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Research article

Efficiency of photobiomodulation on accelerating the tooth movement in the alignment phase of orthodontic treatment—A systematic review and meta-analysis

Tu Huang [a,*], Zihao Wang [b], Juan Li [c]

[a] Department of Orthodontics, 363 Hospital of Genertec, Southwest Medical University, Chengdu, China
[b] Chengdu Jinjiang Center for Disease Control and Prevention, Chengdu, China
[c] Department of Stomatology, 363 Hospital of Genertec, Southwest Medical University, Chengdu, China

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ABSTRACT

Objectives: To investigate the efficiency of photobiomodulation on accelerating the tooth movement in the alignment phase of orthodontic treatment.

Materials and methods: The data search was performed with PubMed, Embase, Scopus, and the Cochrane Library. Randomized clinical trials and controlled clinical trials evaluating the efficiency of photobiomodulation on accelerating tooth movement in the alignment phase were selected, and the characteristics of the included studies were collected in a customized data form. Data analysis was conducted by the random-effects model after risk of bias and certainty of evidence were assessed.

Results: Five randomized clinical trials and three controlled clinical trials were included in the final analysis. All included studies reported positive results except the study of Shehawy et al. The results of the analysis showed that photobiomodulation significantly increased the rate of tooth movement and reduced the treatment duration, compared with the control group. Although the heterogeneity was large among the included studies, it was improved after subgroup analysis.

Conclusions: This systematic review offered evidence that photobiomodulation can accelerate tooth movement in alignment procedures and reduce treatment time. Future studies are needed to find the best PBM protocol for orthodontic practice.

1. Introduction

Orthodontic treatment is an efficient method to solve the healthy and aesthetic problems caused by malocclusion. With the development of orthodontics, an increasing number of children and adults are seeking orthodontic treatment. According to published literature, conventional methods of fixed appliances may last 12–30 months [1]. This lengthy process of orthodontic treatment has troubled both orthodontists and their patients for years. For orthodontic patients, long-term treatment may affect their work and cause many inconveniences in daily life. For orthodontists, a longer treatment duration indicates higher risks of a range of side effects, including root resorption, caries, and periodontal diseases.

Methods aiming to increase the rate of tooth movement and reduce orthodontic treatment time have been researched for a long

* Corresponding author.
E-mail addresses: huangtu0224@sina.cn (T. Huang), wangzihaowawsa@163.com (Z. Wang), Juan_Li9395@163.com (J. Li).

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time. Several methods have been defined as efficient ways to accelerate tooth movement, involving the injection of different biologics around the alveolar socket, surgical techniques, and electric stimulations. Although there is plenty of evidence showing the efficacy of the above methods, they are associated with discomfort and painful experiences for patients [2]. In addition, the apparatuses and biologics required by these invasive operations are not easily available for conventional orthodontic practices. Orthodontists are still searching for a truly noninvasive and user-friendly method to reduce treatment time [2]. Thus, photobiomodulation (PBM) systems have been introduced into the field of orthodontics.

Photobiomodulation is a noninvasive technique that uses low-level lasers (LLLs) or light-emitting diodes (LEDs) at wavelengths from 600 to 1000 nm to provoke a biological reaction [2,3]. The difference between these two sources is that the light from LLLs is coherent, while LEDs produce incoherent light [4]. PBM has been defined as an effective intervention for activating several cellular biological processes, including mitochondrial metabolism, cell turnover, and angiogenesis, resulting in increased wound healing and remodelling processes in skin, bone, and nervous tissues [2]. With a wide range of applications in modern dentistry, many clinical studies have suggested that photobiomodulation was able to increase the rate of canine movement in the space closure phase [5]. However, some studies also published negative results. Several systematic reviews have investigated the relationship between photobiomodulation and accelerated tooth movement. Ge et al. and Imani et al. concluded that applications of PBM with varying wavelengths and energy densities may reduce orthodontic treatment duration, although the optimal dose of PBM remains undetermined [6,7]. In contrast, Almeida et al. reported that there was no evidence supporting that PMB may accelerate tooth movement and reduce orthodontic treatment time [8]. According to these heterogeneous results, it is not reasonable to determine the capacity of PBM in accelerating tooth movement.

In recently published systematic reviews, researchers investigated the relationship between photobiomodulation and canine retraction during the space closure phase. However, as the percentage of patients requiring extractions only ranged from 35% to 45%, all orthodontic patients would undergo the alignment process, while less than half of them would meet the space closure phase [9–12]. Therefore, evaluating the effectiveness of PBM on reducing alignment time may provide more valuable evidence for the wide application of PBM in orthodontic practice. Here, this review aims to systematically evaluate the effectiveness of PBM on accelerating the alignment rate for further application in orthodontic treatment.

