

**REVIEW ARTICLE**

# Good, better, best? The effects of polarization on photobiomodulation therapy

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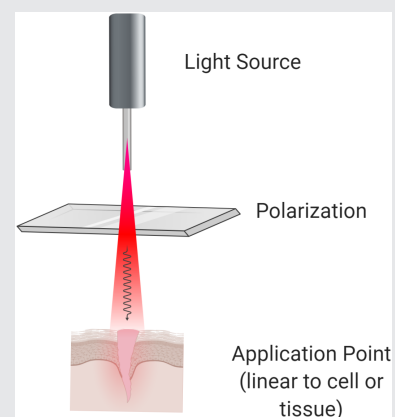
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**Abstract**

Photobiomodulation therapy (PBMT) is a widely adopted form of phototherapy used to treat many chronic conditions that affect the population at large. The exact physiological mechanisms of PBMT remain unsolved; however, the prevailing theory centres on changes in mitochondrial function. There are many irradiation parameters to consider when investigating PBMT, one of which is the state of polarization. There is some evidence to show that polarization of red and near-infrared light may promote different and/or increased biological activity when compared to otherwise identical non-polarized light. These enhanced cellular effects may also be present when the polarized light is applied linear to the tissue direction. Herein, we synthesize the current experimental and clinical evidence pertaining to polarized photobiomodulation therapy; ultimately, to better inform future research into this area of phototherapy.

**KEYWORDS**

low-level light therapy, photobiomodulation, polarization, polarized light therapy

## 1 | INTRODUCTION

Phototherapy encompasses a broad spectrum of therapeutic modalities, all designed to bring about a positive biological effect. The earliest documented evidence of phototherapy dates back to the ancient Egyptians, who worshipped the sun god Ra. Through Ra's perceived power, the worshippers would expose themselves to direct sunlight to increase their energy levels and vitality [1]. In more recent times, a diverse group of

phototherapeutic devices have been developed aimed at treating of a range of conditions, spanning from skin lesions to neurodegenerative diseases. These include: UV therapy, commonly used to treat dermatological conditions such as psoriasis, acne, vitiligo and lichen planus [2, 3]; polarized light therapy, which is used to treat musculoskeletal and dermatological conditions [4, 5]; and broad-spectrum fluorescent light-boxes, which are used to treat seasonal affective disorder [6–10]. Amongst all the phototherapies used clinically, Photobiomodulation

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Therapy (PBMT), appears to be the most widely used and accepted. PBMT is a system of phototherapy that uses low-intensity, non-destructive laser and/or light emitting diode (LED) to create a therapeutic effect [11]. This type of phototherapy dates back to the 1960s, and like many scientific breakthroughs, was discovered by mistake. While working at Semmelweis University in Budapest, Hungary, Endre Mester assessed whether laser could cause cancer in mice. To his surprise, not only did the mice exposed to lasers not develop cancer, the experimental wound inflicted on them healed faster [11]. From this point onward, the medical application of lasers and LEDs has slowly grown, as has the evidence base [12]. PBMT has also been referred to as “cold-laser,” “soft-laser,” “low-level laser/laser therapy” or “biostimulation” [11, 13]. All of these use red and/or near-infrared (NIR) light commonly to create a biological effect. The known efficacious wavelengths that have been investigated range between 600 nm and 1000 nm [12], thus spanning both red and NIR. The full mechanistic effects of PBMT are currently not clear, but its effects are known to occur at both the cellular and molecular level [14].

