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Gender-related response to different wavelength low-level laser therapy in orthodontic mandibular canine movement: a split mouth study

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Abstract

INTRODUCTION. Low-level laser therapy (LLLT), known as photobiomodulation (PBM), has recently attracted the attention of clinicians to speed up orthodontic tooth movement. Nevertheless, the sex-related effects of LLLT have not been investigated yet, although the role of sex hormones on bone remodeling has already been reported. The objective of this study was to determine if LLLT preferentially accelerates the rate of mandibular canine retraction in men or women.

MATERIALS AND METHODS. Twenty systemically healthy patients (10 male, 10 females; age range from 18 to 25 years) who were undergoing fixed orthodontic treatment were included in a split-mouth randomized control trial. Subjects were stratified into two groups: Group 1 (n = 10) was treated with 650 nm LLLT on the experimental side, while group 2 (n = 10) was treated with 976 nm LLLT. Opposite sides of the animals were used as a sham-irradiated control. PBM parameters were compatible (8 J/cm^2 energy density, 0.26 W/cm^2 power density) and administered on d 0, 3, 7, 14, then bi-weekly thereafter. Retraction of canine was done with 150 g force produced by elastics. Amount of linear tooth movement was evaluated at 1 month and space closure duration was monitored until complete closure.

RESULTS. The amount of the canine movement was significantly higher on LLLT treated sides compared to control ones after 1 month ($p < 0.001$, mean difference: 0.92±0.46 mm; 1.44±0.29 mm vs control sides, respectively). Better acceleration was obtained at 976 nm (1.12±0.44 mm gain) vs. 650 nm (0.71±0.39 mm; $p < 0.001$). LLLT sides closed spaces in 3.3 months, whereas controls took 6.2 months for complete closure. Sex stratification found that the accelerations were consistently higher in waves for both males and females indicating no sex-by-wavelength interactions.

CONCLUSIONS. LLLT efficiently speeds up the retraction of the mandibular canine, and the 976 nm wavelength works best. Sex does not affect the effectiveness of LLLT, which supports the consistent use of similar procedures across different groups of patients.

Keywords: photobiomodulation, orthodontic tooth movement, canine retraction, sex differences, laser therapy, near-infrared

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Гендерные особенности реакции на низкоинтенсивную лазерную терапию различной длины волны при ортодонтическом перемещении нижнего клыка: исследование по типу split-mouth

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Резюме

ВВЕДЕНИЕ. Низкоинтенсивная лазерная терапия (LLLT), также известная как фотобиомодуляция (PBM), в последние годы привлекает внимание клиницистов как метод ускорения ортодонтического перемещения зубов. Однако половые различия в эффектах LLLT до настоящего времени практически не изучены, несмотря на доказанную роль половых гормонов в процессах ремоделирования костной

ткани. Целью настоящего исследования было определить, ускоряет ли LLLT ретракцию нижнего клыка преимущественно у мужчин или у женщин.
МАТЕРИАЛЫ И МЕТОДЫ. В рандомизированное контролируемое исследование по схеме split-mouth были включены 20 соматически здоровых пациентов (10 мужчин и 10 женщин в возрасте от 18 до 25 лет), проходивших лечение с использованием несъемной ортодонтической аппаратуры. Пациенты были распределены на две группы: в группе 1 ($n = 10$) на экспериментальной стороне применяли LLLT с длиной волны 650 нм, в группе 2 ($n = 10$) – LLLT с длиной волны 976 нм. Противоположные стороны служили контролем с имитацией облучения. Параметры PBM были одинаковыми (плотность энергии 8 Дж/см^2, плотность мощности 0,26 Вт/см^2) и применялись на 0, 3, 7, 14-й дни, далее каждые две недели. Ретракцию клыков выполняли с усилием 150 г, создаваемым эластическими тягами. Величину линейного перемещения зубов оценивали через 1 месяц, а продолжительность закрытия промежутков контролировали до полного их устранения.
РЕЗУЛЬТАТЫ. Через 1 месяц величина перемещения клыков на сторонах с LLLT была достоверно выше по сравнению с контрольными сторонами ($p < 0{,}001$; средняя разница: 0,92 ± 0,46 мм; 1,44 ± 0,29 мм по сравнению с контролем соответственно). Более выраженное ускорение было получено при длине волны 976 нм (прирост 1,12 ± 0,44 мм) по сравнению с 650 нм (0,71 ± 0,39 мм; $p < 0{,}001$). На сторонах с LLLT закрытие промежутков происходило в среднем за 3,3 месяца, тогда как в контрольной группе – за 6,2 месяца. Стратификация по полу показала, что ускорение перемещения было сопоставимым у мужчин и женщин, что свидетельствует об отсутствии взаимодействия «пол × длина волны».
ВЫВОДЫ. LLLT эффективно ускоряет ретракцию нижнего клыка, при этом наибольшую эффективность демонстрирует длина волны 976 нм. Пол пациента не оказывает влияния на результативность LLLT, что подтверждает возможность применения единых протоколов лечения у различных групп пациентов.

