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Clinical Evaluation of an Electrospun Chitosan/Polyvinyl Alcohol Nanofibrous Membrane Used as an Open-Healing Barrier for Ridge Preservation After Mandibular Premolar Extraction: A Randomized Split-Mouth Clinical Trial Protocol

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Study protocol

Keywords: Barrier membrane, Guided bone regeneration, Guided tissue regeneration, Socket preservation, Clinical trial protocol, Chitosan, Polyvinyl alcohol, Nanofibers

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Table 1 is available in the Supplementary Files section.

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Abstract

Background: Alveolar ridge resorption following tooth extraction may compromise subsequent restorative procedures. Electrospun chitosan/polyvinyl alcohol (CS/PVA) nanofibrous membranes exhibit favorable biological and mechanical properties; however, high-quality clinical evidence supporting their use as standalone barriers under open-healing conditions is limited.

Objectives: This protocol describes a randomized split-mouth clinical trial designed to evaluate the effectiveness of CS/PVA nanofibrous membrane for ridge preservation following mandibular premolar extraction.

Methods: Eligible participants requiring bilateral mandibular premolar extraction will be enrolled. Test sites will receive CS/PVA membrane, while control sites will heal naturally. Primary outcomes include horizontal and vertical ridge dimensional changes, keratinized tissue width, and histomorphometric parameters. Secondary outcomes include soft tissue healing, soft tissue thickness gain, and adverse events. Outcomes will be assessed over a 4-month healing period using blinded evaluation and paired statistical analysis.

Discussion: This trial is designed to address current evidence gaps by isolating the barrier effect of CS/PVA nanofibrous membranes in intact sockets under open-healing conditions.

Trial Registration: Prospective registration (TCTR20251001001).

Keywords

Barrier membrane, Guided bone regeneration, Guided tissue regeneration, Socket preservation, Clinical trial protocol, Chitosan, Polyvinyl alcohol, Nanofibers.

Introduction

Tooth extraction initiates a cascade of biological events that frequently results in significant and irreversible alveolar ridge resorption(Apaza-Bedoya et al., 2024). The loss of periodontal ligament disrupts the vascular supply to the bundle bone, leading to rapid remodeling and dimensional contraction of the socket walls(Araújo et al., 2023). Clinical and radiographic studies have consistently reported horizontal ridge reduction of up to 50% within the first six months following extraction, with the majority of changes occurring during the early healing phase(Zhao et al., 2018). This phenomenon is particularly critical in the posterior mandible, where limited bone availability can compromise prosthetically driven implant placement and necessitates additional augmentation procedures(Aliabadi et al., 2020).

Guided Bone Regeneration (GBR) is a well-established surgical technique that uses barrier membranes to create a secluded space over a bone defect, preventing soft tissue cells from migrating into the defect and allowing osteogenic cells to repopulate and regenerate bone(Z. Yang et al., 2022). Recent evidence confirms that barrier-assisted GBR and socket preservation techniques reduce post-extraction alveolar ridge resorption compared with spontaneous healing, although the magnitude varies across studies and materials(Kim et al., 2023; MacBeth et al., 2017; Mizraji et al., 2023). Effective GBR depends on a biocompatible barrier that maintains space, excludes unwanted cell types, and supports clot stability and vascularization(Caballé-Serrano et al., 2018).

Barrier membranes can be resorbable or non-resorbable, with resorbable options reducing the need for a second surgery but sometimes exhibiting unpredictable degradation or limited mechanical strength(Abtahi et al., 2023). Advances in polymeric membranes, including synthetic and Electrospun designs, have expanded the range of materials available for GBR and ridge preservation, offering tailored mechanical and biological properties that may improve clinical performance and handling(Alqahtani et al., 2023).

The development of electrospun nanofibrous membranes, particularly those made of chitosan (CS) and polyvinyl alcohol (PVA), represents a frontier in biomaterial science due to the high surface-to-volume ratio and tunable properties that better mimic the native extracellular matrix(Sánchez-Machado et al., 2024). CS is a natural biopolymer derived from chitin and is widely used in regenerative medicine for its biocompatibility, biodegradability, and intrinsic mucoadhesive properties(Mokhtari et al., 2025). In addition, CS exhibits broad-spectrum antibacterial activity, which has been shown to occur through the disruption of bacterial cell walls and inhibition of microbial proliferation(Murugan et al., 2025), which is an important advantage when membranes are intentionally left exposed in open-healing protocols. Recent studies on CS/PVA blends confirm improved antibacterial activity and support early soft tissue healing in wound models(Cai et al., 2024; Doan & Tran, 2023).

