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Effects of Laser Photobiomodulation on the Regeneration of Bone Defects Grafted with Bio-Oss® Xenograft: a Systematic Review of Animal Models

Efeitos da Fotobiomodulação a Laser na Regeneração de Defeitos Ósseos Enxertados com Xenograft Bio-Oss®: uma Revisão Sistemática de Modelos Animais

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Abstract

Photobiomodulation with low-power laser has stood out for its effects on metabolism, bone regeneration and its notable osteogenic potential. This study aimed to review the literature regarding the effectiveness of photobiomodulation with low-level laser therapy (LLLT) in inducing bone regeneration in sites grafted with Bio-Oss®, through experimental animal studies. It was a systematic review, based on a search performed in *PubMed/Medline*, *Google Scholar*, Capes Journals, *SciELO* and BIREME databases. Descriptors were selected from DeCS/MeSH and the PICOS strategy was applied. Experimental studies published from 2012 to 2023 were included, according to the PRISMA parameters, registered in the PROSPERO platform. The SYRCLE risk of bias tool was used. Using the search strategy, 1352 articles were identified, and five were included in this qualitative synthesis. Despite the divergence observed in the laser dosimetry protocols adopted by the studies, it was evident that laser photobiomodulation associated with the use of Bio-Oss® promotes bone density gains and a considerable increase in the amount of mineralized tissue in bone defects induced in animals. In addition, the use of laser alone has contributed to an improvement in bone formation in non-grafted sites. The data presented show a potential for improvement in the bone reconstruction process by associating photobiomodulation with low-level laser with the application of the Bio-Oss® inorganic bovine bone xenograft.

Keywords: Low-Level Laser Therapy. Photobiomodulation Therapy. Xenografts. Bio-Oss.

Resumo

A fotobiomodulação com laser de baixa potência tem se destacado pelos seus efeitos no metabolismo, na regeneração óssea e por seu notável potencial osteogênico. Este estudo teve como objetivo revisar a literatura sobre a eficácia da fotobiomodulação com laserterapia de baixa potência (LLLT) na indução da regeneração óssea em locais enxertados com Bio-Oss®, por meio de estudos experimentais em animais. Trata-se de uma revisão sistemática, baseada em busca realizada nas bases de dados PubMed/Medline, Google Acadêmico, Periódicos Capes, SciELO e Bireme. Os descritores foram selecionados no DeCS/MeSH e aplicada a estratégia PICOS. Foram incluídos estudos experimentais publicados de 2012 a 2023, segundo parâmetros PRISMA, cadastrados na plataforma PROSPERO. Foi utilizada a ferramenta de risco de viés SYRCLE. Utilizando a estratégia de busca, foram identificados 1.352 artigos, e cinco foram incluídos nesta síntese qualitativa. Apesar da divergência observada nos protocolos de dosimetria do laser adotados pelos estudos, ficou evidente que a fotobiomodulação laser associada ao uso do Bio-Oss® promove ganhos de densidade óssea e aumento considerável na quantidade de tecido mineralizado em defeitos ósseos induzidos em animais. Além disso, o uso isolado do laser contribuiu para uma melhora na formação óssea em locais não enxertados. Os dados apresentados mostram potencial de melhoria no processo de reconstrução óssea através da associação da fotobiomodulação com laser de baixa intensidade com a aplicação do xenoenxerto ósseo bovino inorgânico Bio-Oss®.

Palavras-chave: *Terapia com Luz de Baixa Intensidade. Terapia de Fotobiomodulação. Xenoenxertos. Bio-Oss.*

1 Introduction

Procedures using bone grafts are currently largely employed, with approximately 2.2 million performed per year all over the world.[1] Among the grafting materials used for bone regeneration, autologous bone is considered the 'gold standard' since it has the properties necessary for bone regeneration, in terms of osteoconduction, osteoinduction and osteogenesis combined.[2,3] However, its collection is associated with various complications, including hematomas, damage to anatomical structures, infections, pain, and unpredictable graft reabsorption.[2-6] Considering this, inorganic bovine bone is a grafting material that has also been explored in the dentistry field due to its properties, characteristics, and similarity to the human bone.[2]

