Doctoral School in Health Sciences

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CHELE Dumitru

EVALUATION OF THE INFLUENCE OF MUCOSAL GRAFTS ON PERI-IMPLANT BIOLOGIC SPACE FORMATION

323.01 – STOMATOLOGY

Summary of Doctor of Medical Sciences Thesis

Chișinău, 2026

The thesis was developed at the Department of oral and maxillofacial surgery „Arsenie Guțan” State University of Medicine and Pharmacy „Nicolae Testemițanu”.

Scientific coordinator
Mostovei Andrei,
PhD med. sci., associate professor

Co-supervisor (Cotutelle)
Consuela Norina Forna,
PhD med. sci., university professor

Guidance committee members:
Bâldea Bogdan,
PhD med. sci., associate professor.
Zănoagă Oleg,
PhD med. sci., associate professor.
Sîrbu Dumitru,
PhD med. sci., associate professor.

The defense will take place at 24.08.2026, at 14.00 in the premises of USMF "Nicolae Testemițanu", bd. Ștefan cel Mare si Sfânt, 165, office 205 in the meeting of the Commission for public defense of the doctoral thesis, approved by the decision of the Scientific Council of the Consortium of 01.07.2026 (minutes no. 14).

The composition of the Commission for public defense of the doctoral thesis:
Ciobanu Sergiu,
Dr. habil. med. sci., associate professor, **president**

Mostovei Andrei,
PhD med. sci., associate professor, Scientific coordinator

Forna Consuela Norina,
PhD med. sci., university professor, Co-supervisor (Cotutelle)

Sîrbu Dumitru,
PhD med. sci., associate professor, referent, Guidance committee member

Uncuța Diana,
Dr. habil. med. sci., associate professor, referent

Cirimpei Vasile,
PhD med. sci., referent

Mighic Alexandr,
PhD med. sci., referent

Author
Chele Dumitru

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1. CONTEMPORARY ASPECTS OF PERI-IMPLANT PHENOTYPE

Background and Significance. Over the past decades, oral implantology has become the method of choice for the rehabilitation of partial and total edentulism, owing to the high survival and clinical success rates of dental implants [1,2]. However, the success of contemporary implant-prosthetic treatment is no longer assessed exclusively through osseointegration, but through the long-term maintenance of peri-implant tissue health, marginal bone level stability, and the achievement of a predictable esthetic outcome. In this context, the peri-implant phenotype represents one of the most important biological factors involved in the success of implant-supported restorations [3,4].

Current evidence demonstrates that peri-implant soft tissue thickness directly influences crestal bone remodeling, the formation of supracrestal tissue attachment, and the long-term stability of dental implants [5]. Thin gingival phenotypes are associated with pronounced marginal bone loss, soft tissue recession, translucency of prosthetic components, and inferior esthetic outcomes compared to thick phenotypes [6,7]. Accordingly, the concept of "peri-implant biological space" or "supracrestal tissue attachment" has become an essential component in modern implant-prosthetic treatment planning [8].

Numerous studies have demonstrated that insufficient soft tissue thickness (<2 mm) leads to compensatory remodeling of the marginal bone in order to re-establish the biological dimensions required by the supracrestal tissues [5]. Furthermore, the absence of an adequate width of keratinized mucosa is associated with plaque accumulation, peri-implant inflammation, discomfort during oral hygiene, and an increased risk of peri-implantitis. For these reasons, peri-implant soft tissue augmentation represents one of the current directions of research and development in oral implantology [9,10,11].

The current therapeutic standard for soft tissue augmentation is the autogenous connective tissue graft, considered the "gold standard" due to its predictability and clinical efficacy [12,13]. However, this technique presents multiple disadvantages, including the need for an additional donor site, increased postoperative morbidity, pain, bleeding, and quantitative limitations of available tissue [14]. In this context, xenogeneic collagen matrices have been proposed as a therapeutic alternative, with the advantage of eliminating the donor site and reducing postoperative discomfort [15]. Nevertheless, evidence regarding their comparative efficacy and impact on peri-implant biological space formation remains insufficient and controversial [12,15,16,19].

No prospective controlled clinical studies evaluating the comparative influence of autogenous and xenogeneic grafts on peri-implant phenotype modification and peri-implant biological space formation have been identified in the Republic of Moldova. This scientific gap underscores the rationale and relevance of the present study.

Aim: To optimize the management of peri-implant soft tissues in implant-prosthetic treatment.

Objectives:

1. To evaluate the role of the gingival phenotype and bone remodeling during the osseointegration period and peri-implant biological space formation.
2. To assess the qualitative and quantitative outcomes of the mucosa and peri-implant bone remodeling following augmentation with autogenous grafts.

3. To assess the qualitative and quantitative outcomes of the mucosa and peri-implant bone remodeling following augmentation with xenogeneic grafts.
4. To comparatively analyze the results obtained following augmentation with autogenous and xenogeneic grafts.

Scientific Novelty

The scientific novelty of this work consists in the fact that, for the first time in the Republic of Moldova, a prospective comparative clinical study was conducted evaluating the use of xenogeneic collagen matrices versus autogenous connective tissue grafts in peri-implant phenotype augmentation. Quantitative and qualitative changes in keratinized mucosa, buccal soft tissue thickness, and marginal bone level stability were comparatively assessed according to the type of material used. The results obtained allowed the formulation of a peri-implant soft tissue management approach adapted to the individual gingival phenotype of the patient.

Research Methodology and Summary of Results

The study represents a prospective controlled clinical trial conducted on 42 patients (66 implants), allocated into two groups: the study group, augmented with xenogeneic collagen matrix (n=33 implants, 21 patients), and the control group, augmented with autogenous connective tissue graft (n=33 implants, 21 patients). Patients with partial edentulism in the posterior mandibular regions, thin gingival phenotype (≤2 mm), and no decompensated systemic conditions were included. Evaluation included clinical parameters (keratinized mucosa width and thickness, gingival phenotype, peri-implant indices), radiological parameters (marginal bone level), and digital parameters (STL-DICOM superimposition, volumetric measurements). Statistical analysis was performed using G*Power 3.1 and dedicated statistical software packages. The main limitations of the study include the relatively small sample size, clinical follow-up limited to the osseointegration period, and the inability to achieve formal randomization due to the difference in morbidity between the two procedures.

Approval of Results

The research was conducted within the Department of Oral and Maxillofacial Surgery and Oral Implantology "Arsenie Guțan", Nicolae Testemițanu State University of Medicine and Pharmacy, Chișinău, Republic of Moldova. The thesis topic was approved at the meeting of the Scientific Council of specialty 323.01 Dentistry on XX.XX.XXXX (minutes no. X). The study was approved by the Research Ethics Committee of Nicolae Testemițanu State University of Medicine and Pharmacy of the Republic of Moldova (no. 19 of 17.06.2022 and no. 2 of 25.11.2025). The research project and the title were approved at the meeting of the Department of Oral and Maxillofacial Surgery and Oral Implantology "Arsenie Guțan" of Nicolae Testemițanu USMP on 23.03.2021 (no. 6).

Publications on the Thesis Topic

The results of the study were disseminated through 15 scientific papers published in national and international specialty journals, 2 oral communications and 4 posters presented at conferences and congresses. 2 invention patents and 2 inovation certificates were obtained. The research was recognized at national and international level through participation in 4 invention forums, distinguished with 4 medals and awards. The complete list of publications on the thesis topic is included at the end of the work.

Volume and Structure of the Thesis

The thesis comprises 130 printed pages of text and consists of an introduction, 4 chapters, general conclusions, bibliography, annexes, declaration of responsibility, and abstract. The core material is structured in sections reflecting, in sequence, the critical analysis of the literature, research material and methods, original results, and their critical analysis. The bibliographic index comprises 138 scientific sources. The illustrative material includes 48 figures, 1 table, and 15 annexes.

Keywords: dental implant, peri-implant phenotype, peri-implant soft tissue, xenogeneic collagen matrix, autogenous connective tissue graft, keratinized mucosa, tissue augmentation, mucosal thickness, marginal bone level, mucogingival surgery.

2. RESEARCH METHODOLOGY

The research represents a prospective controlled clinical study designed for the comparative evaluation of the efficacy of peri-implant soft tissue augmentation using autogenous connective tissue grafts and xenogeneic collagen matrices. The study investigated the influence of these methods on peri-implant biological space formation, gingival phenotype modification, and peri-implant tissue stability during the osseointegration period of dental implants.

Research Design

The study was developed in accordance with the principles of evidence-based medicine and international recommendations for clinical research in oral implantology. The research protocol was approved by the Research Ethics Committee of Nicolae Testemițanu State University of Medicine and Pharmacy, and all procedures were performed in compliance with the principles of the Declaration of Helsinki on biomedical research involving human subjects.

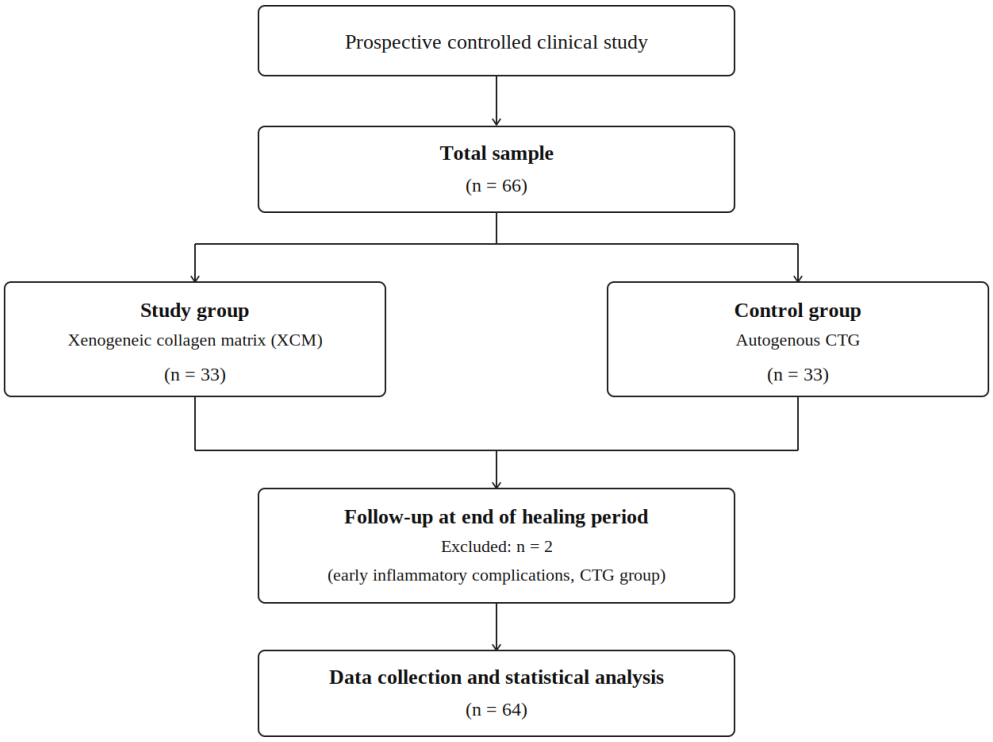


Figure 1. Research design

The research design (Figure 1) was prospective, controlled, with two parallel treatment arms. This design allowed direct comparison of the results obtained through two methods of peri-implant soft tissue augmentation used in contemporary clinical practice.

