Doctoral School in the field of Medical Sciences

As a manuscript
C.Z.U: 616.716.85/.87-007.23-089.844:615.461(043.2)

ZUGRAV Vasile

USE OF POLYMER MESHES IN GUIDED BONE REGENERATION IN THE MAXILLARY

323.01 - DENTISTRY

Summary of the doctoral thesis in medical sciences/dentistry

Chișinău, 2025

The thesis was developed within the Department of Oral and Maxillofacial Surgery and Oral Implantology „Arsenie Guțan” at the Nicolae Testemițanu State University of Medicine and Pharmacy.

Head

Chele Nicolae, PhD, Professor

Members of the guidance committee:

Zănoagă Oleg, PhD, Assoc.Prof

Mostovei Andrei, PhD, Assoc.Prof.

Suharschi Ilie, PhD, Assoc.Prof.

The defense will take place on 20.10.2025 at the "Nicolae Testemițanu" USMF, located at 165 Ștefan cel Mare și Sfânt Blvd., office 204 , during the meeting of the Public Defense Committee for the Doctoral Thesis, as approved by the decision of the Scientific Council of the Consortium of 04.07.2025 (minutes no. 65).

Composition of the Public Defense Committee for the Doctoral Thesis:

President: Ciobanu Sergiu, PhD, Associate Professor

Chele Nicolae, PhD, Professor, Head

Porosencova Tatiana, PhD, Associate Professor, Reviewer

Adrian Camen, PhD, Professor., Reviewer

Solomon Oleg, PhD, Associate Professor, Reviewer

Cristian Niky Cumpătă, PhD, Associate Professor, Reviewer

Mostovei Andrei, PhD, Associate Professor, Reviewer

Grigoriev Vladimir, PhD, Reviewer

Author:

Zugrav Vasile

CUPRINS

INTRODUCTION

The issue of alveolar ridge resorption and restoration remains a pressing concern in dentistry and has recently become the focus of intensive research. Various techniques and methods for restoring bone tissue have been developed to enhance the availability of suitable bone for dental implant insertion. These techniques include autologous bone blocks harvested from intraoral and extraoral donor sites, autologous bone lamellae using the Khoury method, guided bone expansion, osteogenesis through guided bone elongation, and guided bone regeneration (GBR). According to D. Buser, approximately 50% of implantation sites require a surgical procedure for bone restoration to ensure sufficient bone volume for dental implant insertion [3, p.17]. Presently, guided bone regeneration is the preferred technique for rehabilitating defects in the alveolar process to achieve the necessary bone volume for dental implantation [3]. Retzepi M. (2010) emphasized the importance of using a membrane to separate tissues, thereby enhancing the efficiency of guided bone regeneration techniques. The membranes employed in guided bone regeneration must meet several requirements: they should be biocompatible, non-toxic, and non-allergenic while maintaining adequate three-dimensional mechanical space for bone tissue formation.

The first non-resorbable membranes used to augment bone supply were constructed from PTFE (polytetrafluoroethylene). They were improved by incorporating titanium strips to enhance their hardness and plasticity (Buser D 1993). The main advantage of these membranes is their ability to provide excellent mechanical stability and effectively separate the graft from the surrounding gingival soft tissues. However, PTFE and titanium membranes have several disadvantages including the extra surgical steps required for their removal, which can impact wound healing. Additionally, their rigid nature often leads to wound dehiscence when exposed, increasing the risk of infection. To mitigate the risks associated with PTFE and titanium membranes, collagen membranes and resorbable synthetic biopolymers have been introduced. These membranes, made of collagen, have limited utility due to their rapid resorption and fragile structure. Poly-4-hydroxybutyrate (P4HB) is a long-term resorbable polyester known for not creating an acidic during degradation [9]. It received clinical approval from the Food and Drug Administration (FDA) in 2007, followed by the approval of the resorbable P4HB mesh later that year. To address the limitations of existing methods, such as those made from PTFE and titanium requiring additional surgeries for removal and collagen with its short resorption time, we propose researching and developing a novel technique for guided bone regeneration of pre-implant alveolar ridges. This technique involves using resorbable polymeric surgical meshes made from poly-4-hydroxybutyrate (P4HB), which serve as both a barrier and a maintenance solution.

Purpose: To evaluate the treatment of jawbone insufficiency through guided bone regeneration interventions using Poly-4-hydroxybutyrate mesh.

Objectives:

1. Examining the principles and properties of membranes used in guided bone regeneration.
2. Assessing the effectiveness by comparing the use of resorbable poly-4-hydroxybutyrate meshes with titanium meshes in guided bone regeneration.
3. Investigating and establishing the histo-morphological relationships between gingival soft tissues, resorbable meshes, and newly formed bone tissue.
4. Conducting statistical analyses and interpreting the data obtained.

5. Creating an algorithm for utilizing P4HB meshes in guided bone regeneration.

Research hypothesis

The following theories were formulated as research hypotheses:

Null hypothesis I_0: The polymeric mesh, due to its prolonged resorbable character, allows for the generation of newly regenerated bone tissue similar to that obtained through titanium meshes; however, it separately induces the volumetric development of the gingival biotype, an essential factor in implant-prosthetic treatment and the prevention of complications.

Alternative hypothesis I_A: The polymeric mesh does not contribute to the formation of bone tissue and does not influence the gingival biotype.

Scientific research methodology

To achieve the aforementioned goals and objectives, we conducted a clinical cohort study involving 70 patients who underwent guided bone regeneration in the jaw, using the resorbable P4HB synthetic polymer mesh and a perforated titanium membrane. According to the research methodology, the study was developed over five years and involved two groups of 35 patients between 20 and 60. The research examined the effectiveness of the synthetic absorbable P4HB mesh in guided bone regeneration of the jaws, identified its advantages and disadvantages compared to conventional bone regeneration techniques, and established a treatment plan outlining the surgical stages of treatment with this mesh. Based on clinical and paraclinical examinations, contemporary radiological and computed tomography analysis programs were utilized, and control and surveillance measurements were conducted at 1 to 8 months, with the obtained data recorded and subsequently analyzed.

The study was conducted according to the ethical principles of the Declaration of Helsinki and approved by the Ethics Committee of USMF "Nicolae Testemițanu" on 10.06.2020, with No. 43 dated 13.02.2020. This multicenter research was carried out from 2019 to 2024 within the Department of Oral-Maxillofacial Surgery and Oral Implantology "Arsenie Guțan" at the clinical facilities of Î.M.CSMC —Chișinău Municipal Dental Center and the university clinical base SRL "MASTERDENT."

Main scientific results

1. 225 specialized literature sources were reviewed, highlighting the importance of separating and supporting membranes in guided bone regeneration.

2. The key requirements and principles for a separation and support membrane in guided bone regeneration were defined.

3. Seventy bone regeneration surgeries were conducted, utilizing P4HB resorbable meshes and perforated titanium membranes; patient outcomes were monitored, recorded, analyzed, and statistically interpreted, leading to formulated conclusions.

4. The study resulted in the development and proposal of a treatment algorithm for maxillary bone atrophy involving P4HB resorbable polymer in guided bone regeneration.

Practical relevance

The study's practical importance is that we aimed to reduce some of the shortcomings of existing guided bone regeneration methods, such as the use of PTFE and titanium meshes that need additional intervention for their removal and collagenous ones, which have a short resorption time. That's why we proposed the study and development of a new technique for guided bone regeneration

of preimplant alveolar ridges, which consists in the use of resorbable polymeric surgical sutures with a barrier and maintenance function made of poly-4-hydroxybutyrate (P4HB).

Implementation of scientific results

The results of the scientific research were implemented in the research and clinical activity of the Department of Oral and Maxillofacial Surgery and Oral Implantology, "Arsenie Gutan," of the USMF "Nicolae Testemitanu."

Approval of scientific results

The research was discussed and presented at various national and international scientific forums: the Annual Scientific Conference at USMF "Nicolae Testemițanu" in Chișinău, from October 20-22, 2021; and the Scientific Conference commemorating the distinguished scientist Valentin Topalo, also at USMF "Nicolae Testemițanu" in Chișinău, on April 28, 2023. Participation included poster presentations at several international scientific forums: the AIT World Symposium from May 9-11, 2024, in Singapore; the European Association for Osseointegration Congress from September 26 to October 1, 2022, in Geneva, Switzerland; the 14 th edition of the EUROINVENT European Exhibition of Creativity and Innovation from May 26-28, 2022, in Iași, Romania; the 13 th edition of EUROINVENT from May 20- 22, 2021, in Iași, Romania; the International Exhibition of Scientific Research, Innovation, and Inventions PRO INVENT, 19 th Edition, in Cluj- Napoca, Romania, from October 20-22, 2021; the online International Exhibition of Inventions and Innovations “Traian Vuia,” 7 th Edition, in Timișoara, Romania, from October 6-8, 2021; and the 6 th Edition of the International Exhibition of Inventions and Innovations “Traian Vuia” in Timișoara, Romania, on October 15, 2020. The International Student Innovation and Scientific Research Exhibition – “Cadet Inova' 19” – hosted by the “Nicolae Bălcescu” Land Forces Academy in Sibiu, occurred from April 11-13, 2019, and the 11 th edition of EUROINVENT in Iași, Romania, took place from May 16-18, 2019. Based on the research project, the following honors were received: Government Excellence Scholarship and Scientific Field Scholarship for PhD students for 2022, as per DECISION No. HG 6/2022 dated 12. 01. 2022. The approval of the thesis topic occurred during the following meetings: the Meeting of the Department of Oral- Maxillofacial Surgery and Oral Implantology "Arsenie Guțan" (Minutes No. 4 of 17. 01. 2020); the Ethics Committee' s Opinion at USMF "N. Testemițanu" (No. 43 of 13. 02. 2020); and Scientific Seminar 323 in Dentistry (Minutes No. 5 of 11. 11. 2021). Publications related to the thesis topic include 13 scientific papers, 2 oral communications, 9 posters, 2 patents, 2 implementation documents, and 6 participations in various international invention forums, resulting in the following accolades: 3 gold medals, 1 silver, 1 bronze, and a diploma of excellence, along with the Government of the Republic of Moldova' s excellence scholarship and a scientific field scholarship for doctoral students for the year 2022.

