FULL STUDY PROTOCOL

Comparison of Intraoperative Conditions and Schneiderian Membrane Perforation Risk Among Three Surgical Approaches for Lateral Sinus Floor Elevation

A Prospective Randomized Three-Arm Comparative Clinical Trial

NCT Number	NCT07794293
Unique Protocol Id	IAU-DENT-OMFS-LSFE-2026-01
Principal Investigator	Mehmet Kagan Degerliyurt, DDS, PhD
Study Site	Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul Aydin University, Istanbul, Türkiye
Original Protocol and SAP Date	11 January 2021
Reviewed Full Protocol Date	27 September 2026
Study Period	April 2021 - July 2026
Ethics Approval	Istanbul Aydin University Clinical Research Review Board, Approval No. 2021-464

Document status and provenance

This full protocol document was reviewed on 27 September 2026, after completion of the trial, to provide a comprehensive public record of the study methods. The underlying study protocol and statistical analysis plan were originally prepared prospectively on 11 January 2021, before trial commencement, participant recruitment, randomization, study procedures, and data analysis. The present consolidated document was assembled from the original protocol and statistical analysis plan, ethics documentation and contemporaneous study materials. Final implementation details, including final enrollment and analysis software versions, are included where supported by study records. Accordingly, the preparation date of this consolidated document should not be interpreted as indicating that the underlying study protocol or statistical analysis plan were developed retrospectively. No procedures, outcomes, or analyses unsupported by the available study records have been added.

Protocol Synopsis

Item	Protocol Summary
Design	Single-center, prospective, randomized, three-arm, parallel-group comparative clinical trial.
Population	Adults requiring lateral sinus floor elevation (LSFE) for implant rehabilitation of the posterior maxilla and meeting the eligibility criteria.
Allocation	1:1:1 to standard procedure (SP), epinephrine-soaked cotton roll technique (ESCR), or piezoelectric sinus lift (PESL).
Randomization	Computer-generated variable permuted blocks of 6, 9, and 12; sequence generated by an independent statistician; centralized electronic allocation concealment.
Blinding	Operating surgeon not blinded because interventions were visibly different. Participants were not informed of allocation, although effective participant blinding could not be guaranteed. Preoperative CBCT examiners and the independent data/statistical evaluator were blinded to treatment allocation.
Minimum planned sample size	471 participants (157/group), based on Cohen's f = 0.19, 90% power, and two-sided alpha = 0.0125 for four co-primary outcomes.
Final enrollment	504 participants (168/group) after recruitment continued through the predefined recruitment period.
Co-primary outcomes	Intraoperative bleeding, surgical field visibility, procedural simplicity, and operation time.
Principal secondary outcome	Intraoperative Schneiderian membrane perforation (yes/no).
Other analyses	Technique-specific effect modification for bleeding, visibility, and procedural simplicity in relation to perforation; supportive associations of patient- and anatomy-related factors with intraoperative conditions.
Ethics	Istanbul Aydin University Institutional Review Board, Approval No. 2021-464. Written informed consent obtained before enrollment.

Contents

1. Administrative Information
2. Background and Rationale
3. Objectives
4. Trial Design
5. Study Setting and Participants
6. Eligibility Criteria
7. Recruitment and Informed Consent
8. Randomization and Allocation Concealment
9. Blinding and Masking
10. Interventions and Surgical Procedures
11. Preoperative CBCT Assessment and Anatomical Variables
12. Outcome Measures
13. Measurement Reliability
14. Sample Size and Recruitment Framework
15. Statistical Analysis Plan and Final Analysis Implementation
16. Safety and Intraoperative Complication Management
17. Ethics, Funding, and Data Availability
18. Patient and Public Involvement

1. Administrative Information

Official study title: Comparison of Intraoperative Conditions and Schneiderian Membrane Perforation Risk Among Three Surgical Approaches for Lateral Sinus Floor Elevation: A Prospective Randomized Three-Arm Comparative Clinical Trial.

