

STUDY PROTOCOL WITH STATISTICAL ANALYSIS PLAN

Single application 940 nm GaAlAs photobiomodulation immediately after free gingival graft harvesting: randomized controlled trial of early postoperative pain and palatal wound area reduction

Study design	Randomized, parallel-group, sham-controlled clinical trial
Intervention	Single-session 940-nm GaAlAs diode laser photobiomodulation
Comparator	Sham laser irradiation without therapeutic laser energy delivery
Protocol version	Version 1.0
Document date	October 1, 2024
Ethics approval	Ethics Committee, University of Medicine and Pharmacy at Ho Chi Minh City (Approval No. 1976/DHYD-HDDD, 2024)
ClinicalTrials.gov Identifier	NCT07308912

1. Background and Rationale

Free gingival grafting is commonly used to increase keratinized tissue and manage mucogingival deficiencies. Harvesting a graft from the palate creates a secondary-intention donor-site wound that may be associated with postoperative pain and delayed soft-tissue healing. Photobiomodulation therapy (PBMT) using low-level laser energy has been proposed as an adjunctive approach to modulate inflammatory responses, reduce postoperative discomfort, and support wound repair. This trial evaluates whether a single immediate postoperative application of a 940-nm GaAlAs diode laser improves early postoperative pain and palatal donor-site healing after free gingival graft harvesting.

2. Objectives

Primary objective: To evaluate the effect of a single session of 940-nm diode laser PBMT on postoperative pain following free gingival graft harvesting.

Additional objectives: To compare postoperative pain, analgesic consumption, epithelialization of the palatal donor site, and reduction in remaining wound area between study groups at prespecified follow-up time points.

3. Study Design

This was a parallel-group, randomized, sham-controlled clinical trial. Eligible participants requiring an autogenous palatal free gingival graft were randomly allocated to either the laser group or the sham-control group in a 1:1 ratio.

4. Study Setting and Participants

Participants were recruited from patients undergoing periodontal surgery involving free gingival graft harvesting at the Faculty of Dentistry, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam.

Eligibility criteria were as follows:

Inclusion criteria:

- (a) ≥ 18 years of age;
- (b) systemically healthy individuals without conditions affecting wound healing (e.g., diabetes mellitus, immunosuppression, coagulation disorders, or Candida infection);
- (c) full-mouth plaque score (FMPS) and full-mouth bleeding score (FMBS) $<15\%$;
- (d) no previous history of palatal tissue harvesting;
- (e) no use of overdentures or removable partial dentures involving the donor area.
- (f) palatal mucosal thickness ≥ 3 mm at the donor site prior to harvesting, measured at the center of the graft harvesting area approximately 6 mm from the gingival margin in the premolar region.

Exclusion criteria:

- (a) pregnant or breastfeeding women;
- (b) smokers;
- (c) patients with psychiatric disorders;
- (d) patients receiving medications known to interfere with tissue healing or alter pain perception.

5. Randomization, Allocation Concealment, and Masking

Randomization was performed using a computer-generated sequence (random.org) with permuted blocks. Thirty-four opaque, sealed, sequentially numbered envelopes (17 per group) were prepared by an independent assistant who was not involved in participant recruitment, surgery, laser application, outcome assessment, or data analysis. Allocation concealment was maintained, and envelopes were opened sequentially only after completion of surgery.

Participants, the surgeon, and the outcome assessor were blinded to group allocation. All surgical procedures were performed by a single experienced periodontist who remained unaware of treatment assignment. Immediately after surgery, laser or sham irradiation was administered by a separate clinician who was aware of the allocation but was not involved in the surgical procedure or outcome assessment. In the control group, the irradiation procedure was simulated using identical device positioning and handling, while the laser device remained off and no radiation was delivered, thereby maintaining participant blinding. All clinical outcomes were assessed by an independent examiner blinded to group allocation. The statistician was also blinded during data analysis.

6. Surgical Procedure and Postoperative Care

Free gingival grafts were harvested from the palatal donor site using a standardized four-incision technique. A palatal stent was used to protect the donor site. Postoperative medications, oral-hygiene instructions, and follow-up care were standardized across both groups.