Keywords: resorbable mesh, P4HB, titanium membrane, GBR, guided bone regeneration, xenograft, mucogingival flap.

1. ANATOMICAL AND PHYSIOLOGICAL NOTIONS OF ALVEOLAR CREST ATROPHIES

Surgical bone augmentation techniques primarily depend on the organism's regenerative capacity, which stimulates bone modification and the remodeling of the bone graft. Once activated, osteogenesis proceeds through biochemical, histochemical, cellular, and tissue events. Understanding the fundamental processes of bone regeneration is crucial for intervening cautiously

and enhancing the natural osteogenesis process. A significant aspect of bone tissue is its remarkable capability for self-healing, regeneration, and remodeling, all of which are vital functions for the organism [3].

It is well established that a reduction in the vestibulo-oral and coronal-apical dimensions of the dental alveolus precedes tooth extraction. It has been suggested that immediate or early placement of the implant in the postextraction alveolus could stop this physiological bone-destructive process and preserve the dimensions of the alveolar ridge [4,11,12].

Guided bone regeneration is a technique that enables vertical and horizontal bone growth while preventing the movement of graft material or infiltration by soft tissue. Various types of resorbable and non-resorbable membranes, autogenous and allogeneic cortical bone plates, and prefabricated and perforated titanium membranes currently serve as guiding and retaining materials. While these devices offer several advantages, they also come with disadvantages, including gingival dehiscence with exposure, superinfection, additional trauma, and complete resorption of the bone graft. Implant surgery provides a wide variety of barrier-function membranes, yet none fully meet the requirements for optimal bone growth.

2. RESEARCH MATERIAL AND METHODS

2.1 General study data

The research is a controlled clinical trial using conventional diagnostic and treatment methods. In the same way, the advantages and disadvantages of conventional treatment techniques were studied. Based on clinical and paraclinical examination, using contemporary radiological and CBCT programs, analysis, control, and surveillance measures were performed at 1.8 months.

The study was conducted by the ethical principles of the Declaration of Helsinki, approved by the Ethics Committee of USMF "Nicolae Testemitanu" on 10.06.2020, minutes No. 43 of 13.02.2020. The research is multicenter and was carried out during 2019-2024 within the Department of Oro-Maxillo-Facial Surgery and Oral Implantology "Arsenie Gutan" at the clinical bases of the premises of the M.M.CSMC—Chisinau Municipal Stomatological Center and the university clinical base SRL "MASTERDENT."

In this research,70 patients were enrolled for implant-prosthetic rehabilitation, presenting bone defects of the alveolar processes with the impossibility of inserting dental implants, requiring guided bone regeneration surgery with restoration of the bone defect. The number of included patients was calculated according to the ANOVA statistical study program formula based on the following parameters: confidence interval 95.0%; statistical power - 80.0; difference of the result up to 28.0% with the ratios between the groups - 1:1, adjusting the non-response rate, estimated at 10.0%. Thus, the whole sample that represented the research has an admitted error of 5% and must include a minimum of 70 patients, 35 patients in each research lot: research lot L0, 35 patients who were operated using P4HB meshes; and control lot L1, 35 patients who were operated using titanium membranes.

Inclusion criteria: patients with bone atrophy of the jaws; age between 20 and 60 years; patients with normal hemodynamic indices; patients without general pathologies (TB, HIV, pulmonary diseases, cardiac pathologies, etc.)

Exclusion criteria: patients over the age limit; patients with chronic ENT pathologies; general pathologies such as diabetes mellitus, glycemic values >7-8 mmol/l, oncologic pathologies, diseases of the hematopoietic system, autoimmune diseases, liver cirrhosis, and cardiac and respiratory pathologies; patients who refuse to participate in the study; and patients who request to be excluded from the study.

2.2 Investigative methods employed in the research

An anobligatory paraclinical examination for implant surgery is computed tomography, but to have an overall view of both jaws, it is advisable to perform orthopantomography first (figure 1A).

Orthopantomography:

This diagnostic method provides a complex image of both maxillae, which is currently the most common method of analysis and diagnosis in implantology surgery. The panoramic radiographs used in our study were made using the apparatus of the manufacturing company Planmeca. Technical characteristics of the device: The radiation emission dose is expressed in mGy/cm² and ranges from 61 to 258. Exposure time: 12 sec. Deciphering software - Planmeca Romexis 3.8.3.R. Investigation performed in incidence: Orthogonal. Plan: The OPG shows a slightly distorted image due to the projection of a three-dimensional body exposed in a two-dimensional plane.

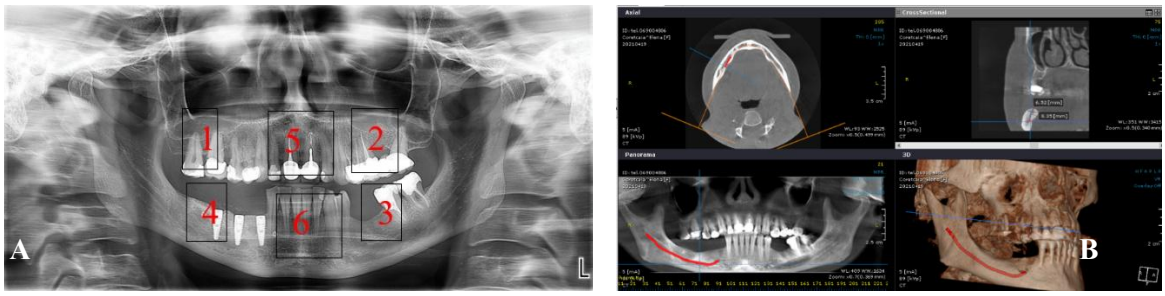

Figure 1**. Radiological examination figure A -OPG indicating the sites that underwent regeneration and figure B CBCT section at the level of the mandible**

Cone Beam Computed Tomography:

Cone Beam Computed Tomography, or CBCT, is a modern radiological method of analysis and diagnosis with high precision, often used in dental implant insertion procedures. The significant advantage of this type of radiography is obtaining a three-dimensional image that allows for the planning of surgical interventions and the avoidance of accidents such as NAI trauma or sinus cavity perforation. Our research used the image obtained by the cone beam computed tomography device Model: CS 9300. The images were processed by the CS Imaging Software. The bone density of the graft after the healing period, according to the Hounsfield scale, the volume of the initially augmented graft, and the volume of regenerated bone after the healing period, were characteristics obtained from CBCT in the research. The illustration in figure 1B represents a three-dimensional image highlighting the bone structures of the jaws, anatomical elements such as the NAI level, the volume of the alveolar ridge in section at the d 4.6 level which is to be augmented using the GBR technique.

Laboratory Examination:

The following blood parameters were examined in the laboratory to assess the general condition of the patients. Medical tests were conducted on the 70 patients participating in the study.

- General Blood Analysis
- Liver samples.
- LDL- low-density lipoprotein.
- HDL – high-density lipoprotein.
- Vitamin D level
- Coagulation parameters
- Alkaline phosphatase

Histological examination:

The histological examination outlined a procedure for sampling the gingival biopsy and the regenerated bone tissue following the healing period, accompanied by their histomorphological analysis. This procedure comprised a clinical stage, which involved the collection of samples, and a laboratory stage, aimed at processing and microscopically evaluating the tissues. The clinical stage facilitated the collection of the macro preparation, while the laboratory stage focused on the histological analysis. The clinical stage for material collection occurred during the second surgical procedure.

2.3. Surgical Protocol

The duration of a surgical intervention varied based on the volume and degree of bone resorption present in each patient; however, regardless of the complexity of the case, the initial surgical procedure did not exceed 120 minutes from the time anesthesia was introduced.

2.3.1. Surgical stage I

Preparation of patients for surgery

All patients received two hours of preoperative antimicrobial medication with 500 mg of Azithromycin (2 tablets per os). After using oral antiseptic solutions – 10% Polividone Iodine and 0.05% Chlorhexidine (CHX) solution, the perioral skin was first treated with a 70% alcohol solution, followed by a 10% Polividone Iodine solution. Then the patient was covered with a sterile field.

The actual surgical stage

Anesthesia

A 4% Articaine solution diluted to 1:100,000 in all patients included in the study was used. The anesthesia method primarily involved peripheral troncular administration, supplemented by loco-regional plexal infiltration to minimize bleeding while preserving the structure of the future flap.

Flap preparation

The flap was created to cover the guided bone regeneration elements in a similar way for all patients. It was also performed according to the technique and recommendations of Nada and the authors in 2020, which consists of obtaining a double-layered vestibular flap created from the periosteum and gingivomucosa while avoiding vertical incisions (figure 2), where a terminal breach on the right of the mandible is highlighted with the creation of a double-layered vestibular flap composed of the periosteum attached to the bone bed and the gingivomucosa detached from it.