Bio-Oss® (Geistlich Biomaterials GmbH, Baden-Baden, Germany) is a deproteinized and sterilized mineral bovine hydroxyapatite with a porosity of 75% to 80%, and with crystal size of approximately 40nm (400x100Å) in the shape of granules and cortical and trabecular blocks.[7,8] It has satisfactory osteoconductive properties, since it allows the neoformation of capillaries, perivascular tissue, and migration of cells from the receptor region through a tridimensional structure.[9,10] According to Galindo-Moreno *et al*., (2013) Bio-Oss® particles integrate themselves into the newly formed bone structure, preserving its volume in the long term. The material made of deproteinized bovine bone cells (DPBB) is obtained from samples of cortical and cancellous bone, and it is commercially available in two particle sizes, 0.25 - 1 and 1 - 2 mm.[11]

In order to recover the compromised anatomy and function, complementary therapies can be used, together with drafts, to reduce the bone healing time and, possibly, reduce complications in the regenerative process. Photobiomodulation Therapy (PBM), using low-level laser therapy (LLLT), has been recommended in tissue regeneration processes due to its photochemical, photophysical and photobiological effects caused by the laser light source, having as advantages the modulation of the inflammation, stimulation of healing and pain control.[12-14] Moreover, it stands out for its effects on the metabolism and bone regeneration, with great osteogenic potential, and for being a non-invasive and relatively inexpensive method, without collateral damage that may interfere in the individual's health.[15,16] Accordingly, studies showed positive effects of PBM on the acceleration of healing in larger bone defects, in the initial and final stages of recovery.[17,18] Understanding the importance of using bone substitutes in regions with bone loss that limits the rehabilitation process is essential for the development of innovation in the field. .

Therefore, this systematic review aims to compile scientific evidence regarding the effectiveness of photobiomodulation with **LLLT** in inducing bone regeneration in sites grafted with Bio-Oss®, assessed in experimental studies performed on animal samples.

2 Material and Methods

2.1 Study Design

This is a systematic review of experimental studies that was conducted in April 2023 according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) methodology, used to assist in the construction of systematic reviews and meta-analyses.[1] This review was submitted to the PROSPERO platform and registered under protocol number CRD42022345570.

2.2 Search Strategy

Only scientific articles available in electronic databases such as *PubMed/Medline*, *Google Scholar*, Capes Journals, *SciELO* and BIREME were selected. The following search strategy was used in all databases: ("Low-Level Light Therapy" OR "LLLT" OR "Laser Biostimulation" OR "Laser Phototherapy" OR "Low Level Laser Therapy" OR "Photobiomodulation Therapy") AND ("Bio-Oss" OR "BioOss" OR "Heterografts" OR "Heterograft" OR "Xenograft" OR "Xenografts"). Records were screened by the title, abstract and full text by two independent investigators. Studies included in this review matched all the predefined criteria according to PICOS ("Population", "Intervention", "Comparison", "Outcomes", and "Study design"), as shown in Table 1.

Table 1 - Inclusion and exclusion criteria according to PICOS

Parameter	Inclusion Criteria
Population	Rats or rabbits
Intervention	Association of PBM with LLLT in filling bone defect with Bio-Oss®
Comparison	Filling bone defects with Bio-Oss® only, autologous bone or a blood clot only
Outcomes	Does the association of PBM with LLLT bring benefi in bone regeneration using the Bio-Oss® graft?
Study design	Experimental studies in animals
	Written in English and having performed histomorphometric analyzes on the sample. No publication date restrictions were imposed.

Source: research data.

2.3 Selection of studies

All the selected articles were tabulated in Microsoft Word (2010 version). In the first stage, two previously calibrated reviewers, A.A.C. and D.A.S.S. performed the search independently in the aforementioned databases. In case of disagreement between them, a third author was called (J.S.V.N). For the reading of titles and abstracts, inclusion and exclusion criteria were applied. Duplicate articles were only considered once. The second stage consisted of reading and selecting full texts. The analysis of agreement between two reviewers in relation to the included studies was performed using Cohen's Kappa test, which exhibits the parameters mild (0.00 to 0.20), regular (0.21 to 0.40), moderate (0.41 to 0.60), high (0.61 to 0.80), and almost perfect (0.81 to 1.00). The value of Cohen's Kappa coefficient in the present study was >0.73, with an agreement classified as high.

