BMJ Open

Photobiomodulation for postoperative pain relief following conventional periapical surgery: a randomised controlled study protocol

Rolf Wilhem Consolandich Cirisola,[1,2] Luis Eduardo Pascuali Moya ,[1,2] María Victoria García Olazabal,[1,2] Daniela Anat Amzallag Wagmann ,[2] Guendalina Palermo Suarez,[2] Carolina Wince ,[1,2] María Laura Hermida Bruno ,[1,2] Daniel Rodriguez Salaberry,[1,2] Ana Paula Taboada Sobral ,[3] Priscila Larcher Longo,[4] Lara Jansiski Motta ,[1,5] Sandra Kalil Bussadori ,[1,5] Cinthya Cosme Gutierrez Duran ,[1] Kristianne Porta Santos Fernandes ,[1] Raquel Agnelli Mesquita-Ferrari ,[1,5] Anna Carolina Ratto Tempestini Horliana [1]

To cite: Cirisola RWC, Moya LEP, Olazabal MVG, *et al*. Photobiomodulation for postoperative pain relief following conventional periapical surgery: a randomised controlled study protocol. *BMJ Open* 2025;**15**:e089986. doi:10.1136/bmjopen-2024-089986

► Pre-publication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-089986).

Received 13 June 2024
Accepted 25 September 2025

For numbered affiliations see end of article.

Correspondence to
Dr Anna Carolina Ratto Tempestini Horliana; annacrth@gmail.com

ABSTRACT

Introduction Photobiomodulation (PBM) has shown promising effects in managing postoperative pain following conventional periapical surgery, although current evidence remains limited. This study aims to assess the effect of PBM on postoperative pain 24 hours after periapical surgery.

Methods and analysis A randomised, controlled, double-blind trial will include 34 patients undergoing periapical surgery in the maxillary region, randomly assigned to an experimental group (n=17) or control group (n=17). The experimental group will receive PBM (GaAlAs diode laser, 808 nm, 100 mW, 4 J/cm², applied at five vestibular points) and placebo ibuprofen immediately and 24 hours postoperatively. The control group will receive simulated PBM and active ibuprofen. The primary outcome is postoperative pain assessed by the visual analogue scale at 24 hours. Secondary outcomes include pain at the seventh day, paracetamol intake, oedema, ecchymosis, soft tissue status and temperature at 24 hours and 7 days. Radiographic evaluation of healing will be performed at 1 and 3 months. Statistical analysis will be conducted based on data distribution, using repeated measures ANOVA (Analysis of Variance) or non-parametric equivalents for longitudinal outcomes, and appropriate tests for categorical variables. Significance will be set at $p<0.05$.

Ethics and dissemination The study was approved by the Human Research Ethics Committee of Universidad Católica del Uruguay (process no. 220914). Results will be disseminated to participants, healthcare professionals, the public and scientific communities.

Trial registration number NCT05935306.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study is limited to a single clinical setting at Universidad Católica del Uruguay, which may affect the generalisability of the findings to other settings or populations.
⇒ Patients with comorbidities, smokers and those using medications affecting bone metabolism or the inflammatory process were excluded, which may limit the applicability of the results to these groups.
⇒ Randomisation and blinding are meticulously maintained using sequentially numbered opaque envelopes and a double-dummy method, minimising bias.
⇒ The sample size calculation is based on previous studies and ensures sufficient power to detect differences between groups, enhancing the reliability of the findings.
⇒ The study includes comprehensive postoperative assessments, such as pain measurement using the visual analogue scale, and secondary outcomes like oedema, ecchymosis, soft tissue healing and bone consolidation, providing a thorough evaluation of treatment effects.

INTRODUCTION

Marked improvement has been found in the success rate of periapical surgery in recent years, with rates of 91%[1] and 82%[2] described in the literature. Despite the advances, discomfort in the postoperative period remains influenced by factors such as surgical trauma, the presence of microorganisms and failure to adhere to postoperative guidelines.[1] These factors directly contribute to postoperative pain. Photobiomodulation (PBM) can be used to diminish postoperative pain and promote healing, which can improve patient adherence to guidelines. Although PBM does not have direct microbiological effects, its ability to

reduce inflammation and promote tissue repair can create an environment less favourable to microbial proliferation.

