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Systematic Review

Effect of Photobiomodulation Therapy Dosage on Orthodontic Movement, Temporomandibular Dysfunction and Third Molar Surgery Outcomes: A Five-Year Systematic Review

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Abstract: (1) Background: This five-year systematic review seeks to assess the impact of oral and perioral photobiomodulation therapies (PBMTs) on the adjunctive management of deeper tissue biofunction, pathologies related to pain and inflammatory disorders and post-surgical events. (2) Methods: The search engines PubMed, Cochrane, Scopus, ScienceDirect, Google Scholar, EMBASE and EBSCO were used with appropriate Boolean operatives. The initial number of 14,932 articles was reduced to 261. Further exclusions performed to identify PBM therapy in third molar surgery, orthodontic and TMJ articles resulted in 19, 15 and 20 of these, respectively. Each paper was scrutinised to identify visible red–NIR laser wavelength PBM applications, concerning dosimetry and outcomes. (3) Results: A dataset analysis was employed using post hoc ANOVA and linear regression strategies, both with a Bonferroni correction ($p < 0.05$). The outcomes of articles related to oral surgery pain revealed a statistically significant relation between PBMT and a positive adjunct ($p = 0.00625$), whereas biofunction stimulation across all other groupings failed to establish a positive association for PBMT. (4) Conclusions: The lack of significance is suggested to be attributable to a lack of operational detail relating to laser operating parameters, together with variation in a consistent clinical technique. The adoption of a consistent parameter recording and the possible inclusion of laser data within ethical approval applications may help to address the shortcomings in the objective benefits of laser PBM.

Keywords: dentistry; laser; orthodontics; photobiomodulation; systematic review; oral surgery; TMJ

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1. Introduction

Photobiomodulation therapy (PBMT), formerly known as low-level laser therapy, is the application of sub-ablative photonic energy to a tissue target for the therapeutic relief of pain and inflammation [1]. The influence of laser photobiomodulation (PBM) as a significant source of adjunctive therapy in clinical dentistry has now received growing acceptance through peer-reviewed research [2]. From early in vitro cellular analyses, the fundamental and downstream effects of the lower levels of photonic energy were observed to be below the threshold associated with damage to the cellular apparatus to be examined [3]. This has allowed for prescriptive applications of chosen wavelengths and appropriate light doses to be applied, both to influence the healing of post-surgical oral and dental conditions and as a stand-alone therapeutic management of inflammatory and syndromic pathologies [4].

The laser photoexcitation of target cellular structures may be seen as ineffective if the photon stream energy density is too low to influence any reaction; equally, if excessively high photoexcitation is delivered, such levels may prove cytotoxic. Between these extremes, an ascending positive reaction, termed biostimulation, contributes to increased cell performance [5]. Recent reviews of evidence-based data have also presented arguments to indicate a zone of inhibition consequent upon a light dose above an upper limit of

biostimulation, but within a tolerable zone below that of any damaging cell effects [6]. This has been termed a hormetic response, and it is a generally favourable stress-induced characteristic of the response of many biological processes upon exposure to increasing amounts of a stressor [7].

Tissue trauma, surgery or pathology characterised by a level of inflammation as a primary reaction, associated negative aspects of pro-inflammatory biochemical and cellular mediators and aspects of inflammation including tissue swelling, pain and structural disruption all pose major clinical challenges to achieving resolution [8,9]. The three primary outcomes of PBM therapy within the confines of a defined clinical strategy are the mitigation of reduced inflammation and pain, analgesia and a process of optimal wound healing within the biological capacity of the tissues to respond, which is a process best described as uneventful [10].

Consensus on the fundamental principles that underpin PBM therapy to normal as well as impaired or dysfunctional tissue suggest that the application of a therapeutic light dose leads to a cellular response, mediated by mitochondrial mechanisms along with downstream effects within anatomical sites [11]. Studies have shown that these changes can modify the peak and duration of the pain and inflammatory responses to trauma or infection, as well as promote good quality, "uneventful" healing and tissue repair [12,13].

Mitochondria represent significant operators of many cellular physiological processes, within the inner membrane of which are located a series of five molecular complexes known collectively as the Electron Transport Chain (ETC). Within the mitochondrion, the ETC creates an electrochemical gradient that leads to the production of adenosine triphosphate (ATP) through a complete system known as oxidative phosphorylation [14]. A by-product of this series of reactions stimulates the manufacture and release of nitric oxide ($NO^{\bullet}$) and reactive oxygen species (ROS), which in turn have an impact on local extracellular vasodilation and the cellular gene transcription of growth factors and local extracellular vasodilation, respectively [15]. Extended concepts of secondary intracellular effects include accentuated pro-mitotic pathways that promote cell division processes as well as enhance cellular resistance to stress or positive cell function. From this early work extended in vitro and in vivo animal studies, which led to human trial studies, together, these applications have provided an evidence base for the direct and indirect outcomes of a chosen specific sub-ablative damage threshold photoirradiation parameters dose [16]. Table 1 provides a summary of tissue and biochemical factors that may be influenced through PBM action.

Table 1. Growth factors associated with PBM therapeutic irradiation, molecular targets and recorded outcomes.

Mediator	Molecules	Action and/or Effects
Growth factors	GDNF, FGF, β FGF, IGF-1 KGF, PDGF, TGF-β, VEGF	Proliferation, Differentiation, Angiogenesis, Migration, Chemotaxis
Anti-inflammatory cytokines	IL-2, IL-4, IL-8, IL-10	Differentiation, Proliferation, Immune activation, Chemotaxis, Angiogenesis
Pro-inflammatory cytokines	IL-1a, IL-1b, IL-6, TNF-α, PGE2, COX2	Stimulate and accelerate inflammation, Angiogenesis, Promote cell migration, Anti- and pro-apoptosis
Heat shock proteins	HSP90, HSP70, HSP25	Chaperone protein, Enhance cell survival
Matrix metalloproteinases	MMP2, MMP9	Cell survival, Prevention of terminal differentiation, Tissue remodelling
Small molecules	ATP, GSH, ROS, Ca^{2+}, NO, H^{+}	Normalisation of cell function; Migration; Angiogenesis; Proliferation

Source: adapted from Kim WS, Calderhead RG. [16]. Abbreviations: GDNF—Glial cell line-derived neurotrophic factor; FGF—Fibroblast growth factor; IGF-1—insulin-like growth factor 1; KGF—Keratinocyte growth factor; PDGF—Plasma-derived growth factor; TGF-β—Transforming growth factor-β; VEGF—Vascular endothelial growth factor; IL—Interleukin; TNF-α—Tumour necrosis factor-α; PGE2—Prostaglandin E2; COX2—cyclooxygenase-2; HSP—Heat shock protein; MMP—Metalloproteinase; ATP—Adenosine triphosphate; GSH—Glutathione; ROS—Reactive oxygen species.

The totality and extent of PBM-mediated activity remains the product of multi-factorial elements, such as the target tissue, target pathology, applied photonic dose (at surface/at depth), wavelength, irradiance (W/cm^2), spot (irradiance) area size, spectral beam profile, gated or continuous wave modes, dose repetition and total energy delivered. Published studies have highlighted the inconsistency of PBM delivery, with a lack of consensus agreement in all clinical aspects of light therapy, resulting in a sizable contribution toward the wide variation in the reported supportive outcomes of PBMT and consequent potential lack of consensus regarding its effectiveness [17].

Opinions have been well established, through peer-review publications, to support the wide scope of PBM within all aspects of clinical dentistry [18–21].

The purpose of this systematic review was to consider three clinical entities in commonplace dental practice, each with differing aetiologies or reasons for treatment, and where randomised clinical trials exist to evaluate the adjunctive support of PBM in affecting the outcome. These are listed as follows:

a. Temporomandibular joint dysfunction syndrome (TMJDS) may encompass a mixed and often complex aetiology, but common symptoms generally arise through muscle pain and spasms together with degrees of trismus; this may be representative of both an acute as well as a chronic inflammatory condition.
b. The surgical removal of mandibular third molars, for whatever reason, may involve the incision and raising of a full muco-gingival flap and bone removal to assist in the location and delivery of the tooth. Such surgical intervention will provoke an acute inflammatory reaction, notably through observed post-operative swelling, trismus and pain.
c. Orthodontic treatment—embracing appliance-based tooth movement and/or tooth arch expansion—offers an opportunity for otherwise stable and healthy supporting tissue to be reorganised to allow the passage of teeth to a new prescribed location in the dental arch. Inasmuch, there may be induced low-stress inflammation associated with such a therapy, and some levels of pain and discomfort are often experienced. In essence, however, the contribution of PBM therapy is claimed to accentuate the osseous and dental supportive soft tissue cellular activity and to promote reductions in pain episodes and the overall active treatment time.

Since each group may exhibit a differing symptomology, if at all, the application of laser PBM may be assumed to promote differing accents of tissue activity and responses, and thus provide some guidance to optimise the delivery parameters to be consistent with the outcome.

The null hypothesis is that within these three distinct therapy groups, each based upon differing degrees of an acute/chronic inflammatory response and PBM application technique, no appreciable differences exist in the outcome of such adjunctive therapy. For each treatment group of published RCTs, the following basic questions were considered:

- Does PBM positively affect and augment the successful outcome of treatment, commensurate with a statistically significant comparison when compared to a control?
- Where inconsistency exists between the three groups, is the outcome of PBM therapy predictability affected according to the underlying status of the treatment area in terms of inflammation or pathology?
- Where inconsistency exists between the groups, is the effectiveness of PBM affected by disparity in light-dose, irradiation spot size or other laser operating parameters?

In general, a systematic review, through the analysis of accepted published data, criteria and conclusions, may be seen as an evolving confirmation of the contemporary evidence base. The limitations of such an analysis derive from the completeness and discipline of the randomised clinical trials, concerning the delivery of the essentials of study reproducibility.

2. Materials and Methods

2.1. Protocol and Registration

The protocol of the present study was submitted and registered with the International Prospective Register of Systematic Reviews (PROSPERO—CRD42024503029) and followed the guidelines of the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for reports [22].

The PICOS questions relating to clinical studies are as follows [23]:

(i) P (Participant): adult patients who received active clinical treatment, associated with one of the three groups of therapy.
(ii) I (Intervention): laser-activated in-office adjunctive PBM therapy.
(iii) C (Control): dental treatment undertaken to address the presenting clinical need, but without adjunctive PBM therapy.
(iv) O (Outcome): clinical assessment of improved outcome and reduction in negative symptoms.
(v) S (Study Type): Randomised clinical trial peer-reviewed published studies.

2.2. Search Strategy

An electronic database search was performed relating to the effects of laser PBM application associated with surgical tooth removal, TMJDS or orthodontic treatment. The data platforms used were ScienceDirect, PubMed, Google Scholar, Cochrane, Scopus and EBSCO, using the following MeSH terms and Boolean operators: (Photobiomodulation OR PBM OR LLLT OR Low level Laser) AND (soft tissue OR oral surgery OR buccal mucosa) for oral surgery, (Photobiomodulation OR PBM OR LLLT OR Low level Laser) AND (orthodontic OR maxillary expansion) for orthodontic tooth movement, (Photobiomodulation OR PBM OR LLLT OR Low level Laser) AND (TMJ) for TMJ, published after 2018. The last search for recently published papers was carried out in February 2024.

The initial article scanning delivered a total of 4491 for oral surgery, 5104 for orthodontic tooth movement and 5337 for TMJ.

After removing ineligible trial articles and duplicated reports, the remaining articles were 82 for oral surgery, 87 for orthodontic tooth movement and 92 for TMJ.

Subsequently, the titles and abstracts of these articles were independently screened by three reviewers (SP, EA, VM), using the inclusion and exclusion criteria listed below. Any disagreements that arose during this process were resolved through discussion between the researchers involved.

The inclusion criteria were as follows:

- Randomised clinical trials;
- Laser PBM therapy associated with wavelengths in the range of 445–1064 nm;
- Articles were written in the English language;
- Control group and appropriate conventional non-PBM therapy;
- A minimum of 10 patients/samples per group;
- An adequate and appropriate protocol description.

