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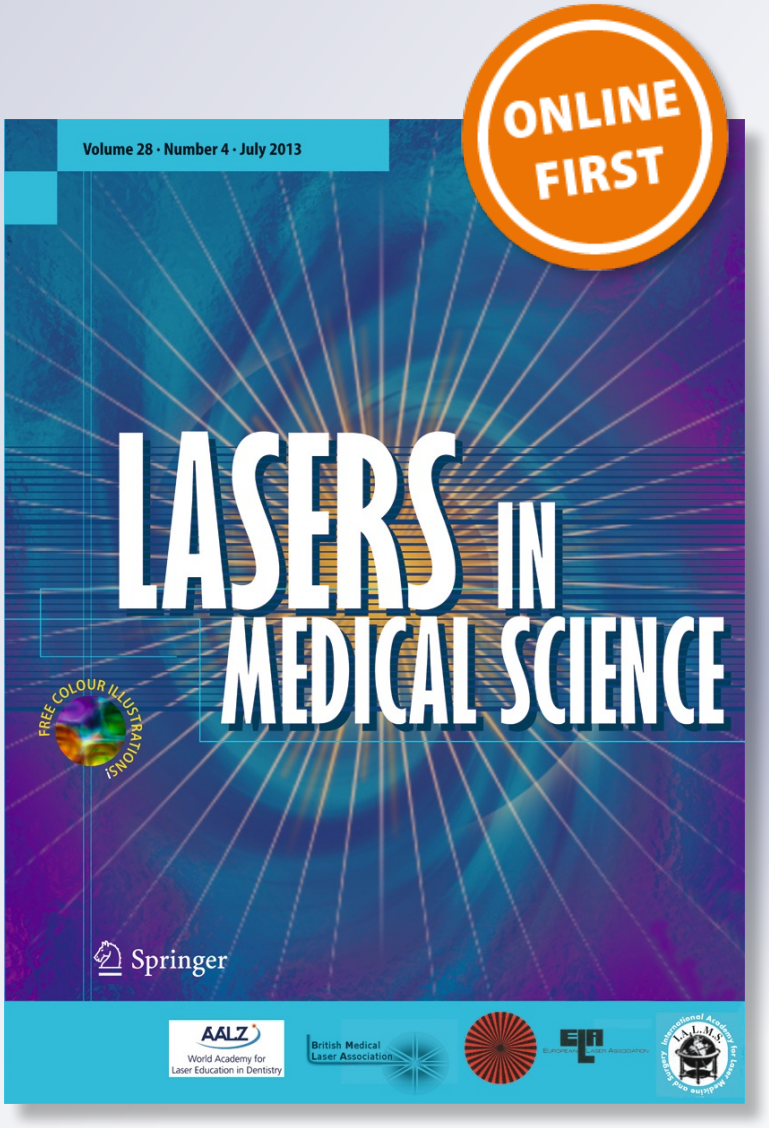

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ORIGINAL ARTICLE

Effect of LED-mediated-photobiomodulation therapy on orthodontic tooth movement and root resorption in rats

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Abstract The aim of this experimental study was to evaluate the effects of light-emitting diode-mediated-photobiomodulation therapy (LPT), on the rate of orthodontic tooth movement (TM) and orthodontically induced root resorption, in rats. Twenty male 12-week-old Wistar rats were separated into two groups (control and LPT) and 50 cN of force was applied between maxillary left molar and incisor with a coil spring. In the treatment group, LPT was applied with an energy density of 20 mW/cm^2 over a period of 10 consecutive days directly over the movement of the first molar teeth area. The distance between the teeth was measured with a digital caliper on days 0 (T0), 10 (T1), and 21 (T2) on dental cast models. The surface area of root resorption lacunae was measured histomorphometrically using digital photomicrographs. Mann–Whitney *U* and Wilcoxon tests were used for statistical evaluation at $p<0.05$ level. TM during two different time intervals (T1–T0 and T2–T1) were compared for both groups and a statistically significant difference was found in the LPT group ($p=0.016$). The TM amount at the first time period (1.31±0.36 mm) was significantly higher than the second time period (0.24±0.23 mm) in the LPT group. Statistical analysis showed significant differences between two groups after treatment/observation period ($p=0.017$). The magnitude of movement in the treatment group was higher (1.55±0.33 mm) compared to the control group (1.06±0.35 mm). Histomorphometric analysis of root resorption, expressed as a percentage, showed that the average relative root resorption affecting the maxillary molars on the TM side was 0.098±0.066 in the LPT group and 0.494±0.224 in the control group. Statistically significant inhibition of root resorption with LPT was determined ($p<0.001$) on the TM side. The LPT method has the potential of accelerating orthodontic tooth movement and inhibitory effects on orthodontically induced resorptive activity.