Principal Investigator: Mehmet Kagan Degerliyurt, DDS, PhD, Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul Aydin University, Istanbul, Türkiye.

Correspondence: mehmetdegerliyurt@aydin.edu.tr; +90 212 411 30 00 ext. 29501; +90 533 548 3260.

Study site: Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul Aydin University, Istanbul, Türkiye.

Original protocol and statistical analysis plan date: 11 January 2021.

Consolidated full protocol date: 27 September 2026.

Study period: April 2021 - July 2026.

Funding: No external funding.

Conflict of interest: The investigators declared no conflicts of interest.

2. Background and Rationale

Lateral sinus floor elevation (LSFE) is an established procedure for implant rehabilitation of the posterior maxilla when residual vertical bone height is insufficient. Schneiderian membrane perforation is among the most frequent intraoperative complications and may be influenced by surgical technique, operator-related factors, and local sinus anatomy. Sinus septa, membrane thickness, residual bone height, and lateral wall morphology have all been investigated as potential contributors to procedural difficulty and perforation risk.

Piezoelectric instrumentation has been introduced to provide selective cutting of mineralized tissue and greater control during lateral-window preparation and membrane elevation. In parallel, local hemostatic adjuncts such as epinephrine-containing cottonoid materials have been proposed to reduce oozing and improve visualization. However, comparative evidence addressing the broader intraoperative environment - including bleeding, visibility, procedural simplicity, and operation time - is limited, particularly when these parameters are evaluated together with Schneiderian membrane perforation.

The trial therefore compared three LSFE approaches under a standardized single-center surgical protocol: a conventional standard procedure, an epinephrine-soaked cotton roll technique, and a piezoelectric sinus lift technique.

The study was designed to evaluate both intraoperative field conditions and membrane perforation while accounting for relevant patient- and anatomy-related variables.

3. Objectives

3.1 Primary Objective

To compare SP, ESCR, and PESL with respect to four co-primary intraoperative outcomes: bleeding, surgical field visibility, procedural simplicity, and operation time.

3.2 Secondary Objectives

- To compare intraoperative Schneiderian membrane perforation among the three surgical techniques.
- To evaluate whether the associations of intraoperative bleeding, visibility, and procedural simplicity with membrane perforation differ according to surgical technique.
- To explore associations of patient- and anatomy-related characteristics with intraoperative conditions and membrane perforation.

4. Trial Design

The study was a single-center, prospective, randomized, three-arm, parallel-group comparative clinical trial with equal allocation (1:1:1). The three intervention groups were SP, ESCR, and PESL. Each participant contributed a single maxillary sinus to the analysis. When both maxillary sinuses met eligibility criteria, one side was independently selected using a separate computer-generated randomization sequence to avoid within-patient clustering.

The trial was conducted as an interventional study with no crossover between treatment groups. All surgical procedures were performed by the same experienced senior oral and maxillofacial surgeon using standardized protocols.

5. Study Setting and Participants

Patients requiring LSFE for implant rehabilitation were screened consecutively at the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul Aydin University. A total of 504 eligible participants ultimately underwent one LSFE procedure each within the trial framework.

Baseline demographic and patient-related variables included age, sex, and smoking status. Surgical and anatomical variables included side of sinus augmentation, residual bone height (RBH), Schneiderian membrane thickness, lateral sinus wall thickness (LWT), and the presence of maxillary sinus septa.

6. Eligibility Criteria

6.1 Inclusion Criteria

- Age 18 years or older.
- Absence of one or more maxillary posterior molars with a healing period of at least 6 months after extraction.
- Clinical indication for LSFE with either simultaneous or delayed implant placement.
- RBH 5 mm or less at the planned implant site, confirmed by CBCT.
- Availability of complete medical, clinical, and radiographic records.

