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Effects of photobiomodualtion therapy on breast cancer-related lymphoedema: A systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Objective: Lymphoedema characterised by the persistent accumulation of the interstitial fluid in peripheral tissues post breast cancer treatments. Photobiomodualtion therapy (PBMT) is widely used as supportive care in patients with breast cancer or breast cancer-related lymphoedema (BCRL). This systematic review and meta-analysis analysed the effectiveness and safety of PBMT for the treatment of BCRL.

Method: PubMed, EMBASE, PEDro, SCOPUS, CINAHL, and Cochrane Central Register of Controlled Trials were searched for RCTs on PBMT published before July 2019. Randomised controlled trials (RCTs) that evaluated the efficacy of PBMT on BCRL were included. The primary outcome was the arm circumference or volume, and secondary outcomes were grip strength and pain scores. This study is registered with PROSPERO (number CRD 42018102107).

Results: We reviewed nine RCTs that included 316 patients and six studies for mata-analysis. We found no significant difference in the reduction of the arm circumference or arm volume after treatment, one month, and three month follow-up between the PBMT and control groups. Studies revealed no significant differences in the reduction in grip strength and pain scores at 0, 1, 2, and 3 month between the PBMT and control groups.

Conclusions: Although PBMT demonstrated a slight improvement in reducing arm circumference and arm volume, the results of our meta-analysis did not show significant benefits in relieving of lymphoedema. Further trials are needed to recruit more participants, and to evaluate the long-term efficacy and safety of PBMT in management of breast cancer-related lymphoedema.

1. Introduction

Lymphoedema is a chronic condition characterised by the persistent accumulation of the interstitial fluid in peripheral tissues, particularly extremities, and is caused by the dysfunction of lymphatic drainage or the absence of lymph nodes.[1,2] The development of lymphoedema is a pertinent problem post breast cancer treatments, such as radiation therapy and axillary lymph node dissection; it results in adverse outcomes in patients, including pain and limited physical function, and negatively affects their quality of life (QOL).[3] Despite the emergence of a novel surgical technique, sentinel node biopsy, which aims to reduce the incidence of lymphoedema, breast cancer-related lymphoedema (BCRL) remains a major concern. The incidence of lymphoedema at 12 months following breast cancer surgery ranged from 12% to 26%.[4–6]

Numerous therapeutic options, including compression garments, complex decongestive physiotherapy (CDP), manual lymphatic drainage (MLD), and remedial exercises,[7,8] have the potential to relieve the symptoms and improve the QOL of patients with BCRL. Among these options, CDP is currently considered an effective therapy for reducing upper-arm lymphoedema in breast cancer survivors. By contrast, the

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efficacy of other physiotherapy methods has been reported to be limited.[9–12] In addition, these therapeutic options are reported to be time consuming and have poor (or unacceptable) adherence. Therefore, an effective and alternative treatment for lymphoedema is required.

In the past two decades, photobiomodualtion therapy (PBMT), previous known as low-level laser therapy, has been widely used as supportive care in patients with breast cancer or BCRL. PBMT (wavelength between 650 and 1000 nm), approved by the US Food and Drug Administration as a therapeutic intervention, is a noninvasive form of phototherapy associated with the use of low irradiance. PBMT is believed to improve lymphatic motility, stimulate lymphangiogenesis, reduce inflammation, soften fibrotic tissues, and alleviate pain.[13] The beneficial effects of PBMT have been reported in relation to various medical conditions, such as wound healing[14] and musculoskeletal disorders.[15,16]

To date, multiple studies have demonstrated the effects of PBMT on lymphoedema following breast cancer surgery. However, consensus on its benefits remains to be reached, most likely because of the small sample sizes of previous studies. Thus, the aim of this systematic literature review and meta-analysis of randomised controlled trials (RCTs) was to analyse the effectiveness and safety of PBMT for the treatment of BCRL.

2. Materials and methods

2.1. Selection criteria

We searched the literature for RCTs that evaluated the outcomes of PBMT in the treatment of BCRL after surgery. We included RCTs that provided the following information: (1) inclusion and exclusion criteria used for patient selection, (2) the definition of lymphoedema, (3) the PBMT technique used, and (4) the evaluation of treatment outcomes. We excluded RCTs that met at least one of the following criteria: (1) inclusion of patients with lymphoedema who did not have breast cancer and (2) inclusion of patients with medical conditions, such as current metastases, pregnancy, photosensitivity, chronic inflammatory diseases, and history of severe trauma.

