

Review Article



Does photobiomodulation on the root surface decrease the occurrence of root resorption in reimplanted teeth? A systematic review of animal studies

Theodoro Weissheimer ,¹ Karolina Frick Bischoff ,² Carolina Horn Troian Michel ,¹ Bruna Barcelos Só ,¹ Manoela Domingues Martins ,¹ Matheus Albino Souza ,² Ricardo Abreu da Rosa ,¹ Marcus Vinícius Reis Só ¹

¹Department of Conservative Dentistry, School of Dentistry, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil

²Department of Restorative Dentistry, School of Dentistry, University of Passo Fundo, Passo Fundo, RS, Brazil



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*Correspondence to

Theodoro Weissheimer, DDS, MSc

Department of Conservative Dentistry, Federal University of Rio Grande do Sul - UFRGS,

2492 Ramiro Barcelos Street, Porto Alegre, RS 90035-003, Brazil.

Email: theodoro.theo@hotmail.com

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ABSTRACT

This review aimed to answer the following question “Does photobiomodulation treatment of the root surface decrease the occurrence of root resorption in reimplanted teeth?” Electronic searches were performed in the MEDLINE/PubMed, Cochrane Library, Scopus, Web of Science, Embase, and Grey Literature Report databases. Risk of bias was evaluated using SYRCLE Risk of Bias tool. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) tool was used to assess the certainty of evidence. In total, 6 studies were included. Five studies reported a reduced occurrence of root resorption in teeth that received photobiomodulation treatment of the root surface prior to replantation. Only 1 study reported contradictory results. The photobiomodulation parameters varied widely among studies. GRADE assessment showed a low certainty of evidence. It can be inferred that photobiomodulation treatment of the root surface prior to replantation of teeth can reduce the occurrence of root resorption. Nonetheless, further clinical studies are needed.

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INTRODUCTION

Traumatic dental injuries (TDIs) comprise 5% of all injuries in children and young adults [1]. In 2018, the worldwide prevalence of TDIs was 15.2% for permanent teeth and 22.7% for primary teeth, with an incidence rate of 2.82 per 100 person-years [2]. TDIs exert a significant negative impact on the oral health-related quality of life of children and adolescents [3], and there are several risk factors associated with their occurrence, such as male sex, age [4,5], greater overjet, inadequate lip coverage, anterior open bite [4-6], overweight, a previous history of TDI, tongue piercing, the use of alcoholic beverages, and sports practice [5].

Among the injuries that can occur following trauma, avulsion is one of the most serious dental injuries. According to the International Association of Dental Traumatology (IADT),

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ORCID iDs

Theodoro Weissheimer 
<https://orcid.org/0000-0001-6810-1877>
Karolina Frick Bischoff 
<https://orcid.org/0000-0001-7805-5253>
Carolina Horn Troian Michel 
<https://orcid.org/0000-0001-8376-7589>
Bruna Barcelos Só 
<https://orcid.org/0000-0002-8144-9760>
Manoela Domingues Martins 
<https://orcid.org/0000-0001-8662-5965>
Matheus Albino Souza 
<https://orcid.org/0000-0002-9412-3807>
Ricardo Abreu da Rosa 
<https://orcid.org/0000-0001-6568-7403>
Marcus Vinicius Reis Só 
<https://orcid.org/0000-0002-1393-5900>

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in situations of tooth avulsion, replantation should be the treatment of choice, with only a few situations precluding this procedure, such as severe caries or periodontal disease, an uncooperative patient, severe cognitive impairment requiring sedation, severe medical conditions such as immunosuppression, and severe cardiac conditions [7]. Nevertheless, the main complications associated with tooth avulsion are external inflammatory root resorption, with a prevalence of 23.2%, and/or replacement resorption, with a prevalence of 51% [8].

External inflammatory root resorption develops following injuries to the pulp and root cementum, and it is associated with the presence of bacterial infection beyond the damaged root surface, which acts a stimulus to clastic cells, contributing to a rapid progression of the resorptive process [9]. Replacement resorption is associated with severe damage to the root cementum (when more than 20% of the root surface is affected, resulting in the exposure of the root dentin) [10,11], the resorptive action of osteoclastic cells, and the subsequent deposition of bone tissue by osteoblastic cells [12].

To date, the only treatment recommended by the IADT for reducing the occurrence of root resorption is the use of systemic antibiotics [7]. Specifically, doxycycline is recommended due to its antimicrobial, anti-inflammatory, and antiresorptive effects [7]. However, the risk of tooth discoloration when using tetracycline or doxycycline, especially in patients under 12 years old [13], and the risk of bacterial resistance to the use of antibiotics [14] are major drawbacks related to the use of systemic antibiotics. Therefore, it seems to be necessary to investigate other treatment modalities in order to reduce the occurrence of root resorption.