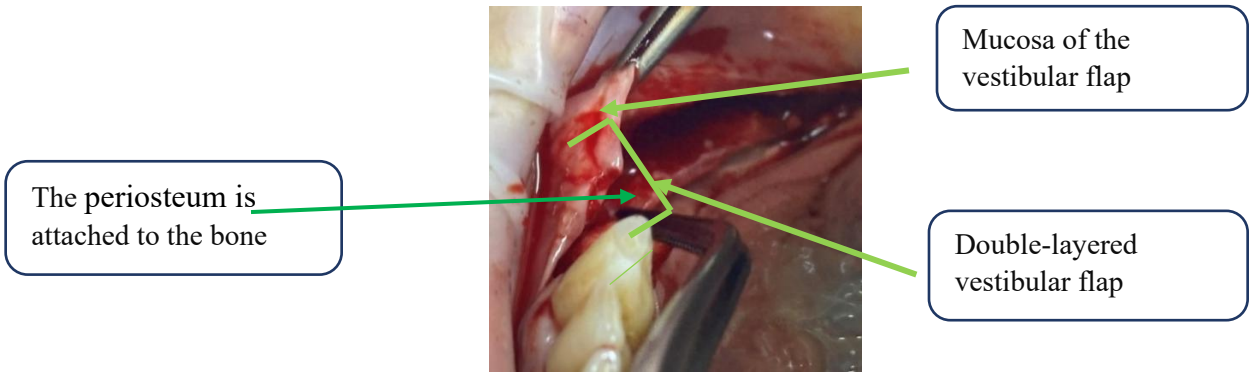

Figure 2. **Creation of the double vestibular flap "DF- double flap"**

In guided bone regeneration procedures involving the mandible and the creation of a sufficiently advanced coronal lingual flap(CALF), the CALF technique was utilized, as proposed by several authors (Nada, Urban). This technique involves lifting the lingual mucogingiva from the alveolar ridge after creating the vestibular flap. The lifting process included highlighting the muscle fibers of the mylohyoid muscle, which were detached from the mucosa using a blunt instrument (figure 3). Here, we can visualize the creation of a coronally advanced lingual flap with the atraumatic detachment of the mylohyoid muscle fibers. The image illustrates the height of the coronal advancement of the lingual mucoperiosteum.

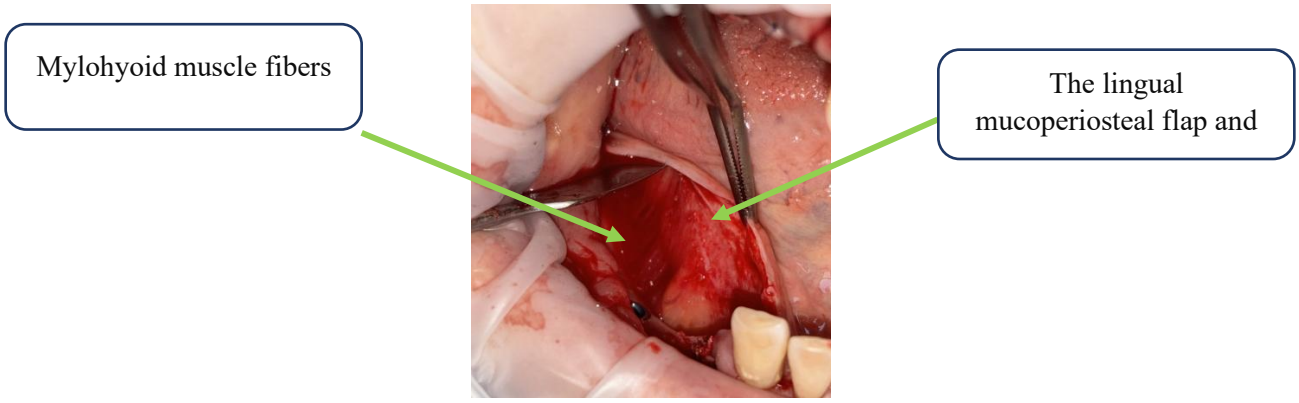

Figure 3. **Advancement of the coronary lingual flap, according to the "CALF" technique**

Preparation of the bone sites

The next phase of the intervention focused on preparing the bone sites for augmentation. After deperiosteation and flap formation, the bone surface was meticulously smoothed with a bone scraper. Next, utilizing the physiodispenser alongside the No. 1 drill, which included the pilot drill, the "Triple Blade Bone Collect" drill, and the disposable scraper "SafesScraper Rwist," several openings were created on the cortical surface in the areas affected by bone defects. The depth of these holes was determined by the thickness of the cortical bone and the presence of bleeding. The goal was to access the bone marrow to promote pluripotent cell migration and facilitate the collection of the patient's bone graft (figure 4). This figure illustrates the surgical procedure for establishing connections with the bone marrow using the Triple Blade Bone Collect cutter. In image A, these holes are created with the cutter positioned for the physiodispenser, while image B displays the holes punctually connecting with the bone marrow.

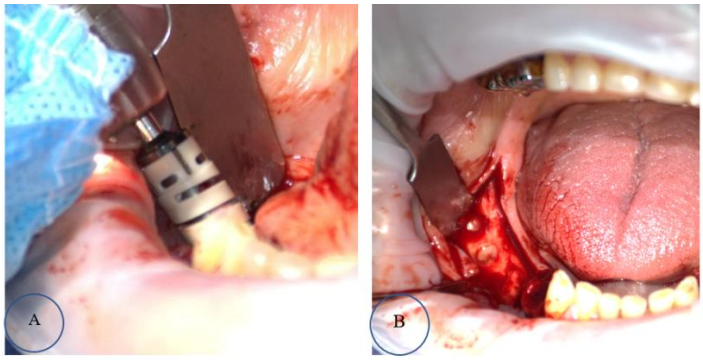

Figure 4**. Augmentation site preparation and bone chip collection using the Triple Blade Bone Collect**

Bone graft preparation

Preparing the bone graft for the augmentation procedure involves the preparation of a mixture composed of mineralized bovine bone and autologous bone particles with a ratio of 4:1, a protocol used in both research groups. The autologous bone particles was obtained by drilling holes into the bone marrow or creating neoalveoli in the case of implant insertion in the same session. In cases where dental implants were not inserted in the same session, the autologous graft was insufficient, so bone was collected from the cortical bone of the augmentation site using the Triple Blade Bone Collect. This multi-purpose drill features a three-blade device and a shock-absorbing housing for collecting bone particles (figure 5A), according to the method described previously.

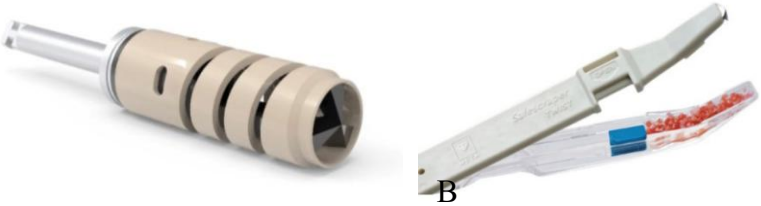

Figure 5. **Devices for bone collection: A. Triple Blade Bone Collector B. Disposable Bone Harvesters "SafeScraper Twist"**

In figure 5B, we can see a disposable instrument composed of a handle, a bone particles collector, and a semicircular blade that, when sliding more aggressively on the surface of the cortical bone, collects bone tissue in the form of particles. For easier shaping and manipulation, the grafting mixture was fixed with autologous blood platelet concentrate, thus obtaining a mixture composed of autologous bone, mineralized bovine bone, and blood platelet concentrate. This mixture presented a gelatinous and semisolid consistency that was well-molded during augmentation (figure 6).

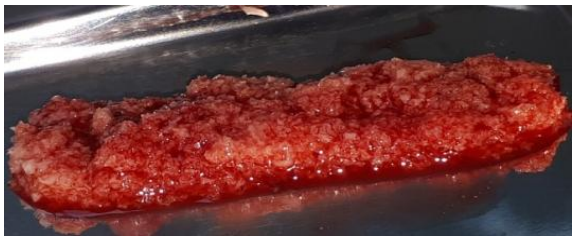

Figure 6. **Graft mixture of mineralized bovine bone, autologous bone particles, and blood platelet concentrate**

Fixation of meshes and barrier membranes

Fixation of poly-4-hydroxybutyrate (P4HB) mesh. In the study group where the resorbable mesh served as a separation and maintenance device, the mesh at the augmentation site subjected to regeneration was prepared differently based on the degree of atrophy of the alveolar processes. They were prepared as follows: in grade V atrophy, where there is resorption both vertically and horizontally and the dental implants were partially inserted into the native bone immediately, the resorbable mesh was fixed separately on each edge of the defect- oral and buccal- with 4 to 6 titanium pins. The number of pins depended on the size of the defect (figure 7A), were are illustrating the dental implants partially inserted into the native bone of the mandible on the right, with two segments of mesh fixed separately, both lingually and buccally. The same procedure was followed in grade VI atrophy, where the defect also involved basal bone atrophy, except that the dental implants were not inserted in the same session.