2.4 Data Extraction and Data Analysis

The following study characteristics were collected in a Word document (2010 version): authors, year of publication, animal model characteristics (species, weight, age, number of animals, bone lesion characteristics), protocol of the photobiomodulation (type of laser, wavelength, output power, energy density, spot size, time, and sites of irradiation), description of the surgical intervention and application of the xenograft, and tests performed. Study quality was assessed by two investigators (A.A.C. and D.A.S.S.) using the Systematic Review Center for Laboratory animal Experimentation (SYRCLE) Risk of Bias tool, which is the adapted version for animal studies of the Cochrane Risk of Bias tool.[20] A meta-analysis was not performed due to heterogeneity in results and lack of original outcome data in the reviewed studies.

2.5 Outcome measures

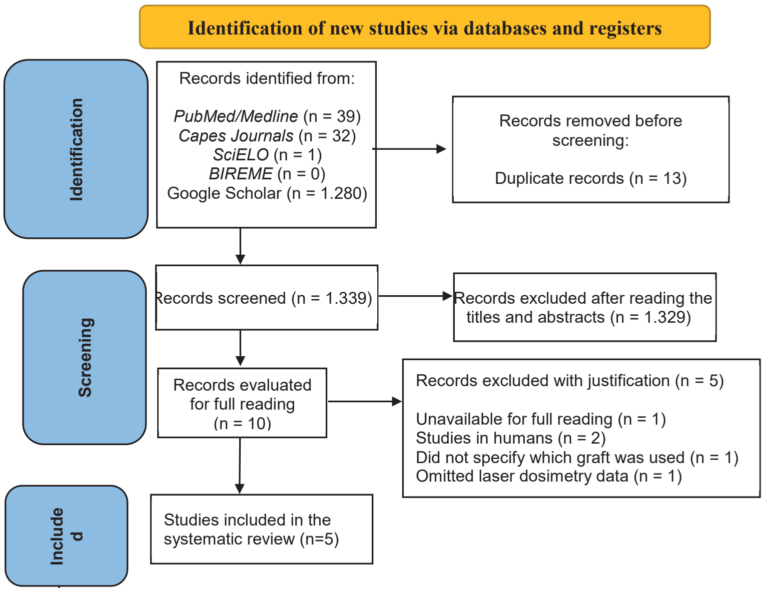
The primary outcome was the effect of laser photobiomodulation on bone regeneration of sites grafted with Bio-Oss® through histomorphometric evaluation. The protocol used and the tissue response to it were considered secondary outcome variables. A descriptive analysis of the studies was performed.

3 Results and Discussion

3.1 Study Selection

In the first stage, 1352 articles were identified in the online databases following the search strategy: 39 were found in *PubMed/Medline*, 32 in *Capes Journals*, 1 in *SciELO*, 0 in *BIREME* and 1.280 in *Google Scholar* gray literature. A total of 13 articles were excluded due to duplicity. One thousand three hundred and thirty-nine articles were excluded in the first stage after reading the titles and abstracts. Of the remaining 10 articles, 5 were excluded with the following justifications: 1 was unavailable for full reading, 2 were studies in humans (1 case report and 1 randomized controlled trial), 1 article did not specify which graft was used and 1 article omitted laser dosimetry data. Consequently, five studies were selected in the eligibility stage and were fully read. Figure 1 illustrates the search strategy performed.

Figura 1 - Article search strategy according to the outlined inclusion criteria. April 2023



Source: research data.

3.2 Risk of Bias

The SYRCLE tool was used, which assesses the risk of bias for animal studies (Table 2). This tool contains the following assessment categories: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias. Ten questions were applied to the articles included in the systematic review, whose answers can be "YES", which indicates low risk of bias, "NO", which indicates high risk of bias, and "UNCERTAIN", which indicates uncertain risk of bias.