Some studies have tested the local application of different substances, such as a gel containing enamel matrix proteins [15], sodium alendronate [16], and propolis and acidulated phosphate sodium fluoride [17], in attempts to reduce the occurrence of root resorption following tooth replantation. However, none of these experimental therapies were effective [15-17]. More recently, researchers have proposed directly applying photobiomodulation to the root surface prior to tooth replantation, aiming to induce morphological changes on the root surface to improve cell adhesion, proliferation, and the subsequent attachment of periodontal tissue [18-20], in addition to an antimicrobial effect [21-23]. These findings led to the assumption that the irradiation of root surfaces prior to replantation could decrease the incidence of root resorption, improving the prognosis of replanted avulsed teeth.

Considering the severe implications of tooth avulsion and the need to investigate alternative therapies to the use of systemic antibiotics, as well as the growing number of studies investigating the use of photobiomodulation on the root surface prior to tooth replantation, the present systematic review aimed to investigate the available evidence by addressing the following question: “Does photobiomodulation treatment of the root surface decrease the occurrence of root resorption in reimplanted teeth?”

MATERIALS AND METHODS

This systematic review followed the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [24], and the protocol was registered in the PROSPERO database (CRD42022349891).

Search strategy

Searches were independently conducted up to June 2022, without year or language restriction, by 2 examiners (T.W. and K.F.B.) in the following electronic databases: MEDLINE/PubMed, Cochrane Library, Scopus, Web of Science, Embase, and Grey Literature Report (grey literature search). The electronic search strategy employed the most cited descriptors in this field according to previous publications, combining Medical Subject Heading (MeSH) terms and text words (tw.). The Boolean operators “AND” and “OR” were applied to combine the terms and create a search strategy. **Supplementary Table 1** presents the search strategies for each database. Additional manual search of the reference lists of the selected studies was performed. All articles selected were imported into the Mendeley reference manager (Mendeley Ltd., London, UK) to catalog the references and facilitate the exclusion of duplicates.

Eligibility criteria

The eligibility criteria were selected according to the PICOS strategy [25-27], as follows:

- Population (P): extracted teeth in animal models;
- Intervention (I): photobiomodulation treatment of the root surface prior to replantation;
- Comparison (C): control group;
- Outcome (O): root resorption;
- Study design (S): studies in animal models.

Studies in which photobiomodulation was not applied directly in the root surface, studies in which root resorption was simulated by means of radicular grooves, studies in which animals presented systemic diseases; studies that evaluated other oral diseases (*e.g.*, periodontitis); systematic reviews with and without meta-analysis, reviews, letters, opinion articles, and conference abstracts were excluded.

Selection of the studies

Study selection was performed by 2 independent authors (T.W. and K.F.B.), who conducted the database search, removed duplicates and screened titles and abstracts. If the title and abstract were not sufficient to determine inclusion, the full text was read for a final decision. After that, potentially eligible studies were then read for full-text assessment using the PICOS criteria. Divergences between reviewers were solved by discussing with a third author (C.H.T.M.).

Data extraction

Two authors (T.W. and K.F.B.) performed data extraction independently. Disagreements were solved by discussing with a third author (C.H.T.M.). The following data were extracted from the studies: authors' names, year of publication, country of first author, animal model, sample size, investigated groups, samples per group, teeth evaluated, photobiomodulation protocol, additional procedures, extra-alveolar time prior to replantation, storage medium, time of outcome assessment, method of root resorption analysis, outcomes, and main findings. In case of missing information, the authors were contacted 3 times by e-mail at intervals of 1 week.

Qualitative assessment

The Systematic Review Centre for Laboratory Animal Experimentation Risk of Bias (SYRCLE RoB Tool) was used to assess the quality of the selected studies [28]. The SYRCLE RoB Tool evaluates 10 domains: selection bias, performance bias, detection bias, attrition bias,

reporting bias, and other sources of bias. For each domain, a study was deemed to have a high risk of bias (if it did not meet 1 or more criteria); an unclear risk of bias (if it did not present the necessary data or partially met 1 or more criteria), or a low risk of bias (if all the requirements were met).

Certainty of evidence

To assess the certainty of the evidence of the included studies, an adapted methodology of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool was used [29]. The GRADE tool has 5 domains that can be downgraded to reduce the assessment of the quality of the evidence. The following domains were included in this study: 1) risk of bias; 2) inconsistency; 3) indirectness; 4) imprecision; and 5) other considerations: assessment of publication bias, significant effect, plausible confounding, and dose-response gradient.

RESULTS

Study selection

The flow diagram of the search strategy is displayed in **Figure 1**.