A total of 42 patients who underwent placement of 66 dental implants were enrolled in the study. Patients were allocated into two groups:

- Control group — augmentation with autogenous connective tissue graft (CTG);
- Study group — augmentation with xenogeneic collagen matrix (XCM).

Each group included 33 implants, allowing a balanced comparison between the two therapeutic methods.

The study population consisted of adult patients requiring implant-prosthetic treatment in the posterior mandibular regions and presenting with a thin gingival phenotype.

Inclusion Criteria:

1. Partially edentulous patients in the posterior mandibular regions requiring implant-prosthetic treatment.
2. Clinically healthy patients with no contraindications to implant-prosthetic treatment.
3. Patients presenting a thin gingival phenotype (≤2 mm).
4. Patients who accept participation in the study and sign the informed consent form.
5. Patients able to attend scheduled follow-up visits.
6. Patients without systemic conditions that may influence tissue regeneration.
7. Sufficient bone volume for prosthetically guided implant placement (width ≥7 mm at the implant platform level, and height ≥10 mm).
8. Presence of fixed keratinized mucosa on the ridge ≥2 mm.
9. Achievement of primary stability ≥20 N/cm.
10. Patients aged between 18 and 80 years.

Exclusion Criteria:

1. Patients with decompensated systemic conditions.
2. Patients refusing to sign the informed consent form.
3. Psychologically unstable or uncooperative patients.
4. Patients unable to attend scheduled follow-up visits.
5. Patients receiving medication that may compromise implant osseointegration.
6. Smokers (>10 cigarettes/day).
7. Patients under oral anticoagulant therapy.
8. Fixed keratinized mucosa width on the ridge <2 mm.
9. Need for bone augmentation at the implant site.

Careful selection of participants aimed to reduce confounding factors and increase the internal validity of the study.

Sample Size Estimation

Sample size was calculated through statistical power analysis using G*Power 3.1. The calculation was based on data reported in the literature regarding changes in peri-implant soft tissue thickness following augmentation procedures. A significance level of 5% and a minimum statistical power

of 80% were selected, allowing identification of a sufficient number of cases to detect clinically relevant differences between groups.

Patient Allocation into Treatment Groups

Patient allocation into the study groups was performed prior to the surgical intervention. Two groups comparable in terms of clinical and demographic characteristics were established.

- The control group underwent soft tissue augmentation using autogenous connective tissue grafts harvested from intraoral donor sites.
- The study group underwent augmentation using a xenogeneic collagen matrix, applied according to the manufacturer's recommendations and contemporary clinical protocols.

Clinical Examination

All patients underwent a standardized clinical examination. The clinical evaluation included:

- assessment of the gingival phenotype;
- evaluation of soft tissue thickness;
- determination of keratinized mucosa width;
- analysis of local conditions for implant placement;
- assessment of peri-implant and periodontal tissue status.

Calibrated periodontal probes were used to measure keratinized mucosa width (Figure 2). The mucogingival junction was identified using established clinical methods.

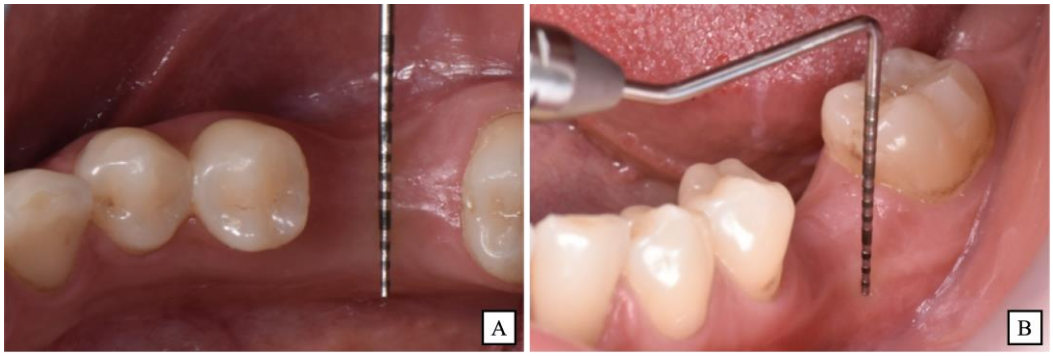


Figure 2. Assessment of keratinized mucosa width: A) occlusal view, B) buccal view.

The gingival phenotype was assessed using both quantitative and qualitative methods, in accordance with the current recommendations of the World Workshop on Periodontal and Peri-Implant Diseases and Conditions.

Imaging and Paraclinical Examination

Imaging examination constituted an essential component of the study. All patients underwent:

- orthopantomography;
- cone beam computed tomography (CBCT);
- digital intraoral scanning.

CBCT imaging (Figure 3) allowed three-dimensional assessment of available bone volume, identification of adjacent anatomical structures, and measurement of peri-implant bone parameters.

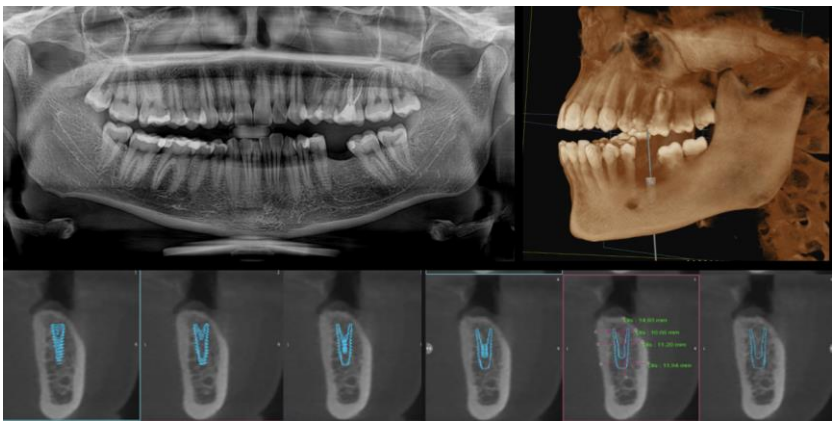


Figure 3. CBCT sections in sagittal, coronal, and axial planes showing available bone volume and adjacent anatomical structures.

Digital intraoral scanning was used to obtain virtual STL models and for three-dimensional analysis of soft tissue changes.

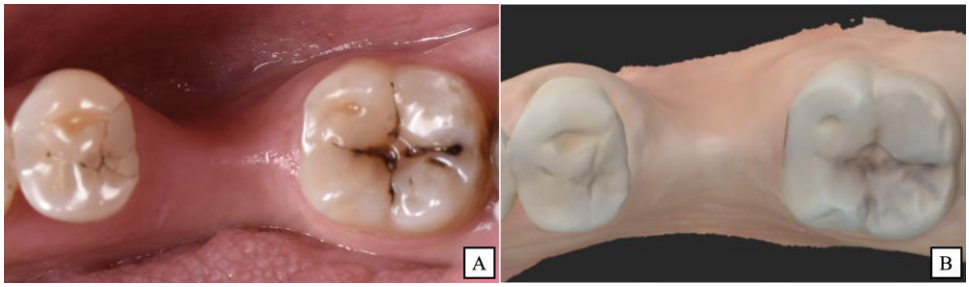


Figure 4. A) Intraoral photograph; B) Intraoral scan (IOS) of the region of interest.

Digital Planning

An innovative element of the study was the use of digital technologies for the evaluation of peri-implant changes. DICOM files from CBCT examinations were superimposed with STL files obtained from intraoral scans (Figure 5).

This method allowed: three-dimensional evaluation of soft tissues; measurement of volume gained following augmentation; assessment of buccal thickness changes; monitoring of peri-implant tissue changes during the healing period.

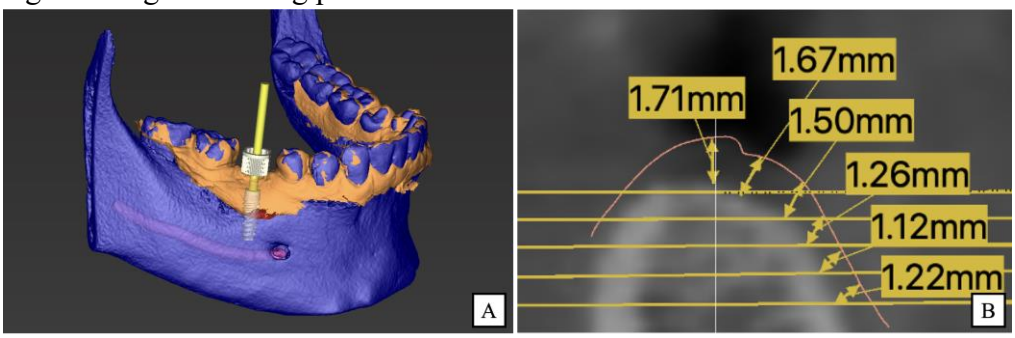


Figure 5. Digital planning through DICOM-STL superimposition: A) Three-dimensional reconstruction of the mandible with IOS overlay; B) Sagittal section in the projection of the planned implant, showing digital measurements of buccal soft tissue thickness at levels 0, 1, 2, 3, and 4 mm, and supracrestal tissue height.

The use of this technology allowed reduction of measurement errors and increased reproducibility of results.

Common Surgical Protocol

Regardless of the study group, all interventions were performed according to a standardized surgical protocol. The common steps included (Figure 6):

- local anesthesia;
- mucoperiosteal flap elevation;
- implant socket preparation;
- dental implant placement;
- primary stability verification;
- positioning of the augmentation material;
- wound closure and suturing.

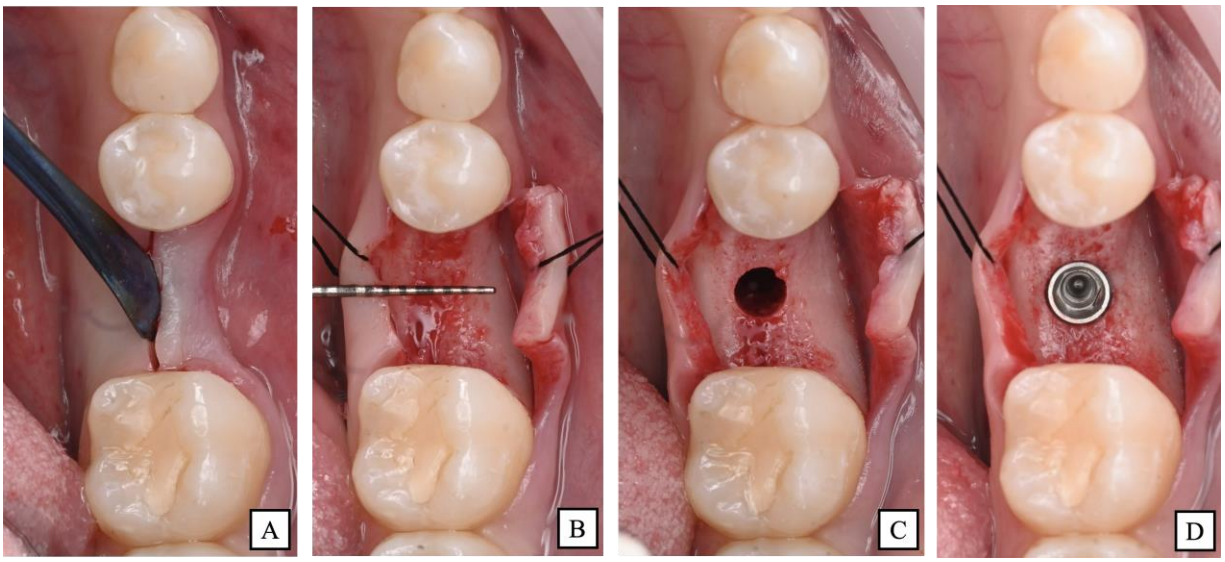


Figure 6. Common surgical steps for both study groups: A) Incision and mucoperiosteal flap elevation; B) Assessment of alveolar ridge width; C) Implant socket preparation according to manufacturer's recommendations; D) Endosseous implant placement.

