



# Evaluating the efficacy of photobiomodulation therapy in the management of chemotherapy-induced peripheral neuropathy: a pilot trial (NEUROLIGHT trial)

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## Abstract

Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of chemotherapy that hinders the patient's health-related quality of life (HRQL). Managing CIPN often requires a chemotherapy dose reduction or premature cessation of treatment. Photobiomodulation (PBM) therapy uses visible or (near)-infrared light to target tissue and stimulate cell repair processes. This trial aimed to evaluate PBM's efficacy in managing CIPN. A randomised, controlled trial was performed with sixty cancer patients with CIPN at Jessa Hospital (Belgium). Patients underwent six PBM sessions with a fluence of 6 J/cm<sup>2</sup> (PBM-1, n=28) or 8 J/cm<sup>2</sup> (PBM-2, n=32). The modified Total Neuropathy Score (mTNS) and Six-Minute Walk Test (6MWT) were performed to assess the CIPN severity and mobility. Questionnaires (Numeric Rating Scale, NRS; Functional Assessment of Cancer Therapy/Gynecologic Oncology Group Neurotoxicity, FACT/GOG-NTX) were administered to evaluate the pain, satisfaction, and HRQL. The trial was registered at clinicaltrials.gov on the 6th of January 2022 (NCT05199389). The mTNS and 6MWT improved significantly over time (P=0.048 and P<0.001, respectively). No significant differences could be detected for the FACT/GOG-NTX total score, nor its neurotoxicity subscale. The pain scores improved over time (P<0.001), with better scores in the PBM-1 group (P=0.034). The NEUROLIGHT trial revealed a significant improvement in CIPN symptoms and mobility. PBM applied with a fluence of 6 J/cm<sup>2</sup> could be more capable of soothing the pain caused by CIPN. No improvements could be detected in HRQL. Future research is necessary to support these findings.

**Keywords** Chemotherapy-induced Peripheral Neuropathy · Photobiomodulation · Supportive Cancer Care · Health-related Quality of Life

## Abbreviations

ASCO	American Society of Clinical Oncology
BMI	Body Mass Index
CIPN	Chemotherapy-Induced Peripheral Neuropathy
ESMO	European Society of Medical Oncology
FACT/GOG-NTX	Functional Assessment of Cancer Therapy/Gynecologic Oncology Group Neurotoxicity
HRQL	Health-Related Quality of Life
mTNS	Modified Total Neuropathy Score
NRS	Numeric Rating Scale
PBM	Photobiomodulation

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SSRI	Selective Serotonin Reuptake Inhibitor
WALT	World Association for Photobiomodulation Therapy

## Introduction

With a global incidence of approximately 20 million new cases in 2022, cancer ranks among the most common diseases of the 21st century [1]. Major healthcare reforms and technological advances have enabled earlier diagnosis and more effective, personalised treatment, significantly improving cancer survival rates across high-income countries [2, 3]. Even with more recent targeted medicines, chemotherapy remains a mainstay cancer treatment due to its efficiency in eliminating rapidly dividing cells [4]. Unfortunately, chemotherapy can result in short- and long-term adverse effects, as it also targets healthy cells with constant cellular renewal [4]. Chemotherapy-induced peripheral neuropathy (CIPN) is a common and challenging complication of several chemotherapy regimens, including taxanes, platinum agents, and vinca alkaloids [3, 5, 6]. Patients diagnosed with CIPN typically experience paraesthesia, pain, disturbed sensation, and muscle weakness and may display significant functional decline and a diminished health-related quality of life (HRQL) [3, 6, 7]. According to a meta-analysis including 31 studies, the overall incidence of CIPN is the highest within the first month after chemotherapy (68.1%) and decreases over time (60.0% at three months and 30.0% at six months or later). However, since the lack of uniformity in CIPN assessment methods makes it difficult to make between-study comparisons, the numbers are likely to be even greater than those reported [8]. Moreover, the incidence, symptoms and severity of CIPN can vary considerably based on the type of antineoplastic drug, dose, duration of exposure, and scheduling [9].

Unfortunately, therapeutic options for patients suffering from CIPN are limited [9]. The American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO) clinical guidelines discuss both pharmacological and nonpharmacological options, with varying grades of recommendation [9, 10]. To date, duloxetine, a selective serotonin reuptake inhibitor (SSRI), remains the sole treatment recommended for the painful symptoms of CIPN [9, 10]. Nonetheless, the effects of SSRIs (and other drugs such as anticonvulsants, tricyclic antidepressants, and opioids) are rarely beneficial and often induce other hampering side effects [9–12]. As a result, a reduction of the chemotherapy dosage or

withdrawal of chemotherapy is often necessary to manage the severity of CIPN, which could affect the treatment outcome [9–12].

