



## The effect of photobiomodulation on chemotherapy-induced peripheral neuropathy: A randomized, sham-controlled clinical trial



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### ABSTRACT

**Background.** Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of cancer therapy with few efficacious treatments.

**Methods.** We enrolled 70 patients with CIPN in a randomized, double-blinded, sham-controlled, cross-over trial to determine if photobiomodulation (PBM) ± physiotherapy reduced the symptoms of neuropathy compared to sham treatment. At the conclusion of follow-up, sham-arm patients could cross-over into a third arm combining PBM and physiotherapy to determine if multimodal treatment had additive effects. Treatment included 30 minute sessions 3-times weekly for 6 weeks using either PBM or sham therapy. Neuropathy was assessed using the modified total neuropathy score (mTNS) at initiation and 4, 8, and 16 weeks after initiating treatment.

**Results.** Sham-treated patients experienced no significant change in mTNS scores at any point during the primary analysis. PBM patients experienced significant reduction in mTNS scores at all time points. Mean changes in mTNS score (and corresponding percent drop from baseline) for sham and PBM-group patients respectively were  $-0.1$  ( $-0.7\%$ ) and  $-4.2$  ( $-32.4\%$ ) at 4 weeks ( $p < 0.001$ ),  $0.2$  ( $0.0\%$ ) and  $-6.8$  ( $-52.6\%$ ) at 8 weeks ( $p < 0.001$ ), and  $0.0$  ( $0.1\%$ ) and  $-5.0$  ( $-38.8\%$ ) at 16 weeks ( $p < 0.001$ ). Patients who crossed over into the PBM/PT-group experienced similar results to those treated primarily; changes in mTNS score from baseline were  $-5.5$  ( $-40.6\%$ ) 4 weeks ( $p < 0.001$ ),  $-6.9$  ( $-50.9\%$ ) at 8 weeks ( $p < 0.001$ ), and  $-4.9$  ( $-35.9\%$ ) at 16 weeks ( $p < 0.001$ ). The addition of physiotherapy did not improve outcomes over PBM alone.

**Conclusion and relevance.** Among patients with CIPN, PBM produced significant reduction in neuropathy symptoms.

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### 1. Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a common side-effect of many modern chemotherapeutic agents. It typically manifests as numbness, paresthesia, pain, and/or burning, though motor dysfunction (typically weakness) and/or autonomic dysfunction can also occur [1,2]. The reported prevalence of CIPN following neurotoxic chemotherapy is 20–51%, but estimates vary considerably depending on the agents assessed, the severity threshold, and mechanism of detection; but because sensory symptoms are not overt, underreporting of both the prevalence and magnitude of CIPN is likely [3,4].

Once present, regression of CIPN symptoms is slow. Lingering or permanent symptoms are common and can significantly impair quality of

life [5,6]. Unfortunately, multiple trials focusing on mitigation of lingering symptoms, especially pain, have been disappointing, with a 2009 National Comprehensive Cancer Network Taskforce unable to recommend any directed therapy [7,8]. Since then, Smith and colleagues have reported the only positive, large, placebo-controlled trial examining pharmacologic treatment for CIPN, observing modest symptom-improvement in platinum-treated patients with painful CIPN who were treated for 5 weeks with duloxetine, a serotonin and norepinephrine re-uptake inhibitor [9].

Increasing study of non-pharmacologic therapies has revealed multiple strategies with potential efficacy in reducing the burden of CIPN [10,11]. Photobiomodulation (PBM) employs non-ionizing, low power, laser light therapy and has been shown in pre-clinical and small trials to improve neural function. In animal models PBM demonstrates alleviation of oxaliplatin-induced mechanical and cold allodynia as well as both nerve regeneration and improved motor recovery after nerve crush injury [12,13]. In humans, two small, sham-controlled studies

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