PBMT has been shown to be clinically effective across a range of pathologies, many of which cause a significant burden to global health services and society more broadly. Given the theorized biological effects of PBMT on cellular factors related to tissue healing, research has been completed that shows PBMT can accelerate the healing of chronic diabetic ulcers [15]. PBMT has also been shown to assist in the treatment of various dermatological conditions such as psoriasis [16], hypertrophic scars and keloids [17] and may have the capacity to modulate various acne-inducing pathways [18]. PBMT has also been used in treating conditions associated with the nervous system. Another key focus of clinical research into PBMT is that of the treatment of pain. Multiple trials have shown PBMT to be effective in promoting analgesia in patients with diagnosed neuropathic pain [19] as well as both chronic and acute low back and neck pain [20] [21] [22]. Trials have also found PBMT to be of benefit in the treatment and management of various forms of osteoarthritis [23, 24] and tendinopathy [25, 26]. Finally, PBMT can also be applied to the sporting population. In fact, PBMT can provide immediate pain relief in sports injuries [27] and when used before exercise, can cause a significant performance improvement in both strength and endurance sports [28].

Despite plausible biological mechanisms and widespread use, there is still more research needed to better quantify the biological effects of PBMT and develop an accepted set of evidence-based guidelines for its use [14]. The application of PBMT is a delicate balance; too little energy will not create any detectable effect and too much

can cause negative effects. This is known as the biphasic dose response or Arndt-Schulz effect [12, 13]. There can be a number of variables manipulated that can contribute to the summation of PBMT dosage, which include: wavelength, irradiance, pulse structure, coherence and polarization [12]. Light waves normally travel across all different planes. Light can be polarized by blocking or absorbing specific planes of light propagation, so the remaining photons travel in a specified plane or planes. There are three main types of polarization: linear polarization, where light travels in a single plane only; circular polarization, where light travels in two distinct linear planes that are perpendicular to one another; and elliptical polarization, where the light travels in an elliptical fashion, by combining two linear segments of light at different amplitudes [29]. Research suggests that linear or circular polarization may induce different or more pronounced cellular effects when compared to otherwise identical, non-polarized light, potentially being more pronounced, when polarized light aligns parallel to its target tissue [30, 31]. Currently, there is a small amount of evidence documenting the effects of polarized PBMT (PPBMT) and fewer still comparing non-polarized PBMT (NPPBMT) and PPBMT. Given that red and NIR light has the largest underpinning body of evidence, it makes sense to investigate the differences between polarized and non-polarized light within this spectrum, before expanding to polychromatic polarized light sources. Therefore, this review will synthesize the current experimental and clinical evidence surrounding narrow-band, monochromatic PPBMT (600-1000 nm), ultimately to better inform this potential area of advancement within the field of PBMT, and help to inform other, broader-spectrum phototherapy research.

## 2 | REVIEW METHODOLOGY

Searches were conducted using CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE, PUBMED, The Cochrane Library and Google Scholar. The following search terms were used: low-level light therapy; photobiomodulation; photobiomodulation therapy; low-level laser therapy; polarization; polarized light; polarized PBMT; polarized low-level light therapy; polarized low-level laser therapy; polarized laser; polarized laser irradiation; polarized light therapy; polarized phototherapy; polarized photobiomodulation; polarized photobiomodulation (Figure 1). American and English spellings were used for all terms. Studies from all years were included. The inclusion criteria were peer reviewed original research, reviews and case studies related to the search topics. Studies that examined non-polarized light



**FIGURE 1** Summary of search strategy and paper exclusion

only, polychromatic light, or light outside of the 600 to 1000 nm range were omitted. Non-English articles that were not able to be translated were excluded. Initial search identified 7590 entries. After exclusion of duplicates and conference abstract titles, an abstract analysis was used to identify potential items. Full-text analysis of all papers was performed to assess appropriateness for inclusion in this review. Reference lists of included articles were also used to locate additional relevant articles. In total 16 number of studies were found related to red and NIR PPBMT (Figure 1). No ethical approval was required for this review.

