

Tooth Movement in Orthodontic Treatment with Low-Level Laser Therapy: A Systematic Review of Human and Animal Studies

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Abstract

Objective: This review attempts to organize the existing published literature regarding tooth movement in orthodontic treatment when low-level laser therapy (LLLT) is applied. **Background data:** The literature discusses different methods that have been developed to motivate the remodeling and decrease the duration of orthodontic treatment. The application of LLLT has been introduced to favor the biomechanics of tooth movements. However there is disagreement between authors as to whether LLLT reduces orthodontic treatment time, and the parameters that are used vary. **Materials and methods:** Studies in humans and animals in which LLLT was applied to increase the dental movement were reviewed. Three reviewers selected the articles. The resulting studies were analyzed according to the parameters used in the application of laser and existing changes clinically and histopathologically. **Results:** Out of 84 studies, 5 human studies were selected in which canine traction had been performed after removing a premolar, and 11 studies in rats were selected in which first premolar traction was realized. There were statistically significant changes in four human studies and eight animal studies. **Conclusions:** Varying the wavelength with a reasonable dose in the target zone leads to obtaining the desired biological effect and achieving a reduction of the orthodontic treatment time, although there are studies that do not demonstrate any benefit according to their values.

Introduction

WHEN AN ORTHODONTIC FORCE IS APPLIED ON A TOOTH, osteogenesis is generated on the tension side, whereas osteoclastogenesis occurs on the pressure side, producing bone remodeling.¹ The literature shows different methods that have been developed to motivate the remodeling and decrease the duration of treatment, as in the case of drug injections,² electrical stimulation,³ ultrasound application,⁴ and the combination of orthodontic treatment with periodontal surgery and bone graft regeneration.⁵ Recently, the application of low-level laser therapy (LLLT) has been introduced to favor the biomechanics of tooth movements. It is assumed that LLLT can increase the tooth movements and lower the risk of root resorption, which leads to an adequate biological response in the periodontal ligament (PDL). In the past, the simplicity of the technique and the fact that LLLT is noninvasive and painless were considered its main advantages. Ozawa et al.⁶ suggested that the effect of the

laser is on the early stages of the proliferation and differentiation of osteoblasts. Until now, a large number of experimental studies on a variety of animal species such as rats, monkeys, dogs, and cats have been conducted to obtain better information about the biomechanical response to orthodontic forces under the use of LLLT. Most of the studies used the relatively inexpensive rat model, which facilitates the use of large samples. The histologic preparation is easier than in other models. Also, most antibodies that are required for cellular and biological techniques are only available for mice and rats. Finally, transgenic strains are almost exclusively developed in small rodents.⁷ On the other hand, many morphologic and physiological differences between a rat and human's alveolar bone and PDL should be considered. The alveolar bone is denser in rats, shows no plate osteons, and its lack of bone marrow is obvious.⁸ A thorough systematic review of the available literature on this topic could be a basis for the appropriate application of LLLT in clinical orthodontics. Therefore,

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the present study will determine the current status of the relationship between orthodontic force and the rate of subsequent tooth movement under the use of LLLT to assess the methods, procedures, and variables applied by different authors in human and animal models and evaluate the aspects that remain to be studied.

Materials and Methods

Search strategy

The following databases were searched: MEDLINE® (1984–2012), Cochrane Database of Systematic Reviews (Issue 4, 2009), EMBASE (1984–2012) and China National Knowledge Infrastructure (CNKI) (1994–2012) including the following languages: English, Spanish, French, Portuguese, and Italian. Table 1 describes the selection and specific use of each term with its respective truncation. All retrieved studies were independently assessed by two reviewers for possible inclusion by using pilot-tested forms. If these two reviewers could not agree, a third reviewer was consulted. In the cases in which additional information was required for discussion or statistical analysis, and was not specifically given in the article, contact with the authors was sought in order to obtain the required information.

Inclusion criteria

We included studies in which LLLT of any wavelength, in pulsed or continuous wave (CW) mode, was applied to obtain orthodontic tooth movements in animals or human subjects. Non-laser light sources (including tungsten filament, xenon arc, metal halide, and fluorescent lamps) have not been reported in relation to orthodontic treatments. Studies were included if the experimental protocol reported was approved by the appropriate Ethics Committee for Animal Experiments or if the human subjects signed an informed consent before the research procedures. Animal studies were included if there was a control group. In human studies, LLLT was applied to the test side and a pseudoapplication was used on the placebo side. Histologic results were evaluated based on vascularization, osteoclastic and osteoblastic activity, collagen fibers, and orthodontic retraction movements on molar and canine teeth.