Table 2 - Evaluation of the risk of bias of articles using the SYRCLE tool. Search period: April 2023

Author/Year	Selection BIAS			Performance BIAS		Detection BIAS		Attrition BIAS	Reporting BIAS	Other
	1	2	3	4	5	6	7	8	9	10
Torquato *et al.* 2021[21]	S	S	?	S	?	?	S	N	S	S
De Oliveira *et al.* 2018[22]	S	S	?	S	?	?	S	S	S	S
Cunha *et al.* 2014[23]	S	S	?	S	?	?	S	S	S	S
Buchaim *et al.* 2022[24]	S	S	?	S	?	?	?	S	S	S
Pomini et al. 2023[25]	S	S	?	S	?	?	?	S	S	S

S - YES (low risk of bias); N - NO (high risk of bias); ? - uncertain (uncertain risk of bias); 1- Allocation sequence: In all articles the case and control groups were randomly allocated; 2- Baseline characteristics: In all articles, the case and control groups underwent surgical intervention, therefore, all of them had an induced bone defect at the beginning of the experiment; 3 - Allocation concealment: No article described whether there was concealment in the allocation of case and control groups; 4 - Random housing: In all articles, the case and control groups were randomly distributed among housing units, being exposed to the same conditions; 5 - Blinding: No article exposed whether the researcher was aware of which animals received which type of intervention; 6 - Randomized outcome evaluation: No article described whether the outcome evaluation of the case and control groups was performed randomly; 7 - Blinding: All articles, except two, described that the researcher was not aware of which animals had received which type of intervention in the evaluation of the outcome; 8 - Incomplete outcome result: Only one article reported sample deaths (Torquato *et al.,* [21] reports the death of 4 animals, with no apparent cause); 9 - Selective outcome reporting: In all studies, no selective reporting of outcomes whose results were significant was performed; 10 - Other sources of bias: No article presented other sources of bias.
Source: research data.

The results on the methodological quality of the studies are presented in Table 2. All articles can be classified as having low risk of bias.

3.3 Study characteristics

While evaluating the five included articles, it could be noticed that all of them were performed in Brazil. These were published between the years 2014–2023. The total population of test subjects was 314 male rats, divided into control groups with a total of 108 animals and intervention groups with a total of 206 animals. The control group animals were always characterized as "coagulum", "blod clot" or "control group", while the intervention groups contained animals that underwent treatment.

The periods chosen for analysis ranged from a minimum of 7 days[21] to a maximum of 90 days.[22] There seems to be a preference for studies performed 30 days after the intervention, with 2 articles falling into this category,[22,23] while 3 articles evaluated results before and after this period.[21,24,25]

Considering all the articles included in this review, the application of PBM in bone lesions was verified in all the 5 articles, 4 involving the calvaria,[21,23,24,25] and 1 in the mandibular branch.[22]

The use of deproteinized inorganic bovine bone (Bio-Oss®) and its association with low-level laser photobiomodulation was observed in all the studies. It is worth mentioning that in the studies by Buchaim et al., (2022)[24] and Pomini et al., (2023)[25], Bio-Oss® was associated with a heterologous fibrin biopolymer, while in all the other studies it was used in its conventional form. The information cited can be better viewed in Table 3.