2. Materials and methods

2.1. Protocol and registration

This review was registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD [CRD42022355857]) and can be consulted at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022355857 [5]. The Cochrane Handbook for Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used to guide this systematic review and meta-analysis [6].

Selection criteria:

The eligibility criteria of this review followed the PICOS criteria:

- Population = Patients receiving PMB as an aid intervention in fixed orthodontic treatment.
- Intervention = PBM used to accelerate tooth movement.
- Compared with = Control groups receiving fixed orthodontic treatment without any other interventions.
- Outcome of interest = Overall alignment time, alignment rate, etc.
- Study type = Randomized controlled trials and controlled clinical trials.

The included articles met the following criteria:

Inclusion criteria:

- Articles in English without any restriction of the publication time.
- The articles must be original peer-review studies that meet all PICOS criteria with the design of randomized clinical trials (RCTs) or controlled clinical trials (CCTs).
- PBM interventions conducted with LEDs or LLLs equipment.
- Studies presenting the parameters of PBM and the individual characteristics of patients.
- Outcome variables were defined as the overall alignment time or alignment rate.

Exclusion criteria:

- The studies included fewer than 10 arches per group.
- Patients of studies exposed to previous orthodontic treatment.
- Patients in studies suffered from systemic diseases or poor oral hygiene.
- Patients of studies diagnosed with mild crowding in selected arches.

2.2. Information sources and search strategy

The electronic search was conducted in the following four databases until the 17th of August 2022: PubMed, Embase, Scopus and Cochrane Library. The search strategies are based on Table 1. The manual search, reviewing the references of included articles, was conducted by two reviewers [Huang and Wang]. No restrictions on status, publication data, or language were imposed in the article research procedure [13].

The titles and abstracts of retrieved records were independently assessed by two investigators [Huang and Wang]. The same

Table 1
Keywords and algorithms used in the search strategy.