Standardization of the surgical procedures was intended to eliminate the influence of operator-related factors on the final outcomes.

Control Group Protocol

The autogenous connective tissue graft was used in the control group (Figure 7). Connective tissue was harvested predominantly from the hard palate and, in specific clinical situations, from the maxillary tuberosity. The principles of modern mucogingival surgery were observed with regard to:

- donor site selection;
- optimal graft thickness;
- protection of anatomical structures;
- graft stabilization at the recipient site.

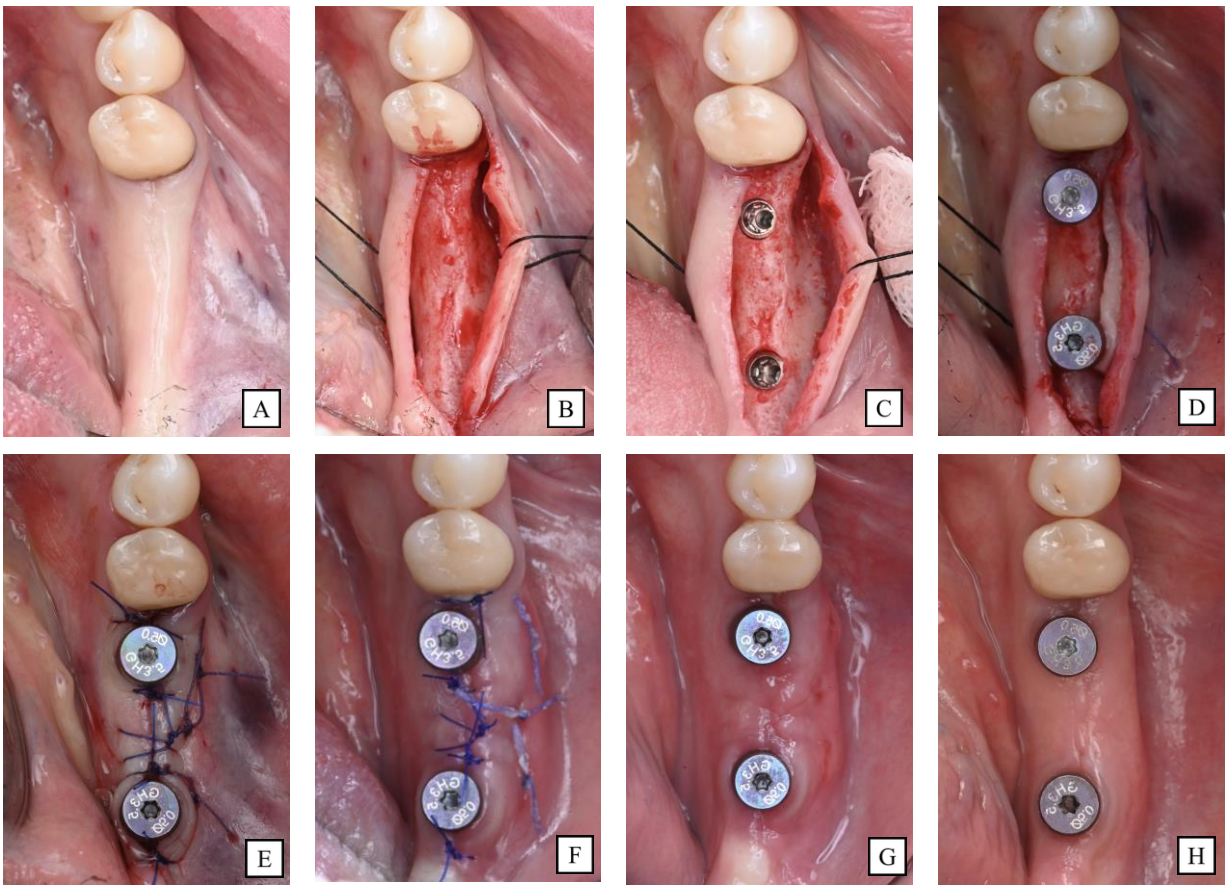
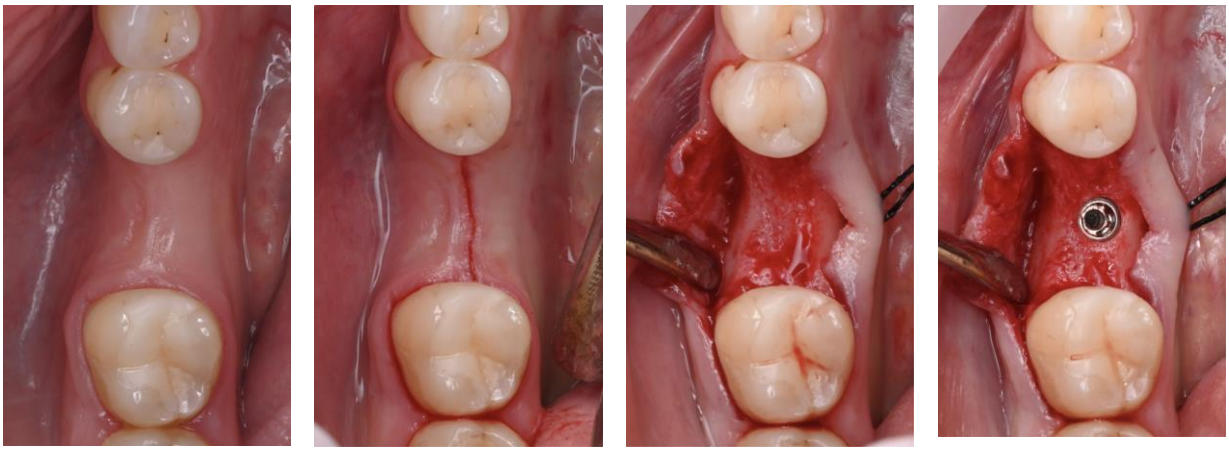


Figure 7. Representative case from the control group: A) Preoperative situation; B) Incision and mucoperiosteal flap elevation; C) Placement of Straumann implants 4mm × 10mm; D) Suturing of the palatal connective tissue graft and healing abutment connection; E) Wound closure with 5.0 sutures; F) Clinical appearance at suture removal, 2 weeks postoperatively; G) Clinical appearance following suture removal; H) Clinical appearance at the end of the osseointegration period (4 months).

Study Group Protocol

A xenogeneic collagen matrix was used in the study group. The material was prepared according to the manufacturer's protocol and individually adapted to the dimensions of the defect. The matrix was positioned buccally to the implant and stabilized using standard suturing techniques (Figure 8). The use of the xenogeneic biomaterial aimed to eliminate donor site morbidity and simplify the surgical procedure.



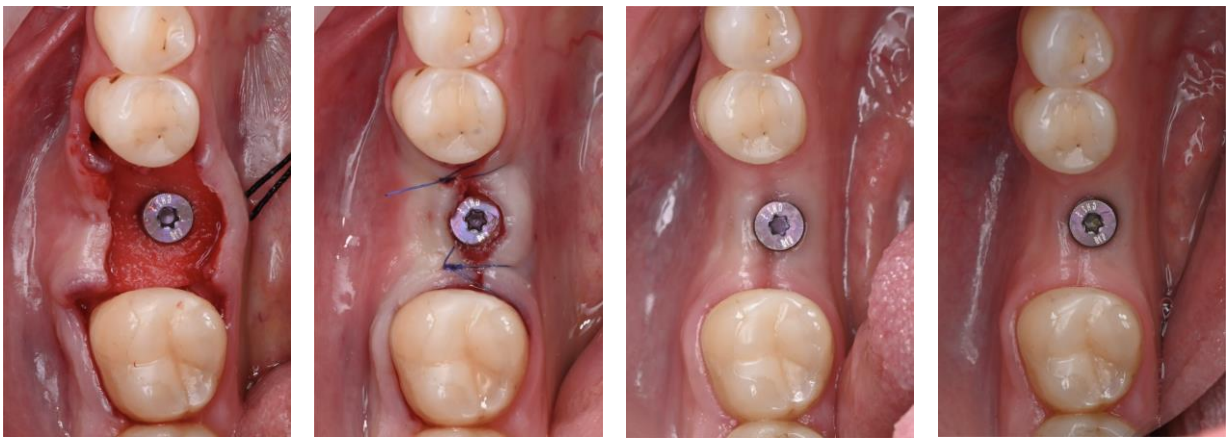


Figure 8. Representative case from the study group: A) Initial clinical situation; B) Mid-crestal incision dividing the keratinized mucosa into two equal portions; C) Mucoperiosteal flap elevation with assessment of soft tissue thickness and alveolar ridge width; D) Implant socket preparation and placement of a Straumann BLX 4mm × 10mm implant; E) Collagen matrix application and stabilization with the healing abutment; F) Wound closure with interrupted 5.0 sutures; G) Clinical appearance at 2 weeks following suture removal; H) Soft tissue appearance 4 months after the intervention.

Postoperative Management

All patients received a uniform postoperative protocol, which included:

- pharmacological treatment;
- local antiseptic measures;
- hygiene and dietary recommendations;
- periodic clinical monitoring.

Healing was followed throughout the entire osseointegration period.

Postoperative Evaluation at the End of the Healing Period

At 3 months postoperatively, a period considered sufficient for the completion of peri-implant soft tissue healing, all patients were re-evaluated clinically, radiologically, and digitally. Radiological evaluation assessed peri-implant bone remodeling through orthopantomography (Figure 9), measuring the distance between the implant platform and the marginal bone level at the mesial and distal aspects. The difference between baseline and postoperative values represented marginal peri-implant bone loss.