Postoperative regimen:

All participants received amoxicillin/clavulanate (875/125 mg) three times daily for 5 days and ibuprofen (400 mg) three times daily for 3 days. Acetaminophen was permitted as rescue analgesia when required. Participants were also instructed to use a 0.12% chlorhexidine mouth rinse for 2 weeks.

7. Interventions

Laser group: After suturing at the recipient site had been completed, the palatal donor-site wound received a single session of 940-nm GaAlAs diode laser photobiomodulation. Irradiation was delivered in continuous-wave mode at an output power of 0.1 W and an energy density of 4 J/cm² for 40 seconds per field across three fields, corresponding to a total delivered energy of approximately 12 J. The applicator was positioned perpendicular to the wound surface at a distance of approximately 0.5 cm, with a treatment field of approximately 1 cm². A palatal stent was placed immediately after irradiation.

Control group: After suturing at the recipient site had been completed, sham laser irradiation was performed using the same procedural approach as in the laser group, including identical device positioning and handling, but with the laser device switched off so that no radiation or therapeutic laser energy was delivered. A palatal stent was subsequently placed.

8. Outcome Measures

8.1 Postoperative pain

Postoperative pain intensity was assessed using a 0–10 visual analog scale (VAS), with 0 indicating no pain and 10 indicating the worst possible pain. Pain was recorded at 2 hours, postoperative day 3, and postoperative day 7.

8.2 Postsurgical analgesic consumption

Post-surgical analgesic consumption was recorded during the early postoperative period in accordance with the study data-collection schedule.

8.3 Epithelialization of the palatal donor site

Epithelialization of the palatal donor site was assessed on postoperative days 7 and 14 using a clinical test with 3% hydrogen peroxide, in accordance with the study assessment protocol.

8.4 Remaining wound area

The palatal donor-site wound was digitally assessed at baseline (day 0) and on postoperative days 3, 7, and 14. Digital impressions were obtained using the TRIOS 3 intraoral scanning system, and the remaining wound area was quantified according to the predefined measurement procedure.

9. Sample Size and Participant Disposition

The planned randomization comprised 34 allocations, with 17 participants assigned to each group. Thirty-three participants were included in the final analysis (laser group, n = 16; control group, n = 17). One participant in the laser group was lost to follow-up because of absence at the postoperative day-3 visit and was excluded from the analysis; routine postoperative care was maintained.

10. Statistical Analysis Plan

Data distribution was assessed using the Shapiro–Wilk test. Baseline characteristics and analgesic consumption were compared between groups using the Mann–Whitney U test. Wound epithelialization was analyzed using the chi-square test or Fisher's exact test, as appropriate. Statistical significance was defined as a two-sided p value < 0.05.

To account for repeated measurements and within-participant correlations, postoperative pain (VAS) and remaining wound area (RWA) were analyzed using linear mixed-effects models (LMMs). Group, time, and the group × time interaction were specified as fixed effects, with age and sex included as covariates and participant ID specified as a random effect. Fixed effects were evaluated using Type III tests with Satterthwaite's approximation. Post hoc pairwise comparisons between groups at each assessment time point were derived from the fitted models. Results were reported as estimated marginal means (EMMs) with corresponding standard errors (SEs).

11. Ethical Considerations

The study was conducted in accordance with the ethical principles governing research involving human participants. Ethical approval was obtained from the Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (Approval No. 1976/DHYD-HDDD, 2024). Written informed consent was obtained from all participants before any study procedures were undertaken.

12. Data Management and Confidentiality

Study data were recorded and managed using coded participant identifiers to protect confidentiality. Access to identifiable source data was restricted to authorized study personnel in accordance with institutional requirements. No personally identifiable participant information is included in documents made publicly available through ClinicalTrials.gov.

13. Protocol Deviations and Amendments

Protocol amendments and deviations, including any changes to masking, the control intervention, or the statistical analysis plan, were to be documented with their corresponding dates and rationale to ensure transparent reporting.

14. References / Supporting Documents

Ethics approval documentation, informed consent materials, case report forms, and other study documents were maintained as part of the study records, as applicable.