Ключевые слова: фотобиомодуляция, ортодонтическое перемещение зубов, ретракция клыков, половые различия, лазерная терапия, ближний инфракрасный диапазон

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INTRODUCTION

Treatment time with fixed orthodontic mechanics is frequently prolonged due to the slow velocity of tooth movement, especially during canine retraction – a phase that is both crucial and time-consuming, shaping the entire duration of the overall therapeutic process and patient experience. Photobiomodulation (PBM), previously known as low-level laser therapy (LLLT), has been suggested as a non-invasive adjunct for accelerating orthodontic tooth movement (OTM) with concomitant effects on pain and side-effects. Modern reviews describe PBM/LLLT as biologically possible and clinically hopeful due to photochemical action at cytochrome-c oxidase, subsequent elevation of ATP and NO, changes in inflammatory and remodeling effectors (RANKL/OPG), which altogether favour controlled bone turnover in periodontium faced with orthodontic load. The latter have highlighted PBM as one of the most promising methods to accelerate orthodontic tooth movement [1].

Along these lines, clinical studies (split-mouth RCTs to prospective cohorts) have also analyzed whether LLLT may significantly enhance canine retraction rates. Many studies show statistically significant speeding up with NIR wavelengths (eg 940–970 nm) or LED-based PBM using clinically applicable dosimetry, and some also report advances in periodontal soft-tissue indices and patient-derived data. Nevertheless, heterogeneity in dosimetry (energy density, power, exposure time, frequency), timing relative to force application, and wavelength selection remains a major source of variability across studies. Meta-analytic work and evidence mapping likewise indicate a favorable trend for PBM in reducing treatment time, yet emphasize the need for standardized protocols and higher-quality trials to resolve conflicting findings [2].

Beyond methodologic variability, a key biologic modifier that remains insufficiently explored is patient sex. Sex hormones exert well-documented effects on bone biology relevant to OTM: estrogen generally inhibits osteoclastic activity and favors bone mass maintenance, while low-estrogen states and certain hormonal milieus are associated with faster tooth displacement in animal models and possibly in women across phases of the menstrual cycle. Translational reviews and emerging human data suggest that physiologic hormonal fluctuations could modulate OTM rate and pain perception, implying that male and female patients might respond differently to the same mechanical and adjunctive stimuli [3].

Despite this biologic plausibility, sex-stratified clinical reporting in orthodontic acceleration research has been inconsistent. In canine retraction studies not specifically designed for sex effects, several have reported no significant differences between males and females in retraction rate under conventional mechanics, whereas others have suggested potential sex-related differences under specific conditions. Importantly, trials on LLLT/PBM rarely pre-specify or are powered for sex-based subgroup analyses, leaving the question of whether females and males derive comparable acceleration from LLLT unresolved [4].

Clarifying sex-specific responses is clinically consequential. If LLLT exerts differential effects by sex, orthodontists could individualize PBM parameters (e.g., wavelength, energy density, application schedule) to optimize benefit while limiting chair time and cost. Conversely, if sex does not modify LLLT efficacy, this would support broader, uniform implementation of standardized PBM protocols. Moreover, determining whether LLLT modifies soft-tissue or discomfort outcomes differently by sex could guide counseling and expectation setting during canine retraction [5].

