European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2021

Review

PAIN IN FIXED ORTHODONTIC TREATMENT. ROLE OF PHOTOBIOMODULATION: DREAM OR REALITY?

P. Caccianiga[1*], I. Carminati[2], G. Caccianiga[1]

[1]School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy;
[2]Private Practicioner, Bergamo, Italy

**Correspondence to:*
Paolo Caccianiga, DDS
School of Medicine and Surgery, University of Milano-Bicocca, 20900 Monza, Italy
e-mail: p.caccianiga@campus.unimib.it

ABSTRACT

Pain is an unpleasant emotional and sensory experience. For many years orthodontists have been looking for an effective method of reducing this feeling of discomfort. As a result, Photobiomodulation (PBM) has recently taken hold in the orthodontic field. Among the countless advantages, it can modulate the painful feeling. The aim of this research is to identify the use of photobiomodulation in subjects undergoing fixed orthodontic treatment, to reduce the pain and discomfort it causes. The research was conducted from the Web of Science, Pubmed and Scopus databases. Only 14 articles met the inclusion and exclusion criteria and were used to conduct the research. The different studies compared, in most cases, patients whose mouth was divided into a part treated with laser therapy and a placebo part. The results show a statistically significant difference in perceived pain between the irradiated and non-irradiated arch. Three authors did not find statistically significant results in favour of low-laser therapy, but it is important to remember that they used different parameters. To obtain generally valid studies with consistent and reproducible results, it is necessary to standardise the different parameters independent of the operator performing the procedure.

KEYWORDS: *photobiomodulation, low-level laser therapy, pain, orthodontic treatment*

INTRODUCTION

Pain is an unpleasant emotional and sensory experience. It is known that it is one of the negative aspects of a fixed orthodontic treatment. It is perceived as discomfort, dull pain, and hypersensitivity in affected teeth (1, 2) and is present in most procedures: separator placement, banding, initial wire engagement, wearing elastics and debonding (3, 4, 5).

About 90% of patients undergoing orthodontic treatment experience a painful sensation (6), and according to O'Connor, it is considered the fourth most frequent reason for apprehension and fear in patients who need to start any fixed treatment (7).

The pain associated with orthodontic appliances is a real problem for the patient since it interferes with chewing

Received: 02 July 2021
Accepted: 25 August 2021

ISSN: 2038-4106
Copyright © by BIOLIFE 2021
This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder. Unauthorized reproduction may result in financial and other penalties. **Disclosure: All authors report no conflicts of interest relevant to this article.**

performance and speech (8).

For many years, orthodontists have searched for an effective method to reduce the discomfort their patients perceive, as this often determines whether to continue therapy (9).

In recent years, Photobiomodulation (PBM) has taken hold in the orthodontic field for the countless advantages it brings: it can induce the activation and proliferation of osteoblasts and osteoclasts, therefore accelerating the remodelling of bone, increase the velocity of orthodontic tooth movement (10, 11, 12) and the efficiency of orthodontic treatment during dental alignment (13); it can also be used to enhance keratin synthesis (14, 15), in case of hypersensitivity, analgesia and inflammatory processes in periodontal tissues (16), but above all, it can modulate the painful feeling as a non-invasive, non-thermal and inexpensive technique without significant adverse effects (17, 18).

PBM's analgesic and anti-inflammatory properties are attributed to increased blood flow, decreased prostaglandin E2 and inhibiting COX-2 enzyme secretion (19, 20).

The aim of this research is to identify in the literature the use of photobiomodulation in subjects undergoing fixed orthodontic treatment to reduce the perception of pain and discomfort that it causes.

MATERIALS AND METHODS

The research was conducted from the Web of Science, Pubmed and Scopus databases. Hand-searching was not performed. Keywords used were "photobiomodulation", "laser", "orthodontic", "dental movement", "tooth movement", and "pain". Inclusion and exclusion criteria were determined prior to reading the retrieved abstracts.