2.2. Search strategy and study selection

An electronic search of the following databases was performed using keywords: PubMed, EmBASE, PEDro, Cochrane Central Register of Controlled Trials, SCOPUS, CINAHL and the ClinicalTrials.gov registry (http://clinicaltrials.gov/). The following terms and Boolean operator were used in MeSH and free-text searches: Lower level laser therapy OR low-energy laser OR low-intensity laser OR laser therapy OR photobiomodulation, breast cancer OR neoplasm, lymphoedema OR lymphedema OR edema. The “related articles” option in PubMed was used to broaden the search. Additional studies were identified by searching the reference sections of all relevant papers. Professionals working in related fields were consulted to identify potential articles. No language restrictions were applied. The last search was performed in July 2019.

2.3. Data extraction

Data were extracted independently by HYC and HHT. Spreadsheets were designed to record the details of RCTs pertaining to participants, inclusion and exclusion criteria, baseline arm circumference and volume for lymphoedema, the type of PBMT used, and outcome measures. The individually recorded decisions of the two reviewers were compared, and consensus was reached through discussion. Any persistent disagreements between the reviewers were resolved through evaluation by a third reviewer, TWH.

2.4. Methodological quality appraisal

The methodological quality of included studies was independently appraised by HYC and HHT by using the Cochrane Risk of Bias 2.0 (RoB 2.0) tool[17] based on the following criteria: (1) adequacy of randomisation, (2) deviations from intended interventions, (3) missing data of dropouts, (4) bias in the measurement of the outcomes, and (5) selection of the reported results.

2.5. Outcomes assessments

The difference in the arm circumference or volume was the primary outcome used to evaluate the efficacy of PBMT. Secondary outcomes were grip strength and pain scores. The primary analysis was based on the results of the included RCTs. The no treatment group and conventional therapy group, including treatment methods such as compression garments, MLD, and remedial exercises, were grouped as the control group. Because of the heterogeneity of the included trials, the follow-up time points of treatment included were immediately and 1–3 months after the end of all treatment sessions.

2.6. Statistical analysis

All statistical analyses were performed using the statistical package Review Manager, version 5.3 (Cochrane Collaboration, Oxford, England). The meta-analysis was performed in accordance with the PRISMA guidelines.[18] When necessary, standard deviations (SDs) were estimated on the basis of reported confidence interval (CI) limits, standard errors, or range values. The effect sizes of continuous outcomes are reported as the weighted mean difference (MD) or standardised mean difference (SMD). The precision of effect sizes was reported at a CI of 95%. A pooled estimate of weighted MDs and SMDs was computed using the DerSimonian and Laird random-effects model.[19] A statistically significant result was indicated by a P value of < 0.05 or a 95% CI not including zero in the weighted MD and SMD. Only if included studies presented adequate clinical and methodological similarities, the data were extracted and pooled. The heterogeneity of each extracted datum was assessed using the I^2 test, with I^2 quantifying the proportion of the total outcome variability that was attributable to variability among the studies.

3. Results

3.1. Characteristics of trials

The review process is outlined in Fig. 1. Our initial search yielded 298 studies, 278 of which were deemed to be ineligible after screening the titles and abstracts. Subsequently, the full text of the remaining 20 reports was screened, and 11 of them were excluded from our final analysis for the following reasons: 2 were not randomised trials, 6 were review papers, 2 were focused on different comparisons, and 1 was case-report paper. Thus, the remaining six eligible studies were included in this meta-analysis[12,20,21,23,24,26]

The main characteristics of the included studies are listed in Table 1. The publication dates of the studies were between 2003 and 2018, and the sample sizes of these studies ranged from 11 to 61 female patients. All the nine included trials evaluated patients who were diagnosed with BCRL, and the age of patients ranged from 36 to 77 years. Of the included studies, nine trials for qualitative synthesis and six trials for quantitative synthesis. F Table 2 presents the methodological quality our trials investigated the outcomes of PBMT and sham laser treatment.[12,21,22,26] Only one trial designed their control group as not receiving any treatment,[24] and the other four trials compared the outcomes of PBMT with those of conventional therapy.[3,20,23,25] All the studies measured the arm circumference or volume as the primary outcome. Regarding secondary outcomes, five trials measured pain