However, pure CS membranes often lack the mechanical strength and flexibility required for consistent clinical handling and space maintenance(Wahba, 2020). The incorporation

of PVA, a hydrophilic and biocompatible synthetic polymer, enhances the mechanical integrity and spinnability of nanofibers, producing scaffolds with more favorable tensile properties and structural stability(Ghoneum et al., 2025). Electrospun CS/PVA blends also demonstrate improved morphology and uniform fiber formation, which are critical for maintaining barrier function in moist and dynamic environments like the oral cavity(Al-Madhagy et al., 2023). Recent materials research shows that optimized CS/PVA electrospinning parameters can significantly enhance fiber consistency and mechanical performance relative to CS alone(Hadipour-Goudarzi et al., 2023; Salleh et al., 2025).

Despite the increasing use of polymeric barrier membranes and their theoretical advantages for ridge preservation, high-quality clinical evidence evaluating their effectiveness as standalone barriers without adjunctive grafting remains limited(Tang & Zhang, 2025). Recent reviews emphasize that most human studies combine membranes with graft materials, which obscures the isolated effect of the membrane on hard and soft tissue healing, and that randomized split-mouth trials with histomorphometric outcomes are scarce(Avila-Ortiz et al., 2019). In an open-healing scenario, a barrier membrane must not only function as a physical partition preventing soft tissue ingrowth into the socket, but also stabilize the blood clot, reduce the risk of alveolar osteitis (dry socket), and facilitate the development of a mature and keratinized tissue band(Dimitriou et al., 2012; Schnutenhaus et al., 2018). Therefore, this randomized split-mouth clinical trial aims to evaluate the effectiveness of an electrospun chitosan/polyvinyl alcohol nanofibrous membrane as a standalone open-healing barrier for ridge preservation, assessing its ability to limit bone resorption and improve soft tissue outcomes compared with natural healing.

Objectives

Primary objectives

To compare horizontal and vertical alveolar ridge dimensional changes, keratinized tissue width, and histomorphometric outcomes between mandibular premolar extraction sockets treated with a nanofibrous electrospun CS/PVA membrane and those healing naturally.

Secondary objectives

To evaluate soft tissue thickness gain, early wound healing, and the occurrence of postoperative adverse events between the two treatment approaches.

Statistical hypothesis

The null hypothesis is that no statistically significant differences exist between test and control sites with respect to the primary and secondary outcomes.

This protocol was developed in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2025 statement(Chan et al., 2025), and the results of the completed trial will be reported in line with the CONsolidated Standards of Reporting Trials (CONSORT) 2025 guidelines(Hopewell et al., 2025).

Study Design and Methodology

Trial Design and Setting

This study is designed as a prospective, randomized, triple-blinded, split-mouth clinical trial with a 1:1 allocation ratio. The trial will be conducted at the outpatient clinics of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Damascus University. Ethical approval from the Biomedical Research Ethics Committee has been obtained, and the trial has been prospectively registered at the Thailand Clinical Trial Registry (ID: TCTR20251001001). The study will be conducted in accordance with the Declaration of Helsinki. Furthermore, this study is designed as an exploratory, superiority clinical trial. Participant recruitment has started on 13/01/2026 and is expected to continue until the required sample size is achieved. Given the exploratory nature and minimal risk of this trial, no independent auditing process is planned.

The study will recruit patients requiring bilateral extraction of non-restorable mandibular premolars. Participants will be screened by 2 assessors, and must meet the following criteria to be eligible for inclusion: 1- adults aged between 18 and 65 years in good general health. 2- presence of bilateral, single-rooted mandibular premolars requiring extraction due to caries, endodontic failure, or trauma. 3- post-extraction sockets must exhibit intact buccal and lingual plates, classified as type 1 (4-walled) sockets. 4- presence of at least two stable, non-mobile adjacent or nearby teeth to support the reference stent.5- ability to understand and sign the informed consent and commit to the four-month follow-up schedule.