The exclusion criteria were as follows:

- Laser wavelength outside the range 445–1064 nm;
- Case studies;
- Narrative review papers;
- Languages other than English;
- Pilot studies and/or case series;
- Experimental studies;
- Animal studies;
- Conference presentation papers or book chapters;
- Editorial articles or opinions;
- Short notes or comments in erratum;
- Press articles in the press;

- Non-retrievable studies.

After the implementation of these criteria, 54 studies were included in this systematic review, spread across oral surgery (n = 19), orthodontic tooth movement (n = 15) and TMJ (n = 20).

In accordance with the PRISMA 2020 statement [22], the details of the selection criteria are presented in Figures 1–3.

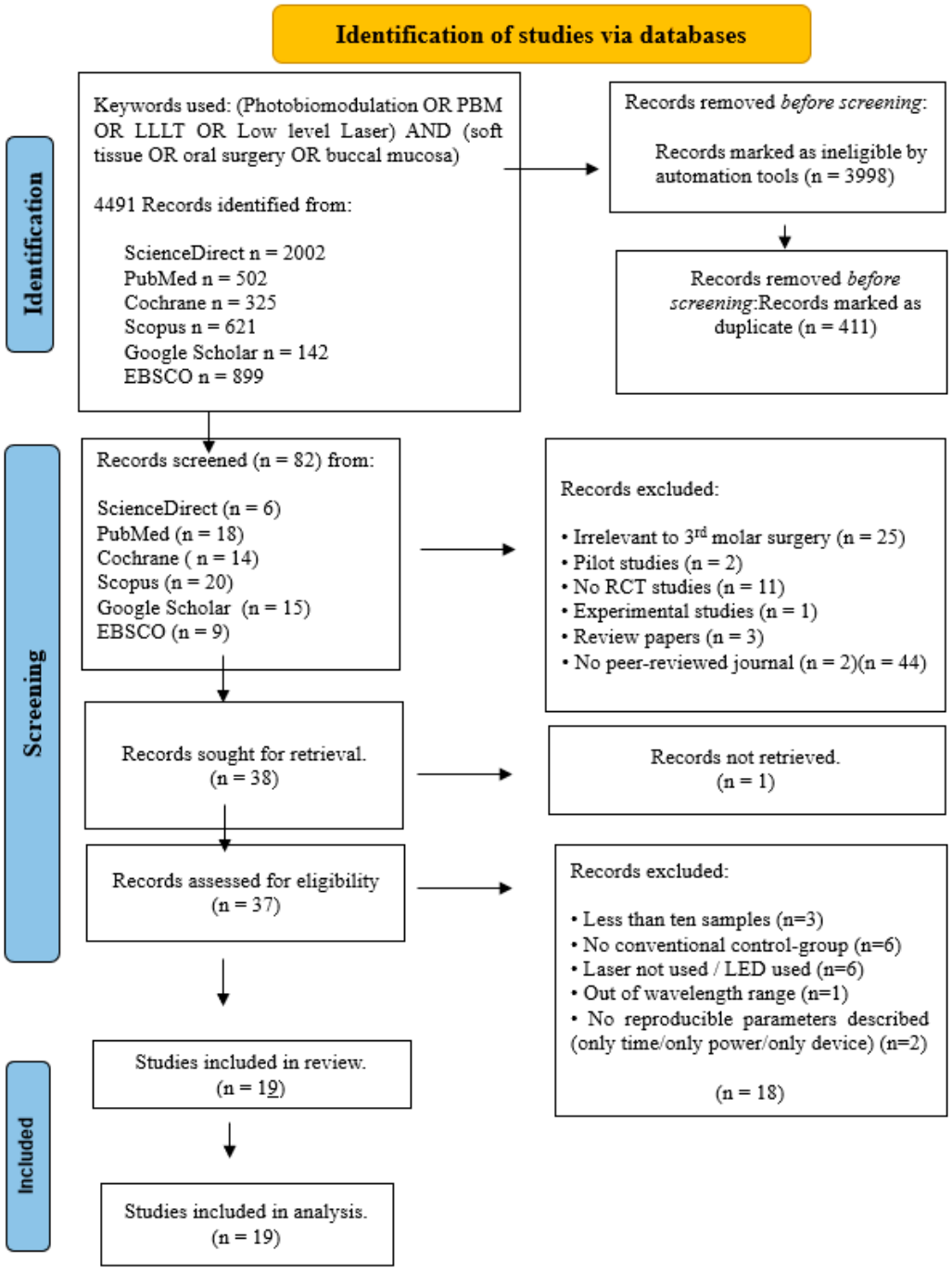

Figure 1. PRISMA flow-chart of selected criteria for the included oral surgery studies.

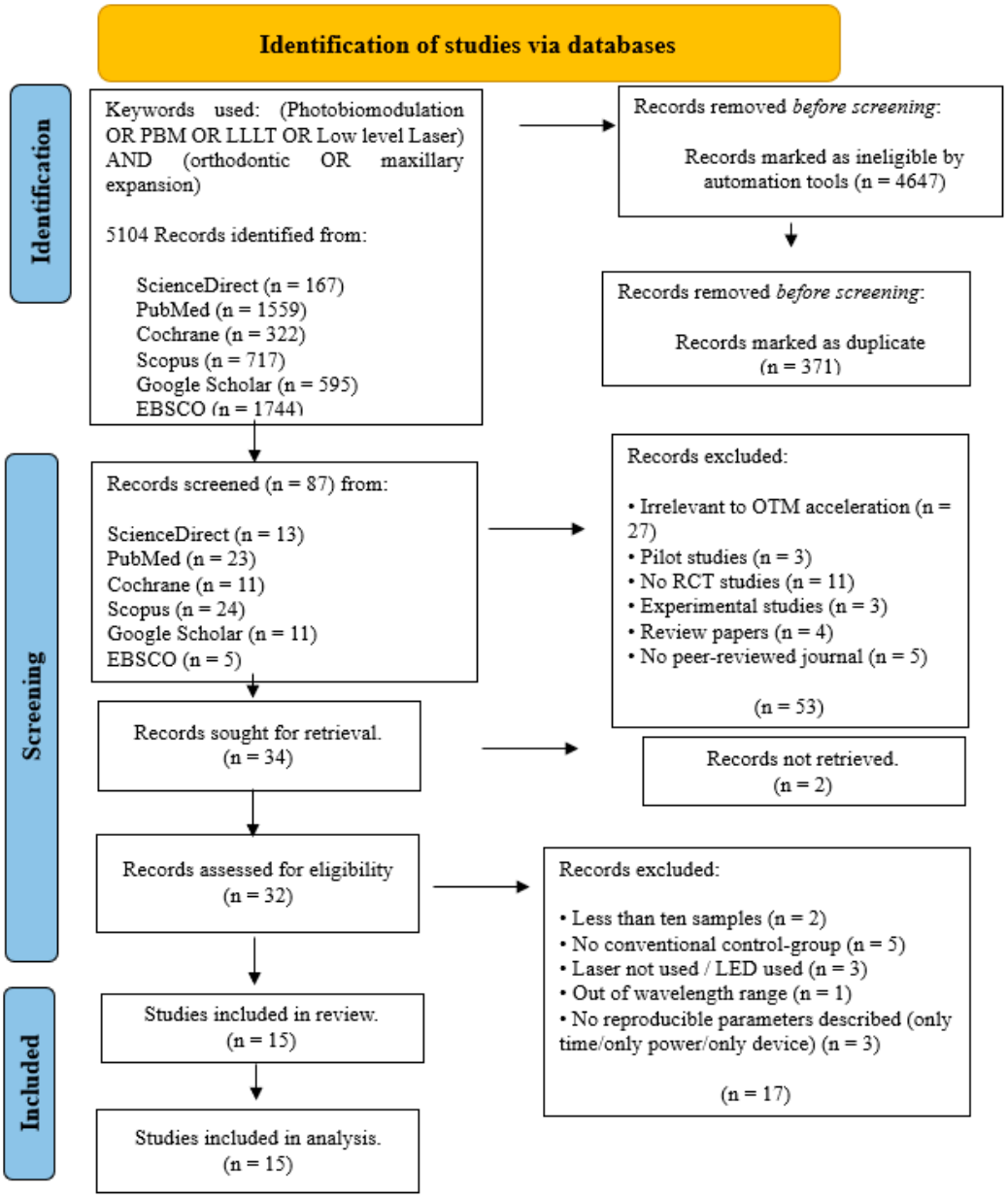

Figure 2. PRISMA flow-chart of selected criteria for the included orthodontic studies.

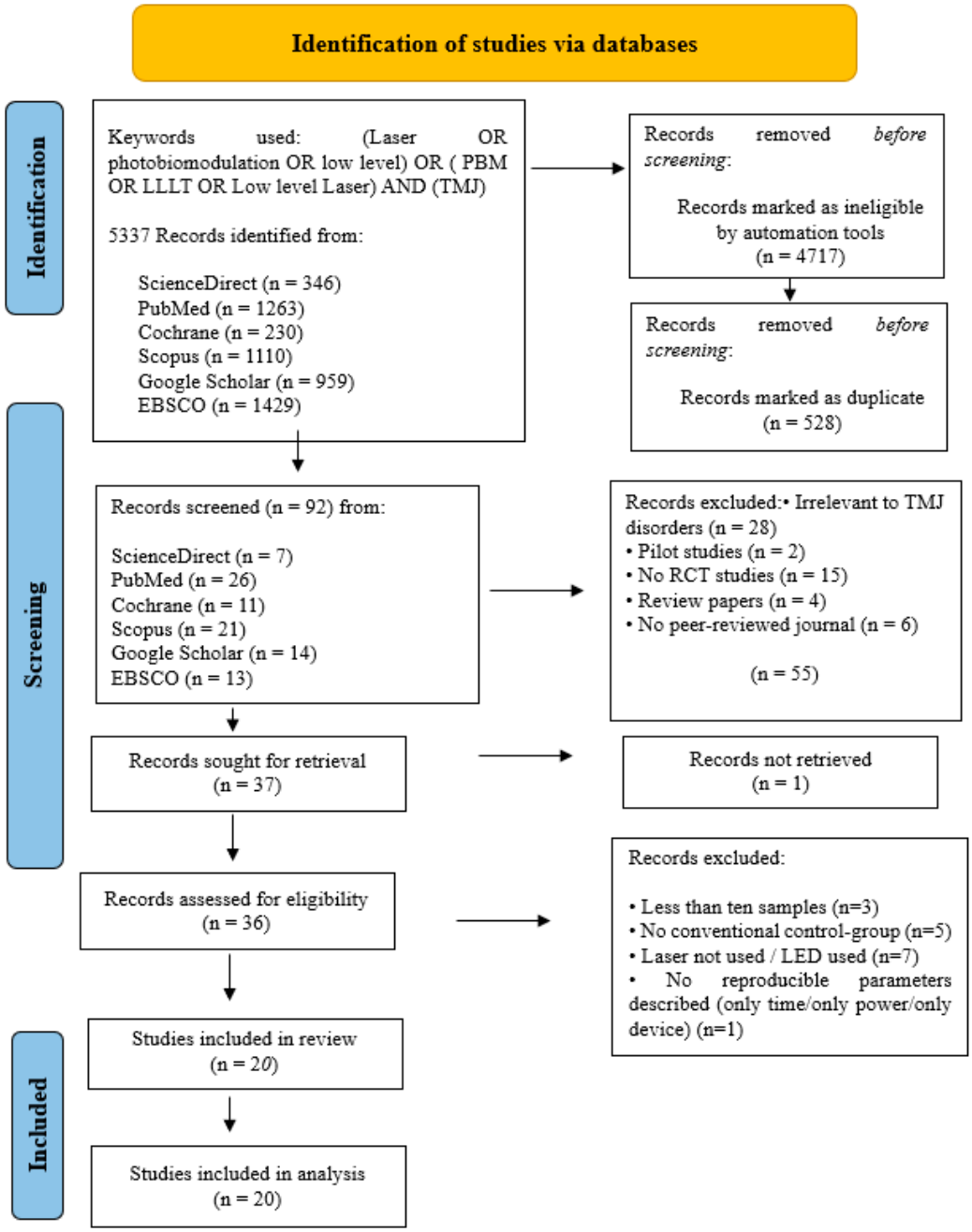

Figure 3. PRISMA flow-chart of selected criteria for the included TMJ studies.