6.2 Exclusion Criteria

- Uncontrolled systemic disease.
- Known bleeding or coagulation disorders, including clinically relevant thrombocytopenia or platelet dysfunction.
- Current use of anticoagulant or antiplatelet medications.
- Pathological sinus mucosal thickening or other radiographic or clinical evidence of sinus disease.
- Untreated periapical or periodontal infection adjacent to the maxillary sinus.
- Antiresorptive therapy.
- History of head and neck radiotherapy.
- Requirement for additional vertical or horizontal bone augmentation procedures other than LSFE.
- Previous LSFE involving the same maxillary sinus.
- In otherwise clinically and radiographically healthy sinuses, Schneiderian membrane thickness greater than 4 mm on preoperative CBCT, used as a study-specific exclusion criterion.

7. Recruitment and Informed Consent

Consecutive patients were screened for eligibility. Written informed consent was obtained before enrollment. Eligibility was confirmed before release of treatment allocation. The a priori power calculation defined a minimum sample-size requirement rather than a fixed stopping boundary; recruitment continued through the predefined recruitment period, with randomization maintained using variable permuted blocks. Final enrollment was 504 participants, with 168 participants in each group.

8. Randomization and Allocation Concealment

Eligible participants were randomized in a 1:1:1 ratio to SP, ESCR, or PESL. The sequence was computer-generated by an independent statistician who was not involved in recruitment, eligibility assessment, treatment delivery, or outcome evaluation. Variable permuted blocks of 6, 9, and 12 were used in random order to maintain balance while limiting predictability.

The allocation sequence was concealed from investigators responsible for enrollment and eligibility assessment. Treatment assignment was released through a centralized electronic allocation system only after eligibility had been confirmed and written informed consent had been obtained. Participants received the intervention to which they were assigned. No interim analyses were planned or performed, and no formal stopping rules for efficacy, futility, or safety were specified.

9. Blinding and Masking

Participants were not informed of treatment allocation; however, because the procedures were inherently different, effective participant blinding could not be guaranteed. Blinding of the operating surgeon was not feasible. Bleeding, visibility, and procedural simplicity were surgeon-reported immediately after surgery and therefore could not be assessed by a treatment-blinded surgeon. Data organization and statistical analyses were performed by an independent evaluator blinded to treatment allocation.

Preoperative CBCT measurements were obtained independently by two examiners. Each examiner was blinded to the other examiner's measurements and to surgical group allocation.

10. Interventions and Surgical Procedures

10.1 Standardized Local Anesthesia and Surgical Access

A standardized local anesthesia protocol was used in all groups. Before incision, 3 mL of Ultracain D-S Forte was administered, corresponding to 120 mg articaine hydrochloride and 0.036 mg epinephrine. Two milliliters were infiltrated directly into the lateral sinus augmentation site, while the remaining 1 mL was distributed to the planned vertical releasing-incision sites and palatal mucosa. A midcrestal incision with vertical releasing incisions was made, followed by elevation of a full-thickness mucoperiosteal flap to expose the lateral wall of the maxillary sinus.

10.2 Standard Procedure (SP)

The lateral bony window was created using a rotary round diamond bur. The window was outlined and removed, and the Schneiderian membrane was elevated using conventional hand instruments.

10.3 Epinephrine-Soaked Cotton Roll Technique (ESCR)

Following completion of the lateral sinus wall osteotomy, a cottonoid was saturated with an additional 1 mL of Ultracain D-S Forte containing 40 mg articaine hydrochloride and 0.012 mg epinephrine. The cottonoid was applied to the surgical field for 5 minutes to induce local vasoconstriction, promote hemostasis, and improve intraoperative visibility. After removal, membrane elevation was continued using conventional hand instruments.

10.4 Piezoelectric Sinus Lift (PESL)

The lateral window was created using US2 and UL4 piezoelectric surgical tips (Woodpecker, Guilin, China). The Schneiderian membrane was subsequently elevated using UL2 and UL5 piezoelectric inserts, supplemented with conventional hand instruments when the piezoelectric inserts were insufficient to achieve the required membrane elevation.