Exclusion criteria will include the following: 1- Patients with uncontrolled metabolic bone diseases, uncontrolled systemic diseases, or those on long-term corticosteroids or bisphosphonate therapy will be excluded. 2- Patients with active periodontal disease, defined as probing pocket depth ≥ 5 millimeters (mm) with bleeding on probing at the extraction sites, or acute periapical infection at the extraction sites that cannot be fully debrided. 3- heavy smokers (≥ 10 cigarettes/day), alcoholics, and pregnant and lactating women. 4- Patients with a known sensitivity to seafood, chitosan, or PVA.

Randomization will be performed using a computer-generated simple random sequence (randomizer.org) to determine the allocation of the CS/PVA nanofibrous membrane to either the left or right extraction site. For randomization purposes, the right side will be coded as”1” and the left side as “2”, with the selected numbering indicating the test site. The generated sequence will be printed, placed into sequentially numbered, opaque, sealed envelopes corresponding to patient enrollment order, and prepared by an assistant not involved in the surgical or outcome assessment procedures. Allocation concealment will be maintained until both teeth are extracted and the integrity of the four socket walls is

confirmed, at which point the envelope will be opened by the surgeon. Participants, outcome assessors, and the data analyst will remain blinded to group allocation throughout the study period.

Surgical protocol

Under local anesthesia (2% lidocaine with 1:100.000 epinephrine), the target teeth on both sides will be extracted with minimal trauma using elevators and forceps, and will be debrided from granulation tissues if present. Following extraction, a 2 mm cervicular mini-flap will be elevated buccally and lingually on both sockets to facilitate measurements, membrane placement, and suturing. An impression for the lower arch will be taken and poured to make a stone cast; all measurements will be taken at this stage.

For the experimental sites, the CS/PVA membranes will be supplied in a sterile form and trimmed chairside to adapt to the socket dimensions; detailed fabrication and physicochemical characterization have been previously described(Al-Madhagy et al., 2022). After membrane adaptation, 3/0 nylon sutures will be placed in a figure 8 pattern. To maintain participant blinding, membrane handling and suturing procedures will be visually simulated at both extraction sites; however, only the test site will receive the CS/PVA membrane, while the control site will be sutured over the natural blood clot.

Postoperative instructions

Patients will be provided with verbal and written instructions. These include: biting on a sterile gauze for one hour, avoiding spitting, and mouth rinsing during the first 24 hours, avoiding hot drinks, and maintain soft diet for the first 48 hours, rinsing with warm normal saline from the day after surgery. prescribed analgesics (acetaminophen 500 mg) to be used when the pain is severe. No systematic antibiotic will be prescribed unless a post-extraction infection occurs. Sutures will be removed after one week.

Postoperative complications, specifically alveolar osteitis (dry socket) or localized surgical site infections, will be defined and systematically recorded as adverse events. Alveolar osteitis will be diagnosed based on the presence of intense pain starting 1-3 days post-extraction, accompanied by a total or partial loss of the blood clot within the alveolar socket. Localized infection will be identified by clinical signs, including suppuration, persistent erythema, or swelling beyond the normal 72-hour inflammatory window. All such occurrences will be documented in the participant's case report form and recorded as binary outcomes (presence/absence). Affected sites will receive appropriate palliative care or pharmacological intervention; however, these participants will remain in the study to preserve the Intention-to-Treat (ITT) population for longitudinal soft and hard tissue monitoring. Adverse events will be monitored and recorded by the principal investigator throughout the follow-up period.

Following the extraction of bilateral, non-restorable mandibular premolars, a computer-generated randomization sequence will be used to assign each socket to either the experimental group (membrane group) or the control group (blood clot group) by an

assistant who is not involved in the study. The assignments will be placed in sequentially numbered, opaque, sealed envelopes. The surgeon will open the envelope only after the extraction is completed and the four –walled integrity of the socket is confirmed, thereby preventing selection bias during the extraction process.