2.3. Data Extraction

Data were independently extracted by the same three reviewers (S.P., E.A. and V.M, working independently) based on the following factors:

- Origin;
- Patient numbers represented in control and test groups;
- Use of randomisation and blinding;
- Laser wavelength applied;
- Laser operation parameters;
- Fluence (as calculated);
- Outcome (statistical significance).

2.4. Quality Assessment

A risk of bias assessment of all included articles was performed following the data extraction by the same independent reviewers (S.P, E.A. and V.M.). The requirements of the systematic review allowed the Cochrane Risk of Bias tool [24] to be adequately modified. Applying the questions listed below provided either positive or negative responses, and these were tabulated and quantified to provide statistically relevant allocations of the bias risk.

The variables evaluated were the following:

- Randomization employed;
- Existence of sample size calculation and required sample number included;
- Blinding employed;
- Baseline situation similar for all groups;
- Laser operating parameters appropriately described, and any associated calculations correct;
- Optimal fluence applied;
- Power meter used to calibrate the laser used;
- Statistical analysis able to be applied to numerical results;
- Outcome data complete;
- Correct interpretation of data and results.

The determination of the degree of bias was based on the relative number of positive and negative responses, with the classification as follows:

- High risk: 0–4;
- Moderate risk: 5–7;
- Low risk: 8–10.

In case of any disagreements arising, these were resolved through discussions between the researchers involved.

3. Results

The results were classified according to each dental field as follows.

3.1. Oral Surgery

3.1.1. Primary Outcomes

The primary objectives of this systematic review were (a) to critically appraise the PBM irradiation protocols and (b) to examine the PBM treatment efficacy in terms of the pain, trismus and oedema reductions compared to those of the positive or negative control groups.

3.1.2. Data Presentation

The data extrapolated and evaluated from the included studies are displayed in Table 2.

Table 2. Data extraction for oral surgery studies.

Published Data by Study—PBM-Adjunctive Third Molar Oral Surgery						
Citation—Oral Surgery	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
De Oliveira, R., et al., 2021 [25]	RCT. Post extraction paraesthesia. Laser vs. laser acupuncture	60 pts (3 groups × 20). No placebo. (i) 20 medication—C (ii) 20 laser—LT (iii) 20 laser acupuncture—LA	808 nm	100 mW irradiation CW mode contact, punctual. Spot: 0.028 cm^2 acupuncture; 6 sites, same parameters.	26 points—1 cm apart (40 s per point). Irrad. 3.57 W/cm^2. 20 sessions (2 × week × 10 weeks)	T1: Before Tx/T 2:5 weeks T3: 10 weeks/ T1, T2: L = LA = C T3: L > LA > C p T1 > 0.05, T2 > 0.05, T3 0.003

Table 2. *Cont.*

Published Data by Study—PBM-Adjunctive Third Molar Oral Surgery						
Citation—Oral Surgery	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Souza, M., et al., 2023 [26]	RCT. Post-extraction OHRQoL. Laser PBM vs. aPDT vs. PBM + aPDT.	40 pts (4 groups × 10). No placebo. (i) 10 extractions without any additional treatment—C (ii) 10 extractions + aPDT (iii) 10 extractions + PBM (iv) 10 extractions + PBM + aPDT	aPDT—660 nm PBM—808 nm	aPDT: 100 mW CW, output energy fluence 300 J/cm^2, spot of 3 mm^2, irradiance of 3.33 W/cm^2 for 90 s PBM: 100 mW CW, output energy of 4 J, fluence of 133 J/cm^2, spot of 3 mm^2, and irradiance of 3.33 W/cm^2 for 40 s	PBM therapy appl. to vestibular and lingual gingiva. Contact/CW modes. Single administration	T0: At extraction, T1: 7 days, T2: 30 days. +ve OHIP-14 scores sig. different in T0—T1 and T0—T2 for all ($p < 0.001$). PBM + aPDT > PBM > other groups. Groups (ii), (iii), (iv) sig. +ve OHRQoL vs. control at T1 (p 0.01–0.043). Best: T1 and T2 with PBM + aPDT.
Momeni, E., et al., 2021 [27]	RCT. Impact of laser PBM on post-op pain, trismus	25 pts. 1 tooth per side. Each pt received (i) PBM to one side and (ii) placebo to contra lateral side.	940 nm	Application/point time 30 s. Fluence at each point (J/cm^2), 10 Power (W), 0.5 CW	Application technique, non-contact. Three application points (three occlusal, buccal, and lingual). Laser applied only on extn day.	VAS pain every day post-op. No sig. diff. between the two groups. Trismus immediately after extn, 2nd and 7th day. No sig. diff. between the two groups ($p > 0.05$). Mean swelling did not differ significantly ($p > 0.05$).
Isolan, C., et al., 2021 [28]	RCT. Impact of laser PBM on post-op pain.	44 pts (101 extns) Random. No placebo. (i) Control (n = 50)—surgical removal (ii) Test (n = 51)—extn + laser PBM	808 nm	Output 50 mW CW. Spot area: 0.4 cm^2 Dose per point: 11 J. Total dose of 66 J.	Laser applied only on extn day. T0—extn day + 6 h T1—24 h; T2 48 h. 6 contact points 2-apical + cervical in buccal, lingual and occlusal.	PBMT showed stat. sig. effect ($p < 0.001$) on VAS pain at T0. Similar VAS pain was observed at T24 ($p < 0.001$) and T48 ($p < 0.001$). PBMT.
Asutay, F., et al., 2018 [29]	RCT. Impact of laser PBM on post-op outcome	45 pts. 3 groups: (i) n = 15 Control—ice (ii) n = 15 Test—laser PBM (iii) n = 15 Test—placebo PBM)	810 nm	Output power: 0.3 W CW, beam area: 3 cm^2, energy density: 4 J/cm^2, energy delivered: 12 J, irradiation time 40 s	Application Non-contact	VAS pain on days #2 and 7. Swelling on days #2 and 7. No stat. sig. differences between all groups for edema and trismus results ($p > 0.05$).
Bianchi de Moraes, M., 2020 [30]	RCT. Impact of laser PBM on post-op outcome	57 patients: 3 groups: (i) (low PBM) 19 (ii) (high PBM) 20 (iii) (placebo) 18	660 nm	For both laser groups, output: 30 mW CW, beam area: 0.03 cm^2, power: 0.03 W, application/point time: (i) 2.25/(ii) 7 s, (i) fluence: 10 J/cm^2, (ii) fluence: 30 J/cm^2	Laser application immediate on days #3 and 7. 4 application points: buccal/lingual/cervical/apical.	Post-op pain (VAS) and swelling. Periodontal condition at 6 months, all cf sham. Stat. sig. more effective in group #i—10-J/cm^2 laser protocol. ($p = 0.017$ for the 10-J/cm^2 group and $p = 0.001$ for the 30-J/cm^2 group)
Mohajerani, H., et al., 2021 [31]	RCT. Impact of laser PBM on post-op outcome	40 pts. 2 groups: (i) n = 20 extn control (ii) n = 20 extns + PBM (laser and LED) Placebo sham applied to control.	810 nm LED 632nm	Output: 500 mW CW. Fluence: 5 J/cm^2. Fluence: 2 J/cm^2	PBM applied immediately post extraction and 24 h later. Irradiation: 2 intraoral (1 lingual and 1 vestibular side of the wound and with 1 cm the from wound), 1 extraoral (masseter area)	Pain: days #3 and # 7 sig. less in PBM group ($p = 0.03$ and 0.01, respectively). Trismus: Sig. less in PBM group on day #3 ($p = 0.006$). On day #7, pain was not significant. Swelling: days #3 and #7 sig. less in PBM group ($p < 0.0001$).

Table 2. *Cont.*

Published Data by Study—PBM-Adjunctive Third Molar Oral Surgery						
Citation—Oral Surgery	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Nunes, C., et al., 2023 [32]	RCT. Impact of laser PBM on post-op outcome	22 pts (44 teeth). 2 groups: (i) n = 22 extn control (ii) n = 22 extn + laser PBM Placebo applied to control.	808 nm	Output: 100 mW CW. Beam diameter: 600 µm. 40 s per area.	PBM applied immed post extraction + 24 h later. Placebo, same. 8 applicat spots: E/O 4 and I/O 4.	VAS pain only sig. diff (PBM group) on days #4 and 5 ($p < 0.05$). Opening: no sig. diff. Edema: no sig. diff.
Feslihan, E., et al., 2019 [33]	RCT. Impact of laser PBM vs. steroid on post-op outcome	30 pts (60) teeth. 2 groups: (i) n = 30 extn control (ii) n = 30 extn + laser PBM No placebo	810 nm	Output: 300 mW CW Fluence: 6 J/cm^2	Applied extra-orally to insertion point of masseter for 60 s. PBMT repeated on post-operative days 1 and 2.	PBMT was also effective in post-operative pain, edema and trismus at a level similar to that of methylprednisolone. No sig. diff. ($p \leq 0.05$)
Nejat, A., et al., 2021 [34]	RCT. Impact of laser PBM on post-op osteitis + pain	80 pts. 2 extns per pt, 1 month apart. 2 groups: (i) Extn + PBM (ii) Extn + placebo	660 nm 810 nm	Output: 200 mW CW (beam area: ~0.64 cm^2, 312.5 mW/cm^2, 1 J, Fluence: 1.6 J/cm^2). 810 nm, 200 mW CW (400 mW/cm^2, 3 J, Fluence: 6 J/cm^2).	Applied at ~1 cm to 4 points on socket at tissue surface at 3 points on buccal and lingual gingiva, for 15 s. PBM immediately after extraction and repeated on days #2, 4, 6.	PBM therapy significantly reduced the rate of AO development. In addition, it significantly reduced pain and the need to take analgesics ($p \leq 0.05$).
Gururaj, S., et al., 2022 [35]	RCT. Impact of laser PBM on post-op outcome	26 pts. 2 groups: (i) n = 13 pts extn control (ii) n = 13 extn + laser PBM. Random allocation. No placebo	810 nm 660 nm	810 nm irradiation at 100 mW CW. 120 s prior and 60 s for both post-extraction irradiations.	810 nm to the site immed before and after extraction. Also, a transcutaneous irradiation of 660 nm 1-day post-op. Control group—no irradiation	Pain: VAS/Healing Turnbull and Howley's Index for soft tissue healing on the 7th and 21st days. *p*: <0.0001.
Ahrari, F., et al., 2020 [36]	RCT. Impact of laser PBM on post-op outcome	40 pts. 4 groups (4 × 10): (i) extn + 660 nm PBM (ii) extn + 810 nm PBM (iii) extn + 660 nm + 810 nm laser (iv) extn + placebo Random allocation.	660 nm 810 nm	Both 660 nm + 810 nm laser: 200 mW CW output. 30 s radiation to lingual, buccal and occlusal surfaces of the socket, 6 J/area. 660 nm fluence: 4.21 J/cm^2. 810 nm fluence: 21.4 J/cm^2.	LLLT was performed after 0.5–1 h of extraction and 2 days later.	VAS over 7 days. Healing evaluated on 3rd + 7th days. No sig. diff. in pain scores ($p > 0.05$). The between-group diffs. in healing scores were small and insignificant ($p > 0.05$). No greater effect vs. placebo laser for reducing the complications.
Tortorici, S., et al., 2019 [37]	RCT. Impact of laser PBM on post-op pain	41 pts. 2 third molar extns for each pt, 2 months apart. Random allocation	940 nm	Output 4 W CW Beam size of 2.8 cm^2 Energy per point was 1200 J in 10 s	First stage pts rec'd placebo laser (PL) 15 min before extraction and PBM immed. post-op. At 2 months—PBM 15 min pre-extn and PL immediately post op.	VAS at 4, 12, 24, 48, 72 and 168 h. Scores sig. lower in first stage at 4 h and 12 h post-op, VAS similar until 168 h. ($p < 0.05$).
Das, A., et al., 2022 [38]	RCT. Impact of laser PBM on post-op outcome	30 pts. 2 groups: (i) n = 15 pts extn control (ii) n = 15 extns + laser PBM. Random allocation. No placebo	660 nm	Output: 0.1-watt CW, Fluence: 6 J/cm^2, 60 s	Application immed. post op and on 1st day post op. I/O—B, L, M, D and E/O facial.	Pain: VAS/Healing on day #2 and 7. $p < 0.05$. PBMT effective in reducing post-op pain, edema and trismus
Ali, M., et al., 2019 [39]	RCT. Impact of laser PBM on post-op swelling, trismus	40 pts. 2 groups: (i) 20—extn + 980 nm PBM (ii) 20—extn + placebo Random allocation.	980 nm	Output 100 mW CW. 30 s per point.	Application at 6 points—3 E/O, 3 I/O.	2nd and 4th day sig. diff in swelling ($p = 0.05$). No sig. diff in trismus.
Ferreira, G., et al., 2022 [40]	RCT. Impact of laser PBM on post-op outcome	21 pts. 42 teeth. (i) 21—extn + PBM (ii) 21—extn + placebo 15-day interval between sides. Random allocation.	660 nm 789 nm	Output: 660 nm, 20 mW CW. I/O, 5 J/cm^2, 10 s, 4 points Output: 789 nm, 60 mW CW. E/O: 30 J/cm^2, 20 s, 8 points	PBM immed. post-op (T1), 24 (T2) and 48 (T3) hours	Pain control, swelling and trismus intensity at T1, T2, T3 and 7 days Pain: no sig. diff. ($p = 0.909$) No differences in swelling ($p = 0.958$) or trismus ($p = 0.837$)