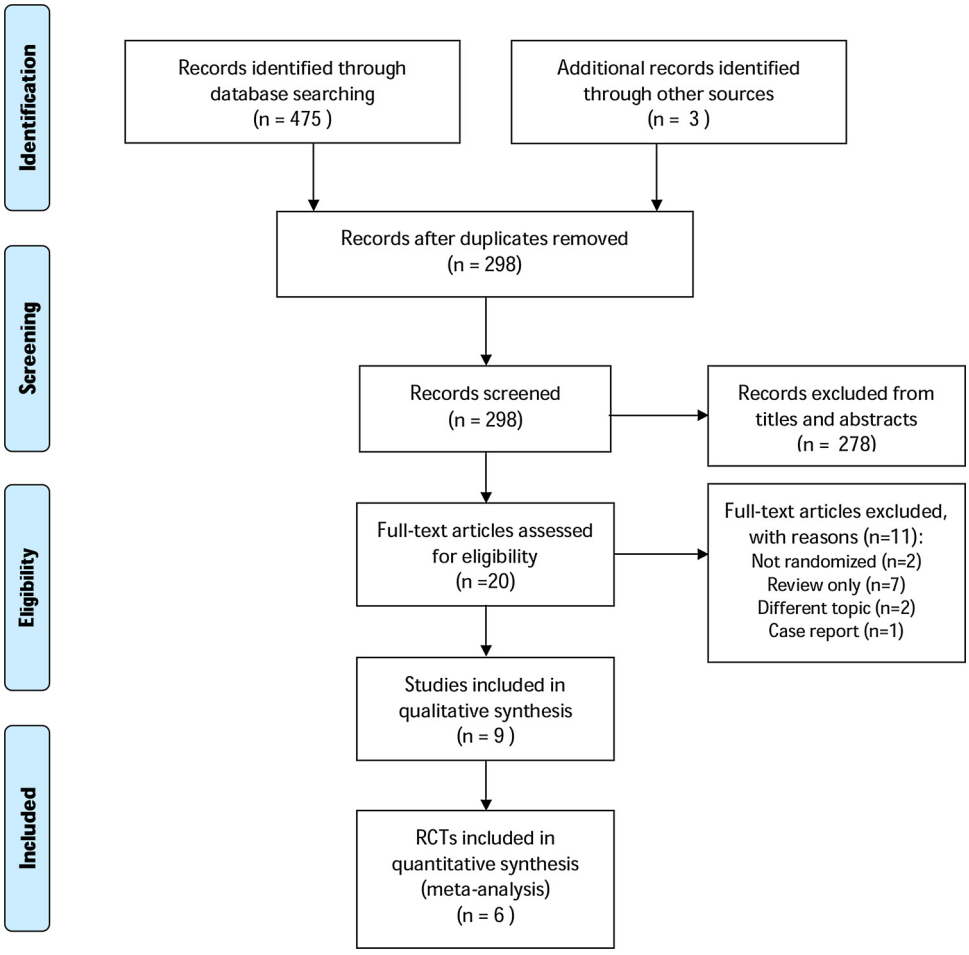

Fig. 1. Flowchart of the selection of clinical trials.

intensity scores and three trials measured grip strength. The duration of PBMT in the intervention group in all the included studies ranged from 4 to 12 weeks, except in the study conducted by Maiya et al[25] who administered PBMT for 10 days. All the studies reported the dosage of laser treatment administered to patients, except for one study.[3] In addition, the dosage used in most of the studies ranged from 1.5 to 2.4 J/cm^2; by contrast, the dosage used was up to 4.89 J/cm^2 [12] and 6 J/cm^2[20] in two studies. The baseline characteristics of patients included in the nine trials are shown in Table 1.

Table 2 presents the methodological quality of the nine included RCTs. All the studies were described as RCTs, and the methods of randomisation allocation reported were all moderate risk. All of them reported the blinding of patients and outcome assessors, except for Lau et al[24] who reported a high risk of detection bias resulting from the single-blinded design of the trial.[24] In most of the studies, outcomes were reported as the mean with its respective SD. However, data of some studies were presented in different forms, such as a line chart,[22] a median with its corresponding interquartile range,[12] and a percentage of difference,[3] which may have resulted in a bias attributable to the selection of reported results. The percentage of patients who were lost to follow-up was acceptable (< 20%) in all the studies.

