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ORIGINAL PAPER

THE RESULTS OF USING A COMBINED DEMINERALIZED FIBRIN-BONE MATRIX IN THE TREATMENT OF RADICULAR CYSTS OF THE JAWS

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Abstract

Introduction. The timely detection, prevention and rehabilitation of patients with chronic inflammatory processes of the bones of the facial skeleton are very important.
The objective of the study was to increase the efficiency of restoration of bone defects of the jaws with allograft material obtained by simultaneous centrifugation demineralised bone granules, autologous bone-derived plastic material, and the patient's venous blood.
Materials and methods. A total of 50 patients aged between 20 and 40 years who had been diagnosed with radicular cysts of the jaws were selected for the study. All patients were divided into groups I and II, who underwent cystectomy and bone grafting. In group I (n=25), patients underwent cystectomy in combination with bone grafting using a scaffold created by simultaneous centrifugation of blood and bone grafting material. In group II (n=25), patients were performed

Résumé

Résultats de l'utilisation de la matrice combinée fibrine-os déminéralisée dans le traitement des kystes radiculaires des mâchoires

Introduction. La détection, la prévention et la réadaptation rapides des patients atteints de processus inflammatoires chroniques des os du squelette facial sont tres importantes.
L'objectif de l'étude était d'augmenter l'efficacité de la restauration des défauts osseux des mâchoires avec du matériel d'allogreffe obtenu par centrifugation simultanée de granules osseux déminéralisés, de matériel plastique autologue dérivé de l'os et du sang veineux du patient.
Matériels et méthodes. Un total de 50 patients âgés de 20 à 40 ans chez qui on avait diagnostiqué des kystes radiculaires des mâchoires ont été sélectionnés pour l'étude. Tous les patients ont été divisés en groupes I et II, qui ont subi une cystectomie et une

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cystectomy in combination with bone grafting using only demineralized bone grafting material.
Results. The results of the postoperative radiological examinations confirm the effectiveness of the filter and the technique developed by us, evidenced by the simultaneous uniform regeneration of bone tissue across the entire thickness of the defect during the 6th month in group I in 21 patients (84%). This is evidenced by the organised architecture of bone tissue with a pronounced trabecular pattern, which correlated with bone density indices from 780.69+18.77 up to 516.31+31.19 HU. In this group of patients, these indices corresponded to intact bone.
Conclusions. The stable combined fibrin scaffold has a pronounced osteoconductive and osteoinductive effect.

Keywords: bone tissue regeneration, bone-plastic material, restoration of bone defects of the jaws, bone grafting.

List of abbreviations:
PRF – platelet-rich fibrin
A-PRF – advanced platelet-rich fibrin
i-PRF – injectable platelet-rich fibrin
rhBMP-2 – recombinant human bone morphogenic protein 2
SEM – scanning electron microscopy
HU – Hounsfield units
SEM – scanning electron microscopy
u/j – upper jaw
l/j – lower jaw

greffe osseuse. Dans le groupe I (n = 25), les patients ont subi une cystectomie associée à une greffe osseuse utilisant un support créé par centrifugation simultanée de sang et de matériel de greffe osseuse. Dans le groupe II (n = 25), les patients ont subi une cystectomie associée à une greffe osseuse utilisant uniquement du matériel de greffe osseuse déminéralisé.
Résultats. Les résultats des examens radiologiques postopératoires mentionnés ci-dessus confirment l'efficacité du filtre et de la technique développée par nos soins. Cette efficacité a été démontrée par la régénération uniforme simultanée du tissu osseux sur toute l'épaisseur du défaut au cours du 6e mois dans le groupe I chez 21 patients (84%). Ceci est démontré par l'architecture organisée du tissu osseux avec un motif trabéculaire prononcé, qui est en corrélation avec des indices de densité osseuse de 780.69±18.77 jusqu'à 516,31±31,19 HU. Dans ce groupe de patients, ces indices correspondaient à un os intact.
Conclusions. L'échafaudage de fibrine combiné stable a un effet ostéoconducteur et ostéoinducteur prononcé.

Mots-clés: régénération du tissu osseux, matériau osseux-plastique, restauration des défauts osseux des mâchoires, plastique osseuse

Introduction

The timely detection, prevention, and rehabilitation of patients with chronic inflammatory processes of the bones of the facial skeleton are very important. Among the chronic inflammatory processes, chronic forms of osteomyelitis and radicular cysts are the most frequent and problematic in the rehabilitation programme, as these pathologies most often lead to bone destruction and require the use of reconstructive plastic surgery[1-3].

Surgical interventions involving dental procedures for chronic inflammatory processes that result in destructive changes of the facial skeleton frequently entail the use of implant materials comprising tricalcium phosphate and hydroxyapatite, to provide supplementary structural support during the process of bone tissue restoration[4-6]. However, when using these materials and standard techniques, there is a problem of restoring the full bone structure, which is associated with untimely degradation of the granulate and development of bone hyperostosis or the formation of connective tissue around the implanted granules. A number of studies have identified the structure of a functional carrier for these tissues or cells, namely a matrix based on biocompatible and biodegradable materials, as playing an important role in tissue reconstruction[7-9].