Table 2. *Cont.*

Published Data by Study—PBM-Adjunctive Third Molar Oral Surgery						
Citation—Oral Surgery	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
El Saeed, A., et al., 2020 [41]	RCT. Impact of laser PBM on post-op outcome	20 pts. 40 teeth. (i) 20—extn + PBM (ii) 20—extn + placebo 3-week interval between sides. Random allocation	980 nm	Output: 0.5 W CW, 50 J total Beam: 12 cm^2 Fluence: 4 J/cm^2	Single application E/O immediately post op.	Swelling, trismus and VAS pain. Sig. diff. between PBM and placebo sides $p > 0.001$
Peimani, A., et al., 2018 [42]	RCT. Impact of laser PBM on post-op outcome	30 pts. 2 groups (n = 15): (i) extn + PBM (ii) extn + placebo 3 week-interval between sides. Random allocation	980 nm	Output: 0.5 W CW. Beam: 7 mm dia. Fluence: 39.06 J/cm^2, 15 J total per site	Single application. E/O mandible. I/O B, L, O. 30 s per site.	Pain, trismus, QoL. Pain VAS day #2–7. No sig. diff in any measurable parameters ($p \leq 0.05$).
Fakour, S., et al., 2020 [43]	RCT. Impact of laser PBM on post-op outcome	40 pts. 2 groups: (i) n = 20 pts extn control (ii) n = 20 extn + laser PBM. Random allocation. No placebo	980 nm	Output: 200 mW CW for 60 s per site. Fluence: 12 J/cm^2	Single application. I/O B and L. E/O angle of jaw.	Trismus and facial swelling assessed on day #2 and 7. No significant positive effects on reducing the post-operation complications.

3.1.3. Quality Assessment

The risk of bias (ROB) assessment results for the oral surgery studies are presented in Table 3.

Table 3. Modified risk of bias table for oral surgery studies.

Modified Risk of Bias—Oral Surgery (n = 19)											
Citation	**Randomisation**	**Sample Size Calc and Number Required**	**Blinding**	**Baseline Situation Similar for All Groups**	**Laser Parameters Complete/Calculations Correct**	**Optimal Fluence Applied**	**Power Meter Used**	**Numerical Results (Statistics)**	**No Missing Outcome Data**	**Correct Assessment of Results**	**Total**
de Oliveira R et al. [25]	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Souza M et al. [26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	9
Momeni E et al. [27]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Isolan C et al. [28]	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	7
Asutay F et al. [29]	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Bianchi de M et al. [30]	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	7
Mohajerani H et al. [31]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Nunes C et al. [32]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7

Table 3. *Cont.*

Modified Risk of Bias—Oral Surgery (n = 19)											
Citation	**Randomisation**	**Sample Size Calc and Number Required**	**Blinding**	**Baseline Situation Similar for All Groups**	**Laser Parameters Complete/Calculations Correct**	**Optimal Fluence Applied**	**Power Meter Used**	**Numerical Results (Statistics)**	**No Missing Outcome Data**	**Correct Assessment of Results**	**Total**
Feslihan E et al. [33]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8
Nejat A et al. [34]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9
Gururaj S et al. [35]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6
Ahrari F et al. [36]	Yes	No	Yes	Yes	No	No	No	Yes	No	Yes	5
Tortorici S et al. [37]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6
Das A et al. [38]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Ali M et al. [39]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6
Ferreira G et al. [40]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8
El Saeed A et al. [41]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	8
Peimani A et al. [42]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9
Fakour S et al. [43]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6

The following are revealed in Table 3:

- Low risk of bias in 6/19 of the articles (31.6%):
  - One [34] scored 9/10;
  - Five [25,26,33,40,42] scored 8/10.
- Moderate risk of bias in 13/19 of the articles (68.4%):
  - Seven [27–32,38] scored 7/10;
  - Five [35,37,39,41,43] scored 6/10;
  - One [36] scored 5/10.
- High risk of bias in none of the studies.

Overall, the mean ± standard error (SEM) Cochrane risk of bias score parameter was 7.00 ± 0.23 out of a perfect value of 10 [95% confidence intervals: 6.52–7.48].

A power meter was employed in only one of the studies. The other negative answers most commonly found concerned (a) laser operating parameters described and correct calculations, and (b) optimal fluence applied, followed by (c) the sample size calculations and numbers included, (d) all relevant outcome data included and (e) a baseline situation similar for all groups.

3.1.4. Data Analysis

It is evident that a wide variety of laser irradiation protocols have been performed. Regarding the wavelengths applied, the vast majority were in the near-infrared range (789–980 nm), while five studies [31,34–36,40] examined a combination of red (632 nm or 660 nm) and infrared (810 nm) wavelengths.

As far as the other parameters are concerned in most of the studies, fluence was up to 30 J/cm^2, treatment was performed in multiple repetitions, and the application was executed either intra-orally, or in a combination of intra- and extra-orally.

As for the treatment outcomes observed, 12/19 studies (63.2%) [25,26,28,30–35,38,39,41] presented a positive result, while 7/19 (36.8%) [27,29,36,37,40,42,43] showed no difference with the control group.

3.2. Orthodontic Movement

3.2.1. Primary Outcomes

The primary goals of this systematic review were (a) to critically appraise the PBM irradiation protocols and (b) to examine the PBM treatment efficacy in terms of speed of tooth movement compared to positive or negative control groups.

3.2.2. Data Presentation

The data extrapolated and evaluated from the included studies are displayed in Table 4.

Table 4. Data extraction for orthodontic studies.

Published Data by Study—PBM-Adjunctive Orthodontic Movement						
Citation—Ortho Movement	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Sagar, J., et al., 2020 [44]	RCT effect of PBM on ortho movement	10 pts. 2 groups: (i) 10—PBM (ii) 10—Control Random allocation	980 nm	Output: 0.3 W CW. Spot: 400 µm dia.	10 applications (5 B, 5 P) per exposure. Exp. time—15 s B, P. Total energy: 9 J (2 × 15 s × 0.3 W) PBM applied on days #0, 3, 7, 14. After every 15th day	Difference in the rate of displacements stat. sig. (p-value of 0.0026)
Farhadian, N., et al., 2021 [45]	RCT effect of PBM on ortho movement	56 pts. 3 groups: (i) 17—LED (ii) 20—PBM laser (iii) 19—placebo Random allocation	810 nm	Power: 100 mW CW. Tip was 3.1 mm, and the energy density was 4 J/cm^2.	PBM used on days 0, 3, 30 and 60 3 points, buccal, and 3 points, palatal; 3 s each point.	Retraction sig. higher in laser group than control (p = 0.004); indicated a 60.8% increase in the rate of OTM as compared with the latter.
Lalnunpuii, H., et al., 2020 [46]	RCT effect of PBM on ortho movement	65 pts. 3 groups: (i) 20 conventional ligation + PBM (ii) 20 self-ligation + PBM (iii) 25 Control Random allocation	660 nm	Output—8 mW CW Fluence—2.29 J/cm^2 Exposure time/point—10 s	2 doses—cervical third, 2 doses—apical third, 1 dose—centre of the root. B + L laser regimen was applied on days 0, 3, 7 and 14 Thereafter, irradiations were performed every 15th day	Statistically significant enhancement in the rate of OTM in the 2 experimental groups (p < 0.05)
Mistry, D., et al., 2020 [47]	RCT effect of PBM on ortho movement	20 pts. 2 groups: (i) 10 ortho + PBM (ii) 10 ortho + sham PBM Random allocation	808 nm	Output: 0.20 W CW Irradiance: 1.97 W/cm^2, 1.72 Joules (J) of energy per point, a total of 13.87 J per visit.	8 points (B, 4 P). 10 s per point. PBM applied at beginning day 0 (T0), day 28 (T1) and day 56 (T2)	LLLT every 4 weeks did not result in differences in the amount of tooth movement, anchorage loss or canine rotation during extraction space closure. (p = 0.27)

Table 4. *Cont.*

Published Data by Study—PBM-Adjunctive Orthodontic Movement						
Citation—Ortho Movement	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Hasan, A., et al., 2022 [48]	RCT effect of PBM on ortho movement	42 patients. 3 groups: (i) 14 fixed posterior bite block + PBM (ii) 14 Bite block (iii) 14 Untreated Random allocation	808 nm	Output: 250 mW CW Energy at 4 J, and the application time was 16 s/point.	6 points—3 B, 3 P applied at the first visit; then, days 3, 7 and 14 of the first month. Afterward, it was applied every 15 days until end of Tx	Correction of the AOB required significantly less mean time in the PBM group compared to the FPBB group ($\bar{x}$ = 7.07, $\bar{x}$ = 9.42 months, respectively; p = 0.001).
Pérignon, B., et al., 2021 [49]	RCT effect of PBM on ortho movement	42 patients. 2 groups: (i) 21 ortho + PBM (ii) 21 ortho placebo Random allocation	970 nm	Output 500 mW CW. Spot: 2 mm dia. Fluence: 30 J/cm^2. Exposure point received 0.9 J.	6 points per tooth, 3 B, 3 P. Second laser application session was carried out 1 month after the first	Distance of movement was sig. greater than that on the placebo side (p = 0.009).
Lo Giudice, A., et al., 2020 [50]	RCT effect of PBM on ortho movement	89 patients. 2 groups: (i) 43 ortho + PBM (ii) 46 ortho + control Random allocation	Multi λ 450 to 835 nm	Biostim panel setting. 6 min of irradiation, producing 48 J/cm^2 of fluence	PBM every 14 days. 3 sessions, total duration of 18 min and 144 J/cm^2 of fluency was administered (i.e., 48 J/cm^2 3 stages).	Treatment time was significantly shorter (p < 0.001) for the PBM group
Matos, D., et al., 2021 [51]	RCT effect of PBM on max. expansion ortho movement	34 pts. 2 groups: (i) 18—PBM (ii) 16—placebo Random allocation	980 nm	Output: 300 mW CW Spot size: 1.26 cm^2 Irrad: 238.8 mW/cm^2 Exposure: 10 s/point Radiant exp: 238.85 J/cm^2 Radiant energy: 3 J/point	6 spots bilaterally distributed along MPS for 10 s. 12 applications over 10 weeks (1, 5, 10 and 15 days, and once a week for 8 weeks)	PBMT did not accelerate bone regeneration in the MPS (p = 0.2273)
Eid, F., et al., 2022 [52]	RCT effect of PBM on ortho movement	20 pts. 2 groups: (i) 10—PBM (ii) 10—PBM Different frequency of application Random allocation	980 nm	Output: 100 mW CW Fluence: 8 J/cm^2	days 0, 3, 7, 14 and every 2 weeks thereafter. Group B, PBM applied every 3 weeks on experimental sides, throughout the study period (12 weeks).	PBM can efficiently accelerate the rate of orthodontic tooth movement to approx 1.4 folds, whether applied with a high frequency or with less frequent applications (p < 0.001).
Isola, G., et al., 2019 [53]	RCT effect of PBM on ortho movement	41 pts. 2 groups: (i) 41—PBM (ii) 41—Control Random allocation	980 nm	Output: 1 W CW Spot size: 600 µm dia. Energy density of 8 J	Buccal/palatal on 3 pts/side (dist, medial and mes.) at baseline and 3, 7, 14 days and every 15 days	Laser group: less mean time required to accomplish space closure compared to the control group (p < 0.001).
Pereira, S., et al., 2020 [54]	RCT effect of PBM on ortho movement	11 pts. 2 groups: (i) 11—PBM (ii) 11—Control Random allocation	780 nm	Mand: output: 40 mW CW; fluence: 10 J/cm^2; exposure: T 10 s. Max B: output: 40 mW; fluence: 10 J/cm^2; expos T: 10 s. Max P: power: 70 mW; fluence: 35 J/cm^2; expos T: 20 s; spot: 0.04 cm^2	Mand: 10 irradiations were carried out each time, 5 on each buccal and lingual. Max B & P: A total of 5 irradiations carried out each time. Laser therapy ended after 90 days	No difference in movement between the irradiated and nonirradiated sides. (p < 0.05)
Zheng, J., et al., 2021 [55]	RCT effect of PBM on ortho movement	12 pts. 2 groups: (i) 12—PBM (ii) 12—Control Random allocation	810 nm	Output: 100 mW CW. Fluence: 6.29 J/cm^2.	Applied 4 points (M, D, B, P), 40 s on each surface. PBM applied on days #1, 7, 14 and 21	PBM appeared to increase IL-1β, RANKL and OPG on day #7.
Özsoy, B., et al., 2023 [56]	RCT effect of PBM on ortho movement	20 pts. 2 groups: (i) 10—PBM (ii) 10—Control Random allocation	980 nm	Output: 20 mW CW Spot: 0.28 cm^2 Fluence: 0.71 J/cm^2 2 J total energy/molar	PBM pn day #0, 3, 7, 14, 21, 42, 63. Total no. of points, 16. 10 s (per point)	Movement on PBM sig. Higher at all time intervals (1–2) (2–3) (p < 0.001)
Abellán, R., et al., 2021 [57]	RCT effect of PBM on ortho movement	20 pts. 2 groups: (i) 10—Control (ii) 10—PBM Random allocation	670 nm	Output: 150 mW CW Av fluence: 11.3 J/cm^2 Irradiance: 4.78 W/cm^2 Spot diameter: 2 mm	Exposure: 3 min/dental surface (total 12 min) Days #0, 1, 2, 3, 4, 7 and in each Tx month.	No significant differences (p > 0.05).
Kamran, M. 2020 [58]	RCT effect of PBM on ortho movement	44 pts. 2 groups: (i) 44—Control (ii) 44—PBM Random allocation	808 nm	Output: 100 mW G-CW, 50 Hz, 50% duty. Fluence: 25 J/cm^2 Area covered: (cm^2) 0.04	Applied for 10 s at 10 points PBM in 4 visits: application days: #0, 3, 7, 14.	PBM group sig. greater in at 1 month (p = 0.04) and 2 months (p < 0.001)