Keywords Low-level laser therapy · Tooth movement · Orthodontics · Rats

Introduction

In orthodontic therapy, tooth movement is a process that combines both pathological and physiological responses to externally applied forces [1]. Histologically, tooth movement has been well described [2]. It is universally accepted that periodontal cells, which are compressed between the alveolar bone and cement, secrete bone-resorbing cytokines to stimulate osteoclast formation and bone resorption in the direction of orthodontic force vector [3].

On the other hand, orthodontically induced inflammatory root resorption (OIIRR) is a common iatrogenic consequence of treatment. It has been considered a side-effect of the cellular activity associated with the removal of necrotic tissue in an overcompressed periodontal ligament (PDL) [4].

To date, several researchers have suggested that there might be ways to prevent OIIRR [5–9] and accelerate tooth movement [10–15]. One of the most commonly studied agents in clinical and animal models is prostaglandin [6, 8, 14, 16].

A. Ekizer (✉)
Department of Orthodontics, Faculty of Dentistry, Erciyes University, Kayseri, Turkey
e-mail: dtekizer@hotmail.com

T. Uysal
Department of Orthodontics, Faculty of Dentistry, Izmir Katip Celebi University, Izmir, Turkey

E. Güray
Ankara, Turkey

D. Akkuş
Faculty of Medicine, Histology and Embryology, Erciyes University, Kayseri, Turkey

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Additionally, the acceleration of TM and prevention of OIIRR caused by the injection of 1,25-dihydroxycholecalciferol (vitamin D3) [14, 17] and hormones such as parathormone [15], thyroid hormones [5, 18], sex hormones [19] in the area of the tooth, where orthodontic force is applied, has been investigated. These methods depend on injections, that could be associated to discomfort and pain, or a sophisticated apparatus that demands applications for a long term to achieve its therapeutic effects.

Photobiomodulation is a current therapeutic approach in which exposure to low-level laser (LLL) light is proposed to have beneficial effects on enhanced tissue regeneration and tissue growth including effects on fibroblastic [20] and chondral [21] proliferation, collagen synthesis [22], wound healing [23–25], bone regeneration [26, 27], and nerve regeneration [28]. It is easy to perform and use thrifty equipments that can be used for several different orthodontic treatments in clinical practice such as accelerating tooth movement [29], reduction of orthodontic post-adjustment pain [30], and accelerating the process of bone regeneration during the consolidation phase after distraction osteogenesis [31]. Previous studies [26, 32] showed that irradiation by light-emitting diode (LED)-mediated-photobiomodulation therapy (LPT) had greater stability. Kawasaki et al. [29] demonstrated that the LLL irradiation can accelerate TM accompanied by alveolar bone remodeling in the rat model and this process included an increase in bone formation and cellular proliferation on the tension side as well as increased number of osteoclasts in the compression side of the moved molars.

LED radiation is a monochromatic near-infrared radiation (NIR). Light in the NIR range of 630–1,000 nm is generated by using low-energy laser or LED arrays that have been shown to improve retinal function in an animal model of mitochondrial dysfunction [25]. The difference between LED radiation and the LLL radiation is that the latter is a laser with the characteristic of coherency, whereas LED light is not coherent; therefore, fewer side effects are expected to result [33]. LED radiation can also be produced at a lower cost compared to the LLL and it can safely be applied to a larger area of the body surface.

The aim of this study was to evaluate the effects of LPT on the rate of TM and OIIRR in rats. The null hypothesis assumed that there is no significant tooth movement and root resorption difference between the LPT group and the non-irradiated control.

Materials and methods

Animals and groups

Twenty male 12-week-old Wistar rats with a mean weigh of 284.65±17.95 g were used. All animals were housed in polycarbonate cages, subjected to a 12-h light–dark cycle at a constant temperature of 23 °C, and fed a standard pellet diet (Expanded pellets; Stepfield, Witham, Essex, UK) with tap water *ad libitum*. The experiment protocol was approved by the University of Erciyes, Regional Animal Research Ethics Committee (no. 07-09/45). This study was organized as a parallel group design with one group receiving the experimental protocol and the other receiving the control. The power analysis was performed with G*Power Ver. 3.0.10 (Franz Faul, Universität Kiel, Germany) software. Based on 1:1 ratio between groups, a sample size of 17 animals would give more than 80 % power to detect significant differences with 0.35 effect size and at $\alpha = 0.05$ significance level. Animals were randomly divided into two equal groups (control and experimental) of 10 rats each. Ten animals had only an orthodontic appliance inserted (control group), whereas 10 rats received both orthodontic force and LPT.

