Influence of Phototherapy on the Kinetics of Orthodontic Tooth Movement: A Meta-Analysis of Randomized Controlled Trials

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Abstract

AIM: This study aims to evaluate the efficacy and safety of phototherapy and the correlation between its parameters in accelerating orthodontic tooth movement. METHODS: A comprehensive search was conducted across several databases from the study's inception to January 25, 2019. Only randomized placebo-controlled trials examining adjunctive phototherapy during orthodontic canine retraction were included. Study quality was assessed using the Jadad score and the Cochrane risk of bias tool. Statistical analysis was performed using comprehensive meta-analysis software v. 3. RESULTS: A total of 21 studies involving 302 patients were eligible; 11 were included in the quantitative synthesis. A meta-analysis of low-quality evidence demonstrated that adjunctive phototherapy outperformed the control group (Hedges' g = 0.68, 95% CI [0.08-1.28], I^2 = 83%, p = 0.03). Subgroup analyses indicated more significant effects with a 940 nm wavelength (Hedges' g = 2.93, 95% CI [2.20-3.65], I^2 = 0%, p = 0.00), 100 mW output power (Hedges' g = 1.17, 95% CI [-0.20-2.55], I^2 = 91%, p = 0.10), and 5 J/cm^2 energy density (Hedges' g = 0.69, 95% CI [-0.03-1.41], I^2 = 10%, p = 0.06). No risks were identified in the six studies that conducted safety investigations. CONCLUSION: Phototherapy can accelerate orthodontic tooth movement without associated risks. Significant effects were observed with higher dosages. Further well-designed, high-quality trials are necessary to identify the exact impact of phototherapy and its parameters.

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1 Introduction

The significantly lengthy process of conventional orthodontic treatment, which varies considerably between 19.9 to 33 months, was the primary concern of orthodontic patients (Tsichlaki et al., 2016). Depending upon the patient's severity of malocclusion and the clinical judgments of practitioners, an average of 3.3 to 5.9 months is required if the case involves tooth extraction (Skidmore et al., 2006; Mavreas et al., 2008) and a further 4 to 6 months to ensure a fully retracted and upright canine on a premolar extraction site, which is the most time-consuming approach to address crowding or protrusion (Shpack et al., 2007; Prasad et al., 2014; Abbas et al., 2016).

A brief orthodontic treatment would be more appealing to patients (Pacheco-Pereira et al., 2016), more cost-effective for practitioners (Turbill et al., 2001), and would prevent potential deleterious effects (Segal et al., 2004; Roscoe et al., 2015). A substantial amount of research has been conducted regarding the interest in accelerating canine retraction during orthodontic treatment from a non-surgical to a surgical approach. However, the acceptance rate among patients for a surgical procedure was low (Zawawi, 2015), as 80% of patients undergoing surgical procedures suffered moderate to severe swelling post-operatively (Al-Naoum et al., 2014).

Concerning the non-surgical approach, phototherapy has been widely investigated and employed in dentistry for decades. It involves the application of athermal and atraumatic coherent light such as low-level laser therapy (LLLT) or non-coherent light such as light-emitting diodes (LED) (Smith, 2005). It alters target cells to promote tissue repair, reduce inflammation, and encourage pain remission and wound healing (Cernavin et al., 1994; Chung et al., 2012). It emits in the red to near-infrared spectrum between 600 and 1000 nanometres (nm), with an energy density from 1 to 20 Joules per cm^2, and power output from 5 to 50 milliwatts (mW) (Huang, 2009; Huang et al., 2011).

The magnitude of the correlation between phototherapy and the stimulation of cells has been proposed by several published clinical trials (**Figure 1**). One of the hypotheses is based on the activation of the mitochondrial cytochrome c oxidase, which is the primary photo acceptor between the red to near-infrared light range of 650 to 950 nm wavelength in mammalian cells, signalling an increase in the following: adenosine triphosphate (Farivar et al., 2014), cyclic adenosine monophosphate (Wu et al., 2013), and intracellular free calcium concentration (Sharma et al., 2012). These changes cause an overall increase in cellular stimulation. Another hypothesis, wherein flavoproteins and porphyrins molecules are activated and combined with oxygen, predicts an acceleration of cellular stimulation (de Freitas & Hamblin, 2016). Finally, another proposed mechanism is that phototherapy directly increases the intracellular free calcium concentration and the pumping activity of sodium-potassium, leading to an overall increase in cellular stimulation (Coombe et al., 2001). The efficacy of phototherapy in the different cellular events described depends primarily upon proper application and dosage (**Figure 2**) (Ohshiro & Calderhead, 1991). For this reason, most of the published clinical trials have applied varying doses in each parameter to establish the most suitable dosage necessary for adequate cell stimulation, due to the existence of the Arndt-Schultz curve (Hamblin & Demidova, 2006).

To date, current systematic reviews have produced mixed results due to inadequate literature searches and small sample sizes. Some support its efficacy but conclude that high-quality clinical trials are necessary to confirm its benefits (Ge et al., 2013; Sousa et al., 2014; He et al., 2016; Imani et al., 2018), while others have provided weak evidence (Long et al., 2013; Sonesson et al., 2016; de Almeida et al., 2016; Farsaii et al., 2017).

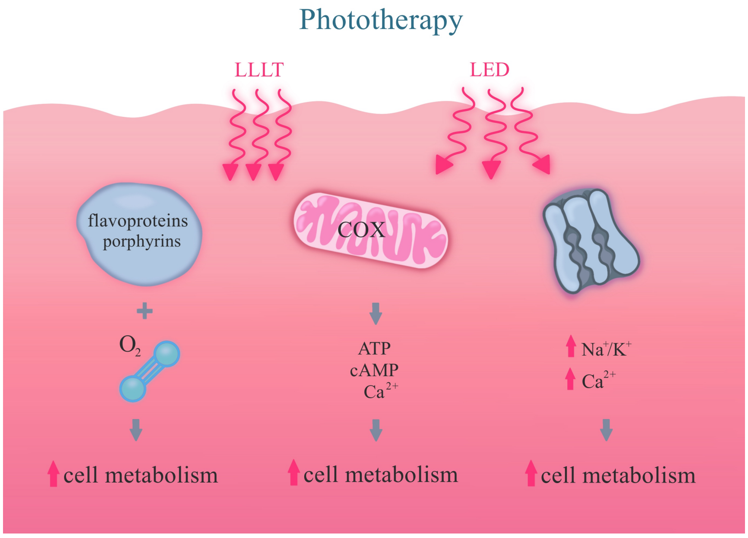


Figure 1. Schematic diagram adapted from several proposed molecular mechanisms of phototherapy, from the emission of LLLT and LED light to the absorption of cellular chromophores or photoacceptors, resulting in the increased stimulation of cells. LLLT: low-level laser therapy; LED: light-emitting diode; COX: cytochrome c oxidase; ATP: adenosine triphosphate; cAMP: cyclic adenosine monophosphate; Ca^{2+}: intracellular free calcium concentration; O_2: oxygen; Na^+/K^+: sodium-potassium pumping activity (Coombe et al., 2001; Sharma et al., 2012; Wu et al., 2013; Farivar et al., 2014; de Freitas & Hamblin, 2016).

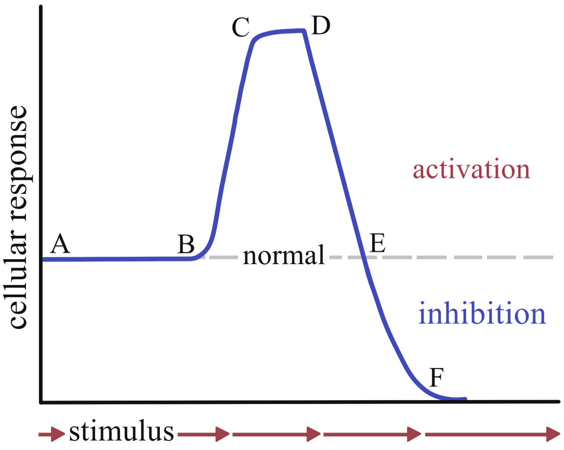


Figure 2. Ohshiro and Calderhead's phototherapy-adapted version of the Arndt-Schultz curve, or biphasic dose-response curve, must be considered. Its parameters are the primary key to predicting cellular stimulation. From point A to B, there will be no cellular response during the application of insufficient energy; as more power is applied from B to C, biostimulation will be achieved. However, bioinhibition will occur from point D to F if too much energy is applied (Amended from Ohshiro & Calderhead, 1991, p. 271).