Electronic databases	Keywords and algorithms
PubMed: 371	#1 ((((((((((((((((((((((((((“Low-Level Light Therapy”[Mesh]) OR (Photodynamic Therapy [Title/Abstract])) OR (Therapy, Photodynamic [Title/Abstract])) OR (Photodynamic Therapies [Title/Abstract])) OR (Therapies, Photodynamic [Title/Abstract]))) OR (Light Therapy, Low-Level [Title/Abstract])) OR (Low Level Light Therapy [Title/Abstract])) OR (Low-Level Light Therapies [Title/Abstract])) OR (Therapies, Low-Level Light [Title/Abstract])) OR (Photobiomodulation Therapy [Title/Abstract])) OR (Photobiomodulation Therapies [Title/Abstract])) OR (Therapies, Photobiomodulation [Title/Abstract])) OR (Therapy, Photobiomodulation [Title/Abstract])) OR (LLLT[Title/Abstract])) OR (Laser Therapy, Low-Level [Title/Abstract])) OR (Low-Level Laser Therapies [Title/Abstract])) OR (Irradiation, Low-Power Laser [Title/Abstract])) OR (Low-Power Laser Therapy [Title/Abstract])) OR (Laser Therapies, Low-Power [Title/Abstract])) OR (Low-Level Laser Therapy [Title/Abstract])) OR (Laser Biostimulation [Title/Abstract])) OR (Biostimulation, Laser [Title/Abstract])) OR (Laser Phototherapy [Title/Abstract])) OR (Phototherapy, Laser [Title/Abstract]) #2 ((((((((((“Orthodontics”[MeSH Terms] OR “orthodontic” [Title/Abstract]) OR (Tooth Movement Techniques [Title/Abstract])) OR (Tooth Uprighting [Title/Abstract])) OR (Tooth Uprightings [Title/Abstract])) OR (Tooth Movement, Minor [Title/Abstract])) OR (Tooth Intrusion [Title/Abstract])) OR (Tooth Intrusions [Title/Abstract])) OR (Tooth Depression [Title/Abstract])) OR (Tooth Depressions [Title/Abstract])) OR ((fixed appliances [Title/Abstract]) OR (fixed appliance [Title/Abstract]))) OR (Dental Alignment [Title/Abstract])) OR (dental leveling [Title/Abstract])) OR (leveling [Title/Abstract] AND alignment [Title/Abstract])) #3 #1 AND #2
Embase: 150	#1 **‘low level laser therapy’**/exp OR **‘low level laser therapy’** OR **‘photodynamic therapy’**/exp OR **‘photodynamic therapy’** OR (**photodynamic** AND (**‘therapy’** OR **‘therapy’**/exp OR **therapy**)) OR **‘photodynamic therapies’**:ti,ab,kw OR **‘light therapy, low-level’**:ti,ab,kw OR **‘low level light therapy’**:ti,ab,kw OR **‘low-level light therapies’**:ti,ab,kw OR **‘photobiomodulation therapy’**:ti,ab,kw OR **‘photobiomodulation therapies’**:ti,ab,kw OR **‘therapies, photobiomodulation’**:ti,ab,kw OR **‘therapy, photobiomodulation’**:ti,ab,kw OR **lllt**:ti,ab,kw OR **‘laser therapy, low-level’**:ti,ab,kw OR **‘low-level laser therapies’**:ti,ab,kw OR **‘low-power laser therapy’**:ti,ab,kw OR **‘low-power laser therapies’**:ti,ab,kw OR **‘low-level laser therapy’**:ti,ab,kw OR **‘low-power laser irradiation’**:ti,ab,kw OR **‘laser biostimulation’**:ti,ab,kw OR **‘biostimulation, laser’**:ti,ab,kw OR **‘laser phototherapy’**:ti,ab,kw OR **‘phototherapy, laser’**:ti,ab,kw #2 **‘orthodontic tooth movement’**/exp OR **‘orthodontic tooth movement’** OR **‘tooth movement techniques’**/exp OR **‘tooth movement techniques’** OR ((**‘tooth’** OR **‘tooth’**/exp OR **tooth**) AND (**‘movement’** OR **‘movement’**/exp OR **movement**) AND **techniques**) OR **‘tooth movement technique’**:ti,ab,kw OR **‘orthodontic tooth movement’**:ti,ab,kw OR **‘orthodontic tooth movements’**:ti,ab,kw OR **‘tooth movement, orthodontic’**:ti,ab,kw OR **‘tooth movements, orthodontic’**:ti,ab,kw OR **‘tooth uprighting’**:ti,ab,kw OR **‘minor tooth movement’**:ti,ab,kw OR **‘minor tooth movements’**:ti,ab,kw OR **‘tooth intrusion’**:ti,ab,kw OR **‘intrusion, tooth’**:ti,ab,kw OR **‘tooth intrusions’**:ti,ab,kw OR **‘tooth depression’**:ti,ab,kw OR **‘dental alignment’**:ti,ab,kw OR **‘dental leveling’**:ti,ab,kw OR (**leveling**:ti,ab,kw AND **alignment**:ti,ab,kw) #3 #1 AND #2
Scopus: 393	#1 (TITLE-ABS-KEY (low-*level* AND light AND therapy) OR TITLE-ABS-KEY (photodynamic AND therapy) OR TITLE-ABS-KEY (low AND level AND light AND therapy) OR TITLE-ABS-KEY (photobiomodulation AND therapy) OR TITLE-ABS-KEY (lllt) OR TITLE-ABS-KEY (laser AND therapy, AND low-*level*)) OR ((TITLE-ABS-KEY (low AND *power* AND *laser* AND *irradiation*) OR TITLE-ABS-KEY (laser AND *biostimulation*) OR TITLE-ABS-KEY (*laser* AND *phototherapy*))) OR ((TITLE-ABS-KEY (*laser* AND *irradiation,* AND *low-power*) OR TITLE-ABS-KEY (*low-power* AND *laser* AND *therapy*) OR TITLE-ABS-KEY (low AND *level* AND *laser* AND *therapy*))) #2 ((TITLE-ABS-KEY (tooth AND movement AND techniques) OR TITLE-ABS-KEY (orthodontics) OR TITLE-ABS-KEY (orthodontic AND tooth AND movement))) OR ((TITLE-ABS-KEY (tooth AND uprighting) OR TITLE-ABS-KEY (tooth AND movement, AND minor) OR TITLE-ABS-KEY (tooth AND intrusion) OR TITLE-ABS-KEY (tooth AND depression))) OR ((TITLE-ABS-KEY (dental AND alignment) OR TITLE-ABS-KEY (dental AND leveling) OR TITLE-ABS-KEY (leveling AND alignment))) #3 #1 AND #2
Cochrane Library: 504	#1 MeSH descriptor: [Low-Level Light Therapy] explode all trees #2 (Photodynamic Therapy): ti, ab, kw OR (Light Therapies, Low-Level): ti, ab, kw OR (Photobiomodulation Therapy): ti, ab, kw OR (LLLT): ti, ab, kw OR (Laser Therapy, Low-Level): ti, ab, kw (Word variations have been searched) #3 (Low-Power Laser Therapy): ti, ab, kw OR (Low-Power Laser Irradiation): ti, ab, kw OR (Laser Biostimulation): ti, ab, kw OR (Laser Phototherapy): ti, ab, kw (Word variations have been searched) #4 #1 OR #2 OR #3 #5 MeSH descriptor: [Tooth Movement Techniques] explode all trees #6 (Movement Technique, Tooth): ti, ab, kw OR (Orthodontic Tooth Movement): ti, ab, kw OR (Tooth Uprighting): ti, ab, kw OR (Tooth Movement, Minor): ti, ab, kw OR (Tooth Intrusion): ti, ab, kw (Word variations have been searched) #7 (Tooth Depression): ti, ab, kw OR (Dental Alignment): ti, ab, kw OR (Dental leveling): ti, ab, kw OR (leveling and alignment): ti, ab, kw (Word variations have been searched) #8 #5 OR #6 OR #7 #9 #4 AND #8

procedure was repeated for the full text assessment of potentially included studies. Disagreements and final decisions were settled by the third author [Li] [13].