Experimental tooth movement

All operations were carried out under general anesthesia by using an intraperitoneal injection of ketamine (1.0 mg/kg body weight; ketamine hydrochloride, Gedeon Richter Ltd, Budapest, Hungary) and xylazine (0.5 mg/kg body weight; Rompoun, Bayer, Leverkusen, Germany) combination. A retractor was used to hold back the soft tissues and to hold the head securely (Fig. 1) [34].

For mesial movement of the upper left first molar by the method of Brudvik and Rygh [35], the wire end of a 4–7 mm length of stainless steel, superelastic closed-coil spring (Elgiloy spring, F-31 0.008×0.032 in.; Rocky Mountain Dental Products Co., Denver, CO, USA) was ligated with the maxillary first molar by a 0.010-in. stainless steel ligature wire (Dentaurum, Ispringen, Germany; Fig. 1). The other side of the coil spring was also ligated with a hole in the left maxillary incisor drilled buccolingually just above the gingival margin by using the same ligature wire. The steel wire was inserted through the hole and bent on the buccal surface of the left incisor. The orthodontic force exerted by the appliance was constant at 50 cN in the beginning of the experiment between the maxillary left molar and incisor in the mesial direction to the molar tooth. The force magnitude was calibrated by a tension gauge once a week and the coil spring was adjusted if needed. Tooth movement was performed for 21 days.

Measurement of tooth movement

On days 0 (T0), 10 (T1), and 21 (T2), silicone impressions (Zetalabor, Zhermack, Rovigo, Italy) of the maxillae of the rats were taken and cast models were made up with dental stone. The amount of orthodontic tooth movement was evaluated by measuring the distance between the most mesial point of the maxillary first molar (M1) and the most distal

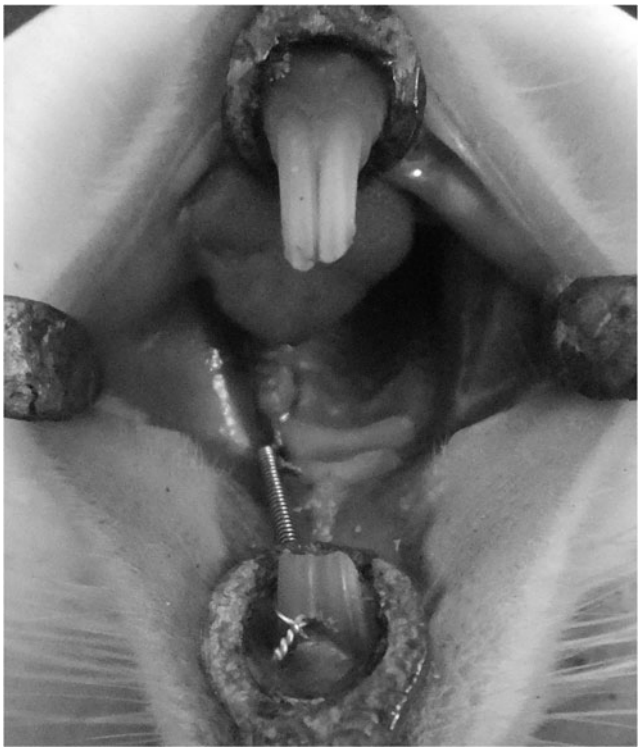

Fig. 1 Ecarteur in situ and schematic view of orthodontic appliance. Closed-coil spring producing force of 50 cN was attached between maxillary left first molar and incisor by stainless steel ligature

point of the ipsilateral incisor (IP) at the gingival level as described by Drevenšek et al. [13]. Measurements were made with an electronic digital caliper (Mitutoyo Co., Miyazaki, Japan) on dental cast models.

Changes in measured distances were calculated and recorded in two time periods. Days 0–10 is called the first period (T1–T0) and days 10–21 is called the second period (T2-T1). The same investigator (AE) performed all measurements and every measurement was repeated three times. The mean value of each triplet was used as the final measurement. Appliance condition and oral hygiene were checked once a week. During the study, the coil spring was adjusted to generate a drawing force at 50 cN if necessary.

LED-mediated photobiomodulation therapy

For LPT, OsseoPulse® LED device (Biolux Research Ltd, Vancouver, Canada; Fig. 2) was used in the present study. The wavelength was 618 nm and the output power was 20 mW/cm^2. Irradiation was performed under general anesthesia to ensure the immobility of the test animal for 20 min once a day for the first period (total exposure time, 200 min). The treatment array was positioned on the cheek surface overlying the experimental side of the animal and the irradiation was applied transcutaneously. All irradiations were done by the same operator (AE). After activation, the LED device