The analysis of literature data indicates a growing interest in autologous materials, which are currently regarded as the "golden standard" of reconstructive technologies. This is due to criteria as histocompatibility, lack of toxicity and the presence of certain factors that directly or indirectly affect the wound healing processes. Such promising biomaterials include platelet-rich fibrin (PRF), having a number of advantages, also including enhanced release of proteins and growth factors, fibroblast proliferation, their ability to migrate and express growth factors[10-14]. The use of these materials was performed both in filling of defects after the extraction of third molars[15] and in other surgical interventions[16-18]. This particular type of plasma has been administered in both gel and injectable forms[18-20].

In addition to practical clinical use, laboratory studies of the properties of this autologous material are ongoing. In particular, Crisci et Barillaro found that leukocyte- and platelet-rich fibrin (L-PRF) and its derivatives (advanced PRF (A-PRF), injectable PRF (i-PRF)) are useful as a basis for stem cells in wound regeneration[21,22]. In particular, the use of PRF technology in combination with bone-plastic material creates optimal conditions for bone regeneration. For example, the results of the study by Kim et al. are noteworthy, as the researchers evaluated the PRF matrix mixed with tricalcium phosphate and recombinant human bone morphogenic protein 2 (rhBMP-2) and its capacity to enhance bone regeneration in sinus lift surgery[23]. However, an analysis of existing techniques has shown that when PRF technology is used in combination with bone grafting material, i-PRF is usually used, as only with this consistency it is possible to fully combine bone granulate and growth factor-rich plasma.

The disadvantage of this technique is the lack of mechanical stability of such a hybrid, combined scaffold. In contrast, an alternative technique has lead to the formation of a mechanically stable gel-like framework in a test tube during centrifugation. In their study, De Almeida et al. and El Bagdadi et al. performed a comparative analysis of the tensile strength of platelet concentrates between two different autologous platelet concentrates (L-PRF versus PRF)[24,25]. However, this type of the gel-like PRF is not fully mixable with bone tissue.

In our opinion, the combination of a mechanically stable fibrin PRF matrix with an integrated bone-plastic material will, on the one hand, ensure the stability of such a scaffold in a bone defect, and on the other hand, due to growth factors, will lead to the stimulation of bone regeneration.

The objective of the study was to enhance the efficacy of bone defect restoration of the jaws with allo-autologous material obtained by the simultaneous centrifugation of granules of demineralised and autologous bone-plastic material and the patient's venous blood.

Materials and methods

To obtain a scaffold created by simultaneous centrifugation of a patient's blood and bone-plastic material, a suitable titanium filter made of lightweight biocompatible titanium alloy Ti-6Al-4V (Patent N° 152966. A61L 33/00, published 03.05.2023) has been developed.

A total of 50 patients, aged between 20 and 40 years and diagnosed with radicular cysts of the jaws, were selected for inclusion into the clinical trial. To ensure the reliability of the analysis of defect recovery dynamics, the size of the defect – which did not exceed 25 mm – was also taken into account during the selection of patients. All subjects examined were practically healthy, exhibiting no concomitant somatic pathology, and no orthopaedic structures were identified in the areas of surgical correction. Additionally, no factors that could directly or indirectly affect the results of the studies were present, including but not limited to pathological conditions of the oral vestibule, tobacco abuse, and poor oral hygiene.

To determine the effectiveness of the combined matrices obtained by us, all patients were divided into two groups, depending on the use of a particular technique. Group I comprised patients (n=25) who underwent cystectomy in combination with bone grafting according to the known method. However, the scaffold itself was prepared according to a protocol developed by the authors (Patent N° 136410. A61C 8/00, A61C 9/00, published 27.08.2019; Patent N° 158126. A61L 31/00, A61L 33/00, Published 01.01.2025) using the filter developed by us. Group II included patients (n=25) who underwent cystectomy in combination with bone grafting according to the standard method using only demineralised bone graft material in the form of CenoBone® granulate (manufactured by Cenobiologics Ltd) and an insulating collagen membrane CenoMembrane®.

Initially, venous blood was extracted from the patient and transferred into a tube with a plasma activator. For this technique, glass vacuum tubes such as MM Medic, were selected. Subsequently, the device developed by the authors was positioned centrally within the tube. Thereafter, granules of demineralised bone-plastic material CenoBone® produced by Ceno Biologics were poured into the middle of the tube. The tube was then closed and placed in a centrifuge and centrifugated for 12 minutes at 2500 rpm, followed by 3 minutes at 3000 rpm.

Following the process of centrifugation, the erythrocyte mass remained in the lower third of the tube, passing through the pores between the bone plastic granules and through the filter part of the device. Conversely, the bone plastic granules remained on the surface of the filter part of the device. In the upper half of the tube, an organised fibrin framework was formed, with platelets and growth factors integrated into the porous bone graft scaffold. Following centrifugation, the combined scaffold was extracted from the tube and applied into the bone defect area, covering it with CenoMembrane®, an insulating collagenous membrane manufactured by Ceno Biologics.

The efficacy of the methodology developed by the authors was assessed by electron microscopy, clinical and radiological parameters.

In order to study the structure of our bone-fibrin scaffold, scanning electron microscopy of the preparations using JEOL-25 TA-220 equipment (Tokyo, Japan) was performed. The specimens for the study were prepared by freeze-drying through the critical point, cut at different angles and mounted on microscope slides with conductive glue, after which they were coated with a layer (20 nm) of chemically pure aluminium (sample ^{999}) in the VUP-5M apparatus (SELMI, Sumy, Ukraine) for the scanning electron microscopy (SEM) with an accelerating voltage of 15-25 kV in the mode of absorbed and secondary scattered electrons.

