ORIGINAL ARTICLE

UDC: 616.31-092.9
DOI: https://doi.org/10.2298/VSP190731040D

CBCT analysis of bone density in bicortical defects after augmentation with alloplastic and xenogeneic bone substitutes – A study on domestic pigs

CBCT analiza gustine kosti u bikortikalnim defektima nakon pojačanja primenom aloplastičnog i ksenogenog koštanog zamenika – studija na domaćim svinjama

Filip Djordjević*, Branko Mihailović*, Raša Mladenović†, Dejan Dubovina*, Mirjana Kostić‡, Jelena Stanišić*, Zoran Vlahović*

University of Priština/Kosovska Mitrovica, Faculty of Medicine, *Department of Dentistry, ‡Institute of Preventive Medicine, Kosovska Mitrovica, Serbia; †University of Kragujevac, Faculty of Medical Sciences, Department of Dentistry, Kragujevac, Serbia

Abstract

Background/Aim. A significant benefit in bicortical defects healing can be achieved by guided tissue and guided bone regeneration. The aim of this study was a cone-beam computed tomography (CBCT) radiographic bone density analysis of bicortical defects healing when treated with guided bone regeneration and two bone substitutes – bovine xenograft and alloplastic bone substitute. **Methods**. The research was performed on domestic pigs in two phases. In the first phase, extraction of all teeth in the intercanine sector was performed in the lower jaw and postextraction wounds were sutured. In the second phase, after the period required for healing, bicortical defects were formed – following the elevation of mucoperiosteal flaps from the vestibular and lingual side in the area of the previously extracted teeth, surgical removal of the cambium layer of periosteum was performed in the area of future defects with sharp surgical scissors and curette. Two defects, 10 mm in diameter, on the left and right side of the medial line were formed and filled with alloplastic bone substitute on the left and xenograft on the right side afterward. After augmentation, the defects were covered by a collagen resorptive membrane on both sides, and the flap was repositioned and sutured. After 12 weeks, experimental animals were sacrificed. The surrounding native bone was used as a control. **Results.** Analysis of bone tissue density showed a statistically significant difference between the examined bone substitutes ($p < 0.01$), with a better effect achieved by the use of alloplastic bone substitute. After applying Bonferroni correction, the difference was still statistically significant. **Conclusion.** Both bone substitutes used in the study showed good osteoconductive properties in the treatment of bicortical defects. Bone tissue density in defects filled with alloplastic bone graft was statistically significantly higher than that in the defects filled with xenograft.

Key words:
alveolar ridge augmentation; bone density; bone regeneration; bone transplantation; cone-beam computed tomography; dental implants; oral surgical procedures; swine.

Apstrakt

Uvod/Cilj. Vođena tkivna i vođena koštana regeneracija omogućuju značajnu korist u zarastanju bikortikalnih defekata. Cilj istraživanja bio je rendgenografska analiza koštanog zarastanja unutar bikortikalnih defekata primenom kompjuterizovane tomografije zasnovane na tehnologiji konusnog snopa (CBCT), kao i komparativna analiza gustine koštanog tkiva u bikortikalnim defektima tretiranim postupkom vođene koštane regeneracije uz korišćenje kolagene membrane i dva tipa koštanih zamenika: goveđeg ksenografta i aloplastičnog koštanog zamenika. **Metode.** U prvoj fazi istraživanja izvršena je ekstrakcija svih zuba interkaninog sektora donje vilice nakon čega su postekstrakcione rane zašivene. U drugoj fazi, nakon perioda zarastanja, pristupilo se formiranju bikortikalnih defekata. Nakon odizanja mukoperiostalnog režnja sa vestibularne i lingvalne strane oštrim makazicama i kiretom uklonjen je kambijalni sloj periosta u predelu budućih defekata. Zatim su sa leve i desne strane od medijalne linije formirana dva bikortikalna defekta promera 10 mm koji su popunjavani koštanim zamenicima i to aloplastičnim na levoj i goveđim ksenograftom na desnoj strani. Nakon popunjavanja defekti su prekriveni kolagenim resorptivnim

Correspondence to: Raša Mladenović, University of Kragujevac, Faculty of Medical Sciences, Department for Dentistry, Svetozara Markovića 69, 34 000 Kragujevac, Serbia. E-mail: rasa.mladenovic@med.pr.ac.rs

membranama obostrano, nakon čega je izvršena repozicija i ušivanje režnja. Nakon 12 nedelja eksperimentalne životinje su žrtvovane. Okolna nativna kost služila je kao kontrola. **Rezultati.** Analiza gustine koštanog tkiva pokazala je statistički značajnu razliku između testiranih zamenika kosti, pri čemu je bolji efekat postignut primenom aloplastičnog koštanog zamenika ($p < 0,01$). Nakon primene Bonferonijeve korekcije, razlika je i dalje bila statistički značajna grupe. **Zaključak.** Oba koštana zamenika korišćena u studiji pokazuju dobra osteokonduktivna svojstva u tretmanu bikortikalnih defekata. Gustina koštanog tkiva u defektima pojačanim aloplastičnim zamenikom je bila statistički značajno veća nego u defektima popunjavanim ksenograftom.