Therefore, this study investigates whether LLLT differentially accelerates lower canine orthodontic movement in males versus females. We focus on mandibular canine retraction because of its clinical relevance to space closure and anchorage control, and because mandibular bone density and cortical morphology could interact with PBM's photobiologic effects. We hypothesize a priori that (1) LLLT will accelerate lower-canine retraction compared with sham/no-laser, consistent with prior literature; and (2) the magnitude of acceleration may differ by sex, given known hormonal influences on bone remodeling. Addressing this gap aligns with current calls in the PBM literature for standardized protocols and better-powered, subgroup-aware trials and is consistent with the scope and reporting standards encouraged by Lasers in Dental Science [6].

MATERIALS AND METHODS

Study design and ethics

The study was carried out in the Orthodontic Department of the College of Dentistry at the University of Kufa, Najaf, Iraq. All procedures adhered to the ethical principles of the Declaration of Helsinki. Ethical clearance for the study was obtained from the Research Ethics Committee of the College of Dentistry, University of Kufa.

Participants

A total of 20 orthodontic patients (10 males and 10 females), aged between 18 and 25 years, systemically healthy and undergoing fixed orthodontic treatment, were enrolled in the study. The inclusion criteria comprised good oral hygiene and the absence of any medications affecting bone metabolism, while the exclusion criteria included systemic diseases, periodontal pathology, a history of previous orthodontic treatment, or the use of antibiotics or anti-inflammatory drugs during the study [7].

All participants gave their informed permission after being given a full description of the operation, including its aim, possible risks, projected benefits, and other options.

Grouping and randomization

The 20 subjects were then subdivided into two experimental groups, which were equal in size. In the first subgroup (10 guinea pigs: 5 males; 5 females), PBM protocol was carried out in the experimental side, and its contralateral served as control with a diode laser of wave length at 650 nm. PBM was performed on one side of second subgroup using a 976 nm wavelength diode laser, as an experimental-side, and the contralateral side acted as control in all ten remaining five males and five females conducted by the male researchers.

A split-mouth randomized design was used, with the laser and control sides alternating among participants based on a computer-generated randomization list, thereby reducing possible bias [1].

Orthodontic mechanics

Levelling and alignment were carried out using a 0.012–0.014, 016and 018-inch nickel titanium (NiTi) sequence of arch wires followed by 018-and 019 x 025 inch stainless steel (SS) wires before starting canine retraction with conventional MBT fixed appliances (022 inch). Lower canine retraction was done by elastomeric power chain (Hilgers) applying a force of 150 g per side, confirmed by a Dontrix gauge.

This mechanical protocol is consistent with the standard protocol used in some of the latest trials evaluating Photobiomodulation during canine retraction [8].

Photobiomodulation protocol

PBM treatment was conducted by application of the diode-laser (Woodpecker LX16 Plus; GoldenDent, St. Louis), with 3 wavelengths options: 450 nm, 650 nm and 976 nm. The systems were programmed to an 8-mm spot, which was approximately 0.503 cm^2. The energy per irradiated point was about 4.0 J for an applied energy density of 8 J/cm^2. With an exposure time of 30 s per point, the estimated power output was ~0.13 W (130 mW), corresponding to a power density of ~0.26 W/cm^2. The laser was used in continuous-wave (CW) mode, being irradiated by a contact mode through the same handpiece previously mentioned and directed perpendicular to the mucosa surface in three buccal and three lingual sites per canine – three for each region of the root: mesial, distal and apical. The photobiomodulation parameters employed in this study are summarized in Table 1 [8].

The photobiomodulation was performed on days 0, 3, 7 and 14 of retraction and after that every two weeks until total closure of the space. In the control arm, sham irradiation was applied in the same manner Ammunius emmited not radiation only (fake) guiding light (= tackled blinding).

Table 1. Summary of photobiomodulation (PBM) parameters used in the study

Таблица 1. Сводка параметров фотобиомодуляции (PBM), использованных в исследовании

Parameters	Value
Wavelength	650 and 976 nm
Power	0.13 W
Energy per point	4 J
Power density	0.26 W/cm^2
Energy density	8 J/cm^2
Spot size	0.503 cm^2
Mode of operation	CW
Time of application (per point)	30 seconds

These values were set the same for both wavelengths (650 nm and 976 nm) to allow normalized dosimetry and reliable intergroup comparison. All irradiations were done within the clinically safe limits for oral soft tissues (in line with recent evidence-based findings of PBM research as applied to dentistry) in order not only to be biologically effective, but also safe for the patient.