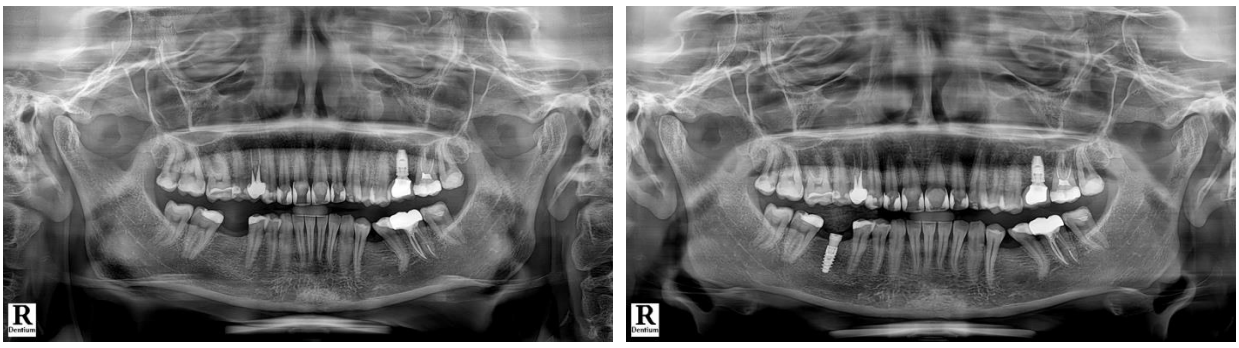


Figure 9. Radiological evaluation: A) Preoperative orthopantomogram; B) Orthopantomogram following the healing period.

Two-dimensional digital evaluation was performed through intraoral scanning and superimposition of postoperative STL files over baseline scans and CBCT images (Figure 10). The following parameters were determined:

- supracrestal soft tissue height;
- buccal soft tissue thickness at the alveolar ridge crest and at 1, 2, 3, and 4 mm apical to it;
- keratinized mucosa width.

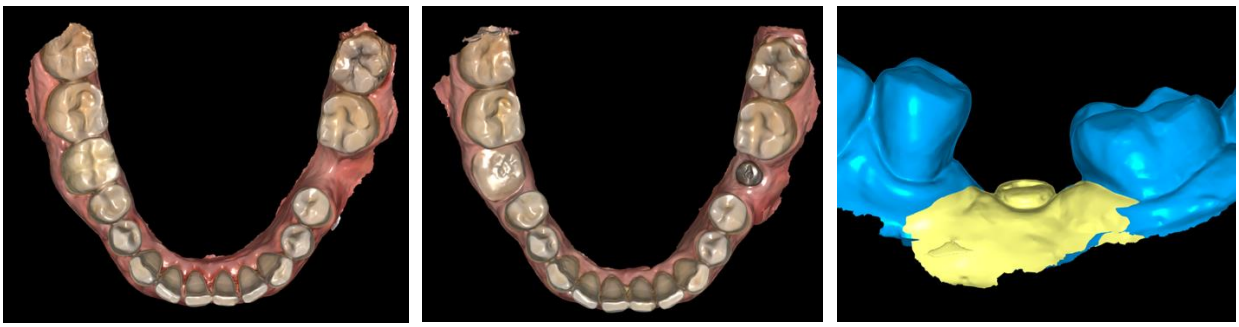


Figure 10. Intraoral scan superimposition: A) Preoperative IOS; B) IOS following the healing period; C) Superimposition of the two scans.

Soft tissue gain was calculated as the difference between postoperative and baseline values (Figure 11). Three-dimensional volumetric analysis was performed through superimposition of preoperative and postoperative STL models. Soft tissue changes were quantified within a standardized region of interest located buccal to the implant. Volumetric gain was determined by calculating the difference between the digital surfaces before and after treatment, with positive values indicating an increase in tissue volume.

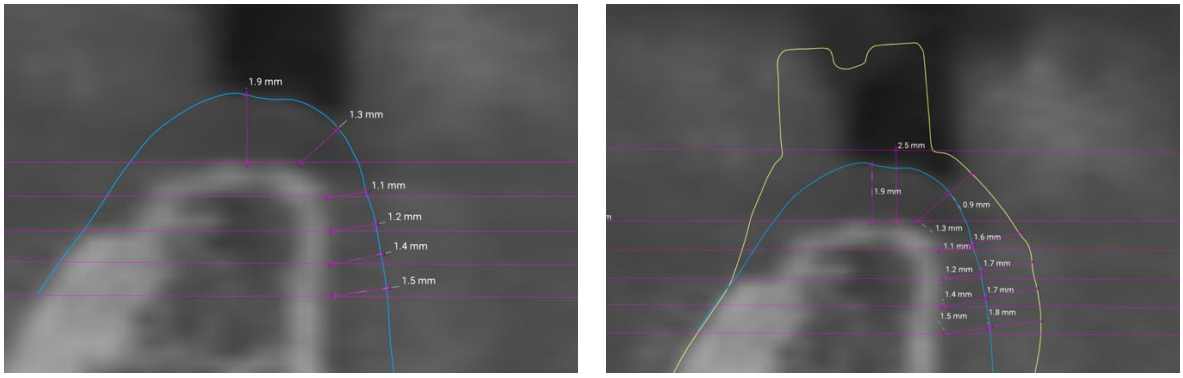


Figure 11. Assessment of buccal soft tissue thickness: A) Preoperative soft tissue thickness measurement; B) Postoperative soft tissue thickness measurement.

All digital and radiological evaluations were performed by the same investigator to ensure reproducibility and methodological consistency.

Study Variables

The primary outcome of the study was the change in buccal soft tissue thickness at the TM1 level. Secondary outcomes included:

- change in keratinized mucosa width;

- change in soft tissue volume;
- gingival phenotype conversion;
- supracrestal tissue height;
- marginal bone level;
- implant stability;
- surgical procedure duration;
- postoperative complications.

Statistical Analysis

Statistical data processing was performed using dedicated statistical software. The following were calculated:

- arithmetic mean;
- standard deviation;
- confidence intervals;
- intergroup differences;
- tests of statistical significance.

The level of statistical significance was set at $p<0.05$.

Statistical analysis allowed objective assessment of the efficacy of the two augmentation methods and determination of the relationship between peri-implant phenotype characteristics and peri-implant tissue stability. The applied methodology enabled comprehensive clinical, radiological, and digital evaluation of peri-implant changes, providing a solid basis for formulating conclusions regarding the efficacy of soft tissue augmentation with autogenous grafts and xenogeneic collagen matrices.

3. ANALYSIS OF OWN RESULTS

The study included 42 patients in whom 66 dental implants were placed. Implants were equally distributed between the two study groups: the control group (autogenous connective tissue graft — CTG) and the study group (xenogeneic collagen matrix — XCM), each comprising 33 implants. Due to early inflammatory complications, two implants from the control group were excluded from the statistical analysis.

Included patients presented a satisfactory general health status, with no decompensated systemic conditions. Primary stability was achieved in all cases, and the groups were comparable at baseline for the majority of analyzed parameters.

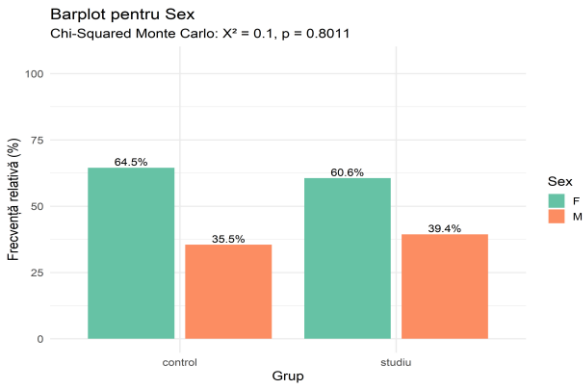


Figure 12. Gender distribution across the study groups.

Sex distribution revealed a predominance of female patients (62.5%), with no significant differences between groups (Figure 12). The mean age of participants was 45.6 ± 13.3 years, with groups being comparable in terms of age (Figure 13).

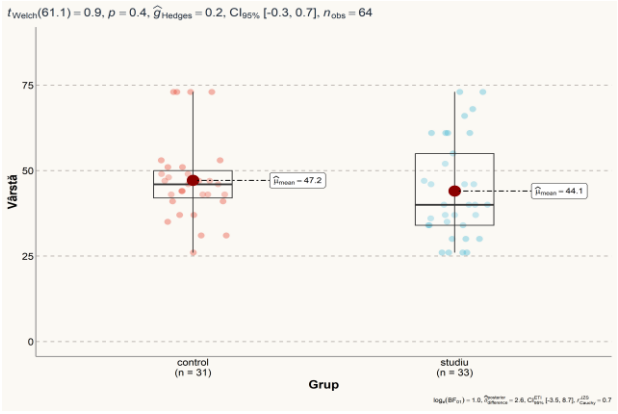


Figure 13. Age distribution across the study groups.

The most frequently treated region was the first mandibular molar (57.8%), followed by the second molar (28.1%) and the second premolar (14.1%) (Figure 14).

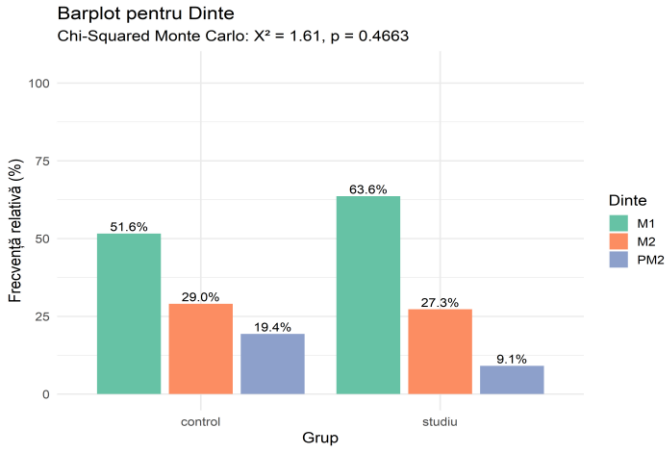


Figure 14. Distribution of implants according to the position of the replaced tooth across the study groups.

Regarding the implant systems used, Dentium implants were the most frequently placed, followed by Straumann implants (Figure 15).

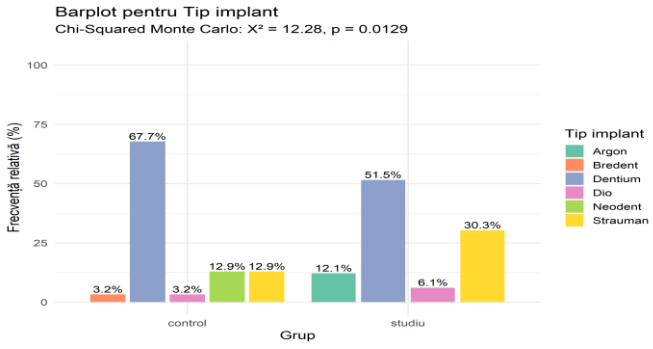


Figure 15. Distribution of implants according to the implant system used across the study groups.

The primary outcome of the study was the assessment of buccal mucosal thickness change at 1 mm apical to the alveolar crest (TM1). At baseline (Figure 16), no significant differences were observed between groups, with a mean thickness of approximately 1.6–1.7 mm.