The existing evidence of the efficacy of phototherapy related to orthodontic tooth movement still contains controversies. A systematic review that incorporates a more significant portion of the available evidence is needed to confirm the effectiveness of phototherapy and its proper dosage required in speeding up tooth movement and to identify undesirable effects.

This study seeks to systematically evaluate and consolidate current evidence regarding the effectiveness of phototherapy in accelerating canine retraction in orthodontic patients. It aims to determine the optimal parameters (including wavelength, output power, and energy density) for phototherapy to be effective and to assess any potential adverse effects on dental and periodontal structures. The central questions addressed include the efficacy of phototherapy in speeding up canine retraction, the dependency of its success on specific parameters, and its safety profile concerning dental and periodontal health.

2 Methods

This review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009) for the eligibility criteria using the PICO format; these included population, intervention, comparison, and outcome. The methodological quality of the individual studies was assessed using the Cochrane risk of bias tool recommended by the Cochrane Handbook (Higgins & Green, 2011).

A comprehensive computerized literature search was undertaken to identify all relevant data, ensuring transparency and reproducibility. The search strategy included search terms and keywords derived from the PICO format. The following databases were searched from the inception of the study through January 25, 2019, without language restrictions: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI), Digital Library of Theses and Dissertations of the University of São Paulo (BDTD), and System for Information on Grey Literature in Europe (SIGLE) for unpublished research. This was supplemented by a manual search of all reference lists from the obtained related studies and previous systematic review articles.

The search strategy included terms derived from the PICO format: (P) Population: Any orthodontic patients, irrespective of age, sex, or race, whose treatment includes bilateral extraction of upper first premolars and conventional canine retraction (”orthodontic”, ”orthodontics”, ”orthodontic appliance”, ”orthodontic treatment”); (I) Intervention: Conventional canine retraction with the application of phototherapy, such as low-level laser therapy or light-emitting diode (”low-level laser therapy”, ”low-level light therapy”, ”LLLT”, ”light-emitting diode”, ”low-power laser irradiation”, ”low-intensity laser therapy”, ”light therapy”, ”laser therapy”, ”phototherapy”, ”phototherapies”, ”LED”, ”photobiomodulation”); (C) Comparison: Conventional canine retraction; (O) Outcome: Rate of canine retraction and incidence of risks in root resorption, alveolar bone resorption, and periodontal tissue destruction (”dental movement”, ”tooth movement”, ”canine retraction”, ”canine distalization”, ”rate”, ”speed”, ”accelerate”).

To be included in this review, studies had to involve healthy human subjects of any age, gender, or ethnicity who had undergone bilateral symmetrical extraction of their upper first premolars and were receiving conventional canine retraction as part of their fixed orthodontic treatment. Additionally, the studies needed to be randomized controlled trials employing a split-mouth design and provide quantitative data on the individual parameters of canine retraction. Importantly, the focus was on studies that compared the rate of canine retraction using phototherapy as the experimental intervention against a placebo or control group.

Studies were excluded from the review if they involved in-vitro experiments or animal subjects, or if the intervention and control groups were not appropriately matched. Moreover, case reports, case series, review articles, and systematic reviews were not considered in the review, as the focus was strictly on randomized controlled trials that provided robust, quantitative, and directly comparable data.

All information from eligible studies will be organized in tabular form for qualitative and quantitative analysis, including details such as first author, publication year, number of patients, average age, gender, specific interventions for each group, treatment duration, and all outcome measures. If any data is missing, the author will be contacted for further clarification. Studies that are deemed ineligible will also be listed along with the primary reason for their exclusion. To evaluate the efficacy of phototherapy, several parameters are essential, including the amount of canine retraction obtained, wavelength, output power, energy density, and the incidence of root resorption, alveolar bone resorption, as well as periodontal tissue destruction.

Two strategies were employed to evaluate the quality of the included clinical studies. Firstly, the Jadad scoring system (Jadad et al., 1996), a five-point scoring method, was considered optimal; a study was deemed high quality when it achieved three points or more. Secondly, the Cochrane risk of bias tool, as recommended by the Cochrane Handbook (Higgins & Green, 2011), was utilised to assess the following domains: random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

Each study was categorised as low risk if all assessed domains had a low risk of bias, unclear risk if any domain had an unclear risk of bias, and high risk if any domain had a high risk of bias.

2.1 Statistics

Means, standard deviations, and sample sizes were extracted in each study to calculate the effect sizes (Hedges' g) and the 95% confidence interval (CI) from the follow-up phase at each time point, whereby a positive effect size would indicate a result favouring phototherapy in comparison with the control group.

The combined overall mean was performed in all included studies for the meta-analysis to explore each parameter of phototherapy and to provide estimates about the appropriate settings necessary to favour the rate of canine retraction. Parameters according to the used wavelength, output power, and energy density at multiple time points and the combined overall mean effect size (Hedges' g) were tested to justify the magnitude of the effect and to evaluate its clinical and practical significance.

To compare phototherapy with the control group, a small effect size is defined as > 0.2 to 0.4, a medium effect size is > 0.5 to 0.7, and a large effect size is > 0.8 (Durlak, 2009). An I^2 index was calculated to assess the degree of heterogeneity. A random-effects method was applied, which is recommended by the Cochrane Handbook due to variations in interventions and sample characteristics among included studies; the findings were depicted by forest plots to describe factors related to the efficacy of phototherapy. All statistical analyses were performed using Comprehensive Meta-Analysis software version 3.

3 Results

A total of 406 studies were identified after removing duplicates. Three hundred and seventy-six studies were excluded after reading the titles and abstracts, as the study designs employed were not applicable. After reviewing the full-text articles for the remaining 31 studies, 21 studies were deemed eligible for inclusion in the qualitative review, and 11 studies were eligible for meta-analysis (**Figure 3**).