The initial screening of databases resulted in 244 studies, with 46 excluded for being duplicates. From the analysis of the titles and abstracts of the 198 eligible papers, 9 studies

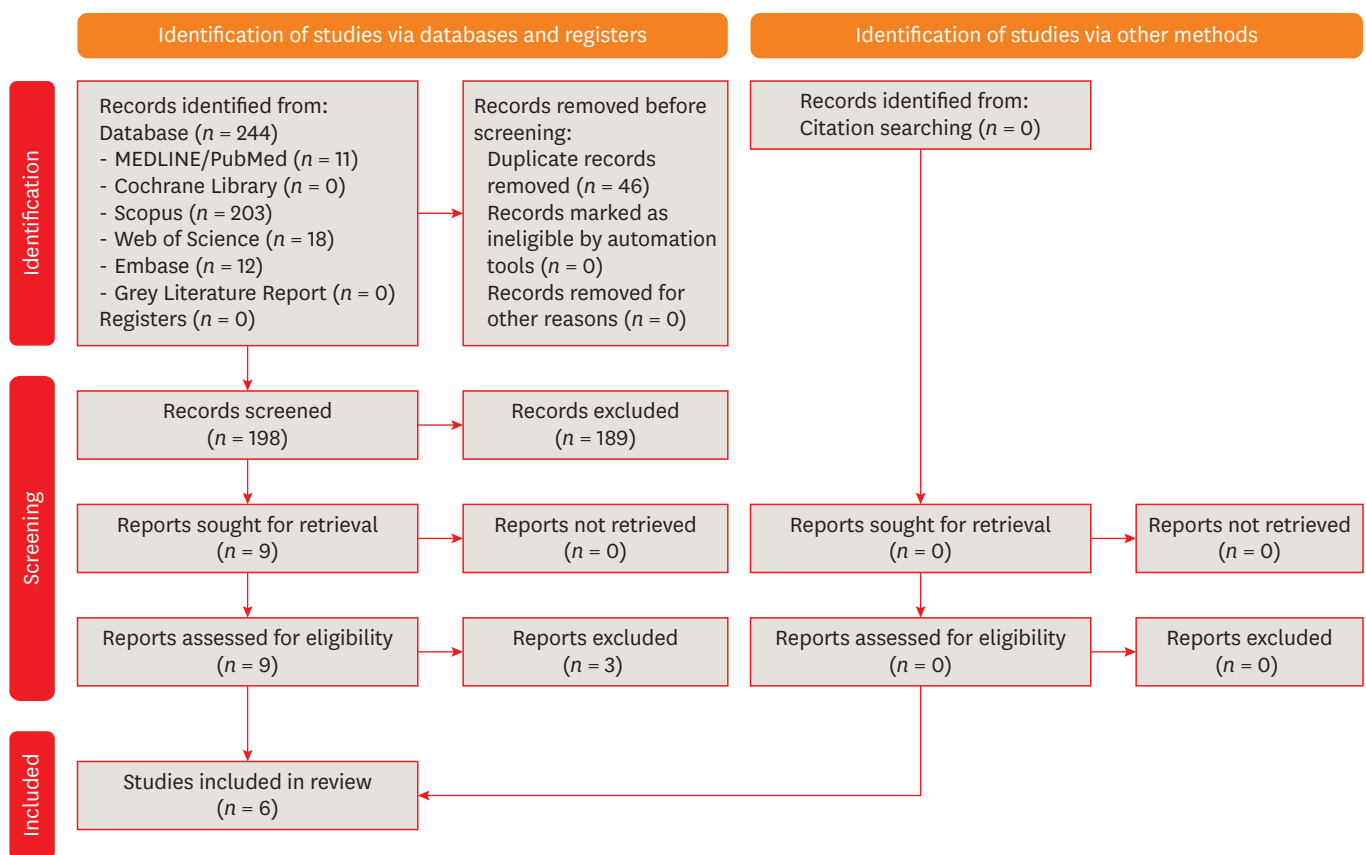


Figure 1. Systematic search process according to the PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analysis.

were selected for full-text reading [30-38]. After full-text reading, 3 studies were excluded [30-32]: 1 study for having performed simulated grooves in root resorption [30], 1 study for not having evaluated the occurrence of root resorption [31], and 1 study for not having applied photobiomodulation directly to the root surface [32].

Finally, 6 studies were included in the present systematic review [33-38].

Data extraction

The characteristics of the included studies are presented in **Table 1**.

All included studies performed their evaluation in maxillary incisors of rat models [33-38]. The photobiomodulation protocol, additional procedures, and storage medium varied among studies. The extra-alveolar time prior to replantation ranged from 0 minutes (immediate replantation) to 60 minutes.

Three studies assessed the outcomes after 15, 30 and 60 days [34-36]; 2 studies after 60 days only [33-38]; and one study after 15 and 30 days [37]. Moreover, root resorption was studied using histomorphometric [33,34,37]; radiographic [34,38]; histological [34,36,38]; and histomorphological [35] methods.

Five studies reported that the application of photobiomodulation on the root surface, prior to replantation, reduced the occurrence of external root resorption [34-38]. Only 1 study did not find any significant differences between the experimental and control groups [33]. Additionally, 1 study found that photobiomodulation in the buccal and palatal mucosa every 48 hours for 15 days resulted in a higher incidence of external inflammatory root resorption and ankylosis [36].