3.2.3. Quality Assessment

The risk of bias (ROB) assessment results for the examined studies are outlined in Table 5.

Table 5. Modified risk of bias table for orthodontic studies.

Modified Risk of Bias—Orthodontics (n = 15)											
Citation	**Randomisation**	**Sample Size Calc & Number Required**	**Blinding**	**Baseline Situation Similar for All Groups**	**Laser Parameters Complete/Calculations Correct**	**Optimal Fluence Applied**	**Power Meter Used**	**Numerical Results (Statistics)**	**No Missing Outcome Data**	**Correct Assessment of Results**	**Total**
Sagar J et al. [44]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Farhadian N et al. [45]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	8
Lalnunpuii H et al. [46]	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	7
Mistry D et al. [47]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Hasan A et al. [48]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Pérignon B et al. [49]	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	8
Lo Giudice A et al. [50]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Matos D et al. [51]	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	6
Eid F et al. [52]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9
Isola G et al. [53]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Pereira S et al. [54]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Zheng J et al. [55]	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7
Özsoy B et al. [56]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	7
Abellán R et al. [57]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Kamran M et al. [58]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7

The following are revealed in Table 5:

- Low risk of bias in 7/15 of the articles (46.7%):
  - Two [52,57] scored 9/10;
  - Five [45,46,49,53,54] scored 8/10.
- Moderate risk of bias in 8/15 of the articles (53.3%):
  - Seven [44,47,48,50,55,56,58] scored 7/10;
  - One [51] scored 6/10.
- High risk of bias in none of the studies.

Overall, the mean ± standard error (SEM) Cochrane risk of bias score parameter was 7.50 ± 0.22 out of a perfect value of 10 [95% confidence intervals: 7.01–7.99].

A power meter was employed in only two of the studies. The other negative answers most commonly found concerned (a) laser operating parameters described and calculations correct, and (b) optimal fluence applied, followed by (c) the sample size calculations and numbers included, (d) the blinding of study researchers and (e) a baseline situation similar for all groups.

3.2.4. Data Analysis

It is evident that a wide variety of laser irradiation protocols have been performed. Regarding the wavelength applied, the vast majority was in the near infrared range (780–980 nm), while one study [50] examined a multi-panel system emitting polychromatic lights in the range of 450 nm to 835 nm.

As far as the other parameters are concerned in most of the studies, fluence was up to 30 J/cm^2, treatment was performed in multiple repetitions, and the application was executed only intra-orally.

As for the treatment outcomes observed, 11/15 studies (73.3%) [44–46,48–50,52,53,55,56,58] presented a positive result, while 4/15 (26.7%) [47,51,54,57] showed no difference from the control group.

3.3. TMJ Studies

3.3.1. Primary Outcomes

The primary goals of this systematic review were (a) to critically appraise the PBM irradiation protocols and (b) to examine the PBM treatment efficacy in terms of pain and trismus reduction compared to positive or negative control groups.

3.3.2. Data Presentation

The data extrapolated and evaluated from the included studies are displayed in Table 6.

Table 6. Data extraction for TMJ studies.

Published Data by Study—PBM-Adjunctive TMJ Therapy						
Citation—TMJ	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Ekici, Ö., et al., 2022 [59]	RCT. Impact of laser PBM on TMJ therapy	132 pts. 4 groups: (i) 38—OS (ii) 38—US (iii) 38—PBM (iv) 38—Control Random allocation	1064 nm	15–20 Hz Fluence 360 J/cm^2	Five times a week for 4 weeks, 15 min per session. 3 applications: 100 cm^2 per 30 s/static masseter and temporal/100 cm^2 in 60 s	Significant improvements were observed in terms of pain, function, disability and quality of life at both the 4th and 12th weeks compared to the control group ($p < 0.001$). QoL scores diff with PBM and US.
Ekici, Ö., et al., 2022 [60]	RCT. Impact of laser PBM on TMJ therapy	76 pts. 2 groups: (i) 38—laser PBM (ii) 38—placebo PBM Random allocation	1064 nm	10.5 W Av. FRP. 10–40 Hz, a probe diameter of 0.5 cm, and a spot size of 0.2 cm^2	Applied 1/day × 15 d × period of 3 weeks. 3 applications: 100 cm^2 per 30 s/static masseter and temporal/100 cm^2 in 60 s	Evaluated for pain, the range of motion of the jaw, disability and quality of life ($p \leq 0.001$)
Chellappa, D., et al., 2020 [61]	RCT. Impact of laser PBM on TMJ therapy	60 pts. 2 groups: (i) 30—PBM (ii) 30—TENS Random allocation	672 nm	Output: 50 mW CW. 3 J/site/4 sites (mass, temp, condyle, i-auricular portion).	Tx on altern days; 2 sessions/week × 3 weeks. Each point: 120 s PBMT, using scanning	VAS scores for pain and movement. Stat. sig. difference between LLLT and TENS groups

Table 6. *Cont.*

Published Data by Study—PBM-Adjunctive TMJ Therapy						
Citation—TMJ	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Shousha, T., et al., 2021 [62]	RCT. Impact of laser PBM on TMJ therapy	112 pts. 3 groups: (i) 37—PBM (ii) 37—splint OST (iii) 38—control Random allocation	940 nm	Output: 0.2 W CW 2 J energy. 10 s with an energy density of 2.5 J/cm^2.	Sessions were scheduled 3 days a week (every other day) for a total of 10 sessions	TMJ opening index (TOI), visual analogue scale (VAS), surface electromyography (sEMG). Sig. diff. in improving VAS, TOI and sEMG
Madani, A., et al., 2020 [63]	RCT. Impact of laser PBM on TMJ therapy	45 pts. 3 groups: (i) 15—PBM (ii) 15—acupuncture (LAT) PBM (iii) 15—placebo Random allocation	810 nm	Output: 200 mW CW, Gaussian beam, spot size: 0.28 cm^2, fluence: 21 J/cm^2	Pre-Tx (T1), after 5 (T2) and 10 (T3) laser appls, +1 m. (T4). Appl 2 × week, 30s/pt × 5 weeks. In LAT, PBM on acupuncture points (ST6, ST7, LI4)	LLLT and LAT were effective in reducing pain and increasing excursive and protrusive mandibular motion in TMD. $p \leq 0.05$.
Brochado, F., et al., 2018 [64]	RCT. Impact of laser PBM on TMJ therapy	51 pts. 3 groups: (i) PBM (n = 18). (ii) Manual MT (n = 16). (iii) Combined CT (n = 17).	808 nm	Output: 100 mW CW, Spot size: 0.03 cm^2, Fluence: 13.3 J/cm^2 and 4 J per point	PBM was applied 12 times (3 times a week for 4 consecutive weeks).	All—↓ in pain and ↑ in jaw movements during treatment and at follow-up (<0.001). CT group sig. diff. in improvement (<0.001).
Rodrigues, C., et al., 2020 [65]	RCT. Impact of laser PBM on TMJ therapy	78 pts. 3 groups: (i) 30—PBM (ii) 29—placebo PBM (iii) 19—control Random allocation	780 nm	Masseter: 30 J/cm^2–60 mW/20 s; the lateral pole of the TMJ (75 J/cm^2–60 mW/50 s).	8 Tx sessions. 2× week, Masseter 30 J/cm^2–60 mW/20 s. TMJ 75 J/cm^2 (60 mW/50 s), performed in 5 pts related to the lateral pole of the mandible head. Placebo HP used.	The active and placebo LLLT showed a reduction in pain during chewing and better recovery levels during the rest of the period ($p > 0.05$), without differences between OMC groups.
Aisaiti, A., et al., 2021 [66]	RCT. Impact of laser PBM on TMJ therapy	100 pts. 4 groups: (i) 25 TMJ—PBM (ii) 25 Myalgia—PBM (iii) 25 placebo TMJ PBM (iv) 25 placebo myalgia Random allocation	810 nm	Output power = 100 mW, 10 Hz. Spot dia = 2 cm, tip at 3 cm from tissue. Both sites: fluence: 6 J/cm^2	Masseter muscle: time per site = 20 s, total time = 60 s TMJ: time per point = 6 s, total time = 30 s.	PBMT: greater reduction in pain scores than placebo ($p = 0.014$). Myalgia: pain intensity decreased over time ($p < 0.001$); no difference between interventions ($p = 0.074$).
Monteiro, L., et al., 2020 [67]	RCT. Impact of laser PBM on TMJ therapy	42 pts. 2 groups: (i) 22—PBM (ii) 20 Placebo Random allocation	635 nm	Output: 200 mW CW. Spot: 0.5 cm^2. PD: 400 mW/cm^2. Exposure: 20 s. Fluence: 8 J/cm^2. Radiant energy: 16 J/pt and 128 J on 4 sessions (av. 8 pts)	Contact mode. No points irradiated: 4 points per side. Area irradiated: 0.5 cm^2 per point. Number and frequency of Tx 4 sessions (1 per week)	Pain: sig. reduction in laser group compared with baseline, $p < 0.001$. Pain during palpation of masticatory muscles was sig. Sig. increase in non-assisted painless mouth opening among laser group ($p = 0.007$).
Magri, L., et al., 2018 [68]	RCT. Impact of laser PBM on TMJ therapy	64 pts. 3 groups: random (i) PBM laser (n = 20), (ii) placebo (n = 21), (iii) controls (without treatment (n = 23)	780 nm	Masseter + temporal = 5 J/cm^2 (20 mW–0.5 W/cm^2), TMJ area = 7.5 J/cm^2 (30 mW–0.8 W/cm^2)	eight sessions, twice a week.	Laser group showed 80% pain reduction; placebo, 85%; and WT, 43% at 4 weeks. $p < 0.05$
Dias, W., et al., 2022 [69]	RCT. Impact of laser PBM on TMJ therapy	34 pts. 2 groups: (i) 17—OF myotherapy + PBM (ii) 17 OF myotherapy + placebo Random allocation	830 nm	Two settings: (i) sessions #1–5: 6 J/fluence of 51 J/cm^2, (ii) session #2: 4 J and fluence of 34 J/cm^2,	First phase (#1–#5), to ease painful condition. Second phase (at the sixth session), to biostimulate functional gains	VAS OHQOL No sig. diff. ($p \geq 0.05$)
Batra, S., et al., 2023 [70]	RCT. Impact of laser PBM on TMJ therapy	20 pts. 2 groups: (i) 10—TMJDS + PBM (ii) 10—TMJDS + TENS Random allocation	660 nm	Output: 100 mW CW. 6 J/ point	60 s/pt, 2 sessions/week × 4 weeks On mass., temporalis, condylar, i-auricular regions	Pain VAS: diff. not statistically significant. Excursive movement: sig. diff. ($p \leq 0.05$)