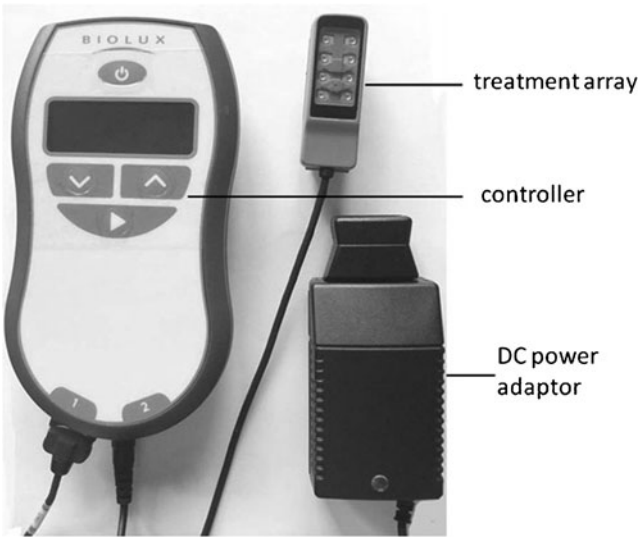

Fig. 2 LED-mediated photobiomodulation therapy device

was automatically deactivated when application time is over. All animals of the two groups were euthanized on day 21 using an overdose of carbon dioxide.

Histological preparation

The appliance-bearing segment of the maxilla were dissected and kept in fixative for 24 h at 4 °C, rinsed in 0.1 M sodium cacodylate buffer containing 0.2 M sucrose, and decalcified in 0.25 M ethylenediaminetetraacetic acid (10 %) at 4 °C for approximately 8 weeks. The specimens were embedded in paraffin and 5 mm parasagittal sections were cut and stained with haematoxylin and eosin.

The slide showing the greatest length of the mesiobuccal root of the first molar and four adjacent slides were evaluated histomorphometrically. Each slide contained five sections. The histomorphometric evaluation design was adopted from Talic et al. [7]. For histomorphometric measurements, photomicrographs were taken digitally with 4× objective lens with a microscope and digital camera system (Olympus CX41/DP25; Olympus Corp., Tokyo, Japan).

To calculate the percentage of OIIRR, two reference points were selected that could be reliably identified on all sections: the cemento-enamel junction and the root bifurcation point. A line was drawn between the reference points. By tracing the pulp area, the computer image analysis software (Analysis 2.1; Soft-Imaging Software GmbH, Münster, Germany) calculated the area (in square micrometer) of the pulp. The whole root was traced and the area (in square micrometers) of the whole root was also calculated by the software (Fig. 3). To determine the percentage of root resorption for each root, the following formula was used: combined surface area of root resorption lacunae divided by the surface area of the whole root minus the surface area of the radicular pulp multiplied by

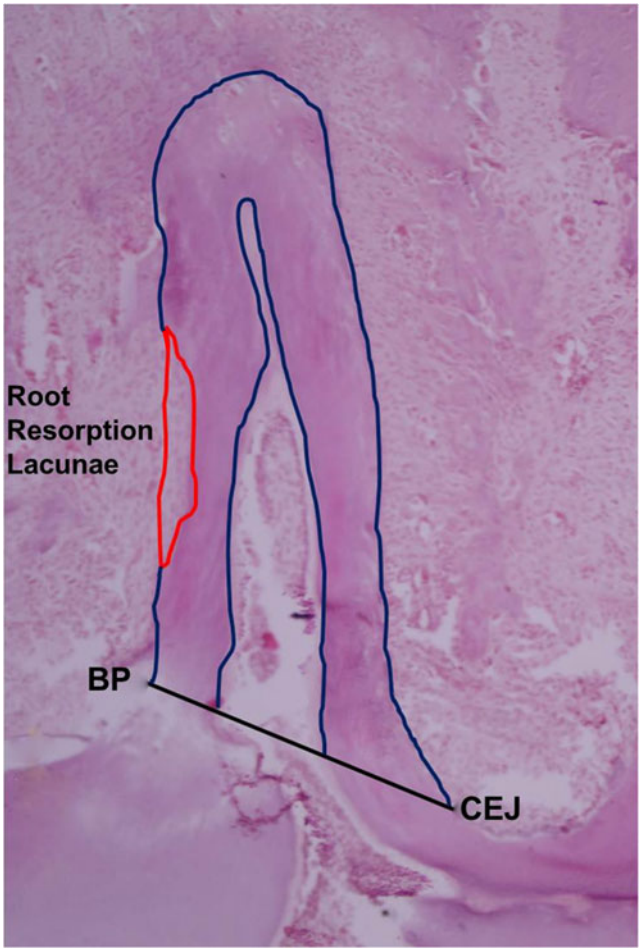

Fig. 3 Area of investigation: sagittal section along the mesio-buccal root. Measurements of the area of root resorption and total root surface using an image analysis system. *BP* bifurcation point, *CEJ* cemento-enamel junction

100. The measurements were taken from four sections at 25 μm intervals and the mean values were calculated.

Statistical analysis

All data were analyzed with the Statistical Package for Social Sciences, 13.0 (SPSS for Windows; SPSS Inc, Chicago, IL, USA). Descriptive statistics were given as mean, standard deviation, minimum, and maximum. Comparison of the amount of tooth movements during different time periods and OIIRR were evaluated by Wilcoxon test. Group differences were studied by the Mann–Whitney *U* test. When the *p* value was less than 0.05, the statistical test was determined as significant.