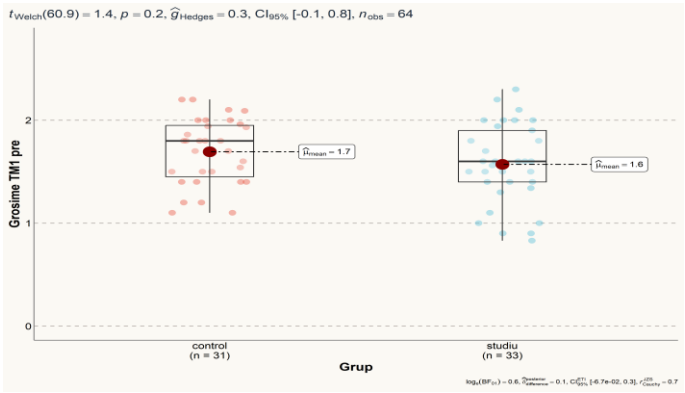


Figure 16. Baseline values of buccal soft tissue thickness (TM1) across the study groups.

At the end of the healing period, mean soft tissue thickness increased in both groups; however, values were significantly greater in the CTG group compared to the XCM group (Figure 17).

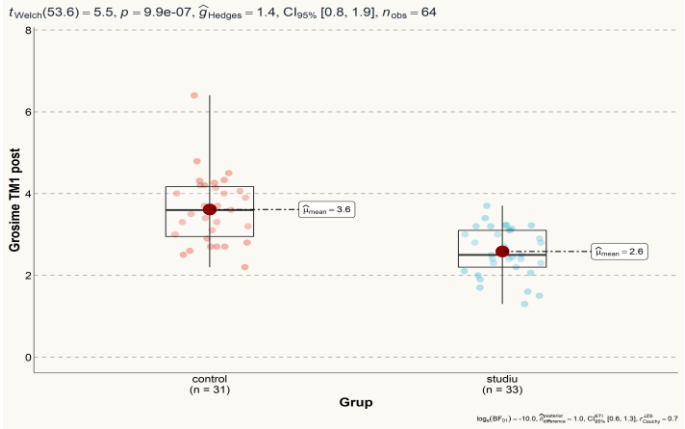


Figure 17. Postoperative values of buccal soft tissue thickness (TM1) across the study groups.

The mean thickness gain (Figure 18) at TM1 level was approximately 1.9 mm in the CTG group and 1.0 mm in the XCM group, the difference being statistically significant. These results demonstrate the superiority of the autogenous connective tissue graft with regard to peri-implant mucosal thickness augmentation.

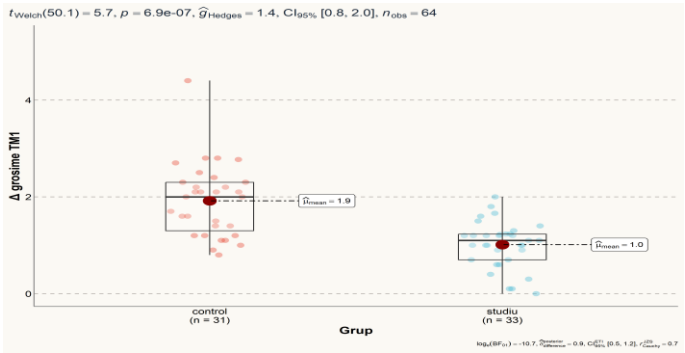


Figure 18. Buccal soft tissue thickness gain (ΔTM1) across the study groups.

Non-inferiority analysis demonstrated that the xenogeneic collagen matrix did not meet the non-inferiority criteria relative to the autogenous graft (Figure 19). Accordingly, the non-inferiority hypothesis for XCM was rejected.

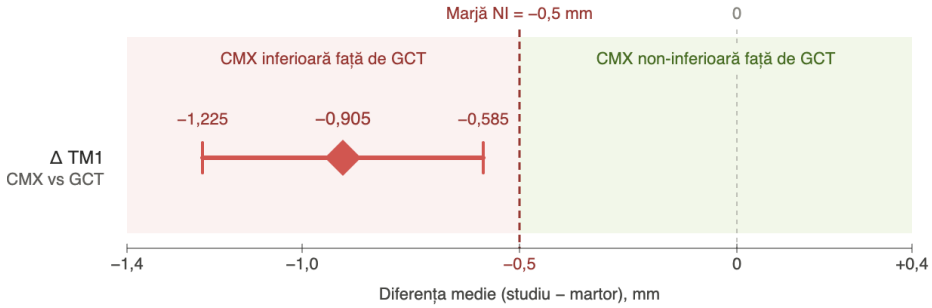


Figure 19. Non-inferiority analysis of buccal soft tissue thickness gain (ΔTM1).

Evaluation of all analyzed buccal levels (TM0–TM4) confirmed the same trend. Mean thickness gain (Figure 20) was significantly greater in the group treated with autogenous connective tissue graft, confirming the superior efficacy of this method for converting the thin peri-implant phenotype to a thick phenotype.

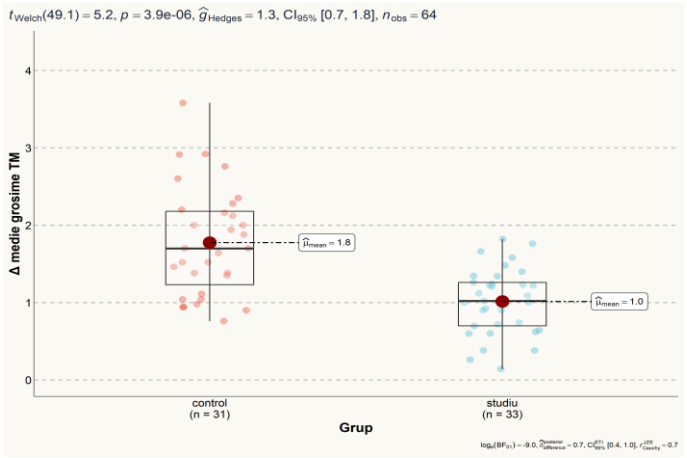


Figure 20. Mean buccal soft tissue thickness gain (ΔTM) across all measured levels in the study groups.

Peri-implant soft tissue height (Figure 21) was comparable between groups both before and after treatment. Although both methods produced a moderate increase in soft tissue height, the differences between groups were not statistically significant.

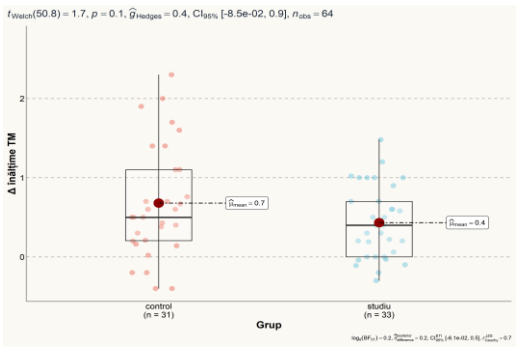


Figure 21. Buccal soft tissue height gain (ΔTM) across the study groups.

Analysis of keratinized mucosa width demonstrated that the groups were comparable at baseline and remained comparable following the healing period (Figure 22). Neither method demonstrated significant superiority for this parameter.

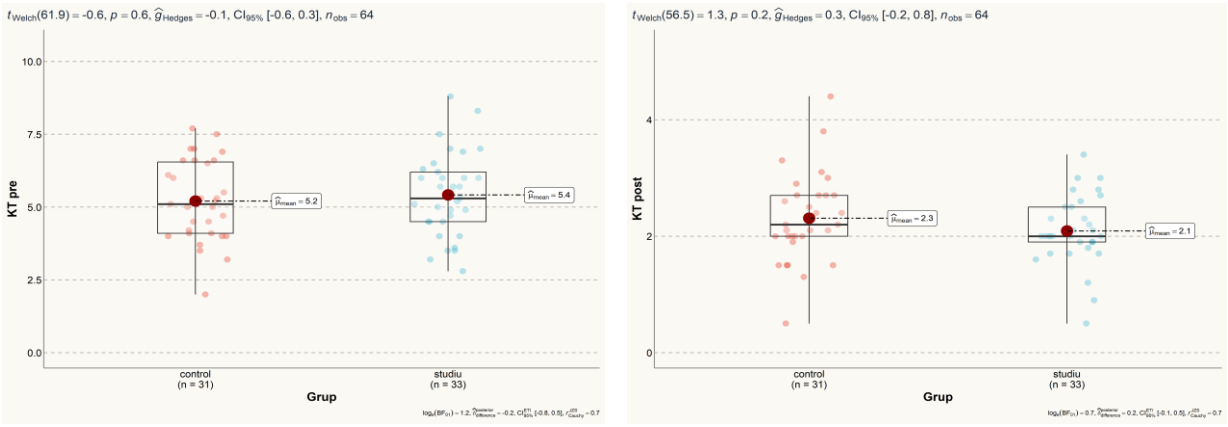


Figure 22. Baseline (KT pre) and postoperative (KT post) values of keratinized mucosa width across the study groups.

Three-dimensional volumetric analysis of peri-implant soft tissues was performed in 37 patients. Mean volumetric gain was approximately twice as large in the CTG group compared to the XCM group (Figure 23). The observed difference was statistically significant and confirmed the superiority of the autogenous graft both in terms of quantitative outcomes and predictability of results.

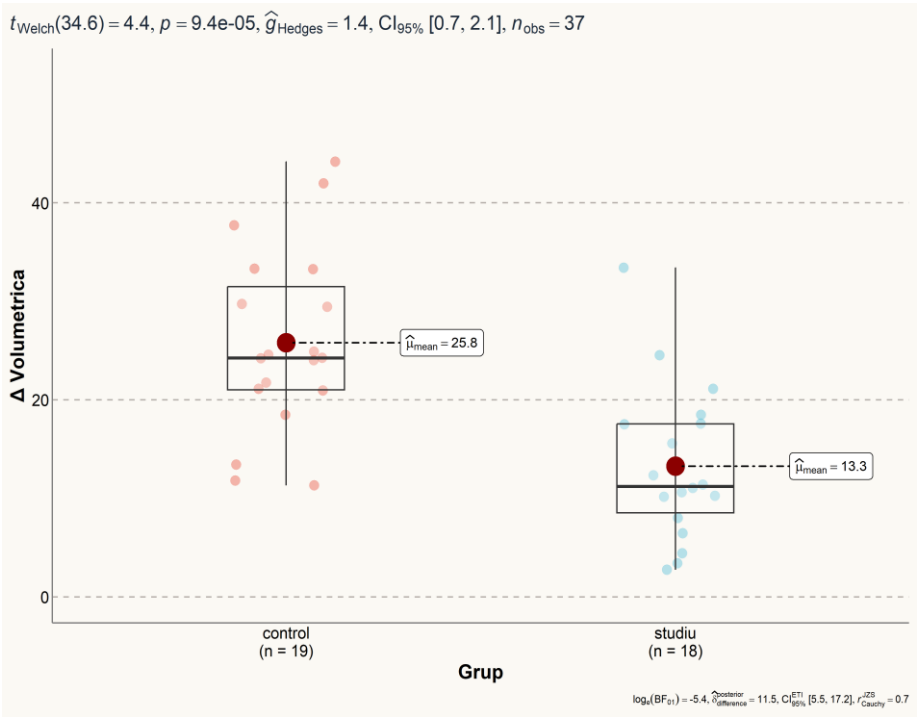


Figure 23. Peri-implant soft tissue volumetric gain (ΔVolumetric) across the study groups.