The inclusion criteria were as follows:

- Articles published in the last 10 years,
- Studies published in the English language,
- Studies conducted on the human species,
- Participants that underwent fixed orthodontic treatment without limitation in gender, age, race and socio-economic status,
- Randomised clinical trials which analysed the effectiveness of PBM in reducing orthodontic pain compared with a placebo group (simulated pain treatment) and/or a control group (no treatment of any kind),
- Studies that used the analogue visual scale (SEA), the numerical evaluation scale or another type of questionnaire to evaluate the duration and intensity of pain.

The exclusion criteria were as follows:

- Articles not written in the English language,
- Studies were cases or letter reports, review articles, cohort studies, opinion articles, abstract and descriptive,
- Studies in vitro studies or animal,
- Participants had pain caused by acute or chronic dental, periodontal or gum disorders,
- Studies of patients compromised by neurological and psychiatric disorders, systemic diseases or chronic pain,
- Participants not subjected to fixed orthodontic treatment such as studies on orthodontic elastomeric separation or similar.

The articles found in the search were selected based on their abstract, title and keywords relevance. Publications addressing relevant questions were read in full and either included for further analysis or excluded.

RESULTS

Three hundred twenty-one results have been identified through database searching: 164 on Web of Science, 71 on Pubmed, and 86 on Scopus. The filters "last 10 years" and "human species" have been applied, finding the following articles: 136 on Web of Science, 52 on Pubmed and 63 on Scopus. After excluding duplicates and reviewing titles and abstracts, 52 articles were evaluated in full text. Only 14 articles met the inclusion and exclusion criteria and were used to conduct the research.

The selected studies that evaluated the effectiveness of PBM for orthodontic pain used different parameters, such as wavelength, power output, energy dose, exposure duration, focal spot area, power density, energy density, and frequency of treatment. Moreover, the subjects examined differ in age, sex, cultural difference, malocclusion and more. Table I

shows the different parameters of each study.

DISCUSSION

For years orthodontic treatment has been accompanied by pain, considered natural and negligible compared to possible problems such as prolonged treatment time, periodontal problems and root resorption (21).

To date, more and more orthodontists are looking for a way to relieve patients' pain. There are several ways to decrease this discomfort, such as using drugs, chewing plastic wafers or gum, eating a diet of softer foods, and using vibratory and transcutaneous electrical stimulation (22, 23).

PBM is one of the latest methods to relieve orthodontic pain. Although the mechanisms of action are not yet clear (16), low-laser therapy has been shown to have neural and anti-inflammatory periodontal regenerative properties. The use of a diode laser in a continuous wave can significantly reduce pain after tooth movement in the first three days (24, 25).