Exclusion criteria

Studies reporting patients with neurologic or psychiatric diseases, underlying systemic diseases, chronic pain, or previous orthodontic treatments were excluded. Literature reviews and reports with no direct orthodontic movement measurements were excluded. Because of the specificity of

TABLE 1. SEARCH STRATEGY WITH DIFFERENT DATABASES

Database	Key words	Period of search	Results	Articles included
MEDLINE® PubMed	(low level laser therapy AND orthodontic movement)	1984–2012	32	20
	(CO ₂ laser AND tooth movement)	1984–2012	1	0
	(CO ₂ laser AND orthodontic movement)	1984–2012	0	0
	(low power laser AND orthodontic movement)	1984–2012	1	1
	(low energy laser AND orthodontic movement)	1984–2012	0	0
	(Ga-Al-As diode laser AND orthodontic movement)	1984–2012	0	0
	(low level laser AND orthodontic movement)	1984–2012	4	4
	(phototherapy AND orthodontic movement)	1984–2012	3	3
Scopus - V.4 (Elsevier). SciVerse	1. (low level laser therapy AND orthodontic movement)	2005–2012	23	15
	2. Dental Movement.mp [mp=title, original title, abstract, name of substance word, subject heading word]			1
Web of Science (Thomson Scientific/ISI Web Services)	(low level laser therapy AND orthodontic movement)	2000–2012	0	0
ProQuest Health & Medical Complete (Cambridge Scientific Abstracts) (ProQuest XML)	1. Low level Laser.mp [mp=title, original title, abstract, name of substance word, subject heading word]	2001–2012	3	0
	2. Dental Movement.mp [mp=title, original title, abstract, name of substance word, subject heading word]			
AMED: Allied and Complementary Medicine Database	(low level laser therapy AND orthodontic movement)	2001–2012	1	0
Biblioteca Cochrane Plus	(low level laser therapy AND orthodontic movement)	2001–2012	11	2
Cumulative Index to Nursing and Allied Health (CINAHL) (EBSCO)	(low level laser therapy AND orthodontic movement)	2000–2012	1	1
Cochrane Library	(low level laser therapy AND orthodontic movement)	2009	13	0

the dynamics and of the mechanisms in which canine retraction is involved, we excluded orthodontic treatments that were not performed with a closed-coil spring, or that were not referred to the molars in experimental animals.

Responses evaluated

We evaluated the orthodontic treatments performed to obtain the tooth movement in terms of the device information, as well as the laser irradiation (LI) and treatment parameters both in humans and in experimental animals (Table 2). We evaluated the post-LLLT effects in terms of morphometric, radiographic, and biological analysis. The biological parameters included were osteoclastogenesis, osteoblastogenesis, vascularization, and collagen fiber formation.

Results

Sixteen of 84 studies initially identified by our search—11 animal studies and 5 human studies—fit our inclusion criteria (Table 2).

Human studies

The five human studies included a total of 66 orthodontic patients, with the number in individual trials ranging from 11 to 20 (Table 3).^{9–13}

Participant selection

Four studies^{9–12} reported recruitment of “healthy” or “normal” participants; moreover, two of them excluded participants with systemic diseases.^{10,12} Both male and female participants were selected in all studies; one study¹³ recruited patients of a reported median age of 20 years (± 3.4), whereas the other four^{9–12} reported patients with ages ranging from 10 to 23 years.

Orthodontic measurements

All the studies measured the retraction of maxillary and mandibular canines,^{9,11,12} or only of maxillary canines.^{10,13} In all the studies, the canines were retracted using a NiTi coil-spring by applying a force of 150 g/side. The amount of tooth movement in millimeters was obtained using a digital caliper to measure the distance either between reference points on the model casts,^{9,11} or between the brackets.¹⁰ One study used an automated three-dimensional (3D) system to assess the bone resorption of the tooth’s alveolar ridges,¹² whereas another study used a stereomicroscope to measure the distance between the medial line and the canine in model casts.¹³ Table 3 shows the relationship between the study and the molar or canine retraction and instruments used, and whether there were statistically used.

