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# Influence of low-level laser therapy on the healing of human bone maxillofacial defects: A systematic review

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ABSTRACT

*Purpose:* This systematic review evaluates the effectiveness of low-level laser therapy (LLLT) to enhance maxillofacial area bone repair.
*Methods:* A comprehensive search of studies published up to February 2017 and listed in PubMed/MEDLINE, Scopus, and Cochrane Library databases was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.
*Results:* The 15 selected studies evaluated a total of 374 patients (mean age, 28.5 years) who were treated with LLLT. Gallium-arsenide (GaAs) and gallium aluminium arsenide (GaAlAs) were the most commonly used devices, and LLLT parameters varied greatly. Wavelengths varied from 500 to 1000 nm. Tooth extraction, distraction osteogenesis, maxillary expansion, periodontal defects, orthodontic movement and maxillary cystic defects were evaluated. From the 15 selected studies, six evaluated bone repair (primary outcomes). Of these, four studies showed improvement in bone formation after using LLLT, two demonstrated improved results for only one follow up period, and one showed no additional benefits. The other 9 studies evaluated secondary parameters related to healing (secondary outcomes) in the maxillofacial area after applying LLLT, including anti-inflammatory, analgesic, and healing accelerator effects, and quality of life related to oral health. There were no adverse or negative effects of LLLT reported.
*Conclusion:* Within the limitation of this review, a possible improvement in bone density can be found when LLLT is applied postoperatively in maxillofacial bony defects. LLLT also seems to promote anti-inflammatory and analgesic effects and accelerate healing, as well as enhance quality of life related to oral health. However, LLLT use protocols need to be standardized before more specific conclusions can be drawn about this subject.


## 1. Introduction

The application of lasers has been considered a technological advance. They are used as an adjuvant because of their therapeutic effect and to biostimulate tissues. Low-level lasers, applied in the red spectral region and near infrared regions, promote cellular photobiomodulation effects and therapeutic responses induced by photochemical, photoelectric, and photoenergetic reactions (1).

Low-level laser therapy (LLLT) has been used by researchers in several health fields to accelerate wound healing in hard and soft tissues. In Medicine, this and other therapies have been applied for surgical scars [2,3], and for wrist and hand fractures [4]. In Dentistry, laser therapy has been clinically used and evaluated for post-surgical tooth extraction [5–8], after rapid maxillary expansion [1,9,10], after connective tissue graft harvesting in the mucosal palate [11], for treatment of jaw osteonecrosis [12,13], and for periodontal defects [14,15].

Bone has the capacity to regenerate and repair itself. However, this capacity may be impaired or lost depending on the size of the defect or the presence of certain diseases [16]. Thus, researchers have directed their efforts to find a therapy that can improve its healing ability. In vivo and in vitro studies have demonstrated that LLLT can improve bone healing by activating the osteogenic factors [17,18]. In addition, LLLT can also stimulate angiogenesis, a key component of bone formation during the early phase of healing [19,20], and induce cell proliferation [18,21]. Although positive results have been reported from clinical, animal, and in vitro and experiments, other studies that investigated the effects of LLLT on bone healing are contradictory [22,23]. Such discrepancies might be attributable to variations in the irradiation protocols and/or the experimental models used [18,24].

The application of LLLT to bone tissue has already been critically evaluated by some authors. Systematic reviews assessed its effect on in vitro proliferation and differentiation of bone cell lines [25], in vivo reduction

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of the duration of osseointegration in dental implants [26], treatment of peri-implantitis [27] or periodontitis [28–30], and accelerating orthodontic tooth movement [31,32]. LLLT was also systematically analyzed as a potential approach for management of osteonecrosis of the jaw [33].

Doeuk et al. [34] performed a systematic review to generally evaluate low level laser treatment in maxillofacial surgery in general way. However, there is no systematic review that evaluates the effect of this therapy in promoting the formation of bone tissue. Thus, the aim of this systematic review is to assess the null hypotheses that there are no differences between bone defects in maxillofacial areas treated with lasers compared to a control group. Published scientific studies were reviewed to assess the information available on this topic to provide a more detailed understanding of the clinical effects of LLLT on enhancing bone repair, and any other relevant circumstances regarding healing in Dentistry.