Table 6. *Cont.*

Published Data by Study—PBM-Adjunctive TMJ Therapy						
Citation—TMJ	**Aim of Study**	**Test Group/ Control/Placebo**	**Laser λ**	**Laser Operating Parameters**	**Application/Repetition**	**Outcome**
Borges, R., et al., 2018 [71]	RCT. Impact of laser PBM on TMJ therapy	44 pts. 4 groups: (i) 11—8 J/cm^2 (ii) 11—60 J/cm^2 (iii) 11—105 J/cm^2 (iv) 11—control placebo Random allocation	830 nm	Output: 30 mW CW. Spot size: 0.116 cm^2. Irradiation: 2.59 W/cm^2. Fluence: J/cm^2 (i–iii) 64 480 840.	Frequency of irradiation 3× week/10 sessions. 8 points (4 per side).	Study did not show effect of PBM over TMJ mobility. Results demonstrated sig. reductions in TMD pain and symptoms in all the PBM protocols used, including the placebo group.
Maracci, L., et al., 2022 [72]	RCT. Impact of laser PBM on TMJ therapy	30 pts. 3 groups: (i) 11—splint (ii) 10—PBM (iii) 9—placebo Random allocation	808 nm	Power: 100 mW, fluence of 80 J/cm^2, 22 s per application, distance of 1 cm between each site.	T0: start of Tx. T1: 1 month after occlusal splint (G1) or 1 month after PBMT (G2) or placebo PBMT (G3).	VAS pain: G1 improvement (p = 0.014). G2 and G3, no sig. diff. OHRQoL, G1 + G2 sig. improvement (p = 0.005) cf. G3.
De Oliveira Chami, V., et al., 2022 [73]	RCT. Impact of laser PBM on TMJ therapy	20 pts. 2 groups: (i) 10—laser group (LG) (ii) 10—placebo group (PG) Random allocation	808 nm	Output: 100 mW, fluence: 80 J/cm^2, 22 s per application, distance of 1 cm between each site.	T1: pre-PBM Tx; T2: after 1st PBM Tx; T3: before 2nd PBM Tx 48 h post 1st; T4: post 2nd Tx; T5: 7d post T2; T6: 30d post T1.	OHRQoL assessed at T1 and T6. Significant increase in mouth opening (p = 0.04) and improvement in QoL (p = 0.003) observed in the LG after 30 days.
Nadershah, M., et al., 2020 [74]	RCT. Impact of laser PBM on TMJ therapy	202 pts. 2 groups: (i) 108—PBM group (ii) 94—placebo group Random allocation	940 nm	Power: 7 W/2.8 cm^2 Fluence: 300 J/cm^2 Irradiance: 7 W/2.8 cm^2	E/O application, 2 min (24 s/appl. pt), 2 cm from skin, 5 points Every 48 h for 10 days	Sig. diff. pain—VAS (p = 0.01).
Mansourian, A., et al., 2019 [75]	RCT. Impact of laser PBM on TMJ therapy	107 pts. 3 groups: (i) 35—PBM group (ii) 33—TENS (iii) 32—control group Random allocation	810 nm	Power: 0.2 W Fluence: 2 J/cm^2	10 s time and every week × 2 months.	Pain VAS: sig. diff. (p = 0.003). At 2 months, no sig. diff. found between the groups. (p = 0.38)
Desai, A., et al., 2022 [76]	RCT. Impact of laser PBM on TMJ therapy	60 pts. 2 groups: (i) 30—placebo group (ii) 30—PBM group Random allocation	633 nm	Power: 30 mW continuous wave.	20 sessions of LLLT applied both in closed mouth and the maximum opened-mouth position, administered over a period of 08 weeks.	Pain VAS, mouth opening, lateral movement: better treatment outcome in PBM laser group but no sig. diffs. (p > 0.8).
Bakry, S., et al., 2021 [77]	RCT. Impact of laser PBM on TMJ therapy	40 pts. 2 groups: (i) 20—PBM group (ii) 20—placebo group Random allocation	635 nm	Power: 200 mW CW. Fluence: 5 Jcm^2.	Applied at the height of the joint capsule with a mouth closed/opened position. 10 doses per joint. The total cycle dose was 100, and the cycle repeated for 10 days (every 2nd day).	One moth—VAS pain/opening—no sig. diff. Three months—sig. diff. from pre-operative state until post-operative state at three months ($p \leq 0.0001$).
Emam, A., et al., 2023 [78]	RCT. Impact of laser PBM on TMJ therapy	100 pts. 4 groups: (i) 25—behavioural therapy (BT). (ii) PBMT (LT) (iii) max. ant. Repos. splint (MARS). (iv) stabilisation splint (SS).	808 nm	70 mW and doses of 105 J/cm	2/week for 4 weeks (total of 8 sessions). Admin. at 5 specific points on the TMJ, as well as the external acoustic canal.	MRM was evaluated for each patient before treatment and after 6 months (p < 0.05). There were significant improvements for SS and MARS on the different movements of MRM, more than those for LLLT and BT ($p \leq 0.05$).

3.3.3. Quality Assessment

The risk of bias (ROB) assessment results for the examined studies are outlined in Table 7.

Table 7. Modified risk of bias table for TMJ studies.

Modified Risk of Bias—TMJ (n = 20)											
Citation	**Randomisation**	**Sample Size Calc & Number Required**	**Blinding**	**Baseline Situation Similar for All Groups**	**Laser Parameters Complete/Calculations Correct**	**Optimal Fluence Applied**	**Power Meter Used**	**Numerical Results (Statistics)**	**No Missing Outcome Data**	**Correct Assessment of Results**	**Total**
Ömer E et al. [59]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Ömer E et al. [60]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Chellappa D et al. [61]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	8
Shousha T et al. [62]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7
Madani A et al. [63]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	9
Brochado F et al. [64]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9
Rodrigues C et al. [65]	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	7
Aisaiti A et al. [66]	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	8
Monteiro L et al. [67]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9
Magri L et al. [68]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9
Dias W et al. [69]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6
Batra S et al. [70]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Borges R et al. [71]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	9
Maracci L et al. [72]	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	8
De O Chami V et al. [73]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	9
Nadershah M et al. [74]	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	7
Mansourian A et al. [75]	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	5
Desai A et al. [76]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7
Bakry S et al. [77]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	7
Emam A et al. [78]	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	6

The following are revealed in Table 7:

- Low risk of bias in 10/20 of the articles (50%):
  - Three [64,71,73] scored 9/10;
  - Seven [63,65–68,72,74] scored 8/10.
- Moderate risk of bias in 10/20 of the articles (50%):

- Eight [59–62,69,70,76,77] scored 7/10;
- One [78] scored 6/10;
- One [75] scored 5/10.

- High risk of bias in none of the studies.

Overall, the mean ± standard error (SEM) Cochrane risk of bias score parameter was 7.50 ± 0.22 out of a perfect value of 10 [95% confidence intervals: 7.03–7.97].

A power meter was employed in eight of the studies. The other negative answers most commonly found concerned (a) laser operating parameters described and calculations correct, and (b) optimal fluence applied, followed by (c) a baseline situation similar for all groups, and (d) the sample size calculations and numbers included.

3.3.4. Data Analysis

It is evident that a wide variety of laser irradiation protocols have been performed. Regarding the wavelength applied, the vast majority was in the near-infrared range (780–940 nm), while five studies [61,67,70,76,77] examined the red wavelengths, and two [59,60], the 1064 nm wavelength.

As far as the other parameters are concerned in most of the studies, the total fluence per session was up to 300 J/cm^2, treatment was performed in multiple repetitions, and the application was executed only extra-orally.

As for the treatment outcomes observed, 12/20 studies (60%) [59–64,66,67,70,73–75] presented a positive result, while 8/20 (40%) [65,68,69,71,72,76–78] showed no difference from the control group.

4. Statistical Analysis

For the three separate group models outlined below, full datasets were primarily subjected to univariate data analysis in order to screen for those that appear to significantly contribute toward the outcome parameters (albeit in a univariate context). ANOVA and linear regression approaches were employed for this purpose, with the output variable being scored 0 for no difference from the control, and +1 for a statistically significant difference observed.

For the ANOVA and LR screening approaches, all publication data points were weighted according to the total number of participants recruited to the study, i.e., a total combination of those in the test and control groups.

Subsequently, these significant variables were then incorporated into Partial Least Squares Regression (PLS-R) or Discriminatory Analysis (PLS-DA) models for the significant 'predictor' variables in order to determine any multicollinearities (cross-correlations) between them. However, in following the univariate selection of variables, which were significant only for the oral surgery datasets examined, all of these multivariate models constructed were found to not be significantly validated (Q^2 statistic values were close to or even less than zero for all models examined). The data analysis was summarised using XLSTAT2021 software BASIC+ (Addinsoft, Paris, France).

4.1. Oral Surgery

Figures 4–7 concern oral surgery data pain (Figures 4 and 5) and biostimulation (Figures 6 and 7).

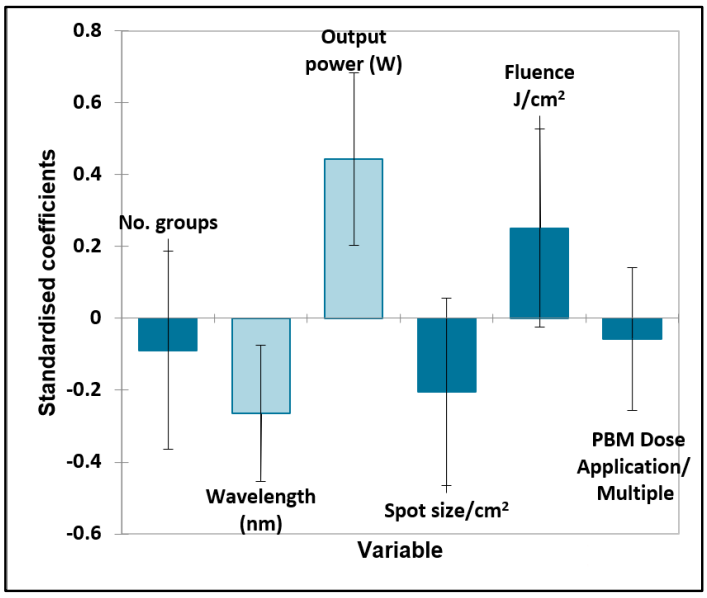

Figure 4. Oral surgery quantitative variables—pain. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for quantitative explanatory variables evaluated using the regression models employed for predicting the outcome variable for pain (0 for no effect, and +1 for a statistically significant influence).