Early clinical outcomes in patients of groups I and II in the postoperative period were assessed by clinical signs such as the presence or absence of pain, edema, the condition and degree of divergence of the wound margins, exudate from the gingival pockets and along the incision line. Radiological analysis was performed before surgery and at 6 and 12 months after surgical treatment. Computed tomography data (TOSHIBA Aquilion PRIME 160-slice MODEL TSX-302A/1C) were used to assess the density and structure of bone tissue. The analysis of bone density and its structure according to Hounsfield HN (1919) (HU) was performed using SimPlant Pro 11.04 software. To compare the bone density, there were used both intact jaw areas and additionally archival computed tomography data of 30 patients from the control group, without bone pathology of the maxillofacial area. The dimensional parameters of odontogenic cysts were determined by the linear dimensions of width, height and depth in three mutually perpendicular directions. The analysis of bone density and structure in patients with radicular cysts of the jaws was performed according to the following sectors: the frontal sector from the canine to the canine, the premolar area and the molar area. The density and structure of bone tissue in the area of radicular cyst were examined at 2, 4, 6 mm from the lateral wall of the defect in contact with the cyst membrane to the periphery.

In all patients, the cystectomy was performed using an angled or trapezoidal incision. The fissure boron was used to resect the root apex (if deemed necessary), followed by cystectomy. The mucocutaneous periosteal flap was then placed and fixed with sutures.

The study was conducted in accordance with the principles of the Helsinki Declaration of Universal Protection of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine. The study protocol was approved by the Local Ethics Committee for all participants. Written informed consent was obtained for the study, as well as for the collection and processing of patient data.

Statistical analysis of numerical data was performed using Microsoft Excel 2019 software (Microsoft Office 2019 (Microsoft). All the quantitative data obtained in the study corresponded to the normal type of distribution according to the Shapiro-Wilk's W test, and therefore the interval (M±m) was used to represent their central tendency: arithmetic mean (Mean) ± Standard error. To assess the reliability of the differences in the results obtained in comparison with the control group, the parametric t-test (Student's test) was used. The reliability of the difference in qualitative data between the comparison groups was determined according to the results of calculating the Chi-squared test with Yates's correction for continuity. A value of $p<0.05$ was considered significant.

Results

The preparations studied by us demonstrate the presence of organized fibrin filaments that are rapidly formed in conjunction with platelet pseudopodia and manifest as a densely interwoven mesh (Fig. 1), which can serve as a reliable framework structure for consolidation, with both osteoblasts migrating into the framework and the mesh that adheres the allogeneic material (Fig. 2). This, in turn, creates all the conditions for contact osteogenesis, when hemocapillaries grow into such a mesh and mineralization of osseous fibers occurs, which massively penetrate the allograft.

Despite the presence of a substantial number of pores of various size on the surface of allo bone, which can function as supplementary retention sites for osteoblasts of autologous bone, the application of platelet-leukocyte mass results in the formation of a biofilm that effectively holds the particles together. Such a biofilm can become the basis for the formation of closed general plates around the allograft in the process of neoosteogenesis after transplantation of such a scaffold into the surgical field. Furthermore, data derived from the scientific literature suggest that the fibrin matrix functions as a source of leukocyte and platelet factors for the promotion of osteoblast growth and angiogenesis[11,12,18]. In the presence of a structural substrate, these factors contribute to the successful osteointegration of the allograft in the immediate postoperative period following transplantation surgery.

Among all 50 patients with radicular cysts of the jaws, 64% were men and 36% were women. Out of the examined age range, 74% of radicular cysts of the jaws were detected in the age group from 28 to 40 years. Accordingly, in the younger age group – 20 to 28 years – the percentage was 26%.

The analysis of complaints demonstrated that in 70% of cases the asymptomatic course of the disease prevailed. In 30% of cases, the patients were periodically disturbed by spontaneous aching pain in the