Qualitative assessment

Figure 2 presents the risk of bias assessment of the included studies [39].

The domains “allocation concealment,” “random housing,” “blinding of participants,” and “random outcome assessment” were classified as having a high risk of bias in all studies. In the domain “baseline characteristics,” all studies were classified as presenting an unclear risk of bias. In the domain “random sequence generation,” 1 study was classified as having a high risk of bias [34], and the other studies as having an unclear risk of bias. In the domain “blinding of outcome assessors,” 1 study presented a high risk of bias [36], and the other studies a low risk of bias. All studies showed low risks of bias in the domains “incomplete outcome data,” “selective reporting,” and “other bias.”

Certainty of evidence

Table 2 summarizes the results of the GRADE assessment.

According to the recommendations for assessing the certainty of evidence from preclinical animal studies [29], the initial certainty was high. “Risk of bias” received a “very serious” classification, and for this reason, the overall certainty was downgraded. “Inconsistency,” “indirectness,” and “imprecision” were classified as “not serious.” In the “other considerations” domain, none of the components were verified and the certainty of evidence was not upgraded. Therefore, the overall certainty of evidence for the included studies was low.

Table 1. Characteristics of the included studies

Authors - country	Year of publication	Animal model (sample size)	Investigated groups (samples per group)	Teeth evaluated	Photobiomodulation protocol	Additional procedures	Extra-alveolar time prior to replantation	Storage medium	Time of outcome assessment	Method of root resorption analysis	Outcomes	Main findings
Saito <i>et al.</i> [33] - Brazil	2011	Male rats (n = 60)	<ul style="list-style-type: none"> Group 1: Maxillary right incisors (n = 10) Control 1 (n = 10) Group 2: Control 2 (n = 10) Group 3: Control 3 (n = 10) Group 4: Laser 1 (n = 10) Group 5: Laser 2 (n = 10) Group 6: Laser 3 (n = 10) 	Maxillary right incisors	<ul style="list-style-type: none"> Palatal root surface/ Alveolar socket GaAlAs continuous-wave diode laser Wavelength: 660 nm (palatal root surface), 830 nm (alveolar socket) Output power: 30 mW (palatal root surface), 40 mW (alveolar socket) Energy density: 57.14 J/cm² (each site) Total energy: 4 J (each site) Total time of irradiation: 2 min and 13 sec (palatal root surface), 1 min and 40 sec (alveolar socket) 	<ul style="list-style-type: none"> Groups 1 and 4: Asepsis with 1% iodine polyvinylpyrrolidone, and irrigation of the alveolar socket with saline solution Groups 2, 3, 5, and 6: Removal of the dental papilla and enamel organ with scalpel, pulp extirpation, root canal irrigation with saline solution, root canal filling with calcium hydroxide Asepsis with 1% iodine polyvinylpyrrolidone, and irrigation of the alveolar socket with saline solution (after laser application in groups 5 and 6) 	<ul style="list-style-type: none"> Group 1: Control 1-4 min Group 2: Control 2-30 min Group 3: Control 3-45 min Group 4: Laser 1-4 min Group 5: Laser 2-30 min Group 6: Laser 3-45 min 	<ul style="list-style-type: none"> Groups 1 and 4: kept dry Groups 2, 3, 5, and 6: saline solution 	After 60 days	<ul style="list-style-type: none"> Histomorphometric analysis 	<ul style="list-style-type: none"> No differences were found in inflammatory and replacement resorption among groups. Areas of ankylosis were greater in group 5. 	<ul style="list-style-type: none"> Treatment of the root surface and the alveolar wound with low-level laser did not improve the healing process of immediate and delayed tooth replantation in rats.
Carvalho <i>et al.</i> [34] - Brazil	2012	Male rats (n = 60)	<ul style="list-style-type: none"> Group 1: Negative control (n = 10) Group 2: Positive control (n = 10) Group 3: Continuous mode laser (n = 10) Group 4: Pulse mode laser (n = 10) 	Maxillary right incisors	<ul style="list-style-type: none"> Root surface GaAlAs high-power diode laser Wavelength: 810 nm Output power: 1,200 mW Total time of irradiation: 30 sec (5 sec in each surface) Incidence angulation: 45° 	<ul style="list-style-type: none"> Removal of the dental papilla, pulp extirpation, root canal preparation and irrigation with 1% sodium hypochlorite and EDTA-T Root canal filling with calcium hydroxide (after laser application in groups 3 and 4) Prior to laser application, immersion of extracted teeth in 1% sodium hypochlorite for 10 min, removal of remaining periodontal ligament with gauze, and washing with saline solution 	60 min	After 15, 30, and 60 days	<ul style="list-style-type: none"> Radiographic analysis Histomorphometric analysis Histological analysis 	<ul style="list-style-type: none"> Histomorphometric and radiographic analyses showed lower incidence of root resorption in the irradiated groups, without differences between irradiated groups. Resorption and ankylosis were observed in histological section after 30 and 60 days, except in group 3. 	<ul style="list-style-type: none"> Root surface treatments with high-powered diode laser irradiation prior to delayed replantation reduced the occurrence of external root resorption. 	