### 3 | A PRIMER ON LIGHT-TISSUE INTERACTIONS

Light is made up of packets of energy known as photons, which constantly travel at the speed of light throughout the known universe. The more photons in number, the brighter the light is. The perceived colour of light is determined by its wavelength on the electromagnetic spectrum. Visible light to humans, is generally defined as a wavelength between 400 and 700 nm. When light interacts with living tissue, it can be absorbed, reflected or transmitted [14]. Generally, only a small amount of light is reflected from biological tissue, this is said to follow Snell's law, which describes the change in direction of a light wave as it transitions between two media. Most light however, is absorbed. Light absorption by biological tissue is characterised by the absorption coefficient ( $\mu_a$ ). It is also important to consider the scattering of light within

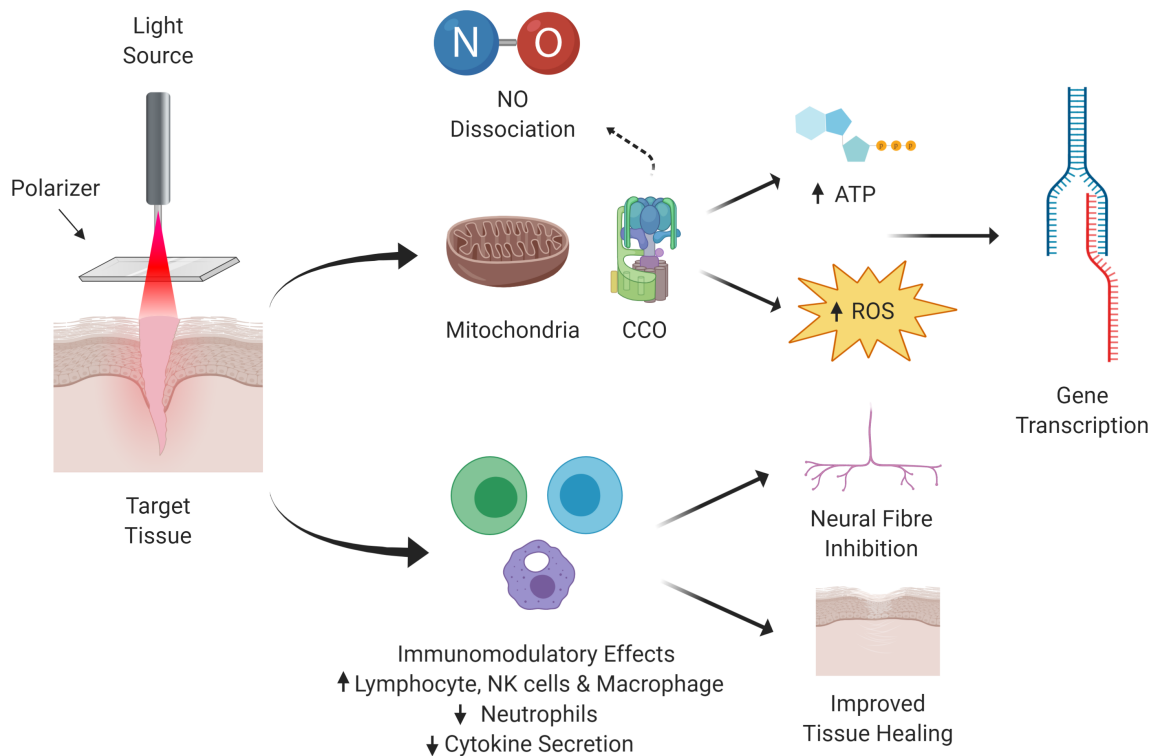
tissue, which is the precursor to light absorption. Scattering is described by the scattering coefficient ( $\mu_s$ ). To determine total light attenuation ( $\mu_t$ )—the reduction in the intensity of light due to absorption and scattering—the scattering coefficient is added to the absorption coefficient. Hence, total light attenuation is expressed as:

$$\mu_t = \mu_s + \mu_a.$$

Focussing on the components of light attenuation, an “optical window” model has been develop to explain the relatively high levels of light penetration of red and NIR light [12]. As wavelengths get closer to the blue end of the spectrum, light is absorbed and scattered more readily in biological tissue. Additionally, at wavelengths greater than 1150 nm, water starts to absorb a significant amount of light energy. PBMT, demonstrated mainly for wavelengths from 600 to 1000 nm, exploits this optical range by generating maximum light penetration and minimum light attenuation [14]. It is important to note that this optical window refers to in vivo applications, and may explain why otherwise wavelengths of light show positive effects in vitro, yet do not translate to human and animal studies. Considering polarisation in this context, it may represent a method of achieving improved light penetration in biological tissues within the 600 to 1000 nm range.