Four-month follow-up and surgical re-entry

At the conclusion of the four-month healing period, sites will undergo a standardized clinical and surgical evaluation prior to implant placement. Following local anesthesia, a mid-crestal incision will be performed using a number 15 blade, followed by the elevation of a full-thickness mucoperiosteal flap. A bone core biopsy will be harvested from the geometric center of the sockets using a 2.0 mm internal diameter trephine bur under sterile saline irrigation to a depth of 6-8 mm. The osteotomy will be expanded to the dimensions of the required implants, followed by implant insertion, flap repositioning, and suturing with 3/0 silk sutures.

Participant timeline

Screening and eligibility assessment will occur prior to extraction. Baseline measurements will be recorded immediately after extraction. Postoperative follow-up visits will be conducted at 7, 14, and 21 days for soft tissue healing assessment. Final clinical measurements and bone core biopsy will be performed at 4 months during implant placement (table 1). The participant timeline was structured in accordance with the SPIRIT 2025 recommendations(Chan et al., 2025).

Outcomes assessment

The primary outcomes of this study are the change in vertical bone height, horizontal ridge width, keratinized tissue width, and histomorphometric outcomes at 4 months post-extraction. Secondary outcomes include soft tissue augmentation and early wound healing parameters.

I. Clinical Morphometric Assessment

Direct clinical measurements will be recorded at baseline (immediately following extraction) and at 4 months during the re-entry surgery. To ensure site-specific accuracy, a customized transparent vacuum stent will be fabricated for each patient, extending to at least two stable adjacent teeth and to the vestibule of the extracted tooth as well (Figure 1). All clinical measurements will be performed by a single calibrated examiner who is blinded to group allocation.

1- Vertical Bone Linear Measurements:

A calibrated periodontal probe will be used to measure the distance from the stent's fixed reference holes to the alveolar crest at five specific points: mid-buccal, mid-lingual. Mesial, distal, and the center of the socket.

The central hole will be used to measure the distance from the stent to the socket floor at baseline, then at 4 months, measuring from the stent to the newly formed bone. This will allow us to calculate the amount of socket fill. The other holes will be used to record the heights of the socket walls and will tell us how much bone resorption/gain.

The Vertical Bone Change (VBC) for each wall will be calculated using the following formula:

$$\boldsymbol{VBC = H_{baseline} - H_{followup}}$$

Where $\boldsymbol{H}$ is the distance from the stent to the bone of a specific wall.

The percent of VBC for each wall will be calculated using the following formula:

$$\%\boldsymbol{VBC} = \left(\frac{\boldsymbol{H_{baseline} - H_{followup}}}{\boldsymbol{H_{baseline}}}\right) \times 100$$

The Vertical Socket Fill (VSF) will be calculated using the following formula:

$$\boldsymbol{VSF = D_{baseline} - D_{followup}}$$

Where $\boldsymbol{D}$ is the distance from the stent to the socket floor/apex**.**

2- Horizontal Ridge Width:

The horizontal bone width will be evaluated using the transgingival ridge mapping technique in conjunction with the reference stent. Three holes will be perforated on the horizontal extension guide of the stent at crestal level (1 mm), then 3 mm, and 5 mm apically on both the buccal and lingual sides. A sharp-tipped Wilson Ridge Mapping Caliper will be inserted through the guide channels, and the overlying soft tissue until the alveolar bone is definitely reached on both buccal and lingual aspects.

The total horizontal width ($\boldsymbol{W}$) at each level will be recorded at baseline and after 4 months. The magnitude of horizontal resorption will be calculated using the formula:

$$\Delta\boldsymbol{W = W_{baseline} - W_{followup}}$$

The percent of width loss will be calculated using the following formula:

$$\%\boldsymbol{loss} = \left(\frac{\boldsymbol{W_{baseline} - W_{followup}}}{\boldsymbol{W_{baseline}}}\right) \times 100$$



Figure 1: The Fabricated transparent, patient-specific Vacuum stent with the hole on the occlusal and buccal surfaces.

3- Keratinized Tissue Width (KWT):

The KWT will be measured from the gingival margin to the mucogingival junction (MGJ) at baseline and after 4 months. The mid-buccal hole of the stent will be used as a reference point to identify the mid-buccal point (upper limit). The MGJ will be identified using the roll test, where the alveolar mucosa is moved coronally with a probe until it meets the immobile keratinized tissue (lower limit).

