokine critical for tissue repair. Recent research by Khan et al. demonstrated that PBM can activate latent TGF-β1 in injured tissue, thereby accelerating healing [15]. In a full-thickness burn wound model in mice, a controlled PBM regimen (810 nm laser, calibrated to avoid thermal effects) resulted in significantly **faster burn wound closure** compared to untreated controls [16]. PBM-treated wounds in these mice showed *elevated TGF-β signaling and reduced inflammatory gene expression*, correlating with better healing outcomes [15] [17]. Importantly, when the same experiment was conducted in genetically modified mice that lack activatable TGF-β1, **PBM no longer improved healing** [17]. This finding implicates TGF-β1 activation as a key pathway by which PBM enhances tissue regeneration. Taken together, both clinical evidence and mechanistic studies indicate that PBM can **significantly improve wound healing** – especially in settings of impaired or delayed healing – by dampening chronic inflammation and kick-starting the body's normal repair machinery. It is now used in some clinics as a complementary therapy for hard-to-heal wounds, with minimal side effects and ease of application.

Neurological Applications and Evidence

Although originally applied to peripheral tissues, photobiomodulation has increasingly been investigated for **neurological benefits**. Transcranial PBM (tPBM) involves directing red/NIR light to the head to stimulate neural tissue. Early-phase studies, including both animal experiments and human trials, suggest that PBM can induce several beneficial changes in the brain's physiology. For example, near-infrared light (typically 808 nm or 810 nm) penetrates the scalp and skull to some degree and can be absorbed by brain cells, particularly in cortical regions. This has been shown to **increase cerebral blood flow and oxygenation, enhance mitochondrial activity in neurons, and reduce neuroinflammation** in the treated areas [18]. Mechanistically, the same mitochondrial and anti-inflammatory effects observed in other tissues also occur in neural cells – PBM boosts ATP production in neurons and glia, moderates oxidative stress, and can shift microglia (brain immune cells) to a less inflammatory state [6]. These changes are hypothesized to improve the brain's resilience and functional capacity, which is being tested in various neurological conditions.

Clinically, the strongest evidence so far has emerged in the realm of **cognitive function and neurodegenerative illness**. A 2025 meta-analysis compiled results from 24 randomized controlled trials (total N = 820) examining PBM's effects on cognitive performance in humans [19] [20]. The trials ranged from healthy adults receiving tPBM to patients with mild cognitive impairment or early dementia. The meta-analysis found **significant cognitive benefits** from PBM therapy compared to sham/placebo treatments [21]. In cognitively impaired individuals, PBM led to measurable improvements in **global cognition** (standardized mean difference [SMD] ≈ 0.66 vs control), as well as specific domains like **working memory** (SMD ≈ 1.4, indicating a large effect) [22]. PBM-treated participants also demonstrated better **attention and executive function**, often evidenced by faster reaction times on neuropsychological tests [22]. Notably, even in healthy individuals, some studies reported modest improvements in attention and memory after PBM, though effects were more pronounced in those with baseline impairment [23]. These findings suggest that PBM can *enhance neural function* or *slow cognitive decline*, making it a promising adjunct or preventive strategy in conditions like Alzheimer's disease, Parkinson's disease (for cognitive aspects), stroke rehabilitation, and traumatic brain injury. Indeed, small pilot trials in **post-stroke patients** and **TBI patients** have reported trends of improved executive function, reduced depression, and better sleep with PBM, though larger confirmatory studies are needed. Overall, while neurological applications of PBM are still an active area of research, the accumulating evidence indicates **meaningful benefits in brain health** are achievable. The therapy is noninvasive and well-tolerated, and if further validated, it could fill an important gap by offering a **safe treatment for neurodegenerative and neuropsychiatric conditions** that currently have limited options.