LI application

Four studies applied LI in direct contact with the alveolar tissues,^{9–12} whereas in the study of Limpanichkul, the probe sheath for the irradiation side had a clear plastic end, which for the pseudo-irradiation on the placebo side was replaced by a sheath covered by a black plastic end,¹³ on 6–10 points. In three studies,^{9,10,12} LI was applied for 10 sec, to a total of 10 points situated around the teeth (5 vestibular, 5 lingual).

Youssef et al.¹¹ applied LI in a differentiated manner in the three vestibular and lingual points by using 10 sec for the cervical and apical application points and 20 sec for the medial point. Limpanichkul et al.¹³ applied LI to eight irradiation points for a standard time of 23 sec situated in three vestibular and lingual points, plus two points distal to the retracted teeth (Table 2).

Laser parameters

Wavelength was reported in all studies, as well as the output power ranging from 0.7 to 100 mW. Pulsed laser parameters such as duration of pulse were consistently reported (Table 2). However, pulse repetition rate (PRR), measured in Hz, was not mentioned. The duration of LI at each point ranged from 10 to 23 sec. We have calculated that energy densities per point ranged from 2 to 4821.4 J/cm² (Table 2), whereas energy per point values were only reported by Sousa et al.¹² (0.2 J of energy per point) and Limpanichkul et al.¹³ (2.3 J/point).

Animal studies

Eleven animal studies were included out of 424 studies. Two hundred and two subjects were irradiated (Table 4).

Participant selection

The animal selected was the Wistar rat. Only male participants were selected in all studies, with weights ranging from 180 to 300 g and ages from 6 weeks to 3 months. One study¹⁴ did not specify the age.

Orthodontic measurements

In all studies, the molars were retracted with a NiTi closed-coil spring ligated with the maxillary first molar cleat by a 0.008 in (0.20320 mm) stainless steel ligature wire. The other side of the coil spring was also ligated, with the holes in the maxillary incisors drilled laterally just above the gingival papilla. The force range was from 10 to 40 g/F. Seven studies evaluated the distance between the tractioned tooth to the incisors, by diverse methods. Five trials detected statistically significant differences in the range of days from day 2 to 21,^{15–20} whereas two studies found no difference in the traction between both groups.^{21,22} Table 4 shows the relationship among each study and the instrument used for measurement and the days in which statistically significant differences were found for each study. The histologic and cell and molecular biology parameters included were those relevant for assessing osteoclastogenesis, osteoblastogenesis, vascularization, and collagen fiber formation (Table 5).

LI application

The application points around the molars and irradiation time are highly variable. Three points (two intraoral and one extraoral) were irradiated by Gama et al.,²¹ although the time was not specified. Three points were irradiated (vestibular, palatal and mesial) for 4 sec by Abi-Ramia et al.¹⁴ and Duan et al.²⁰ Four points were irradiated for 2 min 15 sec per point (buccal, palatal, mesial, and distal) by Yoshida et al.,¹⁵ whereas other authors applied it for 3 min

TABLE 2. DATA SUMMARY OF PHOTOMEDICINE DOSE AND BEAM PARAMETERS IN HUMAN STUDIES AND RAT STUDIES (DEVICE INFORMATION, IRRADIATION PARAMETERS, AND TREATMENT PARAMETERS)

