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ORIGINAL ARTICLE

Comparison of two power densities on the healing of palatal wounds after connective tissue graft removal: randomized clinical trial

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Abstract Connective tissue graft (CTG), which is considered to be among the best techniques for treating gingival recession, has presented stable long-term results. However, this technique causes morbidity and discomfort in the palatine region due to graft removal at that site. A previous study reports that photobiomodulation (PBM) using a dosage of 15 J/cm^2 may improve wound healing and the patient's postoperative comfort. However, no other studies in the literature provide the best application dosage or comparisons between protocols for this purpose. The aim of this study is to compare two power densities of PBM on the wound-healing process of the donor palatine area after CTG removal. In this study, 51 patients presenting buccal gingival recession were randomized into one of the following groups: group 1: CTG procedure for root coverage and PBM application at the donor site using a 60 J/cm^2 dose; group 2: CTG and PBM application using a 30 J/cm^2 dose; or group 3: CTG and sham application. The evaluated parameters were the wound remaining area (WRA), scar and tissue colorimetry (TC), tissue thickness (TT), and postoperative discomfort (D), evaluated at baseline and 7, 14, 45, 60, and 90 days after surgery. Group 1 presented statistically significant smaller wounds at day 7 ($p > 0.05$). None of the patients presented scars at the operated area, and all of the patients reported mild discomfort, with low consumption of analgesic pills. We concluded that the protocol of 60 J/cm^2 provided faster wound healing 7 days after removing the connective tissue graft for root coverage. Trial registration: ClinicalTrial.org (NCT02580357) https://clinicaltrials.gov/ct2/show/NCT02580357.

Keywords Connective tissue graft · Gingival recession · Low-level laser therapy · Wound healing

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Introduction

Gingival recession is the exposure of the root surface due to the displacement of the gingival margin apical to the cementoenamel junction (CEJ) [1]. Studies have demonstrated that the prevalence of gingival recessions seems to increase with age, affecting up to 100 % of the population at 50 years or more, showing that this is an aging problem [2–4]. Gingival recession can have a negative impact on patients' conditions, such as the presence of tooth hypersensitivity and esthetic problems [5]. Due to this fact, many surgical procedures have been developed to treat gingival recession-type defects. The most frequent and predictable is the coronally advanced flap associated with connective tissue graft (CTG) [5–7].

The literature reports that the CTG technique is the gold-standard treatment modality for gingival recession because it can reach root coverage rates of up to 100 % [8, 9] and keep those results stable, even in the long term [10]. However, CTG can also cause morbidity and discomfort for the patient in the palatine region, as a consequence of connective tissue graft

removal. Besides discomfort, necrosis and bleeding can happen at that area [11]. In this way, a treatment for the palatine area to aid wound healing at the donor site would decrease discomfort and, consequently, could be used to avoid side effects.

Some studies have evaluated the influence of photobiomodulation (PBM) in stimulating and accelerating wound healing, by stimulating regeneration processes and increasing the patient's postoperative comfort [12, 13]. The literature describes many laser application parameters, such as wavelengths, power, and laser sources. However, there is no consensus about which is the best approach. Diverse studies have used wavelengths between 680 and 840 nm, which are related to the most efficient tissue biostimulation [12]. Evidence regarding the healing efficacy of low-level laser therapy techniques using gallium aluminum arsenide (Ga-Al-As) infrared lasers at different doses on hard palate wounds in mice showed that laser application has a positive healing effect on the healing process [14].

Randomized controlled clinical studies have recently evaluated the effects of PBM after periodontal plastic surgery procedures for root coverage. The results showed that the laser may have additional beneficial effects for this type of procedure [15, 16]. Another recent study that evaluated the PBM effects in the palatal area after the removal of connective tissue graft to treat gingival recessions observed that patients treated with a dose of 15 J/cm^2 had accelerated closure of their surgical wound and decreased tissue repair time, compared with patients who did not receive laser therapy [17].

Thus, the literature shows that PBM may improve and accelerate palatal wound repair. However, no studies in the literature show the best dosage or protocol in using PBM for this purpose. Therefore, the aim of this study is to compare the influence of two different power densities of low-level laser therapy application in the recovery of a palatine donor-site wound after harvesting a connective tissue graft.