### 4 | PBMT MECHANISMS OF ACTION

As there is scant mechanistic evidence pertaining to PPBMT we will prelude this review by describing the current theoretical mechanisms of NPPBMT (Figure 2). At a cellular level, PBMT appears to interact principally with the mitochondria [32]. The functions of the mitochondria are well known and are being increasingly investigated as a source of pathology [33]. Within mammalian mitochondria, cytochrome c oxidase (CCO)—an enzyme of the mitochondrial respiratory chain, which assists in the transfer of electrons from CCO to molecular oxygen [34]—has been shown to absorb red and NIR light, which then affects its structure and/or function [35]. This molecular photoacceptor is known as a chromophore [36]. When red and NIR light interacts with the CCO chromophore it increases its available energy and thus, increases the mitochondrial ability to generate adenosine triphosphate (ATP) [14]. The precise mechanism of how PBMT affects CCO remains unknown, but the current prevailing theory is based on the interplay between, nitric oxide (NO), oxygen and CCO [12]. It has been shown that NO competes with oxygen to interact with CCO,



**FIGURE 2** Proposed mechanisms of PBMT diagram. PBMT, photobiomodulation therapy

resulting in lowered cellular respiration and decreased ATP production [37]. Polychromatic light has been demonstrated to acutely reverse the inhibition of CCO by NO [38]. Moreover, exogenous NO has been shown to directly inhibit the functional cellular effects of PBMT in vitro [39]. These processes inform this mechanistic theory of PBMT whereby red and NIR light causes the dissociation of NO from CCO at a mitochondrial level, resulting in a higher rate of cellular respiration and increased ATP production [40].

PBMT appears not only to affect mitochondrial function, it has also been shown to have an effect on cellular reactive oxygen species (ROS) [14]. ROS are molecules that are important in redox signalling, oxidative stress, cell signalling, enzyme activation, regulation of cell cycles, and protein synthesis [14, 41, 42]. During many cellular processes, a portion of the oxygen metabolised is converted to ROS. PBMT promotes the metabolism of oxygen, presumably through its effects on the mitochondria, which can lead to an increase ROS production [14]. This has been demonstrated in vitro with PBMT changing the redox potential of a cell toward greater oxidation [43] and increasing ROS generation within the cell [44]. ROS can also activate nuclear factor kappa B (NF- $\kappa$ B) [45]. NF- $\kappa$ B is a transcription factor that can activate a number of genes, including those coded for cytokine and chemokine release, cell adhesion, cell surface receptors,

anti-apoptosis and cellular proliferation [46, 47]. PBMT has been shown to increase NF- $\kappa$ B, presumably through the generation of ROS [45]. NF- $\kappa$ B is generally considered pro-inflammatory and PBMT anti-inflammatory. On face value this does not appear to be compatible, however, it is proposed that both ROS and NF- $\kappa$ B may play a role in the dose-response relationship in PBMT. In the right amount NF- $\kappa$ B can cause reduced apoptosis, and increased cell proliferation and migration—responses thought to be beneficial in tissue healing [48]. Overexposure though, causes an undesired increase in ROS and NF- $\kappa$ B, which could potentially cause the downturn in cellular function when tissue is overexposed to PBMT [48]. More generally ROS can cause the modulation of DNA transcription and thus, may activate genes that play stimulatory or protective roles within the cell [14, 42, 47]. These changes in gene expression have been demonstrated across multiple cell lines. For example, in vitro experiments on fibroblasts have shown that PBMT promotes upregulation of multiple genes involved in DNA repair (MPG), inflammation (LENG5), growth and proliferation (CDK5R1) and metabolism (CANX) [49–51]. Similar changes to key genes involved in adaptation and healing have also been shown in muscle and tendon tissue in vitro and in vivo [52–57]. PBMT is also thought to play a major role in regulating the immune system by modulating many key cells affecting the immune system.