First author, year	Device Information				Irradiation parameters				Treatment parameters				
	Manufacturer	Lasing medium	Center wavelength	Operating mode	Average radiant power	Beam area	Irradiance at target	Exposure duration	Energy per point	Energy density per point	Total energy per tooth	Number of points irradiated	Application technique
Limpanichkul, 2006	Top Laser 250 Sir 100, Medical Innovation, France.	GaAlAs	860 nm	CW	100 mW	0.09 cm ²	1.1 W/cm ²	23 sec	2.3 J	25.6 J/cm ²	204.5 J	8	Contact
Sousa, 2011	Twin Laser, MMOptics Ltda. Brazil.	GaAlAs	780 nm	CW	20 mW	0.04 cm ²	0.5 W/cm ²	10 sec	0.2 J	5.0 J/cm ²	50 J	10	Contact
Youssef, 2008	NS	GaAlAs	809 nm	NS	100 mW	0.5 cm ²	0.2 W/cm ²	10sec/20sec ^b	1 J	2 J/cm ²	12 J	6	Contact
Cruz, 2004	Twin Laser, MMOptics Ltda. Brazil.	GaAlAs	780 nm	CW	20 mW	0.04 cm ²	0.5 W/cm ²	10 sec	0.2 J	5.0 J/cm ²	50 J	10	Contact
Doshi-Metha, 2012	LA3D0001.1; LAMBDA S.p.A., Vicenza, Italy	GaAlAs	800 nm ^c	CW	0.25 mW	0.04 cm ²	0.00625 W/cm ²	8 sec	0.002 J	0.05 J/cm ²	0.5 J	10	Contact
Gama, 2010	Laser Unit; Kondortech, Brazil	NS	790 nm	NS	40 mW	0.0314 cm ²	12.7 W/cm ²	32.5 sec	1.3 J	41.4 J/cm ²	5.2 J	4	NS
Abi-Ramia, 2010	TheraLase; DMC Equipamentos, Brazil	GaAlAs	830 nm	NS	100 mW	0.02 cm ²	4.5 W/cm ²	4 sec	0.4 J	18 J/cm ²	1.2 J	3	Contact
Yoshida, 2009	Osada Inc., Japan	GaAlAs	810 nm	CW	100 mW	0.0028 cm ² ^a	35.71 W/cm ²	135 sec	13.5 J	4821.4 J/cm ²	54 J	4	Contact
Yamaguchi, 2007	Osada Inc., Japan	GaAlAs	810 nm	CW	100 mW	0.0028 cm ² ^a	35.71 W/cm ²	180 sec	18 J	4821.4 J/cm ²	54 J	3	Contact
Fujita, 2008	Osada Inc., Japan	GaAlAs	810 nm	CW	100 mW	0.0028 cm ² ^a	35.71 W/cm ²	180 sec	18 J	4821.4 J/cm ²	54 J	3	Contact
Kawasaki, 2000	Panalas 1000 prototype, Matsushita Industrial Equipment, Inc.	GaAlAs	830 nm	CW	100 mW	0.0028 cm ² ^a	35.71 W/cm ²	180 sec	18 J	4821.4 J/cm ²	54 J	3	Contact
Marquezan, 2010	TheraLase; DMC Equipamentos, Brazil	GaAlAs	830 nm	CW	100 mW	0.0028 cm ² ^a	35.71 W/cm ²	180 sec	18 J	4821.4 J/cm ²	54 J	3	Contact
Habib, 2010	NS	GaAlAs	790 nm	NS	40 mW	0.0314 cm ²	12.7 W/cm ²	180 sec	7.2 J	229.3 J/cm ²	21.6 J	3	NS
Habib, 2012	Laser Unit Kondortech, Brazil	GaAlAs	790 nm	CW	40 mW	0.0314 cm ²	12.7 W/cm ²	180 sec	7.2 J	229.3 J/cm ²	21.6 J	3	NS
Yamaguchi, 2010	Osada Inc., Japan	GaAlAs	810 nm	CW	100 mW	0.0028 cm ² ^a	35.71 W/cm ²	180 sec	18 J	4821.4 J/cm ²	54 J	3	Contact
Duan, 2012	Bio-Flex LDI-200, Canada	GaAlAs	830 nm	CW PW 2.5% PW 4.50% PW 8.50%	180 mW 50% (duty cycle)	0.2 cm ²	0.9 W/cm ²	4 sec 8 sec 8 sec	0.72 J	3.6 J/cm ²	2.16 J	3	Contact

^aThe authors consider that the beam area and irradiance figures are improbable and perhaps should not be relied upon.

^b10 sec in the cervical and apical area and 20 seconds in the middle area.

^cValues reported as used for biostimulation.

CW, continuous wave; PW, pulse wave; GaAlAs, Gallium-Aluminium-Arsenide; Contact (skin contact).