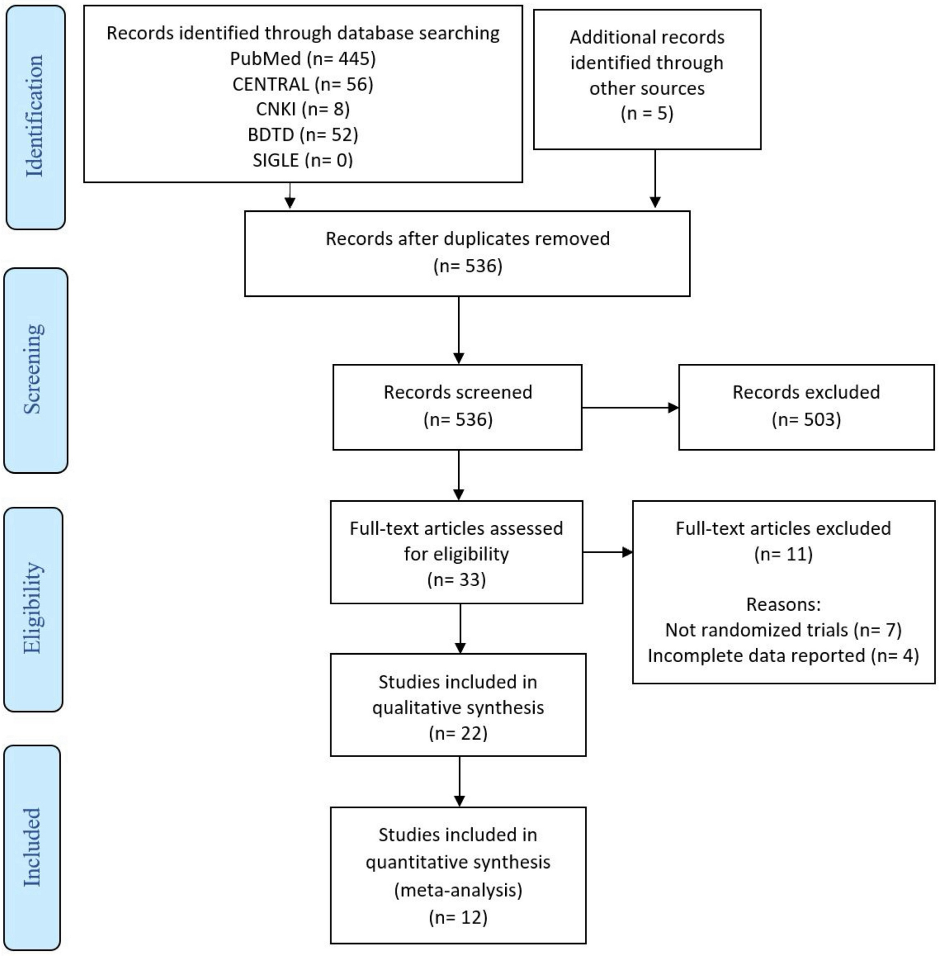


Figure 3. PRISMA 2009 Flow Diagram.

The 21 human studies involved a total of 302 patients aged between 10.5 and 35 years, conducted across various countries (**Table 1**). Geographically, a significant number of studies are from India and Brazil, suggesting a regional focus in orthodontic research or institutional prioritisation within these countries. Brazil appears in four instances, and India leads with seven, indicating a relatively high research activity in these locations. Meanwhile, other countries such as Iran and Turkey are moderately represented. Of the included studies, 18 reviews were written in English, one in Arabic, and two in Portuguese.

The majority of studies have a relatively small sample size, ranging mostly between 10 and 20. Patients in all studies acted as their own controls; thus, 302 experimental canines received phototherapy, and 302 canines were in the control group. Regarding patient demographics, age variation seems substantial across studies, with many authors not reporting standard deviations. Most studies include adolescents and young adults, typically aged between 12 and 25 years, which could be attributed to the common peak age for orthodontic treatment. The gender distribution varies significantly: Some studies report a nearly equal male-to-female ratio, while others exclusively focus on one gender, particularly females in multiple cases. The study durations vary widely, from as short as 1.8 months to as long as 39 months. Such variations could indicate differences in the complexity of orthodontic cases, treatment plans, and outcome measures.

Table 1. General information concerning the included studies. NR = Not Reported; m = months; w = weeks; d = days; M = Male; F = Female; SD = Standard Deviation; S-time = study duration in month.

1st Author, date	Country	Patients (M/F)	Age ± SD	S-time
Cruz, 2004	Brazil	11 (NR)	12-18	2
Limpanichkul, 2006	Thailand	12 (4/8)	20.1 ± 3.4	3
Sousa, 2011	Brazil	5 (NR)	10.5-20.2	4
Hosseini, 2011	Iran	12 (4/8)	12-25	2
Doshi-Mehta, 2012	India	20 (8/12)	12-23	4.5
Souza, 2014	Brazil	11 (NR)	12-17	3
Kansal, 2014	India	10 (NR)	NA	2.1
Heravi, 2014	Iran	20 (3/17)	15-31	1.9
Pereira, 2014	Brazil	11 (7/4)	12-17	3
Garg, 2014	India	18 (NR)	>17	2.8
Dalaie, 2015	Iran	12 (3/9)	20.1	2.2
Yassaei, 2016	Iran	11 (0/11)	14-25	4
Ekizer, 2016	Turkey	20 (7/13)	16.8 ± 1.4	3
El-Hosieny, 2017	Egypt	10 (0/10)	14-18	5.9
Qamruddin, 2017	USA	22 (11/11)	12-25	2.1
Ureturk, 2017	Turkey	15 (7/8)	12-19	3
Kochar, 2017	India	20 (12/8)	16-24	4
Varella, 2018	India	10 (4/6)	14-25	1.8
Guram, 2018	India	20 (8/12)	17-24	39
Arumughan, 2018	India	12 (NR)	17-35	2.8
Ubolviroj, 2018	Thailand	20 (NR)	21.1 ± 3.9	4.8

3.1 Phototherapy and irradiation doses

Different phototherapy types, modes of delivery, dosages, and the number of irradiations were specified in detail for each trial (**Table 2**). The study data reveals patterns in the type of laser used, the frequency of application, and contact methodology. The majority of studies employed the Gallium Aluminium Arsenide (GaAlAs) laser, reflecting a preference for this specific type in phototherapy research.

Direct Contact (DC) application was the most frequently reported contact method, suggesting a potential trend towards ensuring precise application of irradiation doses. The number of spots per tooth varied, but a significant portion reported ten spots per tooth. Irradiation durations showed some variability, with most studies opting for durations around 10 seconds, though extremes ranged from as low as 3 seconds to as high as 1200 seconds in specific cases like LED usage.

Regarding frequency, a considerable number of studies applied phototherapy multiple specific days, though other schedules such as daily, weekly, or bi-weekly were also noted. The heterogeneity in methodologies, especially concerning irradiation durations and frequencies, highlights the experimental nature and individualized protocols in phototherapy research. This diversity underscores the adaptive approaches tailored to specific study designs, yet suggests a need for more standardized protocols to enhance comparability and reproducibility in future investigations.

Table 2. Phototherapy and irradiation doses. Direct Contact (DC), Non-Contact (NC), Not Reported (NR), Not Specified (NS), Gallium Aluminium Arsenide laser (GaAlAs), Aluminium Gallium Arsenide laser (AlGaAs), Arsenic Gallium Aluminium laser (AsGaAl), Gallium Arsenide laser (GaAs), Light Emitting Diode (LED).

1st Author, date	Phototherapy	Contact	Spots/tooth	Irradiation	Frequency
Cruz, 2004	GaAlAs	DC	10	10 s	Once or specific days in a month
Limpanichkul, 2006	GaAlAs	DC	8	23 s	Multiple specific days
Sousa, 2011	AsGaAl	DC	10	10 s	Multiple specific days
Hosseini, 2011	GaAlAs	NR	NS	42-83 s	Multiple specific days
Doshi-Mehta, 2012	AlGaAs	DC	10	10 s	Multiple specific days
Souza, 2014	ArGaAl	DC	10	10 s	Once or specific days in a month
Kansal, 2014	GaAs	DC	10	10 s	Once or specific days in a month
Heravi, 2014	GaAlAs	DC	10	30 s	Multiple specific days
Pereira, 2014	GaAlAs	DC	10	10-20 s	Once or specific days in a month
Garg, 2014	GaAlAs	NC	NS	30 s	Once or specific days in a month
Dalaie, 2015	GaAlAs	NR	8	10 s	Multiple specific days
Yassaei, 2016	GaAlAs	DC	6	8-10 s	Once or specific days in a month
Ekizer, 2016	LED	transcut	NA	1200 s	Daily for a period
El-Hosieny, 2017	GaAlAs	NC	NS	20 s	Multiple specific days
Qamruddin, 2017	GaAlAs	DC	10	3 s	Once or specific days in a month
Ureturk, 2017	GaAlAs	DC	10	10 s	Multiple specific days
Kochar, 2017	AlGaAs	DC	10	10 s	Multiple specific days
Varella, 2018	GaAlAs	NR	10	10 s	Once or specific days in a month
Guram, 2018	GaAlAs	DC	8	10 s	Weekly/Bi-weekly
Arumughan, 2018	GaAlAs	DC	6	10 s	Once or specific days in a month
Ubolviroj, 2018	LED	NC	12	5 s	Weekly/Bi-weekly

3.2 Method of canine retraction, reference points, and measurements used

Various methods, reference points, and measurement tools have been employed to ensure accurate and effective results. **Table 3** provides a detailed breakdown of the studies that were included, noting the specific methods, reference points, and measurement techniques used for each. The primary method employed for canine retraction, as indicated in the studies, involves the use of Nickel Titanium (NiTi) closing springs. A few studies have utilized elastomeric chains (E-chains) as an alternative. The force applied across most studies is consistently set at 150 grams, except for one study by El-Hosieny in 2017, which used a 200-gram force for en masse retraction.

