Effectiveness of low-level laser therapy in accelerating the orthodontic tooth movement: A systematic review and meta-analysis

Skuteczność terapii laserem małej mocy w przyspieszaniu ortodontycznych przesunięć zębowych – systematyczny przegląd piśmiennictwa i metaanaliza

Wesam Mhd Mounir Bakdach^{B–D,F}, Rania Hadad^{A,C,E,F}

Department of Orthodontics, Faculty of Dentistry, University of Damascus, Syria

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;

D – writing the article; E – critical revision of the article; F – final approval of the article

Dental and Medical Problems, ISSN 1644-387X (print), ISSN 2300-9020 (online)

Dent Med Probl. 2020;57(1):73–94

Address for correspondence

Wesam Mhd Mounir Bakdach

E-mail: bakdach-wm@hotmail.com

Funding sources

None declared

Conflict of interest

None declared

Received on July 19, 2019

Reviewed on August 26, 2019

Accepted on September 18, 2019

Published online on March 31, 2020

Cite as

Bakdach WMM, Hadad R. Effectiveness of low-level laser therapy in accelerating the orthodontic tooth movement: A systematic review and meta-analysis. *Dent Med Probl.* 2020;57(1):73–94. doi:10.17219/dmp/112446

DOI

10.17219/dmp/112446

Copyright

© 2020 by Wrocław Medical University

This is an article distributed under the terms of the

Creative Commons Attribution 3.0 Unported License (CC BY 3.0)

(<https://creativecommons.org/licenses/by/3.0/>)

Abstract

Objectives. The aim of the paper was to appraise the current evidence of the effectiveness of low-level laser therapy (LLLT) in accelerating the tooth movement.

Methods. A comprehensive search was performed in 9 databases up to June 2019. Only randomized controlled trials (RCTs) were included. The risk of bias was assessed using the Cochrane Collaboration tool. The quantitative data synthesis was attainable only for the studies evaluating the effect of laser on canine retraction; the qualitative description was used for the rest of the studies. The overall quality of evidence was rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria.

Results. A total of 25 RCTs were included in this review. The radiated upper canines showed a greater retraction – 0.50 mm and 0.49 mm at months 2 and 3, respectively. The radiated lower canines showed a greater retraction – 0.28 mm and 0.52 mm at months 2 and 3, respectively. No statistically significant differences were observed among the upper and lower canines after the 1st month of retraction. When the GRADE approach was utilized, the overall quality of evidence limited confidence in the estimates. The qualitative description revealed enhanced tooth movement when LLLT was applied. The attrition bias was the main risk factor affecting the methodology of the studies.

Conclusions. Low-level laser therapy can speed up the rate of the tooth movement. However, the overall quality of evidence ranged from low to very low and the clinical significance of the obtained statistically significant differences is questionable. Hence, more precise studies are needed. As discussed in this review, it is highly recommended to express and compare the laser dosage with the total number of joules applied per month rather than the previously used J/cm². Moreover, the previous recommendation indicating that lower energy densities (2.5, 5 and 8 J/cm²) are more effective than 20 and 25 J/cm² is misleading.

Key words: orthodontics, acceleration, lasers, low-level laser therapy

Słowa kluczowe: ortodoncja, przyspieszenie, lasery, terapia laserem małej mocy

Introduction

The primary objective of orthodontic treatment is usually to achieve an optimal occlusion with minimal complications within a relatively short period of time.¹ According to a recent systematic review of 22 studies involving 1,089 participants, the mean duration of comprehensive orthodontic treatment with a fixed appliance is 19.9 months.² This long treatment duration is associated with an increased risk of developing white spots, caries, gingivitis, and root resorption.³ Therefore, accelerating the tooth movement, which leads to a reduction in the duration and complications of the treatment, is desirable for both patients and orthodontists.

Over the last decade, numerous studies have been conducted to investigate the efficacy of different interventions in speeding up the tooth movement. One of these interventions is low-level laser therapy (LLLT). Initially, histological research showed that LLLT contributes to inducing remodeling processes in the alveolar bone by increasing the numbers of osteoblasts and osteoclasts.^{4,5} In consequence, an exponential growth in the number of studies conducted to investigate the effectiveness of laser treatment in accelerating the tooth movement has become apparent. Interestingly, LLLT enjoys high patient acceptability and can be easily utilized, especially with the availability of small portable devices.⁶

Electronic literature searches in the PubMed and Scopus databases have yielded some systematic reviews that also concern this issue. Ge et al. demonstrated that LLLT might speed up the tooth movement, adding that relatively low energy densities (2.5, 5 and 8 J/cm²) are more effective than 20 or 25 J/cm² and higher.⁷ de Almeida et al. concluded that there was no evidence showing that the use of laser therapy can accelerate the induced tooth movement.⁸ Imani et al. found that LLLT could increase the rate of the orthodontic movement.⁹ Those differing conclusions in previous publications could be ascribed to variations in review methodology, the number of studies included and the publication dates. Hence, the objective of this review was to provide an updated assessment of the current scientific evidence concerning the efficacy of utilizing LLLT in the acceleration of the tooth movement.

Methods

Research question

The research question of whether or not LLLT accelerates the tooth movement was defined according to the PICOS format:

- **Participants:** Healthy male and female patients (at least 10 patients in each study) at any age and of any ethnic group who underwent orthodontic treatment;
- **Interventions:** Orthodontic treatment assisted by LLLT in order to accelerate the tooth movement;

- **Comparisons:** Orthodontic treatment without laser therapy;
- **Outcomes:** The rate of tooth movement (millimeters of tooth movement per time period) or any equivalent measurement indicating the efficacy of the intervention used;
- **Study design:** Only randomized controlled trials (RCTs) were included in this review in order to minimize confounding factors and to reduce bias.

Search strategy

A comprehensive electronic search was performed independently and in duplicate by the authors, with no limitations on language, year or publication status, from the inception to June 2019 in the following databases: the Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, Trip, CINAHL via EBSCO, PubMed, OpenGrey (for grey literature), and ProQuest (for dissertations and theses). The bibliographies of the included studies and relevant reviews were screened for possible further studies. Ongoing trials were also checked through the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal and ClinicalTrials.gov. More details on the electronic search strategy can be found in Supplementary Table 1.

Study selection and data extraction

The 2 authors independently assessed the studies identified during the search. Initially, a screening process was carried out by assessing titles and abstracts to identify potentially relevant articles. Then, the full-text copies of potentially relevant studies were assessed and subjected to the eligibility criteria. At this stage, to avoid any conflict of interest or any possible bias, a blinding was performed by masking the authors' and the journals' names. Any disagreements between the 2 reviewers were resolved through discussion and consensus.

Finally, information was extracted from the studies, including the authors' names, setting, PICOS data, follow-up period, and main findings. When doubtful information was found, the corresponding authors of the studies were contacted for clarification.

Assessing the risk of bias of the included studies

The risk of bias of the included studies was assessed independently by the 2 authors using the Cochrane Collaboration tool for assessing the risk of bias. The following fields were described as having a high, low or unclear risk of bias: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcome

Supplementary Table 1. Electronic search strategy

No.	Database	Search strategy	Results
1	Cochrane Central Register of Controlled Trials (CENTRAL) from the inception up to June 2019, with no limits	#1 orthodontic* OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement' #2 accelerat* OR expedit* OR speed* OR fast* OR rapid* OR velocity OR duration OR rate OR time #3 laser OR 'laser therapy' OR 'low level laser' OR 'low level laser therapy' OR LLL OR LLLT OR 'low powered laser' OR 'low intensity laser' OR 'low level light therapy' OR 'low level light therapy' OR photobiostimulation OR photobiomodulation OR biomodulation OR irradiat* OR phototherapy OR 'light emitting diode' OR LED OR diode #4 #1 AND #2 AND #3	#4 = 261
2	Scopus from the inception up to June 2019, with no limits	#1 TITLE-ABS-KEY (orthodontic* OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement') #2 TITLE-ABS-KEY (accelerat* OR expedit* OR speed* OR fast* OR rapid* OR velocity OR duration OR rate OR time) #3 TITLE-ABS-KEY (laser OR 'laser therapy' OR 'low level laser' OR 'low level laser therapy' OR LLL OR LLLT OR 'low powered laser' OR 'low intensity laser' OR 'low level light therapy' OR 'low level light therapy' OR photobiostimulation OR photobiomodulation OR biomodulation OR irradiat* OR phototherapy OR 'light emitting diode' OR LED OR diode) #4 #1 AND #2 AND #3	#4 = 923
3	Trip from the inception up to June 2019, with no limits	(orthodontic* OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement') AND (accelerat* OR expedit* OR speed* OR fast* OR rapid* OR velocity OR duration OR rate OR time) AND (laser OR 'laser therapy' OR 'low level laser' OR 'low level laser therapy' OR LLL OR LLLT OR 'low powered laser' OR 'low intensity laser' OR 'low level light therapy' OR 'low level light therapy' OR photobiostimulation OR photobiomodulation OR biomodulation OR irradiat* OR phototherapy OR 'light emitting diode' OR LED OR diode)	76
4	CINAHL via EBSCO TX: All Text; from the inception up to June 2019, with no limits	TX (orthodontic* OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement') AND TX (accelerat* OR expedit* OR speed* OR fast* OR rapid* OR velocity OR duration OR rate OR time) AND TX (laser OR 'laser therapy' OR 'low level laser' OR 'low level laser therapy' OR LLL OR LLLT OR 'low powered laser' OR 'low intensity laser' OR 'low level light therapy' OR 'low level light therapy' OR photobiostimulation OR photobiomodulation OR biomodulation OR irradiat* OR phototherapy OR 'light emitting diode' OR LED OR diode)	214
5	PubMed All Fields; from the inception up to June 2019, with no limits	#1 orthodontic* OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement' #2 accelerat* OR expedit* OR speed* OR fast* OR rapid* OR velocity OR duration OR rate OR time #3 laser OR 'laser therapy' OR 'low level laser' OR 'low level laser therapy' OR LLL OR LLLT OR 'low powered laser' OR 'low intensity laser' OR 'low level light therapy' OR 'low level light therapy' OR photobiostimulation OR photobiomodulation OR biomodulation OR irradiat* OR phototherapy OR 'light emitting diode' OR LED OR diode #4 #1 AND #2 AND #3	#4 = 492
6	OpenGrey up to June 2019	#1 (acceleration OR accelerating OR accelerated OR rapid OR fast) AND (orthodontic OR tooth movement) #2 (orthodontic OR tooth movement) AND (laser OR phototherapy OR photobiomodulation)	8 #1 = 4 #2 = 4
7	ProQuest up to June 2019	ab(orthodontic OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement') AND ab(accelerate OR acceleration OR accelerating OR accelerated OR speed OR fast OR rapid OR velocity OR duration OR rate OR time) AND ab(laser OR 'laser therapy' OR 'low level laser' OR 'low level laser therapy' OR LLL OR LLLT OR 'low powered laser' OR 'low intensity laser' OR 'low level light therapy' OR 'low level light therapy' OR photobiostimulation OR photobiomodulation OR biomodulation OR irradiat* OR phototherapy OR 'light emitting diode' OR LED OR diode)	49
8	World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal advanced search (Title) up to June 2019	(orthodontic OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement') AND (laser OR photobiomodulation)	12
9	ClinicalTrials.gov up to June 2019	(orthodontic OR dental movement* OR 'tooth movement' OR 'orthodontic tooth movement') AND (laser OR photobiomodulation)	22

data (attrition bias); selective outcome reporting (reporting bias); and other sources of bias. Then, an overall risk of bias for each trial included was reported according to the following criteria:

- when all fields were assessed as having a low risk of bias, a low risk of bias was reported;
- when 1 or more fields were assessed as having an unclear risk of bias, a moderate risk of bias was reported;
- when 1 or more fields were assessed as being at high risk of bias, a high risk of bias was reported.

The judgments of both reviewers were compared and any disagreements were discussed until a consensus was reached.

Data synthesis

The data was pooled using the Review Manager (RevMan) v. 5.3 software (the Nordic Cochrane Centre, Copenhagen, Denmark). The inverse variance method with the random effect analysis and mean differences (MDs) with associated 95% confidence intervals (CIs) were chosen as the analysis methods. The amount of variability among the pooled studies was evaluated by applying the χ^2 test and calculating the I^2 index for heterogeneity. The publication bias was assessed visually using funnel plots for outcomes that were evaluated by 10 trials or more. Finally, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines were used to rate the overall quality of evidence.

Results

Literature flow

A total number of 2,057 references were identified in the electronic search. Duplicates and articles that were beyond the scope of the defined question and PICOS were eliminated. As a result, 57 references were potentially relevant, and were therefore checked in depth. The final results included 25 completed RCTs and 10 ongoing RCTs. Figure 1 shows the detailed search process (PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart). The list of the studies excluded after the full-text assessment, with the reasons for exclusion, is provided in Supplementary Table 2.

Description of the studies

Twenty-five completed RCTs, including a total of 570 patients, were conducted to investigate the effects of LLLT on the tooth movement. Of the completed studies included, 2 were theses and 3 were reported in a language other than English (2 in Portuguese and 1 in Persian). Different types of tooth movement were described, including leveling and alignment, canine retraction, and en-masse retraction. Table 1 summarizes the characteristics of the completed studies included, whereas Supplementary Table 3 summarizes the characteristics of the ongoing studies.

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart

RCT – randomized controlled trial.

Supplementary Table 2. Studies excluded and the reasons for exclusion

No.	Study	Reason for exclusion
1	Genc G, Kocadereli I, Tasar F, Kilinc K, El S, Sarkarati B. Effect of low-level laser therapy (LLLT) on orthodontic tooth movement. <i>Lasers Med Sci.</i> 2013;28(1):41–47.	non-randomized controlled trial
2	Domínguez A, Gómez C, Palma JC. Effects of low-level laser therapy on orthodontics: Rate of tooth movement, pain, and release of RANKL and OPG in GCF. <i>Lasers Med Sci.</i> 2015;30(2):915–923.	non-randomized controlled trial
3	Camacho AD, Cujar SAV. Acceleration effect of orthodontic movement by application of low-intensity laser. <i>J Oral Laser Appl.</i> 2010;10:99–105.	non-randomized controlled trial
4	Youssef M, Ashkar S, Hamade E, Gutknecht N, Lampert F, Mir M. The effect of low-level laser therapy during orthodontic movement: A preliminary study. <i>Lasers Med Sci.</i> 2008;23(1):27–33.	non-randomized controlled trial
5	Xu CW, Zhang ZJ, Zhao J, Cao G. The effect of low energy laser on accelerating orthodontic tooth movement. <i>Med J Qilu.</i> 2006;1:45–46.	non-randomized controlled trial
6	Shaughnessy T, Kantarci A, Kau CH, Skrenes D, Skrenes S, Ma D. Intraoral photobiomodulation-induced orthodontic tooth alignment: A preliminary study. <i>BMC Oral Health.</i> 2016;16:3.	non-randomized controlled trial
7	Gui L, Qu H. Clinical application of low energy laser in acceleration of orthodontic tooth movement. <i>Journal of Dalian Medical University.</i> 2008;30:155–156.	non-randomized controlled trial
8	Kuznetsova M, Zueva SM, Gunenkova IV, Ezhova EE, Ozerova EM. The use of the Optodan laser physiotherapeutic apparatus for the prevention of complications and the acceleration of the time in treating anomalies in the position of individual teeth with fixed orthodontic appliances [in Russian]. <i>Stomatologiya (Mosk).</i> 1998;77(3):56–60.	accelerating tooth eruption
9	Altan BA, Sokucu O, Tokar H, Sumer Z. The effects of low-level laser therapy on orthodontic tooth movement: Metrical and immunological investigation. <i>JSM Dent.</i> 2014;2(4):1040.	non-randomized controlled trial
10	Matarese G, Matarese M, Picciolo G, Fiorillo L, Isola G. Evaluation of low-level laser therapy with diode laser for the enhancement of the orthodontic tooth movement: A split-mouth study. <i>Preprints.</i> 2018:2018090273.	non-randomized controlled trial
11	Monea A, Mo M, Pop D, Bersescu G. The effect of low level laser therapy on orthodontic tooth movement. <i>J Optoelectron Adv M.</i> 2015;9(1–2):286–289.	non-randomized controlled trial
12	Mc Quattie Pimentel IC. The effect of light accelerated therapy for orthodontic tooth movement: A prospective split-mouth clinical trial. 2017. (Order No. 10259785). Available from ProQuest Dissertations & Theses Global (1894849499).	only 5 patients included
13	Chung SE, Tompson B, Gong SG. The effect of light emitting diode phototherapy on rate of orthodontic tooth movement: A split mouth, controlled clinical trial. <i>J Orthod.</i> 2015;42(4):274–283.	less than 10 patients included
14	NCT03202355	non-randomized controlled trial
15	ACTRN12610001067066	non-randomized controlled trial
16	Fernandes MRU, Suzuki SS, Suzuki H, Martinez E, Garcez AS. Photobiomodulation increases intrusion tooth movement and modulates IL-6, IL-8 and IL-1 β expression during orthodontically bone remodeling. <i>J Biophotonics.</i> 2019;12(10):e201800311.	non-randomized controlled trial
17	Isola G, Ferlito S, Rapisarda E. Low-level laser therapy increases interleukin-1 β in gingival crevicular fluid and enhances the rate of orthodontic tooth movement. <i>Am J Orthod Dentofacial Orthop.</i> 2019;155(4):456–457.	letter to author
18	Yang H, Liu J, Yang K. Comparative study of 660 and 830 nm photobiomodulation in promoting orthodontic tooth movement. <i>Photobiomodul Photomed Laser Surg.</i> 2019;37(6):349–355.	animal study
19	Cordeiro JM, Sahad MG, Cavalcanti MFXB, et al. Laser photobiomodulation over teeth subjected to orthodontic movement. <i>Photomed Laser Surg.</i> 2018;36(12):647–652.	animal study
20	Ojima K, Dan C, Watanabe H, Kumagai Y. Upper molar distalization with Invisalign treatment accelerated by photobiomodulation. <i>J Clin Orthod.</i> 2018;52(12):675–683.	case report
21	Hsu LF, Tsai MH, Shih AH, et al. 970 nm low-level laser affects bone metabolism in orthodontic tooth movement. <i>J Photochem Photobiol B.</i> 2018;186:41–50.	animal study
22	Narmada IB, Rubianto M, Putra ST. The role of low-intensity biostimulation laser therapy in transforming growth factor β 1, bone alkaline phosphatase and osteocalcin expression during orthodontic tooth movement in <i>Cavia porcellus</i> . <i>Eur J Dent.</i> 2019;13(1):102–107.	animal study

Effects of interventions

The included studies were grouped according to the type of tooth movement achieved and the region of LLLT application (i.e., intra-orally or extra-orally). The vast majority of the included studies used J/cm² to express the dosage used. However, the current recommendations of the World Association for photobiomodulation Therapy (WALT) suggest reporting the low-level laser (LLL) dosage in terms of the total number of joules applied

(J, total energy). Accordingly, we calculated the total number of joules applied per month for each study, using the formula:

$$\text{total number of joules} = \text{power (total watts applied)} \times \text{time (total seconds of application)}$$

per month (Table 1). However, it was unattainable to subcategorize the studies according to the total number of joules applied per month due to a wide variety of doses used.