3.2. Arm circumference

Four studies provided information regarding the reduction of the difference in circumference between the affected and unaffected arms.[20,22,23,25,26] However, only three studies were pooled.[20,23,26] In each of the included trials, the difference in circumference was measured at the beginning and at 0, 1, and 3 months after the treatment. Because of the use of different methods for measurements, SMD was then introduced to eliminate the bias between two trials. The pooled SMD in the limb circumference were – 0.47 (95% CI: –1.34 – 0.39) at 0 month, –0.52 (95% CI: – 0.52 – 0.42) at 1 month, and –0.33 (95% CI: –0.88 – 0.23) at 3 month after treatment; no significant difference was observed after the period of treatment limb circumference between the groups. The I^2 value ranged from 62 to 79% at various time periods, indicating moderate to high heterogeneity across the trials (Fig. 2).

The data reported by Kaviani et al[22] and Maiya et al[25] were excluded due to lack of integrity of data or baseline data.[22,25] However, they reported that the reduction in arm circumference caused by PBMT significantly differed between the treatment and control groups.

3.3. Arm volume

The reduction of the change in volume between the affected and unaffected arms was determined in four trials that evaluated the outcome of PBMT in patients with BCRL.[3,12,21,24] However, only three studies were pooled.[12,21,24] The timing of the outcome assessment was the end of the intervention and 1 month after the intervention. The pooled SMD in the arms volume were 0.04 (95% CI: –0.32 – 0.41) post-treatment, and –0.53 (95% CI: – 1.10 – 0.04) at 1 month after treatment; no significant difference was observed after the period of treatment arms volume between the groups. The I^2 value ranged from 3 to 28% at various time periods, indicating low heterogeneity among studies (Fig. 3).

The results reported by Rinder et al[3] were not pooled because they indicated only the percentage of change rather than the mean and SD.[3] In this study, PBMT was not significantly superior to MLD at the end of

Table 1
Characteristics of Included Studies.

Author [Year]	Inclusion criteria	No. of patients	Age, yr (mean ± SD)	Lymphedema during (month)	Baseline of affected arm (mean ± SD)	Intervention
Qualitative analysis						
Kaviani [2006]	≧3 months hx of PML with radiation therapy.	L: 6	L: 53.7 ± 9.8	L: 6.8 ± 3.8	L^b: 180 ± 18	L: 2 blocks (3 times/w x3 w with 1.5 $^{J}/_{cm^2}$) separated by 8 w rest period
		C: 5	C: 48.7 ± 12.5	C: 6.2 ± 5.3	C^b: 166.5 ± 16.6	C: Sham therapy
Maiya [2008]	with radiotherapy	L: 10	NR	NR	NR	L: 34 min. d x 10 d with 2.4 $^{J}/_{cm^2}$
		P: 10				P: Pneumatic compression + limbs exercise
Ridner [2013]	Age≧21 yr, stage I or II lymphedema	L: 15	L: 66.4 ± 11.3	L: 27 ± 38.52	$L^{\dagger}$: 11.7	L: 20~30 sec/point in each grid; 20 min/session
		M: 16	M: 67.5 ± 10.3	M: 18.9 ± 50.37	$M^{\dagger}$: 23.2	M: 40 min/session
		L + M: 15	L + M: 66 ± 10.2	L + M: 25.2 ± 100.74	L + $M^{\dagger}$: 20.4	L + M: each session 20 min of LLLT +20 min of MLD
Quantitative analysis						
Baxter [2018]	Age≧18 yr, diagnosis of BCRL	L: 8	L: 57.9 ± 9.6	L: 73.2 ± 50.4	L^b: 5.45 ± 3.03	L: 10 min/session; 2 times/w x6 w with 6 $^{J}/_{cm^2}$
		C: 8	C: 64.3 ± 11.1	C: 57.6 ± 70.8	C^b: 8.16 ± 8.00	C: BCRL conventional therapy
Carati [2003]	Age≧18 yr	L: 33	L: 63 ± 11.5 C:	L: 98 ± 15	L^a: 645 ± 413.60	L: 2 blocks (3 times/w x3 w with 1.5 $^{J}/_{cm^2}$) separated by 8 w rest period
		C: 28	65 ± 10.6	C: 43 ± 9	C^a: 888 ± 571.48	C: Sham therapy followed by 8 w rest period then 1 block (3 times/w x3 w with 1.5 $^{J}/_{cm^2}$)
Kozanoglu [2009]	≧3 months hx of PML	L: 25	L: 45.4 ± 9.9	L: 21.4 ± 26.9	L^b: 16.8 ± 9.8	L: 20 min/session x 3 times/w x4 w with 1.5 $^{J}/_{cm^2}$
		P: 25	P: 51.2 ± 10.3	P: 18.8 ± 29.7	P^b:18.9 ± 6.4	P: Pneumatic compression 2 h/session x5 times/w x4 w
Lau [2009]	Age≧18 yr, with radiotherapy or chemotherapy	L: 11	L: 50.9 ± 8.6	L: 43.3 ± 1.0	L^a: 448.2 ± 145.6	L: 20 min/session x 3 times/w x4 w with 2 $^{J}/_{cm^2}$
		C: 10	C: 51.3 ± 8.9	C: 35.6 ± 9.1	C^a: 426.0 ± 166.7	C: No treatment
Omar [2011]	Stage II or III breast cancer	L: 25	L: 54.76 ± 3.33	L: 13.8 ± 1.77	L^b: 109.6 ± 5.9	L: 3 times/w x12 w with1.5 $^{J}/_{cm^2}$
		C: 25	C: 53.36 ± 3.56	C: 14.16 ± 2.23	C^b: 113.3 ± 4.3	C: Placebo with sham therapy
Storz [2017]	≧3 months hx of PML	L: 20	L: 61.06 ± 9.66	NR	L^a: 91.63 ± 272.73	L: 10 min/session; 2 times/w x4 w with 4.89 $^{J}/_{cm^2}$
		C: 20	C: 59.37 ± 10.16		C^a: 160.46 ± 221.24	C: Placebo with sham therapy