Safety and Dosimetry Considerations

One of the advantages of photobiomodulation therapy is its **excellent safety profile** when used correctly. PBM is a non-ionizing, atraumatic intervention – it does not break the skin or expose patients to harmful radiation. However, like any therapeutic modality, proper parameters and precautions are essential to ensure safety. Below we outline key safety and dosimetry considerations for PBM:

- **Non-Thermal Dosages:** By definition, PBM uses "low-level" light that should *not* overheat tissues. Using an appropriate power density and exposure time is critical to avoid unwanted thermal effects. Studies on laser PBM have shown that if irradiance is too high, it can raise tissue temperature above safe levels and even cause cellular damage. For instance, researchers in a burn wound model found that **increasing laser power without adjusting exposure time led to skin surface temperatures exceeding 45 °C and signs of tissue injury**, whereas using a pulsed or on–off protocol to keep temperature <45 °C prevented damage [24]. They optimized a PBM regimen (810 nm at ~70 mW/cm^2 for 5 minutes, delivering ~21 J/cm^2 per session) that enhanced healing **while keeping tissue temperature below 45 °C** [25] [26]. The take-home point is that PBM should be delivered in a **dosimetric "sweet spot"** – enough energy to stimulate cells, but not so much as to produce heat or inhibitory effects. Exceeding the recommended fluence can not only risk burns but also invoke the biphasic response where further increases in dose **reverse** the benefits [4]. Thus, adherence to tested parameters (energy density, power output, treatment duration/frequency) is key to PBM safety.

- **Eye Safety Measures: Protective eyewear is mandatory** for both the patient and the practitioner during PBM treatments, especially when using laser devices. The human retina is highly sensitive to light injury, and inadvertent exposure to a PBM laser (even a reflection from a shiny surface) can cause retinal damage [27]. Because PBM wavelengths are often in the red/NIR range – which the eye may not perceive as bright but can still focus on the retina – it's critical to block all direct viewing of the beam. International laser safety standards classify even moderately powered PBM lasers as a hazard to eyes. Therefore, clinics using PBM enforce strict eye safety: appropriate **wavelength-specific goggles** are worn by all people in the room to filter out the PBM beam [28]. Additionally, one should never shine a PBM device (laser or high-intensity LED) near or into the eyes. With these precautions, **ocular injuries from PBM can be effectively prevented**. It's worth noting that low-level LEDs (as in some LED helmets for tPBM) are more diffuse and less hazardous than collimated lasers, but eye protection is still advised as a general rule.

- **Minimal Side Effects:** When proper protocols are followed, PBM's side effects are **typically mild and transient**. Patients occasionally report a warming sensation, tingling, or erythema at the exposure site, but these usually resolve quickly after treatment [29] [30]. In the consensus guidelines on PBM, experts noted that common side effects (if any) were limited to **minor discomfort, transient redness, or slight swelling**, and these effects were **temporary and self-resolving** [29] [30]. More serious adverse events are exceedingly rare. PBM *rarely* causes burns or blistering – and virtually never does so if the device is kept moving or at the correct distance to avoid hot spots. Likewise, there have been **no reports of significant scarring or lasting injury** from PBM in medical literature [31]. Crucially, because PBM light is non-ionizing (no UV or X-rays involved), it **does not carry a risk of DNA mutation or cancer initiation**. A recent review confirms that red/NIR PBM *does not induce the DNA damage associated with carcinogenesis or photoaging* [32]. This differentiates PBM from ultraviolet therapies or radiation treatments – PBM can be used repeatedly over the long term without cumulative cellular damage. In fact, PBM is often used in cancer patients (for example, to heal oral mucositis from chemotherapy) with no evidence that it promotes tumor growth [33]. Overall, the consensus in the field is that PBM is **a very safe therapy** when applied as directed, with side effects typically minor if they occur at all [29].

- **Contraindications and Precautions:** Although PBM is broadly safe, practitioners follow certain **precautionary guidelines**. Active malignancy is usually listed as a contraindication for PBM on or near the tumor site (out of theoretical caution, since PBM's growth-stimulatory effects on cancer cells are not fully understood). Similarly, PBM is often avoided over the uterus during **pregnancy**, and patients with a history of **epilepsy** are treated cautiously (especially avoiding pulsing frequencies that might trigger seizures) [34]. Patients with known **photosensitivity disorders or those taking photosensitizing drugs** (e.g. some antibiotics or isotretinoin) should be evaluated carefully, as their threshold for light reaction is altered [35]. Other relative contraindications include avoiding direct irradiation over endocrine glands (like the thyroid) or over the gonads, since long-term effects in those areas haven't been fully studied [35]. It's also advised to keep PBM devices a slight distance from **pacemakers or other electronic implants** to prevent any electromagnetic interference, though modern PBM devices generally pose minimal EMI risk [36]. Adhering to manufacturer instructions and published protocols is the best way to ensure safety; indeed, an expert Delphi panel highlighted the importance of **standardizing PBM parameters and treatment reporting** to maintain consistent safety and efficacy [37] [38]. In summary, **when used within recommended guidelines, PBM has an outstanding safety record**. By following precautions (eye protection, proper dosing, and respecting contraindications), healthcare providers can utilize this therapy to harness healing and pain relief with minimal risk.