Specifically, PBMT has been shown to alter M1-related cytokine and chemokine expression via mitochondrial biogenesis and histone modification [58] and to enhance proliferation of peripheral blood mononuclear cells [59]. Additionally, PBMT can cause increased macrophage proliferation and altered differentiation [60], an increase in CD45 lymphocytes and natural killer cells [61] and interestingly, a decrease in the number of neutrophils in areas of inflammation [62]. These immune changes are key mechanisms across other forms of phototherapy [4] and further, are fundamental in producing the pain suppressing effects of PBMT. PBMT is known to modulate multiple substances related to the inflammatory drivers of nociception, which include: Prostanoids (prostaglandins, leukotrienes, eicosanoids); Kinins; Serotonin; Histamine; Cytokines; Neuropeptides; ROS; and ATP [63]. Additionally, PBMT can decrease nociceptive input by inhibiting A and C neural fibres by decreasing axonal flow, thought to work in conjunction with the aforementioned molecular changes [64–66]. It is currently thought that PPBMT works via the same pathways as NPPBMT, however, these effects may be enhanced through polarization (Figure 2).

## 5 | PPBMT IN VITRO EXPERIMENTS

The effect of PPBMT has been evaluated in both connective tissue and immune cell lines with the aim of quantifying PPBMT's effect on tissue healing and the immune response. Collagen is the most abundant protein in mammals and plays a critical role in the wound healing process [67]. One study measured the effect of the polarization angle on NIH/NT3 fibroblasts. It specifically measured vascular endothelial growth factor (VEGF) secretion, differentiation to myofibroblasts and collagen organization after irradiation with a 800 nm polarized light. Cells were irradiated at a 0°, 45°, 90° and 135° polarization angle for 6 minutes daily, for 6 days. This was compared against both a population that was exposed to light polarized in all orientations and a non-irradiated control. The results demonstrated increased cell viability, VEGF secretion and myofibroblast differentiation in all irradiated groups and compared to the non-irradiated control. In addition, the degree of polarization influenced collagen organization. The 0° to 135° samples showed increased collagen alignment at 30° and 130°. This contrasts the “all degree” and control sample that demonstrated peaks at 110° and 180°. However, as there was no NPPBMT sample, this study could not demonstrate a clear advantage of PPBMT [68].

Further, the effects of PPBMT and NPPBMT on Wharton's jelly derived mesenchymal stem cells was assessed. Following a 24-hour incubation period, the cells were irradiated once for 2, 4 or 6 minutes. There was a NPPBMT, PPBMT and control (non-irradiated) group. Cells that were irradiated for 6 minutes showed significantly increased levels of proliferation from the control group, however no significant difference was observed between the PPBMT and NPPBMT group. Furthermore, it was clear that cell counts and colony formation were both significantly higher after PPBMT when cells were plated at higher confluency (500 cells, per 35 mm well). However, scratch wound assays showed no significant improvement in wound closure rates in any group [69]. A limitation of this study includes that only one round of irradiation was performed; other analogous studies have shown that multiple doses of PLLLLT tend to show better outcomes compared to NPPBMT [31, 70]. Nevertheless, this study does provide evidence of some small advantage of PPBMT over NPPBMT.