10.5 Subsequent Surgical Steps and Perforation Repair

In all groups, membrane integrity was evaluated by direct visualization and the Valsalva maneuver. When membrane perforation occurred, repair was performed using leukocyte- and platelet-rich fibrin (L-PRF) combined with a

resorbable collagen membrane (Bio-Gide, Wolhusen, Switzerland), or by repositioning and suturing the Schneiderian membrane to the superior margin of the lateral window followed by L-PRF coverage, as appropriate. After membrane elevation, graft material was placed as indicated. Implant placement was performed during the same procedure when simultaneous implantation had been planned; otherwise, the flap was repositioned and secured with 3/0 non-resorbable silk sutures (Doğsan, Trabzon, Türkiye).

11. Preoperative CBCT Assessment and Anatomical Variables

11.1 CBCT Acquisition

All CBCT examinations were acquired using an ORTHOPANTOMOGRAPH OP 3D unit (PaloDEx Group Oy, Tuusula, Finland; marketed under the KaVo brand) with a 9 x 11 cm field of view in standard-resolution mode and an isotropic voxel size of 300 micrometers. Tube voltage was 95 kV; tube current ranged from 4.0 to 12.5 mA and exposure time from 3.6 to 4.2 seconds according to patient-specific exposure settings. Images were viewed and analyzed using DTX Studio Clinic software (Nobel Biocare AB, Göteborg, Sweden).

11.2 Measurement Definitions

- RBH: measured on a standardized coronal section centered on the planned implant site, along an axis through the center of the intended implant location and perpendicular to the alveolar crest, from the alveolar crest to the sinus floor.
- Schneiderian membrane thickness: measured at the corresponding point along the sinus floor on the coronal section centered on the planned implant site, using the same implant-centered perpendicular reference axis.
- LWT: measured perpendicular to the lateral sinus wall at the midpoint of the planned lateral-window osteotomy.
- Maxillary sinus septa: corticated bony lamellae or projections originating from the sinus floor, extending into the sinus cavity, with a maximum height of at least 2.5 mm; identified preoperatively on CBCT by the senior surgeon and verified intraoperatively.
- Smoking: classified dichotomously as current smoker versus not currently smoking. Active smoking at enrollment qualified as current smoking irrespective of daily cigarette consumption.

12. Outcome Measures

12.1 Co-primary Outcomes

The four co-primary intraoperative outcomes were bleeding, visibility, procedural simplicity, and operation time.

- Bleeding: assessed immediately after completion of surgery by the operating surgeon using an 11-point numerical rating scale (NRS) from 0 to 10; 0 = no bleeding and 10 = excessive bleeding sufficient to compromise the surgical field.
- Visibility: assessed immediately after completion of surgery using an 11-point NRS from 0 to 10; 0 = poorest surgical visibility and 10 = optimal visibility.
- Procedural simplicity: assessed immediately after completion of surgery using an 11-point NRS from 0 to 10; 0 = maximal procedural difficulty and 10 = greatest ease of surgical handling.
- Operation time: measured by stopwatch from initiation of lateral-window osteotomy to completion of Schneiderian membrane elevation, recorded in minutes and rounded to the nearest whole number. Graft placement and implant placement were excluded from the recorded interval.

12.2 Principal Secondary Outcome

Intraoperative Schneiderian membrane perforation was recorded as a binary outcome (yes/no). Membrane integrity was assessed by direct visualization and the Valsalva maneuver.

12.3 Additional Secondary and Supportive Analyses

- Technique-dependent modification of the relationships between bleeding, visibility, procedural simplicity, and membrane perforation.
- Supportive associations of age, RBH, Schneiderian membrane thickness, LWT, sinus septa, and smoking status with intraoperative outcomes and perforation.

13. Measurement Reliability

All preoperative CBCT measurements were performed independently by two examiners before surgery. Examiner 1 was a senior oral and maxillofacial surgeon with more than 20 years of experience in lateral-window sinus floor elevation surgery; Examiner 2 was an oral and maxillofacial surgery resident. Interexaminer reliability was assessed using measurements obtained independently by both examiners for all 504 examinations.