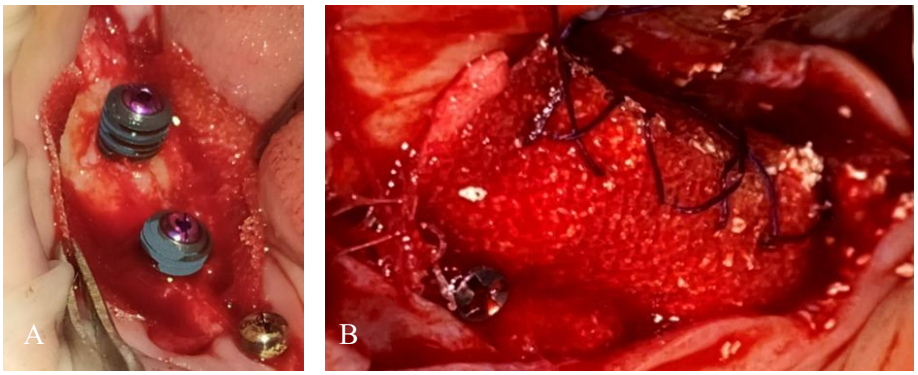

Figure 7. **Fixation of PH4B mesh lingually and buccally with immediate implantation figure A and suture figure B**

After the mesh segments were fixed, a lodge was formed. and in the lodge formed between the bone bed and the two lingual and buccal meshes, the previously prepared grafting mixture was placed. It should be noted that the augmentation covered the dental implants by approximately 1-2 mm. The two mesh segments, oral and buccal, were sutured together at the coronal edges with absorbable thread, thus restoring sufficient tension to the mesh so that the complex formed between the mesh, bone and grafting material was rigid (figure 7B).

In grade IV bone resorption in the vertical plane or knife-edge-shaped alveolus, when there is not enough bone in width, the mesh is composed of a single segment, initially fixed only on a vestibular or oral side, depending on the area and convenience (figure 8A).

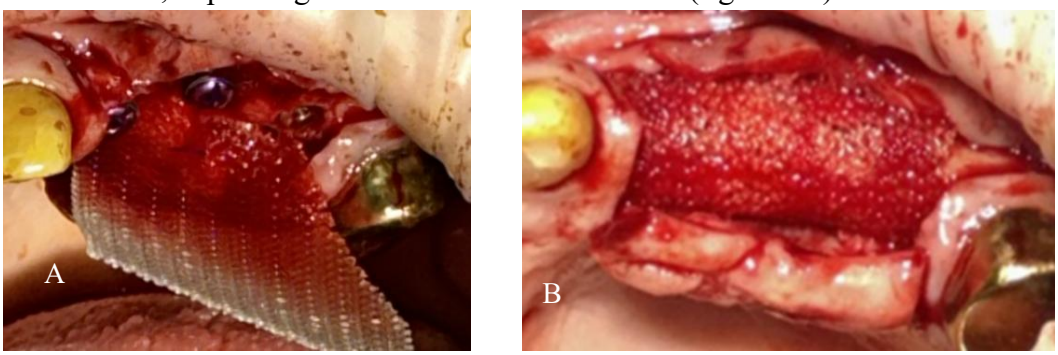

Figure 8. **Fixation of P4HB mesh in grade IV atrophy with immediate implantation**

It is worth noting that in such resorptions, dental implants could be inserted in the same session. After their insertion, the grafting material was added, and we also mention that the augmentation material covered the dental implants 1-2 mm. The mesh was subsequently tensioned and fixed with titanium pins on the opposite side (figure 8B).

Fixation of titanium membrane. In the case of the control group, where a titanium membrane was used as a maintenance and stabilization device, the regeneration site was prepared the same way as in the study group. Regardless of the type of atrophy, the titanium membrane was used only in one piece; its adaptation and shaping were performed with surgical scissors during the operation after measurements were made on the operating field with the graduated probe. Its primary fixation depended on the case, and according to the operator's convenience, its oral or vestibular fixation was also with the help of 4-6 titanium pins (figure 9A).

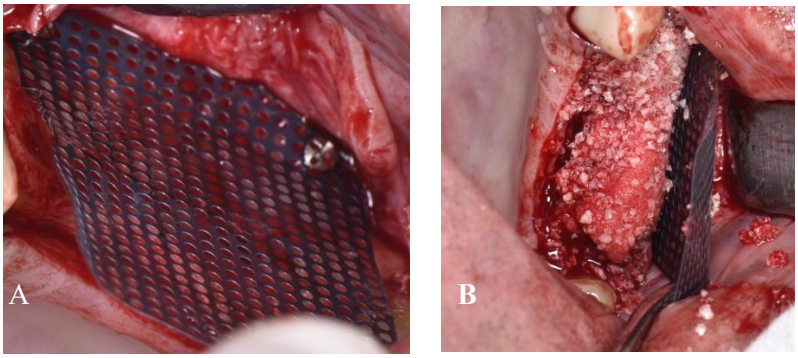

Figure 9. **Adapting the titanium device and securing it with titanium pins.**

Depending on the specific case where immediate implantation was utilized, the implants were placed first, followed by the fixation of the titanium membrane, after which the prepared augmentation material was added. Subsequently, the titanium membrane was tensioned and secured on the opposite side (figure 9B), where we can observe the fixation of the titanium membrane to the vestibular side of the upper jaw on the left and the presence of the augmented graft material.

Suturing the flaps. Suturing the gingivomucosal tissue and achieving primary wound closure were performed in three layers, as recommended by Nada et al. [10]. To reduce the tension of the vestibular flap, the corresponding periosteum was first sutured to the oral mucoperiosteal flap using mattress sutures, serving as the initial stitch to alleviate tension while ensuring no strain on the thread (figure 10A). This figure shows the suture connecting the vestibular periosteum to the mucoperiosteum of the palatal flap using a mattress suture. The second layer of suturing also involves mattress sutures without tension on the thread; however, this level is pulled tight until it approaches the gingival edges of the flaps (figure 10B), illustrating the second layer of mattress suture that reduces flap tension. The third level of suturing provided final closure and sealing of the wound. It consisted of interrupted or continuous sutures, as depicted in figure 12B, where final sutures and sealing with interrupted thread are visible.

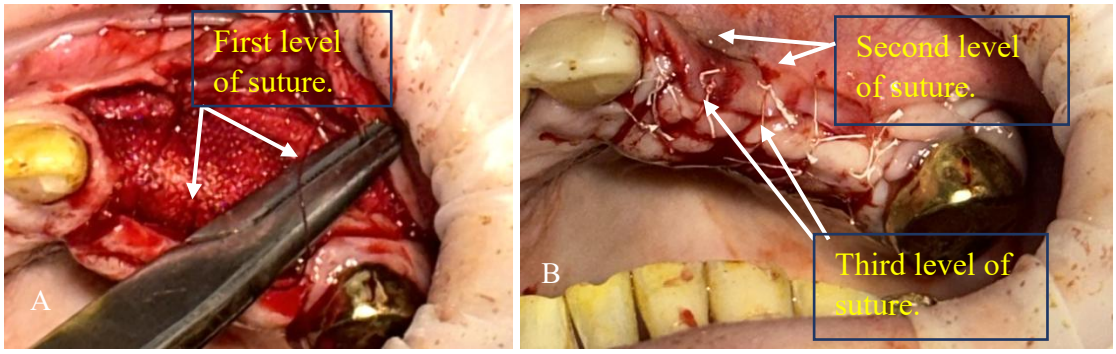

Figure 10. **Upper jaw on the left, oral mucosa periosteum suture**

According to the recommendations of Buser et al. (2021), the sutures should be placed without tension, and the mattress suture used for the vestibular flap to approximate the gingival margins should be performed without applying excessive compression on the tissues [3,6,8]. Additionally, the node in the lower jaw should be positioned vestibularly, while in the maxilla, it should be located palatally. These principles were also adhered to in our research.

2.3.2 Surgical Stage II

The second surgical stage was conducted 8 months after the healing period and consisted of the following phases: clinical, paraclinical, and laboratory. During the clinical phase, the inspection and assessment of the integrity of the soft tissues in the regeneration area were performed. In contrast, the paraclinical phase involved a radiological examination that visualized the state of the regenerated bone tissue and facilitated the measurements necessary for the research. In the laboratory examination, the histomorphology of both the soft tissues and the regenerated bone tissue was studied.

At this stage, in the case of the study group where the resorbable mesh was used, the main aim was to measure the changes in the gingivomucosa and the regenerated bone tissue during the healing period. The bone tissue was collected by pinching with a chisel. In instances where patients required the insertion of dental implants as a secondary part of the surgical intervention after the GBR operation, gingivomucosa was collected from the middle of the alveolar ridge using a scalpel, and bone tissue was collected using 4 mm diameter trephines from the area of the future neoalveolus (figure 11). From the macroscopic image, we can observe the regenerated bone tissue bleeding, with mineralized bovine bone particles incorporated into the newly formed bone tissue, the absence of the resorbable mesh, the condition of the bordering gingiva, and the inserted implants.

