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1.1 Biomechanical effect of one session of low-level laser on the bone-titanium implant interface.

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Abstract

Low-level laser (LLL) has been used on peri-implant tissues for accelerating bone formation. However, the effect of one session of LLL in the strength of bone-implant interface during early healing process remains unclear. The present study aims to evaluate the removal torque of titanium implants irradiated with LLL during surgical preparation of implant bed, in comparison to non-irradiation. Sixty-four Wistar rats were used. Half of the animals were included in LLL group, while the other half remained as control. All animals had the tibia prepared with a 2 mm drill, and a titanium implant (2.2 × 4 mm) was inserted. Animals from LLL group were irradiated with laser (gallium aluminum arsenide), with a wavelength of 808 nm, a measured power output of 50 mW, to emit radiation in collimated beams (0.4 cm(2)), for 1 min and 23 s, and an energy density of 11 J/cm(2). Two applications (22 J/cm(2)) were performed immediately after bed preparation for implant installation. Flaps were sutured, and animals from both groups were sacrificed 7, 15, 30, and 45 days after implant installation, when load necessary for removing implant from bone was evaluated by using a torquimeter. In both groups, torque values tended to increase overtime; and at 30 and 45 days periods, values were statistically higher for LLL group in comparison to control (ANOVA test, $p < 0.0001$). Thus, it could be suggested that a single session of irradiation with LLL was beneficial to improve bone-implant interface strength, contributing to the osseointegration process.

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1.2 Connective tissue graft associated or not with low laser therapy to treat gingival recession: randomized clinical trial

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Abstract

BACKGROUND

To evaluate the treatment of gingival recession with a connective tissue graft (CTG) alone or in combination with low-level laser therapy (CTG + L).

METHODS

Forty patients presenting 40 Miller Class I and II gingival recessions were included. The defects were randomly assigned to receive either CTG (n = 20) or CTG + L (n = 20). A diode laser (660 nm) was applied to the test sites immediately after surgery and every other day for 7 days (eight applications).

RESULTS

The mean percentage of root coverage was 91.9% for the test group and 89.48% for the control group after 6 months ($p > 0.05$). The test group presented more complete root coverage (n = 13, 65%) than the control group (n = 7, 35%) ($p = 0.04$). Dentine sensitivity decreased significantly after 6 months in both groups ($p < 0.001$). The two groups showed improvement in aesthetics at the end of treatment.

CONCLUSIONS
Low-level laser therapy may increase the percentage of complete root coverage when associated with CTG.

TRIAL REGISTRATION
ClinicalTrials.gov NCT02118155.

KEYWORDS
aesthetic; clinical trial; gingival recession; low-level laser therapy; periodontal surgery

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1.3 Current indications for low level laser treatment in maxillofacial surgery: a review.

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Abstract
Low level laser treatment (LLLT) is currently being used for various disorders, but with no convincing scientific evidence. Most recently we have noticed an increase in published randomised controlled trials (RCTs) that have focused on its applications in wound healing, scarring, disorders of the temporomandibular joint (TMJ), oral mucositis, and dental pain. Our aim therefore was to assess the scientific evidence about its current efficacy in maxillofacial surgery. We reviewed PubMed from January 2003 to January 2013 using the key phrase «low level laser treatment». Our inclusion criterion was intervention studies in humans of more than 10 patients. We excluded animal studies and papers in languages other than English, French, and German. We found 45 papers that we screened independently. The resulting full texts were scrutinised by two authors who awarded a maximum of 5 points using the Jadad scale for assessing the quality of RCT, and extracted the data according to sample size, variables of LLLT, the authors' conclusions, and the significance of the result. LLLT seems to be effective for the treatment of oral mucositis after treatment for head and neck cancer. However, it cannot yet be considered a valid treatment for disorders of the TMJ. It seems to improve gingival healing, and myofacial and dental pain.

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1.4 Developments in low level light therapy (LLLT) for dentistry.

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Abstract
OBJECTIVES
Low level light/laser therapy (LLLT) is the direct application of light to stimulate cell responses (photobiomodulation) in order to promote tissue healing, reduce inflammation and induce analgesia. There have been significant studies demonstrating its application and efficacy at many sites within the body and for treatment of a range of musculoskeletal injuries, degenerative diseases and dysfunction, however, its use on oral tissues has, to date, been limited. The purpose of this review is to consider the potential forLLLT in dental and oral applications by providing background information on its mechanism of action and delivery parameters and by drawing parallels with its treatment use in analogous cells and tissues from other sites of the body.

METHODS
A literature search on Medline was performed on laser and light treatments in a range of dental/orofacial applications from 2010 to March 2013. The search results were filtered for LLLT relevance. The clinical papers were then arranged to eight broaddental/orofacial categories and reviewed.

RESULTS
The initial search returned 2778 results, when filtered this was reduced to 153. 41 were review papers or editorials, 65 clinical and 47 laboratory studies. Of all the publications, 130 reported a positive effect in terms of pain relief, fast healing or other improvement in symptoms or appearance and 23 reported inconclusive or negative outcomes. Direct application of light as a therapeutic intervention within the oral cavity (rather than photodynamic therapies, which utilize photosensitizing solutions) has thus far received minimal attention. Data from the limited studies that have been performed which relate to the oral cavity indicate that LLLTmay be a reliable, safe and novel approach to treating a range of oral and dental disorders and in particular for those which there is an unmet clinical need.

SIGNIFICANCE
The potential benefits of LLLT that have been demonstrated in many healthcare fields and include improved healing, reduced inflammation and pain control, which suggest considerable potential for its use in oral tissues.

KEYWORDS
Dental therapy; Low-level laser therapy; Oral disease; Photobiomodulation; Phototherapy

https://www.ncbi.nlm.nih.gov/pubmed/24656472

1.5 Effect of low-level laser therapy on Candida albicans growth in patients with denture stomatitis

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Abstract
OBJECTIVE
The purpose of our report is to present the effect of low-level laser therapy on Candida albicans growth and palatal inflammation in two patients with denture stomatitis.