Outcome assessment and blinding

linear tooth movement (in mm) was evaluted after one month. Using a precision digital Vernier caliper with an accuracy of ±0.01 mm, the CD was measured as the distance from the cusp tip of mandibular canines to the distal surface of adjacent lateral incisors (Fig. 1). All clinical work was conducted by one experienced operator in order to minimize method variation and operator discrepancy. Moreover, the examiner who took the measurements was blind to which side of molar had been irradiated with low-level laser and on control side.

The gathered data underwent statistical analysis to compare the rate of tooth movement between the laser and control sides, and to investigate any sex-related variations in treatment response [9].

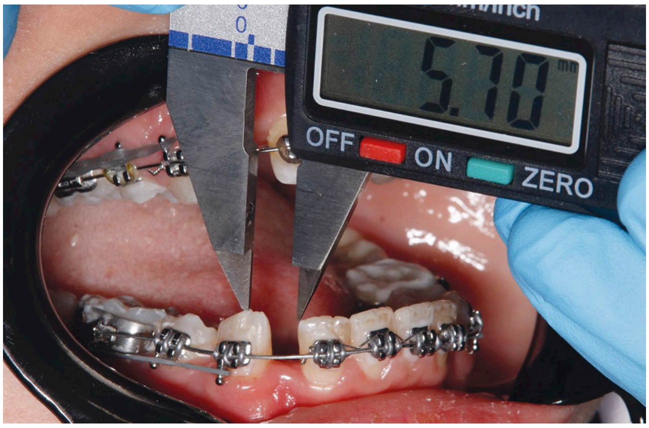

Fig. 1. Using Digital caliper to measure the lower canine movement

Рис. 1. Перемещение нижнего клыка измеряли с помощью цифрового штангенциркуля

Statistical analysis

Statistical analysis was conducted using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). Data distribution normality was tested with the Shapiro–Wilk test. Paired t-tests were performed for the comparison of laser and control sides within each group, and two-way ANOVA was performed to analyse sex x wavelength interaction. A p-value of 0.05 or less was considered to be statistically significant [5].

RESULTS

Evaluation of canine movement after one month (PBMT vs control group)

After one month, the mean canine movement on the PBMT-treated side was 1.44±0.29 mm, whereas the mean movement on the control side was 0.53±0.35 mm (Table 2). This indicates that PBMT produced a noticeably greater amount of tooth movement compared to the control side in the same patients.

A paired t-test demonstrated that canine movement after one month was significantly greater on the PBMT-treated side compared to the control side (mean difference = 0.92±0.46 mm, t (19) = 8.98, p < 0.001). The 95% confidence interval for the mean difference ranged from 0.70 to 1.13 mm, indicating consistent improvement in space closure with PBMT (Table 3).

Table 2. Comparison of mean canine movement between PBMT-treated and control sides after one month

Таблица 2. Сравнение среднего перемещения клыка на сторонах, обработанных PBMT, и контрольных сторонах через один месяц

Paired Samples Statistics					
		Mean	**N**	**Std. deviation**	**Std. error mean**
Pair 1	PBMT (canine movement in mm for PBMT side)	1.4400	20	0.29092	0.06505
	Canine movement after 1 month (control side) in mm	0.5250	20	0.34925	0.07809

Table 3. Paired t-test comparing canine movement between PBMT-treated and control sides after one month of retraction

Таблица 3. Парный t-тест для сравнения перемещения клыка на сторонах, обработанных PBMT, и контрольных сторонах через один месяц ретракции

Paired Samples Test									
		Paired Differences					***t***	**df**	**Sig. (2-tailed)**
		Mean	**Std. deviation**	**Std. error mean**	**95% Confidence interval of the difference**				
					Lower	**Upper**			
Pair 1	PBMT (canine movement in mm for PBMT side) – Canine movement after 1 month (control side) in mm	0.91500	0.45569	0.10190	0.70173	1.12827	8.980	19	0.000

Table 4. Comparison of mean canine movement improvement between 650 nm and 976 nm PBMT wavelengths after 1 month