TABLE 3. DATA SUMMARY OF FIVE QUALIFIED TRIALS IN HUMANS (CHARACTERISTICS OF PATIENTS AND METHOD OF TRACTION)

	No. patients irradiated/ (control group)	Gender/ age	Extracted tooth	Beginning of traction	Prescription appliance/arch	Force	Result
Limpanichkul, 2006	12	4 male, 8 female/ 20.11 ± 3.4 years	Mx first PM right/ left	3 months after extraction	Roth/ Australian Premium Plus arch wire (0.022 × 0.028 in/0.56 × 0.72 mm)	150g	No
Sousa, 2011	13	4 male, 6 female/ 13.1 years	First PM of Mx and Md	3 month after extraction	Andrews (Ormco)/ stainless steel (0.016 in/0.40 mm)	150g	↑
Youssef, 2008	30	Both genders/ 14–23 years	First Pm of Mx and Md	NS	Ricketts (RMO)/ not specified	150g	↑
Cruz, 2004	11	Both genders/ 12–18 years	First Pm Mx	NS	Roth (Dental Morelli)/ 0.017 × 0.025 in (0.43 × 0.64 mm) Niquel-titanium	150g	↑
Doshi-Metha, 2012	20	8 male, 12 female/ 12–23 years	First Pm of Mx and md	After 21 days of 0.019 × 0.025 in (0.48 × 0.63 mm) stainless steel wire placement	McLaughlin Bennett Trevisi (Ortho Organizers)/0.019 × 0.025 in (0.48 × 0.63 mm) stainless steel	150g	↑

↑ Significant measurement's differences existed in the irradiated group, no differences between groups. PM, premolar; Mx, maxillary; Md, mandibular.

at three points (buccal, palatal, and mesial).^{16–19,22,23} The details of laser parameters concerning human studies are shown in Table 2, although the authors of some trials did not specify a certain number of relevant data.

Laser parameters

Wavelength was reported in all studies, as well as the output power, ranging from 40 to 180 mW. Irradiation and treatment laser parameters, such as dose, spot size and beam code, and duration of pulse were consistently reported (Table 2). Only the article by Duan et al.²⁰ compared continuous and pulsed wave.

Biological analysis

Different histochemical techniques were applied to assess the biological processes in animals (Table 4). The only study that assessed the vascularization in the third day found statistically significant differences.¹⁴ However, there was discordance in other biological processes. In the clinical trials that analyzed osteoclastogenesis,^{16–19,23} the process was detected from days 2–19, whereas Marquezan et al.²² did not find differences. Habib et al.²³ found that osteoblastogenesis was statistically significantly higher than the control group on days 7 and 13. However, Fujita et al.¹⁷ did not obtain significant differences. Finally, the collagen fiber formation was analyzed and two clinical trials^{18,23} concluded that between day 1 and 19 there was a statistically significant difference, whereas another study²² found no significant difference. Moreover, Habib et al.²⁴ found that collagen fiber hyalinization was significantly reduced from day 7 to day 19 in the control group whereas it was increased at day 7 with an ulterior significant reduction at day 13 on irradiated subjects. Table 5 shows the relationship between the method used by the authors, the parameters analyzed, and the days when statistically significant differences were found.

Discussion

The results of this review show that there is a difference of opinion as to the benefits of LLLT. The evaluations were based on studies using rats and humans to try to define a course of action or protocol, as a variety of study designs and parameters are reported. Researchers have based their hypotheses on the findings of cell components that occur during orthodontic tooth movement in animal studies and the calculation of the distance in human studies. It is acknowledged that laser wavelength, total delivered energy, PRR and dose, and the optical properties of the irradiated tissues, are all directly related to cell response to laser therapy.²⁵

All of the studies used a CW diode laser, except for the one by Duan et al.,²⁰ which used a CW as well as a pulsed laser. However, there were no significant differences found between both applications. Currently, most commercially available lasers are characterized by a wavelength located in the near infrared band (790–1064 nm)—very versatile—although most studied lasers are those that emit the visible red spectrum (635 at 685 nm). They are used because infrared laser irradiation has a low absorption coefficient in hemoglobin and water, and consequently, a higher penetration

TABLE 4. DATA SUMMARY OF ELEVEN QUALIFIED TRIALS IN ANIMALS (CHARACTERISTICS OF SUBJECTS AND METHOD OF TRACTION)