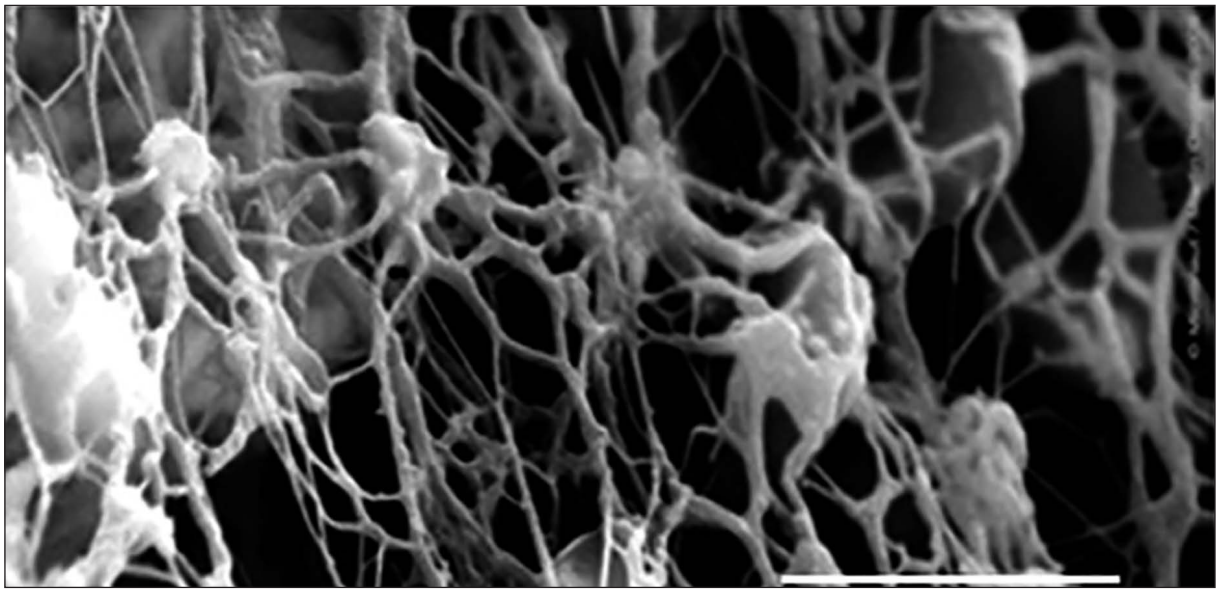
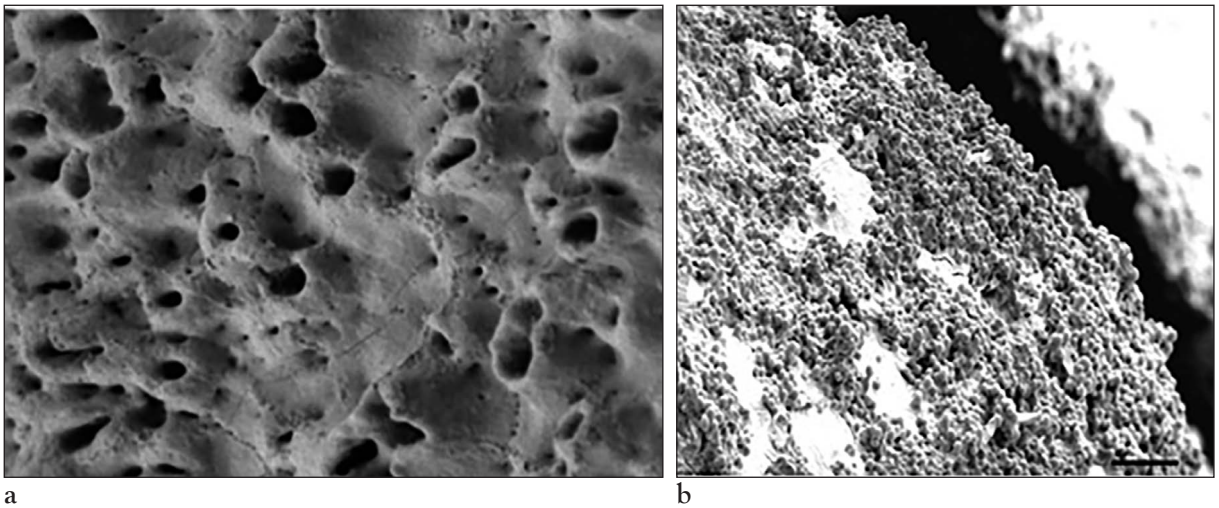


Fig. 1. General view of the platelet preparation. Method: SEM; Accelerating voltage: 15 kV.
Original magnification x 5000, scale bar = 5 μm.



a b

Fig. 2. Image of the allocyst surface before treatment with platelet mass (a) and allo bone fragments after treatment with platelet mass (b). Method: SEM; Accelerating voltage: 25 kV.
Original magnification: a x 5000; b x 2500, Scale bar: a = 20 μm; b = 5 μm.

affected area and pain when biting in the pathologically altered area. A small number of patients (10%) experienced a violation of sensitivity in the lower lip and chin area (Vincent's symptom) in combination with pain.

Based on the computed tomography data, the linear dimensions of the radicular cysts of the jaws were analysed, which showed that in all patients, cysts ranging from 15 to 28 mm in size were detected. The largest percentage of patients (58%) had cysts up to 17 mm in size. A slightly smaller percentage (30%) of patients had cysts up to 20 mm in size, and the remaining patients (12%) had the largest cysts up to 28 mm in size.

When analysing the percentage of cysts located in the upper and lower jaws, the authors referred to the area of localisation rather than to a specific tooth, due to the large size of the lesion and the peculiarities of its location. A detailed analysis of the location of the cysts showed that the incidence of radicular cysts in the upper jaw was 56%, in contrast to the lower jaw, where the percentage was 44%. Based on the radiological examinations, it was found that the most frequent cysts in the upper jaw were in the area of the frontal group of teeth: from the central incisors to the canines (50%). This was followed by a decreasing frequency of cysts in the area of the first and second molars (28.57%) and both upper premolars (21.42%) (Fig. 3).