Results

All animals survived to the end of the study. Orthodontic appliance was well tolerated and the animals gained weight. The body weight of one rat in the experimental group decreased during the expansion period but subsequently recovered. No statistically significant changes in body weight were observed between groups during treatment/observation periods (Table 1).

Orthodontic tooth movement was evidenced by a gradual decrease in the width of mesial of M1 and IP points. Tooth movement during two different time intervals (T1–T0 and T2–T1) were compared for both groups and statistically significant difference was found in the LPT group ($p=0.016$; Table 2). During LPT intervention, the tooth movement during the first time period (T1–T0) (1.31±0.36 mm) demonstrated significant increases as compared with the second time period (T2–T1; 0.24±0.23 mm). However, there were no significant differences between the two investigated time periods in the control group.

Table 3 presents the rate of tooth movement data comparing the LPT group versus the control. The increased amount of overall tooth movement attained with the use of LPT was highly significant at $p<0.05$ level as compared with the control animals that received orthodontic appliances but no additional applications. The magnitude of movement in the treatment group was 1.55±0.33 and 1.06±0.35 mm in the control group.

Histomorphometric analysis showed that the average relative OIIRR of the mesiobuccal root of maxillary molar on the TM side was 0.098±0.066 μm^2 in the LPT group and 0.494±0.224 μm^2 in the control group as shown in Table 4. There was a significant difference in relative root resorption between the two groups ($p<0.001$). According to different TM and OIIRR findings, the null hypothesis of the present study was rejected.

Discussion

Electrical stimulation, LLL therapy, drugs, or different pharmacological agents have been studied in many fields of dentistry and also in orthodontics; but to our knowledge, this is the first time that LPT on experimental TM and OIIRR in animals is investigated. The results of the present study demonstrate that LPT in the infrared spectrum (618 nm) improves

Table 1 Body weight changes (in kilogram) between groups during first and second period

Groups	*N*	T1–T0		T2–T0		Significance	
		Mean	SD	Mean	SD	T1–T0	T2–T0
LPT group	8	0.268	0.196	0.326	0.130	NS	NS
Control group	10	0.276	0.167	0.320	0.155	NS	NS

SD standard deviation, *T0* beginning of study, *T1* end of first period (10th day), *T2* end of experiment (21st day)

Table 2 Descriptive statistics and statistical comparisons of tooth movement during two different time intervals (in millimeter)

Groups	Time period	*N*	Mean	SD	Minimum	Maximum	25th	Percentiles 50th (median)	75th	Statistical comparisons (*p* value)
LPT group	T1–T0	8	1.31	0.36	0.65	1.70	1.04	1.36	1.64	0.016
	T2–T1		0.24	0.23	0.00	1.28	0.02	0.07	0.26	
Control	T1–T0	10	0.49	0.26	0.06	0.84	0.32	0.47	0.79	0.683
	T2–T1		0.57	0.38	0.01	1.07	0.27	0.49	1.15	

N sample size, *SD* standard deviation

TM rate and inhibits OIIRR after the application of orthodontic force.

Most of the animal researches on TM and OIIRR have been presented in rats [5–9, 11, 13–19, 29] as this study. Injections of thyroid hormone [18], osteocalcin [11], and prostaglandin [6, 8, 14, 15] can increase TM without any damage to the periodontal tissues. But in clinical practice, this technique can be associated pain and discomfort. For the purpose of decreasing fear of injection and avoiding pain, some methods to increase bone tissue metabolism by noninvasive ways have been studied, as electric stimulation [10], ultrasound [36], or LLL therapy [29].

OIIRR is a common but unpredictable consequence of TM [7]. Foo et al. [9] observed increases in resorption crater volumes in the TM group compared with the control group. Identifying high-risk patients who may develop root resorption during orthodontic TM is a prerequisite for developing clinical or cellular treatment modalities to prevent or reduce the incidence of OIIRR [7]. However, in clinical practice, most of these methods are associated with pain and discomfort because of the injection procedure as mentioned before.

Luger et al. [37] reported that the scattering through the skin/mucosa reduces the energy level of laser beams to 3–6 % of its original intensity. LED irradiation has a low absorption coefficient in hemoglobin and water, and consequently, a high penetration depth in the irradiated tissue [5]. As the main aim of the current study was to stimulate osteogenic and cementoblastic cells, which are located deep to the soft tissue (e.g., gingiva) in the PDL space, the LED device (618 nm) was selected for this study. Therefore, the authors assumed that the energy of LED irradiation was delivered to the PDL through the mucosa/gingiva and alveolar bone in the present study.