Materials and method

The methodology of the present study adheres to the new CONSORT statement [18] and followed our previous study [17].

This investigation was a parallel, double-blind, randomized clinical trial. The study protocol (ClinicalTrial.org-NCT02580357) was approved by the Institutional Review Board at College of Dentistry—São José dos Campos, State University of São Paulo (132.831-UNESP). Each subject provided informed consent after a thorough explanation of the nature, risks, and benefits of the clinical investigation. The sample of this study comprised 54 patients with class I or II Miller gingival recession who were referred to the Department of Periodontology of São José dos Campos Dental School, UNESP—State University of São Paulo. The subjects were selected in the period between February 2014 and November 2014.

Inclusion criteria

The patients were 20 to 70 years old, of both genders, and presented class I or II Miller gingival recession on vital canines or premolars in the palatine region (donor site) with no pathological or morphological alterations. The patients agreed and signed formal consent to participate in the study after receiving an explanation of the risks and benefits from an individual who was not a member of the present study (resolution no. 196—October 1996, and Ethics and Code of Professional Conduct in Dentistry—CFO 179/93).

Exclusion criteria

Patients presenting the following conditions were excluded: systemic problems that contraindicated the surgical procedure, those under medication that could interfere with the wound healing, those who smoked, those who were pregnant or lactating, and those who had received periodontal surgery in the study area.

Power analysis

The sample size was calculated with the remaining wound area (RWA) considered as the primary outcome variable. The study was powered to detect a minimum clinical difference between treatments of 30 % in the WRA and standard deviation of 5 mm^2. The test indicated that a minimum sample of 12 subjects per treatment arm was needed for a power of 0.8.

Randomization and treatment

The patients were randomly assigned to one of the three treatment groups:

- Group 60 (PBM 60, $n = 18$): Periodontal surgery for root coverage through connective tissue graft and PBM on the donor site using a 60 J/cm^2 dose.
- Group 30 (PBM 30, $n = 18$): Periodontal surgery for root coverage through connective tissue graft and PBM on the donor site using a 30 J/cm^2 dose.
- Group sham (control, $n = 18$): Periodontal surgery for root coverage through connective tissue graft and PBM sham on the donor site.

The patients were randomly allocated with the use of a computer-generated randomization table. The allocation was concealed using a sealed, coded opaque envelope containing the treatment for each specific subject. The sealed envelope containing the treatment assignment was opened immediately after the surgical procedure. Besides the blind randomization (allocation concealment), the patients and the professional

responsible for the surgical procedures were not aware of which treatment each individual had received.

Surgical procedure

The same expert periodontist (MPS) performed all of the surgeries. Before the surgical procedure, all patients were enlightened about the causes and consequences of gingival recession as well as prevention techniques. Factors related to the origin of the gingival recession, such as toothbrush trauma and inflammation caused by biofilm, were controlled through instruction on standardized brushing techniques to avoid the influence of other hygiene methods capable of promoting trauma on soft tissues. Standardized dental floss and toothbrushes were given to the patients. The surgical technique adopted in the recession defects was the trapezoidal-type of CAF, as described by Zucchelli [19]. A connective tissue graft was removed from palate mucosa following the Bruno technique [20]. Briefly, the first incision on the palate was performed perpendicularly to the long axis of the teeth, 2 to 3 mm apical to the gingival margin. The mesial-distal length of the incision was determined by the length of the graft required to cover the recession. Because the selected recessions were in maxillary canines and premolars, the lengths of the graft varied minimally (10–12 mm). The second incision was made parallel to the first one (1–2 mm apically and parallel to the long axis of the teeth) in order to separate the subepithelium connective tissue from the epithelial layer. The incision was carried far enough apically to provide a 7-mm height of connective tissue to cover the denuded root surface. Afterward, another incision parallel to the long axis of the teeth, starting from the first incision, was performed to separate the subepithelium connective tissue from the periosteum. Then, the connective tissue graft was removed from the palate as atraumatically as possible. Single sutures were made on the palate (4–0 silk), and the graft was sutured onto the receptor site.