Orthodontic treatment

Table I. *The different parameters of each study.*

Articles	Study design	Laser	Wavelength and power	Dose	Total energy	Pain measurement	Subject	Orthodontic treatment
Dominguez et al. (2013)	Single-blind RCT (split mouth)	GaAlAs laser	830 nm 100 mW	80 J/cm2, 2.2 J vestibular and palatal surface, for 22 sec each Only one dose: T0	4.4 per tooth	VAS after 2 h (T1), 6 h (T2), 24 h (T3), 2 days (T4), 3 days (T5), and 7 days(T6)	59: 40 F - 19 M AGE: 20-30	mini brackets Equilibrium and self- ligating brackets slot 0.022 inch
Wu et al. (2018)	Double-blinded RCT	GaAlAs diode laser	810 nm 400 mW	2 J/cm2 3 points/side, for 20 sec each Multiple doses: 0h, 2 h, 24 h, 4 d, and 7 d	Not indicated	Quantitative sensory testing (QST) at 0 h, 2 h, 24 h, 4 d, and 7 d	40: 30 F – 10 M Age: 12-33	self-ligating brackets slot 0.022 inch
Sobouti et al. (2015)	Single-blind RCT (split-mouth) placebo-controlled	He-Ne laser	632.8 nm 10 mW	6 J/cm2 buccal and palatal: radical apical for 80 sec and coronal for 40 sec Only one dose: T0	Not indicated	VAS on the 1, 2, 4, and 7 days	27: 11 F – 16 M Age: 12-21	metal pre-adjusted brackets (Extractions)
Isola et al. (2019)	RCT (split mouth)	Diode laser	810 nm 1 W	66.7 J/cm2, 3 points/side for 15 sec each Multiple doses: 0d, 3d, 7d, 14d and every 15d	8 J (2 x 40 s x 100 mW)	VAS at 3, 7, and 14 days	41: 20 F – 21 M Age: 10-18	metal brackets slot 0.022–0.028 inch (Extractions)
Qamruddin et al. (2017)	Single-blinded RCT (split-mouth)	GaAlAs diode laser	940 nm 100 mW	7.5 J/cm2, 5 points/side, 3 sec for each point Multiple doses: T0, T1 and T2	Not indicated	NRS 4h and 24h after each application	20: 10 F – 10 M Age: 12-25	self-ligating MBT brackets slot 0.022-inch (Extractions)
Celebi et al. (2019)	RCT (split-mouth)	GaAlAs diode laser	820 nm 110.3 mW	1.76 J/cm2, 3 points/side for 16 sec each. Only one dose	Not indicated	VAS 2h, 6h, 24h, 2d, 3d and 7d	60: 30 F – 30 M Age: 11-23	fixed orthodontic tratment, slot 0018x0.025 inch
Domiguez A. et al (2013)	RCT	Diode laser	670 nm 200 mW	6.37 W/cm2, 3 surface, 3 min on each surface Multiple doses: 0, 1, 2, 3, 4, and 7 days	108 J	VAS day 0, 1, 2, 3, 4, 7, 30, and 45	10: 5 F – 5 M Age: 12-16	fixed orthodontic treatment slot 0.018 inch (Extractions)
Qamruddin et al. (2018)	single-blinded RCT (split mouth), placebo controlled	GaAlAs diode laser	940- nm 100 mW	7.5 J/cm2, 5 points/side for 3 sec. Only one dose	75 J per tooth	NRS. at consecutive 12 h intervals for 7 days	42: 26 F – 16 M Age: 12-25	Fixed orthodontic treatment slot 0.022-inch (Extractions)
Doshi-Mehta et al (2012)	RCT (split mouth)	GaAlAs diode laser	800 nm 0.7 mW	8 J (2 x 40 sec x 100 mW). 5 points/side Multiple doses: 0, 3, 7, and 14 days	8 J (2 x 40 s x 100 mW).	Visual pain scale at 1, 3, 30 days	20: 12 F – 8 M Age: 12-23	fixed orthodontic treatment slot 0.022-inch (Extraction)
Storniolo-Souza et al. (2020)	double-blind, placebo controlled RCT (split mouth)	ArGaAl-Twin Laser	780 nm 40-70 mW	10-35 J/cm2 5 points/side 10-20 sec each Single monthly dose	4 J for mandible 9 J for the maxilla	VAS at12, 24, 48 and 72 hours	11 Age: ±14	Fixed appliances slot 0.022 × 0.028 inch (Extraction)
Lo Giudice et al. (2019)	RCT	diode laser	980 nm 1 W	24-27 J/cm2 A total of 50 sec Multiple doses: 3 times at intervals of 2 min	150 J/cm2 for mandibular arch	NRS at 2h, 6h, 24 h, from day 2 to 7	84: 43 F – 41 M Age: 16.5±2.8	self-ligating appliance slot 0.022 inch
Alam MK. (2019)	Prospective clinical intervention	GaAlAs laser	940 nm 100 mW	7.5 J/cm2 5 points/side for 3 sec each Only one dose	75 J per tooth	NRS At 4 h, 24 h, 3 d, and 7 d	32 F>M Age: 14-25	Conventional backets and self-ligatin brackets slot 0.022 inch
Al Sayed Hasan (2020)	single-blind, placebo-controlled, RCT	GaAlAs laser	830 nm 150 mW	4.25 J/cm2 2 point/side for 15 sec for each tooth Only one dose	2 J per point	VAS At 1, 6, 24, 48, and 72 h	26 Age 16-24	fixed orthodontic treatment (Extraction)
Guram et al. (2018)	RCT double-blind splint-mouth	Ga-Al-As laser	810 nm 0.2 W	5 J/cm2 8 spots for 10s Multiple doses: each week for 21 days	Not indicated	Wong-Baker Faces Rating Scale days 1 to 7	20 12 F – 8 M Age: 17-24	fixed orthodontic treatment MBT bracket 0.022 inch (Extraction)

RCT: Randomized Clinical Trial; VAS: Visual Analogue Scale; QST: Quantitative Sensory Testing; NRS: Numerical Rating Scale

In this research, studies using elastomeric separators or bands (26), maxillary orthodontic expansion (27, 28), invisible removal aligners (29, 30) or agenesis cases (31) were excluded because the forces used and the perception of pain could be very different from a fixed orthodontic treatment. On the contrary, all studies of patients with each fixed orthodontic treatment have been included.