In the past, to use fewer animals and for ethical considerations, evaluation of the effects of different agents such as prostoglandins against TM was investigated by using a split-mouth study design [8]. One side served as the orthodontic control since it received only a vehicle injection, whereas the other side received the pharmacological agent injection. A split-mouth design was inconvenient for this investigation. The current experimental design was chosen instead of the split-mouth technique to avoid the carry-across effect. We thought that application of LPT on one side also could affect the other side. So, animals were divided into two different groups.

The wavelength delivered by LED is close to that used in LLL (600–1,000 nm) with similar energy. It has been shown that both the LED and the LLL radiation result in photobiomodulation effects LED radiation can be produced at a lower cost compared to the LLL and it can be safely applied to a larger area of the body surface [25].

The TM velocity is greatly dependent on the speed of bone remodeling. Saito and Shimizu [27] studied the effects of LLL on the expansion of midpalatal sutures in rats, comparing the bone regeneration obtained with and without laser treatment. Their results showed that the therapeutic effects of laser are dependent on the total dosage, the frequency, and the duration of the treatment. Their laser-irradiated group showed 20–40 % better results when compared to the control group.

LLL therapy has yielded important outcomes in orthodontics, with positive effects on bone remodeling. The findings of an experimental study [38] in which an orthodontic force was applied to rat incisors to cause experimental tooth movement demonstrated increased expression of fibronectin and collagen type I in the experimental group as a result of LLL irradiation. This result suggests that LLL irradiation facilitates the turnover of connective tissues during tooth movement. In that study, for the LLL source, a gallium aluminum–arsenide laser was used. The wave length was 808 nm and the output power was 96 mW. In this study, we used an OsseoPulse® LED

Table 3 The effect of LPT on the velocity of tooth movement

Groups	Mean	SD	SE	Min	Max	*p* value
LPT group	1.55	0.33	0.13	0.65	2.28	0.02
Control	1.06	0.35	0.11	0.06	1.84	

SD standard deviation, *SE* standard error, *Min* minimum, *Max* maximum

Table 4 The effect of LPT on the root resorption

Groups	Mean	SD	SE	Min	Max	p-value
LPT group	0.098	0.066	0.0709	0.014	0.22	<0.001
Control group	0.494	0.224	0.0208	0.17	0.80	

SD standard deviation, *SE* standard error; *Min* minimum, *Max* maximum

device (Biolux Research Ltd), an energy density of 20 mW/cm^2 per treatment of 20 min over a period of 10 consecutive days directly over the movement of the first molar teeth area for the low-energy LED photobiomodulation source.

In the literature, controversial results regarding the TM velocity as a result of phototherapy have been published. Seifi et al. [12] measured a significant decrease in tooth movement velocity in rabbits after 16 days of 9-day irradiation of 5 mW 850-nm laser (pulsed, contact, 3 min/day) and 10 mW 630-nm laser (continuous, contact, 5 min/day) compared to samples without laser application. In contrary to the latter, our results showed a significant increase in the amount of TM. LPT has been shown to stimulate the intracellular production of adenosine triphosphate (ATP), especially in cells that are wounded or ischemic [39]. The absorption of laser and LED photons by the respiratory chain enzyme cytochrome c oxidase is a response from increasing of ATP production [25, 33]. Cytochrome c oxidase allows a better cell function especially in cells with a sub-optimal metabolic condition [40].

Orthodontic TM starts the process of OIIRR and because of the continuous force applied, cementum repair should not occur [13]. Owman-Moll and Kurol [41] showed cementum repair as early as 2 weeks after cessation of orthodontic TM. This methodology allowed the study of maximum resorptive sites after the 3-week experimental period in the present study, without the possibility of a reparative phase. However, the present study demonstrated significant inhibitory effect of LPT on OIIRR.

The measurement of root resorption craters was adopted from Talic et al. [7] who used percentages instead of total resorption area in square micrometers. It was thought that the applied force could lead to more resorption of smaller teeth. Although the animals were nearly the same weight, individual differences may exist in the size of their teeth, similar to humans. Thus, the percentage of the resorption areas to the root was considered to be appropriate for the assessment of the root resorption instead of the total resorption area.

The Haversian system of the bone is characteristically lacking in rats except in some specific areas such as the periodontal membrane, which involve resorptive surfaces in association with fibrous reattachment [42]. Because of their diminished size and minimal need to compartmentalize bone [43], there is a need to work with advanced animal models as dogs and monkeys or human in literature.