A key treatment objective was the conversion of the thin gingival phenotype to a thick phenotype (Figure 24). This objective was achieved in all patients in the CTG group and in the majority of patients in the XCM group. The thin phenotype persisted in only a small number of patients treated with the xenogeneic matrix.

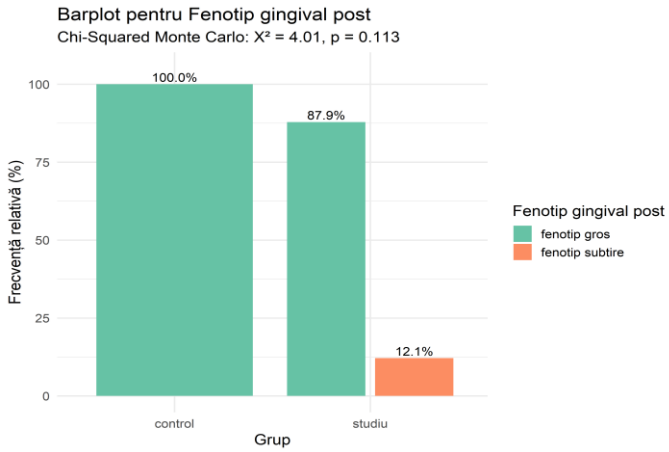


Figure 24. Postoperative gingival phenotype distribution across the study groups.

The need for additional augmentation (Figure 25) through a free gingival graft was low in both groups, with no statistically significant differences.

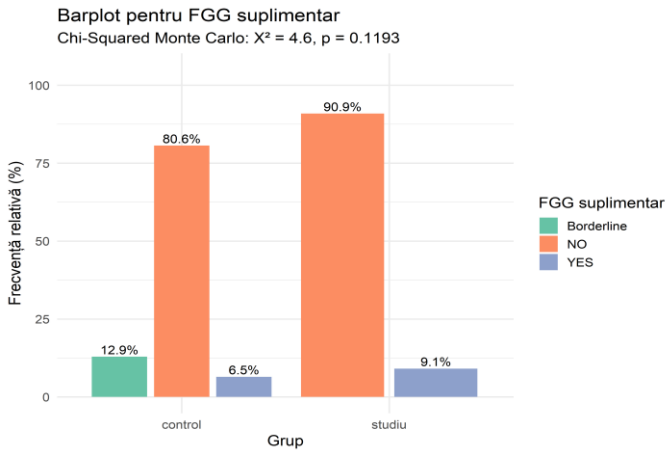


Figure 25. Need for additional free gingival graft (FGG) across the study groups.

Evaluation of preoperative bone characteristics demonstrated that the groups presented similar values for the majority of analyzed parameters. The only significant difference was alveolar ridge height, which was greater in the study group (Figure 26).

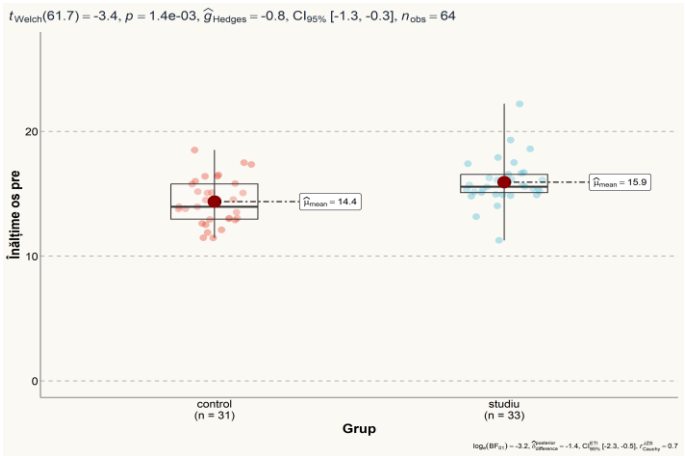


Figure 26. Baseline values of alveolar bone height across the study groups.

Alveolar bone width increased progressively from the crestal to the apical levels in both groups, with no significant differences following the applied statistical corrections (Figure 27).

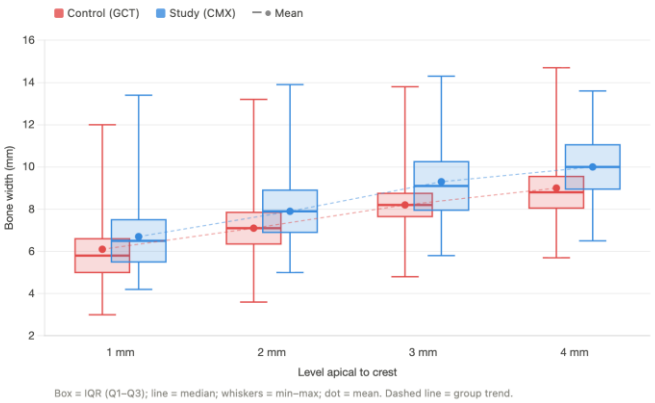


Figure 27. Variation of alveolar bone width according to the apical level relative to the bone crest across the study groups.

Analysis of mesial and distal marginal bone levels revealed minimal bone remodeling in both groups throughout the osseointegration period (Figure 28). The observed marginal bone resorption was limited and comparable between groups, with no statistically significant differences.

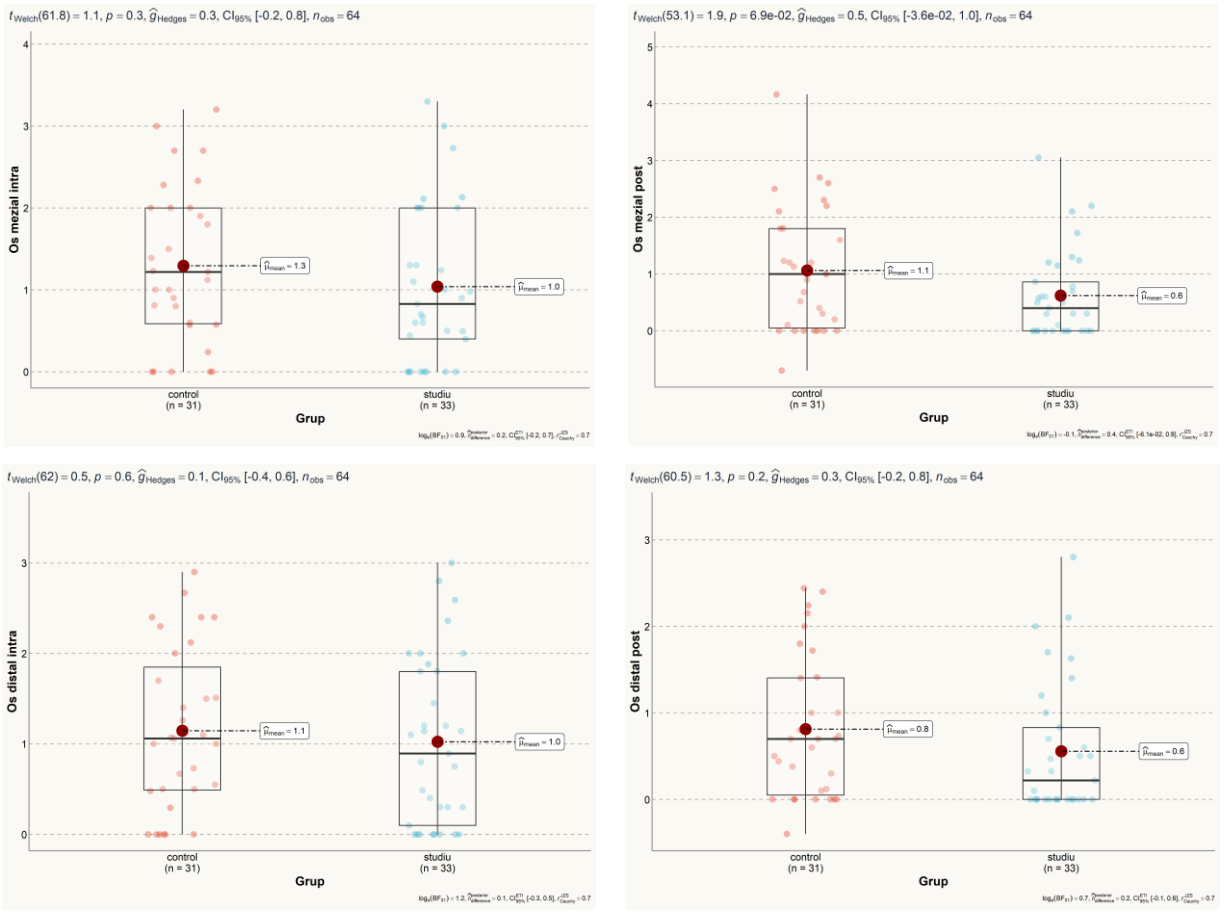


Figure 28. Mesial and distal marginal bone levels: A) mesial preoperative, B) mesial postoperative, C) distal preoperative, and D) distal postoperative, across the study groups.

Surgical procedure duration was significantly greater in the CTG group compared to the XCM group. Procedures requiring autogenous graft harvesting extended the operative time by approximately 30 minutes, reflecting the additional complexity of the technique.

The healing period until prosthetic loading was comparable between groups, with no statistically significant differences (Figure 29).

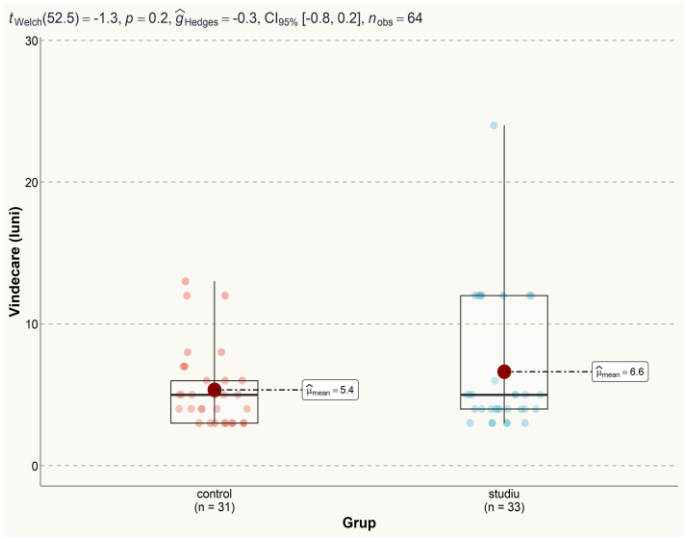


Figure 29. Healing period until prosthetic loading (months) across the study groups.

Postoperative complications were limited in both groups. In the CTG group, complications consisted exclusively of hemorrhage at the palatal donor site, while in the XCM group, only wound dehiscence was observed (Figure 30). The overall complication rate was similar between groups.