BACKGROUND DATA
The most common oral mucosal disorder in denture wearers is denture stomatitis, a condition that is

usually associated with the presence of the yeast Candida albicans. Different treatment methods have been suggested to treat this symptom, none of which is proven to be absolutely effective.

METHODS
Two denture-wearing patients, both with palatal inflammation diagnosed as Newton type II denture stomatitis were treated with low-power semiconductor diode laser (BTL-2000, Prague, Czech Republic) at different wavelengths (685 and 830 nm) for 5 d consecutively. In both patients, palatal mucosa and acrylic denture base were irradiated in noncontact mode (probe distance of 0.5 cm from irradiated area) with different exposure times-5 min (830 nm, 3.0 J/cm2, 60 mW) and 10 min (685 nm, 3.0 J/cm2, 30 mW). The effect of laser light on fungal growth in vivo was evaluated after the final treatment using the swab method and semiquantitative estimation of Candida albicans colonies growth on agar plates. The severity of inflammation was evaluated using clinical criteria.

RESULTS
After lowlevel laser treatment, the reduction of yeast colonies on the agar plates was observed and palatal inflammation was diminished.

CONCLUSION
LLLT is effective in the treatment of denture stomatitis. Further placebo controlled studies are in progress.

https://www.ncbi.nlm.nih.gov/pubmed/15954824

1.6 Effects of low-level laser irradiation on the pathogenicity of Candida albicans: in vitro and in vivo study.

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Abstract
OBJECTIVE
The purpose of this study was to evaluate the effects of low-level laser irradiation (LLLI) on the in vitro growth characteristics and in vivo pathogenicity of Candida albicans in a murine model in the absence of a photosensitizer.

BACKGROUND DATA
C. albicans is an opportunistic commensal organism that causes a wide variety of diseases in human beings, ranging from superficial infections to life-threatening invasive candidiasis. The incidence of C. albicans infection is increasing, because of the greater frequency of acquired immunodeficiency conditions. A high recurrence rate has been reported for vulvovaginal and oralcandidiasis, despite the best available treatments. Therefore, the search for new treatment modalities seems quite rational.

METHODS
Candida culture plates were exposed to common clinical energies of LLLI: 3, 5, 10, and 20 J at 685 nm (BTL Laser 5000, Medicinos Projektai, Czech Republic, Prague, max power output 50 mW) and 3, 5, 10, 30, and 50 J at 830 nm (BTL Laser 5000, Medicinos Projektai, Czech Republic, Prague, max power output 400 mW).

RESULTS
Following LLLI with energies >10 J at both 685 and 830 nm wavelengths, statistically significant effects

were observed in vitro on the turbidimetric growth kinetics of C. albicans and in vivo on the survival rate of infected mice (p value ≤ 0.05). Therefore, this energy could be considered a threshold for clinical investigation.

CONCLUSIONS
Translating our data into the clinical setting, it can be proposed that a direct laser-based approach without using a photosensitizing dye can significantly reduce the pathogenicity of Candida albicans. It can also be concluded that laser light at specific wavelengths could be a possible promising novel treatment for superficial and mucocutaneous C. albicans infections.

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1.7 Effects of low-level laser therapy and epidermal growth factor on the activities of gingival fibroblasts obtained from young or elderly individuals

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Abstract
This study evaluated the effects of low-level laser therapy (LLLT) and epidermal growth factor (EGF) on fibroblasts obtained from young and elderly individuals. Gingival fibroblasts from young (Y) and elderly (E) individuals were seeded in wells of 24-well plates with Dulbecco's modified Eagle's medium (DMEM) containing 10 % of fetal bovine serum (FBS). After 24 h, the cells were irradiated (LASERTable-InGaAsP-780 ± 3 nm, 25 mW, 3 J/cm2) or exposed to EGF (100 µM). After 72 h, cells were evaluated for viability, migration, collagen and vascular endothelial growth factor (VEGF) synthesis, and gene expression of growth factors. Data were analyzed by Kruskal-Wallis and Mann-Whitney tests ($\alpha = 5$ %). Y and E fibroblasts irradiated with laser or exposed to EGF showed increased viability and collagen synthesis. Enhanced cell migration was observed for Y fibroblasts after both treatments, whereas only the LLLT stimulated migration of E cells. VEGF synthesis was higher for Y and E cells exposed to EGF, while this synthesis was reduced when E fibroblasts were irradiated. Increased gene expression of VEGF was observed only for Y and E fibroblasts treated with LLLT. Regardless of a patient's age, the LLLT and EGF applications can biostimulate gingival fibroblast functions involved in tissue repair.

KEYWORDS
Cell biology; Fibroblast(s); Growth factors; Laser(s); Wound healing

https://www.ncbi.nlm.nih.gov/pubmed/27677475

1.8 Influence of low-level laser on bone remodeling during induced tooth movement in rats

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ABSTRACT

Objective

To analyze the effect of low-level laser on bone remodeling during induced tooth movement in rats.

Materials and Methods

A diode laser (808 nm, 100 mW, 54 J on an area of 0.0028 cm2) was used. The application was continuous, punctual, and with contact. Forty-two 70-day-old Wistar rats had the maxillary left first molar moved using a force level of 25 g. In two experimental subgroups the movement was performed over 7 days and in three subgroups the movement occurred over 14 days. In the 7-day movement subgroups, one subgroup received laser irradiation on day 1 only; the other subgroup received laser irradiation on days 1, 3, and 5. In the 14-day movement subgroups, one subgroup received laser irradiation on day 1 only; the second on days 1, 3, and 5; and the third on days 1, 3, 5, 7, 9, 11, and 13. The control group was also divided into two subgroups, and movement occurred over two different periods of treatment (7 days and 14 days) without laser application; these were used as controls for the respective experimental subgroups. Inter-subgroup comparison was performed with Kruskal-Wallis, followed by Mann-Whitney and analysis of variance, followed by Tukey tests within the 7- and 14-day subgroups.