Regarding the penetration effect, no negative side effects could be found in any animal with phototherapy. We thought that this method induce a regional acceleration of metabolic activity with no deep effect. Moreover, the effects of LED irradiation on other osteoclast functions such as stem cell division, chemotaxis, recognition, or attachment should be also studied.

Although other studies such as the effects of different irradiation dosages, the prolonged use of irradiation, or both, on tooth movement and root resorption are still required for clinical use consideration, the introduction of LPT at an early stage of tooth movement in orthodontic treatment seems feasible, and may be of great therapeutic benefit to abbreviate the treatment period.

Conclusion

The present findings suggest that LPT method has the potential of accelerating TM and has inhibitory effects on OIIRR.

References

1. Wise GE, King GJ (2008) Mechanisms of tooth eruption and orthodontic tooth movement. J Dent Res 87:414–434
2. Storey E (1973) The nature of tooth movement. Am J Orthod 63: 292–314
3. Sandy JR, Farndale RW, Meikle MC (1993) Recent advances in understanding mechanically induced bone remodeling and their relevance to orthodontic theory and practice. Am J Orthod Dentofacial Orthop 103:212–222
4. Rygh P (1977) Orthodontic root resorption studied by electron microscopy. Angle Orthod 47:1–16
5. Baysal A, Uysal T, Ozdamar S, Kurt B, Kurt G, Gunhan O (2010) Comparisons of the effects of systemic administration of L-thyroxine and doxycycline on orthodontically induced root resorption in rats. Eur J Orthod 32:496–504
6. Boekenoogen DI, Sinha PK, Nanda RS, Ghosh J, Currier GF, Howes RI (1996) The effects of exogenous prostaglandin E2 on root resorption in rats. Am J Orthod Dentofacial Orthop 109:277–2867
7. Talic NF, Evans C, Zaki AM (2006) Inhibition of orthodontically induced root resorption with echistatin, an RGD-containing peptide. Am J Orthod Dentofacial Orthop 129:252–260
8. Leiker BJ, Nanda RS, Currier GF, Howes RI, Sinha PK (1995) The effects of exogenous prostaglandins on orthodontic tooth movement in rats. Am J Orthod Dentofacial Orthop 108:380–388
9. Foo M, Jones A, Darendeliler MA (2007) Physical properties of root cementum: part 9. Effect of systemic fluoride intake on root resorption in rats. Am J Orthod Dentofacial Orthop 131:34–43
10. Spadaro JA (1997) Mechanical and electrical interactions in bone remodeling. Bioelectromagnetics 18:193–202
11. Kobayashi Y, Takagi H, Sakai H, Hashimoto F, Mataki S, Kobayashi K, Kato Y (1998) Effects of local administration of osteocalcin on experimental tooth movement. Angle Orthod 68:259–266
12. Seifi M, Shafeei HA, Daneshdoost S, Mir M (2007) Effects of two types of low-level laser wave lengths (850 and 630 nm) on the orthodontic tooth movements in rabbits. Lasers Med Sci 22:261–264
13. Drevensek M, Sprogar S, Boras I, Drevensek G (2006) Effects of endothelin antagonist tezosentan on orthodontic tooth movement in rats. Am J Orthod Dentofacial Orthop 129:555–558
14. Kale S, Kocadereli I, Atilla P, Asan E (2004) Comparison of the effects of 1,25 dihydroxycholecalciferol and prostaglandin E2 on orthodontic tooth movement. Am J Orthod Dentofacial Orthop 125: 607–614
15. Soma S, Matsumoto S, Higuchi Y, Takano-Yamamoto T, Yamashita K, Kurisu K, Iwamoto M (2000) Local and chronic application of PTH accelerates tooth movement in rats. J Dent Res 79:1717–1724