Multiple reference points have been used to track and measure the movement of the canine teeth. The most frequently used reference point measurement is "cusp tip of canine to mesiobuccal cusp of the first molar", appearing in 7 out of the 21 studies (almost one-third of the studies). This prevalence suggests that the measurement from the cusp tip of the canine to the mesiobuccal cusp of the first molar is a reliable method for quantifying canine retraction in orthodontic research.

Table 3. Method of canine retraction, reference points and measurement methods. c.s. = coil spring; g = gram; TPA = transpalatal arch; C = canine; M = molar; P = premolar; SP = sutura palatina; PI = papilla incisiva; NR = not reported.

Study	Retraction	Force	Anchorage	Reference points	Gauge
Cruz, 2004	NiTi c.s.	150 g	Nance, TPA	C, 1stM	Digital caliper
Limpanichkul, 2006	NiTi c.s.	150 g	Vertical loop stops	SP, C	Stereomicroscope
Sousa, 2011	NiTi c.s.	150 g	NR	PI, C	3D models
Hosseini, 2011	NiTi c.s.	150 g	Omega loop	PI, C	Digital caliper
Doshi-Meta, 2012	NiTi c.s.	150 g	TPA	C, 1stM	Digital caliper
Souza, 2014	NiTi c.s.	150 g	TPA	PI, C	OrthoAnalyzer
Kansal, 2014	E-chain	150 g	TPA	C, 1stM	Digital caliper
Heravi, 2014	NiTi c.s.	150 g	Vertical loop	C, 1stM	OrthoAnalyzer
Pereira, 2014	NiTi c.s.	150 g	TPA	C, 1stM	Digital caliper
Garg, 2014	NiTi c.s.	150 g	TAD	C, 2ndP	Digital caliper
Dalaie, 2015	NiTi c.s.	150 g	NR	C, 1stM	Digital caliper
Yassaei, 2016	NiTi c.s.	150 g	TPA	C, 1stM	Digital caliper
Ekizer, 2016	NiTi c.s.	150 g	TAD	PI, rugae	OrthoAnalyzer
El-Hosieny, 2017	NiTi c.s.	200 g	TAD	PI, rugae, C, SP	Scanner
Qamruddin, 2017	NiTi c.s.	150 g	NR	C, rugae	Digital models
Ureturk, 2017	NiTi c.s.	150 g	NR	C, 2ndM, SP	OrthoAnalyzer
Kochar, 2017	NiTi c.s.	150 g	Nance	C, 1stM	Digital caliper
Varella, 2018	NiTi c.s.	150 g	NR	C, rugae	Software
Guram, 2018	NiTi c. loops	150 g	NR	C, 1stM	Digital caliper
Arumughan, 2018	NiTi c.s.	150 g	NR	C, 2ndP	Digital caliper
Ubolviroj, 2018	NiTi c.s.	150 g	Ligation	C, 1stM	Synapse program

3.3 Effect on the rate of canine retraction and characteristics of overall studies

The study data on the rate of canine retraction indicates several trends and patterns related to frequency, heterogeneity, and specialities (Supplementary **Table S4**). The data encompasses multiple studies with varying parameters such as wavelength, output power, and energy density, focusing on the effects of these variables on phototherapy outcomes over 30, 60, and 90 days. A conspicuous observation is that the wavelengths used in the studies range predominantly between 618 nm and 980 nm, with a notable concentration around 780 nm and 810 nm, suggesting a preference or optimal efficacy for this range in phototherapy applications.

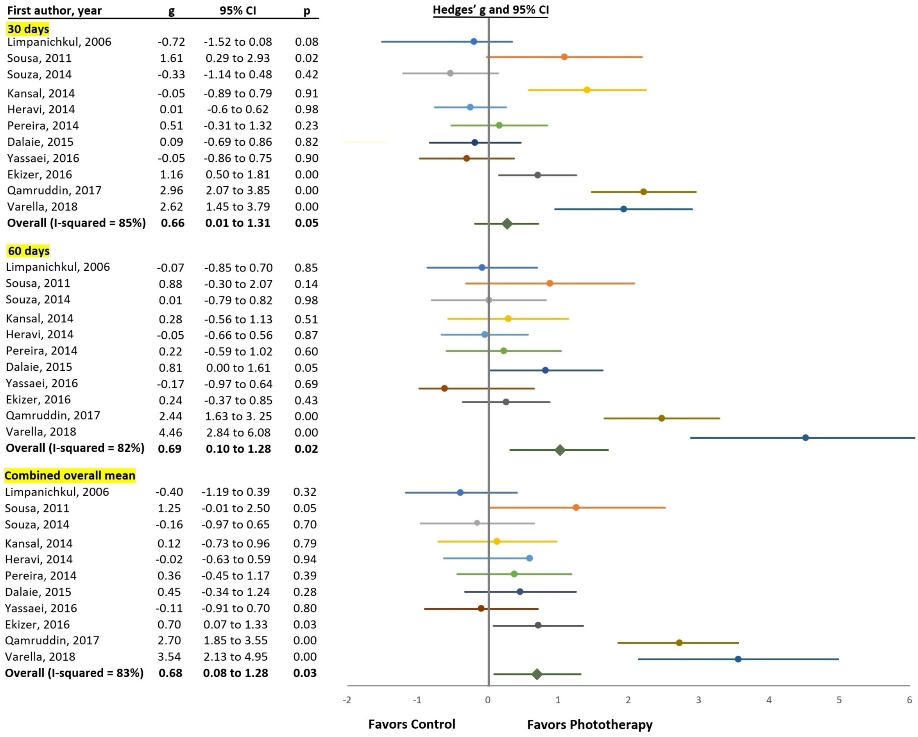
The heterogeneity of the studies is evident in the broad range of output powers employed, from as low as 0.2 mW up to 1200 mW, and the diversity in energy densities and radiation doses. This variability makes direct comparisons challenging, as seen from multiple exclusions due to "incomparable data." However, several studies reported statistically significant differences in outcomes between phototherapy and control groups. The mean values and standard deviations for phototherapy versus control demonstrate this variability, with some studies showing marked improvement in the treated groups, such as Sousa (2011), where phototherapy significantly increased the canine retraction rate compared to the control.

Specialties within these studies also highlight trends pertinent to treatment durations and parameter effectiveness. For instance, many studies report data at specific intervals (30, 60, 90 days), allowing temporal analysis of phototherapy effects. Studies with higher power outputs and energy densities tend to show significant results earlier in the timelines, indicating a potential correlation between these parameters and the rapidity of therapeutic outcomes.

Moreover, the reasons for exclusion often cite incomparable data, which underscores the importance of standardized protocols in future research to enable more robust meta-analyses. Some studies like those of Sousa (2011) consistently report significant differences in outcomes, suggesting the effectiveness of specific phototherapy protocols, although variations in methodology across studies complicate a singular conclusion.

The analysis reveals a prominent focus on the wavelength range of 780 nm to 810 nm, with substantial variability in other treatment parameters. Despite this heterogeneity, significant therapeutic outcomes are frequently reported, especially with higher intensity treatments over shorter durations.