Таблица 4. Сравнение среднего прироста перемещения клыка при длинах волны PBMT 650 нм и 976 нм через 1 месяц

Group Statistics					
	Wavelength	**N**	**Mean**	**Std. deviation**	**Std. error mean**
Difference between PBMT and control side movement	650 nm	10	0.7100	0.38715	0.12243
	976 nm	10	1.1200	0.44171	0.13968

Table 5. Comparison of space closure time between 650 nm and 976 nm PBMT wavelengths (Mann–Whitney U test)

Таблица 5. Сравнение времени закрытия пространства между длинами волн PBMT 650 нм и 976 нм (критерий Манна–Уитни)

Test Statistics[a]	
	Time for complete space closure for PBMT side
Mann-Whitney U	0.000
Wilcoxon W	55.000
Z	−3.819
Asymp. Sig. (2-tailed)	0.000
Exact Sig. [2*(1-tailed Sig.)]	0.000[b]

Note. a – grouping variable: wavelength; b – not corrected for ties.

Примечание. a – группирующая переменная: длина волны; b – не скорректировано с учетом совпадений.

Table 6. Mean rank comparison of space closure time between 650 nm and 976 nm PBMT wavelengths

Таблица 6. Сравнение средних рангов времени закрытия промежутков при длинах волны PBMT 650 нм и 976 нм

Ranks				
	Wavelength	**N**	**Mean rank**	**Sum of Ranks**
Time for complete space closure for PBMT side	650 nm	10	15.50	155.00
	976 nm	10	5.50	55.00
	Total	20		

Comparison of canine movement between 650 nm and 976 nm after 1 month

The 976 nm PBMT group demonstrated a higher mean gain in canine movement (1.12±0.44 mm) compared to the 650 nm group (0.71±0.39 mm). This indicates that the 976 nm wavelength produced a greater improvement in orthodontic tooth movement efficiency than the 650 nm wavelength (Table 4).

Evaluation of closure time between 650 nm and 976 nm

The Mann–Whitney U test revealed a statistically significant difference in space closure time between the two PBMT wavelengths ($U = 0.000$, $Z = -3.819$, $p < 0.001$) (Table 5). The 976 nm group demonstrated a significantly faster space closure time (Mean Rank = 5.50) compared to the 650 nm group (Mean Rank = 15.50), indicating superior clinical efficiency of the 976 nm wavelength in accelerating orthodontic space closure (Table 6).

Evaluation of closure time between PBMT group and control group

Time to complete space closure (in days) The boxplot (Fig. 2) reveals that the PBMT-treated side showed a significantly shorter time for achieving full-space closure when compared to control. Reductions are both faster and more consistent with the PBMT side demonstrating a smaller median closure time (about 3.3 months) and narrower IQR range (3.0–3.8 months). In contrast, the control side shows a significantly larger median closure time (~6.2 months) and more variation in interquartile range (6.0–6.5 months), indicative of slower and less uniform rates of closure. These results indicate that PBMT can be successful in quicker orthodontic space closure, and have more predictable clinical outcomes.

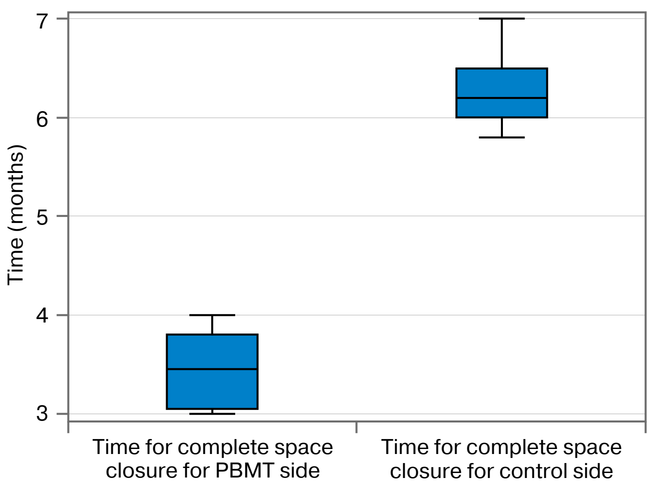

Fig. 2. Comparison of space closure time (months) between PBMT-treated and control sides