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Table 1. (Continued) Characteristics of the included studies

Authors - country	Year of publication	Animal model (sample size)	Investigated groups (samples per group)	Teeth evaluated	Photobiomodulation protocol	Additional procedures	Extra-alveolar time prior to replantation	Storage medium	Time of outcome assessment	Method of root resorption analysis	Outcomes	Main findings
Vilela et al. [35] - Brazil	2012	Male rats (n = 72)	<ul style="list-style-type: none"> Group 1: Control (n = 36) Group 2: Laser (n = 36) 	Maxillary left incisor	<ul style="list-style-type: none"> Root surface/Alevolar None InGaAlP continuous-wave diode laser Wavelength: 685 nm (each site) Output power: 50 mW (each site) Spot size: 0.02 cm² Optical power density: 2.5 W/cm² (each site) Energy density: 200 J/cm² (each site) Total energy: 4 J (each site) Distance from root/irradiated tissue: 1 mm 	None	<ul style="list-style-type: none"> Not reported 	<ul style="list-style-type: none"> Kept dry for 15 min and then stored in saline solution 	<ul style="list-style-type: none"> After 15, 30 and 60 days 	<ul style="list-style-type: none"> Histomorphological analysis 	<ul style="list-style-type: none"> Increased root resorption in the control group was observed in all periods evaluated when compared to the laser group. 	<ul style="list-style-type: none"> Laser therapy resulted in less occurrence of root resorption.
Carvalho et al. [36] - Brazil	2016	Male rats (n = 60)	<ul style="list-style-type: none"> Group 1: Control 1 (n = 15) Group 2: Control 2 (n = 15) Group 3: Laser (n = 15) Group 4: Laser for 15 days (n = 15) 	Maxillary right incisors	<ul style="list-style-type: none"> Root surface/Alevolar socket/Buccal and palatal mucosa Laser application in buccal and palatal mucosa only in group 4, every 48 hr for 15 days GaAlAs continuous-wave diode laser Wavelength: 780 nm (each site) Output power: 70 mW (each site) Spot size: 0.04 cm² Energy density: 16.8 J/cm² (root surface), 4.2 J/cm² (alveolar socket), 4.2 J/cm² (buccal and palatal mucosa) Total time of irradiation: 320 sec (root surface), 60 sec (alveolar socket), 120 sec (buccal and palatal mucosa) 	<ul style="list-style-type: none"> Removal of the dental papilla and enamel organ with scalpel, pulp extirpation, root canal irrigation with saline solution, root canal filling with calcium hydroxide Prior to replantation, irrigation of the alveolar socket with saline solution 	<ul style="list-style-type: none"> 40 min 	<ul style="list-style-type: none"> Group 1: kept dry Groups 2, 3, and 4: UHT skimmed milk 	<ul style="list-style-type: none"> After 15, 30 and 60 days 	<ul style="list-style-type: none"> Histological analysis 	<ul style="list-style-type: none"> After 15 days, group 4 exhibited moderate external inflammatory root resorption. After 30 days, groups 1, 2, and 4 presented intense external inflammatory root resorption, and different levels of ankylosis. Group 3 remained without external inflammatory root resorption and ankylosis up to 60 days. 	<ul style="list-style-type: none"> Laser application to the root surface and alveolar socket resulted in no external inflammatory root resorption or ankylosis. Association of laser application in buccal and palatal mucosa every 48 hours for 15 days resulted in a higher incidence of external inflammatory root resorption and ankylosis.

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Table 1. (Continued) Characteristics of the included studies