Table 1. Characteristics of the studies included: PICOS, follow-up period and main findings

No.	Study/Setting	Participants	Intervention	Laser application schedule	Total energy dose per month	Comparison	Outcomes	Study design	Follow-up	Main findings
1	Varella et al. 2018 ¹³ India	10 (M + F) patients U 1 st premolars extraction mean age: 17.7 years	<ul style="list-style-type: none"> – U canine retraction – conventional brackets + NiTi closed-coil springs – GaAlAs laser 940 nm, 100 mW, 8 J/cm² 	5 pts B, 5 pts Ln 10 s each pt for 3 consecutive days at the beginning of canine retraction, 4 weeks later and 8 weeks later	30 J	OT + LLLT vs OT + sham	<ul style="list-style-type: none"> – RTM – IL-1β secretion 	RCT SMD	8 weeks	<ul style="list-style-type: none"> – LLLT accelerates OTM – an increased level of IL-1β in the LLLT group
2	Samara et al. 2018 ²⁸ UAE	60 patients U 1 st premolars extraction mean age: 20.4 years	<ul style="list-style-type: none"> – en-masse retraction – conventional brackets + NiTi closed-coil springs – OrthoPulse® device 850 nm, 33 mW/cm², 6 J/cm² 	3 min per arch daily	178.2 J per arch	OT + LLLT vs OT	RTM	RCT parallel	till complete space closure	LLLT accelerates OTM
3	Arumughan et al. 2018 ²⁹ India	12 patients 1 st premolars extraction age: 17–35 years	<ul style="list-style-type: none"> – U canine retraction and en-masse retraction distributed equally – conventional brackets + NiTi closed-coil springs – GaAlAs laser 810 nm, 100 mW 	5 pts B, 5 pts Ln 10 s each pt every 3 weeks	10 J/ 3 weeks	OT + LLLT vs OT	RTM	RCT SMD	84 days	LLLT accelerates OTM
4	Al-Okla et al. 2018 ¹² UAE	38 (M + F) patients U crowding >4 mm without extraction age: 12–40 years	<ul style="list-style-type: none"> – leveling and alignment – conventional brackets – OrthoPulse device, 850 nm, 65 mW, 0.065 J/cm² 	5 min per arch daily	585 J per arch	OT + LLLT vs OT + sham	<ul style="list-style-type: none"> – RTM – root resorption 	RCT parallel	6 months	<ul style="list-style-type: none"> – LLLT accelerates OTM – root length at a 6-month interval was shorter in the LLLT group
5	Guram et al. 2018 ¹⁴ India	20 (M + F) patients 1 st premolars extraction mean age: 20.5 years	<ul style="list-style-type: none"> – U + L canine retraction – conventional brackets + sectional closing loops – GaAlAs laser 810 nm, 0.2 W, 5 J/cm², 2 Hz, continuous mode 	4 pts B, 4 pts Ln on the canine 10 s each pt weekly for 21 days	48 J/ 3 weeks	OT + LLLT vs OT + sham	<ul style="list-style-type: none"> – RTM – pain experience 	RCT SMD	till complete canine retraction	LLLT accelerates OTM and reduces pain experience
6	Qamruddin et al. 2017 ¹⁵ Pakistan	22 (M + F) patients 1 st premolars extraction mean age: 19.8 $\pm$ 3.1 years	<ul style="list-style-type: none"> – U canine retraction – self-ligating brackets + NiTi closed-coil springs – GaAlAs laser 940 nm, 100 mW, 7.5 J/cm², continuous mode 	5 pts B, 5 pts Ln on the U canine 3 s each pt on days 0, 21 and 42	3 J/ 3 weeks	OT + LLLT vs OT + sham	<ul style="list-style-type: none"> – RTM – pain experience 	RCT SMD	9 weeks	LLLT accelerates OTM and reduces pain experience
7	Caccianiga et al. 2017 ¹¹ Italy	36 (M + F) patients L mild crowding mean age: 16.9 years	<ul style="list-style-type: none"> – alignment – self-ligating brackets – diode laser 980 nm, 1 W, 150 J/cm² per session, continuous mode 	the mandible divided into 6 dental segments, each segment containing 2 teeth: (36/35) (46/45) irradiated for 9 s, the remaining segments for 8 s; it was repeated 3 times at intervals of 2 min between the sessions a single monthly administration	150 J	OT + LLLT vs OT	treatment duration	RCT parallel	till complete crowding resolution	treatment duration was shorter in the LLLT group

No.	Study/Setting	Participants	Intervention	Laser application schedule	Total energy dose per month	Comparison	Outcomes	Study design	Follow-up	Main findings
8	AlSayed Hasan et al. 2017 ¹⁰ Syria	26 (M + F) patients U mild crowding with extraction mean age: 20 years	– leveling and alignment, – conventional brackets, – GaAlAs laser 830 nm, 150 mW, 2.25 J/cm ² , continuous mode	2 pts B, 2 pts Ln on each root of the 6 maxillary anterior teeth 30 s each pt the 1 st month: on days 0, 3, 7, and 14, the 2 nd month: every 15 days	72 J/tooth for the 1 st month, then 36 J/tooth	OT + LLLT vs OT	– time for alignment – alignment improvement percentage	RCT parallel	till complete crowding resolution	LLLT accelerates OTM
9	Kochar et al. 2017 ¹⁶ India	20 (M + F) patients 1 st premolars extraction mean age: 20 years	– U + L canine retraction – conventional brackets + NiTi closed-coil springs – GaAlAs laser 810 nm, 100 mW, 5 J/cm ² , continuous mode	5 pts B, 5 pts Ln on the canine 10 s each pt days: 0, 3 and 7 of force application	30 J	OT + LLLT vs OT + sham	– RTM – pain experience	RCT SMD	till complete canine retraction	LLLT accelerates OTM and reduces pain experience
10	Üretürk et al. 2017 ¹⁷ Turkey	15 (M + F) patients U 1 st premolars extraction mean age: 16.20 ± 1.32 years	– U canine retraction – self-ligating brackets + NiTi closed-coil springs – GaAlAs laser 820 nm, 20 mW, 5 J/cm ² , continuous mode	5 pts B, 5 pts Ln on the U canine 10 s each pt, 0.2 J/pt on days 0, 3, 7, 14, 21, 30, 33, 37, 44, 51, 60, 63, 67, 74, 81, 84, and 90	10 J	OT + LLLT vs OT + sham	– RTM – the IL-1β and TGF-β1 levels in GCF – periodontal indices	RCT SMD	90 days	LLLT accelerates OTM, increases the IL-1β and TGF-β1 levels with no sign of gingival inflammation
11	Nahas et al. 2017 ³⁰ UAE	40 (M + F) patients L anterior crowding mean age: 21.8 years	– leveling and alignment – self-ligating brackets – extra-oral LED device (OrthoPulse) 850 nm, 90 mW/cm ² , 108 J/cm ² on the surface of the cheek	20 min daily	3,240 J	OT + LLLT vs OT	RTM	RCT parallel	till complete alignment	LLLT accelerates OTM
12	Ekizer et al. 2016 ³² Turkey	20 (M + F) patients U 1 st premolars extraction mean age: 16.77 ± 1.41 years	– canine retraction – conventional brackets + NiTi closed-coil springs + mini-screw application – extra-oral LED device 618 nm, 20 mW/cm ²	20 min daily for 21 days	508 J	OT + LLLT vs OT + sham	– RTM – mini-screw stability – the IL-1β level	RCT SMD	3 months	LLLT accelerates OTM and increases the stability of mini-screws, but has no effect on the IL-1β level
13	Yassaei et al. 2016 ¹⁸ Iran	11 (F) patients 1 st premolars extraction mean age: 19.00 ± 4.21 years	– U canine retraction – conventional brackets + NiTi closed-coil springs – GaAlAs laser 980 nm, 100 mW, 5.6 J/cm ² , continuous mode	3 pts B, 3 pts Ln on the U canine the apical third for 8 s, the cervical and middle ones for 10 s on days 0, 7, 14, 21, and 28 of each month	28 J	OT + LLLT vs OT + sham	– RTM – the IL-6 level in GCF	RCT SMD	11 months	no significant results for accelerating OTM and the IL-6 level
14	Caccianiga et al. 2016 ³³ Italy	21 (M + F) patients moderate crowding in the mandibular arch mean age: 26.0 ± 5.4 years	– alignment – aligners applied 12 h/day – extra-oral diode laser 980 nm, 1 W, 150 J/cm ² , continuous mode	laser applied on the maxil- lary and mandible arch 3 applications for each arch each application for 50 s, a total of 150 s for each arch laser applied every other week	300 J	OT + LLLT vs OT	No. of aligners fitted correctly and No. of treatments finished successfully	RCT parallel	42 weeks	patients have to wear aligners for fewer hours when laser is applied