Table 3 - General study characteristics. Search period: April 2023

Author Year	Population	Methodology	Results	Outcomes
Torquato *et al.* 2021[21]	68 adult male rats (Rattus norvegicus, albinus, Wistar), 90 days old, and approximately 300 g in weight.	The animals were randomly assigned to the following experimental groups: **C** (blood clot); **B** (Bio-Oss®); **L** (Low-level laser therapy); **B+L** (Bio-Oss® + Low-level laser therapy);	Proportion of the area of new bone formation within the defect (%) after 7, 30 and 60 days, respectively. **C** (0.03 ± 0.07/0.25 ± 0.1/0.37 ± 0.97); **B** (0 ± 0/0.06 ± 0.04/0.19 ± 0.07); **L** (0 ± 0/0.28 ± 0.22/0.39 ± 0.13); **B+L** (0 ± 0/0.14 ± 0.09/0.22 ± 0.06); At 60 days, groups **L** and **C** had the highest proportion of new bone formation. However, the **B+L** group had more than twice as much bone neoformation as the **B** group in 30 days.	If a faster regeneration is necessary, PBM could be applied for short-term results.
De Oliveira *et al.* 2018[22]	90 adult male rats (Rattus norvegicus albinus, Holtzman) with approximately 3-months age, with body weights between 200 and 250 g.	The animals were randomly divided into two groups according to the use of laser irradiation: a **control group** and a **laser group**. Each of these groups was subdivided into three groups according to the type of biomaterial used: **COA** (Coagulum); **DBB** (Deproteinized bovine bone/Bio-Oss®) **HA/bTCP** (biphasic ceramic comprising hydroxyapatite and b-tricalcium phosphate);	The **test group** presented higher amounts of bone in the grafted site than did the **control group** for all subgroups and study periods, except for the **HA/bTCP** subgroup at 30 days. Furthermore, the grafted sites in subgroups **DBB** and **HA/bTCP** of the test group had less amount of biomaterial than those in the control group at 60 days.	The use of LLLT stimulated bone healing with the use of osteoconductive biomaterials and the formation of bone tissue in non-grafted sites.
Cunha *et al.* 2014[23]	60 male Wistar rats (Rattus norvegicus) weighing between 250 and 300g.	The animals were randomly assigned to the following experimental groups: **C** (control—filled with blood clot); **LLLT** (low-level laser therapy); **AB** (autologous bone); **ABL** (autologous bone + low-level laser therapy); **OB** (inorganic bovine bone); **OBL** (inorganic bovine bone + low-level laser therapy);	The groups irradiated with laser, **LLLT** (47.67% ± 8.66%), **ABL** (39.15% ± 16.72%), and **OBL** (48.57% ± 28.22%), presented greater area of new bone formation than groups **C** (9.96% ± 4.50%), **AB** (30.98% ± 16.59%), and **OB** (11.36% ± 7.89%), which were not irradiated. Moreover, they were significantly better than group **C**.	The LLLT accelerated the healing of bone defects and the resorption of the graft material particles.

Author Year	Population	Methodology	Results	Outcomes
Buchaim *et al.* 2022[24]	36 male Wistar rats (Rattus norvegicus) aged 90 days, body mass of approximately 390g.	The rats were randomly assigned to the following experimental groups: **BC** (defect filled with blood clot); **BC-PBM** (defect filled with blood clot associated with PBM); **XS** (defect filled with the association of the xenogeneic biomaterial with fibrin biopolymer); **XS-PBM** (defect filled with the association of the xenogeneic biomaterial with fibrin biopolymer associated with PBM therapy);	At 14 days, the **BC-PBM** group showed the highest percentage of new bone formation (8.93 ± 1.42) with a significant difference in relation to the **BC**, **XS** and **XS-PBM** groups (5.89 ± 0.85, 4.31 ± 0.49 e 6.01 ± 1.42, respectively). In the 42-day postoperative period, the **BC-PBM** and **XS-PBM** groups had a higher percentage of new bone deposition, with a significant difference in relation to the groups with the same treatment (11.22 ± 2.10 and 9.47 ± 1.45, respectively) and without PBM (**BC** 7.06 ± 1.10 and **XS** 5.82 ± 0.73, respectively).	Laser PBM enabled the biomodulation of the inflammatory process, with a more organized deposition of collagen fibers in the defect area and, consequently, a more homogeneous bone conformation and an improvement in the formation of new bone.
Pomini et al. 2023[25]	60 male Wistar rats (Rattus norvegicus) aged 90 days, weighing approximately 320g.	The animals were randomly assigned to the following experimental groups: **BCL** (defect filled with blood clot associated with PBM therapy); **HF** (defect filled with heterologous fibrin biopolymer); **HFL** (defect filled with heterologous fibrin biopolymer associated with PBM therapy); **PHF** (defect filled by deproteinized bovine bone particles incorporated into heterologous fibrin biopolymer); **PHFL** (defect filled by deproteinized bovine bone particles incorporated into heterologous fibrin biopolymer associated with PBM therapy);	At 14 days, the bone volume was significantly higher in the groups PHF, 10.45 ± 3.31 mm^3 and PHFL, 9.94 ± 1.51 mm^3 and lower in the groups BCL/HF/HFL, mean 4.51 ± 1.25 mm^3. At 42 days, the bone volume significantly increased in the groups that received BCL (10.78 ± 3.27 mm^3), HFL (8.44 ± 1.68 mm^3) and PHFL (15.35 ± 2.09 mm^3). Laser application and did not show significant differences in the HF groups (4.83 ± 1.17 mm^3) and PHF (13.32 ± 2.33 mm^3). Percentagewise, the PHFL group showed 23% greater than BCL and 57% greater than HFL.	The use of laser radiation was capable of inducing functional bone regeneration through the synergistic combination of biomaterials.