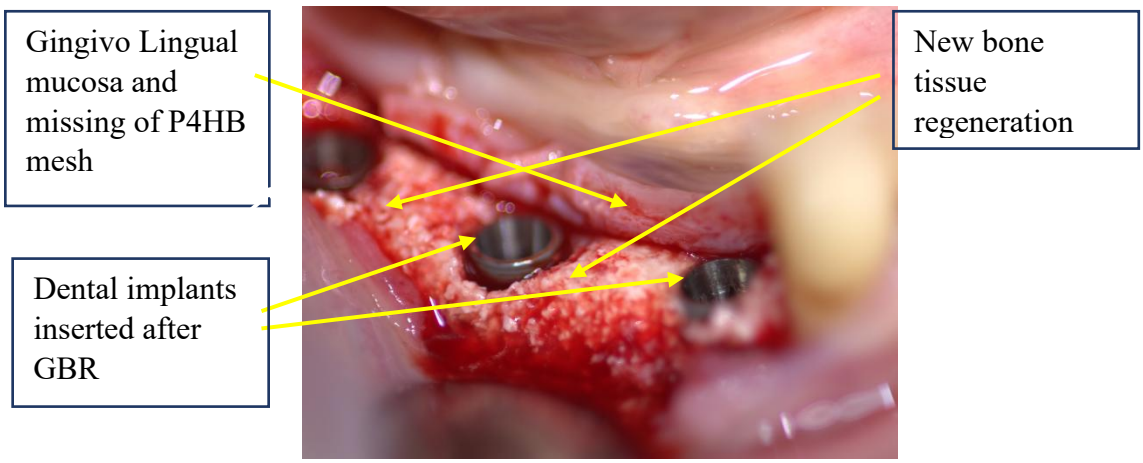

Figure 11**. Opening the regeneration area at the mandible level in the second surgical stage and insertion of implants**

In the control group, where the titanium membrane was used, patients underwent incisions with mucoperiosteal detachments, followed by removing the membrane and fixation pins. The gingivomucosal tissue in this case was not sampled for histological analysis; only the macropreparation of the regenerated bone tissue was collected according to the same principle as in the study group (figure 12). In figure 12A, we can see the creation of the incisions with mucoperiosteal detachment and the exposure of the titanium membrane, which was fixed additionally in this case, as well as by the implants inserted in the first session. In figure 12B, we can observe the regenerated bone tissue bleeding and the integrated dental implants.

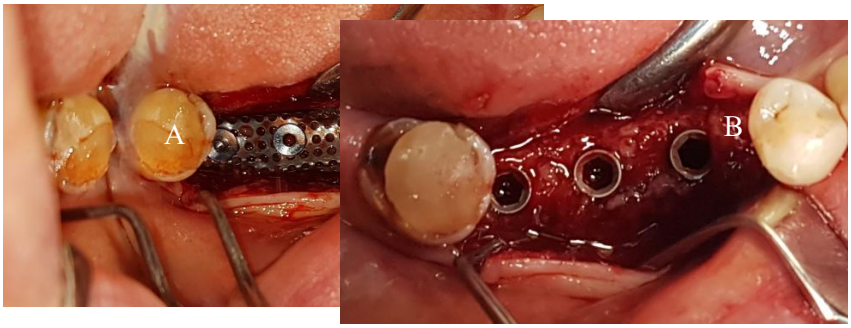

Figure 12. **Image A - Opening of the augmentation area with exposure of the titanium membrane, B - exposure of the newly formed bone and the healed implants inserted in the first stage**

2.3.3 Biopsy and Histological Analysis

The laboratory examination and histomorphological analysis consisted of a clinical and laboratory examination. In the clinical stage, the gingival biopsy was taken from the patients in the study group, as well as the regenerated bone tissue from all patients, and the laboratory stage

included the histomorphological analysis of the biopreparations, the macropreparation collected from both research groups was placed in 10% formalin solution and sent to the laboratory for analysis.

2.4 Statistical processing of the obtained results

The collected data were processed using R Studio (Version 2024.04.1+748), facilitating productive statistical analysis. For the numerical variables, the following descriptive statistics were estimated: minimum value, maximum value, mean value with standard deviation, and median value with interquartile deviation (AI). The comparative evaluation of numerical variables between the control group and the study group was conducted using non-parametric tests for independent and dependent groups (variants of the Mann-Whitney-Wilcoxon test depending on the relationships between the researched groups), employing box plots, jitter plots, and violin plots in combination. Correlation analysis between numerical variables was performed using the Spearman ρ test, with results adjusted using the Holm method.. For categorical variables, absolute and relative frequencies were estimated using bar plots, including 95% confidence intervals for relative frequencies. Hypothesis testing was conducted using Pearson's Chi-square test (Monte Carlo variant with 10,000 repetitions). The threshold value (p) was set at 0.05 for all statistical tests applied in this work.

3.RESULTS

3.1. General Characteristics of the Study Groups and Variables

The average age of respondents and gender was 53.1 years (AI=10, 95%CI 51.55), the median 53.0 years (AI 14.8), the minimum 27.0 years, and the maximum 60.0 years. The biological gender in our research was predominantly represented by the female gender, with 46 respondents, which constitutes 65.7% (95% CI 53.76), and the male gender, represented by 24 respondents, constituted 34.3% (95% CI 24.47).

Comparative evaluation of the Graft-Bone Thickness (GOA) added in dynamics. This parameter was calculated to observe how the separation device influences the three-dimensional stability. Applying the $V_{Wilcoxon}$ test for the study group (figure 13A), we obtain the value of = 420, p= 1.23e-05, the biserial r_{rank} test = 0.93 (95%CI 0.86, 0.97); thus, we can state that there are statistically significant differences in our study group. From figure 13A we can see a tendency to decrease the bone thickness during the bone healing period in the study group, this can be explained by the property and malleable character of the mesh which is not as rigid as the titanium membrane, yields to the pressures in the oral cavity and maintains less bone regeneration height. Clinically, no difficulties were recorded in the second surgical stage. In the case of this variable calculated for the control group, the following was highlighted (figure 13B): the $V_{Wilcoxon}$ test we obtain the value of = 212.50, p= 6.76e-04, the biserial r_{rank} test = 0.84 (95%CI 0.69, 0.92). The test showed statistically significant differences in our control group with clinical importance representing a widespread phenomenon among the population. From figure 13B we can see a trend without change in bone thickness during the bone healing period, clinically it can be explained by the property of the titanium membrane which is rigid and maintains its three-dimensional shape.

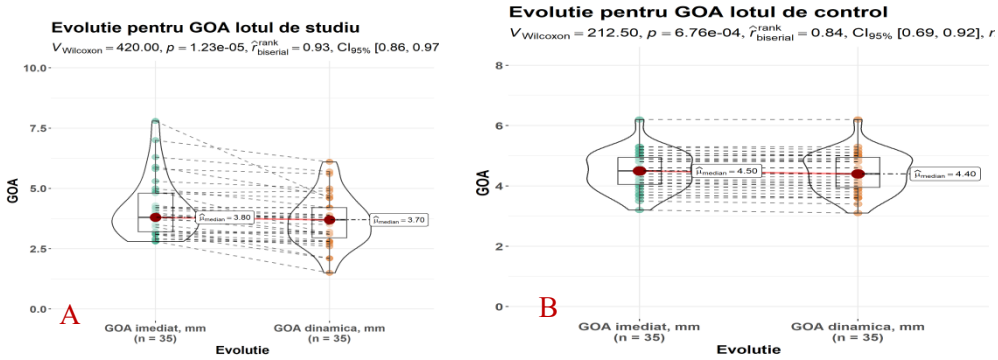

Figure 13. **Violin plot, completed with jitter plot (points) for the GOA variable in evolution A- study group, B- control group. Wilcoxon test**

Comparative evaluation of variable gingival thickness (GG) in dynamics. This variable was calculated to illustrate the changes in the thickness of the gingivomucosal tissue during the bone healing period in patients operated on with absorbable mesh and titanium. Performing the $V_{Wilcoxon}$ test for the study group (figure 14A), we obtain a value of 177, p = -0.04, and biserial r_{rank} test = -0.41 (95% CI -0.67, -0.05). Thus, we conclude that our research indicates statistical differences for this variable and clinical significance demonstrating a moderate phenomenon at the population level. The evolution of GG in the study group shows a tendency to increase during the bone healing period, a clinical phenomenon attributed to the resorbable mesh. This can be explained by the resorption properties of the biopolymer mesh (Phasix Mesh), which is characterized by an aseptic inflammatory reaction leading to its substitution in fibroconnective tissue (Deeken et al., 2020) [8]. Performing the $V_{Wilcoxon}$ test for the control group, we obtain (figure 14B) a value of 300, p = 9.32e-06, and biserial r_{rank} test = 1.0 (95% CI 1.0, 1.0). Consequently, we state that the test showed significant statistical differences in our control group. This indicates that the difference in GG evolution for the control group presents statistical significance and very high practical significance. From figure 14B, we observe a tendency for reduced gingival thickness, which, due to its modeling and adaptation during the operation, along with its sharp edges and porous nature, causes irritation of the oral mucosa through thinning. Towards the bone, the irritation manifests as a form of fibroconnective tissue, referred to by the authors as "pseudoperiosteum" (*Jung et al., 2014*) [11].