Results

The subgroup with three laser applications showed significantly greater osteoclastic activity and bone resorption than the other subgroups in the 7-day movement subgroups.

Conclusions

Low-level laser application significantly increased the osteoclastic but not the osteoblastic activity during the initial phases of tooth movement. In addition, the osteoclastic activity was dose-dependent. (Angle Orthod. 2013;83:1015–1021.)

KEY WORDS

Experimental animal model; Laser therapy; Orthodontic movement

INTRODUCTION

Low-level laser (LLL) has demonstrated analgesic, anti-inflammatory, and biostimulatory effects.1 Among all methods studied to accelerate induced dental movement and consequently decrease orthodontic treatment time, low-level laser is minimally invasive, extremely simple, safe, and fast to apply.2 In spite of these advantages, studies on low-level laser have shown contradictory findings. Although some studies showed an increase in osteoclastic activity or tooth movement with low-level laser,3–5 others found no differences between irradiated and nonirradiated groups,6,7 and some concluded that the speed of tooth movement decreased in lased compared with nonlased samples.8 Because of the aforementioned divergent results, the aim of this study was to analyze the influence of low-level laser application on osteoclastic and osteoblastic activities and on degree of bone neoformation during induced tooth movement in Wistar rats.

Table 1. Specimen Distribution According to Group, Number of Laser Applications, and Time of Humane Killing

Subgroup[a]	Laser Frequency	No. of Laser Administrations	Day Killed
C7d	No administration	0	Day 7
I1ap7d	Day 1 only	1	Day 7
I3ap7d	Days 1, 3, and 5	3	Day 7
C14d	No administration	0	Day 14
I1ap14d	Day 1 only	1	Day 14
I3ap14d	Days 1, 3, and 5	3	Day 14
I7ap14d	Days 1, 3, 5, 7, 9, 11, and 13	7	Day 14

[a] C7d indicates control subgroup, 7-day tooth movement; I1ap7d, experimental subgroup that received one laser application over 7 days; I3ap7d, experimental subgroup that received three laser applications over 7 days; C14d, control subgroup, 14-day tooth movement; I1ap14d, experimental subgroup that received one laser application over 14 days; I3ap14d, experimental subgroup that received three laser applications over 14 days; I7ap14d, experimental subgroup that received seven laser applications over 14 days.

MATERIALS AND METHODS

Permission to conduct this study was granted by the Ethics Committee in Animal Experimentation of Potiguar University (RN – Brazil). Forty-two 70-day-old female Wistar rats weighing 170–190 g were used for this experiment. During the experimental period, the animals remained inside appropriate cages at a constant temperature ranging between 23uC and 25uC, in a 12-hour light/dark environment and provided with food and water ad libitum. The animals were divided into two groups: the experimental, or irradiated group (I), which had 30 rats, and the control group (C), which had 12 rats. The experimental group was divided into five subgroups containing six rats each, according to laser irradiation frequency and duration of treatment (Table 1). In two experimental subgroups, movement was induced over 7 days, and in the remaining three subgroups, movement was induced over 14 days. In the two 7-day movement subgroups, one received laser irradiation on day 1 only, and the other was irradiated on days 1, 3, and 5. In the three 14-day movement subgroups, one received laser irradiation on day 1 only; the one on days 1, 3, and 5; and one on days 1, 3, 5, 7, 9, 11, and 13. The control group was also divided into two subgroups of six rats each. In these subgroups movement was also induced for two different periods of time (7 days and 14 days) but these rats received no laser application (Table 1). All procedures were carried out under general anesthesia, with 0.3 mL/ 100 g body weight intramuscular injection of tiletamine chlorhydrate 125 mg/zolazepam chloridrate 125 g (Zoletil 50, Virbac, Sa˜o Paulo, Brazil).

A modified model described by Heller and Nanda9 was used to move the maxillary left first molar in both groups. Tooth movement was performed by means of nickel titanium closed coil springs (Morelli,Sorocaba, Brazil) using both maxillary central incisors as anchorage. The closed coil spring characteristics were standardized at 0.25 mm of wire diameter, 0.76 mm internal diameter, and 7 mm total length. The coil was fixed to the teeth with a 0.25-mm stainless steel wire ligature. To calibrate the force magnitude, the spring was fixed to the first molar above the proximal contact point. The closed coil spring was stretched until a force of 25 g was achieved before fixation around both maxillary incisors. The teeth were covered by photocured resin around the ligature wire to improve coil spring retention (Figure 1). Gallium-aluminum-arsenide laser (Whitening Laser II – DMC, Sa˜o Carlos, SP, Brazil) was used to generate low-level laser irradiation. The wavelength was 808 nm (infrared laser), and a continuous emission regimen was used. The output power was set to 100 mW, the optic fiber diameter corresponded to 0.6 mm, and the energy density was 642 J/cm2/point (Table 2). Dosimetry was obtained by the following formula:

$$\left(J/cm^2\right) = \left(\frac{P(W) \times T(s)}{A(cm^2)}\right),$$

considering area (A) as p 3 R2 (radius of the optic fiber active point). Following the protocol used by Kawasaki and Shimizu,3 irradiation was applied in three points by the punctual method with 3 minutes of contact for each point, totaling 9 minutes. The application points were the buccal, palatal, and mesiocervical aspects of the first left maxillary molar. Laser was applied 1, 3, or 7 times in each animal during the experimental period, with 48-hour intervals, according to the subgroup (Table 1).

Table 2. Phototherapy Parameters

Phototherapy Parameters	Values
Energy density	1926 J/cm^2
Energy	54 J
Output power	100 mW
Wavelength	808 nm
Color	Invisible
Emition regimen	Continuous
Optic fiber diameter	0.6 mm
Distance of application	In contact/punctual
Time	3 min/3 points of application (9 min total)

Figure 1. Appliance used to move the maxillary left first molar.