Photobiomodulation (PBM) therapy is a noninvasive form of phototherapy that uses visible and/or near-infrared light to trigger a cascade of intracellular reactions. PBM can stimulate proliferation and reduce pain and inflammation [13]. Preliminary research suggests that PBM results in improved restoration of damaged synapses, synaptogenesis, and accelerated axonal regeneration [14–16]. Recently, a randomised, placebo-controlled trial with 32 breast cancer patients, focusing on preventing CIPN, was performed in which PBM was applied twice a week during taxane treatment. This pilot trial showed promising results for the use of PBM in preventing CIPN [17]. Nevertheless, more research is necessary to investigate the curative effect of PBM on CIPN and to further optimise PBM parameters, such as the treatment frequency and dosage.

The current trial aimed to evaluate the efficacy of PBM in a curative setting in cancer patients with different aetiologies who were diagnosed with CIPN. Second, the effect on the patient's HRQL was assessed while the PBM dosage was optimised.

## Materials and methods

### Study design

A randomised, single-blinded, controlled pilot trial (NEUROLIGHT trial), which evaluated the effectiveness of PBM for the management of CIPN, was conducted at Jessa Hospital (Hasselt, Belgium) from February 2022 to November 2023. Patients were divided into two groups based on the fluence applied during PBM treatment: PBM-1, receiving PBM treatment with an energy density of 6 J/cm<sup>2</sup>, or PBM-2, receiving PBM treatment with 8 J/cm<sup>2</sup>. The ethics committees of Jessa Hospital and the University of Hasselt both approved the study (B2432021000036), the study was registered at ClinicalTrials.gov (NCT05199389), and the study was conducted in accordance with the Declaration of Helsinki.

### Participants

Patients were eligible for inclusion if they were diagnosed with CIPN by their physician, aged 18 years or above, and had a Fitzpatrick skin type between I and V. Patients had to be treated with paclitaxel, docetaxel, oxaliplatin, cisplatin, thalidomide, bortezomib or vincristine and received their last administration at least two weeks prior to inclusion.

The exclusion criteria were an interruption of more than two consecutive PBM treatments and CIPN symptoms prior to receiving chemotherapy. Stable doses of medication prescribed for peripheral neuropathy (e.g., pregabalin, duloxetine) were allowed as long as the dosage remained constant during the study period. Patients were recruited at the oncology department of the Jessa Hospital (Hasselt, Belgium), and written informed consent was obtained before the start of the study.

## Randomisation

Eligible patients were randomised by a research assistant (1:1) into the PBM-1 (6 J/cm<sup>2</sup>) or PBM-2 (8 J/cm<sup>2</sup>) group. Randomisation was performed using the Castor<sup>®</sup> data management software's variable block randomisation model with possible block sizes of 4, 6, or 8. Patients were blinded to the allocated intervention group.

## Intervention

Patients in both groups received PBM twice a week for three weeks. A trained operator provided PBM using the class IV MLS<sup>®</sup> M6 laser (ASA Srl, Vicenza, Italy). This device combines two laser diodes of two different wavelengths (905 and 808 nm), peak power (25 W and 1.1 W), and emission mode (pulsed and continuous). The two laser beams work simultaneously and synchronously with coincident propagation axes with a power density of 0.168 W/cm<sup>2</sup>. A fluence of 6 J/cm<sup>2</sup> or 8 J/cm<sup>2</sup> was used for the PBM-1 and PBM-2 groups, respectively. Patients were treated bilaterally at the plantar surface of the hands and feet with a beam spot of 150 cm<sup>2</sup>. More specific PBM parameters can be found in Supplementary Table 1. All patients wore safety glasses during treatment to prevent eye damage.

## Outcome measures

Data were collected at baseline, after six PBM sessions, three weeks, six months, and one year post-PBM.

### Neuropathy severity

The validated modified Total Neuropathy Score (mTNS) was defined as the primary endpoint to establish whether the patient's symptoms associated with CIPN improved. The mTNS assesses six domains of peripheral neuropathy: sensory and motor symptoms, pin sensibility, quantitative vibration thresholds, strength, and deep tendon reflexes. Scores range from 0 to 24, with higher scores indicating a more severe grade of neuropathy [18]. The mTNS was

scored separately for the upper and lower limbs, after which a mean score was calculated.

### Mobility

In addition, the patient's mobility was investigated by performing the six-Minute Walk Test (6MWT). The 6MWT measures the distance an individual can walk over six minutes on a hard, flat surface and is adjusted for sex, age, and BMI [19]. Due to space limitations, the 6MWT was executed over a 10-meter course. The basic reference equations for the 6MWT over a 10-meter course, developed by Beekman et al., were applied [20].

### Quality of life

The validated Functional Assessment of Cancer Therapy/Gynecologic Oncology Group Neurotoxicity (FACT/GOG-NTX) questionnaire was used to assess the patient's HRQL [21]. Questions from the different subscales (physical well-being, social/family well-being, emotional well-being, functional well-being, and neurotoxicity) were rated on a 5-point Likert scale. A higher total score (0–160) indicates a better HRQL, and a higher neurotoxicity score (0–52) represents less severe neurotoxic symptoms. A license was obtained to permit the use of this questionnaire.