Source: research data

3.4 Laser parameters

It was not possible to obtain a standard laser protocol among the analyzed studies, as they differ in all the parameters, except for the emission mode, which was continuous wave (CW) in all the studies. Regarding the type of laser, all the studies used GaAlAs (gallium-aluminum-arsenide) lasers. The wavelength used in the studies covered a wide range of values, from 660 to 830 nm. The output power used in the studies ranged from 30 to 100 mW. As for the parameters of spot size and irradiance, each study presented different data, making it impossible to obtain a gradation. The energy density used in the studies ranged from 6.20 to 354 J/cm2, with each study having a different value from the other. The dosimetry parameters can be evaluated in Table 4.

Table 4 - Laser dosimetry parameters, described in each study

Laser Parameters	Laser Type	Wavelength (nm)	Output Power (mW)	Spot Size (cm^2)	Energy Density (J/cm^2)	Irradiance (W/cm^2)	Emission Mode
Torquato et al. 2021[21]	GaAlAs	660	30	0.04	45	0.75	CW
De Oliveira et al. 2018[22]	GaAlAs	808	100	0.0028	354	35.38	CW
Cunha et al. 2014[23]	GaAlAs	780	100	0.05	210	2	CW
Buchaim et al. 2022[24]	GaAlAs	830	30	0.116	6.20	0.258,62	CW
Pomini et al. 2023[25]	GaAlAs	808	100	0.028	214.29	3.57	CW

Source: research data.

The present study focused on conducting a systematic literature review, to assess the effectiveness of photobiomodulation with LLLT in inducing bone regeneration in sites grafted with Bio-Oss®.

As beforementioned, autologous bone graft is the 'gold standard' for bone defect maintenance, since it provides osteogenic cells, extracellular matrix and molecular signs of bone induction and differentiation.[26,27] However, its collection leads to a secondary donor surgical site, resulting in some morbidity to the patient.[28]

Tapety *et al.*[29] and Shamsoddin *et al.*[30] describe that Bio-Oss® graft is the most reliable xenograft biomaterial, widely used in Dentistry due to its capacity to promote sustainable, predictable, and adequate bone formation with lower infection levels, even in the early stages of new bone formation. Despite its excellent osteoconduction,[6,17] it lacks osteoinductive properties, which has motivated researchers to find ways to improve its *in vivo* behavior even more.[31] In the light of this context, we performed a systematic review of literature in order to clarify the benefits of associating PBM using laser light with Bio-Oss® xenograft in healing bone defects induced in animals.

Rats represent 95.48% of all the animals used in the evaluated studies, which demonstrate a preference for these animals in the empirical study, due to the easy handling because of their small size, and cost of acquisition, being generally chosen for preclinical studies that involve bone reconstruction and regenerative processes in general.[32,33]

However, literature reports that the skeletal system of rats tends to differ from the human's for not having a Haversian system and shows a limited bone remodeling.[34] These deficiencies create barriers in the use of this model while assessing bone lesions. But rabbits show a skeletal system similar to humans, so they can be considered more appropriate to be used in these cases.[34,35]

There are many advantages in the use of rabbit models. First, the presence of the Haversian system in their skeletal system. Second, its cortical reconstruction activity is similar to the humans'. Moreover, the transformation and maturation of the rabbit bone are faster than the rat's, which may lead results more relevant to the clinical practice.[36] For this, we suggest that studies related to the subject discussed here, carried out in rabbits or larger animals, would have greater scientific value in justifying a possible synergistic effect of laser in the regeneration of bone defects in humans.