No.	Study/Setting	Participants	Intervention	Laser application schedule	Total energy dose per month	Comparison	Outcomes	Study design	Follow-up	Main findings
15	Dalaie et al. 2015 ¹⁹ Iran	12 (M + F) patients U + L 1 st premolars extraction mean age: 20.1 years	<ul style="list-style-type: none"> – U + L canine retraction – conventional brackets + sectional closing loops – GaAlAs laser 880 nm, 100 mW, 5 J/cm², continuous mode 	4 pts B, 4 pts Ln on the canines 10 s each pt	*	OT + LLLT vs OT	<ul style="list-style-type: none"> – RTM – pain experience 	RCT SMD	67 days	no significant results for accelerating OTM or reducing pain
16	Kansal et al. 2014 ²⁰ India	10 (M + F) patients U 1 st premolar extraction	<ul style="list-style-type: none"> – U canine retraction – conventional brackets – GaAs diode laser 904 nm, 12 mW, 4.2 J/cm² 	5 pts B, 5 pts Ln on the U canines 10 s each pt on days 1, 3, 7, 14, 21, 28, 35, 42, 49, and 56 during the canine retraction phase	7.2 J for the 1 st month	OT + LLLT vs OT	RTM	RCT SMD	63 days	no significant results for accelerating OTM
17	Pereira 2014 ²² Brazil (thesis)	11 patients U + L 1 st premolars extraction mean age: 14.04 years	<ul style="list-style-type: none"> – U + L canine retraction – conventional brackets + closing coil springs – 780 nm wavelength 	5 pts B, 5 pts Ln on the canines the L canine B and Ln, and the U canine B – 40 mW power, 10 J/cm ² energy density, 10 s each pt, 0.4 J/pt; the U canine Ln – 70 mW power, 35 J/cm ² energy density, 20 s each point, 1.4 J/pt application each month	U: 9 J L: 4 J	OT + LLLT vs OT	<ul style="list-style-type: none"> – RTM – root and bone resorption 	RCT SMD	3 months	no significant results for accelerating OTM
18	Heravi et al. 2014 ²¹ Iran	20 (M + F) patients U 1 st premolars extraction mean age: 22.1 ± 5.3 years	<ul style="list-style-type: none"> – U canine retraction – conventional brackets + vertical loop – GaAlAs laser 810 nm, 200 mW, 21.4 J/cm²/pt, continuous mode 	5 pts B, 5 pts Ln on the U canines 30 s each pt days: 0, 3, 7, 11, and 15 of force application; on day 28, force adjusted and the same protocol repeated	300 J	OT + LLLT vs OT + sham	<ul style="list-style-type: none"> – RTM – pain experience 	RCT SMD	56 days	no significant results for accelerating OTM or reducing pain
19	Souza 2014 ²³ Brazil (thesis)	11 patients U + L 1 st premolars extraction age: 12–17 years	<ul style="list-style-type: none"> – U + L canine retraction – conventional brackets + closed-coil springs – 780 nm wavelength, 40 mW power, 10 J/cm² energy density 	5 pts B, 5 pts Ln on the canines the L canine B and Ln, and the U canine B – 40 mW power, 10 J/cm ² energy density, 10 s each point, 0.4 J/pt; the U canine Ln – 70 mW, 35 J/cm ² energy density, 20 s each pt, 1.4 J/pt	U: 9 J L: 4 J	OT + LLLT vs OT	<ul style="list-style-type: none"> – RTM – pain experience 	RCT SMD	3 months	LLLT was effective only in accelerating mandibular canine retraction and in the 1 st month only
20	Kau et al. 2013 ³¹ USA	90 (M + F) patients irregularity index > 2 mm mean age: 18 ± 7 years	<ul style="list-style-type: none"> – alignment – conventional brackets – extra-oral OrthoPulse device, 850 nm, 60 mW/cm² 	a single exposure of 20 min/day = 72 J/cm ² a single exposure of 30 min/day = 108 J/cm ² a single exposure of 60 min/week = 216 J/cm ²	72 J/day, 2,160 J/month 108 J/day, 3,240 J/month 216 J/day, 6,480 J/month	OT vs OT + LLLT 20 min/day or 30 min/day or 60 min/week	RTM	RCT parallel	till complete alignment	LLLT accelerates OTM

No.	Study/Setting	Participants	Intervention	Laser application schedule	Total energy dose per month	Comparison	Outcomes	Study design	Follow-up	Main findings
21	Doshi-Mehta and Bhad-Patil 2012 ⁶ India	20 (M + F) patients U 1 st premolars extraction age: 12–23 years	– U canine retraction – conventional brackets + NiTi closed-coil springs – GaAlAs laser 810 nm, 0.25 mW, continuous mode	5 pts B, 5 pts Ln on the U canines 10 s each pt the 1 st month; on days 0, 3, 7, and 14 every 15 days till complete retraction	**	OT + LLLT vs OT + sham	– RTM – pain experience	RCT SMD	till complete canine retraction	LLLT accelerates OTM and reduces pain
22	Sousa et al. 2011 ²⁴ Brazil	10 (M + F) patients 1 st U or L premolars extraction mean age: 13.1 years	– canine retraction – conventional brackets + closed-coil springs – diode laser 780 nm, 20 mW, 5 J/cm ² , continuous mode	5 pts B, 5 pts Ln on the canines 10 s each pt on days 0, 3 and 7 after each activation (every month)	6 J	OT + LLLT vs OT + sham	RTM	RCT SMD	90 days	LLLT accelerates OTM
23	Hosseini et al. 2011 ²⁵ Iran	12 (M + F) patients 1 st U or L premolars extraction mean age: 16.9 ± 3.4 years	– U canine retraction – closed-coil springs – GaAlAs laser 890 nm, pulsed mode	on the buccal and palatal mucosa by a slow movement of the probe at the beginning of the 1 st month (6 J every 48 h) laser applied in the 1 st month only	72 J	OT + LLLT vs OT	RTM	RCT SMD	2 months	no significant results for accelerating OTM
24	Limpanichkul et al. 2006 ²⁶ Thailand	12 (M + F) patients U 1 st premolars extraction mean age: 20.11 ± 3.40 years	– U canine retraction – self-ligating brackets on U canines – GaAlAs laser 860 nm, 100 mW, 25 J/cm ² , 2.3 J/pt, continuous mode	4 pts B, 4 pts Ln on the canines 23 s each pt on days 0, 1 and 2 after each activation (repeated at the end of the 1 st , 2 nd and 3 rd month)	55.2 J	OT + LLLT vs OT + sham	RTM	RCT SMD	3 months	no significant results for accelerating OTM
25	Cruz et al. 2004 ²⁷ Brazil	11 (M + F) patients U 1 st premolars extraction age: 12–18 years	– U canine retraction – conventional brackets + closed-coil springs – GaAlAs laser 780 nm, 20 mW, 5 J/cm ² , continuous mode	5 pts B, 5 pts Ln on the canines 10 s each pt 4 days of each month	8 J	OT + LLLT vs OT	RTM	RCT SMD	2 months	LLLT accelerates OTM

M – males; F – females; U – upper; L – lower; NiTi – nickel-titanium; GaAlAs – gallium-aluminum-arsenide; LED – light-emitting diode; GaAs – gallium-arsenide; pt(s) – point(s); B – buccal; Ln – lingual; OT – orthodontic treatment; LLLT – low-level laser therapy; RTM – rate of tooth movement; IL-1 β – interleukin 1 beta; TNF- β 1 – tumor necrosis factor beta 1; GCF – gingival crevicular fluid; IL-6 – interleukin 6; SMD – split-mouth design; OTM – orthodontic tooth movement.* Days of application were not mentioned, and no response to our email inquiry was received. ** On page 291, it is stated that for the biostimulation effect, the output power was 0.25 mW, a total of 10 pts (5 B and 5 Ln) were subjected to irradiation with an exposure time of 10 s/pt, and the result was 2 × 50 s × 0.25 mW = 0.025 J/session; however, it is also stated on the same page that the total amount of energy applied per session was 8 J (2 × 40 s × 100 mW). We asked for clarifications via email, but received no response.