Postoperative maintenance

After the surgery, the participants were requested to take 500 mg of sodium dipyrone every 4 h for 3 days in case of pain, to not chew rigorously, and to avoid brushing and flossing in the treated area for a period of 2 weeks. During this period, plaque control was performed using 0.12 % chlorhexidine rinse used twice a day. The sutures were removed after 7 days, and all of the patients were recalled for prophylaxis and reinforcement of motivation and instruction for atraumatic tooth brushing during the study period.

PBM protocol

The irradiation was performed with a Ga-Al-As diode laser (TheraLase 30 W, DMC Ltda, São Carlos, Brazil) that continuously emitted a 660-nm wavelength with a power of 30 mW for all of the groups. The patients allocated for group 60 received the following protocol for laser application: Two points of irradiation were performed using a total energy density (fluence) of 60 J/cm^2 and a time of 60 s (30 J/cm^2 per point, application time of 30 s per point and total area of irradiation of 0.06 cm^2). The patients allocated to group 30 received the following protocol for laser application: Two points of irradiation were performed using a total energy density (fluence) of 30 J/cm^2 and a time of 30 s (15 J/cm^2 per point, application time of 15 s per point and total area of irradiation of 0.06 cm^2). During irradiation, the tip of the laser probe (0.2 cm of diameter) was placed perpendicularly, with slight contact on the area. Laser therapy was initiated in the immediate postoperative period (just after sutures) and was repeated by six more applications performed every other day, with a total of seven laser applications. The power of the equipment was calibrated prior to each application. The patients allocated to the control group received sham irradiation. For this, black rubber protection was placed at the tip of the laser device, which did not allow the light to reach the tissue, as previously described [17]. The applications were performed by a researcher (CAS) different from the one who measured the study parameters.

Parameters

The following parameters were recorded according to Dias et al. [17]:

1) Postoperative discomfort (D): Through air spray for 5 s over the operated site, sensitive function was measured at 7, 14, 45, and 60 days after the surgical procedure. After air spray was applied, the patients were required to use a visual analogue scale (VAS) of 100 mm to assess their discomfort; the scale extremes ranged from “no pain” to “extreme.” In addition, the patients were asked to report the number of analgesics they took during the first week.
2) Tissue thickness (TT): The tissue thickness of the palatine masticatory mucosa was assessed before the procedure and 3 months after the procedure, through four fixed points marked 5 and 7 mm from the gingival margin in the operated region. One stent was made to standardize the points to be measured. The stent was positioned and the points were marked with a periodontal probe. Then, the stent

was removed and measurements were taken. For this, an endodontic spacer with a rubber cursor was put onto the marked points for it to reach the palatine bone plate. Then, the cursor was taken to the tissue carefully in order to not pressure it. The distance between the spacer tip and the cursor was measured using a digital pachymeter.

3) Scar and colorimetry tissue (CT): Tissue color similarity between the region adjacent to the operated area and the postoperative image, as well the presence or absence of scars or keloids in the operated area, was analyzed through photographs. The photographs were exported to image software (Adobe Photoshop CS 3, München, Germany), and two areas were used: one from the wound and another adjacent area. The areas were compared (ΔE) using brightness parameters (L), the red-green chroma scale, and the yellow-blue chroma scale (b) according to the equation [21]:

$$\Delta E = \left[(L.wound–L.adjacent)^2 + (a.wound–a.adjacent)^2 + (b.wound–b.adjacent)^2\right]^{1/2}$$

4) Remaining wound area (RWA): The defect area was measured after 7, 14, 30, 45, and 60 postoperative days. For this, standardized photographs were taken (in terms of brightness, distance, and angle). A scale was used as a reference to measure the area. These photographs were exported to image software (Image J—NIH, Bethesda, USA), and the wound area was measured in square millimeters.