In addition, the effects of PPBMT on the immune system have been studied. A study found that linearly PPBMT and NPPBMT caused an immunosuppressive effect, in terms of cellular proliferation, on human lymphocytes when compared to a halogen irradiated control sample. In addition, the immunosuppressive effect of the linear PPBMT was found to be 20% greater than the NPPBMT sample [71]. A major limitation of this study was a lack of exact protocol reporting, making replication impossible.

Despite the previous experiments showing possible advantages of PPBMT over NPPBMT there are studies casting doubt on the increased efficacy of PPBMT over NPPBMT. One study investigated the effects of irradiating HeLa cells with linearly polarized red laser light (637 nm). The experiment contained four trial groups; three groups were irradiated with a 99.4%, 60.9% and 34.2% polarization coefficient respectively, while a non-irradiated group was used as a control. Despite the number of cells adhering to the glass surface (a measure of their biological activity) being significantly higher in the irradiated groups, there was no difference between the two experimental groups. This led to the conclusion that degree of polarization had no additional effects [72]. That said, the absence of comparison to a 0% polarization and the high exposure radiation intensity could have been confounding factors in the study.

## 6 | PPBMT ANIMAL MODELS

There have been a few studies showing positive effects of PPBMT on wound healing in animal models. One



experiment measured the effects of PPBMT on the healing of artificially induced wounds in mice. The mice were irradiated with either linear or perpendicular PPBMT (632.8 nm), with the angle of polarization being relative to their spinal cord. Each mouse had their own control wounds that were not irradiated. The results demonstrated that the irradiated wounds healed faster than the non-irradiated wounds and additionally, that parallel polarization caused faster and more complete healing compared to perpendicular [73]. The same research group used a similar methodology to assess collagen birefringence in skin repair in response to PPBMT (632.8 nm). The results demonstrated that the wounds irradiated with parallel PPBMT with respect to the rats spinal cord showed higher birefringence, indicative of a higher degree of collagen organisation and therefore wound healing, when compared to perpendicular polarization [74]. Researchers have also studied the differences in light-tissue interaction between healthy and healing rat skin. An experiment found that in the first 3 days of healing, the polarized laser lost significantly more intensity when passing through the healing tissue when compared to the non-irradiated, injured control as well as healthy tissue. The authors suggested that this effect was possibly due to the large number of inflammatory cells and debris in the healing tissue [75]. A similar methodology to assess collagen birefringence in healthy rat tendons. One Achilles tendon was irradiated with PPBMT and the other no exposed to light as a control. The PPBMT was orientated parallel relative to the tendon. It was found that the irradiated tendon exhibited enhanced collagen alignment relative to the control and the authors suggested that this effect may be applicable in the treatment of pathological tendons [76]. However, there was no comparison to non-parallel PPBMT or NPPBMT and therefore it is uncertain if the reported effects are due to the incident polarisation or PBMT more broadly.

The effects of PPBMT on healing of rabbit tissue was also noted. A comparison of parallel, perpendicular and 45-degree PPBMT relative to the wound against a non-irradiated controls was assessed. It was clear that, the fastest healing wounds were those irradiated with the parallel polarized light, followed by the perpendicular and 45 degree light respectively [70]. Despite positive results, as there were only four animals examined in this experiment, making the results less reliable - more wound models could have been used for a stronger result. PPBMT has also been shown to have an effect on the viscoelastic properties of soft tissues. A soft tissue sample was taken from the pleura of an animal and irradiated with PPBMT either perpendicular or parallel to the direction of tissue stretch. Tissue viscoelasticity was assessed via displacement sensor and stretch load cell before and

after radiation. The results showed that the sample irradiated parallel to the stretch direction exhibited the greatest increase in viscoelastic capacity. The authors hypothesized that this effect could be due to changes in collagen organisation, however no direct mechanistic evidence of this was reported, nor was the type of animal sample [77].