In one of these studies, patients treated by straight-wire technique with Equilibrium brackets (Dentaurum, Ispringen, Ger many) or with In-Ovation C (GAC/Dentsply, Tokyo, Japan) self-ligating brackets (32) were compared. The results show that there is not a significant difference in average pain between bracket groups during the first week of active orthodontic treatment ($p > 0.05$) (33).

The level of dental crowding of treated patients was also not the same. Some patients had slight crowding (34) or levels up to 5 mm (33). Other subjects had 3-5 mm maxillary dental crowding (21, 35).

In the study of Lo Giudice et al., 90 subjects were divided into three groups with different crowding: mild (3-5 mm), moderate (5-7 mm), and severe (>7 mm). The authors did not find differences in the pain perceived among examined patients with mild, moderate and severe mandibular anterior crowding. However, there is no specific indication for the usage of PBM according to the amount of crowding (36).

However, in some treatments, the patients were subjected to bilateral extraction of the first upper premolars and retraction of the canines to correct protrusion and dental crowding; this means that greater force was used to get more displacement of some teeth. In addition, banding and the Nance button were used to obtain good posterior anchorage transpalatal bars (35,37-44).

Laser procedures

In most studies, the procedure was carried out in an isolated room, using protective glasses for the operator, patient and dental assistant (39). In order to confuse the patient and allow the placebo effect, the non-irradiated side was treated in the same way but with the machine turned off. To prevent the perception of the beeping emitted by the laser, music was played at a high volume (39, 41). In this way, patients could not distinguish between the placebo and experimental sides (37).

An article indicates a beneficial effect even on the side not treated with lasers, indicating a generalised effect within the trigeminal system. However, there have been no effects on extra-trigeminal sensitivity. The authors hypothesise that PBM may have reduced peripheral sensitisation of Aδ fibres and C-related nerve fibres (34).

One of the effects of laser therapy with split-mouth is the probability of carry-across effects of the laser beam from one side to the other (45). Therefore, many authors used a plastic shield like a barrier at the midline to limit the laser beam's penetration and, perchance, alter the results (39, 41).

The lasers used had different wavelengths and power. In addition, the irradiated dosimetry, energy density, timing, points on each side and number of monthly applications were also not the same. For example, in one of these studies, patients were first subjected to the alignment and levelling stages with nickel-titanium archwires, and then when the canine retraction began, with 0.018-in-stainless steel wires, laser therapy was used (37).

In the Domìnguez and Velàsquez study, laser treatment was carried out during the final stage of orthodontic treatment, when stainless steel archwires 0.019x0.025 inch were used (33). These results, in addition to the other studies, make us think that PBM is effective in modulating painful sensation at all stages of orthodontic treatment, or a 3-week low-laser therapy model can be convenient in clinical practice as it coincides with conventional orthodontic appointments (39).

Dosages and ways of energy distribution

Low-level laser therapy usually uses the following parameters: a power density between 5 and 150 mW x cm-2, red and NIR wavelength range of 600-1000 nanometers, applied for 30 to 60s per point. The resulting therapeutic effect depends on energy density measured in joules (J) per cm2 (46, 47).

The effects of PBM depend upon the different tissues, cell type, irradiation parameters, time of exposure and redox state of the cell (48). There is a biphasic dose response which underlines the existence of optimal irradiation and dose parameters. In order to make laser therapy effective, the parameters need to be within the biostimulatory dose windows (49).