Examiner calibration

The same-blinded examiner was responsible for performing the clinical parameters and photograph measurements (FLSN). The examiner was calibrated by evaluating the tissue thickness of ten patients who were not enrolled in the study on two separate occasions. The values obtained were submitted to analysis by an intraclass correlation test. The calibration was accepted if the measurements of these two examinations were similar at a 90 % level. In the second calibration procedure, the examiner was calibrated to measure area (using photographs). Likewise, ten photographs of other patients who were not participating in the study were taken at distinct moments; these measures were submitted to an intraclass correlation test. The examiner was trained until the coefficient agreement reached 90 % for the area measurement.

Statistics

All of the data were expressed as mean ± standard deviation or expressed in percentages during the descriptive phase. Data were analyzed according to distribution by the Shapiro-Wilk test. For the remaining parameter analysis of wound area, tissue colorimetry, tissue thickness, and postoperative discomfort, two-way repeated measures ANOVA was performed for intra- and intergroup analysis, and a Tukey test was perform to detect the interactions. A *T* test was used for an intergroup comparison of the number of analgesics taken. The presence or absence of scars was measured with a Q-square test. Statistical analysis was performed using Sigma Plot 12.0. In all tests, a significance level of 0.05 was chosen.

Results

In total, 54 patients were randomized to one of the three groups and received treatment. However, three were excluded because they did not adhere to the laser protocol or missed one or more laser session applications. None of them presented adverse effects to the procedures and/or laser application protocol during the follow-up period. Figure 1 demonstrates the flow chart of the patients, and Table 1 shows the patients' demographic characteristics.

Postoperative discomfort (D)

The patients reported just mild discomfort after the procedure, and none reported moderate or extreme discomfort. The VAS scale results were low for all groups. Regarding the number of analgesics taken by the patients in the first seven postoperative days, group sham presented an average of 2.2 ± 2.0 of 500 mg sodium dipyrone pills per patient, while in the groups that received laser, this average was 1.3 ± 2.0 pills per patient for group 60 and 1.33

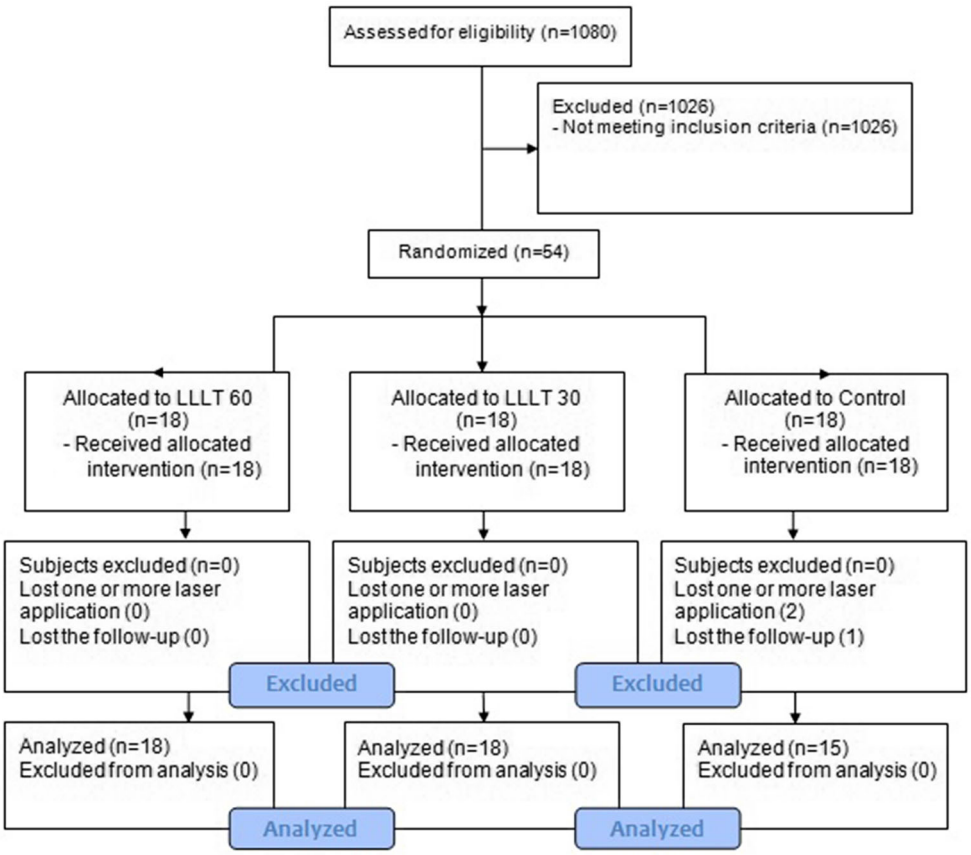

Fig. 1 CONSORT flow chart of the patients

± 1.5 pills for group 30. There was no statistically significant difference among the groups (Table 2).