### Pain

A Numeric Rating Scale (NRS) ranging from 0 (no pain) to 10 (worst pain imaginable) was used to assess the patient's pain level due to CIPN.

### Patient satisfaction

Patients scored their overall satisfaction regarding the PBM treatment and their willingness to recommend the products to others using an NRS ranging from 0 (not satisfied/willing to recommend) to 10 (extremely satisfied/highly recommended).

### Patient data

Patient's personal, disease- and treatment-related characteristics were collected via patient questionnaires and the patient's medical records.

### Statistical analysis

R: A Language and Environment for Statistical Computing (R Core Team (2023), R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses.

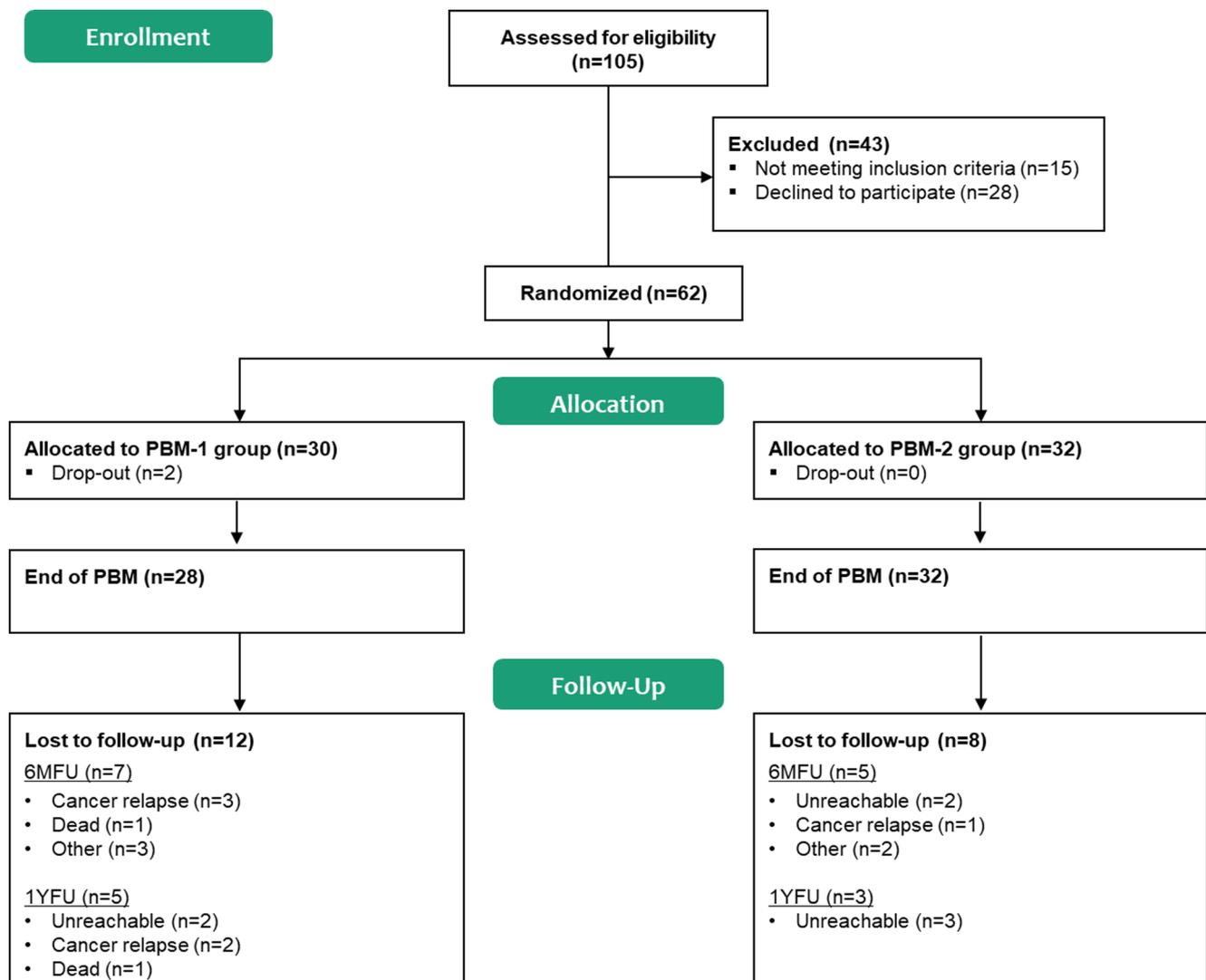
The Shapiro-Wilk test was used to test the normality of the data. Continuous data are displayed as mean  $\pm$  standard deviation or median (25th – 75th percentile). Differences in patient- and therapy-related characteristics between both groups were analysed using chi-square tests, Fisher's exact tests, or unpaired t-tests, as appropriate. A linear mixed model was used to determine differences in outcome over time, compared between the two groups, and between the two groups over time. The significance level was set assuming a significance level of 5% ( $P < 0.050$ , two-tailed).