The data presented in **Figure 4** show that the majority of effect sizes were positive, suggesting that phototherapy enhanced the rate of canine retraction compared to the control group, with medium to large effect sizes observed at both 30 days (Hedges' g = 0.66, 95% CI [0.01 to 1.31]) and 60 days (Hedges' g = 0.69, 95% CI [0.10 to 1.28]). However, analyses of heterogeneity were statistically significant at 30 days ($I^2 = 85\%$, p = 0.05) and 60 days ($I^2 = 82$, p = 0.02). The combined overall mean across all time points was also computed, and the pooled effect size of phototherapy resulted in a significant medium to large effect size (Hedges' g = 0.68, 95% CI [0.08 to 1.28]), but a considerable degree of heterogeneity was discovered ($I^2 = 83\%$, p = 0.03).



First author, year	g	95% CI	p
30 days			
Limpanichkul, 2006	-0.72	-1.52 to 0.08	0.08
Sousa, 2011	1.61	0.29 to 2.93	0.02
Souza, 2014	-0.33	-1.14 to 0.48	0.42
Kansal, 2014	-0.05	-0.89 to 0.79	0.91
Heravi, 2014	0.01	-0.6 to 0.62	0.98
Pereira, 2014	0.51	-0.31 to 1.32	0.23
Dalaie, 2015	0.09	-0.69 to 0.86	0.82
Yassaei, 2016	-0.05	-0.86 to 0.75	0.90
Ekizer, 2016	1.16	0.50 to 1.81	0.00
Qamruddin, 2017	2.96	2.07 to 3.85	0.00
Varella, 2018	2.62	1.45 to 3.79	0.00
Overall (I-squared = 85%)	**0.66**	**0.01 to 1.31**	**0.05**
60 days			
Limpanichkul, 2006	-0.07	-0.85 to 0.70	0.85
Sousa, 2011	0.88	-0.30 to 2.07	0.14
Souza, 2014	0.01	-0.79 to 0.82	0.98
Kansal, 2014	0.28	-0.56 to 1.13	0.51
Heravi, 2014	-0.05	-0.66 to 0.56	0.87
Pereira, 2014	0.22	-0.59 to 1.02	0.60
Dalaie, 2015	0.81	0.00 to 1.61	0.05
Yassaei, 2016	-0.17	-0.97 to 0.64	0.69
Ekizer, 2016	0.24	-0.37 to 0.85	0.43
Qamruddin, 2017	2.44	1.63 to 3. 25	0.00
Varella, 2018	4.46	2.84 to 6.08	0.00
Overall (I-squared = 82%)	**0.69**	**0.10 to 1.28**	**0.02**
Combined overall mean			
Limpanichkul, 2006	-0.40	-1.19 to 0.39	0.32
Sousa, 2011	1.25	-0.01 to 2.50	0.05
Souza, 2014	-0.16	-0.97 to 0.65	0.70
Kansal, 2014	0.12	-0.73 to 0.96	0.79
Heravi, 2014	-0.02	-0.63 to 0.59	0.94
Pereira, 2014	0.36	-0.45 to 1.17	0.39
Dalaie, 2015	0.45	-0.34 to 1.24	0.28
Yassaei, 2016	-0.11	-0.91 to 0.70	0.80
Ekizer, 2016	0.70	0.07 to 1.33	0.03
Qamruddin, 2017	2.70	1.85 to 3.55	0.00
Varella, 2018	3.54	2.13 to 4.95	0.00
Overall (I-squared = 83%)	**0.68**	**0.08 to 1.28**	**0.03**

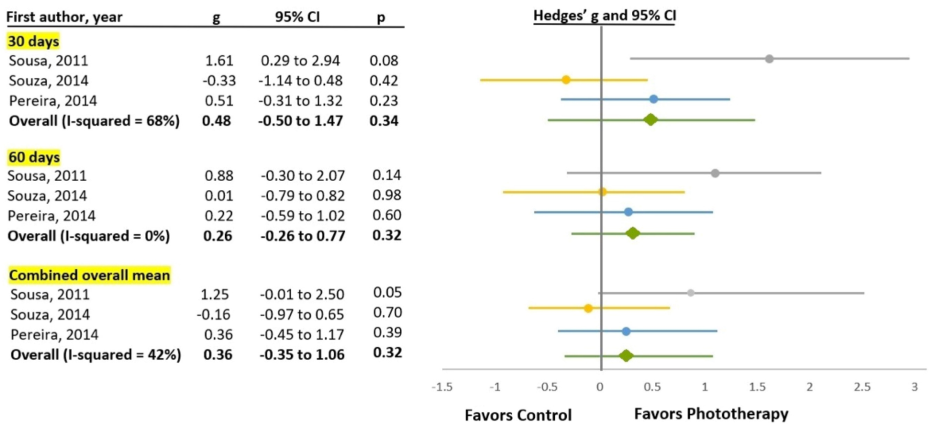
Figure 4. Forest plot evaluating the overall effect of phototherapy. g: Hedges' g; CI; Confidence interval; p: p-value.

To investigate the influence of wavelength on canine retraction speed each parameter was assessed, specifically examining how 780 nm and 940 nm wavelengths affect the impact of phototherapy on the rate of canine retraction. The majority of the calculated effect sizes indicated a positive influence of phototherapy.

3.4 Effect of wavelength, output power and energy density on the rate of canine retraction

The study investigated the impact of phototherapy on the rate of canine retraction by analysing the effects of 780 nm and 940 nm wavelengths, as well as output powers of 20 mW and 100 mW. All estimated effect sizes revealed a consistent benefit of phototherapy across these parameters.

Most studies using 780 nm wavelength (**Figure 5**) showed a small to medium effect size at both 30 days (Hedges' g = 0.48, 95% CI [-0.50 to 1.47]), with moderate to substantial heterogeneity ($I^2 = 68\%$, p = 0.34), and 60 days (Hedges' g = 0.26, 95% CI [-0.26 to 0.77]), with analyses of heterogeneity that were not statistically significant ($I^2 = 0\%$, p = 0.32). The combined overall mean only resulted in a small to medium effect size (Hedges' g = 0.36, 95% CI [-0.35 to 1.06]) with moderate heterogeneity ($I^2 = 42\%$, p = 0.32).



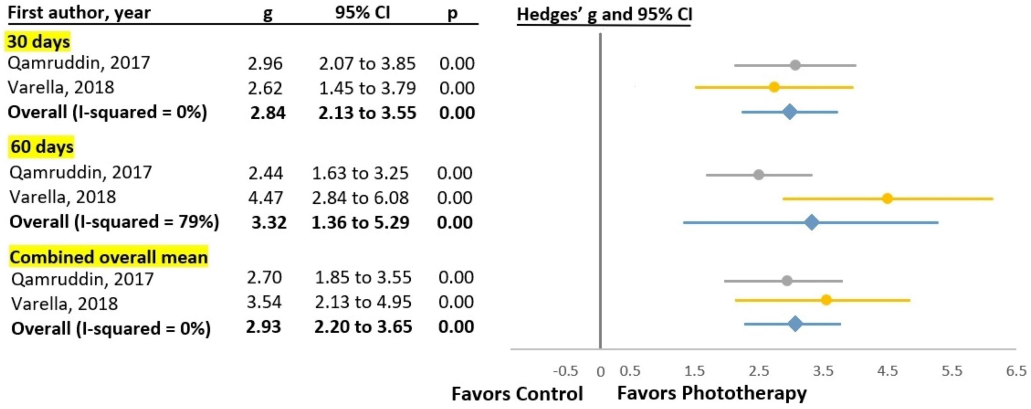
First author, year	g	95% CI	p
30 days			
Sousa, 2011	1.61	0.29 to 2.94	0.08
Souza, 2014	-0.33	-1.14 to 0.48	0.42
Pereira, 2014	0.51	-0.31 to 1.32	0.23
Overall (I-squared = 68%)	**0.48**	**-0.50 to 1.47**	**0.34**
60 days			
Sousa, 2011	0.88	-0.30 to 2.07	0.14
Souza, 2014	0.01	-0.79 to 0.82	0.98
Pereira, 2014	0.22	-0.59 to 1.02	0.60
Overall (I-squared = 0%)	**0.26**	**-0.26 to 0.77**	**0.32**
Combined overall mean			
Sousa, 2011	1.25	-0.01 to 2.50	0.05
Souza, 2014	-0.16	-0.97 to 0.65	0.70
Pereira, 2014	0.36	-0.45 to 1.17	0.39
Overall (I-squared = 42%)	**0.36**	**-0.35 to 1.06**	**0.32**

Figure 5. Forest plot evaluating 780 nm on the rate of canine retraction. g: Hedges' g; CI; Confidence interval; p: p-value.