Non-steroidal anti-inflammatory drugs (NSAIDs), particularly ibuprofen, are commonly prescribed for pain management.[3] However, evidence demonstrates the need for caution, especially in high-risk cardiovascular patients, with the recommendation of low doses of shorter duration for maximal effectiveness.[4 5] There is a growing need for alternatives to NSAIDs for these patients. Ethically, initial hypothesis testing often involves healthy populations,[6] prioritising healthy individuals over situations in which NSAIDs are unsafe (patients with heart conditions). The present study suggests replacing ibuprofen with PBM following periapical surgery, potentially extending its effectiveness to vulnerable populations in the future.

PBM is a therapeutic modality involving the use of low-level light sources (typically below 500 mW) with non-ionising irradiation across both the visible (400–760 nm) and near-infrared (760–1000 nm) portions of the electromagnetic spectrum.[7] Despite its use for nearly fifty years, the widespread acceptance of PBM remains limited due to uncertainties with regards to cellular and molecular mechanisms.[8] A pivotal chromophore in PBM is cytochrome c oxidase in mitochondria.[8–12] The primary hypothesis posits that photons facilitate the dissociation of inhibitory nitric oxide from the enzyme, resulting in heightened electron transport, mitochondrial membrane potential and ATP production.[8]

While PBM has yielded positive results with regard to the control of postoperative pain following third molar surgery,[13–18] there is limited evidence on its use in periapical surgery.[19–21] The literature reports optimal radiant exposure ranging from 3–85.7 J/cm^2 for reducing postoperative pain in third molar surgeries,[16 22 23] with wavelengths ranging from 650–980 nm.[16 22 23] With periapical surgery, however, radiant exposure ranges from 3 to only 15 J/cm^2[19–21] and conflicting results are found regarding wavelength. For instance, one study[19] found little benefit from a wavelength of 680 nm (red portion of the spectrum), possibly due to limited tissue penetration. In contrast, promising results were found in other studies using a wavelength of 810 nm (infrared portion).[20 21]

Radiographic follow-up is essential for monitoring the healing process and evaluating the long-term success of surgical interventions.[22] Follow-up provides valuable insights into the health status of the periapical region, allowing for timely intervention if complications arise.[22] Periapical radiographs and cone-beam CT (CBCT) demonstrate similar overall success rates,[23] although CBCT offers a more detailed evaluation of bone regeneration, particularly when strict healing criteria are applied.[24] However, depending on the study design, especially when involving larger patient samples, periapical radiographs may be preferred due to their lower cost and reduced radiation exposure. A study by some authors[25] found that CBCT images showed a lower healing tendency than periapical radiographs. However, both imaging methods demonstrated substantial healing, with a 77.7% reduction in apical radiolucency after 1 year.

Moreover, healing of pre-existing periapical lesions is most pronounced between 3 months and 2 years, highlighting the importance of radiographic follow-up even after shorter follow-up periods.[26] This reinforces the need for extended radiographic monitoring, particularly in cases with initial periapical pathology or maxillary teeth, which are associated with poorer healing outcomes.

This paper outlines a study for investigating whether PBM can effectively change postoperative pain from baseline (immediately after surgery) to 24 hours after surgery in patients having undergone conventional periapical surgery compared with 'gold standard' treatment (ibuprofen), using the visual analogue scale (VAS) to measure pain intensity.

MATERIALS AND METHODS

According to the standard protocol items: recommendations for interventional trials statement,[27] this randomised, controlled, double-blind study meets the criteria for designing a clinical trial (online supplemental file 1). The study received approval from the Human Research Ethics Committee of the Universidad Católica del Uruguay (UCU) under process number 220 914. The approval document is available in its original language (online supplemental file 2) and English (online supplemental file 3). The original research protocol is also provided in its original language (online supplemental file 4) and English (online supplemental file 5). Following verbal and written explanations of the study, all volunteers who agree to participate will sign a statement of informed consent in their original language (online supplemental file 6). This document is also provided in English (online supplemental file 7). Any complications or changes will be reported to the ethics committee and disclosed in publications. Personal information on the participants will be safeguarded for confidentiality throughout the trial. The study was registered at ClinicalTrials.gov under the identifier NCT05935306 (online supplemental file 8).