<i>First author, year</i>	<i>No. irradiated/ (control group)</i>	<i>Age and mean weight</i>	<i>Force</i>	<i>Result</i>
Gama, 2010	15/15	3 months/ 250–300 g	40g/F	=
Abi-Ramia, 2010	20/25	NS- 300 g	0.4 N	↑
Yoshida, 2009	30/30	6 weeks /180 g	10g/F	↑
Yamaguchi, 2007	25/25	6 weeks /180 g	10g/F	↑
Fujita, 2008	25/75	6 weeks /180 g	10g/F	↑
Kawasaki, 2000	24/24	6 weeks /180 g	10g/F	↑
Marquezan, 2010	18/18	12 weeks /250 g	40cN	↓
Habib, 2010	15/15	3 months/250–300 g	40g/F	↑
Habib, 2012	15/15	3 months/250–300 g	40g/F	↑
Yamaguchi, 2010	25/25	6 weeks /180 g	10g/F	↑
Duan, 2012	44/8	6 weeks /200–250 g	10g/F	↑

↑ Significant differences existed in the irradiated group; ↓ Significant biological differences existed in the control group; = No differences between groups.

depth in the irradiated soft tissues than visible radiation.¹¹ Wavelengths used in these studies were between 780 and 860 nm and there is no direct relationship between the wavelength type and the irradiation benefit.

The higher the output power, the less time it takes to obtain the energy required; however, too much power or too much power density may be unsuccessful or achieve negative results, as has been shown in other applications of LLLT.²⁶ In the literature review, the output power varied from 20 to 180 mW. Approximately 50% of the diode laser beam (60 mW) penetrates to a depth of 1.0 mm in human and bovine mandibular cortical bone.²⁷ Therefore, most of the studies used 100 mW power and the probe tip was in contact

with the gingiva so as not to reflect the laser light. However, other studies with lower output power and similar other parameters have verified their hypotheses.^{10,12,21,23,24}

The irradiation has an accumulative effect that means that part of the administered dose may accumulate in the next irradiation. Therefore, researchers should be cautious not to exceed the biostimulating dose range or reach the inhibition range. An example of biostimulation and inhibitory effect is found in the study of Marquezan et al.²² that revealed on day 2 of tooth movement that the number of osteoclasts in comparison tended to increase with the negative number in the control group (no orthodontic movement) ($p < 0.05$). During this period, the quantity of osteoclasts in the laser-

TABLE 5. RELATIONSHIP BETWEEN THE BIOLOGICAL PARAMETERS ASSESSED, THE HISTOCHEMICAL TECHNIQUES, AND THE TIMING WHEN A STATISTICALLY SIGNIFICANT DIFFERENCE WAS FOUND

<i>Biological parameters</i>	<i>Histochemical technique</i>	<i>First author and year</i>	<i>Days / differences</i>	
			<i>Yes</i>	<i>No</i>
Vascularization	HE	Abi-Ramia, 2010	3 ^a	
Osteoclasts	TRAP	Kawasaki, 2000	2 ^b	
		Yamaguchi, 2007	2 ^c , 4 ^c , and 7 ^c	
		Yamaguchi, 2010	2 ^c , 4 ^c , and 7 ^c	
		Fujita, 2008	2 ^c , 4 ^c , and 7 ^c	
		Marquezan, 2010		No
		Yamaguchi, 2010	2 ^c , 3 ^c , 4 ^c , and 7 ^c	
Osteoblasts	MMP-9, cathepsin K, and integrin subunits of $\alpha(v)\beta3$ RANK and RANKL (M-CSF)/(CSF-1) HE and Sirius red	Fujita, 2008	2 ^b and 3 ^b	
		Yamaguchi, 2007	2 ^b , 3 ^b , 4 ^b , and 7 ^c	
		Habib, 2010	7 ^d and 19 ^e	
		Habib, 2010	7 ^d and 13 ^d	
Collagen fibers	Picro-sirius red	Fujita, 2008		No
		Maquezan, 2010		No
Hyalinization	PCNA HE and Sirius red	Habib, 2010	13 ^e and 19 ^e	
		Kawasaki, 2000	1 ^b and 2 ^b	
		Habib, 2012	7 ^e and 9 ^f	

^aNonstatistically significant differences; ^{b-f}statistically significant differences; ^b($p < 0.01$), ^c($p < 0.05$), ^d($p = 0.015$), ^e($p = 0.007$), ^f($p = 0.048$).