It is essential to remember that a higher dosage than the optimal can have negative therapeutic outcomes; on the contrary, a lower dosage than the optimal value might have a diminished effect (50). For the success of the treatment

wavelength and energy (in J), energy density (J/cm2) is necessary, but also the original power, power density and duration parameters (49, 51).

In the studies examined, the wavelength is between 632 and 980 nm, energy varies between 0.7 and 400 mW, and total energy is not indicated in all studies. In addition, all studies indicating the amount of energy are within the efficacy window. These different protocols make it difficult to compare and quantify the beneficial effects on patients (52).

Statistically significant results

In most cases, the different studies compared patients whose mouth was divided into a part treated with laser therapy and a placebo part. The results show a statistically significant difference in perceived pain between the irradiated and non-irradiated arch (33, 34,41, 44).

In their study, Sobouti et al. contributed about a 12.1% reduction of a painful sensation on the laser side compared with the matched placebo side (37).

Another study shows that the irradiated side significantly reduced the average range of dental pain at 3, 7, and 14 days after laser treatment (38, 42). In the study of Dominguez et al., results show that the highest pain intensity occurs in the first 48 h on the treated side (40).

In a study by Alam et al., all patients are randomly divided into 4 groups: PBM + self-ligating bracket, PBM + conventional bracket, non-PBM + self-ligating bracket, and non-PBM + conventional bracket function. Authors revealed PBM + self-ligating results as the best and PBM + conventional as the 2nd best in lessened pain perception (53).

Another study found a statistically significant difference between the placebo/control and irradiated groups. In the first case, the peak of pain appeared on the second day ending around days 6-7. In the second case, the peak of pain came after 6 hours and disappeared on day 4; patients then found a reduced duration of pain (36).

In three studies, the results do not show a statistically significant difference in relieving orthodontic pain sensation following laser therapy (21, 43, 35).

In a study by AlSyed et al., however, the mean pain scores found in the laser group were less than those of the placebo group in all studied time points; this indicates some clinical efficiency of LLL despite the absence of statistical significance (35).

Appearance of pain

Articles used for this research agree that the onset of pain occurred 2-4 hours after the archwire insertion was activated, up to a peak at 24 hours. The painful sensation decreased and disappeared within 7 days (21, 33, 34, 39, 41), in accordance with Koritsanszky et al. (54).

Age and sex difference

It is known that pain perception can be affected by different individual parameters, such as age, sex, pain threshold, the magnitude of the applied force, emotional status, cultural differences, and previous pain experiences (55, 56, 57).

In several studies, however, no significant difference was found in the pain sensation between males and females, nor between adolescents and adults (39, 41).

The inclusion of both genders and different ages favours generalizability, but it is also important to remember that the most sensitive age might be between 13 and 16 years old (6). In these split-mouth designs, each patient was matched with himself/herself so that variations in the subject's demographics did not confuse the results (37).

Different methods of measuring pain

The recording of the painful sensation was done with different parameters. Some studies have used the Visual Analogue Scale (VAS). It is a widely accepted method for measuring and showing differences in pain reported by patients; it is reliable, accepted by patients, sensitive, and reproducible. Although it is a subjective method, it is one of the best methods because of its reliability in scoring pain at different time points when a significant difference among participants is expected (58, 59).

Other articles used a questionnaire based on a numeric rating scale (NRS) of evaluation to investigate the effects of laser therapy on pain sensation. It is highly correlated with VAS (60). This choice also allowed younger patients to comprehend the data collection method (61). Additionally, NRS can be administered verbally during a phone call (62).

Type of machinery and employee operator

Often the method of administration of laser therapy is unclear but, most importantly, not reproducible. In many studies, the protocol involves using the device at different points of the mouth and for a variable period. To increase the method's reliability, many authors had orthodontic treatment and laser applications performed by the same operator (21, 33, 34, 36, 38, 43).

Unfortunately, even the individual operator cannot reproduce his work similarly over time. Therefore, the handpiece is not easily used in a repeatable way at each session (Fig. 1).

In a recent study by Lo Giudice in 2020, ATP38 was used. Depending on the therapeutic indication, the device is equipped with a multi-panel system and a combination of wavelengths ranging from 450 to 835 nm. One of the advantages of using a static device is that the session is independent of the operator; this can enhance the standardisation of the dosage administered since the operator error is eliminated, and it can make the effect reproducible (Fig. 2) (63).