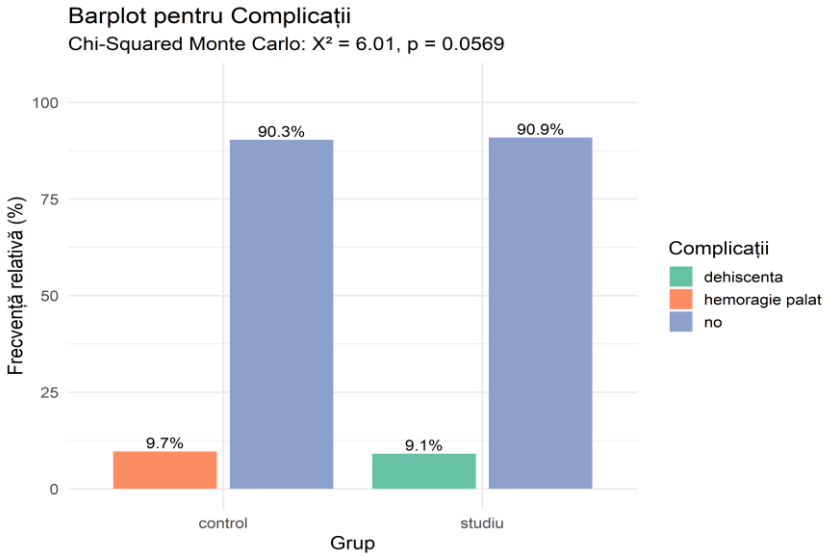


Figure 30. Frequency of postoperative complications across the study groups.

Bone density distribution according to the Misch classification was comparable between groups, with D2 bone type predominating (Figure 31).

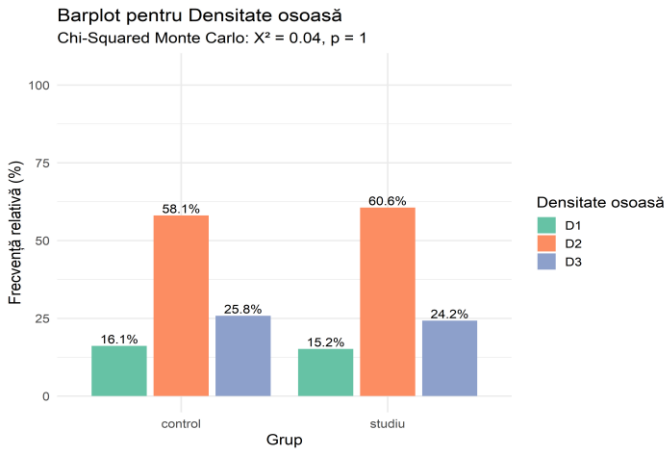


Figure 31. Bone density distribution according to the Misch classification across the study groups.

Primary implant stability, assessed through insertion torque and Periotest values, showed no significant differences between groups (Figure 32). These results confirm that both groups benefited from similar osseointegration conditions and implant stability.

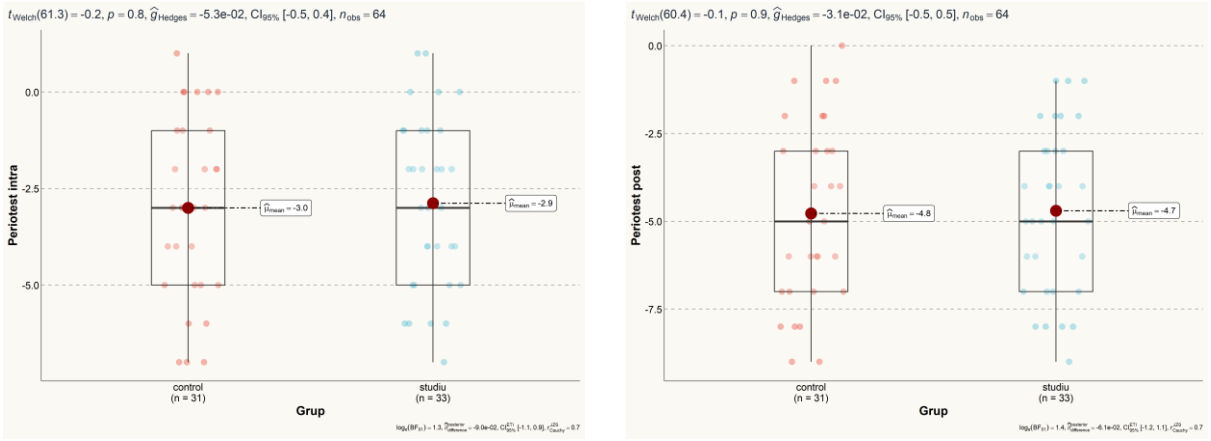


Figure 32. Preoperative (A) and postoperative (B) Periotest values across the study groups.

Overall, the results of the study demonstrate that both the autogenous connective tissue graft and the xenogeneic collagen matrix can be used for peri-implant soft tissue augmentation. However, the autogenous graft yielded superior results with regard to tissue thickness gain, volumetric gain, and predictability of gingival phenotype conversion, while the xenogeneic matrix significantly reduced surgical procedure duration and eliminated donor site morbidity.

4. DISCUSSIONS

The peri-implant phenotype represents one of the determining factors of long-term implant-prosthetic treatment success, influencing both the biological stability of the implant and the final esthetic outcome. In situations where the gingival phenotype is deficient, soft tissue augmentation becomes an important step in ensuring favorable conditions for the formation and maintenance of the peri-implant biological space. The literature considers the autogenous connective tissue graft (CTG) as the gold standard in soft tissue augmentation; however, the morbidity associated with

the donor site has led to the emergence of biomaterial-based alternatives, of which xenogeneic collagen matrices (XCM) are the most extensively studied. The primary aim of the study was the comparative evaluation of the efficacy of the two methods in peri-implant phenotype augmentation.

The study design was conceived to reflect current clinical practice as closely as possible. For ethical reasons, patients were informed about the advantages and disadvantages of each method and voluntarily selected their treatment group. Although this approach may introduce a certain risk of selection bias, the comparability of the groups at baseline reduces the influence of this factor on the interpretation of results. The groups were similar with regard to sex, age, implant location, bone volume, and implant stability parameters, allowing the observed differences to be attributed exclusively to the augmentation technique used.

The primary outcome of the research was the change in peri-implant buccal mucosal thickness at the TM1 level. The data obtained demonstrated that both methods resulted in an increase in soft tissue thickness; however, the autogenous connective tissue graft generated a significantly greater gain compared to the xenogeneic collagen matrix. Non-inferiority analysis did not confirm the equivalence of XCM to CTG, indicating that the xenogeneic substitute cannot fully reproduce the biological effect of autogenous tissue. These results are consistent with data reported in the international literature, which describes CTG as the most predictable method for peri-implant soft tissue thickening.

An important observation in the study was the maintenance of CTG superiority across all investigated levels (TM0–TM4). Not only did punctual mucosal thickness increase, but the entire buccal soft tissue profile presented greater values in the group treated with the autogenous graft. This suggests that autogenous connective tissue exerts a three-dimensional effect on the peri-implant phenotype, favoring the development of a more stable and remodeling-resistant tissue volume. The results confirm observations reported by other authors demonstrating that autogenous tissues exhibit superior biological integration and reduced postoperative contraction compared to xenogeneic biomaterials.

Three-dimensional volumetric analysis represented one of the strengths of the study. The use of STL file superimposition and digital evaluation allowed objective assessment of volume changes. Results demonstrated a nearly twofold volumetric gain in the CTG group compared to the XCM group. From a clinical perspective, this difference is significant as soft tissue volume contributes to emergence profile stability, marginal bone protection, and the achievement of a predictable esthetic outcome. Furthermore, increased peri-implant volume may reduce the risk of recession and prosthetic component exposure, particularly in cases with a thin gingival phenotype. Regarding keratinized mucosa width, results revealed no significant differences between the two treatment methods. This observation suggests that both autogenous grafts and xenogeneic matrices can contribute to the maintenance of an adequate band of keratinized mucosa. Current literature supports the importance of a minimum width of 2 mm for reducing plaque accumulation, limiting peri-implant inflammation, and facilitating oral hygiene. In the present study, both methods provided favorable conditions for the maintenance of peri-implant health.

Supracrestal soft tissue height was also analyzed. No significant differences were found between groups, suggesting that both CTG and XCM allow the formation of adequate supracrestal attachment necessary for implant biological stability. The literature considers a height of approximately 3 mm necessary for the complete development of peri-implant attachment. In the present study, both methods allowed the achievement of values compatible with the maintenance of marginal bone stability.

Analysis of implant stability and marginal bone level demonstrated minimal differences between groups. Periotest values, insertion torque, and marginal bone changes were comparable between groups. This finding indicates that both augmentation methods provided favorable biological conditions for osseointegration, and confirms that the differences observed at the soft tissue level were not influenced by variations in implant stability or initial bone volume.

Surgical procedure duration represented one of the few domains in which XCM demonstrated a clear advantage. Procedures performed with the xenogeneic matrix required significantly less operative time, as they eliminated the need for autogenous graft harvesting. Furthermore, complications associated with the donor site were absent in the XCM group. In contrast, patients treated with CTG presented episodes of bleeding and discomfort at the palatal donor site. These results confirm observations reported in the literature and explain the growing interest in alternative biomaterials in modern clinical practice.

Conversion of the thin gingival phenotype to a thick phenotype represents one of the primary objectives of soft tissue augmentation. In the present study, this objective was achieved in all patients in the CTG group and in the majority of patients in the XCM group. The results confirm the efficacy of both methods while demonstrating the superiority of the autogenous graft with regard to the predictability of the final outcome. From a biological perspective, the thick phenotype is associated with greater soft and hard tissue stability, reduced risk of recession, and more favorable esthetic outcomes.

Regarding the optimal timing of the intervention, the present study supports performing augmentation simultaneously with dental implant placement. This approach allows reduction of the number of surgical interventions, limits operative trauma, and optimizes total treatment time. The results confirm conclusions from recent studies recommending peri-implant phenotype management from the initial phases of implant-prosthetic treatment.

The clinical protocol developed based on the research findings proposes the use of CTG in cases where the primary objective is achieving maximum and predictable soft tissue thickness and volume gain. In situations where reduction of morbidity and patient comfort are prioritized, the xenogeneic collagen matrix may represent a valid alternative, provided that a reduced tissue gain is accepted.

The main limitations of the study were the relatively small number of patients, the absence of classical randomization, and the follow-up period limited to the osseointegration phase. Furthermore, the research focused exclusively on the posterior mandibular regions, which limits extrapolation of results to other anatomical regions, particularly the anterior esthetic zone.
Research perspectives include extension of the monitoring period following prosthetic loading, evaluation of long-term result stability, and analysis of the behavior of both methods in the anterior maxillary regions. Additional studies comparing different types of biomaterials and analyzing their impact on peri-implant esthetics and patient satisfaction are also warranted. The results of such research could contribute to the development of personalized peri-implant phenotype management protocols and to the optimization of modern implant-prosthetic treatment.

5. CONCLUSIONS

1. The deficient peri-implant phenotype, defined by buccal mucosal thickness below 2 mm, represents a documented biological and esthetic risk factor in implant-prosthetic therapy. Its preoperative assessment through standardized methods and simultaneous surgical

correction at the time of implant placement constitute a valid strategy that does not compromise osseointegration, does not affect marginal bone level stability, and allows the achievement of an adequate peri-implant biological space. The integrated digital methodology — STL and DICOM file superimposition, linear measurements at five reference levels, and three-dimensional volumetric analysis — enabled objective and reproducible quantification of peri-implant tissue changes and represents a methodological protocol transferable to future clinical studies.