Patients visiting the UCU clinic who need periapical surgery will be invited to participate in the study. Treatment will be performed at the surgical unit of the University Health Clinic of UCU in Montevideo, Uruguay, from 28 June 2024 to December 2025. The data supporting this study's findings will be made available without restriction at the time of publication. The authors will include a supplementary file containing the means, medians and variance measures.

Sample description

Male and female individuals at the University Health Clinic with a diagnosis of apical periodontitis and an apical lesion smaller than 10 mm with or without a fistula diagnosed clinically and radiographically in the maxillary region (any teeth 15 to 25) will be invited by the main researcher, who will obtain informed consent.

Recruitment

To ensure impartiality and integrity, past assignments will remain undisclosed to the recruiting person, and measures will be in place to prevent the administering researcher from modifying patient inclusion in the trial.

Inclusion criteria

- Patients with chronic periapical lesions (smaller than 10 mm in diameter) who have undergone endodontic treatment.
- Only one tooth (corresponding to one periapical cavity) will be considered for the study.
- Only asymptomatic teeth will be included in the study.
- Patients will be evaluated if the only tooth affected by an infectious focus is the one referred for the intervention.
- No comorbidities (eg, diabetes, hypertension, etc).
- Age between 18 and 70 years.
- Both genders.
- Healthy permanent teeth with good oral hygiene.

Exclusion criteria

- Medications that affect bone metabolism and the inflammatory process (eg, corticosteroids, bisphosphonates).
- Smokers, pregnant or lactating women.
- Use of anti-inflammatory drugs in the 3 weeks before surgery.
- Disruption of treatment progress by missing scheduled appointments for any reason.
- Lack of adherence to guidelines or presence of an injury in the acute phase (pain, swelling, exudate).
- Multiple lesions/teeth will be excluded.
- Patients who develop postoperative infection requiring antibiotic therapy will be excluded from the study.
- Presence of periodontal probing depth ≥4 mm and/or clinical attachment loss.[28]

Patients who have complications during the study period will be treated either at the UCU clinic or outside regular hours at the mobile coronary unit (UCM), as agreed between the UCU and UCM. All patients will be informed that any adverse effects that occur are intrinsic to the surgical procedure, and resolution will follow the standard protocol in such cases. Participants will receive support from the researchers for any issues arising from the study.

Sample size calculation

The total sample will consist of 24 patients, ensuring a power (1–β error probability) of 0.95 and a significance level (α) of 0.05, based on an estimated effect size of 0.61. The original sample size calculation was performed using G*Power V.3.1 and is presented (online supplemental file 9). The sample size calculation was based on data from a previous study by Metin *et al* that evaluated postoperative pain using the (VAS, 0–10 cm). In that study, the mean pain score at 24 hours postoperatively was 1.91±1.76 in the PBM group and 3.14±2.04 in the control group, which aligns closely with the primary outcome of the present study. A repeated measures ANOVA-based calculation indicated that 24 participants would be required. To account for potential dropouts, an additional 10 patients (5 per group) will be included. Although outcomes will be assessed at multiple time points, the sample size calculation was based on the 24-hour postoperative pain score, as this is considered the most clinically relevant time point for evaluating PBM efficacy (figure 1).

Calibration and examiner training

To maximise the reproducibility of the assessments, a single examiner will undergo training on using the VAS and determining temperature.

Randomisation

Treatment immediately following surgery will be randomly assigned as either active or simulated PBM. Using an online programme and a random sequence generator (https://www.sealedenvelope.com/), a random sequence will be generated. Sequentially numbered opaque envelopes will contain the treatment allocation for each patient and will be sealed under the supervision of an individual not otherwise involved in the study. Randomisation will be performed in seven blocks, each comprising six patients, for a final allocation ratio of 1:1. Six additional patients will be included in each group to compensate for the dropout rate predicted in any clinical study (20%). After suturing, the administering investigator will select and open an envelope within the assigned block, preserving the sequence of the remaining envelopes, and implement the specified treatment or simulation. This method ensures that only the administering researcher will be aware of treatment allocation.

Patient and public involvement

In this study, patients and the public were not involved in any stages of the research process. There was no participation in setting research priorities, developing research questions and outcome measures, or in the design and conduct of the study. Similarly, patients and the public were not involved in choosing methods, participant recruitment or the dissemination of the study results.