HE, hematoxylin and eosin; TRAP, expression of tartrate-resistant acid phosphatase; MMP-9, matrix metalloproteinase; RANK and RANKL, receptor activator of nuclear factor- κ B/RANK ligand (RANKL) system; (M-CSF)/(CSF-1), colony-stimulating factor system/colony-stimulating factor-1; OPG, osteoprotegerin; PCNA, proliferating cell nuclear antigen.

irradiated group (day 2) was similar to the quantity in the unirradiated group (day 2). On day 7, the number of osteoclasts tended to decrease ($p < 0.05$), except when LLLT was applied daily (day 7). Therefore, on day 2, there were no statistically significant differences from the other articles⁴⁻⁶ but on day 7, when irradiation was used every 24 h, they noticed an increase in osteoclast production. When Marquezan et al.²² wanted to evaluate the expression of immature collagen on the tension side, they found that after day 7, laser applications inhibited the expression effect. Therefore, Abergel et al.²⁸ demonstrated that small doses with appropriate periods of time in between were more effective than treatments that were very close on fibroblast cultures. Habib et al.²³ found increased amounts of collagen matrix on the pressure side and tension side in irradiated subjects at days 13 and 19 when compared with unirradiated animals using longer irradiation intervals. The right combination of parameters can achieve the desired biological target. For example, Hawkins and Abrahmase²⁹ presented results suggesting that the cumulative effect of lower doses (2.5 or 5 J/cm²) determined the stimulatory effect, whereas multiple exposures at higher doses (16 J/cm²) resulted in an inhibitory effect with more damage. Perhaps in canine distalization treatments, the appropriate course is applying frequent irradiations is for 2 weeks, followed by weekly irradiation for the rest of the treatment. Limpanichkul et al.¹³ used higher doses of laser (25 J/cm²/2.3 J per point/18.4 J per tooth) and this dose might have no effect on the speed of tooth movement in humans. According to Goulart et al.,³⁰ higher doses of LLLT could present inhibitory effects on tooth movement. The irradiations were performed after activating the coil, and the intervals varied according to the study: it was performed every 48 h by Limpanichkul et al.¹³; at 3 and 7 days by Sousa et al.¹² and Youssef et al.¹¹; and at 3, 7, and 14 days by Cruz et al.¹⁰ Most studies²⁻⁵ agree that irradiation intervals should be long; they agree to distribute the total energy density to the highest possible number of points according to canine anatomy. Youssef et al.¹¹ reported 6 points; 8 points were reported by Limpanichkul et al.¹³; and Sousa et al.,¹² Cruz et al.,¹⁰ and Doshi-Metha et al.⁹ reported 10 points.

The studies performed clinical^{4,10,16} or radiographic measurements (computed microtomography)⁶ or on animal models.^{11,13,16-19} In clinical and model measurements, the coronal reference points were used as a reference, with the laser benefit being positive or negative. It should be noted that the measured distance is affected by the inclination of the teeth. However, in the study by Yoshida et al.,¹⁵ distances were measured in the apical zone, closer to the center of resistance, thus enhancing the viability of their measurements.

Finally, in human studies, we should be cautious when evaluating the measurements, because of the systemic effects of phototherapy.²⁷ In human studies, the contralateral canines were used as a control, and it is uncertain if the applied dose may have had an effect on that area. Patients were their own controls in order to reduce the variability and allow a smaller number of patients in the sample.^{13,14}

A recent review by Long et al.³¹ suggests that LLLT, electrical current, and pulsed electromagnetic fields are safe, but have not proven to be effective to accelerate orthodontic tooth movement, whereas corticotomy is reported as able to, and other interventions, such as dentoalveolar or periodontal

distraction, are considered promising in accelerating tooth movement. However, our results show that LLLT is effective in reducing the time for orthodontic treatment, both in humans and in animal experiments.

Conclusions

Variation in the wavelength, with a reasonable dose in the target zone, helps obtain the desired biological effect, achieving a reduction of the orthodontic treatment time, although there are studies that do not report any benefit according to their values.

It remains to determine the dose limits that produce biostimulatory effects, bioinhibitory effects, or nonsignificant results.

Because of the wide variety of combinations of irradiation and the different protocols applied, more studies should be performed in this field with a consensus set of unified criteria.

Author Disclosure Statement

No competing financial interests exist.

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