Authors - country	Year of publication	Animal model (sample size)	Investigated groups (samples per group)	Teeth evaluated	Photobiomodulation protocol	Additional procedures	Extra-alveolar time prior to replantation	Storage medium	Time of outcome assessment	Method of root resorption analysis	Outcomes	Main findings
Matos et al. [37] - Brazil	2016	Male rats (n = 60)	<ul style="list-style-type: none"> Group 1: Maxillary right incisors (n = 10) Control 1 (n = 10) Group 2: Control 2 (n = 10) Group 3: Control 3 (n = 10) Group 4: Control 4: Laser 1 (n = 10) Group 5: Laser 2 (n = 10) Group 6: Laser 3 (n = 10) 	Maxillary right incisors	<ul style="list-style-type: none"> Root surface/Alveolar socket/Buccal and palatal mucosa Laser application in buccal and palatal mucosa, every 48 hr for 5 sessions GaAlAs continuous-wave diode laser (root surface and alveolar socket) InGaAlP continuous-wave diode laser (buccal and palatal mucosa) Wavelength: 808nm (root surface and alveolar socket), 660 nm (buccal and palatal mucosa) Output power: 100 mW (each site) Optical power density: 3.6 W/cm² (each site) Energy density: 61 J/cm² (each site) Total energy: 10.2 J (root surface and alveolar socket), 17 J (buccal and palatal mucosa) Total time of irradiation: 102 sec (root surface), 17 sec (alveolar socket), 170 sec (buccal and palatal mucosa) 	<ul style="list-style-type: none"> Removal of the dental papilla with a scalpel, pulp extirpation, root canal irrigation with saline solution, root canal filling with calcium hydroxide Prior to replantation, irrigation of the alveolar socket with saline solution 	45 min	<ul style="list-style-type: none"> Groups 1 and 4: kept dry Groups 2 and 5: UHT cow milk Groups 3 and 6: soy milk 	After 15 and 30 days	<ul style="list-style-type: none"> Histomorphometric analysis 	<ul style="list-style-type: none"> Group 1 presented larger areas of root resorption. After 30 days, groups 2 and 3 presented no difference in root resorption. After 30 days, laser application significantly reduced root resorption in group 4. After 30 days, laser application reduced root resorption in groups 5 and 6, without differences when compared to groups 2 and 3. 	<ul style="list-style-type: none"> Laser application, as well as cow and soy milk, reduced the occurrence of root resorption

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Table 1. (Continued) Characteristics of the included studies

Authors - country	Year of publication	Animal model (sample size)	Investigated groups (samples per group)	Teeth evaluated	Photobiomodulation protocol	Additional procedures	Extra-alveolar time prior to replantation	Storage medium	Time of outcome assessment	Method of root resorption analysis	Outcomes	Main findings
Carvalho et al. [38] - Brazil	2017	Male rats (n = 50)	<ul style="list-style-type: none"> Group 1: Negative control (n = 10) Group 2: Positive control (n = 10) Group 3: Fibroblast growth gel (n = 10) Group 4: Laser (n = 10) Group 5: Laser + Fibroblast growth gel (n = 10) 	Maxillary right incisors	<ul style="list-style-type: none"> Root surface Continuous-wave high-power diode laser Wavelength: 808 ± 10 nm Output power: 1,200 mW Optical power density: 7.14 W/cm² Energy density: 214.3 J/cm² Total energy: 45 J Incidence angulation: 45° Total time of irradiation: 30 sec (5 sec on each surface) 	<ul style="list-style-type: none"> Removal of dental papilla with scalpel in all groups Groups 3 and 5: Application of 50 µg of 0.2% basic fibroblast growth gel in 3% hydroxypropylmethylcellulose gel in the palatal root surface and in the alveolar socket Groups 3, 4, and 5: Pulp extirpation, root canal preparation and irrigation with 1% sodium hypochlorite and EDTA-T, and root canal filling with calcium hydroxide Prior to laser application, immersion of extracted teeth in 1% sodium hypochlorite for 10 min, removal of remaining periodontal ligament with gauze, and washing with saline solution Prior to replantation, irrigation of the alveolar socket with saline solution 	<ul style="list-style-type: none"> Group 2: Immediate replantation Groups 1, 3, 4, and 5: 60 min 	Kept dry	After 60 days	<ul style="list-style-type: none"> Radiographic analysis Histological analysis 	<ul style="list-style-type: none"> Radiographic analysis showed fewer resorptive areas in group 5 than in the negative control. Radiographically, groups 3, 4, 5, and the positive control did not differ regarding areas of external root resorption. Histological analysis showed lower mean values of ankylosis, replacement, and inflammatory resorption for group 4 than in the negative control, without differing from positive control. 	<ul style="list-style-type: none"> Laser application with or without application of fibroblast growth gel, reduced the occurrence of external root resorption and ankylosis.

GaAlAs, gallium-aluminum-arsenate; InGaAlP, indium-gallium-aluminum-phosphorus; UHT, ultra-heat treatment; EDTA-T, ethylenediaminetetraacetic acid-tetrapon.

Table 2. Certainty of the evidence from the included studies according to the GRADE approach for preclinical animal studies

Number of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall certainty of evidence
6 studies	Very serious*	Not serious	Not serious	Not serious	None	⊕⊕○○ LOW

GRADE, Grading of Recommendations, Assessment, Development, and Evaluations.

*Several domains had studies with an unclear or high risk of bias.