### Role of the funding source

The funder of the study only funded the PhD project and had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

A total of 105 patients diagnosed with CIPN were assessed for eligibility between February 3<sup>rd</sup>, 2022 and October 20<sup>th</sup>, 2022. Among these patients, 59% were deemed eligible and agreed to participate in the trial. Thirty patients were randomised to the PBM-1 group and thirty-two patients to the PBM-2 group. Twelve patients were lost to follow-up in the PBM-1 group and eight in the PBM-2 group (Fig. 1). There were no significant differences regarding the demographic, disease- and treatment-related data between the two groups, except for BMI (Table 1). Compared with the PBM-1 group, the PBM-2 group had a significantly greater BMI ( $26.69 \pm 3.95$  and  $24.41 \pm 3.77$ , respectively;  $P = 0.026$ ). The study population was predominantly female, with a mean age of  $63.79 \pm 11.45$  years in the PBM-1 group and  $60.97 \pm 11.84$  years in the PBM-2 group. The most



**Fig. 1** Consort flowchart. PBM: Photobiomodulation; 6MFU: Six-month follow-up; 1YFU: One-year follow-up

**Table 1** Patient-, disease- and treatment-related characteristics

Characteristics	PBM-1 (n = 28)		PBM-2 (n = 32)		P <sup>a</sup>
	Mean ± SD		Mean ± SD		
Age (years)	63.79 ± 11.45		60.97 ± 11.84		0.353
BMI (kg/m <sup>3</sup> )	24.41 ± 3.77		26.69 ± 3.95		0.026
mTNS score at baseline*	9.67 ± 2.73		9.92 ± 2.74		0.752
	n	%	n	%	P <sup>b</sup>
Sex					0.232
Female	19	67.86	26	81.25	
Male	9	32.14	6	18.75	
Smoking					0.224
Current	2	7.14	2	6.25	
Former	11	39.29	6	18.75	
Never	15	53.57	24	75.00	
Alcohol consumption					0.827
Never or < 1 unit a week	13	46.43	13	40.63	
1-3 units a week	10	35.71	14	43.75	
4-10 units a week	4	14.29	5	15.63	
10-20 units a week	1	3.57	0	0.00	
Exercise frequency					0.950
Never	3	10.71	4	12.50	
Once a week	5	17.86	7	21.88	
2-3 times a week	11	39.29	14	43.75	
3-4 times a week	5	17.86	4	12.50	
≥ 5 times a week	4	14.29	3	9.38	
Tumor location					0.230
Breast	14	50.00	19	59.38	
Head- and neck	1	3.57	1	3.13	
Prostate	1	3.57	0	0.00	
Colorectal	4	14.29	3	9.38	
Ovarian	1	3.57	1	3.13	
Endometrial	0	0.00	2	6.25	
Bladder	0	0.00	1	3.13	
Lung	0	0.00	1	3.13	
Other	7	25.00	4	12.50	
T-stage					0.405
x	1	7.14	2	6.25	
1	3	10.71	7	21.88	
2	14	50.00	15	46.88	
3	8	25.00	8	25.00	
4	2	7.14	0	0.00	
N-stage					0.139
x	1	7.14	2	6.25	
0	6	21.43	15	46.88	
1	14	50.00	9	28.13	
2	6	21.43	5	15.63	
3	1	0.00	1	3.13	
M-stage					1.00
x	4	14.29	4	12.50	
0	16	57.14	19	59.38	
1	8	28.57	9	28.13	
Type of chemotherapy <sup>†</sup>					
Paclitaxel	13	46.43	22	68.75	0.080
Docetaxel	3	10.71	0	0.00	0.096
Oxaliplatin	11	39.29	6	18.75	0.078
Cisplatin	0	0.00	3	9.38	0.241
Carboplatin	5	17.86	6	21.88	0.756

**Table 1** (continued)

Characteristics	PBM-1 (n = 28)		PBM-2 (n = 32)		
Last chemotherapy session					0.448
< 1 year	15	57.14	14	43.75	
≥ 1 year	13	42.86	18	56.25	
	n	%	n	%	p <sup>b</sup>
Type of CIPN medication <sup>†</sup>					0.258
Duloxetine	5	17.86	6	21.88	
Pregabalin	6	21.43	13	40.63	
Gabapentin	0	0.00	1	3.13	
None	17	60.71	17	53.13	

\*The mTNS score was scored for the upper and lower limbs, after which a mean was calculated