Conclusion

Photobiomodulation therapy has emerged as a versatile treatment modality with **broad applications** in systemic health, wound repair, and even neurology. Its mechanism of action – leveraging light to stimulate cells' own repair and anti-inflammatory pathways – represents a unique, drug-free approach to healing. Evidence is strongest for PBM's ability to **accelerate tissue healing and reduce inflammation**, as seen in chronic wounds and musculoskeletal injuries, but growing research supports its benefits in neurological function and possibly other systemic conditions. Equally important, PBM offers this therapeutic benefit **without significant side effects**, provided treatments are delivered at appropriate dosages with standard safety measures. Clinical adoption of PBM is increasing in fields like sports medicine, dermatology, dentistry, and rehabilitation, often as an adjunct to standard care. As research continues (especially with more high-quality trials in neurological and internal medical conditions), our understanding of optimal PBM protocols will sharpen. In the meantime, current data suggest that PBM can be a **valuable tool to promote healing and modulate inflammation** across a variety of scenarios – all while maintaining a high margin of safety for patients [32] [29]. In summary, photobiomodulation exemplifies an innovative convergence of physics and medicine: by shining light on the problem (quite literally), we can engage the body's natural healing processes and achieve outcomes that were previously difficult or impossible, from closing a chronic wound to sharpening a senior's memory, all with minimal risk.

Sources: Recent peer-reviewed studies and reviews on PBM's mechanisms and clinical applications, including consensus guidelines and meta-analyses [1] [6] [7] [10] [15] [21], as well as safety assessments from expert panels and research findings on PBM dosimetry and adverse effects [24] [29] [32] [27]. These sources affirm the discussed therapeutic effects and safety considerations, reflecting the current state of evidence in photobiomodulation therapy.

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1 3 5 6 13 14 Mechanisms and applications of the anti-inflammatory effects of photobiomodulation
https://www.aimspress.com/article/id/1434

2 8 Photobiomodulation at molecular, cellular, and systemic levels - PubMed
https://pubmed.ncbi.nlm.nih.gov/37310556/

4 Photobiomodulation with Blue Light on Wound Healing: A Scoping Review - PMC
https://pmc.ncbi.nlm.nih.gov/articles/PMC9959862/

7 Systemic Effects of Photobiomodulation on Blood Components in the Treatment of Community-Acquired Pneumonia - PubMed
https://pubmed.ncbi.nlm.nih.gov/34935510/

9 15 16 17 24 25 26 33 Accelerated burn wound healing with photobiomodulation therapy involves activation of endogenous latent TGF-β1 | Scientific Reports
https://www.nature.com/articles/s41598-021-92650-w?error=cookies_not_supported&code=695ba9b5-cfa6-4f8e-9aa2-dad7ab0d9c9d

10 11 12 A Systematic Review and Meta-Analysis of the Effects of Low-Level Laser Therapy in the Treatment of Diabetic Foot Ulcers - PubMed
https://pubmed.ncbi.nlm.nih.gov/32394760/

18 Transcranial photobiomodulation for the brain: a wide range of ...
https://journals.lww.com/nrronline/fulltext/2024/03000/transcranial_photobiomodulation_for_the_brain__a.8.aspx

19 20 21 22 23 Photobiomodulation effects on cognitive function - a systematic review and meta-analysis of randomized controlled trials - PubMed
https://pubmed.ncbi.nlm.nih.gov/40394373/

27 34 35 36 Effects of Photobiomodulation Therapy (PBMT) in the Management of Postoperative Pain After Third Lower Molar Extraction: A Narrative Review | MDPI
https://www.mdpi.com/2077-0383/14/15/5210

28 29 30 31 32 37 38 Evidence-based consensus on the clinical application of photobiomodulation
https://www.odontologos.com.co/assets/doc/news/2025-10-22_113621eScholarship_UC_item_68j64451.pdf