Supplementary Table 3. Characteristics of the ongoing studies on the tooth movement facilitated by low-level-laser therapy (LLLT): Study design and intervention

No.	Study/Setting	Study design	Intervention
1	NCT03646942, 2017, Syria (recruiting)	RCT	lingual fixed orthodontic appliance
2	CTRI/2018/05/014328, 2017, India	RCT	fixed orthodontic appliance
3	CTRI/2018/04/013156, 2017, India	RCT	fixed orthodontic appliance
4	CTRI/2018/03/012316, 2018, India	RCT	fixed orthodontic appliance
5	CTRI/2017/07/009153, 2016, India	RCT	fixed orthodontic appliance
6	NCT02181439, 2014, France (completed)	RCT	intermaxillary elastics II
7	NCT02954133, 2016, USA (active, not recruiting)	RCT	aligners
8	NCT02267850, 2014, USA (completed)	RCT	fixed orthodontic appliance
9	NCT02267824, 2014, USA (completed)	RCT	fixed orthodontic appliance
10	DRKS00014964, 2018, Germany (pending)	RCT	fixed orthodontic appliance

Fig. 2. Forest plot of the comparison between the LLLT and control groups at months 1, 2 and 3 of upper canine retraction

SD – standard deviation; CI – confidence interval; df – degrees of freedom.

Effect of intra-oral LLLT in accelerating leveling and alignment

Three parallel-design RCTs assessed the efficacy of intra-oral LLLT in accelerating leveling and alignment, either by assessing the overall treatment time needed for crowding resolution^{10,11} or by assessing the rate of tooth movement.¹² All 3 studies indicated that LLLT is effective in accelerating the tooth movement. However, the data could not be pooled due to the differences in the treatment scenarios: upper alignment with extraction, lower alignment without extraction and upper alignment without extraction, respectively.

Effect of intra-oral LLLT in accelerating upper canine retraction

Sixteen split-mouth-design RCTs assessed the efficacy of intra-oral LLLT in accelerating upper canine retraction.^{6,13–27} Noteworthy, the studies by Yassaei et al. and Sousa et al. were not included in data pooling.^{18,24} In Yassaei et al.'s study, the analyzed sample comprised fewer than 10 patients due to the early closed extraction spaces at the beginning of the retraction phase.¹⁸ In the case of the trial by Sousa et al., the data was obtained from a mixture of the upper and lower canines.²⁴ Therefore, these 2 studies were omitted to provide an accurate comparison. The amount of retraction at month 1 was assessed by 9 trials, comprising 226 canines.^{13,17,19–23,25,26} The pooled estimate showed no statistically significant differences

between the radiated and non-radiated groups (Fig. 2, 1.1.1: WMD (weighted mean difference) = 0.21; 95% CI (–0.09, 0.51); $p = 0.16$). Heterogeneity was very significant ($\chi^2 = 48.40$; $p < 0.001$; $I^2 = 83\%$). According to GRADE, the overall quality of evidence supporting this outcome is very low (Table 2).

The degree of retraction at month 2 was assessed by 12 trials, comprising 336 canines.^{13–16,19–23,25–27} The pooled estimate showed a greater canine retraction (0.50 mm) in the radiated group (Fig. 2, 1.1.2: WMD = 0.50; 95% CI (0.29, 0.72); $p < 0.001$). Heterogeneity was very significant ($\chi^2 = 192.25$; $p < 0.001$; $I^2 = 94\%$). According to GRADE, the overall quality of evidence supporting this outcome is very low (Table 2).

The degree of retraction at month 3 was assessed by 6 trials, comprising 204 canines.^{6,14,17,22,23,26} The pooled estimate showed a greater canine retraction (0.49 mm) in the radiated group (Fig. 2, 1.1.3: WMD = 0.49; 95% CI (0.02, 0.96); $p = 0.04$). Heterogeneity was very significant ($\chi^2 = 71.03$; $p < 0.001$; $I^2 = 93\%$). According to GRADE, the overall quality of evidence supporting this outcome is low (Table 2).

Effect of intra-oral LLLT in accelerating lower canine retraction

Five split-mouth-design RCTs assessed this outcome.^{14,16,19,22,23} Three trials including 68 canines assessed the degree of retraction at month 1.^{19,22,23} The pooled estimate showed no significant differences between the radiated

Fig. 3. Forest plot of the comparison between the LLLT and control groups at months 1, 2 and 3 of lower canine retraction

Table 2. Summary of findings according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines

Certainty assessment			Summary of findings						Comments	
No. of studies	risk of bias	inconsistency	indirectness	imprecision	other considerations	No. of patients	effects			certainty
							relative (95% CI)	absolute (95% CI)		
upper canine retraction facilitated by LLLT (month 2)										
12 RCTs	serious	not serious	serious	not serious	publication bias strongly suspected	171 SMD	–	MD 0.50 higher (0.29 lower to 0.72 higher)	⊕⊕⊕⊕ very low ^a	
This outcome was also measured at month 1 in 9 RCTs (113 patients, SMD); the difference was not significant between both groups (–0.09 lower to 0.51 higher) with evidence quality very low ^b ⊕⊕⊕⊕. Also measured at month 3 in 6 RCTs (89 patients, SMD); the mean retraction in the intervention group was 0.49 higher (0.02 lower to 0.96 higher) with evidence quality low ^c ⊕⊕⊕⊕.										
lower canine retraction facilitated by LLLT (month 2)										
5 RCTs	serious	not serious	serious	not serious	none	74 SMD	–	MD 0.28 higher (0.17 lower to 0.40 higher)	⊕⊕⊕⊕ low ^d	
This outcome was also measured at month 1 in 3 RCTs (34 patients, SMD); the difference was not significant between both groups (–0.37 lower to 1.50 higher) with evidence quality low ^e ⊕⊕⊕⊕. Also measured at month 3 in 3 RCTs (42 patients, SMD); the mean retraction in the intervention group was 0.52 higher (0.40 lower to 0.63 higher) with evidence quality low ^f ⊕⊕⊕⊕.										

High quality: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate quality: We are moderately confident in the effect estimate – the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low quality: Our confidence in the effect estimate is limited – the true effect may be substantially different from the estimate of the effect. Very low quality: We have very little confidence in the effect estimate – the true effect is likely to be substantially different from the estimate of effect.

^a Decline 1 level for the risk of bias: allocation concealment was high in ¹⁵ and unclear in ^{14, 16, 19, 21, 22, 23, 26, and 27}; blinding of outcome assessment was unclear in ^{21, 26 and 27}; outcome data attrition was unclear in ^{14, 16, 19, 21, 26, and 27}; 1 level for indirectness (differences in the population age); and 1 level for strongly suspected publication bias.

^b Decline 1 level for the risk of bias: allocation concealment was unclear in ^{17, 19, 21, 22, 23, and 26}; blinding of outcome assessment was unclear in ^{17, 21 and 26}; outcome data attrition was unclear in ^{17, 19, 21, and 26}; 1 level for indirectness (differences in the population age); and 1 level for strongly suspected publication bias.

^c Decline 1 level for the risk of bias: allocation concealment was unclear in ^{6, 14, 17, 22, 23, and 26}; blinding of outcome assessment was unclear in ^{17 and 26}; outcome data attrition was unclear in ^{6, 14, 17, and 26}; and 1 level for indirectness (differences in the population age).

^d Decline 1 level for the risk of bias: allocation concealment was unclear in ^{14, 16, 19, 22, and 23}; outcome data attrition was unclear in ^{14, 16 and 19}; and 1 level for indirectness (differences in the population age).

^e Decline 1 level for the risk of bias: allocation concealment was unclear in ^{19, 22 and 23}; outcome data attrition was unclear in ¹⁹; and 1 level for indirectness (differences in the population age).

^f Decline 1 level for the risk of bias: allocation concealment was unclear in ^{14, 22 and 23}; outcome data attrition was unclear in ¹⁴; and 1 level for indirectness (differences in the population age).

MD – mean difference.

and non-radiated groups after the 1st month of retraction (Fig. 3, 2.1.1: WMD = 0.56; 95% CI (–0.37, 1.50); $p = 0.24$). Heterogeneity was very significant ($\chi^2 = 13.74$; $p = 0.001$; $I^2 = 85\%$). According to GRADE, the overall quality of evidence supporting this outcome is low (Table 2).

Five trials including 148 canines assessed the degree of retraction at month 2.^{14,16,19,22,23} The pooled estimate showed a greater tooth movement (0.28 mm) in the radiated group (Fig. 3, 2.1.2: WMD = 0.28; 95% CI (0.17, 0.40); $p < 0.001$). Heterogeneity was low ($\chi^2 = 2.75$; $p = 0.60$; $I^2 = 0\%$). According to GRADE, the overall quality of evidence supporting this outcome is low (Table 2).

Three trials including 84 canines assessed the degree of retraction at month 3.^{14,22,23} The pooled estimate showed a greater tooth movement (0.52 mm) in the radiated group (Fig. 3, 2.1.3: WMD = 0.52; 95% CI (0.40, 0.63); $p < 0.001$). Heterogeneity was low ($\chi^2 = 2.00$; $p = 0.37$; $I^2 = 0\%$). According to GRADE, the overall quality of evidence supporting this outcome is low (Table 2).