After study completion, intraexaminer reliability was evaluated separately for each examiner using independently selected random samples of 100 CBCT examinations. Repeat measurements were performed without access to the original measurements, with no more than 20 CBCT examinations reassessed per examiner per day to minimize fatigue-related error. Measurements obtained by the senior surgeon were used for subsequent statistical analyses.

Reliability was quantified using intraclass correlation coefficients based on a two-way model with absolute agreement and single measurements, with 95% confidence intervals.

14. Sample Size and Recruitment Framework

Sample size was determined a priori using a three-group one-way ANOVA framework for the primary between-group comparisons. A small-to-moderate standardized effect size (Cohen's f = 0.19) was assumed. With 90% power and a conservative two-sided alpha level of 0.0125 to account for the four co-primary outcomes, the required total sample size was approximately 470 participants. The calculation was performed using R version 4.0.4.

To maintain equal allocation across three groups, the minimum sample size was set at 471 participants (157 per group). The power calculation therefore defined a minimum requirement rather than a fixed stopping boundary. Recruitment continued through the predefined recruitment period while randomization was maintained with variable permuted blocks, resulting in a final enrollment of 504 participants (168 per group).

15. Statistical Analysis Plan and Final Analysis Implementation

The statistical analysis plan was originally prepared prospectively on 11 January 2021. The analytic framework described below reflects that plan together with final implementation details documented during study completion. Final analyses were performed using R version 4.6.0 and IBM SPSS Statistics for Windows, version 22.0.

15.1 General Principles

Continuous variables were summarized using mean and standard deviation, with medians and interquartile ranges additionally reported for the intraoperative outcomes in the principal tables. Categorical variables were summarized as number and percentage. Distributional characteristics were assessed using the Shapiro-Wilk test and visual inspection of histograms. All tests were two-sided, with $p < 0.05$ considered statistically significant unless multiplicity adjustment was specified.

15.2 Primary Outcome Analyses

Unadjusted differences among SP, ESCR, and PESL for bleeding, visibility, procedural simplicity, and operation time were evaluated using the Kruskal-Wallis test, followed by Dunn post-hoc pairwise comparisons with Holm correction when the global test was significant.

Adjusted analyses used separate multivariable linear regression models for each co-primary outcome. Surgical technique was the main exposure. Adjustment variables were age, RBH, sinus septa, smoking status, Schneiderian membrane thickness, and LWT. Heteroskedasticity-consistent HC3 covariance estimates were used. Adjusted estimated marginal means with 95% confidence intervals and pairwise adjusted mean differences were calculated. Pairwise p-values were Holm-adjusted within each outcome, and global technique-effect p-values were additionally Holm-adjusted across the four co-primary outcomes.

15.3 Membrane Perforation Analysis

Crude membrane perforation rates were compared among techniques using the chi-square test. A multivariable binary logistic regression model evaluated the association between surgical technique and perforation while adjusting for age, RBH, sinus septa, smoking status, Schneiderian membrane thickness, and LWT. Adjusted odds ratios with 95% confidence intervals were reported.

15.4 Interaction Analyses

Effect modification by surgical technique was evaluated separately for bleeding, visibility, and procedural simplicity. Three multivariable logistic regression models were fitted with perforation as the dependent variable and one surgical technique x intraoperative parameter interaction term per model. Each model was adjusted for age, RBH, sinus septa,

smoking status, Schneiderian membrane thickness, and LWT. Global interaction effects were assessed with 2-degree-of-freedom likelihood-ratio tests comparing models with and without the interaction term. The three global interaction p-values were Holm-adjusted. Technique-specific slopes were expressed as odds ratios with 95% confidence intervals, and pairwise slope comparisons were Holm-adjusted within each interaction model.