Group composition

All participants will undergo the same conventional periapical surgical procedure.[28]

G1—sham group—conventional treatment + simulated PBM + postoperative ibuprofen (n=17 patients). The patients in this group will undergo identical treatment to that of the G2 group, except that PBM will be simulated rather than active. The researcher responsible for administering PBM will simulate radiation by placing the device at four equidistant points over the lesion, forming the vertices of a flat square positioned 1 cm apart. A point at the centre of the square will also receive simulated irradiation. These are the same locations as those described for the PBM group, but the equipment will remain off. The

	Study period						
	Record	Randomization	Post-Operative				Closure
TIME	-T_1	0	T_0	T_1 (24h)	T_2 (7d)	T_3 (30 days)	T_4 (90 days)
Record:							
Eligibility screen	x						
Informed consent	x						
Clinical examiner calibration	x						
Assignment		x					
INTERVENTIONS:							
Control group			x	x	x		
Experimental group			x	x	x		
Evaluations:							
VAS			x	x	x		
Analgesics			x	x	x		
Soft tissue healing			x	x	x		
Ecchymosis			x	x	x		
Edema			x	x	x		
Local and systemic temperature			x	x	x		
Periapical radiographs			x			x	x

Figure 1 Standard protocol items: recommendations for interventional trials flow diagram of study—Author created (Rolf Wilhem Consolandich Cirisola and co-authors). VAS, visual analogue scale.

laser tip will be positioned perpendicular to the mucosa in direct contact. To prevent the participants from identifying their group allocation, the activation sound of the device (beep) will be recorded and played back during the application of simulated PBM. During laser application, both the patient and operator will use protective eyewear adequate for the wavelength of the laser. Simulations will be performed with the same laser equipment (Therapy XT—ANVISA RDC Standard 185/2001—DMC, São Paulo, SP, Brazil) (figure 2).

G2—Intervention group—Conventional treatment + PBM + placebo ibuprofen (n=17 patients). All participants will undergo the same surgical procedure. The patients will receive active PBM (as detailed in table 1). The irradiated region will consist of four equidistant points on the lesion, forming the vertices of a flat square positioned 1 cm apart. A point at the centre of the square will also be irradiated. Placebo ibuprofen will be administered.

Paracetamol will be provided to all participants for pain management to be taken as needed in both groups. This is an outcome of the study (comparison of the quantity of analgesics taken in the different groups).

The dosimetric parameters and number of PBM applications are described in table 1.

Description of technique used for periapical surgery

Anaesthesia will be administered, and haemostasis will be controlled to ensure the absence of pain and minimal bleeding during surgery. The next phase will involve incising soft tissues and dissecting to gain access to the area of interest.

Once the target region is reached, access to the lesion and apex through the bone will be achieved, followed by curettage of the peri-radicular lesion to remove inflamed and contaminated tissues. Next, apex resection will be carried out to eliminate the infected apical portion and