The animals were humanely killed in a carbonic gas chamber 7 or 14 days after force application. Their heads were submerged in 10% formaldehyde solution for 48 hours. After fixation, the samples were decalcified using 7.5% nitric acid for 5 days. The left maxillary hemi-arches were then divided and embedded in paraffin, sectioned with a rotary microtome of 4 mm in thickness, perpendicular to the occlusal plane of the first molar up to the radicular pulp level. Finally, the samples were stained with hematoxylin and eosin. Histologic evaluation was performed using a binocular microscope (CX31, Olympus, Tokyo, Japan). The blades were photographed using a digital camera (Olympus) connected to a computer. Two examiners who were blinded to the study groups performed the readings.

The analyzed area corresponded to the inter-root region, especially the distal aspect of the mesial root, the mesial aspect of the distal root, and under the furcation. For interpretation, the same parameters were performed for histologic graduation in the experimental and control groups. The most evident manifestation of the cellular events in each specimen was recorded. The presence of active osteoblastic and osteoclastic cells and the amount of alveolar bone in the inter-root region were analyzed. Osteoblastic activities were interpreted by counting the young cells that had a cuboid shape in bone surfaces and that presented basophilic cytoplasm and polarized nucleus, arranged in palisade, in two fields of large magnification; these were classified as low (1 to 10 cells), moderate (11 to 25 cells), or intense (more than 25 active cells) (Figure 2). The osteoclasts were considered when their outline was irregular, filling the Howship's lacuna, or near bone; the activity was registered as low (maximum of three osteoclasts per region), moderate (four to six cells), and intense (more than six, cells) (Figure 2). These analyses were performed in three inter-root regions (distal root, mesial root, and furcation). A 103 magnification ocular lens placed on the right ocular with a micron graduated, 1 mm long ruler (1/0.01 mm of graduation) was used to measure the distance from the furcation wall to the nearest vertical alveolar bone present. The smallest measurement in each blade was recorded, and the greater the distance, the greater the bone loss (Figure 3).

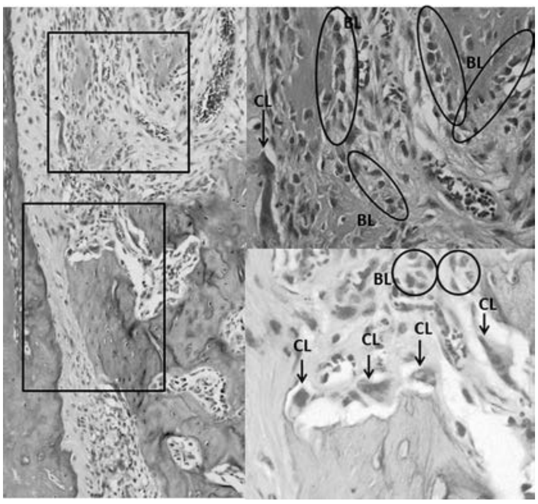

Figure 2. Photomicrography for histologic evaluation. Osteoblasts (BL in circle) and osteoclasts (CL, arrows). Hematoxylin and eosin 400×.

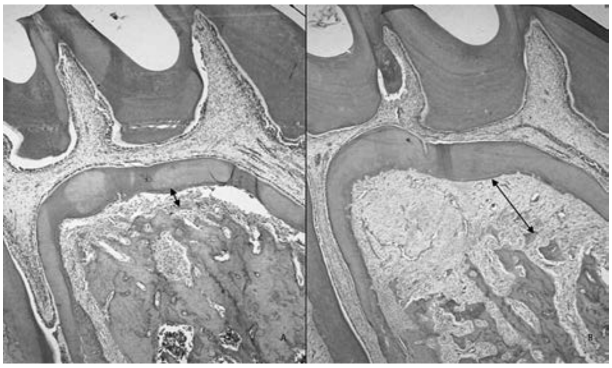

Figure 3. Photomicrography of the distance between the furcation region and alveolar bone (arrow). (A) Specimen of the subgroup C7ap; hematoxylin and eosin (HE) 40×. (B) Specimen of the experimental subgroup that received three laser applications over 7 days (I3ap7d); HE 40×.

Statistical Analyses

Inter-subgroup comparisons of the magnitude of osteoclastic and osteoblastic cellular activity were performed with Kruskal-Wallis tests, followed by Mann-Whitney tests, for the animals in which movement was induced for 7 and for 14 days and their respective control subgroups. Analysis of variance and then Tukey tests were performed to compare the distances between the furcation and the inter-root alveolar bone within the 7- and 14-day movement subgroups and their respective control subgroups. Results were considered statistically significant at P , .05.

RESULTS

Among the 7-day tooth movement subgroups, the experimental subgroup that received three laser applications (I3ap7d) had a significantly greater osteoclastic cellular activity than the control group (C7d) and the experimental subgroup that received one laser application (I1ap7d) (Table 3). There was no inter-subgroup difference among the 14-day tooth movement subgroups (Table 4). Among the 7-day tooth movement subgroups, the experimental subgroup with three laser applications (I3ap7d) had a significantly greater amount of bone loss than the other groups (Figure 3; Table 5). There was no inter-subgroup difference among the 14-day tooth movement subgroups (Table 6).

DISCUSSION

Decalcification with 7.5% nitric acid in the determined time and concentration was adequate to prevent structural cellular changes.10 Cell marking was not necessary because it is perfectly possible for an experienced examiner to count them by observing their characteristics as described in the methodolgy.11 The dosimetry used in this study was similar to the one proposed by Kawasaki and Shimizu,3 but the frequency of applications and force magnitude were distinct. Kawasaki and Shimizu used a daily frequency of laser application, whereas in this research the irradiations consisted of one, three, and seven applications within a 48-hour interval (Table 1). Twenty-five grams of force were applied instead of 10 g3 and this difference may have exacerbated the laser stimuli. Twenty-five grams of force for moving rat teeth is the amount often found in the literature.12 Therefore, the additional laser stimuli may be responsible for the differences between bone resorption and bone formation in our results.