16. Lee WC (1990) Experimental study of the effect of prostaglandin administration on tooth movement—with particular emphasis on the relationship to the method of PGE1 administration. Am J Orthod Dentofacial Orthop 98:231–241
17. Baran S, Hamamci O, Akalar M (1996) An investigation of the effects of the local use of 1:25 dihydroxycholecalciferol (1:25 D) on tension sites during experimental tooth movement in rats. J Marmara Univ Dent Fac 2:557–561
18. Shirazi M, Dehpour AR, Jafari F (1999) The effect of thyroid hormone on orthodontic tooth movement in rats. J Clin Pediatr Dent 23: 259–264
19. Haruyama N, Igarashi K, Saeki S, Otsuka-Isoya M, Shinoda H, Mitani H (2002) Estrous-cycle-dependent variation in orthodontic tooth movement. J Dent Res 81:406–410
20. Almeida-Lopes L, Rigau J, Zangaro RA, Guidugli-Neto J, Jaeger MM (2001) Comparison of the low level laser therapy effects on cultured human gingival fibroblasts proliferation using different irradiance and same fluence. Lasers Surg Med 29:179–184
21. Schultz RJ, Krishnamurthy S, Thelmo W, Rodriguez JE, Harvey G (1985) Effects of varying intensities of laser energy on articular cartilage: a preliminary study. Lasers Surg Med 5:577–588
22. Majaron B, Srinivas SM, Huang H, Nelson JS (2000) Deep coagulation of dermal collagen with repetitive Er:YAG laser irradiation. Lasers Surg Med 26:215–222
23. Lowe AS, Walker MD, O'Byrne M, Baxter GD, Hirst DG (1998) Effect of low intensity monochromatic light therapy (890 nm) on a radiation-impaired, wound-healing model in murine skin. Lasers Surg Med 23:291–298
24. Hawkins D, Abrahamse H (2006) Effect of multiple exposures of low-level laser therapy on the cellular responses of wounded human skin fibroblasts. Photomed Laser Surg 24:705–714
25. Eells JT, Wong-Riley MT, VerHoeve J, Henry M, Buchman EV et al (2004) Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy. Mitochondrion 4:559–567
26. Ekizer A, Uysal T, Guray E, Yuksel Y (2012) Light-emitting diode photobiomodulation: effect on bone formation in orthopedically expanded suture in rats-early bone changes. Lasers Med Sci. doi:10.1007/s10103-012-1214-0
27. Saito S, Shimizu N (1997) Stimulatory effects of low-power laser irradiation on bone regeneration in midpalatal suture during expansion in the rat. Am J Orthod Dentofacial Orthop 111:525–532
28. Anders JJ, Geuna S, Rochkind S (2004) Phototherapy promotes regeneration and functional recovery of injured peripheral nerve. Neurol Res 26:233–239
29. Kawasaki K, Shimizu N (2000) Effects of low-energy laser irradiation on bone remodeling during experimental tooth movement in rats. Lasers Surg Med 26:282–291
30. Lim HM, Lew KK, Tay DK (1995) A clinical investigation of the efficacy of low level laser therapy in reducing orthodontic postadjustment pain. Am J Orthod Dentofacial Orthop 108:614–622
31. Hubler R, Blando E, Gaiao L, Kreisner PE, Post LK, Xavier CB, de Oliveira MG (2010) Effects of low-level laser therapy on bone formed after distraction osteogenesis. Lasers Med Sci 25:213–219
32. Uysal T, Ekizer A, Akcay H, Etoz O, Guray E (2012) Resonance frequency analysis of orthodontic miniscrews subjected to light-emitting diode photobiomodulation therapy. Eur J Orthod 34:44–51
33. Karu TI, Pyatibrat LV, Kolyakov SF, Afanasyeva NI (2005) Absorption measurements of a cell monolayer relevant to phototherapy: reduction of cytochrome c oxidase under near IR radiation. J Photochem Photobiol B 81:98–106
34. Houston WJ (1964) A new design of rat mouth prop. J Dent Res 43: 458
35. Brudvik P, Rygh P (1993) The initial phase of orthodontic root resorption incident to local compression of the periodontal ligament. Eur J Orthod 15:249–263
36. Hadjiargyrou M, McLeod K, Ryaby JP, Rubin C (1998) Enhancement of fracture healing by low intensity ultrasound. Clin Orthop Relat Res S216–229
37. Luger EJ, Rochkind S, Wollman Y, Kogan G, Dekel S (1998) Effect of low-power laser irradiation on the mechanical properties of bone fracture healing in rats. Lasers Surg Med 22:97–102
38. Kim YD, Kim SS, Kim SJ, Kwon DW, Jeon ES, Son WS (2010) Low-level laser irradiation facilitates fibronectin and collagen type I turnover during tooth movement in rats. Lasers Med Sci 25:25–31
39. Liu Q, Liu X, Liu B, Hu K, Zhou X, Ding Y (2012) The effect of low-intensity pulsed ultrasound on the osseointegration of titanium dental implants. Br J Oral Maxillofac Surg 50:244–250
40. Karu TI, Pyatibrat LV, Afanasyeva NI (2005) Cellular effects of low power laser therapy can be mediated by nitric oxide. Lasers Surg Med 36:307–314
41. Owman-Moll P, Kurol J (1998) The early reparative process of orthodontically induced root resorption in adolescents—location and type of tissue. Eur J Orthod 20:727–732
42. Kraw AG, Enlow DH (1967) Continuous attachment of the periodontal membrane. Am J Anat 120:133–147
43. Milne TJ, Ichim I, Patel B, McNaughton A, Meikle MC (2009) Induction of osteopenia during experimental tooth movement in the rat: alveolar bone remodelling and the mechanostat theory. Eur J Orthod 31:221–231