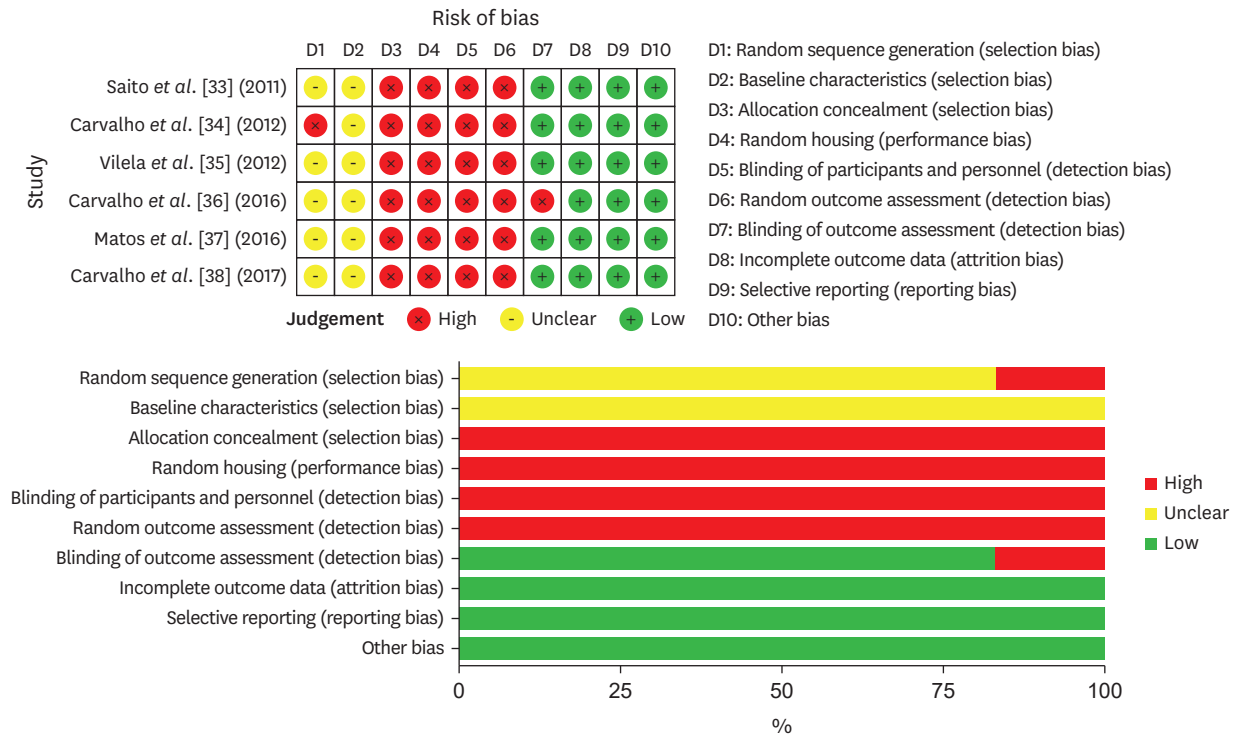


Figure 2. Quality assessment of the included studies according to the risk of bias tool for preclinical animal studies – (SYRCLE’s RoB tool).

DISCUSSION

The prognosis of avulsed teeth following replantation is unpredictable. Many teeth are lost, mainly due to the occurrence of root resorption [40,41]. Therefore, there is a constant need to investigate alternative therapies to reduce the incidence of root resorption. For this reason, in the present systematic review, searches were performed in 6 electronic databases, aiming to evaluate the available evidence on the effectiveness of photobiomodulation of the root surface prior to replantation of teeth on reducing the occurrence of root resorption.

When investigating the effects of photobiomodulation, it is important to understand that it involves several parameters. Among these, wavelength is the most important, since it determines the light penetration depth into the tissues [42], which is also associated with the thermal effect caused by the light [43]. In general, a red-light laser presents a wavelength ranging from 620 to 740 nm, and an infrared-light laser has a wavelength ranging from 780 to 1000 nm [43]. Parameters such as energy density and duration of irradiation are also important because they determine the irradiation dose absorbed by the cells, directly affecting the expected biological effects [44].

Methodologies varied widely among the included studies. However, when evaluating the information presented by those studies, there are a few possible explanations for their findings. Only 2 studies [33,35] performed photobiomodulation using a low-level red-light laser (660 nm and 685 nm, respectively). The red-light laser mechanism of action involves stimulating cell metabolism and tissue repair, favoring a greater effectiveness and response of tissues exposed to an insult [45]. This method also exerts anti-inflammatory effect, by modulating cell influx, hemorrhagic formation, and inflammatory metabolites [45], even in the presence of bacterial by-products [46]. One of these studies concluded that photobiomodulation of the root surface did not decrease the occurrence of root resorption [33]; while the other concluded that it resulted in less occurrence of root resorption [35]. These inconsistent findings may be related to the manner in which photobiomodulation was applied. While in the study by Saito *et al.* [33], photobiomodulation was applied only to the palatal root surface of teeth and, after replantation, to the middle third of the palatal surface of the alveolar socket with an infrared light (830 nm); in the study by Vilela *et al.* [35], application was performed over the entire root surface, on the interior of the alveolus and, after replantation, on the entrance and palatal surface of the alveolar socket. Therefore, it is possible to hypothesize that the non-homogeneous photobiomodulation application in the study by Saito *et al.* [33] could be the reason for the absence of an improved protective effect against root resorption in the irradiated groups, since only 1 root surface was irradiated, and the non-irradiated surface did not receive a sufficient amount of radiation to stimulate the cell metabolism, tissue repair, and anti-inflammatory effects.