Abbreviations: C control; Hx history; M manual lymphatic drainage (MLD); L LLLT; P pneumatic compression; PML postmastectomy lymphedema; SD: standard deviation; W week.
[a]difference between sum of the circumferences of the affected and unaffected arms (mL); [b]difference between sum of the circumferences of the affected and unaffected arms (cm); [†]arm volume % difference(median).

Table 2
Assessment of Methodological Quality of Included Trials (RCT evaluated by RoB 2.0).

Author [year]	Bias caused by adequacy of randomisation	Bias caused by deviations from intended interventions	Bias caused by missing data of dropouts	Bias in measurement of the outcomes	Bias in selection of the reported results	Overall risk of bias
Baxter [2018]	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate
Carati [2003]	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate
Kaviani [2006]	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Moderate
Kozanoglu [2009]	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate
Lau [2009]	Moderate risk	Low risk	High risk	Moderate risk	Low risk	High
Maiya [2008]	Moderate risk	Low risk	Moderate risk	Low risk	Low risk	Moderate
Omar [2011]	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate
Rinder [2013]	Moderate risk	Low risk	Low risk	Low risk	High risk	High
Storz [2017]	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Moderate

the treatment.

3.4. Grip strength

Three studies compared the difference in grip strength between the PBMT and control groups[12,23,26] In all these studies, the baseline of grip strength was measured at the beginning of the treatment, and grip strength was then measured at their designated follow-up sessions. The pooled mean difference in the grip strength were 1.18 (95% CI: –2.16 – 4.52) at 0 month, –1.93 (95% CI: –5.15 – 1.29) at 1 month, 0.67 (95% CI: –2.72 – 4.06) at 2 month and –0.89 (95% CI: – 3.04 – 1.25) at 3 month after treatment; no significant difference was observed after the period of treatment grip strength between the groups. The I^2 value ranged from 0 to 76% at various time periods, indicating low to high heterogeneity across the trials (Fig. 4).

3.5. Pain score

The reduction of difference in the pain score was determined in five studies.[12,20–23,25] However, only four of them were pooled.[19,20,21,23] Three trials measured pain severity on a 10-point scale,[12,20,21] and the other trial used a 0–100-mm visual analogue scale, which was then converted into a 10-point scale.[23] The pooled mean difference in the pain score were –0.14 (95% CI: –0.58 – 0.31) at 0 month, 0.21 (95% CI: –0.27 – 0.68) at 1 month, 0.00 (95% CI: –1.87 – 1.87) at 2 month and 0.01 (95% CI: –0.99 – 1.02) at 3 month after treatment. The I^2 value ranged from 0 to 65% at various time periods, indicating low to medium heterogeneity across the trials. The effect of PBMT on pain relief did not significantly differ between the end of the treatment and at subsequent follow-up assessments (Fig. 5).