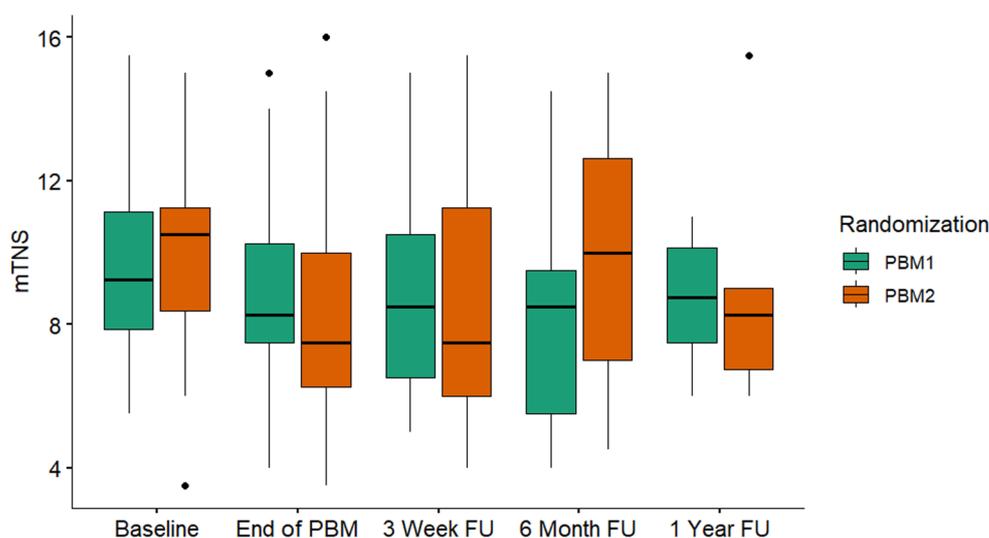
†The percentages may not add up to 100% due to combinations of treatments

<sup>a</sup>unpaired t-test (two-tailed)

<sup>b</sup>Chi-square tests (two-tailed) or Fisher's exact tests, as appropriate

*BMI* Body Mass Index, *CIPN* Chemotherapy-induced peripheral neuropathy, *mTNS* Modified Total Neuropathy Score, *PBM* Photobiomodulation, *SD* Standard Deviation

**Fig. 2** Neuropathy severity based on the modified total neuropathy score. The mTNS was scored separately for the upper and lower limbs, after which a mean score was calculated. A higher score indicates a more severe grade of peripheral neuropathy. Outliers are displayed as dots. Linear mixed models revealed a significant decrease over time ( $P=0.048$ ). mTNS: modified Total Neuropathy Score; PBM: photobiomodulation; FU: Follow-up



commonly observed diagnosis was breast cancer, for which patients received mainly paclitaxel.

Linear mixed models revealed a significant difference over time ( $P=0.048$ ) but not between the groups ( $P=0.970$ ) or between the groups over time ( $P=0.910$ ). In the PBM-1 group, the mTNS score ranged from 9.25 (7.88–11.13) at baseline to 8.50 (6.50–10.50) at the end of PBM and 8.75 (7.50–10.12) at the one-year follow-up. A similar evolution was detected in the PBM-2 group, where the mTNS score ranged from 10.50 (8.38–11.25) at baseline to 7.50 (6.00–11.25) at the final PBM session and 8.25 (6.75–9.00) at the one-year follow-up (Fig. 2).