Table 3. Cellular Activity in the 7-Day Tooth Movement Subgroups (Kruskal-Wallis Followed by Mann-Whitney Tests)[a]

	C7d (N = 6)			I1ap7d (N = 6)			I3ap7d (N = 6)			
	Median	25%	75%	Median	25%	75%	Median	25%	75%	*P
Osteoclasts	1.5[y]	1.0	2.0	1.0	1.0[y]	2.0	2.0[z]	2.0	3.0	.0057
Osteoblasts	2.0	1.0	2.0	2.0	1.0	2.0	1.0	1.0	1.0	.253

[a] C7d indicates control subgroup, 7-day tooth movement; I1ap7d, experimental subgroup that received one laser application over 7 days; I3ap7d, experimental subgroup that received three laser applications over 7 days.

* Statistically significant at $P < .05$. Different letters represent statistically significant differences.

Table 4. Cellular Activity in the 14-Day Tooth Movement Subgroups (Kruskal Wallis Test)[a]

	C14d (N = 5)			I1ap14d (N = 5)			I3ap14d (N = 5)			I7ap14d (N = 5)			
	Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%	*P*
Osteoclasts	1.0	0	1.0	1.0	0	1.0	0	0	0.1	1.0	1.0	2.0	.429
Osteoblasts	1.0	1.0	2.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	2.0	.824

[a] C14d indicates control subgroup, 14-day tooth movement; I1ap14d, experimental subgroup that received one laser application over 14 days; I3ap14d, experimental subgroup that received three laser applications over 14 days; I7ap14d, experimental subgroup that received seven laser applications over 14 days.

Table 5. Bone Remodeling Represented by the Distance Between Furcation (F) and Alveolar Bone (AB) in the 7-Day Subgroups (ANOVA Followed by Tukey Tests)[a]

	C7d (N = 6)		I1ap7d (N = 6)		I3ap7d (N = 6)		
	Mean	SD	Mean	SD	Mean	SD	**P*
F – AB (μm)	55.5[y]	21.23	71[y]	15.47	161[z]	16	.000

[a] C7d indicates control subgroup, 7-day tooth movement; I1ap7d, experimental subgroup that received one laser application over 7 days; I3ap7d, experimental subgroup that received three laser applications over 7 days.

* Statistically significant at $P < .05$. Different letters represent statistically significant differences.

Tissue changes were greater on the mesial aspect of the distal root than on the mesial aspect of the mesial root. This finding was previously reported.13 Therefore, it was decided to analyze the region under the furcation of the mesial aspect of the distal root (compression) and of the distal aspect of the mesial root (tension), instead of the both aspects of the same root as other authors had done,3 enabling simultaneous visualization of the bone remodeling events (Figure 3).

Our results showed that osteoclastic activity was influenced by laser phototherapy, demonstrating greater stimulation with the increase of application frequency, in the 7-day experimental subgroups (Tables 3 and 4). The osteoclasts appeared in greater amounts in the 7-day period and decreased after 14 days of force application. These findings suggest that laser is capable of activating the pre-osteoclasts from the periodontal ligament to become mature but does not induce bone marrow cells to differentiate into new preosteoclasts fast enough. Fujita and colleagues14 also found stimulation only in the early stages. It seems that when the pre-osteoclast cells present in the ligament come to an end, the laser effect in the process of bone resorption is inexpressive. In this way, laser should ideally be recommended only at the initial period of force application, as demonstrated in our findings and according to the literature.15 It may be reasonable to assume that the effect of laser in stimulating the osteoclasts is dependent on the number of existing pre-osteoclasts, once the laser increases the speed in which these cells are activated, as has also been previously demonstrated.3 Osteoblasts were not significantly influenced by lowintensity laser in the dosage used in this study (Tables 3 and 4). The 7-day experimental subgroup that received three laser applications showed the numerically smallest osteoblastic activity. There was a similar response in the 14-day experimental subgroups. It has been previously demonstrated that laser does not have a significant effect on osteoblastic proliferation or activation, and is only beneficial to maintain cellular viability.16 On the other hand, a positive result of laser osteoblastic stimulation was found in other studies.17 These facts suggest that there is a limit of stimulation for osteoclastic and osteoblastic cells, or even an ideal dosage for each cell type that cannot be surpassed to achieve a stimulatory response, as has already been demonstrated in the literature.18

The result in this study was bone loss with consequent increase of the connective tissue area between the furcation wall and the inter-root alveolar bone during the experiment, which was more intense in the experimental subgroup that received three laser applications over 7 days (I3ap7d; Table 5). The increase of connective tissue area means that bone resorption was larger than bone apposition, or bone apposition was not fast enough to balance bone remodeling with the applied dosage in the first 7 days of movement (Figure 3). Therefore, considering that bone remodeling for tooth movement depends on the synchronized activity of both cells, it is not practical that different ideal dosages are necessary to stimulate each cell type. The explanation for no significant difference among the 14-day subgroups (Table