There has also been a combined *in vivo* and *in vitro* study conducted on wound healing in mice. Researchers took NIH3T3 fibroblast cells from wild mice and irradiated them with a 627 nm LED device at varied intensities. The experiment used five groups: an unlit control, a non-polarized light, and three types of polarized light: linearly polarized, right circularly polarized and left circularly polarized. *In vitro*, the linearly and right circularly polarized group demonstrated the greatest cellular proliferation. The authors suggested these changes were due to an increase in the irradiation absorbance value. The most efficacious intensity was reported to be between 2 and 8 J/cm<sup>2</sup>. *In vivo*, a full thickness skin defect of 20 mm in diameter was created in mice. These wounds were irradiated using the same protocols as the *in vitro* study. It was found that the linearly and right circularly polarized light demonstrated the best healing effect at 7 days post-injury. Additionally, the right circularly polarized light promoted significantly increased expression of the type 1 procollagen mRNA compared to the control. However, there was no significant difference in type 3 procollagen mRNA expression between groups [30]. Interestingly, the authors did note a small temperature change 0.1°C per/min. The authors were confident that this small change did not influence their results, however analysis of heat-shock proteins would have been pertinent here to support this claim.

The effects of PPBMT on spinal cord injuries (SCI) have also been noted. One protocol induced an artificial spinal cord contusion using a weight-drop device. Before the injury site was surgically repaired the contusion was irradiated with either parallel or perpendicular PPBMT relative to the spinal cord. These rats were compared to a control group that was injured but did not receive any irradiation. The spinal cord was re-exposed and irradiated for five consecutive days. The results demonstrated that both irradiated groups recovered faster from the injury, with the parallel polarization group demonstrating a significantly better functional evaluation compared to the perpendicular group. Both irradiated groups also demonstrated a significantly smaller cavity formation induced by the contusion compared to control and that parallel polarization caused an approximate 40% greater light transmission through the spinal cord, compared to perpendicular irradiation. Interestingly, they also showed that there were no significant differences

between irradiated and control groups in spinal cord ATP content. This contradicts the key proposed mechanism of PBMT in which it acts on mitochondrial synthesis of ATP, implicating other biological mechanisms at play generating a therapeutic effect. The authors hypothesized that the improved functional recovery of the parallel irradiation was due to more efficient tissue light propagation [31]. However, the light penetration was measured on a healthy rat spinal cord, limiting its application to SCI. Given that other research has found that light penetration through injured tissue is less than in healthy tissue [75], the findings would be more applicable if demonstrated on injured spinal cord tissue. All these studies demonstrate the plausible effects of PPBMT in animal wound healing but raise further questions about the underpinning mechanisms of PPBMT and the optimum dosage at different stages in healing processes.

## 7 | LIMITATIONS

While the research above paints a thought-provoking picture of the efficacy and mechanisms of PPBMT, there remain many key limitations and questions. Firstly, there are conflicting findings pertaining to the light-tissue interactions of polarized light. Human and animal tissue exhibits anisotropic mechanical behaviour, meaning that their mechanical properties can vary in a three-dimensional space throughout the body. This is thought to be mainly due to the variation of collagen fibres in tissues [78, 79]. A key limiting factor in the transmission of light through tissues is scattering, particularly in the dermis due to collagen fibre density and its three-dimensional structure [80]. One study found the orientation of polarization that causes the least light scattering in human skin is correlated to the alignment of collagen tissue, and may have significant implications for phototherapy [80]. Another study found that in denser biological tissues, linearly polarized light is maintained better than circularly polarized light [81]. Furthermore, it has been shown that the more superficial layers of the skin (epidermis, papillary dermis) allow penetration of polarized light with only a small amount of depolarization [82].