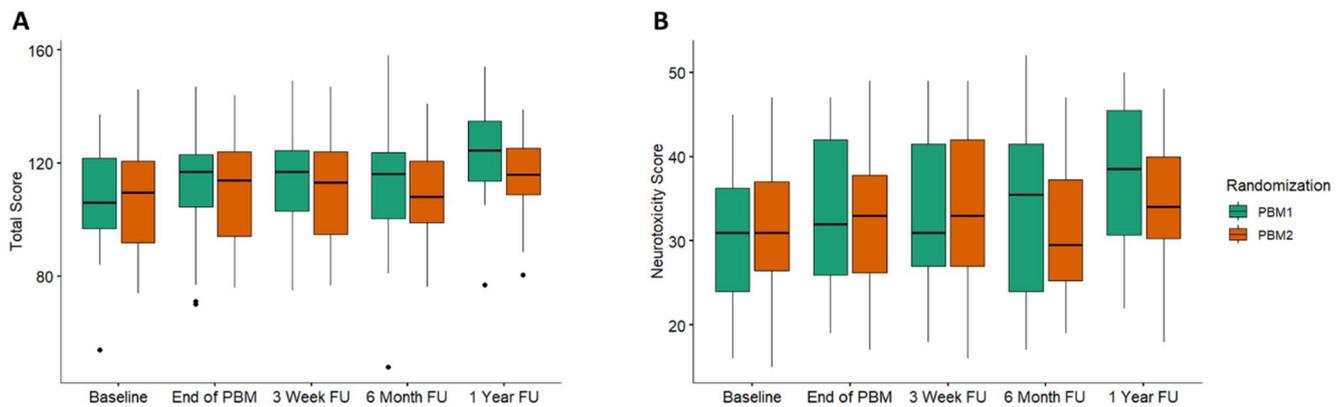
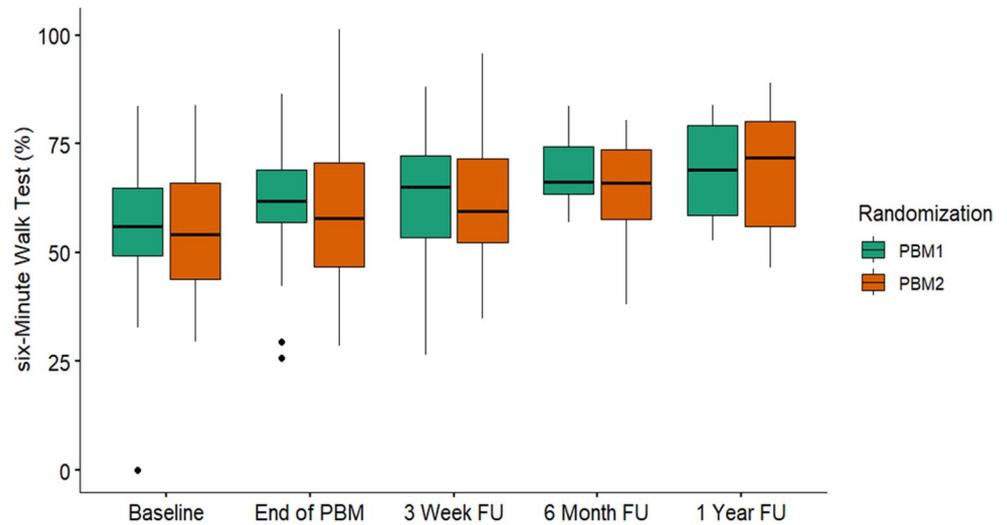
The 6MWT improved significantly over time in both groups, as shown by the linear mixed models' significant time effect ( $P<0.001$ ). No significant differences were detected between the groups ( $P=0.546$ ) or between the groups over time ( $P=0.634$ ). An increase of 13.13% was detected in the PBM-1 group (55.95 (49.25–64.95) at

baseline to 69.08 (58.52–79.31) at the one-year follow-up). The PBM-2 group, on the other hand, showed a 17.62% improvement in mobility (54.19 (43.83–66.12) at baseline compared to 71.81 (56.12–80.11) at the one-year follow-up, Fig. 3).

Linear mixed models did not show any significant time, group or group-by-time effects for the FACT/GOG-NTX total score ( $P=0.095$ ,  $P=0.864$ , and  $P=0.559$ , respectively) or neurotoxicity subscale ( $P=0.268$ ,  $P=0.816$ , and  $P=0.652$ , respectively, Fig. 4).

The pain scores given by the patients differed significantly over time and between the two groups, as indicated by the significant time effect ( $P<0.001$ ) and group effect ( $P=0.034$ ). The group-by-time effect was borderline significant ( $P=0.050$ ). Figure 5 shows that the pain scores of the PBM-1 group decreased over time from 5.00 (3.00–7.00) at baseline to 3.00 (2.00–5.00) at the last PBM session, and 2.00 (0.75–3.25) at the one-year follow-up, whereas those

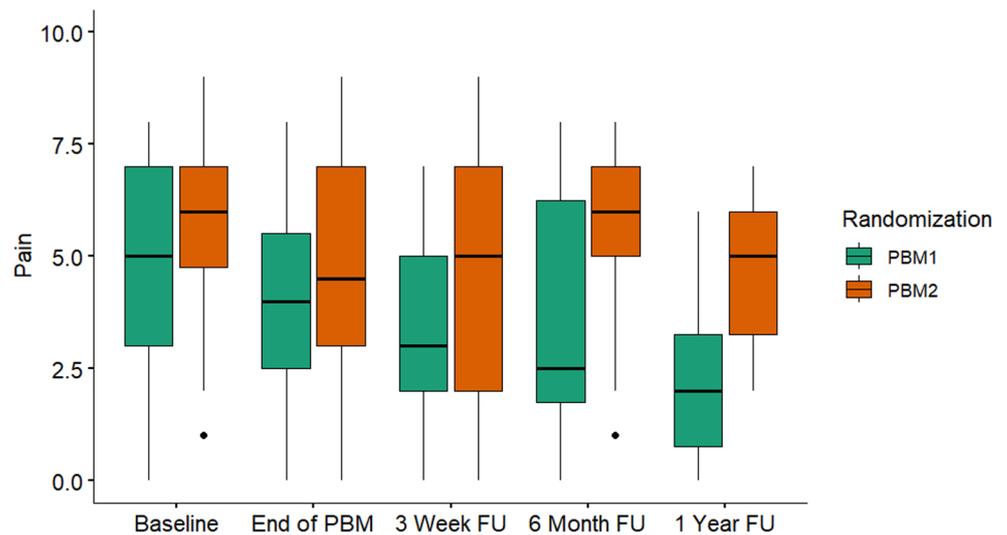
**Fig. 3** Mobility based on the six-minute walk test. Percentages are calculated using reference standards based on the patient's sex, BMI, and age, wherein a higher score indicates better mobility. Outliers are displayed as dots. Linear mixed models revealed a significant time effect ( $P < 0.001$ ). PBM: Photobiomodulation; FU: Follow-up