6) is based on the early laser-stimulating effect already mentioned. After the seventh day, the laser activated the osteoclasts less intensively, allowing time for the non-irradiated group to achieve a bone resorption degree similar to that of the irradiated group. Considering that the number of osteoblasts during the 7- and 14-day periods of movement is relatively the same according to the literature19 and that the osteoclasts are stimulated only at the first period of experiment in irradiated group, a statistically significant difference is present only among the 7-day subgroups. The literature is not clear about the differences between different cell responses and the ideal dosage for each cell type. In any event, if there were a laser radiation modulation band for each cellular type, it would be impractical to stimulate processes that involve many different and synchronized tissues, such as tooth movement. After an accelerated movement by laser stimulation, relapse would be facilitated and greater anchorage reinforcement or greater retention time would be necessary. If this hypothesis is confirmed, the correct indication for laser phototherapy would be regeneration of tissues with similar metabolic pattern.
Studies involving epithelial, connective,20 and bone21 regeneration, or even dental implant osteointegration, 22 showed positive results in the irradiated groups. Conversely, studies on the effects of laser on tooth movement are divergent and inconclusive.3–8 In rats, low-level laser irradiation facilitated turnover of connective tissues during tooth movement and was dependent on dosage and frequency of laser application. 23 The dosage used in this study seemed to be stimulatory for the connective tissue cells, including osteoclasts, but inhibitory or less stimulatory for osteoblasts, consequent to the lack of synchrony in bone remodeling. Furthermore, in respect to tooth movement, synchrony between cellular events would be more important than the speed in which they occur.24 In other words, the ideal situation would be to increase the speed of the events, maintaining the physiological tissue organization. Considering these aspects, it would be interesting to test other laser dosages in tooth-movement stimulation.

CONCLUSIONS

N Osteoclastic activity was greatest in the 3-day laser irradiation administration subgroup, which received laser irradiation on days 1, 3, and 5 in the first 7 days of movement. Therefore, osteoclastic activity was dose-dependent. N Osteoblastic activity was not influenced by laser irradiation.

Table 6. Bone Remodeling Represented by the Distance Between Furcation (F) and Alveolar Bone (AB) in the 14-Day Subgroups (ANOVA)[a]

	C14d (N = 5)		I1ap14d (N = 5)		I3ap14d (N = 5)		I7ap14d (N = 5)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*
F – AB (μm)	222	77.96	287	27.84	225.4	94.50	310.4	92.48	.222

[a] C14d indicates control subgroup, 14-day tooth movement; I1ap14d, experimental subgroup that received one laser application over 14 days; I3ap14d, experimental subgroup that received three laser applications over 14 days; I7ap14d, experimental subgroup that received seven laser applications over 14 days.

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12. Verna C, Hartig LE, Kalia S, Melsen B. Influence of steroid drugs on orthodontically induced root resorption. Orthod Craniofac Res. 2006;9:57–62. Table 6. Bone Remodeling Represented by the Distance Between Furcation (F) and Alveolar Bone (AB) in the 14-Day Subgroups (ANOVA)a C14d (N 5 5) I1ap14d (N 5 5) I3ap14d (N 5 5) I7ap14d (N 5 5)
Mean SD Mean SD Mean SD Mean SD P F – AB (mm) 222 77.96 287 27.84 225.4 94.50 310.4 92.48 .222 a C14d indicates control subgroup, 14-day tooth movement; I1ap14d, experimental subgroup that received one laser application over 14 days; I3ap14d, experimental subgroup that received three laser applications over 14 days; I7ap14d, experimental subgroup that received seven laser applications over 14 days. 1020 COSSETIN, JANSON, DE CARVALHO, DE CARVALHO, HENRIQUES, GARIB
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1.9 Laser applications in oral surgery and implant dentistry.

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Abstract

Lasers have been used for many years in oral surgery and implant dentistry. In some indications, laser treatment has become state of the art as compared to conventional techniques. This article is a comprehensive review of new laser applications in oral surgery and implant dentistry. One of the most interesting developments over the last years was the introduction of the 9.6-microm CO(2) laser. It has been shown in the recent literature that the use of this new device can preserve tissue with almost no adverse effects at the lightmicroscopic level. In contrast, modifications of approved CO(2) laser therapies of premalignant lesions resulted in higher recurrence rates than the conventional defocused laser technique. However, several studies indicate that other wavelengths such as Nd-YAG (lambda = 1,064 nm) or diode lasers (lambda = 810 nm) may be also of value in this field. In many other indications, the use of lasers is still experimental. Intraoperatively used photodynamic therapy or peri-implant care of ailing implants with the CO(2) laser seems to be more of value than conventional methods. However, further studies are required to assess standard protocols. Over the past years, research identified some new indications for laser treatment in oral surgery and implant dentistry. Moreover, well-known laserapplications were defined as state of the art. Nevertheless, further studies are required for laser treatment in oral surgery and implant dentistry.

https://www.ncbi.nlm.nih.gov/pubmed/17268764

1.10 Laser-activated transforming growth factor-β1 induces human β-defensin 2: implications for laser therapies for periodontitis and peri-implantitis.

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Abstract

BACKGROUND

There is increasing popularity of high-power lasers for surgical debridement and antimicrobial therapy in the management of peri-implantitis and periodontal therapy. Removal of the noxious foci would naturally promote tissue healing directly. However, there are also anecdotal reports of better healing around routine high-power laser procedures. The precise mechanisms mediating these effects remain to be fully elucidated. This work examines these low-dose laser bystander effects on oral human epithelial and fibroblasts, particularly focusing on the role of human α-defensin 2 (HBD-2 or DEFB4A), a potent factor capable of antimicrobial effects and promoting wound healing.

MATERIAL AND METHODS

Laser treatments were performed using a near-infrared laser (810 nm diode) at low doses. Normal human oral keratinocytes and fibroblast cells were used and HBD-2 mRNA and protein expression was assessed with real time polymerase chain reaction, western blotting and immunostaining. Role of transforming growth factor (TGF)-α1 signaling in this process was dissected using pathway-specific small molecule inhibitors.

RESULTS
We observed laser treatments robustly induced HBD-2 expression in an oral fibroblast cell line compared to a keratinocyte cell line. Low-dose laser treatments results in activation of the TGF-α1 pathway that mediated HBD-2 expression. The two arms of TGF-α1 signaling, Smad and non-Smad are involved in laser-mediated HBD-2 expression.

CONCLUSIONS
Laser-activated TGF-α1 signaling and induced expression of HBD-2, both of which are individually capable of promoting healing in tissues adjacent to high-power surgical laser applications. Moreover, the use of low-dose laser therapy itself can provide additional therapeutic benefits for effective clinical management of periodontal or peri-implant disease.