Effect of intra-oral LLLT in accelerating anterior en-masse retraction

Two RCTs evaluated this outcome.^{28,29} According to Samara et al., the patients treated with LLLT exhibited a significantly higher velocity of space closure by 0.22 mm/month than the non-radiated patients.²⁸ According to Arumughan et al., each round of laser application (21 days) accelerated the orthodontic tooth movement by 12.55% as compared to the conventional retraction technique.²⁹ However, the data from the 2 studies could not be pooled, because Arumughan et al.'s sample consisted of en-masse retraction and canine retraction distributed equally between the experimental and control groups.

Effect of extra-oral LLLT in accelerating leveling and alignment

Two RCTs assessed the efficacy of extra-oral LLLT in accelerating leveling and alignment.^{30,31} According to Nahas et al., the time was significantly reduced (by 22%) in the test group as compared to the control group (68.3 vs 87.8 days, respectively; $p < 0.043$).³⁰ According to Kau et al., the mean rates of change in Little's Irregularity Index were 0.49 and 1.12 mm/week for the control and experimental groups, respectively.³¹ However, the data from the 2 studies could not be pooled, because Nahas et al. used self-ligating brackets, whereas Kau et al. used conventional brackets.

Effect of extra-oral LLLT in accelerating upper canine retraction

One RCT comprising 40 upper canines from 20 patients assessed the efficacy of extra-oral LLLT in accelerating canine retraction using conventional brackets by evaluating the rate of tooth movement (mm/day).³²

The results showed a greater tooth movement in the radiated group, by 0.54 mm in the 1st month, 0.24 mm in the 2nd month and 0.22 mm in the 3rd month of retraction.

Effect of extra-oral LLLT in accelerating leveling and alignment using aligners

One RCT assessed the efficacy of extra-oral LLLT in accelerating leveling and alignment using aligners.³³ Caccianiga et al. allocated 21 patients to either the radiation group or the control group. All the patients were instructed to wear each aligner for 12 h per day for 2 weeks. In the control group, this 12-h protocol failed and was replaced by wearing aligners for 22 h per day. On the other hand, the 12-hour protocol was suitable for the radiated group, meaning the patients had to wear aligners for fewer hours when laser was applied.

Risk of bias in the included studies

Our analysis found that 4 studies were at low risk of bias, 17 studies were at moderate risk of bias and 4 studies were at high risk of bias. The principle risk factor affecting the methodology of laser studies was incomplete outcome data (attrition bias): 8% were at high risk of attrition bias, with more than 20% of the total sample size missing, and 48% were at unclear risk of bias. Figures 4 and 5 show the summary and graph of the risk of bias of the studies. More details on the assessment of the risk of bias with the supporting reasons for each assessment can be found in Supplementary Table 4.

Publication bias

The publication bias was assessed visually using standard funnel plots for the outcomes evaluated by 10 studies or more (i.e., the 1st and 2nd month of upper canine retraction). Figure 6 shows the funnel plots of the effect estimate against standard error (SE) for the outcomes. The shapes of the 2 funnel plots were deemed to be asymmetrical, which revealed the existence of the publication bias.

Discussion

The present systematic review comprised 570 patients from 25 completed RCTs, which reflects the interests of orthodontists in utilizing LLLT for accelerating tooth movement.

The pooled results of canine retraction facilitated by intra-oral LLLT showed no differences in the tooth movement at end of the 1st month, but significant differences after the 2nd and 3rd month. Since radiation has a cumulative effect, it seems that a 1-month period might be needed to achieve the biostimulation effects necessary to stimulate acceleration.

Supplementary Table 4. Assessment of the risk of bias with the supporting reasons for each assessment

No.	Study/Setting	Selection bias (randomization)	Selection bias (allocation concealment)	Performance bias
1	Varella et al. 2018 India	Low Risk "The experimental side was assigned by means of a lottery method with a sealed envelope."	Low Risk "The experimental side was assigned by means of a lottery method with a sealed envelope."	Low Risk The participants only were blinded (it was confirmed by contacting the corresponding author). According to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
2	Samara et al. 2018 UAE	Low Risk "Randomization and allocation concealment to the patient were achieved by asking each patient to draw a sealed envelope containing the allocation."	Low Risk "Randomization and allocation concealment to the patient were achieved by asking each patient to draw a sealed envelope containing the allocation."	Low Risk "It was not possible to conceal the treatment from both the patients and clinicians." However, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
3	Arumughan et al. 2018 India	Low Risk "The experimental side and the control side were randomly selected by an individual who was not part of the study." The method of randomization was not mentioned in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk Concealment was not described in the article. An email was sent to the corresponding author, but there was no response.	Low Risk The study did not address this outcome. However, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
4	Al-Okla et al. 2018 UAE	Low Risk "The subjects were randomly divided into 2 groups." The method of randomization was not mentioned in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk Concealment was not described in the article. An email was sent to the corresponding author, but there was no response.	Low Risk It was a double-blind clinical trial. Moreover, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
5	Guram et al. 2018 India	Low Risk "The 4 quadrants were randomly divided into the laser and control groups." The method of randomization was not mentioned in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk Concealment was not described in the article. An email was sent to the corresponding author, but there was no response.	Low Risk "Neither the participant nor the 1 st evaluator knows the grouping." Moreover, according to the criteria of judging the of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
6	Qamruddin et al. 2017 Pakistan	Low Risk "The maxillary arch was divided into the experimental and placebo groups by flipping a coin."	High Risk It was confirmed by an email, since the author stated that there was no allocation concealment.	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
7	Caccianiga et al. 2017 Italy	Low Risk "The subjects were randomly allocated to receive orthodontic treatment with a fixed appliance plus the administration of LLLT." The SPSS Statistics software was used to generate an allocation sequence.	Low Risk "Each subject was assigned a study number that was concealed until the date of bonding a fixed appliance."	Low Risk The study did not address this outcome. However, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
8	AlSayed Hasan et al. 2017 Syria	Low Risk A simple randomization technique was used. "Each patient was asked to select a folded piece of paper from a box containing 26 pieces of paper."	Low Risk Allocation concealment was done (it was confirmed by contacting the corresponding author).	Low Risk Although there was no blinding, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
9	Kochar et al. 2017 India	Low Risk "The randomly selected split-mouth design was used." The method of randomization was not described in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk Concealment was not described in the article. An email was sent to the corresponding author, but there was no response.	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.

Detection bias	Attrition bias	Reporting bias	Other bias
Low Risk The outcome assessor was blinded (it was confirmed by contacting the corresponding author).	Low Risk No dropouts, as mentioned in the corresponding author's email.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk "The study models were pooled and coded. All measurements were obtained by a single investigator who was blinded to the group allocation of the study models."	High Risk More than 20% (25%) of the sample were dropped. Moreover, the missing data was not balanced in the numbers and reasons across the groups.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk "The photobiomodulation devices were provided by Biolux Research, which had no role in the design or execution of this study."
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response. It is mentioned that the distance was measured 3 times, and the mean value is used for the data.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	High Risk More than 20% (31%) of the sample were dropped. Moreover, the missing data was not balanced in the numbers across the groups.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk "This study was self-funded by the authors and their institution."
Low Risk The outcome was instrumentally measured and rechecked by another investigator for verification.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk It was confirmed by an email, since the author stated that the outcome was instrumentally measured and rechecked by other assessors without any knowledge of the grouping.	Low Risk The missing outcome data was less than 20% (18%). Moreover, the missing data was balanced in the numbers, with similar reasons for the missing data across the groups.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk As illustrated on the CONSORT flow chart, there was no missing data.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
High Risk The outcome assessor was not blinded (it was confirmed by contacting the corresponding author).	Low Risk As illustrated on the CONSORT flow chart, there was no missing data.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk "All measurements were recorded by the same person. He/she was blinded to the control and lased sides."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.

No.	Study/Setting	Selection bias (randomization)	Selection bias (allocation concealment)	Performance bias
10	Üretürk et al. 2017 Turkey	Low Risk "The canines were randomly separated into 2 groups consisting of 30 teeth." The method of randomization was not described in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk Concealment was not described in the article. An email was sent to the corresponding author, but there was no response.	Low Risk The study did not address this outcome. However, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
11	Nahas et al. 2016 UAE	Low Risk "The patients were randomly assigned to one of the 2 groups utilizing simple randomization by asking them to draw a sealed envelope."	Low Risk They used a sealed envelope to conceal allocation.	Low Risk Although there was no blinding, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
12	Ekizer et al. 2016 Turkey	Low Risk "Randomization was accomplished with random LPT application side selection by coin tossing."	Low Risk "The treatment allocation was concealed in envelopes labeled with the study identification number."	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
13	Yassaei et al. 2016 Iran	Low Risk "All irradiations were performed by 1 operator in 1 maxillary quadrant which was randomly selected." The method of randomization was not described in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk The participants and the clinicians responsible for the treatment stages were blinded. Moreover, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
14	Caccianiga et al. 2016 Italy	Low Risk "The block randomization method was used. Each block contained 4 patients."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk Although there was no blinding, according to the criteria of judging risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
15	Dalaie et al. 2015 Iran	Low Risk "The 4 quadrants were randomly selected in a complete block randomization manner using the Microsoft Excel software."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
16	Kansal et al. 2014 India	Low Risk "The right and left quadrants were assigned to either of the groups randomly at a coin toss to eliminate the left and right side bias, if any."	Low Risk "Random selection was done by 1 operator, who conveyed to the person doing the laser application as to which quadrant of the patient belongs to the laser group."	Low Risk According to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
17	Pereira 2014 Brazil (thesis)	Low Risk Laser was applied randomly only in 1 of the canines in the maxilla and in 1 of the canines in the mandible.	Unclear Risk The study did not address this outcome.	Low Risk According to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
18	Heravi et al. 2014 Iran	Low Risk "In each patient, one side was randomly allocated to laser treatment and another side to the placebo application." The method of randomization was not described in the paper. An email was sent to the corresponding author, but there was no response.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.