**Fig. 4** Quality of life based on the FACT/GOG-NTX total score (A) and neurotoxicity subscale (B). A higher score represents a better quality of life and less severe neurotoxicity symptoms. Outliers are displayed as dots.

FACT/GOG-NTX: Functional Assessment of Cancer Therapy/Gynaecologic Oncology Group – Neurotoxicity; PBM: Photobiomodulation; FU: Follow-up

**Fig. 5** Pain scored on the numeric rating scale. A higher score indicates a higher level of pain. Outliers are displayed as dots. Linear mixed models revealed a significant time effect ( $P < 0.001$ ) and group effect ( $P = 0.034$ ). PBM: Photobiomodulation; FU: Follow-up



of the PBM-2 remained relatively constant (6.00 (4.75–7.00), 5.00 (2.00–9.00) and 5.00 (3.25–6.00), respectively).

The satisfaction grade regarding the PBM treatment differed significantly over time ( $P=0.003$ ), but no significant differences were detected between the groups ( $P=0.595$ ) or between the groups over time ( $P=0.907$ ). The PBM-1 group scored their highest level of satisfaction at the end of PBM (7.00 (5.00–8.00)), whereas PBM-2 scored their highest level of satisfaction at the three-week follow-up (7.00 (4.00–9.00)). The analysis of the recommendation grade did not yield any significance ( $P_s>0.141$ ). Finally, patients did not report any adverse events during their PBM treatment or during their follow-up period.

## Discussion

The results of the current NEUROLIGHT trial suggest that PBM could reduce CIPN severity and associated pain while improving the patient's mobility. The number of long-term cancer survivors is expected to increase in the following decades due to the increasing age of the population and advancements in cancer diagnosis and treatment [22, 23]. As a result, more patients could be diagnosed with CIPN in the future [23]. Consequently, developing effective strategies to prevent or manage CIPN is essential (16, 17).

Patients who underwent PBM presented a significant decrease in the mTNS score and, therefore, improvement in CIPN severity regardless of the applied fluence. These results align with previous research investigating the use of PBM for the management of CIPN [17]. In a randomised controlled trial by Argenta et al. (2017), cancer patients diagnosed with CIPN post-chemotherapy received thrice weekly PBM sessions for six weeks (class IV K-laser, 800–970 nm, and 6.75–12 W). Patients treated with PBM ( $n=30$ ) demonstrated a significant decrease in mTNS of 52.6% ( $P<0.001$ ), whereas there was no evidence of improvement in the control group ( $n=40$ ). Thirty-eight patients in the control group crossed over to receive PBM and experienced a significant decrease in mTNS of 50.9% ( $P<0.001$ ) [24]. Moreover, Hsieh et al. (2016) performed a prospective cohort study with 17 gastrointestinal cancer patients treated with oxaliplatin-based chemotherapies. PBM (GaAlAs diode laser, 780 nm, 80 mW, and 48 J/cm<sup>2</sup>) was applied thrice weekly for four weeks. They reported improved CIPN symptoms using the Pain Quality Assessment Scale, Chemotherapy-Induced Neurotoxicity Questionnaire, Oxaliplatin-Specific Neurotoxicity Scale, touch-detection threshold, and cold-triggered pain withdrawal latency [25].

Moreover, our patients' mobility improved significantly over time, as reflected by the increase in the 6MWT percentage ( $P<0.001$ ). Studies have shown that CIPN severity

is associated with gait, balance, and mobility deficits and that the 6MWT is suitable for evaluating mobility impairments due to CIPN [6, 26]. However, several other factors can influence the results of the 6MWT. For example, some patients included in the NEUROLIGHT trial simultaneously underwent radiotherapy treatment or recently finished it. A meta-analysis by Li C.L. et al. (2024) indicated that patients experience radiotherapy-induced fatigue over three months post-treatment [27].

No significant improvement was detected in the HRQL, as measured by the FACT/GOG-NTX total score or its neurotoxicity subscale. CIPN symptoms and the resulting decreased mobility interfere with a patient's HRQL, daily functioning, socialisation, and psychological distress [3, 6, 7, 28]. However, in our trial, the improvements observed in the mTNS and 6MWT were not associated with improvements in HRQL. Similar results were detected in a phase II, sham-controlled clinical trial performed by Teng C. et al. (2022). Patients suffering from CIPN at least three months post-chemotherapy were included, and PBM was applied to 26 nerve points (Acupak CL Mini Laser, Class II, 658 nm, 8 mW, and 1–2 J/point). Although patients reported sustained CIPN improvement, their HRQL scores remained stable [29].