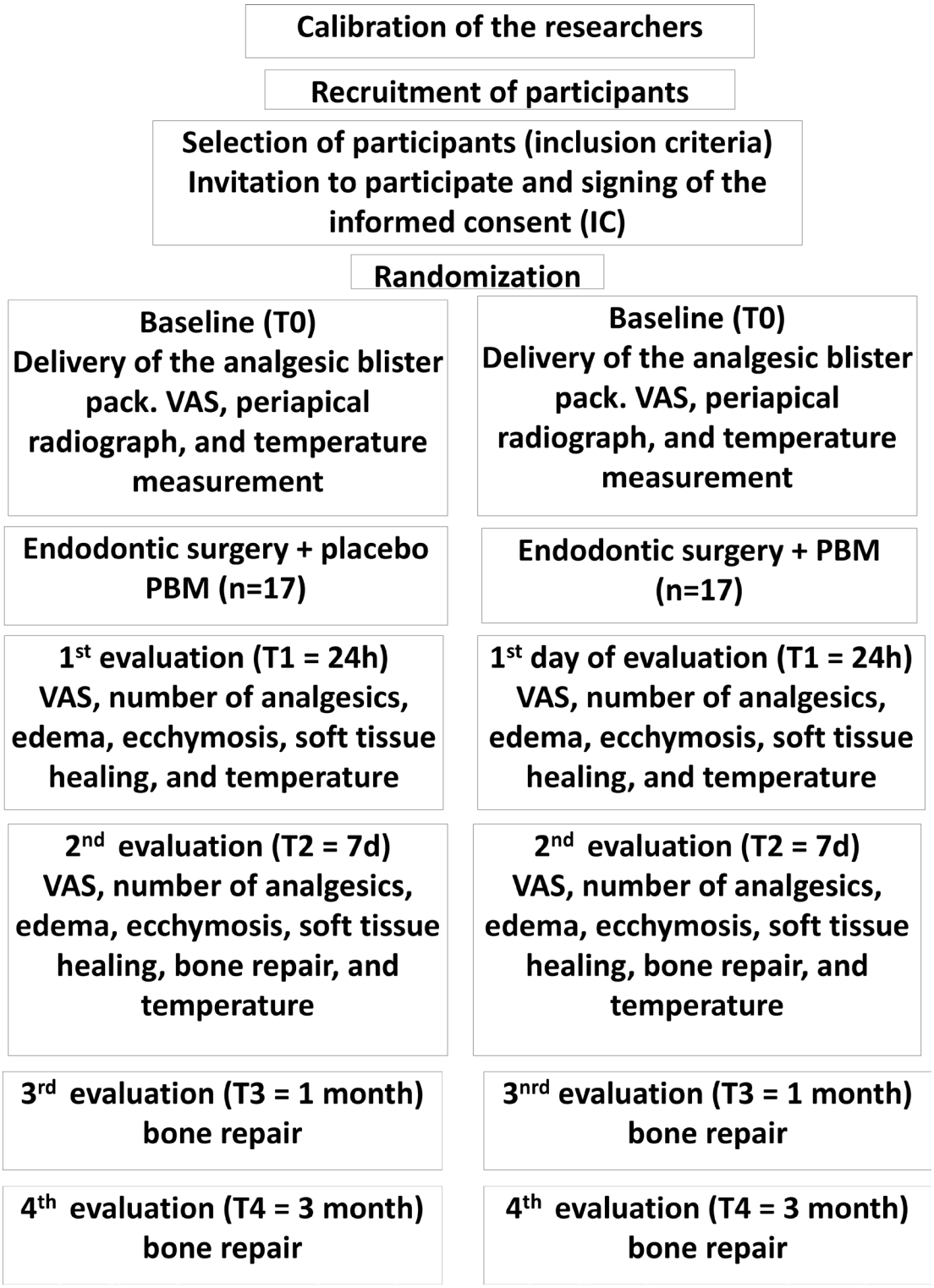

Figure 2 Flow diagram of study—Author created (Rolf Wilhem Consolandich Cirisola and co-authors). d, day; h, hours; PBM, photobiomodulation; t, time; VAS, Visual Analogue Scale.

enable proper root canal cleaning. The apex of the tooth will then be prepared for retrograde filling with biomaterial, which is essential for preventing the recurrence of infection. After retrograde filling, the flap will be repositioned and sutured to promote proper soft tissue healing. Postoperative instructions will also be provided.

Study outcomes

The primary outcome was pain in the postoperative period, assessed using a 10 cm VAS, where 0 represented 'no pain' and 10 represented 'worst pain imaginable'. The main analysis focused on the change in pain intensity at 24 hours postoperatively compared with baseline

Table 1 Dosimetric parameters[19 21]

Parameters	Values/treatment
Wavelength (nm)	808
Operating mode	Continuous
Radiant power (mW)	100
Irradiance (mW/cm^2)	200
Beam area (cm^2)	0.5
Exposure time (s)	20
Radiant exposure (J/cm^2)	4
Radiant energy (J)	2 J per point
Total energy (J)	10
Number of irradiated points	Five points on vestibular face One point in the centre of lesion +4 equidistant points in quadrangular pattern with 1 cm between points
Application technique	In contact at 90 degrees to surface
Number of sessions and frequency	Two postoperative sessions (24 hours and 7 days)

J, Joule; W, Watts.

(immediate postoperative period), as this time point is considered the most clinically relevant for evaluating the effectiveness of PBM in managing acute postoperative pain.