2.3. Data extraction and summery measure

The mean and standard deviations (SDs) of overall alignment times (days) or alignment rate (mm/week) were extracted from the included studies and defined as outcome data.

Other information of studies, including the first author, publication year, country, number of patients in the PBM/control group, details of PMB (equipment, wavelength, exposure point, exposure time, energy density/session, etc.), and the characteristics of the participants were collected in a customized data form.

2.4. Risk of bias assessment

The Cochrane Handbook for Systematic Reviews of Interventions was used for risk of bias assessment of included RCTs. The scale consists of six domains. Trials with low risk of bias in six domains were determined to be low risk. Trials with unclear risk of bias for one or more domains were determined as unclear risk. Trials with at least one item defined as having a high risk of bias were determined to be high risk.

Methodological index for non-randomized studies (MINORS) was used for risk of bias assessment of included CCTs. The evaluation scale has 12 items. The first eight items are used for studies without a control group, and the last four items are applied to studies with a control group along with the first eight items, with a maximum score of 24. In this study, a score of 0–12 was defined as low-quality literature, 13–18 as moderate-quality literature, and 19–24 as high-quality literature.

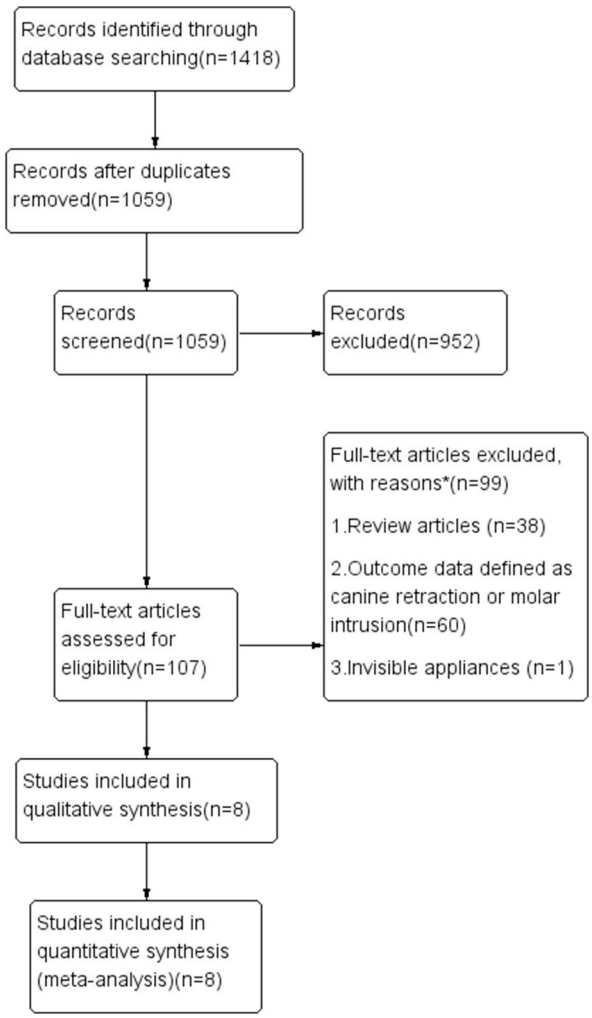

Fig. 1. PRISMA flow diagram for the study search.

Table 2
Characteristics of the included studies.

Study ID	Study design	Number in PBM group	Number in control group	Mean age(years)	Equipment
Caccianiga 2017 Italy [3]	RCT	18	18	Total 16.9 ± 2.5 PBM 17.1 ± 2.5 Con 16.8 ± 2.6	Semiconductor Diode laser
Ghaffar 2022 Egypt [20]	RCT	12	12	18–25	Semiconductor Diode laser
Giudice 2020 Italy [19]	RCT	43	46	18.4 ± 2.8	ATP38
Hasan 2017 Syria [17]	RCT	13	13	16–24	Semiconductor Diode laser
Kau 2016 America [16]	CCT	73	17	PBM 20 Con 17	OrthoPulse™
Nahas 2016 United Arab Emirates [4]	RCT	18	16	PBM 21.8 ± 5.3 Con 21.1 ± 10.2	OrthoPulse™
Shaughnessy 2016 America [2]	CCT	18	10	Total 13.9 ± 1.7 PBM 14.1 ± 1.7 Con 13.5 ± 1.8	OrthoPulse™
Shehawy 2020 Egypt [18]	CCT	15	15	19.2 ± 3.1	Semiconductor Diode laser