Detection bias	Attrition bias	Reporting bias	Other bias
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response. Noteworthy, the movements were measured using the Ortho Analyzer™ software, whereas the reference points were selected manually.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk “The alignment of the 6 lower anterior teeth was evaluated by a single investigator who was blinded regarding the patients’ group allocation.”	Unclear Risk Although the missing data was less than 20% (15%), it was not equally distributed between the 2 groups. Furthermore, the reasons for dropping out were different.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk It is mentioned that the devices were provided by Biolux Research and American Orthodontics. None of the sponsors (listed companies) had any role in the design or execution of this study.
Low Risk “The measurements of the data were done by a clinician blinded to the assignment.”	Low Risk As illustrated on the CONSORT flow chart, there was no missing data.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk As illustrated on the CONSORT flow chart, there was no missing data.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was had no response.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk “... were aware of the irradiation side and the results were recorded by a third party.”	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk “The distance measurement was done by the 3 rd operator, who had no knowledge about which quadrant had been considered in the laser group.”	Low Risk No dropouts occurred. The same sample number as mentioned in the methods part was mentioned again in the results part.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Low Risk The measurements were performed by an examiner other than the operator who applied the laser, which allowed a double-blind study, as the examiner did not know which side was the irradiated one when performing the clinical measurements.	Low Risk No dropouts, as shown in the results tables.	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.
Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response. Noteworthy, the movements were measured using the Smile Analyzer™ software; the reference points were selected by one investigator and confirmed by another one.	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response	Low Risk All the outcomes defined in the methods section were measured and reported.	Low Risk None.

No.	Study/Setting	Selection bias (randomization)	Selection bias (allocation concealment)	Performance bias
19	Souza 2014 Brazil (thesis)	Low Risk Laser was applied randomly only in 1 of the canines in the maxilla and in 1 of the canines in the mandible.	Unclear Risk The study did not address this outcome.	Low Risk According to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
20	Kau et al. 2013 USA	Low Risk "The subjects were randomized into groups with varying treatment exposure times."	Low Risk It was confirmed by contacting the corresponding author.	Low Risk According to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
21	Doshi-Mehta and Bhad-Patill 2012 India	Low Risk "A randomly assigned incomplete block was used."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
22	Sousa et al. 2011 Brazil	Low Risk "The laser application was performed by 1 operator at the predetermined point areas, in only 1 of the canines randomly chosen."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk Although the participants only were blinded, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
23	Hosseini et al. 2011 Iran	Low Risk "In this randomized clinical trial ..." The method of randomization was not mentioned.	Low Risk It was confirmed by contacting the corresponding author.	Low Risk According to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
24	Limpanichkul et al. 2006 Thailand	Low Risk "Block randomization was used to allocate the side of the maxillary teeth (the left and right sides) to be subjected to LLLT and the placebo sides."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author, but there was no response.	Low Risk The participants and the clinicians responsible for the treatment stages were blinded. Moreover, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.
25	Cruz et al. 2004 Brazil	Low Risk "The left and right halves of the upper arcades were randomly divided into the described groups. The method of randomization was not described in the paper. An email was sent to the corresponding author, but there was no response."	Unclear Risk The study did not address this outcome. An email was sent to the corresponding author; however, the corresponding author could not give definite answers, as the research had been done a long time ago.	Low Risk The study did not address this outcome. However, according to the criteria of judging the risk of bias, a low risk of bias is considered when the outcome is unlikely to be influenced by a lack of blinding.

CONSORT – Consolidated Standards of Reporting Trials; LPT – laser phototherapy.

Note: The attrition bias was considered as at: low risk if the missing data was less than 10% or less than 20%, but with a balanced number and similar reasons for dropping out across the groups;

unclear risk if the missing data was between 10% and 20% with an unequal number and different reasons for dropping out across the groups;

and high risk if the missing data was more than 20%.

Detection bias	Attrition bias	Reporting bias	Other bias
<p>Low Risk</p> <p>The analysis was performed at least 3 months after the end of the laser application with the objective of the examiner not to remember which was the irradiated and non-irradiated side of each patient, giving the study a double-blind character.</p>	<p>Low Risk</p> <p>No dropouts, as shown in the results tables.</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>None.</p>
<p>Low Risk</p> <p>Assessor blinding was achieved, as confirmed by the corresponding author.</p>	<p>Low Risk</p> <p>No dropouts, as confirmed by the corresponding author.</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>The trial was sponsored by Biolux Research. This company manufactures the devices used in this clinical trial. The authors did not state clearly that sponsors had no role in the design or execution of this study.</p>
<p>Low Risk</p> <p>"The measurement recorder was blinded to the experimental and control sides."</p>	<p>Unclear Risk</p> <p>The study did not address this outcome. An email was sent to the corresponding author, but there was no response</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>None.</p>
<p>Low Risk</p> <p>"Both the patient and the evaluators were not informed which tooth was irradiated."</p>	<p>Unclear Risk</p> <p>The study did not address this outcome. An email was sent to the corresponding author, but there was no response</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>None.</p>
<p>Low Risk</p> <p>It was confirmed by contacting the corresponding author.</p>	<p>Low Risk</p> <p>The missing data was less than 20% (8%).</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>None.</p>
<p>Unclear Risk</p> <p>The study did not address this outcome. An email was sent to the corresponding author, but there was no response.</p>	<p>Unclear Risk</p> <p>The study did not address this outcome. An email was sent to the corresponding author, but there was no response.</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>None.</p>
<p>Unclear Risk</p> <p>The study did not address this outcome. An email was sent to the corresponding author; however, the corresponding author could not give definite answers, as the research had been done a long time ago.</p>	<p>Unclear Risk</p> <p>The study did not address this outcome. An email was sent to the corresponding author; however, the corresponding author could not give definite answers, as the research had been done a long time ago.</p>	<p>Low Risk</p> <p>All the outcomes defined in the methods section were measured and reported.</p>	<p>Low Risk</p> <p>None.</p>

	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
Al Okla et al. 2018	+	?	+	?	-	+	+
AlSayed Hasan et al. 2017	+	+	+	-	+	+	+
Arumughan et al. 2018	+	?	+	?	?	+	+
Caccianiga et al. 2016	+	?	+	?	?	+	+
Caccianiga et al. 2017	+	+	+	?	+	+	+
Cruz et al. 2004	+	?	+	?	?	+	+
Dalaie et al. 2015	+	?	+	+	?	+	+
Sousa et al. 2011	+	?	+	+	?	+	+
Doshi-Mehta and Bhad-Patil 2012	+	?	+	+	?	+	+
Ekizer et al. 2016	+	+	+	+	+	+	+
Guram et al. 2018	+	?	+	+	?	+	+
Heravi et al. 2014	+	?	+	?	?	+	+
Hosseini et al. 2011	+	+	+	+	+	+	+
Kansal et al. 2014	+	+	+	+	+	+	+
Kau et al. 2013	+	+	+	+	+	+	?
Kochar et al. 2017	+	?	+	+	?	+	+
Limpanichkul et al. 2006	+	?	+	?	?	+	+
Nahas et al. 2017	+	+	+	+	?	+	+
Pereira 2014	+	?	+	+	+	+	+
Qamruddin et al. 2017	+	-	+	+	+	+	+
Samara et al. 2018	+	+	+	+	-	+	+
Souza 2014	+	?	+	+	+	+	+
Üretürk et al. 2017	+	?	+	?	?	+	+
Varella et al. 2018	+	+	+	+	+	+	+
Yassaei et al. 2016	+	?	+	?	+	+	+

Fig. 4. Risk of bias summary: The review authors' judgments about each item of the risk of bias for the studies included

Fig. 5. Risk of bias graph: The review authors' judgments about each item of the risk of bias, presented as percentages across all the studies included

Although relevant grey literature, dissertations and non-English RCTs were sought in order to reduce the potential for the publication bias, the resultant asymmetrical funnel plots might be affected by the significant heterogeneity presented among the included studies.

It is worth highlighting that reporting the total number of joules applied per time period rather than J/cm² is recommended for expressing the laser dosage in future trials. This recommendation is clinically important, as it allows a precise comparison between different protocols, and thus allows avoiding confusion. To illustrate this, Kochar et al. and Cruz et al. used the same energy density (5 J/cm²), but the total amount of energy applied was 30 J/month and 8 J/month, respectively.^{16,27} Adding to the confusion, Guram et al. used 5 J/cm², whereas Limpanichkul et al. used 25 J/cm², but calculating the total amount of energy applied resulted in 48 J/3 weeks and 55.2 J/month, respectively.^{14,26} This means the systematic review results of Ge et al., where 5 and 8 J/cm² were reported to be more effective than 20 and 25 J/cm², constitute a misleading way of comparing different study protocols.⁷

Finally, the methodology of the studies utilizing physical stimuli was mostly affected by incomplete outcome data (attrition bias). Applying physical stimulation requires a highly compliant patient, who is actively interested in a shorter orthodontic treatment. Laser protocols often involve laser applications at several daily appointments, which requires high compliance to ensure efficacy.