Tissue thickness (TT)

The preoperative average was 3.4 ± 1.0 mm for group 60, 3.7 ± 0.6 mm for group 30, and 3.4 ± 0.5 mm for group sham, with no statistically significant differences among the groups. After 90 days, the thickness measurements were 3.5 ± 1.1 mm for group 60, 3.4 ± 0.5 mm for group 30, and 3.2 ± 0.5 mm for group sham, with no statistically significant differences among the groups. When the intragroup comparison was performed, the differences between baseline and 3 months postoperative were not significant for the three groups, showing that palatine mucosa tissue thickness returns to its initial measurement up to 90 days after the procedure (Table 2).

Scar and tissue colorimetry (TC)

Colorimetry analysis revealed that all of the groups presented similar color patterns. None of the patients presented scars at the operated area. During the 7-day and 14-day periods, all three groups presented statistically different color patterns from the non-operated area. However, during the 45-day and 60-day periods, the wounds from both groups presented similar color patterns to the non-operated area (Table 2). When the three groups were compared, group 60 and group 30 showed a significant difference from the sham group at 14 days ($p > 0.05$).

Table 1 Patient characteristics at baseline ($n = 51$)

	G60 ($n = 18$)	G30 ($n = 18$)	G sham ($n = 15$)	p value
Age	43.2 ± 9.8	47 ± 9.3	40.01 ± 7.6	0.1
Gender	5 males	11 males	7 males	–
	13 females	7 females	8 females	–
Length of graft (mm)	12.17 ± 2.0	11.24 ± 2.1	12.91 ± 3.6	0.08

p values: one-way ANOVA

Table 2 Parameters at baseline, 7, 14, 30, 45, 60, and 90 days

		Baseline	7 days	14 days	30 days	45 days	60 days	90 days
TC	G60	–	16.4 ± 8.1Aa	14.4 ± 5.1Aa	9.7 ± 4.5Ba	8.0 ± 2.9Ba	5.3 ± 3.7Ba	–
	G30	–	12.0 ± 6.5Ab	14.3 ± 6.1Aa	9.7 ± 5.2Ba	7.7 ± 4.0Ba	6.8 ± 3.0Ba	–
	Sham	–	13.4 ± 7.4Aa	11.5 ± 4Ab	7.6 ± 2.9Ba	7.9 ± 4.1Ba	4.7 ± 2.3Ba	
TT (mm)	G60	3.4 ± 1.0Aa	–	–	–	–	–	3.5 ± 1.1Aa
	G30	3.7 ± 0.6Aa	–	–	–	–	–	3.4 ± 0.5Aa
	Sham	3.4 ± 0.5Aa	–	–	–	–	–	3.2 ± 0.5Aa
P	G60	–	1.3 ± 2.0a	–	–	–	–	–
	G30		1.33 ± 1.5a	–	–	–	–	–
	Sham	–	2.2 ± 2.0a	–	–	–	–	–

Uppercase letters—different letters means statistically significant difference within groups (lines)—two-way repeated measures ANOVA. Lowercase letters—different letters means statistically significant difference among groups (column)—two-way repeated measures ANOVA

TC scar and tissue colorimetry, *TT* tissue thickness, *P* pain measured by the number of analgesics pills taken

Remaining wound area (RWA—mm^2)

For the remaining wound area measurement, all three groups presented statistically significant reductions during the observation period. In an intragroup comparison, the wound areas at day 7 were statistically greater than they were at day 14, which were statistically greater than at day 30. That is, the wound always had a statistically significant closure from the previous period in all three groups (Fig. 2). The differences were not statistically significant at days 30, 45, and 60. The intergroup comparison showed that the PBM 60 group presented statistically smaller wounds at day 7 compared to group 30 and group sham (50.15 ± 18.49, 65.74 ± 25.08, and 62.91 ± 23.27 mm^2, respectively, $p = 0.01$). However, the measures did not show statistically significant differences at 14, 30, 45, and 60 days, and no wounds were visible at day 60. Figure 3 shows the evolution of wound closure in the three groups.