KEYWORDS
defensins; lasers; low-level light/laser therapy; peri-implantitis; periodontitis; photobiomodulation therapy

https://www.ncbi.nlm.nih.gov/pubmed/27396269

1.11 Laser-activated transforming growth factor-β1 induces human β-defensin 2: implications for laser therapies for periodontitis and peri-implantitis.

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There is increasing popularity of high-power lasers for surgical debridement and antimicrobial therapy in the management of peri-implantitis and periodontal therapy. Removal of the noxious foci would naturally promote tissue healing directly. However, there are also anecdotal reports of better healing around routine high-power laser procedures. The precise mechanisms mediating these effects remain to be fully elucidated. This work examines these low-dose laser bystander effects on oral human epithelial and fibroblasts, particularly focusing on the role of human α-defensin 2 (HBD-2 or DEFB4A), a potent factor capable of antimicrobial effects and promoting wound healing.

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KEYWORDS
defensins; lasers; low-level light/laser therapy; peri-implantitis; periodontitis; photobiomodulation therapy

https://www.ncbi.nlm.nih.gov/pubmed/27396269

1.12 Low-level laser therapy supported teeth extractions of two patients receiving IV zolendronate.

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Abstract
BRONJ (bisphosphonate-related osteonecrosis of jaws) is a frequently encountered disease, particularly in the maxillofacial region, and a consequence of bisphosphonate use. Treatment of BRONJ remains controversial, as efficiency of medical and surgical approaches as well as a combination of these methods with supportive treatments have not been clearly demonstrated in the literature. In recent years, laser usage alone or in combination with the main therapy methods, has become popular for the treatment of bisphosphonate-related osteo-necrosis of jaws. In this article, we present the successful management of two dental patients who had high potentials for BRONJ development as a result of chemo and radiotherapy combined with IV zoledronic acid application. Multiple consecutive teeth extractions followed with primary wound closure and LLLT applications were performed under high doses of antibiotics prophylaxis. Satisfactory wound healing in both the surrounding soft and hard tissues was achieved. LLLT application combined with atraumatic surgical interventions under antibiotics prophylaxis is a preferable approach in patients with a risk of BRONJ development. Adjunctive effect of LLLT in addition to careful infection control on preventing BRONJ was reported and concluded.

https://www.ncbi.nlm.nih.gov/pubmed/20669038

1.13 Low-level laser use in dentistry.

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Abstract
The use of laser light at power levels below that capable of direct tissue change (protein denaturation, water vaporisation and tissue ablation), has been advocated in diverse branches of medicine and veterinary practice, yet its acceptance in general dental practice remains low. However, the scope for using low-level laser light (LLLT) has emerged through many applications, either directly or indirectly tissue-related, in delivering primary dental care. The purpose of this article is to explain the mechanisms

of action and to explore the uses of this group of lasers in general dental practice.

https://www.ncbi.nlm.nih.gov/pubmed/17293815

1.14 Mechanical evaluation of the influence of low-level laser therapy in secondary stability of implants in mice shinbones

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Abstract
The present work evaluates mechanically the bone-implant attachment submitted or not to low-level laser therapy, with wavelength of 795 nm, in a continuous way, with power of 120 mW. The implant was placed in one of the shinbones of 24 mice, randomly distributed into two groups. The experimental group was submitted to six laser applications, divided into four points previously established, two lateral and two longitudinal, six times 8 J/cm2 with an interval of 2 days, totaling the dose of 48 J/cm2. The control group did not receive laser therapy. The interval between applications was 48 h and the irradiations began immediately after the end of the implant surgeries. The two groups were killed on the 14th day and a bone block of the area was removed where the implant was inserted. A torque machine was used to measure the torque needed for loosening the implants. A statistically significant difference was observed between the two groups. The experimental group presented larger difficulty for breaking up the implant interface with the bone block than the control group. It can be concluded that with the animal model and the protocol of irradiation present in this study, the lasertherapy demonstrated capacity to increase the attachment bone implant.

https://www.ncbi.nlm.nih.gov/pubmed/20393769

1.15 Photobiomodulation and implants: implications for dentistry.

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Abstract
The use of dental implants has become a mainstay of rehabilitative and restorative dentistry. With an impressive clinical success rate, there remain a few minor clinical issues with the use of implants such as peri-implant mucositis and peri-implantitis. The use of laser technology with implants has a fascinating breadth of applications, beginning from their precision manufacturing to clinical uses for surgical site preparation, reducing pain and inflammation, and promoting osseointegration and tissue regeneration. This latter aspect is the focus of this review, which outlines various studies of implants and laser therapy in animal models. The use of low level light therapy or photobiomodulation has demonstrated its efficacy in these studies. Besides more research studies to understand its molecular mechanisms, significant efforts are needed to standardize the clinical dosing and delivery protocols for laser therapy to ensure the maximal efficacy and safety of this potent clinical tool for photobiomodulation.

KEYWORDS
Dental implants; Low-level laser therapy; Peri-implantitis; Phototherapy

https://www.ncbi.nlm.nih.gov/pubmed/24455438

1.16 The current status of low level laser therapy in dentistry. Part 1. Soft tissue applications.

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Abstract

Despite more than 30 years of experience with low level laser therapy (LLLT) or 'biostimulation' in dentistry, concerns remain as to its effectiveness as a treatment modality. Controlled clinical studies have demonstrated that while LLLT is effective for some specificapplications, it is not a panacea. This paper provides an outline of the biological basis of LLLT and summarizes the findings of controlled clinical studies of the use of LLLT for specific soft tissue applications in dentistry. Areas of controversy where there is a pressing need for further research are identified.