Assessment of KWT will be calculated based on the following formula:

$$\Delta \boldsymbol{KWT} = \boldsymbol{KWT_{baseline}} - \boldsymbol{KWT_{followup}}$$

4- Soft Tissue Augmentation (Soft Tissue Thickness Gain):

Soft tissue thickness (STT) will be assessed at 4 months during re-entry surgery by a graded probe at two anatomical locations utilizing the stent holes: the mid-buccal aspect and the center of the socket during the re-entry surgery (4 months). The central STT will be calculated by subtracting the stent-to-bone distance from the stent-to-mucosa distance, as shown in the following formula:

$$STT_{central} = D_{bone} - D_{mucosa}$$

5- Soft Tissue Healing:

The qualitative assessment of early wound healing will be calculated at 7, 14, and 21 days post-extraction using the Healing Index by Landry et al(Landry, 1985). The index will assess five clinical parameters to determine the overall state of the wound, these are: the tissue color, bleeding on palpation, presence of granulation tissue, incision or wound margins (presence of epithelization and connective tissue exposure), and presence of suppuration. The clinical sites will be scored on a scale of 1 to 5 by a single blinded examiner. A score of 1 will indicate a very poor healing, while a score of 5 will indicate an excellent socket healing.

II. Histological and Histomorphometric Analysis:

Histomorphometric protocol and subsequent analysis will be performed following the method described by Elizalde-Mota et al. with some modifications (Elizalde-Mota et al., 2024). Upon surgical re-entry at four months, bone core biopsies will be harvested from the center of experimental and control sites using a sterile 2.0 mm internal diameter trephine bur. The samples will be immediately fixed in 10% neutral buffered formalin for 48 hours, and subsequently decalcified in 5% formic acid or a similar decalcifying agent for approximately 3-5 days.

Following decalcification, the specimens will be dehydrated in a series of graded alcohols, cleared in xylene, and embedded in paraffin blocks. Longitudinal sections of 4-6 µm thickness will be cut through the middle of each core using a precise microtome. The primary sections will be stained with Hematoxylin and Eosin (H&E) staining, which provides detailed views of cell nuclei and cytoplasm. Additionally, Masson's Trichrome Staining will be utilized to differentiate between mineralized bone and organized collagenous connective tissue, facilitating the identification of newly formed bone and pseudo-periosteum beneath the resorbable membrane.

The histomorphometric evaluation will be performed using high-resolution digital imaging and ImageJ software. The total area of each core will be analyzed to quantify the following parameters as a percentage of the total biopsy area:

- **New Vital Bone (VB%):** percentage of newly formed mineralized tissue characterized by osteocytes in lacunae.

$$\boldsymbol{VB}\% = \left(\frac{\boldsymbol{Area\ of\ vital\ bone}}{\boldsymbol{Total\ biopsy\ area}}\right) \times 100$$

- **Connective Tissue/Marrow Space (CT%):** percentage of non-mineralized structures, including fibrous tissue and vascular components.

$$\boldsymbol{CT}\% = \left(\frac{\boldsymbol{Area\ of\ connective\ tissue + Marrow}}{\boldsymbol{Total\ biopsy\ area}}\right) \times 100$$

- **Residual Material (RM%):** percentage of any remaining membrane remnants, if present.

$$\boldsymbol{RM}\% = \left(\frac{\boldsymbol{Area\ of\ Residual\ Membrane}}{\boldsymbol{Total\ biopsy\ area}}\right) \times 100$$

Statistical analysis plan:

Sample size calculation

The required sample size for this split-mouth study was determined using a power analysis (G*POWER V1.3.9.4., Franz Faul, Universität Kiel, Germany), accounting for paired comparisons, and based on the primary outcome of horizontal ridge width change. Assuming an alpha level of 0.05 and a desired power of 95%, an effect size of 1.7 was chosen based on the study of Rapani et al.(Rapani et al., 2025); the required sample size is 7 patients (14 alveolar sockets); however, additional participants will be recruited to account for potential dropouts.