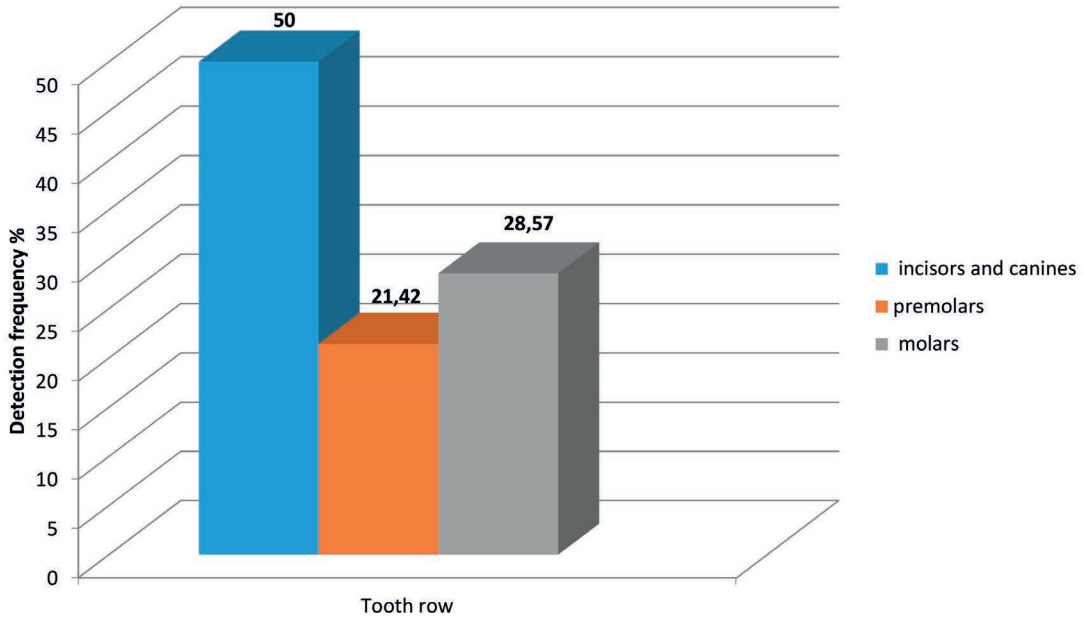


Fig. 3. Incidence of radicular cysts in the upper jaw.

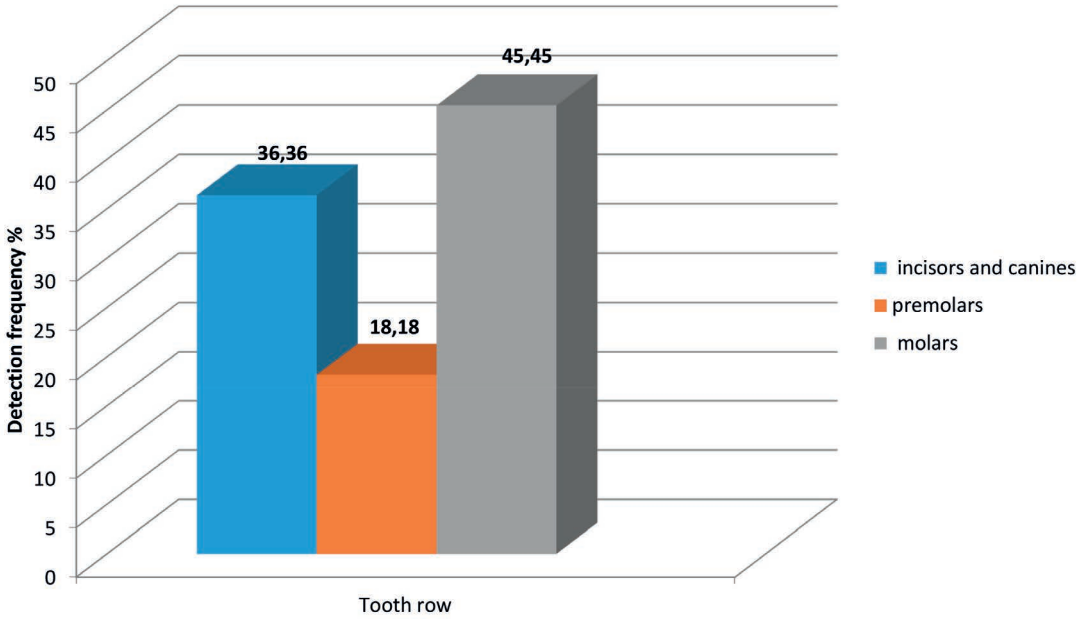


Fig. 4. Incidence of radicular cysts in the lower jaw.

During the examination of the lower jaw, on the contrary, radicular cysts of the jaws were most frequently found in the area of the molars (45.45%) and the anterior group of teeth (36.36%). Less frequently, radicular cysts of the mandible were detected in the area of premolars (18.18%) (Fig. 4).

The analysis of the bone density of the jaws of patients before treatment showed significant differences from the control group. Thus, the greatest difference was observed both in the area of direct contact with the cyst membrane from 1274.69 up to 1064.45 HU, and in the areas remote from this zone (Table 1). The detailed analysis showed no significant correlation between the jaw section and bone tissue density in the area of direct contact with the cyst membrane and the remote 2 mm area. However, in the 2 mm zone, the bone tissue density differed from the area of direct contact with the cyst membrane and ranged from 1126.28 up to 803.03 HU. The bone tissue density was slightly lower in the 4 mm area further from the cyst. There, the values ranged from 913.93 up to 565.76 HU, varying from the anterior to the distal part of the jaw. The same correlation was observed in the 6 mm zone. The analysis of bone tissue density

Table 1. Indices of bone tissue density in patients with radicular cysts of the jaws before surgical treatment.