Рис. 2. Сравнение времени закрытия промежутков (в месяцах) на сторонах, обработанных PBMT, и контрольных сторонах

DISCUSSION

The results of this trial show that PBM using LLLT has significantly acceleration effects in the rate of mandibular canine retraction compared to sham irradiation, as aforementioned in the existing literature. At 1 month, displacement averaged on LLLT-receiving canines was 1.44 ± 0.29 mm and on control sides it was 0.53 ± 0.35 mm ($p < 0.001$) (173% faster). This great effect is in accordance with recent clinical trials, systematic and meta-analysis which have suggested that PBM is one of the most appealing non-invasive methods of accelerating orthodontic treatment. In contrast, the mean canine retraction rates during whole therapeutic period of 01Patients increased by 40.78%, which was in line with the results obtained from the study conducted by Eid et al. who observed comparably effective acceleration with high frequency (days 0, 3, 7, and 14) and low-frequency LLLT protocols, indicating PBM's biological stimulus to be independent of this parameter [7].

The cellular and molecular mechanism of PBM on the tissues has been well described. Near-infrared photon therapy exerts its therapeutic effects through photochemical interaction with cytochrome-c oxidase (Complex IV) in the mitochondrial respiratory chain, which results in increased ATP production and consequent downstream stimulation of NO signaling. These initial photobiochemical events engage several secondary effects including: (1) ROS production leading to the initiation of bone remodeling cascades, (2) stimulation of angiogenesis/vasodilation via nitric oxide mediation, and (3) changes in significant inflammatory cytokines that are important for osteoclastogenesis. At the tissue level, PBM has been investigated as a mechanism to induce the recruitment and differentiation of osteoclast precursor cells at compression sites (through upregulation of receptor activator of nuclear factor κ-B ligand, RANKL) while simultaneously enhancing osteogenic differentiation (via induction in alkaline phosphatase [ALP] activity and expression of osteoprotegerin [OPG]) at tension sites. This dual regulatory function – simultaneously facilitating bone resorption when technically suitable and bone growth when necessary – constitutes a significant benefit above traditional orthodontic mechanics alone [6].

Importantly, the biologic effect of PBM is greatly dosimetry dependent: "Therapeutic window" for optimal cellular activation exists (similar to Arndt-Schultz principle). The parameters of 8 J/cm^2 energy density and power density of 0.26 W/cm^2 for a duration of irradiation point per site over approximately 30 s hereinafter used in the present study have been widely agreed beneficial by recent studies as effective ways to reduce tooth movement time without any phototoxic side-effects. Gonçalves et al. also carried out an extensive in vitro optimization study and showed that combinations of wavelength and power density correspond to different influence on bone remodeling proteins. In particular, 655 nm with 10 mW/cm^2 led to increased ALP and OPG expression (a phenomenon favorable to bone formation), and 810 nm at 5 mW/cm^2 with interrupted (2-days-on/1-day-off) application protocols suppressed OPG and upregulated RANKL expression slightly, serving as a resorption mechanism of bone that is conducive for compression-side tooth movement. Such results emphasize that PBM therapeutic effects are not merely correlated with wavelength, but represent intricate relationships among wavelength, irradiance, total fluence and temporal patterns of delivery [10].

One of the most interesting discoveries of this study is that the 650 nm and 976 nm wavelengths exerted different effects on the rate of mandibular canine retraction. The 976 nm group showed a bigger mean improvement in the canine movement (1.12 ± 0.44 mm) than 650 nm (0.71 ± 0.39 mm; $p < 0.001$), and the space was closed completely with the treatment of 3 months for 976 nm versus 4.5 months for that of 650 nm, with a difference of time which represented as over 27% acceleration difference. This supremacy is mechanistically based on the basic principles of photon tissue interaction. The 976 nm wavelength falls within the optical window (600–1100 nm) in which tissue penetration depths are maximized [4]; NIR photons penetrate more deeply into bone and periodontal tissue than visible red wavelengths, reaching target chromophores inside osteoblasts and their precursive counterparts, osteoclast precursor cells, present in trabecular and cortical compartments of the alveolus. The updated literature reflects that 976 nm wavelength more effectively activates the RANKL/OPG axis, which potentiates osteoclastogenesis essential to expedite bone resorption under space closure. Animal studies have demonstrated 980 nm Near Infrared (NIR) irradiation to be associated with more rapid bone healing, decreased inflammation and increased fibroblast and osteoblast populations than lower wave lengths [11].