All quantitative data will be recorded and uploaded to a centralized electronic database (Open Science Framework, OSF)(Foster & Deardorff, 2017). Descriptive statistics will be presented as means and standard deviation, or medians and interquartile ranges when appropriate. The distribution of each continuous variable will be assessed for normality using the Shapiro-Wilk test. If the data meet the assumptions of normality, the paired t-test will be employed to determine the significant differences between the experimental membrane site and the control site within the same patient. For variables that deviate from the normal distribution or for ordinal data, the Wilcoxon Signed-Rank test will be applied.

All statistical tests will be two-tailed, with the threshold for statistical significance set at $p < 0.05$. Multi-level horizontal width assessments will be subjected to a Bonferroni correction where appropriate to account for multiple comparisons.

A sensitivity analysis will be conducted to evaluate the robustness of the primary outcomes. The primary analysis will follow the ITT principle, including all randomized participants regardless of postoperative complications, to reflect real-world clinical effectiveness. Subsequently, a per-protocol (PP) sensitivity analysis will be performed, excluding sites that developed alveolar osteitis or infection, to assess the treatment effect under ideal biological conditions. Discrepancies between ITT and PP results will be evaluated to determine if pathological resorption secondary to complications significantly confounded the observed efficacy of the membrane. All analyses will be performed using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, USA) software.

Given the split-mouth design of the study, loss to follow-up will result in simultaneous missing data for both test and control sites within the same participant. Therefore, participants who fail to attend the scheduled follow-up visits will be excluded from the

analysis and, if such a loss occurs before the minimum required sample size is reached, additional participants will be recruited to preserve statistical power.

Discussion

The clinical management of extraction sockets remains a cornerstone of implant dentistry, yet the challenge of balancing bone preservation with minimally invasive techniques persists(Yankov, 2023). This protocol evaluates a CS/PVA nanofibrous membrane in an open-healing, 4-walled socket model to address the limitations of current collagen-based barriers, which often lack the anti-microbial resilience required when left exposed to the oral environment(Abdo et al., 2023). By utilizing a split-mouth design in the posterior mandible, we isolate the biomaterial's performance from patient-specific systemic variables, providing a controlled assessment of its barrier function and antimicrobial efficacy.

The primary outcomes are designed to measure the membrane's ability to shield the neutral blood clot. In 4-walled sockets, the buccal plate is particularly susceptible to osteoclast-mediated resorption following the loss of bundle bone(Ickroth et al., 2025). Our use of a fixed-stent coordinate system for measurement is a critical methodological choice; it prevents the geometric shift error common in studies that measure from a resorbing crest, ensuring that the 1, 3, and 5 mm horizontal data points remain spatially consistent over the four-month period. This measurement approach follows methodologies described in well-designed ridge preservation trials to minimize positional bias(Aguilar Porta et al., 2025; Khan et al., 2024).

A unique aspect of this protocol is the emphasis on soft tissue augmentation as a secondary outcome. While most alveolar ridge preservation research focuses exclusively on bone, the quality and thickness of the overlying mucosa (the biotype) are essential for long-term stability of the future dental implants(Shafizadeh et al., 2022). It is anticipated that the delayed resorption profile of the CS/PVA membrane acts as a scaffold not just for osteoprogenitor cells, but for fibroblasts, potentially converting a thin biotype into a thick, keratinized cuff through the formation of an organized connective tissue matrix(Al-Madhagy et al., 2023; Nathan et al., 2023).

The inclusion of histomorphometric analysis from trephine cores serves as the biological gold standard for this trial. By calculating vital bone percentage in sockets without bone graft substitutes, we can directly attribute the osteogenic outcome to the membrane's barrier function(Avila-Ortiz et al., 2019). The absence of graft particle eliminates the confounding variable of residual biomaterial, allowing a clear view of the natural trabecular architecture facilitated by the CS/PVA interface. This approach is consistent with histomorphometric protocols used in recent ridge preservation studies evaluating membrane interventions(Benekou et al., 2025; F. Yang et al., 2023).