The pain scores decreased significantly over time and differed between the two groups. Although both groups showed a decrease in pain, lower pain scores were detected in the PBM-1 group. The borderline group-by-time effect also suggested that PBM applied with a fluence of 6 J/cm<sup>2</sup> could be more capable of soothing the pain accompanied by CIPN. However, the considerable spread of data, depicting the duality of CIPN symptoms, should be considered. Research shows that 77% of CIPN patients report severe numbness and tingling, whereas only 33% report shooting or burning pain [30]. Additionally, patients suffering from painful CIPN reported worse HRQL scores in comparison to patients experiencing nonpainful CIPN [30, 31]. This division highlights the need to distinguish nonpainful and painful CIPNs in further research to optimise management options.

Compared with the PBM-1 group, the PBM-2 group had a significantly greater BMI ( $26.69\pm 3.95$  and  $24.41\pm 3.77$ , respectively,  $P=0.03$ ). The literature shows that overweight patients ( $BMI>25$  kg/m<sup>2</sup>) are impacted more by CIPN than patients within the normal BMI range are [32]. Nevertheless, although BMI is commonly used to measure obesity, it is not the most reliable indicator of adiposity [32, 33]. Research suggests that body fat distribution is the key indicator of obesity risk and can be assessed via simple measurements (e.g., waist circumference or waist-hip ratio) or scans (e.g., dual X-ray absorptiometry) [32, 34]. This possible confounder should be taken into account in future trials.

No definitive conclusions can be drawn regarding the optimal PBM fluence for the management of CIPN, as only the pain score differed significantly between the two groups. Unfortunately, limited research is available on the optimal PBM dose for managing CIPN. A comprehensive position paper by The World Association for Photobiomodulation Therapy (WALT) on potential therapeutic applications of PBM within supportive cancer care concluded that no clinical treatment guidelines could be provided due to inadequate data [35]. Based on the existing research, they recommend treatment with a wavelength of 780–970 and a fluence of 7.5–48 J/cm<sup>2</sup>. However, they stress the need for well-designed, multicentric clinical trials to validate and further optimise these recommendations [35].

The NEUROLIGHT trial was not without limitations. First, the small sample size did not allow the conduction of correlation analysis regarding the type of chemotherapy received (e.g. taxanes vs. platinum agents), the number of cycles administered, the time since cessation of chemotherapy (<1 year or >1 year), the previous lines of CIPN-inducing chemotherapies received, nor neuropathy-inducing comorbidities (e.g. diabetes). These factors could be important as not all chemotherapy regimens have the same likelihood of inducing CIPN, there could be a cumulative dose effect, and the accompanying symptoms tend to improve spontaneously shortly after the completion of the patient's chemotherapy [36, 37]. Furthermore, no control group was included in this trial, and a placebo effect could partly explain the beneficial results observed during this trial. Finally, the impact of potential concurrent therapies with pharmacological agents such as duloxetine and pregabalin was not assessed. On the other hand, The NEUROLIGHT trial has multiple strengths, including well-defined PBM parameters, an optimisation of the dose intensity, a good balance of patient-, medical and treatment-related factors suggesting that the randomisation was effective, the use of validated grading tools and questionnaires, and a one-year follow-up.

There is a clear need for future sham-controlled clinical trials with larger sample sizes to fully optimise the PBM parameters. Moreover, the different types of CIPN (acute vs. chronic and painful vs. nonpainful) should be differentiated to enable personalised treatment.

## Conclusion

The NEUROLIGHT trial revealed a significant improvement in CIPN symptoms and mobility, regardless of the applied fluence. Additionally, the results suggest that PBM applied with a fluence of 6 J/cm<sup>2</sup> could be more capable of soothing the pain caused by CIPN. No significant improvements in

HRQL were detected. More research is necessary to support these findings and validate the use of PBM in the management of CIPN.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s10103-026-04852-1>.

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**Author contributions** All authors have contributed significantly to this article and agree to its publication in this final form. Conceptualisation: M.C., J.L., J.R., J.M.; Methodology: M.C., L.J., J.R., J.M.; Project administration: M.C., J.L., J.R., J.M.; Formal analysis: M.C.; Visualisation: M.C.; Investigation: M.C., J.L., J.R., S.H., P.P., J.M.; Writing – original draft: M.C., J.L.; Writing – review and editing: M.C., J.L., J.R., S.H., P.P., J.M.; Funding acquisition: M.C., J.L., J.R., J.M.; Supervision: J.M.

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**Data availability** Data can be made available upon reasonable request.

## Declarations

**Informed consent** Was obtained from all individual participants included in the study.

**Competing interests** The authors declare no competing interests.

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