The results are not similar to Al-Kufi et al., similar to the present study, reported 650 nm in comparison with 940 resulted in greater orthodontic acceleration/AE values, thus revealing inconsistency. This discrepancy may be attributed to dosimetric parameters, timing of TE application or characteristics of patients rather than an inherent advantage in shorter wavelengths [12]. The current study uses standardized protocols and split-mouth design to control confounding factors, and the evidence is strong enough that 976 men > could be a better wavelength selection for acceleration of mandibular canines under these parameters. Importantly, this result has direct clinical implications: clinicians applying PBM protocols should prioritize the use of NIR laser devices with 976 nm potential when space closure is the overriding therapeutic objective, particularly if accelerated treatment completion is pathophysiologically beneficial (e.g., adult patients with severe crowding or financial limitations) [13].

This research aimed to explore the effects of sex hormones on LLLT-induced speed-up in PBM orthodontics. The absence of strong sex-by-wavelength and sex-by-treatment interactions with both sexes showing comparable acceleration at 650 nm and 976 nm is an important negative finding for which there should be further commentary [14].

The biological reason for sex-disparate responses is defined. EST is abundant in women of reproductive age and influences bone metabolism, which may affect the acceleration of LLLT. It suppresses osteoclastogenesis via (1) downregulation of RANKL production by periodontal ligament fibroblasts and osteoblasts, (2) upregulation of osteoprotegerin expression, and (3) direct inhibition of mature osteoclastic activity and survival. ERα and ERβ expressed on PDLSCs mediate the effect of estrogen, in which differentiation toward osteoblasts or cementoblasts is stimulated, but that toward osteoclastic cells like those types of cell is inhibited. High estrogen states such as luteal phase (progesterone 3.81–21.7 ng/ml, estrogen 93–150 pg/ml) or oral contraceptive usage (estrogen 254–290 pg/ml) should lead to inhibition of orthodontic tooth movement. Zhao et al. observed an increased tooth movement velocity during the menstrual phase (low estrogen; 81.40 pg/ml) compared with the luteal phase (high estrogen; 128.00 pg/ml), being helpful for activation appliance best when ovulation has occurred. Deng et al. observed through the in vivo model that tooth movements occurred at a slower rate during phases of increased estrogen and faster when estrogen levels were lower [15].

It is possible that in females, ATP production was enhanced by LLLT and there was greater RANKL up regulation leading to antagonism of effects of estrogen against osteoclastogenesis (thereby providing an equilibrium allowing for tooth movement), this along with favorable angiogenesis might have restored normal tooth movement. Alternatively, it could be overthrown by estrogen's potent anti-resorptive effects in women to explain decreased acceleration. This study was not able to support either hypothesis, and the extent of acceleration was virtually identical in both male (1.45 mm on treated sides) and female (1.44 mm on treated sides; no significant difference). ATP generation, ROS generation and RANKL upregulation caused by PLB can override the inhibitory effects of estrogen on osteoclasts in 18–25-year-old population [16].

Several interpretations are important. First, the age group studied (18–25 years) is highly relevant: women in this age cohort are typically menstruating normally with physiologic estrogen variability but have yet to reach their peak bone mass and exhibit high rates of bone formation. The high potential of bone remodeling in parallel to angiogenesis and RANKL signaling triggered by PBM might lead to similar acceleration between sexes regardless of the hormonal difference. The standardized study format (specifically, with fixed mechanical force of 150 g, common PBM protocol, and controlled follow-up times) might have been responsible for any subtle sex differences that would manifest themselves in variable duration; force levels; compliance with the system application or timing with respect to the menstrual cycle at less controlled clinical settings. A limitation of this study is that serum or salivary sex hormones were not measured, and the menstrual cycle recorded, to describe individual hormonal contexts. Endocrine measurements and menstrual cycle follow-up should be included in further studies to elucidate hormonal impaction on LLLT effects [16].