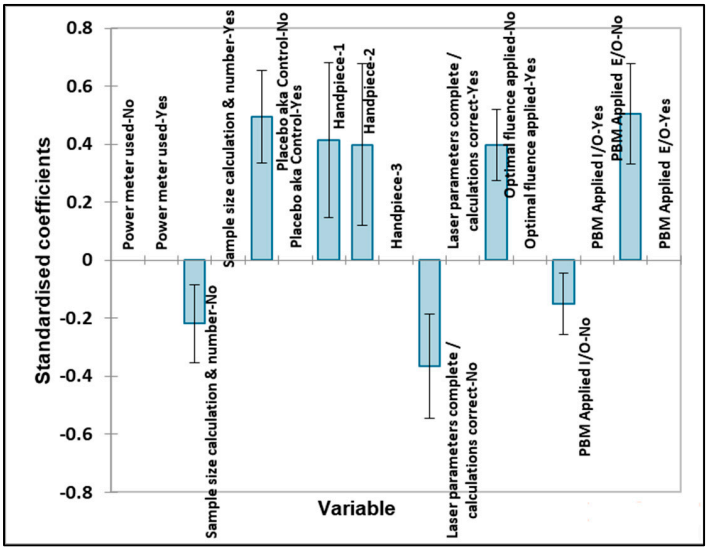

Figure 5. Oral surgery qualitative variables—pain. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for qualitative explanatory variables evaluated using the ANOVA models employed for predicting the outcome variable for pain (0 for no effect, and +1 for a statistically significant influence).

For the quantitative variables, the output power and wavelength were both statistically significant, with the positive effect increasing with the output power level but inversely related to the wavelength in nm, i.e., the lower the wavelength (and higher the energy) used, the better the effect. Fluence and spot size were also close to significance, with enhanced effects observed at higher fluences and larger spot sizes.

Significantly improved outcomes were found with the inclusion of a placebo (control) group, the use of handpieces #1 (bare fibre) and #2 (single tooth), the optimal application of fluence and no extraoral (E/O) PBM applied. Negative outcomes were significantly caused

by no prior sample size calculation, no laser parameters being completed and no intraoral (I/O) PBM applied, as might be expected.

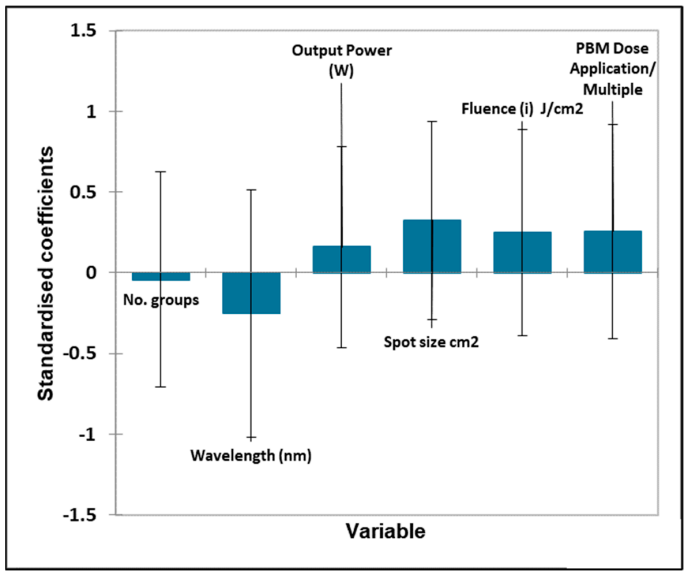

Figure 6. Oral surgery quantitative variables—biostimulation. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for quantitative explanatory variables evaluated using the regression models employed for predicting the outcome variable for biostimulation (0 for no effect, and +1 for a statistically significant influence).

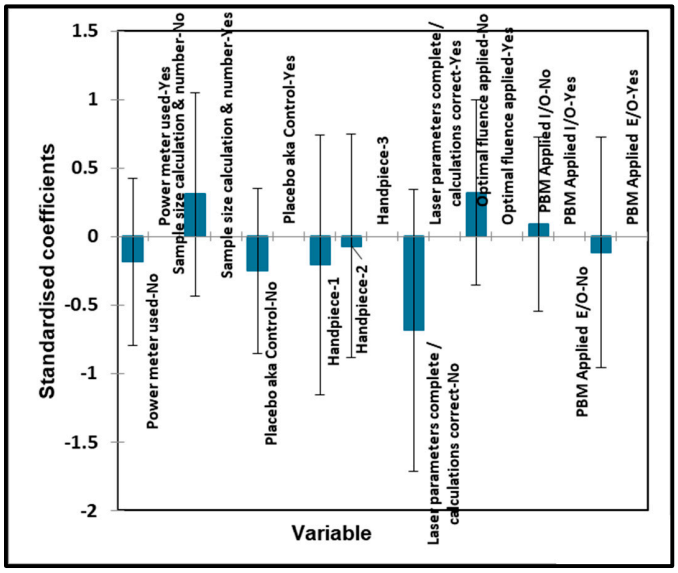

Figure 7. Oral surgery qualitative variables—biostimulation. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for qualitative explanatory variables evaluated using the ANOVA models employed for predicting the outcome variable for biostimulation (0 for no effect, and +1 for a statistically significant influence).

The Bonferroni-corrected *p* value required for statistical significance was found to be 0.00625, so therefore, all of the above significant variables were found to have a significant contributory effect on the pain outcome.

None of the quantitative variables were found to be statistically significant for this outcome score.

Again, no significant effects of any of the qualitative variables were found for the biostimulation output variable.

4.2. Orthodontic Tooth Movement

No significant contributions were found for any of the quantitative variables considered.

Respectively, an analysis of the qualitative variables associated with orthodontic tooth movement was performed. Unfortunately, this model was computationally blocked since there were too many variables and an insufficient number of studies reported. However, there were no significant correlations found between the outcome significance and all 'predictive' variables. Therefore, it can be attested that none of these variables significantly contributed toward the outcome variable (Figure 8).

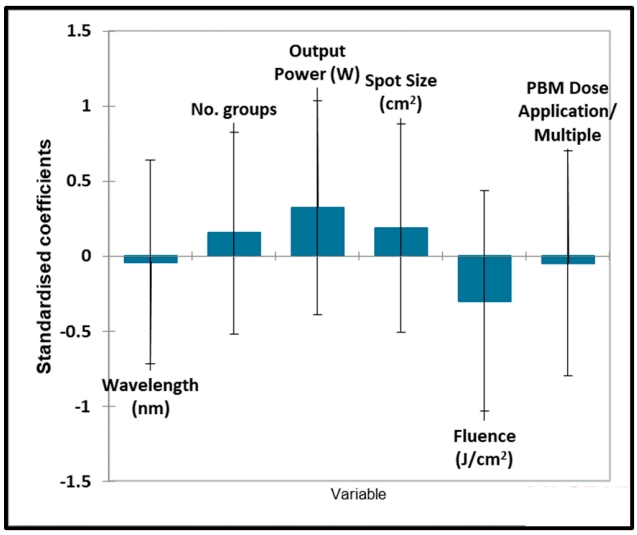

Figure 8. Orthodontic tooth movement quantitative variables. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for quantitative explanatory variables evaluated using the regression models employed for predicting the outcome variable for orthodontic tooth movement (0 for no effect, and +1 for a statistically significant influence).

4.3. TMJ

Figures 9–12 concern the quantitative and qualitative variables associated with TMJ pain and the quantitative and qualitative variables associated with TMJ biostimulation, respectively.

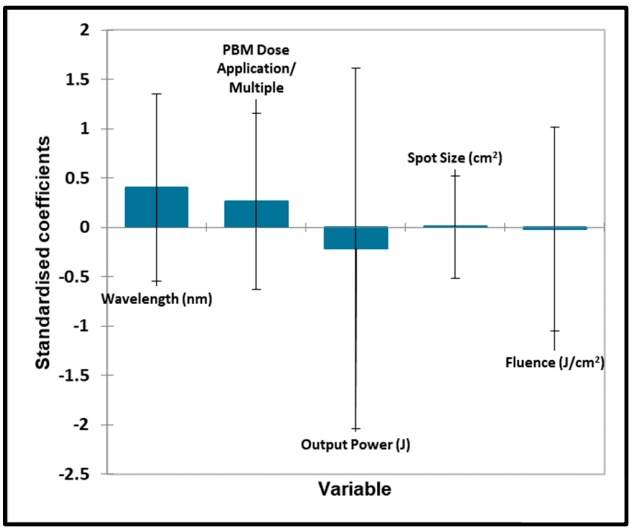

Figure 9. TMJ quantitative variables—pain. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for quantitative explanatory variables evaluated using the regression models employed for predicting the outcome variable for pain (0 for no effect, and +1 for a statistically significant influence).

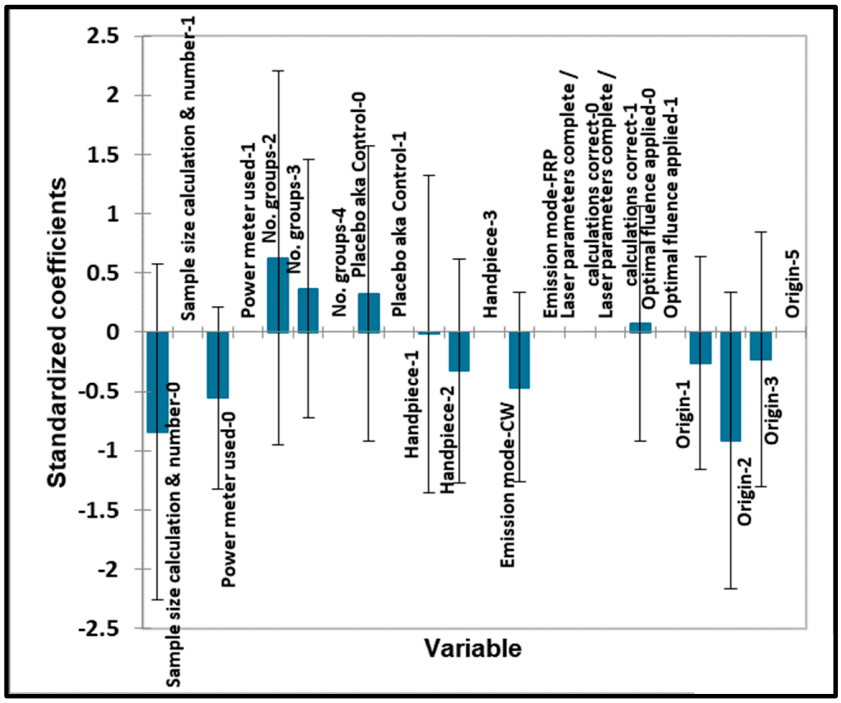

Figure 10. TMJ qualitative variables—pain. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for qualitative explanatory variables evaluated using the ANOVA models employed for predicting the outcome variable for pain (0 for no effect, and +1 for a statistically significant influence).

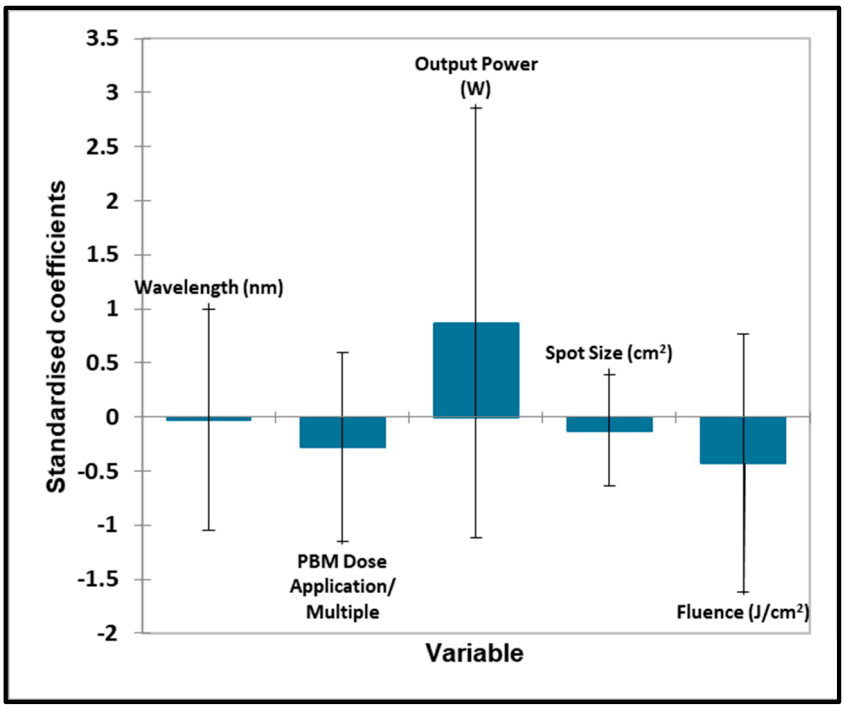

Figure 11. TMJ quantitative variables—biostimulation. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for quantitative explanatory variables evaluated using the regression models employed for predicting the outcome variable for biostimulation (0 for no effect, and +1 for a statistically significant influence).