Anatomical areas	*Areas mm*	*Indications for treatment*	*Control*	*Reliability*
1	2	3	4	5
Incisors and canines u/j	Defect	-	627.34±16.89	-
	0	1138.97±35.05		<0.05
	2	877.69±13.04		<0.05
	4	678.41±17.70		<0.05
	6	648.24±18.87		>0.05
Premolars u/j	Defect	-	510.45±18.73	-
	0	1085.38±39.04		<0.05
	2	826.41±20.89		<0.05
	4	683.59±16.75		<0.05
	6	558.45±20.57		>0.05
Molars u/j	Defect	-	489.76±27.91	-
	0	1064.45±45.32		<0.05
	2	823.17±26.06		<0.05
	4	587.34±20.20		<0.05
	6	467.79±29.20		>0.05
Incisors and canines l/j	Defect	-	887.93±32.02	-
	0	1274.69±33.29		<0.05
	2	1126.28±46.68		<0.05
	4	913.93±36.66		<0.05
	6	829.24±26.67		>0.05
Premolars l/j	Defect	-	657.52±17.54	-
	0	1147.48±35.73		<0.05
	2	928.97±37.63		<0.05
	4	737.17±25.99		<0.05
	6	684.86±19.01		>0.05
Molars l/j	Defect	-	474.45±25.62	-
	0	1088.38±33.45		<0.05
	2	803.03±30.81		<0.05
	4	565.76±29.40		<0.05
	6	438.52±13.33		>0.05

Note: u/j – upper jaw, l/j – lower jaw.

also overlapped with its structure, namely the zone of contact with the cyst membrane, a zone of osteosclerosis, which passed at 2 and 4 mm into the area of increased bone compaction, which was reflected in the form of a change in the trabecular pattern (Fig. 5).

The analysis of clinical data from groups I and II showed some differences between the two groups. Thus, during the 3rd day of the examination, all patients of groups I and II showed an increase in collateral edema. However, 7 (28%) patients in group II had serous discharge during the 3rd – 4th day, in combination with granules of osteoplastic material along the incision line, and 3 (12%) patients had a slight divergence of sutures. On the contrary, in group I, only 4 (16%) patients had a slight serous discharge from the surgical wound, namely, from the incision line, at the above mentioned time. During

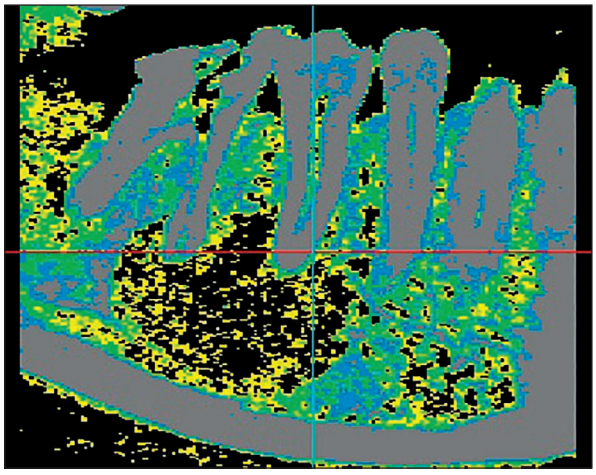


Fig. 5. A 32-year-old patient: bone tissue density indices in the area of radicular cyst of molars and premolars of the lower jaw.



Fig. 6. A 37-year-old patient with the diagnosis of radicular cyst of the upper jaw on the left in the area of teeth 24, 25 and 26: a – cystectomy (defect area); b – defect area filled with combined scaffold; c – computed tomography (transverse reconstruction of the area of tooth 25 before surgery); d – computed tomography (panoramic view of the defect area before surgery); e – computed tomography (transverse reconstruction of the tooth 25 area 10 months after surgery); f – computed tomography (panoramic view of the defect area 10 months after surgery).

the 6th – 7th day after cystectomy and bone grafting, only 5 (20%) out of 7 patients in group II had a slight discharge from the surgical wound, while in group I these changes were observed in only 2 (8%) patients. At the repeated clinical examination during the 12th – 14th day, 5 (20%) patients in group II had the inflammatory changes in the form of a slight discharge of exudate and material from the postoperative wound, whereas no such changes were observed in group I at the indicated time. Thus, analysing these clinical data, it can be concluded that serous discharge in patients in the postoperative period could, in our opinion, be associated with infection of the bone graft area, both with the existing infection in the wound due to the pathological process and with repeated infection of root canals due to the divergence of the surgical wound sutures.

The performed analysis of computed tomography data in group II at the 6-month follow-up period post-surgery revealed that 8 (32%) patients had no signs of bone defect healing, of which 5 (20%) patients were confirmed the progressive inflammatory changes manifesting as fistula formation. Only 7 (28%) patients exhibited signs of complete bone replacement, as evidenced by the formation of a trabecular pattern. In the remaining 10 (40%) patients, signs of peripheral

bone restoration at 2/3 were observed, accompanied by a pronounced trabecular pattern in combination with areas of pronounced disordered calcification. Subsequent to a 12-month interval, a repeated examination revealed that 3 out of 8 patients in group II exhibited complete restoration of bone tissue, while the central portion of the defect remained unaltered. This phenomenon was most commonly observed in patients with large cysts and defect walls represented only by a sclerotic cortical bone layer.