Study ID	Wavelength (nm)	Irradiation points	Energy density per session(J/cm^2)	Laser session
Caccianiga 2017 Italy [3]	980	Four dental segments (right first premolar-canine, right lateral-central incisors, left central-lateral incisors, left canine-first premolar)	150	Once a month
Ghaffar 2022 Egypt [20]	940	Labially at the vestibule	25.7	First month: day 3, 7, 14; starting from the second month: every 14 d
Giudice 2020 Italy [19]	450–835	Surface of the cheek	144	Every 14 days
Hasan 2017 Syria [17]	830	Each maxillary incisor's root at four points (two buccal, two palatal)	54	First month: day 0, 3, 7, 14; starting from the second month: every 15 d
Kau 2016 America [16]	850	Surface of the cheek	72, 108, 216	Every day/every week
Nahas 2016 United Arab Emirates [4]	850	Surface of the cheek	108	Every day
Shaughnessy 2016 America [2]	850	Labially at the vestibule	9.5	Every day
Shehawy 2020 Egypt [18]	635	Six mandibular anterior teeth where each root area was divided into 10 points, 5 facially and 5 lingually	12	First month: day 0, 3, 7, 14; and repeated from the second month

Study ID	Extraction	Orthodontic mechanics and clinical assessment
Caccianiga 2017 Italy [3]	None extraction	Wire sequences: 0.014-in thermal NiTi, then 0.016 × 0.022-in and 0.017 × 0.025-in thermal NiTi archwires. Treatment was considered finished when LII was less than 1 mm.
Ghaffar 2022 Egypt [20]	None extraction	Wire sequences: 0.016-in thermal NiTi, then 0.016 × 0.022-in thermal NiTi archwires. Treatment was considered finished when LII was less than 1 mm.
Giudice 2020 Italy [19]	None extraction	Wire sequences: 0.014-in thermal NiTi, then 0.016 × 0.022-in and 0.019 × 0.025-in thermal NiTi archwires. Treatment was considered finished when LII was less than 1 mm.
Hasan 2017 Syria [17]	Extraction of first premolars	Wire sequences: 0.014-in thermal NiTi, then advanced through a progression of stiffer arch wires. Treatment was considered finished when LII was less than 1 mm.
Kau 2016 America [16]	None extraction	Wire sequences: 0.014-in thermal NiTi or 0.016-in thermal NiTi, then advanced through a progression of stiffer arch wires. Treatment was considered finished when LII was less than 1 mm.
Nahas 2016 United Arab Emirates [4]	None extraction	Wire sequences: 0.014-in thermal NiTi, then 0.016 × 0.022-in and 0.017 × 0.025-in thermal NiTi archwires. Treatment was considered finished when LII was less than 1 mm.
Shaughnessy 2016 America [2]	None extraction	Wire sequences: 0.014-in thermal NiTi, then 0.018-in thermal NiTi archwires. Treatment was considered finished when LII was less than 1 mm.

(*continued on next page*)

Table 2 (*continued*)

Study ID	Extraction	Orthodontic mechanics and clinical assessment
Shehawy 2020 Egypt [18]	None extraction	Wire sequences: 0.012-in thermal NiTi, then 0.014-in and 0.016-in thermal NiTi archwires. Treatment was considered finished when LII was less than 1 mm.

Two reviewers [Huang and Wang] independently assessed the risk of bias, and the differences between the reviewers were resolved by the third author [Li].

2.5. Level of Evidence

Level of Evidence assessment was conducted with the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system by two independent reviewers [Huang and Wang]. The evaluation was based on six domains: study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias.

2.6. Statistical analysis

Meta-analysis was performed by Review Manager 5.3 after the data had been aggregated. The PBM effect with the results was expressed as the mean difference (MD) with a 95% confidence interval (CI) [14]. Statistical heterogeneity was assessed using the I^2 test. Meta-analyses were performed using random-effects models with significant heterogeneity ($I2 > 50\%$) and using fixed-effects models if nonsignificant heterogeneity was found ($I2 \leq 50\%$) [15].

2.7. Focused question

In this systematic review, we focused on the effect of PBM on the alignment phase instead of space closure. Based on this objective, we systematically evaluated the influence of PBM on the following factors: overall alignment time and alignment rate. Moreover, we investigated the causes of heterogeneity among studies by a clinical subgroup analysis.