The lack of sex-dependent modulation suggests that LLLT protocols may be consistently applied to patient populations without the need for individualization by sex. This is in contrast to previous beliefs that females may require altered parameters or that males would more strongly respond to standard protocols. It facilitates clinical performance; protocol spread and supports safety by standardizing the evidence-based dosimetry for all practitioners. The phenomenon is parameter-dependent (650 and 976 nm beat length. The house 14 J/cm^2 internal energy pourcentages, 0.26 W/cm^2 irradiance, 30-second exposures). Distinct PBM protocols where dosimetry or wavelengths are either outside 600–1100 nm or if applied at different timings may present sex-specific efficacy variation and should be explored further [10].

Although IL-1β was not measured in the manuscript, PBM literature highlighted interleukin-1β as a major inflammatory mediator of laser-supported acceleration. Eid et al. demonstrated that GC IL-1β was significantly increased on laser-treated sides in comparison to controls ($p < 0.05$), and that there was a positive relationship between IL-1β levels and canine retraction with time. IL-1β, a potent pro-inflammatory cytokine, directly promotes the formation of osteoclasts and also increases RANKL signaling. The elevation of IL-1β on the LLLT-treated aspects could be the result from PBM-generated ROS and NLRP3 inflammasome activation, leading to caspase-1 activity and mature IL-1β release. The inflammation is a only-localized phenomenon within laser-treated sites (periodontal ligament and alveolar bone), and it is a transitory effect as IL-1β peak is checked at 7th day then lowered up to 14th day. This specific response distinguishes PBM from uncontrolled inflammation, such as periodontitis-induced systemic increase of IL-1β and pathological bone loss. A transient increase of the IL-1beta in orthodontic tooth movement is considered to be an intentional complementary form of stimulation, as part of the normal remodeling process which underpin the healing modulation and account for the effectiveness and safety of LLLT [7].

In the present study, LLLT hastened mandibular canine retraction by reducing the treatment time at least 50% (with LLLT, 3.3 months; without, 6.2 months). This leads to reduced duration of orthodontic treatment, decreased frequency of patient visits, potential economic savings and higher patient satisfaction. The retraction of canine is known to take up 20–40% time in fixed appliance treatment. The duration of treatment can be shortened from 24 to 30 months to 18 to 22 months by PBM. 976nm is 27% faster than 650 nm for selecting equipment. PBM clinicians should utilize 976 nm near infrared diode laser systems if available; and when not available, 650 nm is an established though less effective option for treatment. The standardized parameters in the study (energy density of 8 J/cm^2, irradiance of 0.26 W/cm^2, 30-second exposure on each site, treatment on days 0, 3, 7 and 14 there after biweekly) propose a protocol that clinicians can implement today. The absence of sex-dependent modulation simplifies the clinical decision-making by using the same PBM protocols in both males and females, without any adjustments. This suggests that future PBM studies do not necessarily have to write on sex-specific outcomes or power-analysis per sex subgroup, although longitudinal designs with endocrine assessments are important for etiological understanding. The safety profile of LLLT as a low-risk adjunctive modality, in which the therapy is applied within biologically safe exposure limits and there have been no reports of adverse effects. While surgical approaches (corticotomy, piezocision) with maxillary corticotomy reduce the amount of tissue injury and risk of infection, PBM is atraumatic, painless intervention which does not show side effects within evidence-based dosimetry level [1; 11].

CONCLUSIONS

This RCT demonstrates that PBM using 650 nm- or 976 nm-wavelength diode lasers significantly accelerates MC retraction; the latter is more effective. Sex does not modulate acceleration suggesting a standardized protocol for all subjects. These results support the role of PBM as a non-invasive auxiliary approach in orthodontics and provide practice-related parameters for future application.

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AUTHOR'S CONTRIBUTION

The author made a substantial contribution to the preparation of the manuscript, including the conception and design of the study, data collection, analysis and interpretation of data, critical revision of the article for important intellectual content, and final approval of the version to be published.

ВКЛАД АВТОРОВ

Автор внес существенный вклад в подготовку рукописи, включая разработку замысла и дизайна исследования, сбор, анализ и интерпретацию данных, критический пересмотр статьи с точки зрения значимого интеллектуального содержания и окончательное одобрение версии для публикации.