The following will be the secondary outcomes of the study:

Pain will also be assessed on the seventh day after surgery; however, this is defined as a secondary outcome, since other postoperative parameters—such as oedema, ecchymosis and soft tissue condition—will be evaluated. Based on the literature, we do not expect significant pain at this later stage.[21 29]

The quantity of analgesics taken in the specific periods. The number of analgesics taken in the first 24 hours and the 7 days following surgery will be recorded. Paracetamol will be the sole analgesic administered to the patients and recommended for usage solely in cases of pain.[29] A monitoring procedure will be implemented to follow the adherence of the patients: each patient will be instructed to bring their analgesic package to the follow-up sessions to determine usage.

Oedema: a scale[21] will be used to quantify the extent of oedema. This scale has scores ranging from 0–3: 0=no oedema, 1=intraoral oedema, 2=extraoral oedema and 3=diffuse oedema.[21] This outcome will be measured at baseline, 24 hours and 7 days after surgery.[21]

Ecchymosis refers to bleeding in the subcutaneous tissue caused by the rupture of one or more capillaries, often resulting from surgical trauma and characterised by a diameter >1 cm. The assessment scale for ecchymosis is defined as follows: 0=no colour change, 1=spot smaller than 4 cm in diameter, 2=spot between 4 and 10 cm in diameter, 3=spot larger than 10 cm in diameter.[21] This assessment will be performed at baseline, 24 hours and 7 days after surgery.[21]

Soft tissue healing. Score 1: no opening along the incision line, no drainage (pus or exudate), no inflammation and no pain. Score 2: no opening along the incision line, no drainage, mild swelling and mild pain. Score 3: no opening along the incision line, active drainage, advanced inflammation and moderate to severe pain. Score 4: opening along the incision line, active drainage, advanced inflammation and persistent pain. Soft tissue healing will be assessed at baseline, 24 hours and 7 days after surgery.[21]

Bone consolidation will be assessed using periapical radiography to investigate two-dimensional changes in the bone defects. Consistent with the same equipment and employing the parallelism technique, periapical radiographs will be taken in the immediate preoperative period for comparative analysis with those taken at one and 3 months. The area of the defect will be determined by multiplying the longest mesiodistal and superoinferior diameters visible on the radiographs. On all radiographs, the longest diameter of the lesion will be measured. The periapical index will be determined, with the following interpretation: 0=no lesion, 1=periapical radiolucency with a diameter of 0.5 to 1 mm, 2=periapical radiolucency with a diameter of 1.1 to 2 mm, 3=periapical radiolucency with a diameter of 2.1 to 4 mm, 4=periapical radiolucency with a diameter of 4.1 to 8 mm and 5=periapical radiolucency >8.1 mm in diameter. This assessment will be performed in the baseline as well as at one and 3 months.[21]

In both groups, temperature will be measured locally (at the surgical site) and systemically (at the glabella). This assessment will occur in the immediate postoperative period of periapical surgery, specifically at baseline, 24 hours and 7 days after surgery.

Statistical plan

All statistical analyses will be conducted according to the type and distribution of each variable. The Shapiro-Wilk test will assess the normality of continuous variables.

For continuous outcomes, such as postoperative pain (VAS), temperature (local and systemic) and analgesic consumption, a two-way repeated measures ANOVA will be used to evaluate differences between groups across multiple time points (baseline, 24 hours and 7 days). The two-way repeated measures ANOVA will allow the assessment of both time (within-subject factor) and group (between-subject factor) effects and their interaction. If the data is not normally distributed, the Friedman test will be used for within-group comparisons, and the Mann-Whitney U test will be used for between-group comparisons at each time point.

For categorical outcomes such as oedema, ecchymosis and soft tissue healing, comparisons between groups at each time point will be performed using the χ^2 test or Fisher's exact test, as appropriate, depending on the data distribution and expected cell sizes.

Baseline demographic and clinical characteristics (eg, age, sex, group allocation) will be summarised using means and SD for continuous variables, and frequencies and percentages for categorical variables. Between-group comparisons at baseline will be performed using independent samples t-tests or Mann-Whitney U tests for continuous variables, and χ^2 or Fisher's exact tests for categorical variables.

To control potential Type I errors due to multiple comparisons, Bonferroni correction will be applied where necessary. The significance level will be set at $p<0.05$ for all analyses.