3. Results

3.1. Search results and characteristics

Eight studies were included in this systematic review, involving five RCTs and three CCTs (Fig. 1). The characteristics of the included studies are shown in Table 2.

For the orthodontic mechanics, there were differences in the size of the first arch wire, and the sequence of following arch wire progression, although the same finish criteria, Little's Irregularity Index less than 1 mm, was used in clinical assessment. Six studies used 0.014-in NiTi to start the alignment procedure, while Ghaffar et al. and Shehawy et al. chose 0.016-in NiTi and 0.012-in NiTi as the first arch wire, respectively.

In terms of PBM intervention, five studies used overall alignment time as an outcome indicator, while two studies chose alignment rate. Shaughnessy et al. published their results with the above two outcome indicators. Other characteristics of PBM intervention, including equipment, energy density, irradiation points, and PBM sessions, differed among these studies. Five studies employed LLLs equipment at the wavelength range of 450–940 nm, while 3 trials employed LEDs equipment at a wavelength of 850 nm. The total energy density used per month also showed a huge difference, ranging from 48 to 3240 J/cm^2, across these studies. In addition, researchers chose different anatomical positions as the irradiation points in their trials, including the surface of the cheek, root area of anterior teeth, and labial vestibule.

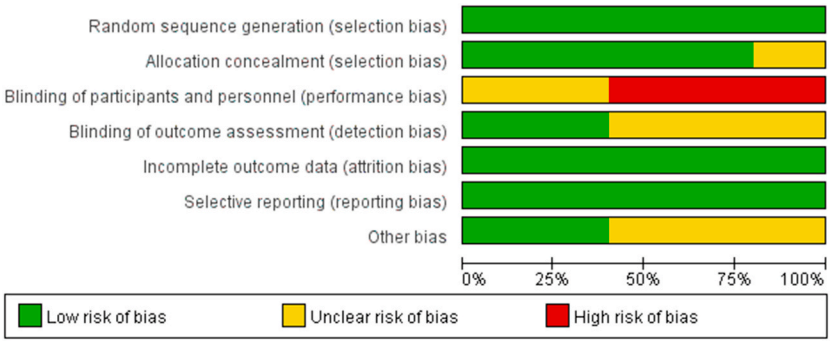

Fig. 2. Risk-of-bias graph.

3.2. Risk of bias

The risk of bias of the included RCTs is shown in Figs. 2 and 3. Due to the nature of these studies, blinding of the patients and operators was almost impossible. Therefore, the domain of blinding of participants and personnel was not defined as having a low risk of bias in all studies. Out of the five RCTs, three trials were assessed as high risk of bias, and two were unclear risk of bias.

The quality of CCTs is shown in Table 3. Included CCTs had a low risk of bias for most of the criteria evaluated, except for bias in failure to follow up, study size, and adequate control group. All CCTs were assessed as high-quality trials with a low risk of bias.

3.3. Level of evidence

The GRADE assessment of evidence resulted in a low quality of evidence. There were serious concerns with the risk of bias and inconsistency domains. (More details are provided in Table 4).

3.4. The efficacy of PBM

The results of the meta-analyses are shown in Figs. 4 and 5. All included studies evaluated the difference in dentition and demographic characteristics between the experimental and control groups and showed nonsignificant differences. Out of the eight trials, most of them reported positive results showing that PBM intervention could accelerate tooth movement in alignment procedures and reduce the treatment duration, except the study of Shehawy et al. [2–4,16–20].

Six of the eight included studies measured the same outcome data (alignment time). The meta-analysis of these six studies involving 237 arches showed that the application of PBM significantly reduced the treatment time of the alignment process, compared with the control group. The standard mean difference of LEDs was −33.60 (95% CI −68.43, 1.23), and the heterogeneity was considerable (P = 0.09, I2 = 65%). The standard mean difference of LLLs was −56.37 (95% CI −62.50, −50.24), and the heterogeneity was negligible (P = 0.61, I2 = 0%). The overall *P* values < 0.00001.