The use of male animals in all the examined studies suggests a gender preference for test subjects. There are grounds for performing studies with male rats, because it avoids the possible influence of female inhibitory hormones on the bone tissue, in addition to the lower risk of fracture and larger bone mass.[37,38]

During this review, different laser dosimetry elements were observed. Each article used a specific wavelength: out of the five evaluated studies, four used near infrared[22,23,24,25] and only one used red laser.[21] While verifying that PBM acts directly on the mitochondria, the wavelength parameter seems to have a great influence on the therapeutic process, with visible wavelengths (red) activating the mitochondrial respiratory chain and the non-visible wavelengths (infrared) acting on the cell membrane. The infrared spectrum is the most used one in reconstructive processes, since it presents lower energy loss while penetrating the tissue, about 37% reaching 2 mm deep.[30,39]

As for the bone neoformation rate, De Oliveira *et al.*[22] reports that the use of osteoconductive biomaterials can induce better bone formation in grafted sites than in non-grafted sites, since the biomaterials that are not reabsorbed fill in possible bone gaps that may eventually appear. Buchaim *et al.*[24], found more bone in the group without biomaterial (BC-blood clot) or in the group with laser irradiation (BC-PBM) and no graft, which suggests a significant benefit of PBM in the formation of new bone. On the other hand, micro-computerized tomography showed that, in the groups that used Bio-Oss®, there was a larger amount of mineralized tissue, which clinically suggests that, if the preservation of the original bone structure is the objective of the treatment in the long term, the use of a biomaterial, such as Bio-Oss®, becomes recommended.[21]

Regarding the energy density applied to the tissue during PBM, all the studies differ in their protocols, making it impossible to compare them. However, one specific study stood out when describing the application an of energy density of 354 J/cm^2 on the irradiated tissue.[22] This amount of energy applied could be justified by the small site to be irradiated (rat's mandible branch) and consequently by the spot size of the device of Ø ~600µm (0.002826 cm²), and as reported by the authors, 1J/point was used. Despite the positive outcome reported in the study, a meta-analysis performed by Cronshaw *et al.*[40], described that factorial statistical analyses identified an association between applications of laser therapy in smaller optical surfaces and a general lower level of clinical success reported in the treatment of superficial and deep targets.

The association of PBM as an enhancer of bone formation has been very widespread in the literature. However, there is a limitation regarding the performance of clinical studies in this aspect, due to various factors. Despite the notable effectiveness of grafting with Bio-Oss®, it still presents a high cost, both for application in clinical studies, and for the day-to-day of some professionals. Moreover, even if researchers develop a clinical study in this field, it is not feasible to perform a collection and subsequent histological evaluation of the newly formed tissue, due to the exposure of the patient to various surgical times, which may even affect the results obtained.

In addition, it could be observed a notable difference in the standardization of the methodologies described in the study with photobiomodulation with low-level laser therapy, and the absence of important data, as power density, energy per point, beam area, spot area and application time. The variability of parameters seems to be common in studies with PBM, raising doubts regarding its reproducibility and, consequently, the production of satisfactory and safe results. On the other hand, despite not having standardization for the dosimetry applied, there was a consensus among the studies on the outcome obtained.

4 Conclusion

At the end of this systematic review, it can be verified that the data presented in recent literature showed a potential to improve the bone reconstruction process by associating photobiomodulation with LLT with the application of Bio-Oss® inorganic bovine bone xenograft. However, due to the significant variability observed in low-power laser irradiation protocols, it is suggested that new experimental studies be conducted to establish a standard protocol that can be used in future laboratory and clinical settings.

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