DISCUSSION

PBM has effectively reduced postoperative pain following third molar surgery.[13–18] However, there is limited evidence on its use in periapical surgery,[19–21] which underscores the need for further investigation into PBM's potential benefits and applicability in this specific context. Our primary motivation is to explore the potential of laser therapy as an alternative to ibuprofen for pain control in healthy patients. If our hypothesis is confirmed, future studies could test these findings in populations with contraindications to ibuprofen use, such as high-risk cardiovascular patients.

To enhance blinding efficiency, we will adopt the double-dummy method. This approach enables a comparison between active treatment (PBM) and the gold standard control treatment (ibuprofen), while minimising expectation bias. Regarding outcomes, we emphasise the essential role of radiography in evaluating secondary outcomes in periapical surgery studies. Although our study focuses on PBM efficacy within the first 24 hours postsurgery, radiographs at one and 3 months will be taken to understand the long-term impact of treatment. These additional assessments will enrich the analysis of the results, providing insights into the effectiveness of PBM and its long-term effects compared with ibuprofen.

This study has several limitations. First, it was conducted in a single clinical setting at UCU, which may limit the generalisability of the findings to other populations or healthcare environments. Additionally, the follow-up time points were limited to 24 hours and 7 days postoperatively. These time points were selected based on previous studies indicating they are adequate for capturing immediate and short-term postoperative responses, such as pain and oedema.[30 31] However, both pain perception and inflammatory processes, such as oedema, can fluctuate significantly within the first few days after surgery. Therefore, additional intermediate time points, such as 48 or 72 hours postoperatively, may have provided more comprehensive insights into the evolution of these outcomes, particularly when using sensitive tools like the VAS for pain and objective measures for oedema.

Regarding radiographic assessments of bone consolidation, evaluations were performed at 1 and 3 months postoperatively. However, a 2-month follow-up time point could have added valuable information on the progression of bone healing.

In summary, the methods employed in this study reflect a comprehensive effort to assess the effectiveness of PBM at reducing postoperative pain, which has significant implications for pain management across various patient populations.

Author affiliations
[1]Postgraduate Program in Biophotonics-Medicine, Universidade Nove de Julho (UNINOVE), Sao Paulo, Brazil
[2]Universidad Católica del Uruguay (UCU), Montevideo, Uruguay
[3]Universidade Metropolitana de Santos (UNIMES), Santos, Brazil
[4]Postgraduate Program in Aging Science, Universidade São Judas Tadeu (USJT), Universidade Sao Judas Tadeu, Sao Paulo, Brazil
[5]Postgraduate Program in Rehabilitation Sciences, Universidade Nove de Julho, São Paulo, Brazil

Contributors Conceptualisation: RWCC, KPSF, RAM-F and ACRTH. Data curation: LEPM, MVGO, DAAW, CW and GPS. Formal analysis: MLHB, DRS, APTS and PLL. Project administration: LJM, SKB and CCGD. Roles/Writing: RWCC, ACRTH, KPSF, RAM-F and CCGD. Validation: APTS, PLL and ACRTH. Guarantor: ACRTH.

Funding National Council for Scientific and Technological Development, Grant/Award Number 316287/2023-7.

Disclaimer The investigators do not plan an interim analysis, as no serious adverse events are expected. However, adverse events (major and minor) will be recorded.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Luis Eduardo Pascuali Moya https://orcid.org/0009-0004-9213-5363
Daniela Anat Amzallag Wagmann https://orcid.org/0009-0000-0765-9164
Carolina Wince https://orcid.org/0000-0003-3942-7143
María Laura Hermida Bruno https://orcid.org/0000-0001-7708-5186
Ana Paula Taboada Sobral https://orcid.org/0000-0002-6846-6574
Lara Jansiski Motta https://orcid.org/0000-0002-7774-4345
Sandra Kalil Bussadori https://orcid.org/0000-0002-9853-1138
Cinthya Cosme Gutierrez Duran https://orcid.org/0000-0001-9055-1524
Kristianne Porta Santos Fernandes https://orcid.org/0000-0001-7156-9286
Raquel Agnelli Mesquita-Ferrari https://orcid.org/0000-0001-5142-9526
Anna Carolina Ratto Tempestini Horliana https://orcid.org/0000-0003-3476-9064

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