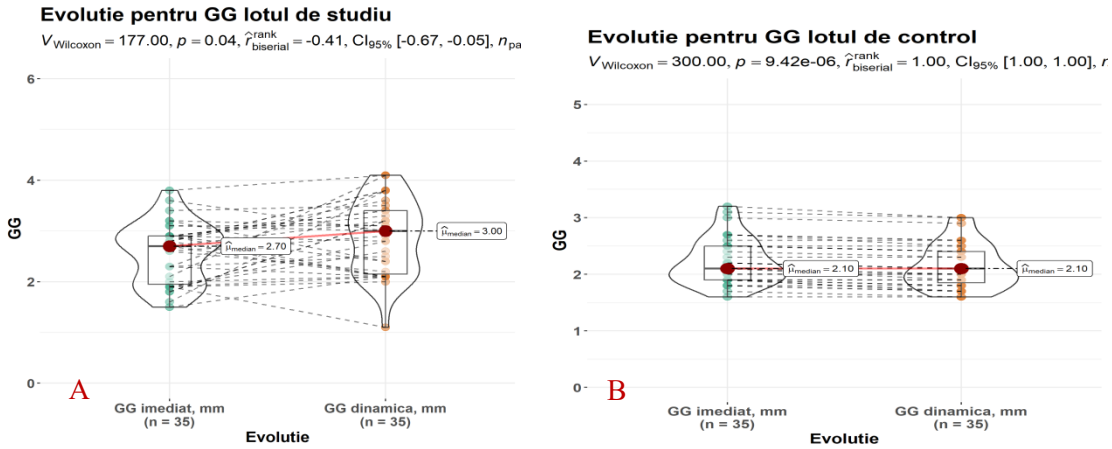

Figure 14. **Violin plot, completed with jitter plot (points) for the GG variable in evolution A- study group, B-control group. Wilcoxon test.**

3.2. Histological examination results

Our research performed 70 histomorphological examinations of newly regenerated bone tissue and 35 histomorphological examinations of gingival tissue. Gingival tissue was studied only in the case of the research group to highlight the impact of the resorbable polymer mesh on the gingiva. Histology of the gingival tissue (postoperative hematoxylin-eosin staining figure 15) shows the following:

- Keratinized squamous cell epithelium, the submucosal layer considerably thickened at the base of fibrous connective tissue, rich in capillaries with discrete lymphocytic infiltrate with unitary monocytes (figure 15A).

- In the basal part of the gingival mucosa, the foreign body – the mesh is embedded in fibrous connective tissue without macrophage reaction, and in some places, perivascular hemorrhages follow ablation(figure 15B).

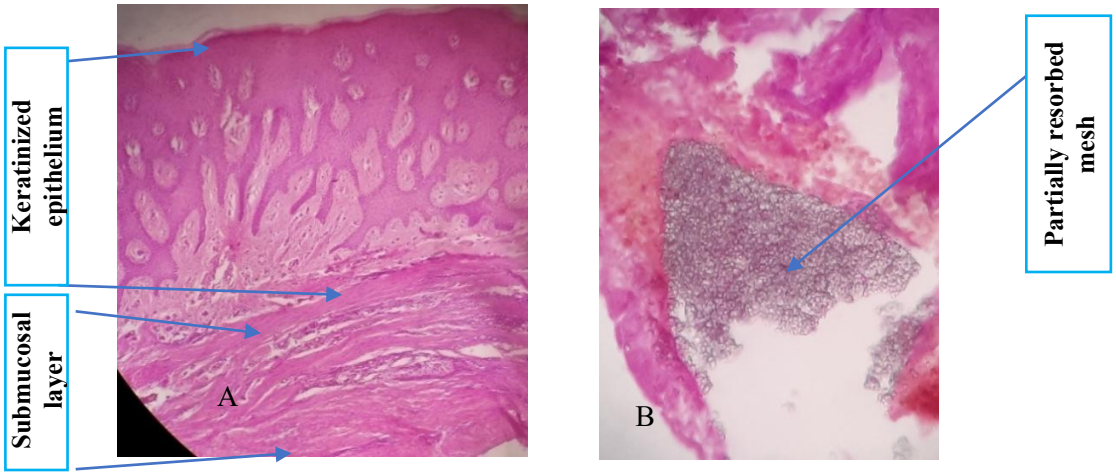

Figure 15. **Histological examination of the gingival mucosa in the case of P4HB use after the healing period**

The histology of bone tissue (hematoxylin-eosin staining) (figure 16) reveals newly formed immature bone tissue in the upper part of the biopreparation, characterized by a rich supply of blood vessels and well-defined osteoblastic cells, along with the presence of an acellular foreign body – a xenograft. The basal part of the biopsy consists of mature mineralized bone, exhibiting an increased layer of blast cells characteristic of medullary bone, with occasional traumatic perivascular hemorrhages.

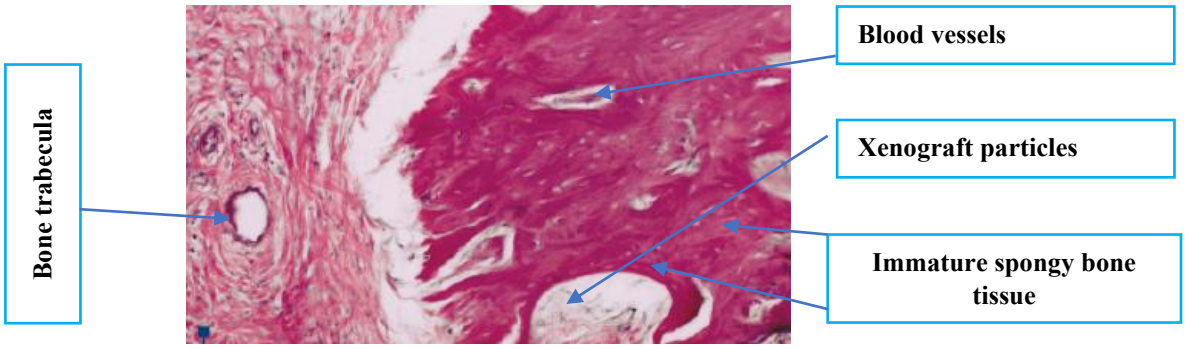

Figure 16**. Histology of bone tissue (hematoxylin-eosin staining) after the healing period**

DISCUSSIONS

Guided bone regeneration remains a preferred method for treating bone atrophy in the jaws, but it poses significant challenges in modern implantology. Any element used in guided bone regeneration must satisfy at least the biological and mechanical conditions necessary to achieve optimal results in the shortest time possible. Synthetic and resorbable polymer meshes, along with perforated titanium membranes, mostly meet all biological conditions required for bone regeneration. The size and value of microperforations in both devices significantly enhance the blood supply to the underlying tissues without hindering nutrient flow. It is important to highlight that the affinity of the polymer mesh component for biological tissues is a critical factor in reducing the risk of dehiscence [1,5]. A major advantage of these membranes is their complete resorption, eliminating the need for additional removal interventions. Another benefit is that the aseptic inflammatory resorption reaction promotes the growth of fibrous connective tissue that plays a supportive role.

1. After studying 225 specialized literary sources, researchers determined that 41 of them reflect requirements for the covering and separating membranes used in guided bone regeneration. The primary characteristics that these devices must meet include biocompatibility, non-toxicity, and non-allergenicity, along with the three-dimensional mechanical maintenance of space. An obvious classification was provided by Wang and Boyapati, who state that during the period of bone remodeling, the augmentation material must maintain stability and be separated from the gingival epithelium. Thus, they formulated and proposed the PASS principle, which encompasses several membrane requirements: P - primary closure; A - angiogenesis; S - primary stability; S - space maintenance.

2. Following the comparative evaluation of the two research techniques, we obtained significant results, particularly concerning bone graft stability values. Patients who underwent guided bone regeneration using resorbable polymer mesh exhibited a regenerated graft thickness that showed no major changes compared to the initial values, and these values did not vary in the control group (Mann-Whitney p= 4.78e-04). Another parameter that exhibited statistically and clinically significant values according to the Mann-Whitney test was the thickness of the gingivomucosal tissue over time (p=3.41e-06, biserial rank =0.64); these values demonstrated that the techniques applied in our research are comparable. The treatment technique involving resorbable biopolymer meshes made from poly-4-hydroxybutyrate in guided bone regeneration indicates that this method is promising in dentoalveolar surgery and is simpler to apply. This method has fewer surgical steps and allows for a faster postoperative recovery for patients. In this study, 70 histomorphological examinations of newly regenerated bone tissue and 35 histomorphological examinations of crestal gingival tissue were conducted after the osteoformation period. Eight cases developed wound dehiscence with exposure of the mesh in the oral cavity more than two months after the initial intervention. We specify that these cases were classified as class I and II according to Fontana and were remedied by the partial removal of the exposed mesh along with lavage of the removable graft, anticipating secondary regeneration.

3. The histomorphological examination of the newly regenerated bone tissue using H-E staining revealed 62 cases of newly formed bone tissue rich in well-defined blood vessels and osteoblastic cells, with 32 cases in the control group and 30 cases in the study group. This result was

obtained where gingival dehiscence did not occur, preventing exposure of the meshes in the oral cavity. The remaining 8 cases showed bone tissue encapsulated in fibro-epithelial tissue in the upper part of the biopsy, and newly formed bone tissue in the lower part, comprising 3 cases in the control group and 5 cases in the study group. The quality of the newly regenerated bone tissue in the study group from the histomorphological examination exhibited the same characteristics as that in the control group. The crestal gingival tissue from the study group, examined through the same morphohistological process, revealed keratinized squamous epithelium in 30 cases. The submucosal layer was considerably thickened at the base of the fibrous connective tissue, which was rich in capillaries with discrete lymphocytic infiltrate and unitary monocytes. The remaining 5 cases showed gingival tissue in the healing process (scar tissue) in areas with foreign particles embedded in the fibroconjunctive tissue (the graft that was not subjected to staining). From these results, we can conclude that the research hypothesis is confirmed and the alternative hypothesis rejected. We also conclude that synthetic bioresorbable meshes made from P4HB provide promising results that warrant further study.