Three of the eight included studies measured the same outcome data (alignment rate). The meta-analysis of three studies involving 148 arches showed that the application of PBM significantly increased the rate of tooth movement, compared with the control group. The standard mean differences were 0.74 (95% CI 0.54, 0.95) and 0.08 (95% CI −0.33, 0.49) with LEDs and LLLs, respectively, with an

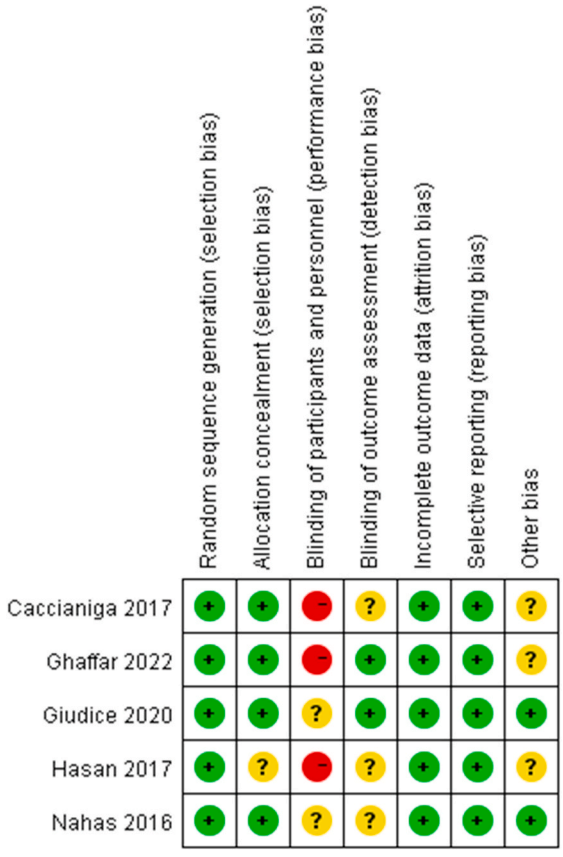

Fig. 3. Risk-of-bias summary.

Table 3
Methodological index for controlled clinical trials.

Studies (first author)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Total
Kau al	2	2	2	2	2	2	2	1	1	2	2	2	22/24
Shaughnessy al	2	2	2	2	2	2	2	2	1	2	2	2	23/24
Shehawy al	2	2	2	2	2	2	0	2	1	2	2	2	21/24

Study categories: Q1: A clearly stated aim; Q2: Inclusion of consecutive patients; Q3: Prospective collection of data; Q4: Endpoints appropriate to the aim of the study; Q5: Unbiased assessment of the study endpoint; Q6: Follow-up period appropriate to the aim of the study; Q7: Loss to follow up less than 5%; Q8: Prospective calculation of the study size; Q9: An adequate control group; Q10: Contemporary groups; Q11: Baseline equivalence of groups; Q12: Adequate statistical analyses.

overall P value $= 0.004$.

4. Discussion

One novelty of this systematic review is that we conducted an analysis of PBM effectiveness in the alignment phase. Although the efficacy of PBM on tooth movement in the alignment phase has not been supported by any published systematic review, there were several perspectives referring to PBM in the space closure process. First, PBM intervention can accelerate the rate of canine retraction, thus reducing the treatment duration of space closure. Studies of Fini et al. and Imani et al. offered evidence that orthodontic movement of human canines was accelerated by PBM based on the results of many RCTs and quasi-RCTs. Second, the biological impact of PBM relies upon the irradiation dose and appropriate protocols [7,21]. According to published literature, the wavelengths of LLLs and LEDs are similar, ranging from 750 to 920 nm [22–24]. In contrast, the type of light equipment, energy density, and application protocol were not similar among these studies. Most of the researchers conducted their studies with a total energy density of 50–250 J/CM2 per month. PBM was applied to patients 2–4 times a month in almost all trials. However, most studies suggested the efficacy of PBM on tooth movement, despite the inconsistent protocols.

In this review, our results showed that PBM may reduce treatment duration by accelerating tooth movement in the alignment procedure, which was consistent with the results in the space closure phase. Our study provided the missing pieces of published research by offering evidence that PBM played a positive role not only in tooth movement in the space closure phase but also in the alignment procedure. Therefore, based on the combination of this review and previous literature, PBM may accelerate tooth movement throughout the whole orthodontic process. In addition, this review also offered evidence that may promote the establishment of comprehensive guidance for the widespread use of PBM in orthodontic practices.

Another novelty of this systematic review is that we performed a clinical subgroup analysis to investigate the causes of heterogeneity. Evaluation of both overall alignment time and alignment rate presented high heterogeneity among the included studies. Out of the clinical factors potentially related to efficacy, we found that 'type of PBM equipment' was significantly associated with heterogeneous results across studies. However, the heterogeneity was negligible ($P = 0.61$, $I2 = 0\%$) with LLLs after subgroup analysis, while considerable heterogeneity still existed with LEDs in the evaluation of overall alignment time. The remaining heterogeneity with LEDs may be related to the impossibility of obtaining the same values of Little's Irregularity Index for all patients at treatment commencement. Changes in the heterogeneity in alignment rate evaluation supported our hypothesis. The heterogeneity with LEDs was negligible after subgroup analysis in the evaluation of alignment rate.