Included studies using 940 nm wavelength (**Figure 6**) supported the efficacy of phototherapy relative to the control group at both time points. A large effect size was found after 30 days (Hedges' g = 1.25, 95% CI [0.66 to 1.84]), with no heterogeneity ($I^2 = 0\%$, p = 0.00), and after 60 days (Hedges' g = 3.32, 95% CI [1.36 to 5.29]), with substantial heterogeneity ($I^2 = 79\%$, p = 0.00). The combined overall mean favours phototherapy, with a large effect size (Hedges' g = 2.93, 95% CI [2.20 to 3.65]) and no heterogeneity ($I^2 = 0\%$, p = 0.00).

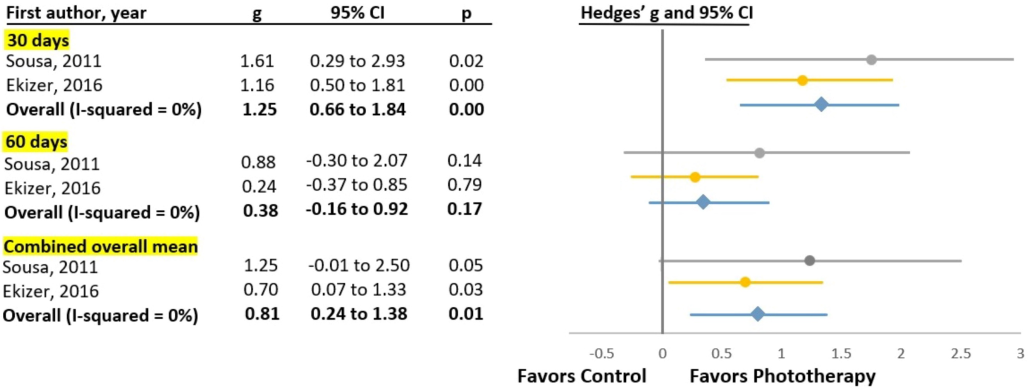
Studies using 20 mW (**Figure 7**) demonstrated positive effect sizes at both time points; a large effect size was evident at 30 days (Hedges' g = 1.25, 95% CI [0.66 to 1.84]), while at 60 days, the effect size was small to medium (Hedges' g = 0.38, 95% CI [-0.16 to 0.92]). Moreover, analyses of heterogeneity were not statistically significant (30 days: $I^2 = 0\%$, p = 0.00; 60 days: $I^2 = 0\%$, p = 0.17). The combined overall mean suggests a statistically significant effect (p = 0.01), indicating a large effect size in favour of phototherapy relative to the control group (Hedges' g = 0.81, 95% CI [0.24 to 1.38]), with no heterogeneity between the results from the trials ($I^2 = 0\%$, p = 0.01).

A large effect size was discovered at two time points with 100 mW (**Figure 8**), specifically 30 days (Hedges' g = 0.95, 95% CI [-0.47 to 2.37]) and 60 days (Hedges' g = 1.38, 95% CI



First author, year	g	95% CI	p
30 days			
Qamruddin, 2017	2.96	2.07 to 3.85	0.00
Varella, 2018	2.62	1.45 to 3.79	0.00
Overall (I-squared = 0%)	**2.84**	**2.13 to 3.55**	**0.00**
60 days			
Qamruddin, 2017	2.44	1.63 to 3.25	0.00
Varella, 2018	4.47	2.84 to 6.08	0.00
Overall (I-squared = 79%)	**3.32**	**1.36 to 5.29**	**0.00**
Combined overall mean			
Qamruddin, 2017	2.70	1.85 to 3.55	0.00
Varella, 2018	3.54	2.13 to 4.95	0.00
Overall (I-squared = 0%)	**2.93**	**2.20 to 3.65**	**0.00**

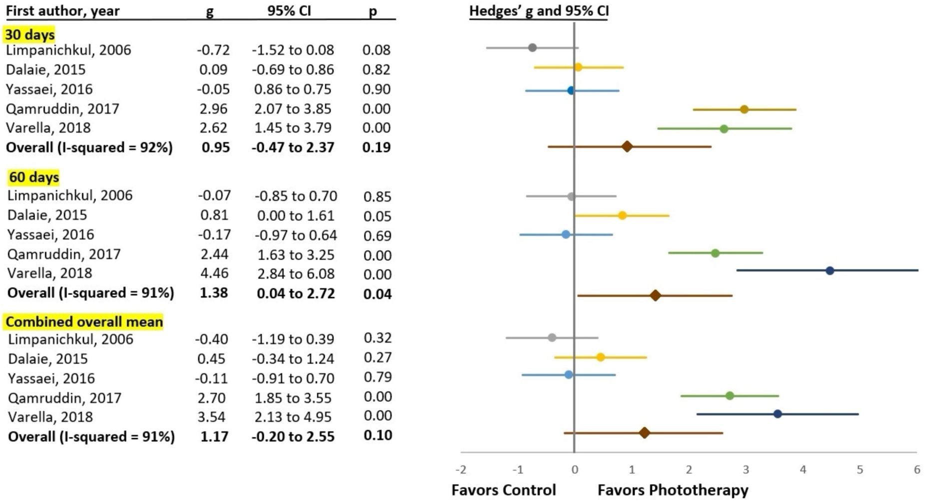
Figure 6. Forest plot evaluating 940 nm on the rate of canine retraction. g: Hedges' g; CI; Confidence interval; p: p-value.



First author, year	g	95% CI	p
30 days			
Sousa, 2011	1.61	0.29 to 2.93	0.02
Ekizer, 2016	1.16	0.50 to 1.81	0.00
Overall (I-squared = 0%)	**1.25**	**0.66 to 1.84**	**0.00**
60 days			
Sousa, 2011	0.88	-0.30 to 2.07	0.14
Ekizer, 2016	0.24	-0.37 to 0.85	0.79
Overall (I-squared = 0%)	**0.38**	**-0.16 to 0.92**	**0.17**
Combined overall mean			
Sousa, 2011	1.25	-0.01 to 2.50	0.05
Ekizer, 2016	0.70	0.07 to 1.33	0.03
Overall (I-squared = 0%)	**0.81**	**0.24 to 1.38**	**0.01**

Figure 7. Forest plot evaluating 20 mW on the accumulated rate of canine retraction. g: Hedges' g; CI; Confidence interval; p: p-value.

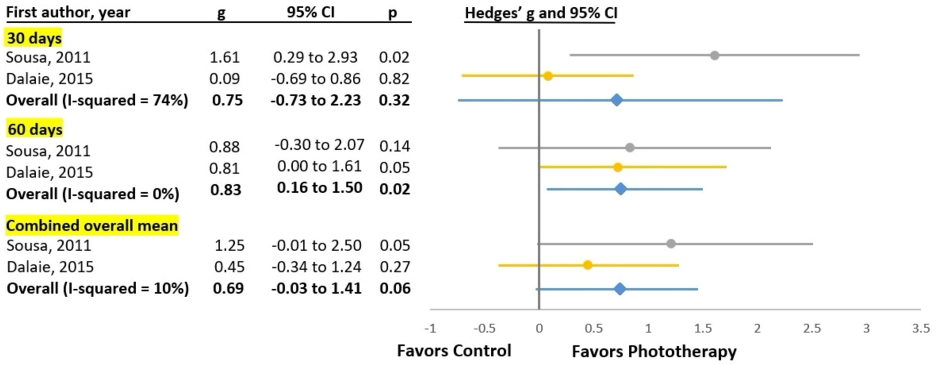
[0.04 to 2.72]). However, there is a considerable degree of heterogeneity between the trials (30 days: $I^2 = 92\%$; 60 days: $I^2 = 91\%$), suggesting that the analysis for each time point is uncertain, as each trial yielded inconsistent results. The test for the combined overall mean has a large effect size (Hedges' g = 1.17, 95% CI [-0.20 to 2.55]), but this indicates that there is no statistically significant effect ($p = 0.10$), and substantial heterogeneity exists between trials at each of these time points ($I^2 = 91\%$).