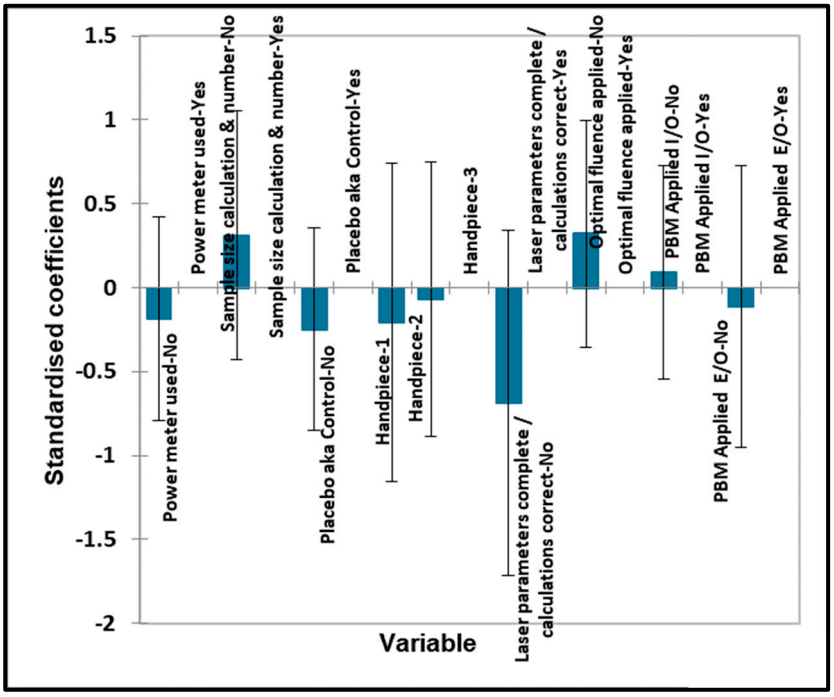

Figure 12. TMJ qualitative variables—biostimulation. Plot of estimated standardised coefficients ± 95% confidence intervals (CIs) for qualitative explanatory variables evaluated using the ANOVA models employed for predicting the outcome variable for biostimulation (0 for no effect, and +1 for a statistically significant influence).

Unfortunately, no significant contributions toward the outcome variable were found for all quantitative 'predictor' variables considered.

In Figures 9 and 10, no significant contributions were found for any of the qualitative 'predictor' variables. No significant contributions were found for any of the quantitative 'predictor' variables evaluated. No significant contributions were found for any of the qualitative 'predictor' variables evaluated.

5. Discussion

Through a systematic review, this study developed an analysis of the many variables associated with PBM therapy, applied in three areas of dental/oral surgical treatments, using randomised clinical human trials [25–78]. The basis of this investigation sought treatments related to the underlying nature of inflammation in general, whether acute, chronic or, in the case of elective orthodontic tooth movement, pre-operatively non-existent, to determine if any pertinent conclusions might be drawn. Although rather simplistic in its generalisation, the application of PBM may be seen to address conditions that are standalone pathologies or conditions contemporary with and consequent of surgical intervention with oral, dental hard and soft tissue diseases or trauma. As such, the presence of acute or chronic inflammation, with associated tissue imbalance (pain, oedema and trismus), may present an opportunity for beneficial PBM therapy. In addition, there may be opportunities to positively influence the status of otherwise 'normal' tissue that may be associated with a clinical procedure, such as orthodontic therapy as well as adjunctive applications associated with regenerative therapies such as stem cells [79] and the hard and soft tissue graft osseointegration of dental implants [80]; other areas of PBM influence include burning mouth syndrome [17], following nerve damage caused by oral surgery [81] and idiopathic tooth hypersensitivity [82,83].

The data extraction and groupings were subjected to a statistical evaluation in order to seek those elements of therapy that represent possible significance and allow meaningful comparisons to be identified. The focus of selection of published papers was to identify

the empirical use of laser photobiomodulation within three areas of adjunctive therapy; the intention was to conduct a refine analysis to enable direct comparisons across the three treatment groups. Additionally, the short time frame of the published randomised clinical trials reflects the high level of research activity during the past five years; however, when compared to the extended span of decades of preceding research, it is questionable as to how little consensus has emerged in terms of a standardisation of laser application techniques, or of the many elements of a general PBM light dose during all phases of treatment.

The objectives of this systematic review originated around three areas of interest: 'Was the influence of PBM therapy primarily related to the presenting condition?', 'Was any benefit influenced by the reported operating technique and surgical anatomy?', and 'Was any benefit of PBM therapy related to the chosen operating parameters?'. As seen from the statistical analysis, there appears to be no significant difference between the three treatment groups to allow for an indication regarding the comparative usefulness of PBM therapy with any underlying clinical condition. Therefore, to draw any significance concerning tissue status appears equivocal.

The prime PBM outcomes of reduced inflammation, analgesia and uneventful healing are potent claims that have been refined through many studies, offering the promise of adjunctive support in the clinical management of disease, disorder or injury. From Table 1, many biochemical mediators have been shown to be influenced through applied PBM therapy; although several areas of activity may be a consequence of an inflammatory response as a precursor to tissue repair, the influences of PBM may be judged as wide ranging.

The choice of three areas of treatment allows some analysis of the applied light doses to be conducted relative to the surgical site. Indeed, as has been researched extensively, the inherent Gaussian distribution of the majority of photonic emission beams, together with the anisotropic nature of oral and dental soft and hard tissue, has considerable effect on the potential attenuation of the surface applied dose, resulting in variable degrees of beam scattering, non-target absorption at depth and a consequently reduced fluence at sub-surface surgical sites [10,17]. The clinical objectives of biostimulation and/or pain mitigation relative to the three anatomically heterogenous treatment areas pose consequently differing dose delivery challenges to the clinician. Key to effective PBM at depth is the employment of an optimal surface fluence in order to accommodate the beam density reduction as it passes through tissue layers.

The influence of varying (non-PBM) treatment protocols, such as surgical access preferences or (orthodontic) appliance therapy, has been demonstrated to have influence on the outcomes [84–90]. Across the three groups, the variation in clinical outcome, as a measure of the effective PBM application, however, appears to be related to the laser operating parameters. This may be related to and draws upon the inherent nature of the laser being used (wavelength, emission mode, delivery mechanism, output power range). Consequent to this, operator-applied permutations of an overall light dose ('spot' size, fluence, irradiation, average power) together with the dose regimen (frequency of application, repetition, total energy) may significantly influence the therapeutic benefits offered by PBM. A third area of influence may be seen in terms of the nature of the clinical condition (pathology, wound trauma, otherwise 'normal' tissue modulation), along with the anatomical site in terms of a possible three-dimensional irradiation, and the effects of photon absorption and scattering. However, with the exception of outcomes relating to oral surgical molar removal, no statistical significance was found.

The influences of variable elements may be considered as follows [91]:

Group structure—test/control/placebo: Many positive outcomes were reported in the included studies, albeit with little statistical significance. Within the orthodontic movement group, the majority of studies utilised a split-mouth design as a control; within the TMJ group, an element of significance related to the influence of a placebo photonic delivery. Hence, it appears that within third molar oral surgery studies, adjunctive PBM effects were measured against a pure surgical treatment, albeit with some variation in the applied light dose and intra-oral verses extra-oral differences.

Wavelength/emission mode: Across all groups, there appears no significance. Even allowing for the extensive emergence of PBM and PBM-type effects with short visible wavelengths, as well as mid- and far-IR, the choice of predominantly visible diode red and NIR wavelengths constitutes a logical choice. However, in view of the wide variation in applied fluences relative to tissue type and surgical site, there has been no opportunity to analyse differences in outcomes across the wavelength range chosen.

Power meter: According to recent primary research [92], the significant variation in the optic fibre delivery fluence arising from impurities may exert considerable influence. That only very few (in number) of the studies analysed cited the use of a power meter or calibration must be seen as a source of error in the results and outcomes of such studies.

Delivery/spot size: Across the groups, some variation was shown in the 'spot' size, i.e., beam diameter, along with contact versus non-contact tip-to-tissue application. Non-contact, non-focused beams will undergo considerable variation in irradiation, which, in tandem with the effects of a non-linear Gaussian spectral beam profile, impacts the fluence values with even short distances. In many instances, no record of such measurements occurred.

Applied fluence/computed/relative to therapeutic optimal dose: during the past twenty years, a gradual acceptance of photonic 'dose' values relative to cellular and then whole-tissue radiation has defined therapeutic PBM delivery. Biphasic light-dose delivery may provide biostimulation, with ascending energy density values leading to a hormetic zone associated with cellular/tissue inhibition; at higher levels, this may lead to permanent damaging effects. Allowing for a nominal standard deviation, the biostimulatory fluence is observed at 5 Joules/cm^2; above 10 Joules/cm^2, with an average of 15 Joules/cm^2, cell/tissue inhibition may be observed. Moreover, an upper value of 30 Joules/cm^2 has been proposed as the threshold of damaging effects. However, the biological capacity of tissues to withstand photo-induced stress is a function of the rate of the dose delivery, expressed as irradiance (W/cm^2). High-intensity photon exposure induces a potential damaging photothermal response; conversely, the accumulated energy expressed as fluence (J/cm^2) may be high with extended low-value irradiance settings, as well as with repeated treatments. From our analysis of all groups, there is wide and significant variation in the fluence values applied, with most instances citing low or sub-therapeutic values.

Application/number/repetition/relative to anatomical site and dose variation with depth: It has been seen earlier that because of the non-isotropic nature of oral soft and hard tissues, with dental hard tissue structures, considerable variation exists between the chosen laser wavelength and associated absorption of applied fluence. Additionally, such phenomena may influence the applied dose at depth, with the reduction in fluence approaching 70–90% at 10 mm in oral soft tissue. The analysis of the applied target dose at depth versus the surface value, across the treatment groups and individual treatment schedules, showed significant variation and may contribute to a compromise in the effectiveness of PBM irradiation at tissue depth.

Significance of outcomes: Taken individually or collectively, the measurable variation in laser-relevant elements needs to be considered and set against the outcomes of individual randomised clinical trials. The consequence of this strict systematic review raises the significance of RCT data in defining ongoing evidence-based knowledge and the application of PBM therapy in dentistry. It is outside the scope of this review to define the extent of discipline to be applied to the parameters of clinical PBM delivery, but the study design and full disclosure of the delivery values should still be fully evaluated at the ethical approval stage of studies.

6. Conclusions

An analysis of randomised clinical trials relating to photobiomodulation was carried out within a specific five-year period and within three areas of adjunctive therapy. A detailed data extraction and analyses have allowed the scrutiny of the inter-group differences of PBM effectiveness and revealed a common benefit of such adjunct therapy. The scrutiny of a large amount of data relating to recorded laser operating and calculated dose

parameters has revealed inconsistent statistical differences, when data group comparisons were applied. From the evaluations of all aspects of this study, we conclude that PBM offers positive benefits in a wide range of clinical treatment modalities. However, in considering the current spread of data recording that exists within contemporary randomised clinical trials, and in agreement with other study findings, there is a substantive need for a standardisation in PBM therapy dose parameters. With greater discipline applied to effectively record such parameters and easier comparisons between RCT outcomes, the effectiveness and predictability of adjunctive PBM treatments may become more attainable.

Author Contributions: Conceptualisation, S.P.; methodology, S.P., E.A. and V.M.; validation, E.A. and V.M.; formal analysis, S.P., E.A. and V.M.; investigation and data extraction, S.P., E.A. and V.M.; writing—original draft preparation, S.P.; writing—review and editing, S.P., V.M., E.A., M.C., E.L. and M.G.; statistical analysis, M.G.; visualisation, S.P.; supervision, M.G.; project administration, S.P. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflicts of interest.

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