Discussion

The literature is vast regarding to the use of low-level laser therapy, which has been commonly associated with healing and anti-inflammatory properties. Some clinical studies have also shown the benefits of this therapeutic modality in the oral mucosa of humans [15–17]. In a previous study, our group showed that the PBM using a 15 J/cm^2 dosage was able to accelerate the palatal wound closure after connective tissue graft harvesting, compared to in patients who did not receive laser therapy. We concluded that PBM irradiation can accelerate wound healing on palatine mucosa after connective tissue removal for root coverage techniques [15].

The present study aimed to compare the influence of two different power densities of photobiomodulation (PBM) in the recovery of the palatal donor site after connective tissue graft technique for root coverage. Despite the research demonstrating that PBM can accelerate wound healing, no studies in the

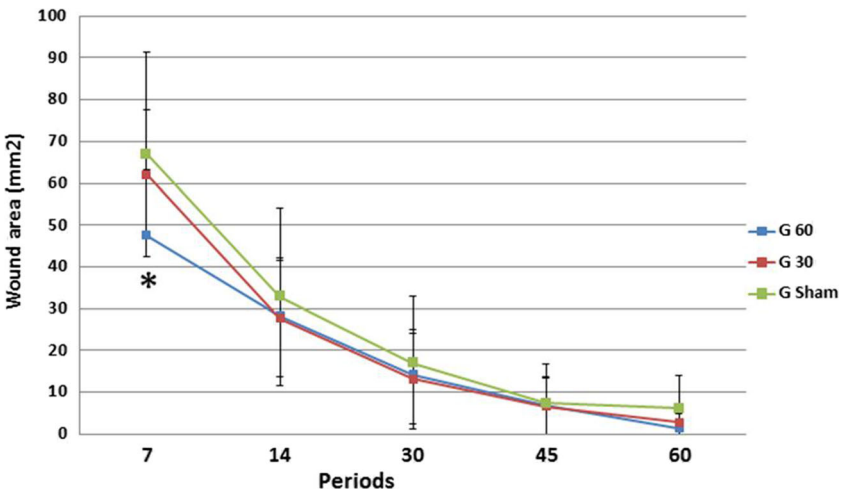

Fig. 2 Wound area variation (in mm^2) of the two groups. The *asterisk* denotes statistically significant difference between groups—two-way repeated measures ANOVA

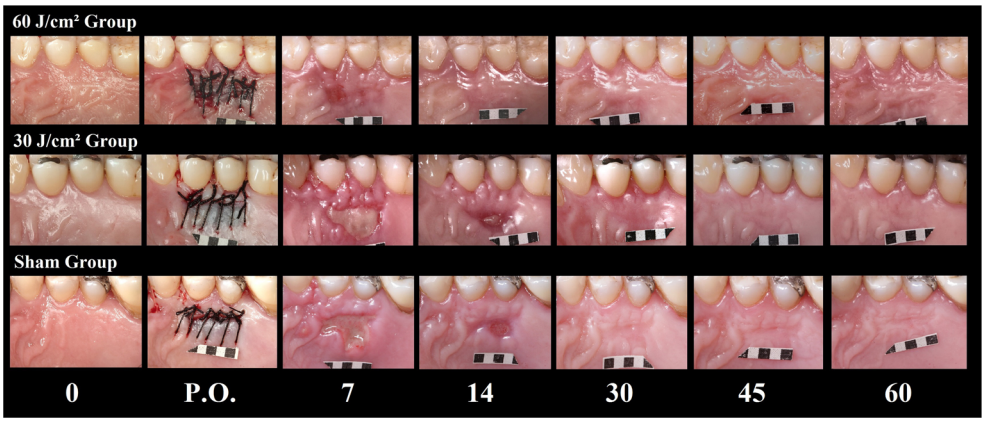

Fig. 3 Clinical view of the wound healing of the three groups. *0* before surgery, *P.O.* postoperative view, *7* after 7 days, *14* after 14 days, *30* after 30 days, *45* after 45 days, *60* after 60 days