Comment in Low level laser therapy. [Aust Dent J. 1997]

https://www.ncbi.nlm.nih.gov/pubmed/9316312

1.17 The current status of low level laser therapy in dentistry. Part 2. Hard tissue applications

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Abstract

While most applications of low level laser therapy (LLLT) in dentistry are directed toward soft tissues, in recent years there has been increasing interest in tooth-related or hard tissue applications of LLLT. This report provides an overview of applications of LLLT in the treatment of dentine hypersensitivity and pain arising from the periodontal ligament, and describes the phenomenon of lethal laser photosensitization and its applications in the treatment of dental caries. Technical aspects of LLLT equipment and safety concerns are also discussed.

https://www.ncbi.nlm.nih.gov/pubmed/9409045

1.18 The effects of CO2 laser with or without nanohydroxyapatite paste in the occlusion of dentinal tubules.

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Abstract
The aim of this study was to evaluate a new treatment modality for the occlusion of dentinal tubules (DTs) via the combination of 10.6 µm carbon dioxide (CO2) laser and nanoparticle hydroxyapatite paste (n-HAp). Forty-six sound human molars were used in the current experiment. Ten of the molars were used to assess the temperature elevation during lasing. Thirty were evaluated for dentinal permeability test, subdivided into 3 groups: the control group (C), laser only (L-), and laser plus n-HAp (L+). Six samples, two per group, were used for surface and cross section morphology, evaluated through scanning electron microscope (SEM). The temperature measurement results showed that the maximum temperature increase was 3.2 °C. Morphologically groups (L-) and (L+) presented narrower DTs, and almost a complete occlusion of the dentinal tubules for group (L+) was found. The Kruskal-Wallis nonparametric test for permeability test data showed statistical differences between the groups ($P < 0.05$). For intergroup comparison all groups were statistically different from each other, with group (L+) showing significant less dye penetration than the control group. We concluded that CO2 laser in moderate power density combined with n-HAp seems to be a good treatment modality for reducing the permeability of dentin.

https://www.ncbi.nlm.nih.gov/pubmed/25386616

1.19 The effects of CO2 laser with or without nanohydroxyapatite paste in the occlusion of dentinal tubules.

Al-Maliky MA1, Mahmood AS2, Al-Karadaghi TS2, Kurzmann C1, Laky M3, Franz A4, Moritz A5

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https://www.ncbi.nlm.nih.gov/pubmed/25386616

1.20 Efficacy of laser therapy in the management of bisphosphonate related osteonecrosis of the jaw (BRONJ) : a systematic review

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OSTEOPOROSE

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Efficacy of laser therapy in the management of bisphosphonate-related osteonecrosis of the jaw (BRONJ): a systematic review.

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Abstract

Bisphosphonate-related osteonecrosis of the jaw is a well-known potential side effect of long-term bisphosphonate therapy; the primary objective of the treatment should be to improve patient quality of life through pain and infection management, to prevent the development of new lesions, and to slow disease progression. In recent years, the use of laser for bisphosphonate-related osteonecrosis of the jaw has become more widespread, due to its use of administration and widely reported beneficial effects on tissue healing. The present systematic review of the literature sought to elucidate whether low-level laser therapy has positive effects on the treatment of bisphosphonate-related osteonecrosis of the jaw. We conducted a systematic search of the PubMed, EMBASE, and Cochrane Library electronic databases, with no restrictions on language or year of publication. Search strategies were formulated using keywords and Boolean operators. The electronic search strategy retrieved 55 records. From 55 articles, 16 were selected for full-text review, and of these, 10 were ultimately included for data analysis in this review. Our findings show that treatment modalities including laser were associated with superior outcomes in terms of cure or improvement of bisphosphonate-related osteonecrosis of the jaw lesions as compared with conventional surgical and/or conservative drug therapy. It can be concluded that combined treatment with antibiotics, minimally invasive surgery (including Er:YAG laser surgery), and low-level laser therapy in the early stages of the disease should be the gold standard for bisphosphonate-related osteonecrosis of the jaw management.

KEYWORDS:

Bisphosphonate-related osteonecrosis of the jaw; Laser therapy; Neoplasm; Neoplasm metastasis; Osteoporosis

1.21 Photobiomodulation therapy: management of mucosal necrosis of the oropharynx in previously treated head and neck cancer patients

Joel B. Epstein, Paul Y. Song, Allen S. Ho,Babak Larian, Arash Asher, René-Jean Bensadoun - 2016

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COMMENTARY

Photobiomodulation therapy: management of mucosal necrosis of the oropharynx in previously treated head and neck cancer patients

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Abstract Necrosis of the oral mucosa following head and neck cancer radiation therapy presents considerable clinical management challenges. We report three cases of symptomatic persisting oral ulcerations where the addition of photobiomodulation therapy resulted in a rapid resolution of the oral lesions and in patient symptoms. These cases suggest that photobiomodulation may represent an adjunct to care of these difficult to manage complications in oncology.

Keywords Photobiomoduation · Low level laser therapy · Mucosal wound healing · Post-radiation mucosal necrosis

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Post radiation fibrosis and risk of oral mucosal ulceration and osteonecrosis are known risks of a high-dose radiation therapy, even with intensity modulated radiation therapy (IMRT) and proton beam techniques. Management of these lesions requires a confirmation of the absence of malignancy, promotion of conservative wound healing, and prevention of further injury; however, an effective management is challenging, and patients may suffer from persisting and symptomatic lesions and limited oral function.

Photobiomodulation (PBM) therapy, previously known as the low-level laser therapy (LLLT), has been shown to promote a repair of bone and connective tissue, by biostimulation of cellular repair, angiogenesis, and anti-inflammatory effects [1–6]. These features suggest a potential role for PBM in modulation/repair of chronic wounds that may be applicable in the management of oral soft tissue necrosis following head and neck radiation therapy (RT).

We treated three patients with chronic postradiation oral mucosal wounds with the addition of PBM therapy to clinical care. PBM therapy was provided twice weekly to the sites of necrosis following the methods as

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