For graphical presentation, covariate-standardized predicted probabilities of perforation were estimated by averaging model-based predictions over the empirical distribution of the adjustment covariates. Curves and 95% confidence intervals were restricted to the observed score range within each surgical technique to avoid extrapolation.

15.5 Supportive Analyses

Spearman rank correlation coefficients were used to examine relationships among bleeding, visibility, and procedural simplicity. Associations of sinus septa and smoking status with intraoperative outcomes were assessed using the Mann-Whitney U test with rank-biserial correlations as effect-size estimates. Associations of age, RBH, Schneiderian membrane thickness, and LWT with intraoperative outcomes were assessed using Spearman rank correlations. These analyses were considered supportive and exploratory and were not adjusted for multiple comparisons.

15.6 Missing Data and Analysis Set

All randomized participants received the allocated intervention and were analyzed in the groups to which they were randomized. No missing observations were present for variables included in the primary multivariable analyses; therefore, no imputation was required for those analyses.

16. Safety and Intraoperative Complication Management

Participants were monitored intraoperatively, as part of routine surgical care, for unexpected surgical or medical adverse events. Bleeding and Schneiderian membrane perforation were protocol-defined study outcomes and were not classified as unintended harms. Any additional intraoperative complication requiring unplanned intervention or deviation from the planned surgical procedure was to be recorded as an unintended effect.

Membrane integrity was evaluated by direct visualization and the Valsalva maneuver. Perforations were treated according to the repair protocol described in Section 10.5. No separate longitudinal adverse-event endpoint was specified because the trial outcomes were intraoperative.

17. Ethics, Funding, and Data Availability

The study received approval from the Istanbul Aydin University Institutional Review Board (Approval No. 2021-464). Written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the Declaration of Helsinki.

The research received no external funding. The investigators declared no conflicts of interest.

Data supporting the study findings are available from the corresponding author upon reasonable request, subject to institutional and ethical restrictions.

18. Patient and Public Involvement

Patients and members of the public were not involved in the design, conduct, analysis, interpretation, or reporting of the study.

References

1. Vercellotti T, De Paoli S, Nevins M. The piezoelectric bony window osteotomy and sinus membrane elevation: introduction of a new technique for simplification of the sinus augmentation procedure. Int J Periodontics Restorative Dent. 2001;21(6):561-567.

2. Wallace SS, Mazor Z, Froum SJ, Cho SC, Tarnow DP. Schneiderian membrane perforation rate during sinus elevation using piezosurgery: clinical results of 100 consecutive cases. Int J Periodontics Restorative Dent. 2007;27(5):413-419.

3. Seoane J, Lopez-Nino J, Garcia-Caballero L, Seoane-Romero JM, Tomas I, Varela-Centelles P. Membrane perforation in sinus floor elevation - piezoelectric device versus conventional rotary instruments for osteotomy: an experimental study. Clin Implant Dent Relat Res. 2013;15(6):867-873. doi:10.1111/j.1708-8208.2012.00447.x.

4. Jordi C, Mukaddam K, Lambrecht JT, Kuhl S. Membrane perforation rate in lateral maxillary sinus floor augmentation using conventional rotating instruments and piezoelectric device - a meta-analysis. Int J Implant Dent. 2018;4(1):3. doi:10.1186/s40729-017-0114-2.

5. Lin YH, Yang YC, Wen SC, Wang HL. The influence of sinus membrane thickness upon membrane perforation during lateral window sinus augmentation. Clin Oral Implants Res. 2016;27(5):612-617. doi:10.1111/clr.12646.

6. Testori T, Weinstein T, Taschieri S, Wallace SS. Risk factors in lateral window sinus elevation surgery. Periodontol 2000. 2019;81(1):91-123. doi:10.1111/prd.12286.

7. Marx RE, Garg AK. A novel aid to elevation of the sinus membrane for the sinus lift procedure. Implant Dent. 2002;11(3):268-271. doi:10.1097/00008505-200207000-00012.