literature compare different low-level laser irradiation protocols or the optimal dose for better and faster wound healing in human palatine mucosa. The results of this study showed that the group that received 60 J/cm^2 presented statistically smaller remaining wound areas at day 7 postoperative, compared to the group receiving 30 J/cm^2 and the sham group, although statistically significant differences no longer existed among the groups at day 14.

This result can probably be explained by the effects of the GaAlAs laser wavelength and the applied dose on the secretory activity of fibroblasts, as well as their influence on the pro- and anti-inflammatory cytokines during early stages of repair, as previously reported [12, 14, 22]. A study conducted by Mendez et al. [23] compared the influence of 20 and 50 J/cm^2 doses on skin wound closure in rats; after 3 days repair, the group treated with 50 J/cm^2 had histologically significant regressions of inflammation and the presence of organized collagen matrix, with reduced collagen deposition noted after 5 days of healing. Another recent study evaluated the influence of a 72 J/cm^2 dose on skin wound repair in rats, confirming the effectiveness of PBM in the first week of repair by reducing the inflammatory response and increasing collagen synthesis, as well as by reducing pro-inflammatory markers such as IL-1β and TNF-α and increasing anti-inflammatory cytokine IL-10 [24]. Thus, high doses of PBM also appear to provide optimum results, which may be a consequence of the attenuation of light during penetration, which means that when a large amount of energy is used, more energy is left to act within the tissues after attenuation, whether by reflection, absorption, or scattering of the transmitted light [23].

The color difference between the operated area and the area adjacent to the wound was also measured to better evaluate the wound-healing process, in which the original color may represent the level of inflammation and/or tissue repair. From this analysis, we observed a statistically significant difference in color between the groups that received PBM, compared to the control group, at 14 days after the procedures, suggesting some influence of PBM on tissue erythema and angiogenesis during the inflammatory phase of repair [24]. Another evaluated parameter was the thickness of the palatal tissue at the site from which the graft was removed, for which the PBM showed no statistically significant differences between the groups, according to other clinical studies that observed rapid recovery of the palatal mucosa [17, 25].

Despite the beneficial anti-inflammatory and tissue repair results of PBM, this study did not found differences related to postoperative discomfort or the number of analgesics taken by patients. Furthermore, the average VAS scale was mild discomfort for all groups, corroborating the randomized clinical study conducted by Dias et al. [17]. In that study, the authors explain these results mainly by two factors: the subjectivity in the measurement of pain and the use of the VAS scale, which, despite being a valid method, tends to present a wide range of results. However, some limitations should be emphasized. The first is related to the discomfort measurement in response to an external stimulus. In the present study, the palatal mucosa was stimulated by a standard air jet. Ideally, a more accurate method for stimulus could be needed to obtain a more realistic representation of an uncomfortable situation suffered by the patient, such as thermal or even tactile stimuli. Another limitation may be related to the surgical wound model once the adopted model requires graft removal at a subepithelial level, thus preserving the epithelium layer and leading to healing by first intention.

Other clinical studies need to be performed. Studies are needed that evaluate other doses and laser application protocols on new models of surgical wounds for which the application of PBM may have a beneficial effect, as well as those allowing the epithelialization process in palatine mucosa to be observed. Thus, within the limitations of the present study, we can conclude that PBM performed at 60 J/cm^2 provided faster wound closure in palatine mucosa after 7 days of a connective tissue graft removal for root coverage.

Compliance with ethical standards The study protocol (ClinicalTrial.org-NCT02580357) was approved by the Institutional Review Board at College of Dentistry—São José dos Campos, State University of São Paulo (132.831-UNESP). Each subject provided

informed consent after a thorough explanation of the nature, risks, and benefits of the clinical investigation.

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