Fig. 1. *It is difficult to use the hand-piece in a repeatable way at each session.*

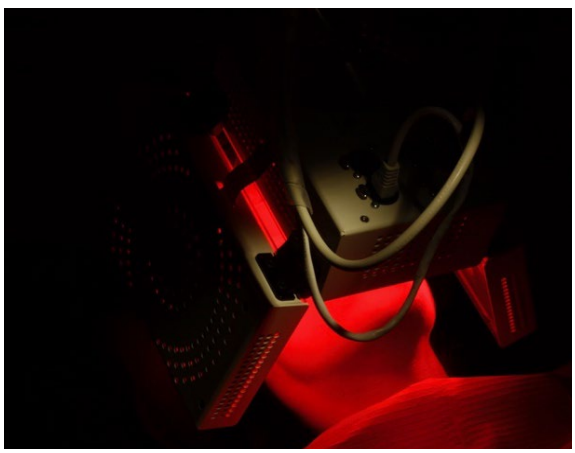

Fig. 2. *ATP38 in use.*

CONCLUSION

This search shows that most authors observed that pain reduction could not be attributed to placebo-based mechanisms. Instead, they said that laser therapy effectively reduces painful sensations during different stages of orthodontic treatment. Other authors showed no statistically significant results in favour of photobiomodulation, but it is important to remember that they used different parameters, including technical specifications and application modes. In this regard, even just one parameter can influence the effect of PBM. Additionally, results depend also on the participants' variability.

To obtain generally valid studies with consistent and reproducible results, it is necessary to standardise the different parameters that are independent of the operator performing the procedure.

Hopefully, suggesting the spread of devices similar to ATP38, the scientific validity of PBM research in orthodontia will increase.

Author Contributions

PC and GC designed the research study; IC performed the research; PC and GC wrote the manuscript. All authors contributed to editorial changes and approved the final version. The authors declare no conflict of interest.

REFERENCES

1. Kavaliauskiene A, Smailiene D, Buskiene I, Keriene D. Pain and discomfort perception among patients undergoing orthodontic treatment: results from one month follow-up study. *Stomatologija*. 2012;14(4):118-125.
2. Panda S, Verma V, Sachan A, Singh K. Perception of pain due to various orthodontic procedures. *Quintessence International (Berlin, Germany: 1985)*. 2015;46(7):603-609. doi:10.3290/j.qi.a33933
3. O'Connor PJ. Patients' perceptions before, during, and after orthodontic treatment. *Journal of clinical orthodontics: JCO*.

2000;34(10):591-592.