## 2. Material and Methods

This systematic review is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist structure [35] and in accordance with a model proposed in previously published reports [36,37]. Moreover, this study was registered on the international prospective register of systematic reviews (PROSPERO CRD42016041899). Two independent investigators (C.S.S. and H.F.F.O.) conducted an electronic search of PubMed/MEDLINE, Scopus, and Cochrane Library for articles published up to February 2017, using the following search terms: low-level laser therapy AND bone repair OR low-level laser therapy AND bone healing OR low-level laser therapy AND bone regeneration. These researchers manually searched for articles published in the following journals: Laser in Medical Science, Photomomedicine and Laser Surgery, and the Journal of Photochemistry and Photobiology B Biology. They also conducted a search of the non-peer reviewed reports and currently unpublished registered trials. All differences in choices between the investigators were analyzed by a third investigator (F.R.V.), and consensus was reached through discussion.

Studies were independently selected and classified as included or excluded by the two researchers (C.S.S. and H.F.F.O.), based on the title and abstract of the articles. Eligible studies included randomized controlled trials (RCTs), studies that compared LLLT and other treatments to promote bone formation, studies that had at least 10 participants, and studies published in English. Exclusion criteria were retrospective or prospective studies, in vitro or animal studies, computer simulations, case reports, studies that evaluated only one type of treatment without a comparison group, and published report reviews. A specific question was formulated based on the population, intervention, control, and outcome (PICO) criteria. The focused question was: "Is LLLT effective in promoting bone regeneration in the maxillofacial area?" Based on these criteria, the population was the participants who were treated with low-level laser therapy in the maxillofacial area to promote bone regeneration, the intervention was low-level laser therapy, and the comparison was control groups. The primary outcome was bone formation, and secondary outcomes were anti-inflammatory, analgesic, and healing accelerator effects, as well as quality of life related to oral health.

Data extracted from the articles were sorted as quantitative or qualitative by one of the researchers (C.A.A.L.) and then checked by two others (F.R.V. and V.S.E.B.). Any disagreements were resolved through discussion until consensus was reached. The quantitative and qualitative data were tabulated for ease of comparison (Tables 1, 2 and 3).

Two investigators (C.A.A.L. and V.E.S.B.) assessed the methodological quality of studies according to the Jadad scale, which ranges from 0 to 5, with studies that scored greater than or equal to 3 considered to be high quality [38] (Table 4). The Cochrane collaboration criteria for judging risk of bias were used to assess the quality of the studies included in the review.

The kappa coefficient value was calculated to determine inter-reader agreement in the study selection process for publications in the PubMed/MEDLINE, Scopus, and Cochrane Library databases.

**Table 1**
Qualitative characteristics of the studies related to patients.

| Author | Study design | Gender | Systemic conditions | Sample size | Mean of age (years) | Study site |
|---|---|---|---|---|---|---|
| Ferreira et al., 2016 | Groups evaluated in different subjects | F/M | Healthy | 14 | 11 | University |
| Zaky et al., 2016 | Groups evaluated in different subjects | Not described | Excluded as study subjects if they have any systemic disease that interferes with bone healing | 16 | 32 | Research Center |
| Abd-Elaal et al., 2015 | Split mouth | F/M | Healthy | 10 | 31 | Hospital |
| Domínguez et al., 2015 | Split mouth | F/M | Healthy | 10 | 13 | University |
| Garcia et al., 2015 | Groups evaluated in different subjects | F/M | Healthy | 39 | 8 | Hospital |
| Eslamian et al., 2014 | Split mouth | F/M | Healthy | 37 | 24 | University |
| Mozzati et al., 2012 | Split mouth | F/M | Patients waiting for liver transplantation | 20 | – | University |
| Mozzati et al., 2011 | Split mouth | F/M | Healthy | 10 | 22,5 | University |
| Angeletti et al., 2010 | Groups evaluated in different subjects | F/M | Healthy | 13 | 24 | University |
| AboElsaad et al., 2009 | Groups evaluated in different subjects | F/M | Healthy | 20 | 45 | Hospital |
| Angelov et al., 2009 | Groups evaluated in different subjects | F/M | Healthy | 60 | 48 | Particular Clinic |
| Chondros et al., 2009 | Groups evaluated in different subjects | F/M | Healthy | 24 | 49 | University |
| Youssef et al., 2008 | Split mouth | F/M | Healthy | 15 | 18,3 | University |
| Ozcelik et al., 2008 | Split mouth | F/M | Excluded patients with uncontrolled or poorly controlled systemic conditions | 22 | 40 | University |
| Fernando et al., 1993 | Split mouth | F/M | Healthy | 64 | 34 | Hospital |