Two studies [36,37] investigated the effects of low-level infrared-light lasers (780 nm and 808 nm, respectively) and reported a lower occurrence of root resorption when laser application was performed. In addition to the stimulation of cell metabolism and tissue repair, favoring a greater effectiveness and response of tissues exposed to an insult [47], this method demonstrated direct effects on the proliferation, attachment, spreading, and orientation of periodontal ligament fibroblasts [20,48,49]. It has also been suggested that this treatment can promote a greater increase of collagen type I and III, accelerating the dynamic of collagenization and facilitating a more favorable repair process [50,51]. Thus, it can be hypothesized that the application of low-level infrared-light laser on the root surface can maintain the cell viability of the periodontal ligament attached to the root surface, as well as locally stimulating repair and controlling the inflammatory response, thereby preventing the occurrence of root resorption.

Two studies [34,38] investigated the use of high-power infrared-light lasers (810 nm and 808 nm, respectively) and also concluded that their application reduced the occurrence of root resorption. In addition to the above-mentioned effects promoted by infrared light, the high-power laser setting promoted morphological alterations of the root surface, such as melting and fusion of the dental structure, thus making it more homogeneous, favoring the adhesion of connective tissue fibers and cells, facilitating new cementum formation, and rendering the surface a more resistant to the action of microorganisms and clastic cells [19,52,53].

As an additional finding, 1 study [36] reported that regular application (every 48 hours for 15 days) of infrared-light laser photobiomodulation to the buccal and palatal mucosa resulted in a higher incidence of external inflammatory resorption and ankylosis. The authors hypothesized that this finding may be related to the stimulation of differentiation and activation of osteoclasts [36]. It has been suggested that mitochondrial cytochrome C absorbs the energy of the laser and this absorption enhances cellular activity by increasing

ATP synthesis [54]. Therefore, since osteoclasts are multinucleated cells with highly active mitochondria, the laser rapidly affects these cells [55,56].

Regarding the risk of bias assessment of the included studies, several drawbacks were observed. None of the studies had information regarding allocation concealment, methods of randomly housing the animals, approaches to blinding researchers, or whether the animals were selected at random for outcome assessment. Thus, in the “allocation concealment,” “random housing,” “blinding of participants and personnel,” and “random outcome assessment” domains, a high risk of bias was attributed to all studies. Five studies [33,35-38] stated that the animals were randomized, but did not describe how this randomization was performed; and 1 study [34] did not provide information about random sequence generation at all. Therefore, an unclear and high risk of bias in the “random sequence generation” domain was attributed to these studies, respectively. Regarding the “baseline characteristics” domain, authors should report the characteristics of the animals used in the study, including information on sex, age and weight. All studies had an unclear risk of bias, as they provided partial information on these characteristics. In the “blinding of outcome assessment” domain, only 1 study [36] had a high risk of bias because it did not contain information on whether the outcomes were evaluated in a blinded manner. Finally, in the “incomplete outcome data,” “selective reporting,” and “other bias” domains, all studies had low risks of bias.

Based on the guidelines for assessing the certainty of evidence in preclinical animal studies [29], the certainty was initially classified as high. Due to the limitations presented by the included studies, during the risk of bias assessment, the domain “risk of bias” was classified as “very serious” and the initial certainty was downgraded 2 levels. No limitations were detected in the domains “imprecision,” “indirectness,” and “inconsistency.” Since no other considerations (assessment of publication bias, significant effect, plausible confounding, and dose-response gradient) were verified, the “other considerations” domain remained unchanged. Therefore, the GRADE analysis demonstrated a low certainty of evidence.

Despite having been performed with an *a priori* protocol involving systematic searches of 6 electronic databases, the present systematic review has some limitations. First, it is known that the storage medium in which the avulsed tooth is kept prior to replantation can influence the periodontal ligament cell viability [57]. Only 1 study evaluated 2 storage media (soy and UHT cow milk) and did not find differences between groups [37]. Therefore, it was not possible to determine whether the storage medium influenced the investigated outcomes. Additionally, it was not possible to determine whether any of the tested protocols had any advantage over another, since different protocols were not tested between groups in the same study.

CONCLUSION

Based on the presented results, it is possible to infer, with a low certainty of evidence, that the application of photobiomodulation to the root surface of teeth prior to replantation can reduce the occurrence of root resorption. Further well-designed studies are needed to improve the quality of the available evidence and to determine a clinical protocol with standardized laser parameters.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Search strategy in each database

[Click here to view](#)

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