4. Leonida A, Paiusco A, Rossi G, Carini F, Baldoni M, Caccianiga G. Effects of low-level laser irradiation on proliferation and osteoblastic differentiation of human mesenchymal stem cells seeded on a three-dimensional biomatrix: in vitro pilot study. *Lasers in Medical Science*. 2012;28(1):125-132. doi:10.1007/s10103-012-1067-6
5. 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. *Photomedicine and Laser Surgery*. 2017;35(8):421-426. doi:10.1089/pho.2016.4215
6. Celebi F, Turk T, Bicakci AA. Effects of low-level laser therapy and mechanical vibration on orthodontic pain caused by initial archwire. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2019;156(1):87-93. doi:10.1016/j.ajodo.2018.08.021
7. Xiaoting L, Yin T, Yangxi C. Interventions for pain during fixed orthodontic appliance therapy. *The Angle Orthodontist*. 2010;80(5):925-932. doi:10.2319/010410-10.1
8. Kim WT, Bayome M, Park JB, Park JH, Baek SH, Kook YA. Effect of frequent laser irradiation on orthodontic pain. *The Angle Orthodontist*. 2012;83(4):611-616. doi:10.2319/082012-665.1
9. Alam MK. Laser-Assisted Orthodontic Tooth Movement in Saudi Population: A Prospective Clinical Intervention of Low-Level Laser Therapy in the 1st Week of Pain Perception in Four Treatment Modalities. *Pain Research and Management*. 2019;2019:1-11. doi:10.1155/2019/6271835
10. Wu S, Chen Y, Zhang J, et al. effect of low-level laser therapy on tooth-related pain and somatosensory function evoked by orthodontic treatment. *International Journal of Oral Science*. 2018;10(3):22. doi:10.1038/s41368-018-0023-0
11. AlSayed Hasan MMA, Sultan K, Ajaj M, Voborná I, Hamadah O. Low-level laser therapy effectiveness in reducing initial orthodontic archwire placement pain in premolars extraction cases: a single-blind, placebo-controlled, randomized clinical trial. *BMC Oral Health*. 2020;20(1). doi:10.1186/s12903-020-01191-7
12. Lo Giudice A, Nucera R, Perillo L, Paiusco A, Caccianiga G. Is Low-Level Laser Therapy an Effective Method to Alleviate Pain Induced by Active Orthodontic Alignment Archwire? A Randomized Clinical Trial. *Journal of Evidence Based Dental Practice*. 2019;19(1):71-78. doi:10.1016/j.jebdp.2018.11.001
13. Sobouti F, Khatami M, Chiniforush N, Rakhshan V, Shariati M. Effect of single-dose low-level helium-neon laser irradiation on orthodontic pain: a split-mouth single-blind placebo-controlled randomized clinical trial. *Progress in Orthodontics*. 2015;16(1). doi:10.1186/s40510-015-0102-0
14. Isola G, Matarese M, Briguglio F, et al. Effectiveness of Low-Level Laser Therapy during Tooth Movement: A Randomized Clinical Trial. *Materials*. 2019;12(13):2187. doi:10.3390/ma12132187
15. Qamruddin I, Khursheed Alam M, 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. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2017;152(5):622-630. doi:10.1016/j.ajodo.2017.03.023
16. 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. *Lasers in Medical Science*. 2013;30(2):915-923. doi:10.1007/s10103-013-1508-x
17. Qamruddin I, Alam MK, Abdullah H, Kamran MA, Jawaid N, Mahroof V. Effects of single-dose, low-level laser therapy on pain associated with the initial stage of fixed orthodontic treatment: A randomized clinical trial. *The Korean Journal of Orthodontics*. 2018;48(2):90. doi:10.4041/kjod.2018.48.2.90
18. Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: A clinical investigation. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2012;141(3):289-297. doi:10.1016/j.ajodo.2011.09.009
19. Storniolo-Souza J, Lima LM, Pinzan A, Alvarez F, Pereira SC da C, Janson G. INFLUENCE OF LOW-LEVEL LASER IRRADIATION ON ORTHODONTIC MOVEMENT AND PAIN LEVEL - A RANDOMIZED CLINICAL TRIAL. *Orthodontic Waves*. 2020;79(2-3):105-112. doi:10.1080/13440241.2020.1820800
20. Guram G, Reddy RK, Dharamsi AM, Syed Ismail PM, Mishra S, Prakashkumar MD. Evaluation of Low-Level Laser Ther-

apy on Orthodontic Tooth Movement: A Randomized Control Study. *Contemporary clinical dentistry*. 2018;9(1):105-109. doi:10.4103/ccd.ccd_864_17

21. Pandis N, Walsh T, Polychronopoulou A, Katsaros C, Eliades T. Split-mouth designs in orthodontics: an overview with applications to orthodontic clinical trials. *European Journal of Orthodontics*. 2013;35(6):783-789. doi:10.1093/ejo/cjs108
22. Bjordal JM. Low Level Laser Therapy (LLLT) and World Association for Laser Therapy (WALT) Dosage Recommendations. *Photomedicine and Laser Surgery*. 2012;30(2):61-62. doi:10.1089/pho.2012.9893
23. Domínguez A, Velásquez SA. Effect of Low-Level Laser Therapy on Pain Following Activation of Orthodontic Final Archwires: A Randomized Controlled Clinical Trial. *Photomedicine and Laser Surgery*. 2013;31(1):36-40. doi:10.1089/pho.2012.3360
24. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. *Pain*. 1986;27(1):117-126. doi:10.1016/0304-3959(86)90228-9