4. Analyzing the statistical results of this study, we can conclude that we obtained statistically significant values in each group, particularly regarding the parameters related to gingival volume over time (control group Wilcoxon test p= 9.32e-06, rank biserial = 1.0; study group Wilcoxon test p= 0.004, rank biserial = 0.41) and the stability of the thickness of the regenerated bone tissue (control group Wilcoxon test p= 6.76e-04, rank biserial = 0.84; study group Wilcoxon test p= 1.23e-05, rank biserial = 0.93). Another important statistical point is the presence of correlations through the Spearman Test for the aforementioned parameters; this test revealed strong and interdependent correlations close to the maximum values, such as the volume of newly regenerated bone tissue compared to the initial volume, which had a value of 0.96, and the thickness of the initial and final graft, which obtained a value of 0.93. These values indicate that, regardless of the technique we used in our research, they were interconnected. In contrast, the thickness of the gingivomucosa over time compared to the initial thickness had an average value of 0.62, suggesting that this characteristic is influenced by factors beyond the biology of gingival regeneration itself, indicating that the polymer mesh affected the final thickness of the gingivomucosa.

5. As a result of the research conducted, a treatment plan was established, and an algorithm for using the resorbable P4HB mesh in guided bone regeneration in the jaw was created. We can report that the surgical steps do not differ from conventional techniques using non-resorbable meshes, except that the additional intervention to remove them is absent. In this research, important values of the stability of the respective mesh were obtained through the Wilcoxon test concerning the graft thickness over time (the study group showed a statistically significant value of p= 1.23e-05, with the biserial rank test = 0.93 and an absolute clinical effect). However, the distribution on the graph indicated a slight decreasing trend in this parameter, particularly at the maximum values. These values result from the polymer mass, which is more malleable and yields to pressures in the oral cavity, especially at high values, and significantly reduces the vertical size of the graft.

PRACTICAL RECOMMENDATIONS

1. When performing guided bone regeneration operations in the jaw due to atrophy of the alveolar processes, it is essential to consider the specific type of atrophy involved. A thorough clinical and paraclinical analysis, including necessary examinations, is advised. We suggest preoperative preparation of the patient with professional oral hygiene, followed by prophylaxis with broad-spectrum antibiotics the day before the operation.

2. Another recommendation is the technique of mobilization and advancement of the muco-gingival flap. First, the patient's gum volume will be considered, as well as the incision level on the middle of the alveolar ridge. The technique of modeling and advancement of the muco-gingival flap is also performed according to the recommendations of Nada and the authors—recommendations that we also considered in our research. The advancement of the vestibular flap will be achieved through the superior or coronal incision of the flap without initial deperiosteation. The mobilization of the submucosa will depend on the need for advancement. The authors recommend that the advancement should exceed the height of the crowns of the neighboring teeth. At the end of the vestibular flap advancement, the periosteum from the bone bed will be deperiosteated. In the case of the lingual flap, deperiosteation should be avoided, but the advancement technique will include debridement of the mylohyoid muscle using an instrument similar to a smoothing device. The authors also recommend that advancing the muco-gingival flap be performed at the beginning of the operation, as hemostasis and better visibility occur toward the end of the operation.

3. The preparation of the bone graft will particularly take into account the type of atrophy and the residual bone volume. Authors such as Istavan Urban recommend that when restoring bone volume with a height greater than 4 mm, it is mandatory to use a mixture of bone graft obtained from mineralized bovine bone and autologous bone in a ratio of at least 4:1. We recommend incorporating this principle into guided bone regeneration when using resorbable synthetic biopolymer mesh; the autologous bone will be collected from the regeneration site with the help of special devices or from the creation of new alveoli when inserting dental implants in the same session.

4. The adaptation and fixation of the P4HB resorbable synthetic polymer mesh in guided bone regeneration of the jaw will also consider the type of atrophy of the alveolar process, particularly in advanced stages such as grade VI or class C. Primary fixation of the mesh will be accomplished using titanium pins from either the oral or vestibular side, depending on the operator's preference. Following this, a graft mixture will be added to the bone bed, and final fixation will continue similarly, utilizing at least 3 titanium pins on the opposite side. We strongly recommend that the resorbable synthetic polymer mesh be kept under tension. The edges of the mesh will be trimmed with surgical scissors to eliminate any sharp edges that could irritate the mandibular-periosteal flap.

5. The gingivomucosal suture will be performed in three layers: the first layer will include a suture to maintain the vestibular periosteum toward the oral flap. We mention and recommend that this suture must be free and tension-free. The next layer of suture will involve a suture thread to maintain the vestibular and oral flaps until approaching the edge of these flaps. We also recommend that this suture be tension-free and not strangulate the gingivomucosal. The final suture will consist of interrupted or continuous sutures at the edges of the gingivomucosal.

BIBLIOGRAPHY

1. Bottino, M. C., Thomas, V., Janowski, G. M., A novel specially designed and functionally graded electrospun membranes for periodontal regeneration. In: *Acta Biomater*. 2011, no. 7, pp. 216–224.

2. Buser D, Dula K, Belser U, et al. Localized ridge augmentation using guided bone regeneration. Surgical procedure in the maxilla. In: Int *J Periodont Restorat Dent*. 1993, no. 13, pp. 29-45.

3. Buser, D. *30 years of guided bone regeneration*. Third edition, Quintessence Publishing Co, Inc, 2021.

4. Chele N. Determinants of osseointegration in implantology. In: . *Medicina Stomatologică*. 2015, no. 3(36), pp. 29-32. ISSN 1857-1328.

5. Chele, N.; **Zugrav, V**. The use of polymer meshes in guided bone regeneration. *Medicina Stomatologică*. 2021; 3 (59): 18-25. ISSN 1857-1328.

6. Cucchi Al., Vignudelli E., Napolitano A., Marchetti C., Corinaldesi G. Evaluation of complication rates and vertical bone gain after guided bone regeneration with non-resorbable membranes versus titanium meshes and resorbable membranes. A randomized clinical trial. In: *Clinical implant dentistry and related research*. 2017, no. 5, pp. 821-832.

7. Cucchi, Alessandro, Elisabetta Vignudelli, Debora Franceschi, Emanuele Randellini, Giuseppe Lizio, Antonino Fiorino, and Giuseppe Corinaldesi. "Vertical and horizontal ridge augmentation using customized CAD/CAM titanium mesh with versus without resorbable membranes. A randomized clinical trial. In: *Clinical Oral Implants Research* 32. 2021, no. 12, pp: 1411-1424.

8. Dahlin C, Gottlow J, Linde A, Nyman S. Healing of maxillary and mandibular bone defects using a membrane technique. An experimental study in monkeys. In: *Scand J Plast Reconstr Surg Hand Surg*. 1990, no. 24, pp. 13–19.

9. DenOtter TD, Schubert J. *Hounsfield Unit*. 2023, Mar 6. In: StatPearls [Internet]. Treasure Island (FL): *StatPearls Publishing*; 2024 Jan. PMID: 31613501.

10. Nada Z., Noha D., Samah B., Azza EA, Omniya AA, Hani N. Clinical comparison of different flap advancement techniques to periosteal releasing incision in guided bone regeneration: A randomized controlled trial. In: Clin *Implant Dent Relat Res*. 2020, no. 1, pp. 10.

11. Paolantonio M, Dolci M, Scarano A, et al. Immediate implantation in fresh extraction sockets. A controlled clinical and histological study in man. In: *J Periodontol*. 2001, no. 72, pp. 1560–1571.

12. Stig Hansson, Halldin A. Alveolar ridge resorption after tooth extraction: A consequence of a fundamental principle of bone physiology. In: *Journal of Dental Biomechanics*. 2012, no. 3.

13. **Zugrav, V**.; Chele, D.; Motelica, G.; Mostovei, A.; Dabija, I.; Chele, N. Biopolymeric membrane—a new concept in guided bone regeneration. Case series. *Ediţie consacrată comemorării distinsului savant Valentin Topalo*.. 2023; 1 (62):76-81. ISSN 1857-1328.

LIST OF PUBLICATIONS AND PARTICIPATIONS IN SCIENTIFIC FORUMS

of Mr. Zugrav Vasile, Department of Oral-Maxillofacial Surgery and Oral Implantology "Arsenie Guțan", carried out for the doctoral thesis in medical sciences/stomatology, on the topic: Use of polymer meshes in guided bone regeneration in the jaws, 323.01, "Nicolae Testemitanu" State University of Medicine and Pharmacy of the Republic of Moldova

SCIENTIFIC WORKS

- ✓ **Articles in accredited national scientific journals**
- ✓ **articles in category B journals**

1. **Zugrav V**., Chele D., Chele N., Cucu G. The importance of mucogingival flaps in guided bone regeneration in the jaws. In: *Mold J Health Sci*.2024;11(4). https://doi.org/10.52645/MJHS.2024.11.(4).30-37

- ✓ **articles in C-category journals**

2. Chele N., **Zugrav V.** The use of polymer meshes in guided bone regeneration. In: *Medicina Stomatologică*. 2021; 3 (59): 18-25. ISSN 1857-1328.

3. **Zugrav V**., Chele D., Motelica G., Mostovei A., Dabija I., Chele N. Biopolymer membrane — a new concept in guided bone regeneration. Case series. In: *Ediție consacrată comemorării distinsului savant Valentin Topalo*. 2023; 1(62):76-81. ISSN 1857-1328.

4. Mîndru A., **Zugrav V**., Motelica G., Chele D., Chele N. Determining the risk of injury to the inferior alveolar nerve after extraction of impacted mandibular 3rd molars. In: *Medicina Stomatologică*. 2023; 1 (62): 82-89. ISSN 1857-1328.

5. Dabija I., Mostovei A., Chele D., Motelica G., **Zugrav V**., Ciobanu V., Goraș A., Chele N. Evaluation of dental implant integration following sinus lifting interventions with sinus membrane perforation. In: *Medicina Stomatologică*. 2023; 2 (63): 158-167. ISSN 1857-1328.