The data reported by Kaviani et al[22] and Maiya et al[25] were not considered because of lack of integrity of data or baseline data.[22,25] However, both of them reported that PBMT may be effective in relieving pain in patients.

4. Discussion

Since the emergence of PBMT as a novel therapeutic strategy for the treatment of BCRL, it has received considerable attention over the past two decades. RCTs are considered a gold standard of evidence; hence, nine published RCTs that investigated the effects of PBMT were included in this systematic review and six for meta-analysis. However, because of the conflicting results of these studies, the effectiveness of PBMT treatment has not been clearly established. The primary aim of this systematic review and meta-analysis was to conduct an overall comparison of the effects of PBMT among the studies. Our results did not reveal a significant benefit of PBMT in the management of BCRL. All outcomes including arm circumference, arm volume, grip strength, and pain scores did not significantly differ between the PBMT and control groups. However, evaluating the effectiveness of the laser treatment is not the same when compared to a control group or placebo control than when comparing it to another treatment. It is possible that the laser treatment does not show differences from other treatments but it shows greater effectiveness than using the control or placebo. If there are no differences between the laser effectiveness and another treatment, the clinical decision to apply it or not will depend on the costs, risks, adherence to treatment, etc. of both interventions.

Arm circumference and volume usually indicate the severity of lymphoedema and are directly associated with upper-arm mobility and QOL. However, because of the lack of guidelines regarding the minimal

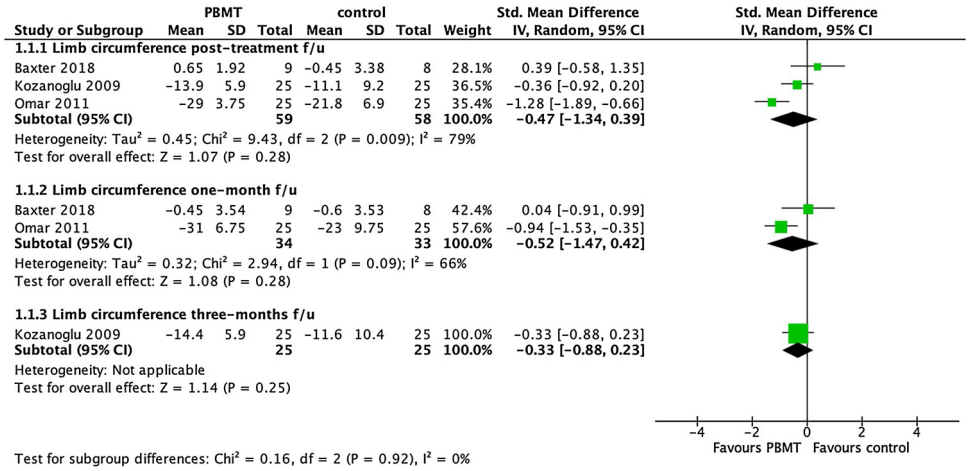

Fig. 2. Forest plot of the comparison of the effect of with or without photobiomodualtion therapy (PBMT) on the reduction of arm circumference of BCRL from three clinical trials. The first author names and the 95% confidence interval (CI) are included.

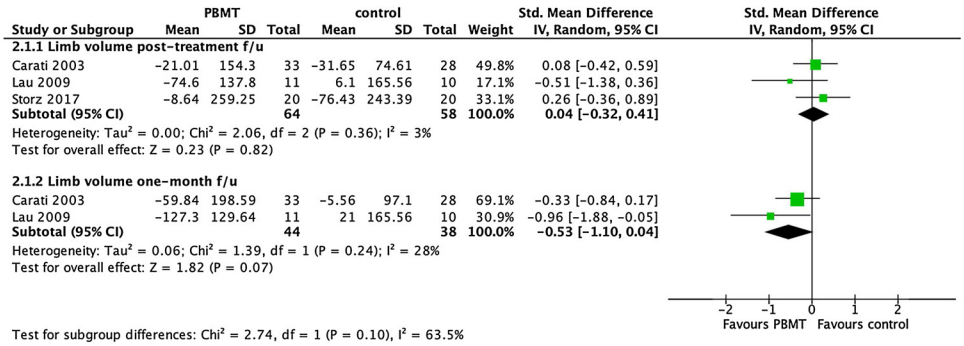

Fig. 3. Forest plot of comparison of the effect of with or without photobiomodualtion therapy (PBMT) on the reduction of arm volume of BCRL from three clinical trials. The first author names, the standard deviations (SDs) of the mean, and the 95% confidence interval (CI) are included.