First author, year	g	95% CI	p
30 days			
Limpanichkul, 2006	-0.72	-1.52 to 0.08	0.08
Dalaie, 2015	0.09	-0.69 to 0.86	0.82
Yassaei, 2016	-0.05	0.86 to 0.75	0.90
Qamruddin, 2017	2.96	2.07 to 3.85	0.00
Varella, 2018	2.62	1.45 to 3.79	0.00
Overall (I-squared = 92%)	**0.95**	**-0.47 to 2.37**	**0.19**
60 days			
Limpanichkul, 2006	-0.07	-0.85 to 0.70	0.85
Dalaie, 2015	0.81	0.00 to 1.61	0.05
Yassaei, 2016	-0.17	-0.97 to 0.64	0.69
Qamruddin, 2017	2.44	1.63 to 3.25	0.00
Varella, 2018	4.46	2.84 to 6.08	0.00
Overall (I-squared = 91%)	**1.38**	**0.04 to 2.72**	**0.04**
Combined overall mean			
Limpanichkul, 2006	-0.40	-1.19 to 0.39	0.32
Dalaie, 2015	0.45	-0.34 to 1.24	0.27
Yassaei, 2016	-0.11	-0.91 to 0.70	0.79
Qamruddin, 2017	2.70	1.85 to 3.55	0.00
Varella, 2018	3.54	2.13 to 4.95	0.00
Overall (I-squared = 91%)	**1.17**	**-0.20 to 2.55**	**0.10**

Figure 8. Forest plot evaluating 100 mW on the rate of canine retraction. g: Hedges' g; CI; Confidence interval; p: p-value.

Each time point demonstrated a positive effect size when using an energy density of 5 J/cm^2 (**Figure 9**). A medium to large effect size was observed after 30 days (Hedges' g = 0.75, 95% CI [-0.73 to 2.23]), accompanied by considerable heterogeneity ($I^2 = 74\%$, $p = 0.32$), and after 60 days (Hedges' g = 0.83, 95% CI [0.16 to 1.50]), where no significant heterogeneity was noted ($I^2 = 0\%$, $p = 0.02$). The overall combined mean yielded a medium to large effect size (Hedges' g = 0.69, 95% CI [-0.03 to 1.41]), with no significant heterogeneity ($I^2 = 10\%$). However, it suggests that there is no statistically significant effect ($p = 0.06$).



First author, year	g	95% CI	p
30 days			
Sousa, 2011	1.61	0.29 to 2.93	0.02
Dalaie, 2015	0.09	-0.69 to 0.86	0.82
Overall (I-squared = 74%)	**0.75**	**-0.73 to 2.23**	**0.32**
60 days			
Sousa, 2011	0.88	-0.30 to 2.07	0.14
Dalaie, 2015	0.81	0.00 to 1.61	0.05
Overall (I-squared = 0%)	**0.83**	**0.16 to 1.50**	**0.02**
Combined overall mean			
Sousa, 2011	1.25	-0.01 to 2.50	0.05
Dalaie, 2015	0.45	-0.34 to 1.24	0.27
Overall (I-squared = 10%)	**0.69**	**-0.03 to 1.41**	**0.06**

Figure 9. Forest plot evaluating 5 J/cm^2 on the rate of canine retraction. g: Hedges' g; CI; Confidence interval; p: p-value.

3.5 Root Resorption, alveolar bone resorption and periodontal tissue destruction

The studies included reported varying degrees of findings, with several authors documenting no observed effects or not reporting their findings. Root resorption was noted as not observed in five instances (Cruz, 2004; Sousa, 2011; Kansal, 2014; Dalaie, 2015; Ubolviroj, 2018). Notably, Ubolviroj (2018) reported minimal resorption in two teeth across both groups. However, most studies either reported NR (not reported) or indicated a lack of observation.

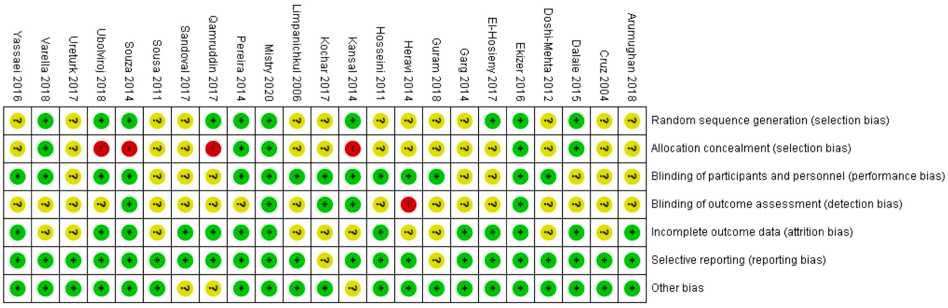
In terms of alveolar bone resorption, this aspect was reported as not observed in multiple studies (Cruz, 2004; Sousa, 2011; Doshi-Mehta, 2012; Kansal, 2014; Dalaie, 2015; Ubolviroj, 2018). A considerable number of studies did not provide any data on alveolar bone resorption.

Similarly, periodontal tissue destruction was often reported as not observed across various studies, including Cruz (2004), Sousa (2011), Doshi-Mehta (2012), and Ubolviroj (2018). Again, several studies had no reported data on this topic.

In summary, the majority of the studies did not report significant evidence of root resorption, alveolar bone resorption, or periodontal tissue destruction, with many entries indicating either a lack of observation or incomplete data reporting. This indicates a potential trend towards stability of these tissues within the evaluated contexts, but further detailed studies may be warranted to confirm these observations and provide comprehensive insights.

3.6 Risk of Bias

All included studies were randomised trials; however, the quality of evidence determined by the Jadad scale scoring system and the Cochrane risk of bias tool (**Figure 10**) was low due to the unclear risk found in all domains except for selective reporting. The scale comprises three main components: randomization, blinding, and the management of withdrawals and drop-outs. The total score for each study reflects the quality of its design and execution, with higher scores indicating a lower risk of bias.



Yassaei 2016	Varella 2018	Ureturk 2017	Ubolviroj 2018	Souza 2014	Sousa 2011	Sandoval 2017	Qamruddin 2017	Pereira 2014	Mistry 2020	Limpanichkul 2006	Kochar 2017	Kansal 2014	Hosseini 2011	Heravi 2014	Guram 2018	Garg 2014	El-Hosieny 2017	Ekizer 2016	Doshi-Mehta 2012	Dalaie 2015	Cruz 2004	Arumughan 2018	
?	+	?	+	+	?	?	+	+	+	?	?	+	?	?	?	?	+	+	?	+	?	?	Random sequence generation (selection bias)
?	+	?	-	-	?	?	-	+	+	?	?	-	?	?	?	?	?	+	?	+	?	?	Allocation concealment (selection bias)
+	+	?	+	+	?	?	?	+	+	+	+	+	+	+	+	?	?	+	+	?	?	?	Blinding of participants and personnel (performance bias)
?	?	?	?	+	?	?	?	?	+	?	+	+	?	-	?	?	?	+	?	?	?	?	Blinding of outcome assessment (detection bias)
+	?	?	+	+	?	+	+	+	+	?	?	?	+	?	?	+	+	+	?	+	?	+	Incomplete outcome data (attrition bias)
+	+	+	+	+	+	+	+	+	+	+	?	+	+	+	?	+	+	+	+	+	+	+	Selective reporting (reporting bias)
+	+	+	+	+	+	?	?	+	+	+	+	?	+	+	+	+	+	+	+	+	+	+	Other bias

Figure 10. Cochrane risk of bias tool.