As with all reviews, ours has strengths and limitations. With regard to strengths, we applied an extensive electronic search, sought grey literature, dissertations and non-English references, checked ongoing registered trials, used the Cochrane Collaboration tool for the assessment of the risk of bias, assessed the publication bias, and finally rated the overall evidence quality using the GRADE criteria. We tried to group LLLT studies according to the total number of joules applied per month, but there was no similarity among the studies in terms of the dosage used. Therefore, a wide variety of LLLT dosimetry in the included studies is considered a limitation of this systematic review.

Fig. 6. Funnel plots of the effect estimate against standard error (SE)

A – month 1 of upper canine retraction facilitated by LLLT; B – month 2 of upper canine retraction facilitated by LLLT.

Conclusions

Low-level laser therapy can speed up the rate of the orthodontic tooth movement, and consequently decrease the treatment time. However, the quality of evidence ranged from low to very low and the clinical significance is questionable, so more precise studies are needed. It is highly recommended to express and compare the laser dosage in future trials by the total number of joules applied per time period rather than the previously used J/cm².

ORCID iDs

Wesam Mhd Mounir Bakdach <https://orcid.org/0000-0001-6523-0075>
 Rania Hadad <https://orcid.org/0000-0002-8426-143X>

References

- Roscoe MG, Meira JB, Cattaneo PM. Association of orthodontic force system and root resorption: A systematic review. *Am J Orthod Dentofacial Orthop.* 2015;147(5):610–626.
- Tschlakai A, Chin SY, Pandis N, Fleming PS. How long does treatment with fixed orthodontic appliances last? A systematic review. *Am J Orthod Dentofacial Orthop.* 2016;149(3):308–318.
- Talic NF. Adverse effects of orthodontic treatment: A clinical perspective. *Saudi Dent J.* 2011;23(2):55–59.
- Huang H, Williams RC, Kyrkanides S. Accelerated orthodontic tooth movement: Molecular mechanisms. *Am J Orthod Dentofacial Orthop.* 2014;146(5):620–632.
- Yoshida T, Yamaguchi M, Utsunomiya T, et al. Low-energy laser irradiation accelerates the velocity of tooth movement via stimulation of the alveolar bone remodeling. *Orthod Craniofac Res.* 2009;12(4):289–298.
- Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: A clinical investigation. *Am J Orthod Dentofacial Orthop.* 2012;141(3):289–297.
- Ge MK, He WL, Chen J, et al. Efficacy of low-level laser therapy for accelerating tooth movement during orthodontic treatment: A systematic review and meta-analysis. *Lasers Med Sci.* 2015;30(5):1609–1618.
- de Almeida VL, de Andrade Gois VL, Andrade RN, et al. Efficiency of low-level laser therapy within induced dental movement: A systematic review and meta-analysis. *J Photochem Photobiol B.* 2016;158:258–266.
- Imani MM, Golshah A, Safari-Faramani R, Sadeghi M. Effect of low-level laser therapy on orthodontic movement of human canine: A systematic review and meta-analysis of randomized clinical trials. *Acta Inform Med.* 2018;26(2):139–143.
- AlSayed Hasan MMA, Sultan K, Hamadah O. Low-level laser therapy effectiveness in accelerating orthodontic tooth movement: A randomized controlled clinical trial. *Angle Orthod.* 2017;87(4):499–504.
- Caccianiga G, Paiusco A, Perillo L, et al. Does low-level laser therapy enhance the efficiency of orthodontic dental alignment? Results from a randomized pilot study. *Photomed Laser Surg.* 2017;35(8):421–426.
- Al Okla N, Bader DM, Makki L. Effect of photobiomodulation on maxillary decrowding and root resorption: A randomized clinical trial. *APOS Trends Orthod.* 2018;8(2):86–91.
- Varella AM, Revankar AV, Patil AK. Low-level laser therapy increases interleukin-1 β in gingival crevicular fluid and enhances the rate of orthodontic tooth movement. *Am J Orthod Dentofacial Orthop.* 2018;154(4):535–544.
- Guram G, Reddy RK, Dharamsi AM, Ismail PM, Mishra S, Prakash-kumar MD. Evaluation of low-level laser therapy on orthodontic tooth movement: A randomized control study. *Contemp Clin Dent.* 2018;9(1):105–109.
- Qamruddin I, Alam MK, Mahroof V, Fida M, Khamis MF, Husein A. Effects of low-level laser irradiation on the rate of orthodontic tooth movement and associated pain with self-ligating brackets. *Am J Orthod Dentofacial Orthop.* 2017;152(5):622–630.
- Kochar GD, Londhe SM, Varghese B, Jayan B, Kohli S, Kohli VS. Effect of low-level laser therapy on orthodontic tooth movement. *J Indian Orthod Soc.* 2017;51(2):81–86.
- Üretürk SE, Saraç M, Fıratlı S, Can ŞB, Güven Y, Fıratlı E. The effect of low-level laser therapy on tooth movement during canine distalization. *Lasers Med Sci.* 2017;32(4):757–764.
- Yassaei S, Aghili H, Afshari JT, Bagherpour A, Eslami F. Effects of diode laser (980 nm) on orthodontic tooth movement and interleukin 6 levels in gingival crevicular fluid in female subjects. *Lasers Med Sci.* 2016;31(9):1751–1759.
- Dalaie K, Hamed R, Kharazifard MJ, Mahdian M, Bayat M. Effect of low-level laser therapy on orthodontic tooth movement: A clinical investigation. *J Dent (Tehran).* 2015;12(4):249–256.
- Kansal A, Kittur N, Kumbhojkar V, Keluskar KM, Dahiya P. Effects of low-intensity laser therapy on the rate of orthodontic tooth movement: A clinical trial. *Dent Res J (Isfahan).* 2014;11(4):481–488.
- Heravi F, Moradi A, Ahrari F. The effect of low level laser therapy on the rate of tooth movement and pain perception during canine retraction. *Oral Heal Dent Manag.* 2014;13(2):183–188.

22. Pereira SC da C. Influência do laser de baixa intensidade na movimentação ortodôntica-avaliação clínica e radiográfica (doctoral thesis) [in Portuguese]. Universidade de São Paulo, Brazil, 2014.
23. Souza JMS de. Avaliação da influência do laser de baixa intensidade na movimentação ortodôntica e supressão da dor (doctoral thesis) [in Portuguese]. Universidade de São Paulo, Brazil, 2014.
24. Sousa MV, Scanavini MA, Sannomiya EK, Velasco LG, Angelieri F. Influence of low-level laser on the speed of orthodontic movement. *Photomed Laser Surg.* 2011;29(3):191–196.
25. Hosseini MH, Mahmoodzadeh Darbandi M, Kamali A. Effect of low level laser therapy on orthodontic movement in human [in Persian]. *J Dent Med.* 2011;24(3):156–164.
26. Limpanichkul W, Godfrey K, Srisuk N, Rattanayatikul C. Effects of low-level laser therapy on the rate of orthodontic tooth movement. *Orthod Craniofac Res.* 2006;9(1):38–43.
27. Cruz DR, Kohara EK, Ribeiro MS, Wetter NU. Effects of low-intensity laser therapy on the orthodontic movement velocity of human teeth: A preliminary study. *Lasers Surg Med.* 2004;35(2):117–120.
28. Samara SA, Nahas AZ, Rastegar-Lari TA. Velocity of orthodontic active space closure with and without photobiomodulation therapy: A single-center, cluster randomized clinical trial. *Lasers Dent Sci.* 2018;2(2):109–118.
29. Arumughan S, Somaiah S, Muddaiah S, Shetty B, Reddy G, Roopa S. A comparison of the rate of retraction with low-level laser therapy and conventional retraction technique. *Contemp Clin Dent.* 2018;9(2):260–266.
30. Nahas AZ, Samara SA, Rastegar-Lari TA. Decrowding of lower anterior segment with and without photobiomodulation: A single center, randomized clinical trial. *Lasers Med Sci.* 2017;32(1):129–135.
31. Kau CH, Kantarci A, Shaughnessy T, et al. Photobiomodulation accelerates orthodontic alignment in the early phase of treatment. *Prog Orthod.* 2013;14:30.
32. Ekizer A, Türker G, Uysal T, Güray E, Taşdemir Z. Light emitting diode mediated photobiomodulation therapy improves orthodontic tooth movement and miniscrew stability: A randomized controlled clinical trial. *Lasers Surg Med.* 2016;48(10):936–943.
33. Caccianiga G, Crestale C, Cozzani M, et al. Low-level laser therapy and invisible removal aligners. *J Biol Regul Homeost Agents.* 2016;30(2 Suppl 1):107–113.