clinically important difference in the reduction of arm circumference or volume, determining the effectiveness of PBMT is difficult. Even in the RCTs included in the present review, the conclusion regarding the therapeutic value of PBMT is conflicting. By contrast, PBMT was reported to alleviate pain in patients in a retrospective study and meta-analysis.[27] Evidence for pain reduction by PBMT in BCRL is not available because we did not observe a significant difference in pain reduction in our meta-analysis, and the included studies reported conflicting results for pain reduction. However, other potential causes of pain in BCRL, including musculoskeletal-related diseases, cervical radiculopathy, brachial plexopathy, mononeuropathy/polyneuropathy (e.g., chemotherapy-induced peripheral neuropathy), postmastectomy pain syndrome, and bone metastases, also cannot be ignored.[28] All the reviewed studies did not evaluate the potential causes of pain, which may have led to overestimation or underestimation of pain in BCRL.

PBMT was reported to have a benefit in softening surgical scarring and fibrous tissues[29] which may be responsible for excess lymphatic fluid accumulation. However, the optimal dosage, wavelength, and frequency of laser treatment remain undetermined. In all our reviewed studies, wavelengths between 808 nm and 905 nm and energy densities between 1.5 J/cm^2 and 2.4 J/cm^2 were most commonly used, which might be related to the efficacy of therapy.[21–26] The application of a high amount of total energy (4.89 and 6 J/cm^2) might exert opposite effects due to higher tissue destruction rather than healing.[12,20] Heterogeneity across therapy sessions based on different times of treatment results in difficulty in comparing outcomes among the included studies. For laser treatment, Storz et al[12] used emitting continuous waves, which were reported to have a lower ability of reaching deeper tissues compared with pulsed waves.[30] However, most of our included studies did not report the type of laser applied, leading to a bias in evaluation. Finally, the emitting zone is also crucial to the effect of therapy. Because of the nonuniformity of the irradiated anatomical area, all studies had their own emitting areas, ranging from one spot to several spots along the upper arm, which may have directly affected the total energy received.[23,26] Therefore, to further determine the effectiveness of PBMT, a well-designed radiation schedule and an appropriate protocol of laser treatment are required in the future.

Before deciding whether PBMT is a favorable treatment option, physicians must consider the possibility of its adverse effects. Although no obvious side effects of PBMT were observed, we still cannot rule out the chance of causing another damage due to the lack of long-term follow-up. In the study, PBMT did not increase the risk of cellulitis[31] however, patients must undergo appropriate medical management when they observe the symptoms and signs of cellulitis. Although a study reported that laser may cause malignant changes in tissues,[13] evidence for the same is not available.

The I^2 value of 0% – 62% for each outcome evaluation indicated the presence of moderate heterogeneity across our selected studies. This finding can be attributed to heterogeneity among patients' demographics, outcome evaluation methods, variable laser settings, and time