There is also conflicting evidence regarding the effects of PPBMT *in vitro*. One study found no change in cell function with PPBMT and have suggested that polarization does not change the efficacy of PBMT [72]. However, as this study used HeLa cells, which are not linearly cylindrical structured like collagen fibres or axons, a hypothesis might be that the morphology of a specific cell renders them susceptible to PPBMT. Polarized light penetration can also be affected by the anisotropic nature of

the skin and can be depolarized after about 1 mm [76]. However, evidence has shown that polarized light can penetrate healthy human skin to at least 1.2 mm with only marginal depolarization [83]. Furthermore, it has been demonstrated in animal nerve tissue that PPBMT applied perpendicular to the axis of the white matter tracts caused a significant increase in light penetration when opposed to perpendicular PPBMT [84]. In an attempt to model *in vivo* circulatory conditions one study looked at the amount of depolarization through animal tissue with and without fluid flow through the tissue. The results demonstrated that polarization was largely unaffected when passing through static tissue or, when the fluid flow was parallel to the polarization direction. Polarization was partially lost when flow was perpendicular to the polarization direction and when the rate of fluid movement was increased [85]. Considering all this, in conjunction with the known effects of PPBMT in animal models [31, 70] it seems plausible that polarized light aligned parallel to cylindrical, or linear biological microstructures such as myofibrils, axons or collagen fibres [79] may represent a more efficacious method to administer PBMT. With the advancement of 3D cell culture and 3D bioprinting, the potential advantages of PPBMT may be able to be quantified *in vitro*, representing a cost saving and ethical advantage over traditional animal research. However, more *in vitro* research is required to confirm this, and to reveal whether any advantages of PPBMT found *in vitro*, would persist *in vivo*.

Secondly, most of the experiments did not compare PPBMT to NPPBMT and further, did not use a light control outside the 600 to 1000 nm range, only a non-irradiation control. Therefore, it is impossible to confidently state whether the reported effects of PPBMT are significantly different from NPPBMT or even polychromatic, visible light sources. It is also unclear if the reported increases in efficacy are due to the increased penetration of PPBMT or if they are caused by the increase in relative irradiation intensity caused by the polarization effect. Thirdly, it remains unclear if the plane polarized light emitted by some helium-neon (he-ne) lasers is a factor to consider when interpreting the findings within this field [86]. Few, if any, PBMT research using he-ne lasers report their polarization state. Given that there is a potential biological difference caused by this effect, any future research using he-ne lasers, should report if they emit plane polarized light or not, and how that light is orientated to the target tissue. Finally, to our knowledge, there have been no human studies conducted that compare PPBMT and NPBMT, making clinical generalization of the relative efficacy impossible based on the current evidence.

## 8 | CONCLUSION

PBMT has been shown to be an efficacious system of phototherapy for treating varied common conditions that affect the population. Its proposed mechanisms are centred on increasing available ATP and changes in gene expression. The polarization of PBMT presents as an interesting variable to investigate further. Some evidence has shown when compared to NPPBMT, PPBMT can cause quicker and more organised wound healing and that it may be able to penetrate biological tissue more effectively when applied in a parallel orientation relative to the tissue being irradiated. However, more detailed mapping of cellular and molecular responses to the therapy is required to show a clear differentiation between PPBMT and NPPBMT, and other phototherapy modalities more broadly. Future research should be directed at ascertaining more detailed mechanistic evidence in vitro and in vivo, as well as comprehensively examining light-tissue interactions. Overall, PPBMT appears to be a promising advancement in phototherapy, though more research is needed to validate these claims to allow for its clinical utilization.

### ACKNOWLEDGMENTS

The authors were supported by the Immunology and Translational Research Group, within the Mechanisms and Interventions in Health and Disease Program, Institute Health and Sport, Victoria University, Australia. Nicholas Tripodi was supported by the Victoria University Postgraduate Scholarship and Jack Feehan by the University of Melbourne Postgraduate Scholarship.


### CONFLICT OF INTEREST

The authors declare no conflict of interest with this article.

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**How to cite this article:** Tripodi N, Feehan J, Husaric M, et al. Good, better, best? The effects of polarization on photobiomodulation therapy. *J. Biophotonics*. 2020;13:e201960230. <https://doi.org/10.1002/jbio.201960230>