In addition, the clinical trials included in this review presented great heterogeneity of irradiation parameters and PBM protocols, thus leading to inevitably heterogeneous results. For this reason, it was not possible to define the best protocol for PBM use in orthodontic practice. Future studies are needed to explore a standard PBM protocol to achieve more efficient tooth movement in patients undergoing orthodontic treatment [25].

5. Conclusion

This systematic review analyzed clinical evidence regarding the PBM efficacy of tooth movement in alignment procedures. The results showed that PBM accelerated tooth movement, compared with the control group. As lower heterogeneity was achieved after subgroup analysis, the type of PBM equipment may be associated with the efficacy. The best protocol for PBM application in orthodontic practice has not yet been established due to the great heterogeneity of irradiation parameters and PBM protocols in the published literature. Future studies are needed to explore a standard and efficient PBM protocol for accelerating tooth movement and reducing treatment duration.

Author contribution statement

Tu Huang; Zihao Wang and Juan Li: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Table 4
Results of quality assessment across studies.

Quality assessment							No of patients		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PBM	Control		
Alignment Time (Better indicated by lower values)										
6	randomized trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	122	115	ÅÅOO LOW	IMPORTANT
Alignment Rate (Better indicated by lower values)										
3	randomized trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	106	42	ÅÅOO LOW	IMPORTANT

[1] The heterogeneity was considerable among these studies.
[2] No blinding of the patients and operators.

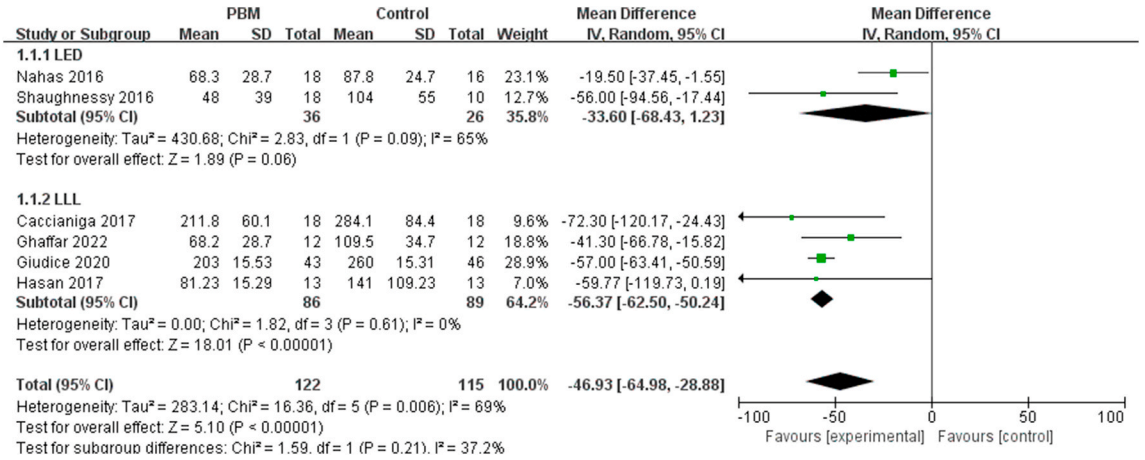

Fig. 4. Forest plot of the overall alignment time.

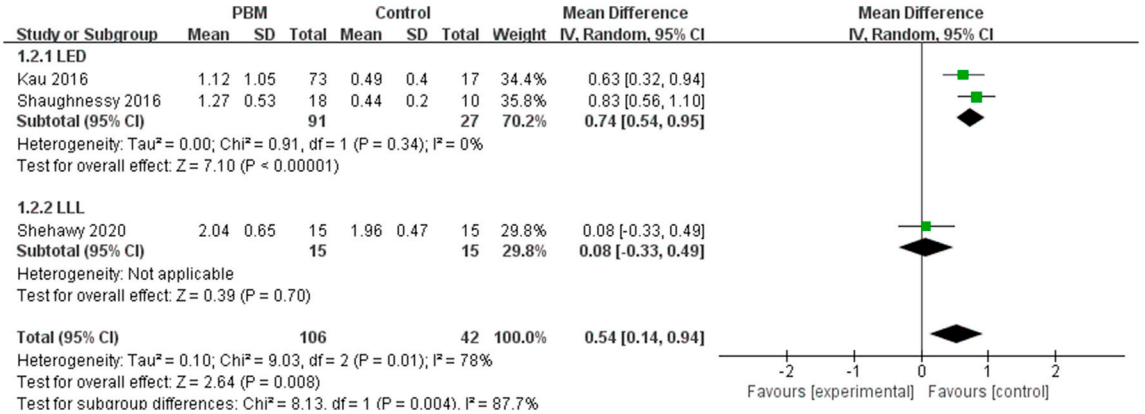

Fig. 5. Forest plot of the alignment rate.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no competing interests.

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