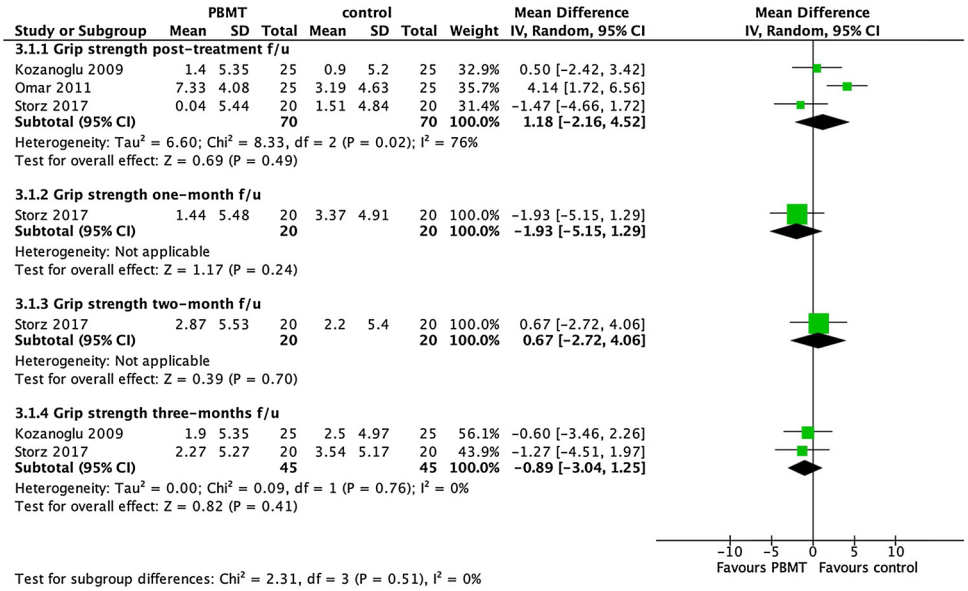

Fig. 4. Forest plot of comparison of the effect of with or without photobiomodualtion therapy (PBMT) on the difference of grip strength of BCRL from three clinical trials. The first author names, the standard deviations (SDs) of the mean, and the 95% confidence interval (CI) are included.

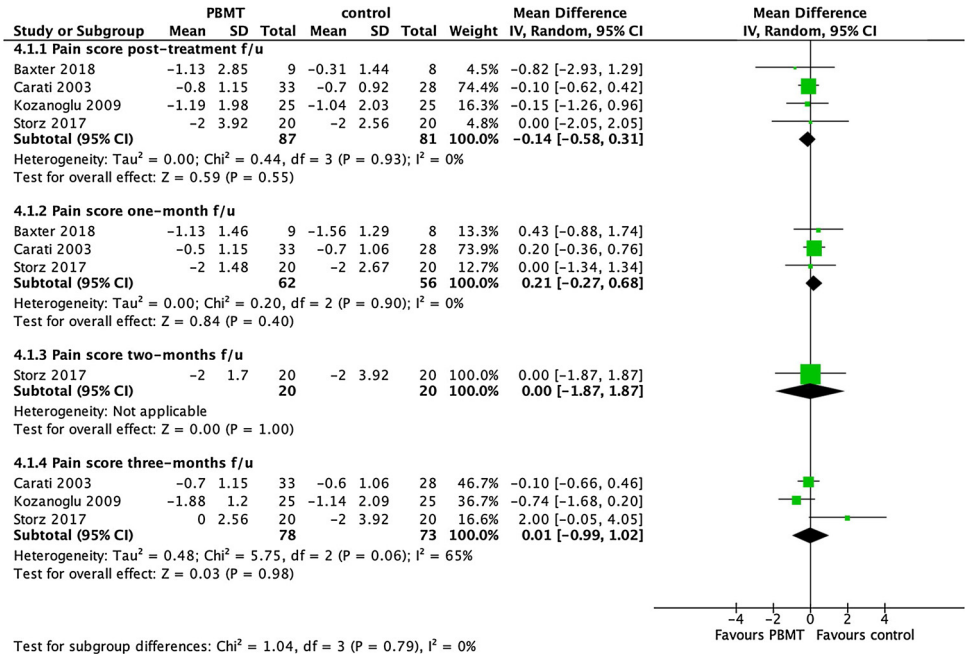

Fig. 5. Forest plot of comparison of the effect of with or without photobiomodualtion therapy (PBMT) on the difference of pain score of BCRL from four clinical trials. The first author names, the standard deviations (SDs) of the mean, and the 95% confidence interval (CI) are included.

of outcome assessments.

Our study has several limitations. First, according to the methodological quality of original studies, two studies were found to have a high risk of bias based on the RoB 2.0 rating scale[3,24] which may affect their reliability. In addition, the process of distribution, the blinding of outcome investigators, and the variability of outcome-evaluating principles may have biased the evaluations of the effect of PBMT. Second, most of the included studies had recruited a small number of patients, and one study had only 10 patients in each treatment group, thereby diminishing the statistical power of their results. Furthermore, most of them did not perform a long-term evaluation of the effects of PBMT on BCRL.

5. Conclusion

Although PBMT demonstrated a slight improvement in reducing arm circumference and arm volume, the results of our meta-analysis did not show significant benefits in relieving of lymphoedema. Overall, some limitations of reviewing the included studies existed, and these must be considered in future studies. According to the results of our meta-analysis, further trials are needed to establish the long-term efficacy and safety of PBMT in the management of BCRL.

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Declaration of Competing Interest

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