The analysis of the bone structure of group I in the area of bone graft both at the 6th and 12th months after surgery showed the presence of a pronounced trabecular pattern. Therefore, 6 months following cystectomy and bone graft, out of 25 patients in group I, 21 (84%) exhibited complete restoration of the defect by bone tissue, while the remaining 4 patients (16%) had bone regeneration of only 2/3 of the bone cavity volume. One year after surgery, it was observed that bone regeneration had occurred in all 25 patients. In patients of group I, where the method developed by us was applied, complete restoration of the cortical layer of bone tissue was observed throughout (Fig. 6).

The bone density analysis was performed during the 6th and 12th months after surgery (Tables 2 and 3).

The analysis of the dynamics of bone density in the postoperative period showed no significant difference between the patients of groups I and II, at both the 6th and 12th months of follow-up.

Table 2. Indices of bone density in Hounsfield units (HU) in patients of groups I and II, 6 months after surgery.

Anatomical areas	*Areas mm*	*Group I*	*Group II*	*Groups I, II – control (p<0.05)*
1	2	4	5	6
Incisors and canines of the u/j	Defect	576.28±20.61	591.48±17.89	627.34±16.89
	0	576.28±20.61	591.48±17.89	
	2	774.72±23.09*	755.03±26.83*	
	4	646.38±21.56	658.21±19.00	
	6	619.66±23.61	624.72±22.67	
Premolars of the u/j	Defect	512.90±25.30	504.14±25.20	510.45±18.73
	0	512.90±25.30	504.14±25.20	
	2	746.52±22.34*	728.90±26.11*	
	4	623.86±22.20*	616.17±21.72*	
	6	527.97±17.50	533.10±16.14	
Molars of the u/j	Defect	508.62±22.37	520.86±19.56	489.76±27.91
	0	508.62±22.37	520.86±19.56	
	2	689.62±35.28*	677.93±32.88*	
	4	574.69±21.14*	567.76±20.87*	
	6	457.07±28.42	474.31±28.94	
Incisors and canines of the l/j	Defect	583.14±19.98*	559.62±21.18*	887.93±32.02
	0	583.14±19.98*	559.62±21.18*	
	2	1108.48±43.75*	977.34±36.03	
	4	872.97±31.23	809.14±25.61	
	6	823.52±22.46	784.79±21.12*	
Premolars of the l/j	Defect	527.00±28.53*	542.52±26.01*	657.52±17.54
	0	527.00±28.53*	542.52±26.01*	
	2	885.69±35.16*	798.69±42.01*	
	4	719.07±24.34*	705.72±19.74	
	6	672.24±20.53	659.31±16.28	
Molars of the l/j	Defect	545.00±30.96	557.24±27.45*	474.45±25.62
	0	545.00±30.96	557.24±27.45*	
	2	756.38±25.15*	692.86±23.51*	
	4	550.69±26.74*	542.24±27.18	
	6	445.31±13.29	416.10±14.46	

Note: * – reliability when comparing the results. u/j – upper jaw, l/j – lower jaw.

Table 3. Indices of bone tissue density in Hounsfield units (HU) in patients of groups I and II, 12 months after surgery.

Anatomical areas	*Areas mm*	*Group I*	*Group II*	*Groups I, II – control (p<0.05)*
1	2	4	5	6
Incisors and canines of the u/j	Defect	617.48±12.81	609.14±20.01	627.34±16.89
	0	617.48±12.81	609.14±20.01	
	2	678.66±27.22	649.97±28.36	
	4	637.90±20.58	640.59±19.20	
	6	617.31±23.28	621.62±22.48	
Premolars of the u/j	Defect	523.52±25.28	508.41±25.36	510.45±18.73
	0	523.52±25.28	508.41±25.36	
	2	597.41±29.33*	548.66±22.90	
	4	521.62±21.74	539.07±22.31	
	6	522.66±16.83	524.76±19.17	
Molars of the u/j	Defect	518.34±22.21	527.21±16.20	489.76±27.91
	0	518.34±22.21	527.21±16.20	
	2	521.66±24.17	519.86±18.39	
	4	506.69±22.50	491.34±18.10	
	6	471.86±28.34	479.41±25.25	
Incisors and canines of the l/j	Defect	780.69±18.77*	718.21±17.89*	887.93±32.02
	0	780.69±18.77*	718.21±17.89*	
	2	869.93±40.60	892.83±31.55	
	4	853.48±32.80	811.00±18.65*	
	6	815.03±20.55	795.79±14.94*	
Premolars of the l/j	Defect	615.34±27.91	567.34±24.83*	657.52±17.54
	0	615.34±27.91	567.34±24.83*	
	2	663.93±39.82	646.10±33.71	
	4	658.72±25.28	633.72±18.08	
	6	645.21±25.06	651.76±17.28	
Molars of the l/j	Defect	516.31±31.19	514.41±28.58	474.45±25.62
	0	516.31±31.19	514.41±28.58	
	2	537.00±17.78*	567.10±15.67*	
	4	488.55±20.54	504.45±20.93	
	6	459.76±15.30	438.59±17.49	

Note: * – reliability when comparing the results obtained. u/j – upper jaw, l/j – lower jaw.