6. Chele D., Chele N., Motelica G., Mostovei A., Dabija I., **Zugrav V**., Beliniuc S. Early type 2 flapless insertion of dental implants in one surgical session. 5-year follow-up evaluation. In: *Medicina Stomatologica*. 2023; 2 (63): 11-24. ISSN 1857-1328.

7. **Zugrav V**., Chele N. New approaches in the treatment of gingival dehiscence in Guided Bone Regeneration. Literary synthesis. In*: Medicina Stomatologica*. 2024; 4:(65): 6-15. ISSN 1857-1328

• Abstracts/summaries/theses in the proceedings of national and international scientific conferences

- ✓ **international**

8. **Zugrav V**., Chele N., Dabija I., Mostovei A. The role of the polymeric absorbable membrane in guided bone regeneration. In: *Clin Oral Impl Res*, 29th Annual Scientific Meeting of the European Association for Osseointegration September 29th – October 1st 2022. Geneva, Switzerland September 29th-October 1st 2022; 33 (Suppl. 24), EAO-¬434 / PO-¬206. DOI: 10.1111/clr.14001, pp. 208.

9. Chele N., **Zugrav V**. Method for restoring bone defects of the jaws. In*: Proceedings of the 14th edition of EUROINVENT European Exhibition of Creativity and Innovation*;(Catalogues &

Publications 14th Edition), Iași, Romania; 26-28 May, 2022: ISSN Print: 2601-4564 Online: 2601-4572, pp.180-181.

10. Chele N., **Zugrav V**. Use of polymer mesh in guided bone regeneration. In: *Proceedings of the 13th edition of EUROINVENT European Exhibition of Creativity and Innovation*;(Catalogues & Publications 13th Edition), Iași, Romania; 20-22 May, 2021. ISSN Print: 2601-4564 Online: 2601-4572, pp. 196.

11. **Zugrav V**., Chele N. Method for restoring bone defects of the alveolar processes in implant-prosthetic rehabilitation. In: Materials of the International Exhibition of Scientific Research, *Innovation and Inventions PRO INVENT, XIX Edition*. (Catalog), Cluj-Napoca, Romania, October 20-22, 2021. ISSN 2810 – 2789, pp. 176-177.

12. **Zugrav V.**, Chele N. Method for restoring bone defects of alveolar processes in the implantprosthetic rehabilitation. In: The scientific bulletin addendum. The official catalogue of the "cadet inova" exhibition research and innovation in the vision of young researchers.*"Cadet INOVA'19"*.(The Scientific Bulletin Addendum No. 4/2019), Sibiu, Romania; April 11-13, 2019, ISSN 2501-3157, pp. 261.

13. **Zugrav V.,** Chele N. Method for restoring bone defects of alveolar processes in the implant prosthetic rehabilitation. In: *Proceedings of the 11th edition of EUROINVENT European Exhibition of Creativity and Innovation*.(Catalogues & Publications 11th Edition), Iași, Romania; 16-18 May, 2019. ISSN Print: 2601-4564 Online: 2601-4572, pp. 197-198.

- ✓ **national**

14. Zugrav V., Chele N. The use of polymer meshes in guided bone regeneration. In*: Annual Scientific Conference of USMF "Nicolae Testemițanu"*. Chisinau, October 20-22, 2021. CZU:61:57 (082)=135.1=111 C35, pp 462.

15. Negru N., Hîțu D., **Zugrav V.,** Carajelascov V., Juc D., Gatman D. Management of oromaxillofacial diseases associated with endocrine pathologies in outpatient surgery. *Annual Scientific Conference, USMF "Nicolae Testemițanu"*, Chisinau, October 19-21, 2022. In: Journal of Health Sciences of Moldova, Suppl. 2022; 29 (3), ISNN 2345-1467, pp 519.

16. Mîndru A., **Zugrav V**., Chele N. Alternative extraction techniques for impacted third molars to reduce the risk of inferior alveolar nerve damage. *Annual Scientific Conference, USMF "Nicolae Testemițanu"*, Chișinău, October 19-21, 2022. In: Journal of Health Sciences of Moldova, Suppl. 2022; 29 (3), ISNN 2345-1467, pp 514.

• Patents, patents, registration certificates, materials at the invention salons

- ✓ **patents**

17. **Zugrav V**., Chele N. Method for restoring bone defects of the alveolar processes in implant-prosthetic rehabilitation. Invention patent MD 1288. BOPI, page 50-51, 31.10.2018..

18. **Zugrav V**., Chele N. Method for restoring bone defects of the jaws. Invention patent MD 1503. BOPI, page. 51-52, 28.02.2021

- ✓ **materials from the international invention exhibitions**

Gold Medal

19. **Zugrav V**., Chele N. Gold Medal for invention: Method for restoring bone defects of alveolar processes in the implantprosthetic rehabilitation. At: *The 11th edition of EUROINVENT European Exhibition of Creativity and Innovation*, Iași, Romania. May 16-18, 2019.

20. **Zugrav V.,** Chele N. Gold Medal for invention: Method for restoring bone defects of alveolar processes in implantprosthetic rehabilitation. At: *International Exhibition of Inventions and Innovations "Traian Vuia" Timișoara, 6th edition*, Timișoara, Romania. October 15, 2020.

21. Chele N., **Zugrav V**. Gold Medal for invention: Method for restoring bone defects of the jaws. In: *Proceedings of the 14th edition of EUROINVENT European Exhibition of Creativity and Innovation,* 26-28 May, 2022, Iași, Romania.

Silver Medal

22. Chele N., **Zugrav V**. Silver Medal for invention: The use of polymer meshes in guided bone regeneration. At: *International Exhibition of Inventions and Innovations "Traian Vuia" Timișoara, 7th edition,* Timișoara, Romania. Online. October 06-08, 2021.

23. **Zugrav V**., Chele N. Silver Medal for invention: Method for restoring bone defects of alveolar processes in the implantprosthetic rehabilitation. At: *The International Student Innovation and Scientific Research Exhibition – "Cadet Inova'19"* – "Nicolae Bălcescu" Land Forces Academy Sibiu, April 11-13, 2019.

Bronze Medal

24. **Zugrav V.,** Chele N. Bronze Medal for invention: Method for restoring bone defects of alveolar processes in implant-prosthetic rehabilitation*. International Salon of Scientific Research, Innovation and Invention PRO INVENT, XIX Edition*. Cluj-Napoca, Romania, October 20-22, 2021.

Diploma of Excellence

25. Chele N., **Zugrav V**. Diploma of Excellence for: Use of polymer mesh in guided bone regeneration. At: *13th edition of EUROINVENT European Exhibition of Creativity and Innovation,* 20-22 May, 2021, Iași, Romania.

• Participation with communications at scientific forums:

- ✓ **national**

26. **Zugrav V**., Chele N. The use of polymer meshes in guided bone regeneration. *Annual Scientific Conference, USMF "Nicolae Testemițanu",* (Program-Invitation) page 45, Chișinău, 20-22 October, 2021.

27. **Zugrav V**., Chele N. The use of polymer meshes in guided bone regeneration. *Ediţie consacrată comemorării distinsului savant Valentin Topalo*, USMF "Nicolae Testemițanu", Chișinău, April 28, 2023.

• Participation with posters at scientific forums:

- ✓ **international**

28. Chele D., **Zugrav V.,** Mostovei A., Chele N. Absorbable biopolymeric mesh: A new concept in Guided Bone Regeneration. *ITI World Symposiom. Singapore*, May 9-11, 2024.

29. *Zugrav V*., Chele N., Dabija I., Mostovei A. The role of the polymeric absorbable membrane in Guided Bone Regeneration*. European Association for Osseointegration Congress*. Geneva, Switzerland, September 26 – October 1, 2022.

30. Chele N., **Zugrav V.** Method for restoring bone defects of the jaws*. Proceedings of the 14th edition of EUROINVENT European Exhibition of Creativity and Innovation*. Iași, Romania, 26-28 May, 2022. ISSN Print: 2601-4564. Online: 2601-4572.

31. Chele N., **Zugrav V**. Use of polymer mesh in guided bone regeneration. *Proceedings of the 13th edition of EUROINVENT European Exhibition of Creativity and Innovation.* Iași, Romania, 20-22 May, 2021.

32. **Zugrav V**., Chele N. Method for restoring bone defects of alveolar processes in implant-prosthetic rehabilitation. *International Exhibition of Scientific Research, Innovation and Invention PRO INVENT, XIX Edition*. Cluj-Napoca, Romania, 20-22 October, 2021.

33. Chele N., **Zugrav V**. Use of polymer mesh in guided bone regeneration. *International Exhibition of Inventions and Innovations "Traian Vuia" Timișoara, 7th edition*. Timișoara, Romania, October 6-8, 2021 (Online).

34. **Zugrav V.,** Chele N. Method for restoring bone defects of alveolar processes in implant-prosthetic rehabilitation. *International Exhibition of Inventions and Innovations "Traian Vuia" Timișoara, 7th edition*. Timișoara, Romania, October 15, 2020.

35. **Zugrav V**., Chele N. Method for restoring bone defects of alveolar processes in the implant prosthetic rehabilitation. *The International Student Innovation and Scientific Research Exhibition - "Cadet Inova'19"* - "Nicolae Bălcescu" Land Forces Academy Sibiu, Romania, April 11-13, 2019.

36. **Zugrav V.,** Chele N. Method for restoring bone defects of alveolar processes in the implant prosthetic rehabilitation. *The 11th edition of EUROINVENT European Exhibition of Creativity and Innovation*. Iasi, Romania, May 16-18, 2019.