2. The autogenous connective tissue graft produced a mean buccal mucosal thickness gain of 1.9 ± 0.8 mm at TM1 and 1.8 ± 0.7 mm across all five evaluated levels (TM0–TM4), with a three-dimensional volumetric gain of 25.8 ± 9.3 mm^3 and complete gingival phenotype conversion in 100% of cases, achieving a mean postoperative mucosal thickness of 3.6 mm, exceeding the 2 mm biological threshold at all treated sites.
3. The xenogeneic collagen matrix produced a mean gain of 1.0 ± 0.5 mm at TM1 and a volumetric gain of 13.3 ± 7.9 mm^3, with gingival phenotype conversion in 87.9% of cases and a mean postoperative mucosal thickness of 2.6 mm, confirming the clinical efficacy of augmentation concurrent with implant placement and the achievement of the 2 mm biological threshold as a minimum therapeutic objective.
4. Non-inferiority analysis demonstrated that XCM does not meet the non-inferiority criteria relative to CTG for the primary soft tissue thickness outcome, with a mean difference of −0.9 mm (CI 95%: −1.22, −0.58) exceeding the pre-established clinical margin of −0.5 mm. Both procedures produced comparable results for postoperative keratinized mucosa width (2.3 vs. 2.1 mm; $p=0.2$), supracrestal tissue height ($p=0.10$), marginal bone level, and implant stability assessed through Periotest and insertion torque. Surgical duration was significantly greater in the CTG group (64.0 vs. 32.8 minutes; $p<0.001$), and the complication profile differed: late palatal hemorrhage exclusively in the CTG group, wound dehiscence exclusively in the XCM group.

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LIST OF PUBLICATIONS AND SCIENTIFIC CONFERENCE PRESENTATIONS

by **Dumitru Chele,**

Department of Oral and Maxillofacial Surgery "Arsenie Guțan"

prepared in connection with the Doctor of Medical Sciences dissertation entitled

„Evaluation of the influence of mucosal grafts on peri-implant biologic space formation”,

Specialty 323.01 – Stomatology,

Nicolae Testemițanu State University of Medicine and Pharmacy of the Republic of Moldova

SCIENTIFIC PUBLICATIONS

- **Articles published in international scientific journals:**
  - ✓ **Articles published in journals indexed in Web of Science (ISI), Scopus, and other international bibliographic databases***

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- **Patents, invention patents, registration certificates, and exhibits presented at invention exhibitions:**

19. Jian M., Ficai A., Ficai D., Nacu V., Cobzac V., Mostovei A., Solomon O., **Chele D**. Grefă pentru restabilirea defectelor osoase. Brevet de invenţie MD 1890 Z. BOPI nr.2/2026.

20. Chele N., Topalo V., Dabija I., **Chele D.** Metodă de augmentare ghidată pe verticală în atrofii maxilare severe cu instalarea simultană a implanturilor dentare endoosoase. Brevet de invenţie MD 1445 Z. BOPI 02/2021.

ACTIVE PARTICIPATION IN SCIENTIFIC FORUMS

- **Oral presentations at scientific meetings:**
  - ✓ **National scientific meetings with international participation**

21. **Chele D**. Managementul țesuturilor moi periimplantare în tratamentul implanto-protetic. Comunicare orală prezentată la: Conferința științifică cu participare internațională în memoria profesorului universitar Valentin Topalo; 28 aprilie 2023; Chișinău, Moldova.
22. **Chele D**. Implantarea ghidată versus convențională. Comunicarea prezentată la: Conferința națională cu participare internațională „Digital Technologies in Multidisciplinary Dentistry"; 9–10 septembrie 2023; Chișinău, Moldova.

- **Poster presentations at scientific meetings:**
  - ✓ **international**

23. **Chele D**, Mostovei A, Dabija I, Mostovei M, Chele N. Implant prosthetic rehabilitation in the esthetic zone: Case series. Comunicarea științifică EAO-500 / PO-207 prezentată în cadrul celui de-al 29-lea Congres Științific Anual al European Association for Osseointegration (EAO); 29 septembrie – 1 octombrie 2022; Geneva, Elveția.
24. **Chele D.** Comparative efficacy of connective tissue grafts from tuberosity and palate: a clinical study. Poster. In the ITI World Symposium 2024; 9–11 mai 2024; Singapore. 2024
25. **Chele D.** Absorbable biopolymeric mesh: A new concept in Guided Bone Regeneration. Poster. In the ITI World Symposium 2024; 9–11 mai 2024; Singapore. 2024
26. **Chele D.** Marginal Bone Loss and Related Factors of 1,040 Dental Implants Placed in Fresh Extraction Sockets: An Observational Retrospective Clinical Study. ePoster. In the 40-th Annual Congress of Academy of Osseointegration (AO); 27–29 martie 2025; Seattle, WA, SUA. 2025

ADNOTARE

Chele Dumitru

„Evaluarea influenței grefelor de mucoasă în formarea spațiului biologic peri-implantar”

Teză de doctor în științe medicale, Chișinău 2026

Structura tezei: lucrarea este expusă pe 130 pagini de text imprimat, constă din introducere, 4 capitole, concluzii generale, recomandări practice, indice bibliografic cu 123 de referințe și 15 anexe. Materialul ilustrativ include 48 de figuri, 1 tabel și 15 anexe. Rezultatele obținute sunt publicate în 15 de lucrări științifice publicate, 2 comunicări orale și 4 postere.

Cuvinte-cheie: implant dentar, fenotip peri-implantar, țesut moale peri-implantar, matrice de colagen xenogenă, grefă autogenă de țesut conjunctiv, mucoasă cheratinizată, augmentare tisulară, grosime mucoasă, nivel osos marginal, chirurgie muco-gingivală.

Scopul lucrării constă în optimizarea managementului țesuturilor moi peri-implantare prin evaluarea comparativă a eficacității clinice a matricei de colagen xenogene față de grefa autogenă de țesut conjunctiv în augmentarea fenotipului peri-implantar.

Obiectivele cercetării: Evaluarea rolului fenotipului gingival și al remanierelor osoase în perioada de osteointegrare și formare a spațiului biologic peri-implantar; evaluarea ofertei calitative și cantitative ale mucoasei peri-implantare și a remanierelor osoase obținute prin grefare cu țesuturi autogene și xenogene; analiza comparativă a rezultatelor clinice și estetice obținute în urma grefării cu grefe autogene față de cele xenogene; elaborarea unui protocol clinic de management adaptat fenotipului gingival individual al pacientului.

Noutatea și originalitatea științifică: Pentru prima dată în Republica Moldova a fost realizat un studiu clinic comparativ prospectiv privind utilizarea matricei xenogene de colagen față de grefa autogenă de țesut conjunctiv în augmentarea fenotipului peri-implantar. Totodată, a fost elaborat un protocol de conduită clinică individualizat, bazat pe particularitățile fenotipului gingival al pacientului, care ghidează decizia terapeutică.

Rezultatele obținute care contribuie la soluționarea unei probleme științifice importante constau în demonstrarea faptului că matricea de colagen xenogenă poate constitui o alternativă viabilă la grefa autogenă în creșterea grosimii mucoasei peri-implantare.

Semnificația teoretică a studiului: Studiul a evidențiat că matricea de colagen xenogenă, utilizată în scopul augmentării țesuturilor moi peri-implantare, oferă rezultate clinice satisfăcătoare, cu avantajul unei recuperări postoperatorii mai ușoare și al eliminării disconfortului asociat zonei donatoare. Totodată, au fost elucidate corelațiile dintre grosimea inițială a mucoasei peri-implantare și remanierea nivelului osos marginal.

Valoarea aplicativă a lucrării: Implementarea protocolului elaborat va permite extinderea indicațiilor de augmentare a țesuturilor moi peri-implantare la pacienții cu contraindicații relative sau absolute față de recoltarea grefei de la situsul donor palatal, oferind o alternativă terapeutică cu morbiditate redusă.

Implementarea rezultatelor științifice: Rezultatele studiului sunt aplicate în procesul didactic al Catedrei de chirurgie oro-maxilo-facială și implantologie orală „Arsenie Guțan" a IP USMF „Nicolae Testemițanu" și sunt implementate în activitatea practică a Clinicii Stomatologice Universitare nr. 2 a IP USMF „Nicolae Testemițanu".

SUMMARY

Chele Dumitru

"Assessment of the influence of mucosal grafts on the formation of the peri-implant biologic width"

Doctoral thesis in medical sciences, Chișinău 2026

Thesis structure: the work is presented over 130 printed pages, comprising an introduction, 4 chapters, general conclusions, practical recommendations, a bibliography of 123 references and 15 annexes. Illustrative material includes 48 figures, 1 table and 15 annexes. Results have been published in 15 scientific papers, 2 oral communications and 4 posters.

Keywords: dental implant, peri-implant phenotype, peri-implant soft tissue, xenogeneic collagen matrix, autogenous connective tissue graft, keratinized mucosa, tissue augmentation, mucosal thickness, marginal bone level, mucogingival surgery.

Aim of the study: to optimize peri-implant soft tissue management through a comparative evaluation of xenogeneic collagen matrix versus autogenous connective tissue graft in augmenting the peri-implant phenotype.

Research objectives: assessment of gingival phenotype and bone remodeling during osseointegration and peri-implant biological space formation; evaluation of peri-implant mucosal characteristics and bone remodeling following augmentation with autogenous and xenogeneic tissues; comparative analysis of clinical and aesthetic outcomes; development of an individualized management protocol based on the patient's gingival phenotype.

Scientific novelty and originality: for the first time in the Republic of Moldova, a prospective comparative clinical study was conducted evaluating xenogeneic collagen matrix against autogenous connective tissue graft for peri-implant phenotype augmentation. An individualized clinical protocol was developed, grounded in the patient's gingival phenotype characteristics, to guide therapeutic decision-making and ensure predictable mucosal thickness augmentation.

Results contributing to the resolution of an important scientific problem: xenogeneic collagen matrix was shown to be a viable alternative to autogenous connective tissue graft for increasing peri-implant mucosal thickness, with a more favorable morbidity profile and without palatal tissue harvesting, broadening the accessibility of peri-implant mucogingival augmentation.

Theoretical significance: the study demonstrated that xenogeneic collagen matrix yields comparable clinical outcomes to autogenous connective tissue graft, with easier postoperative recovery and no donor-site discomfort. Correlations between initial peri-implant mucosal thickness and marginal bone level remodeling were elucidated.

Applied value: the developed protocol extends augmentation indications to patients with contraindications to palatal harvesting, offering a safe, reproducible, low-morbidity alternative that supports long-term aesthetic and biological stability of implant-supported restorations.

Implementation of scientific results: findings have been incorporated into the teaching activities of the Department of Oral and Maxillofacial Surgery "Arsenie Guțan" of the State University of Medicine and Pharmacy "Nicolae Testemițanu" and applied at University Dental Clinic No. 2 of the same institution.