The most pronounced difference was observed between patients after bone grafting and the control group. Thus, during the 6th month following bone grafting, the bone tissue density was significantly lower than in the control group. This difference was most pronounced in the area of the incisors and canines of the lower jaw, where the index was 34.32% lower than in the control group. A significant disparity was also identified in the area of the lower premolars, where the bone density in the area of bone grafting was found to be 19.85% lower. A decrease in bone density at 8.13% in the postoperative period was also noted in the anterior sector of the upper jaw. This tendency, in our opinion, is due to the presence of existing, but not yet fully formed bone tissue. On the contrary, 12 months after the surgical intervention, an increase in bone density in the area of the former defect was observed, which corresponded to intact indices.

As for the other areas, i.e. those in direct contact with the membrane and those at 2, 4 and 6 mm distance, no clear trend in the difference between the two groups and no direct dependence was observed. The only clear dependency was observed between these indices and the postoperative period. The decrease in bone tissue density in the areas of contact with the membrane from the 6th up to the 12th month of postoperative period was due to bone tissue remodelling leading to a decrease in its compaction.

Discussion

In our opinion, severe cases of osteosclerosis and bone tissue compaction in the 2-6 mm zone surrounding the cyst may be indicative of a rapid increase in cyst volume, which may lead to a certain degree of mechanical pressure on the adjacent bone tissue, leading to a compensatory restructuring of the bone. This phenomenon plays a significant role in cystectomy and bone grafting, as the area of compaction and severe osteosclerosis is often characterised by a deficiency in capillary network. This can lead to the negative results in bone grafting, which may be manifested in the lack of bone remodelling in the area of bone augmentation.

The comparison of the density and structure of the newly formed bone tissue in groups I and II did not reveal any significant differences, which is due to the same physiological processes of bone regeneration. However, a comparative analysis of the volume of the newly formed bone tissue and the area of the defect filled by the newly formed bone, the difference between 84% positive result in group I and only 28% positive result in group II at the 6th month after surgery proves the effectiveness of the developed methodology. This fact, in our opinion, is due, on the one hand, to the dense three-dimensional organisation of fibrin fibres and bone granules formed during centrifugation due to the filter design and centrifugal force, and, on the other hand, to the osteoinductive properties of the scaffold itself. The regenerative potential of fibrin matrix at low speed was also studied by Kubesch et al. The results demonstrated that PRF-medium was more porous, had a significantly higher in vivo vascularization rate, and included significantly more human cells[11]. The osteoinductive effect can also be influenced by components in the demineralized bone graft, such as bone proteins. The best experimental results with bone proteins were obtained by Kim et al[23]. A group of animals who were implanted matrix with rhBMP-2 had significantly faster and larger bone growth in the formation area than the control group. The osteoinductive properties of the scaffold, in our opinion, ensure uniform germination of the capillary network throughout the defect. These properties also create conditions for accelerated and uniform simultaneous bone tissue remodelling. This is evidenced by a fully organised bone architecture with a pronounced trabecular pattern, which in group I completely covered the defect in 84% of cases. This correlated with the bone tissue density, which in this group of patients corresponded to intact bone, which, in our opinion, was a radiological confirmation of complete bone regeneration. Conversely, in group II, the analysis of computed tomography data revealed complete bone restoration in 28% of cases. However, in 40% of patients, partial bone restoration was found, which, in the authors' opinion, is due to faster regeneration in the bone-material contact zone, as opposed to the centre of the granular framework, where the germination of the capillary network can occur at a later stage and a kind of the "dead zone" can be created with faster germination of the capillary-poor connective tissue that competes with bone tissue. The results obtained in this study differ somewhat from those reported by other authors[5,6]. For example, results of easy-graft studies showed that all of the defect area was riddled with large bony trabeculae, that actively carry out the process of compaction of bone. Easy-graft is an osteoconductive material based on β-tricalcium phosphate (β-TCP) and can lead to the formation of more compact bone tissue. However, the formation of more compact bone tissue is not always justified for future dental implantation in the area of bone grafting. That is why the results of our research were aimed at restoring bone tissue whose structure is more similar to intact bone.

Conclusions

The results of the radiological examination of radicular cyst area indicate a pronounced bone tissue compaction in the bone-cyst membrane contact zone. Our stable combined fibrin scaffold has a pronounced osteoconductive and osteoinductive effect, which is reflected in the complete restoration of bone tissue throughout the thickness of the defect. The clinical and radiological analysis demonstrated the effectiveness of the technique developed by us, as evidenced by positive results in the form of complete bone tissue restoration in 84% of patients in group I and only in 28% of patients in group II.

Author Contributions:

Conceptualization, Y.I.Y., A.V.P.; methodology, N.Y.K., I.R.Y.; software, A.V.P.; validation, M.M.R.; formal analysis, A.V.P.; investigation, Y.I.Y., A.V.P.; resources, M.M.R. and I.R.Y.; data curation, M.M.R. and A.V.P.; writing–original draft preparation, Y.I.Y.; writing–review and editing, A.V.P.; visualization, Y.V.R.; supervision, M.M.R.; project administration, M.M.R. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as

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