The scoring reveals a range of results among the studies. Several studies achieved high total scores, indicating robust methodologies with effective randomization, blinding, and management of drop-outs. For instance, Souza (2014), Ubolviroj (2018), and Ekizer (2016) received scores of 5, suggesting strong methodological quality. A total score of 4 was also attained by studies such as Kansal (2014), Dalaie (2015), and Varella (2018), indicating a commendable quality level.

Conversely, there were studies with lower total scores, highlighting potential vulnerabilities in their design. Cruz (2004) garnered a score of 1, reflecting significant methodological shortcomings, particularly in blinding and the management of withdrawals. Other studies, such as Heravi (2014) and Garg (2014), also received scores of 2, indicating moderate concerns regarding their design and execution.

Overall, the data exhibit variability in the methodological quality among the studies assessed. While several studies demonstrate rigorous designs, others present notable risks of bias that may impact the reliability of their findings. Future research might benefit from adopting more stringent methodological guidelines to enhance the overall quality and validity of the evidence generated.

4 Discussion

This review and meta-analysis aims to quantitatively compare studies that have evaluated phototherapy in terms of whether it accelerates the rate of upper canine retraction during orthodontic treatment relative to the conventional canine retraction on a split-mouth design in humans. It also evaluates the different types of parameters that cause the phototherapy to take effect and investigates its undesirable effects.

To the best of our knowledge, this is the most extensive review and meta-analysis that has evaluated phototherapy. It has demonstrated that it could improve the rate of canine retraction and uncovered a marked improvement after a follow-up compared with the control group. Concerning its parameters, a subgroup analysis was available regarding the effect of wavelength and output power, in which a 940 nm wavelength and 100 mW output power significantly improved the rate of orthodontic tooth movement. Furthermore, the results suggested a healthy response from the roots of the teeth, periodontal tissues, and alveolar bone.

The improvement in the acceleration of tooth movement based on the overall estimate was supported by a comparable study (Imani et al., 2018), which evaluated six randomized trials, uncovering significant efficacy in favour of phototherapy. However, another meta-analysis with six randomized trials yielded no evidence that phototherapy could induce orthodontic tooth movement (De Almeida et al., 2016).

A clear correlation between phototherapy parameters and the acceleration of orthodontic tooth movement was the secondary aim of this study. Various ranges in wavelength, output power, and energy density were applied in each study, as the researchers explored the specific dose needed to achieve the best result.

A subgroup analysis exhibited a trend towards greater efficacy following a 940 nm wavelength as opposed to a 780 nm wavelength. A similar study confirmed that a lesser wavelength was ineffective due to lower penetration in the tissue chromophores (Long et al., 2013; De Freitas & Hamblin, 2016). The observed correlation was defined based on Ohshiro and Calderhead's phototherapy-adapted version of the Arndt-Schultz curve, explaining that a dosage that is too low has no biological effect, whereas a dosage that is too high will cause plateauing (Ohshiro & Calderhead, 1991).

Additionally, the proximity of application is essential; the direct contact application on the tissue surface will prevent energy loss more than a non-contact method (Yamagishi, 1994). It contributes a more precise understanding that wavelength plays a significant role in determining the extent of penetration of phototherapy (Enwemeka, 2001; Hamblin & Demidova, 2006). A proper starting point for future research would involve the use of a 940 nm wavelength relative to a higher wavelength to evaluate which is more useful to accelerate tooth movement.

Another subgroup analysis based on output power demonstrated a significant efficacy of a 100 mW as opposed to a 20 mW output power. A similar study observed a 20 mW output power being inefficient in accelerating tooth movement (Long et al., 2013). A plausible explanation for the application of varying output power in each study could be yielded by inspecting the appropriate amount needed to accelerate tooth movement due to the observation that approximately 50% of phototherapy radiation at 60 mW output power penetrates to a depth of 1.0 mm in human cortical bone (Yamagishi, 1994). A potential area for examination could be the use of 100 mW output power; this could be compared to a higher output power to determine which can accelerate tooth movement.

An analysis of the energy density of $5\,\mathrm{J/cm^2}$ indicated an improved rate of acceleration in tooth movement. The reported lower energy density also produced a favourable effect based on a previous meta-analysis compared to a higher energy density (Ge et al., 2013; He et al., 2016). In contrast, a comparable study (Long et al., 2013) found no significant effect on lower energy density, and this finding is consistent with another review that found the higher the energy intensity, the more substantial is the biostimulation effect that can be gained during the process (Atasoy et al., 2017). The use of low and high energy density in each study was intended to optimize the power needed to reach a positive response, as the so-called Arndt-Schultz curve, or biphasic dose-response, indicates that the application of a mild dose of energy has no biological effect, a moderate dose of energy has a biostimulatory impact, and a maximum dose of energy has a bioinhibitory outcome (Huang et al., 2009). Additional testing is needed regarding the application of $5\,\mathrm{J/cm^2}$ energy density to compare it to a higher dosage and to explore the extent to which the dose will be necessary to reach an indicative value.

Another aim of this study was to investigate the health of the roots, periodontal tissues, and alveolar bone based on the application of phototherapy; the majority of the included studies that tackled those issues reported that none was found, except for one trial which suggested minimal root resorption between the phototherapy and control group (Ubolviroj et al., 2018). This result was consistent with previous systematic reviews that observed the risks during trials (Jawad et al., 2012; Sousa et al., 2014; Gkanditis et al., 2014). Although nothing was found, the majority of the studies have been of relatively short duration to detect any risks. Future research with long study durations and a larger sample size is recommended to examine whether there are underlying risks with prolonged exposure to phototherapy.

There are plenty of limitations across the trials, including complex patient characteristics, low sample size, biomechanical principles on orthodontic treatment, types of phototherapy and its parameters, time points of data collection, measuring devices, and methodological quality. Regarding a split-mouth design, an en-masse retraction should be avoided to not affect the retraction movement on the control side (Davis et al., 2018), and a proper shield should be used against the control group to prevent carry-over effect during the exposure of phototherapy from the experimental group (Pandis et al., 2013).

In technical aspects of phototherapy, all studies used different ranges of parameters, such as wavelength, output power, energy density, application protocol, and exposure. Authors should standardise the phototherapy parameters before establishing their clinical trials (Jenkins & Carroll, 2011).

Regarding the biomechanical principles concerning orthodontic tooth movement, different materials and degrees of force were exerted during canine retraction. The installation of the anchorage device, stable reference points, detailed pre- and post-baseline scores, and precise measuring devices should be practiced to ensure an accurate comparison.

In the studies selected for the meta-analysis, although a positive effect size was found in the overall rate and subgroup analysis, the outcomes were restricted in terms of statistical power and are regarded as equivocal due to their substantial heterogeneity and the low number of studies included. Overall, the methodological quality of the included studies implies a low level of recommendation. Therefore, this study should be interpreted with caution.

Conclusions

Based on the present findings, phototherapy could improve the rate of orthodontic tooth movement without risk. However, considering the limitations described, future research could involve the combination of a 940 nm wavelength, 100 mW output power, and 5 J/cm^2 energy density. This could be compared to a higher dosage using a stringent methodology to enhance homogeneity for quantitative analysis. Such research would elucidate the exact effect of phototherapy and its optimal dose.

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Ethical approval

No ethical approval was required for this study as it did not involve human participants, animal subjects, or sensitive data. This study falls under the category of data collection without participant identification.

Consent for publication

Not applicable.

Authors' contributions

The author(s) declare that all the criteria for authorship designated by the International Committee of Medical Journal Editors have been met. More specifically, these are: (a) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (b) Drafting the work or revising it critically for important intellectual content; AND (c) Final approval of the version to be published; AND (d) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

The author(s) declare that there are no competing interests related to this work.

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