Furthermore, the decision to maintain participants with postoperative complications for an Intention-To-Treat analysis, supported by a sensitivity analysis, enhances the external validity of the study(Gupta, 2011). This approach reflects real-world clinical challenges,

such as localized infection or alveolar osteitis, while the sensitivity analysis ensures that the Pre-Protocol efficacy remains scientifically robust. This ensures the study addresses not only the material's potential under ideal conditions but also its performance under clinically relevant healing conditions.

Although the CS/PVA membrane typically undergoes complete enzymatic resorption within the first three months, its early-stage stability remains a challenge(Sbricoli et al., 2020). Without an underlying structural support, the membrane may be prone to central collapse, potentially reducing the vertical space available for regeneration and leading to a dipped ridge profile. Furthermore, the split-mouth design, while controlling for systemic variables, cannot entirely eliminate carry-over effects or patient-specific chewing preferences that may disproportionally expose one site to mechanical trauma(Qin et al., 2022).

The generalizability of these findings is also restricted by the strict exclusion of compromised sockets (types 2 and 3) and patients with systemic comorbidities like uncontrolled diabetes. Consequently, the results may not reflect the membrane's efficacy in sites with buccal plate dehiscence or impaired healing capacity.

Conclusion

In conclusion, this split-mouth randomized protocol seeks to determine if the chitosan/polyvinyl alcohol nanofibrous membrane can predictably preserve ridge dimensions in premolar mandibular sockets without supplementary grafting. While the material's biomimetic architecture is promising, its ability to maintain vertical space and enhance soft tissue quality under open-healing conditions remains to be definitively proven. This trial is designed to generate preliminary clinical and histological evidence on the feasibility of nanofibrous barriers as a standalone, minimally invasive alternative to traditional ridge preservation techniques.

Declarations

Abbreviations

CS: Chitosan.

PVA: Polyvinyl alcohol.

CS/PVA: Chitosan/polyvinyl alcohol.

GBR: Guided bone regeneration.

SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials.

CONSORT: CONsolidated Standards of Reporting Trials.

TCTR: Thailand Clinical Trial Registry.

mm: millimeters.

ITT: Intention-to-Treat.

VBC: Vertical Bone Change.

H: the distance from the stent to the bone of a specific wall.

VSF: Vertical Socket Fill.

D: the distance from the stent to the socket floor/apex**.**

W: total horizontal width.

KTW: Keratinized Tissue Width.

MJC: mucogingival junction.

STT: Soft tissue thickness.

H&E: Hematoxylin and Eosin.

VB: new vital bone.

CT: Connective Tissue/Marrow Space.

RM: Residual material.

OSF: Open Science Framework.

PP: Per-protocol.

Ethics approval and consent to participate

The Institutional Review Board and Ethical Committee of Damascus University approve the study (No: DN-180225-422). The study will be done in alignment with the guidelines of the Helsinki Declaration, and all participants will be asked to provide written informed consent.

Trial Registration

Thailand Clinical Trial Registry (TCTR). Registration number (ID: TCTR20251001001), Registered on 01/10/2025 (prospective registration).

URL: https://www.thaiclinicaltrials.org/show/TCTR20251001001.

Consent for Publication

Not applicable.

Protocol and statistical analysis plan

This manuscript describes the full study protocol and prespecified statistical analysis plan. Any protocol amendments will be documented and reported with justification. All analyses will be conducted according to the predefined plan prior to unblinding.

Data availability

De-identified data generated from this study will be deposited in the Open Science Framework (OFS) repository upon study completion, subject to ethical approval and participant confidentiality requirements.

Dissemination policy: the results of this trial will be submitted for publication in peer-reviewed scientific journals regardless of the direction or magnitude of findings. Findings may also be presented at national or international scientific conferences in the field of oral and maxillofacial surgery and implant dentistry.

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Competing interests

The authors declare no financial or non-financial competing interests.

Patient and public involvement

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

Adverse events (Harms)

All adverse events will be monitored and recorded throughout the study period. Events will be reported descriptively as present or absent, including their nature and severity when applicable.

Author contributions

Gamil Al-Madhagy: concept/design, data analysis and interpretation plan, drafting article, critical revision of article, and approval of the article.

Khaldoun Darwich: concept/design, data analysis and interpretation plan, drafting article, critical revision of article, and approval of the article.

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