Ključne reči:
alveolarni greben, podizanja; kost, gustina; kost, regeneracija; transplantacija kosti; tomografija, kompjuterizovana, konusna; implantati, stomatološki; hirurgija, oralna, procedure; svinje.

Introduction

Bicortical, “tunnel” or transosseous defects are defined as defects characterized by lack of buccal and oral bone cortex or occurring when a surgical accessory bone window is formed on one side, with already present erosion on another cortical lamella. These defects typically have a 3-wall configuration with the mesial, distal, and craniocaudal walls, but without buccal or oral. In this type of defect, the rapid proliferation of the connective tissue can interfere with the bone structure ingrowth from the sidewalls of the defect, leading to so-called fibrous healing [1]. Authors who dealt with the problem of these defects consider that a significant benefit in their healing can be achieved by guided tissue, bone regeneration, primarily in the sense of preventing the onset of scarring fibrous healing [2–4].

The main element of guided bone regeneration is a barrier membrane, which is placed into the space between the mucoperiosteal flap and the bone defect, preventing the penetration of the gingival epithelial and connective tissue into a defect, and enabling regeneration, not reparation of the tissue [5]. In addition to the membrane, different types of bone substitutes are also used for the treatment of bone defects within the guided bone regeneration. Their role is not only to support the membrane and stabilize the blood clot but also in accelerating the healing period and contributing formation of a higher quality bone due to their osteoconductive, osteoinductive, and osteogenic properties [6].

The main method for assessing bone healing in augmented defects, which is still considered the gold standard, is histological analysis. However, as it is not adequate for analysis in clinical conditions, some radiographic noninvasive methods of bone tissue analysis are also suggested [7, 8]. In this context, microradiography is cited as a method that provides reliable data on trabecular architecture and density of bones without spatial deformations [9]. The introduction of the cone-beam computed tomography (CBCT) contributed to a significant reduction in the scanning time, radiation dose, costs, and also the possibility of its use in dental clinics as a piece of standard equipment. CBCT scanners can be used in various diagnostic procedures in dentistry, providing precise diagnostic data not only in the region of interest but also in the surrounding structures [10]. Soardi et al. [11] also stated that there is no statistically significant difference in determining bone tissue density between microradiography or CBCT devices.

The aim of this study was to analyze bone healing of bicortical defects treated with the guided bone regeneration and two bone substitutes (bovine xenograft and alloplastic bone substitute) using CBCT.

Methods

The study was approved by the Ethics Committee of the Faculty of Medical Science in Kosovska Mitrovica, with headquarters in Kosovska Mitrovica, Serbia (No. 09-423-1/26.03.2018). The research was carried out on ten domestic pigs with an average weight of 25 kg.

Surgical procedure

Surgical procedures were carried out in the ambulance of the domestic pigs’ farm of the Agricultural High School in Lesak, Serbia. Before every surgical intervention, the animals were deprived of food and water for a period of 12 h. Premedication was performed by intramuscular (im.) injection of midazolam at a dose of 0.5 mg/kg (Midazolam® Panpharma 5 mg/5 mL, Rotexmedica GmbH Arzneimittelwerk, Germany). After fifteen min, the animals were introduced into anesthesia by i.m. administration of 1 mL/10 kg combined ketamine solution as an anesthetic, xylazine as a sedative, and atropine as an anticholinergic (100 mg/20 mg/1 mg *per* mL of solution, KET-A-XYLR Sens, Peru). To control pain and intraoperative bleeding in the area of the surgical field, local anesthesia was used (4 mL articaine chloride/adrenaline hydrochloride, 40 mg/mL/0.012/mL, Ubistesin Forte, 3M ESPE, Germany).

Surgical procedures were performed in two phases. In the first phase, after introducing the animals to short-term anesthesia and then with local anesthesia, the extraction of lower teeth in the intercanine sector was performed. The post-extraction wounds were sutured (Figure 1) with resorptive sutures (Polisorbtm 3–0, Covidien, Switzerland).

In the second phase, after 9 weeks required for healing of postextraction wounds [12], mucoperiosteal flaps from the vestibular and lingual side in the area of the previously extracted teeth were elevated, and bicortical defects were formed after removal of the cambium layer of periosteum with sharp surgical scissors and curette. Two defects on the left and right side of the medial line were formed with a round trepan bur with 10 mm diameter, with the use of a contra-angle handpiece with 700–800 rpm and with manda-

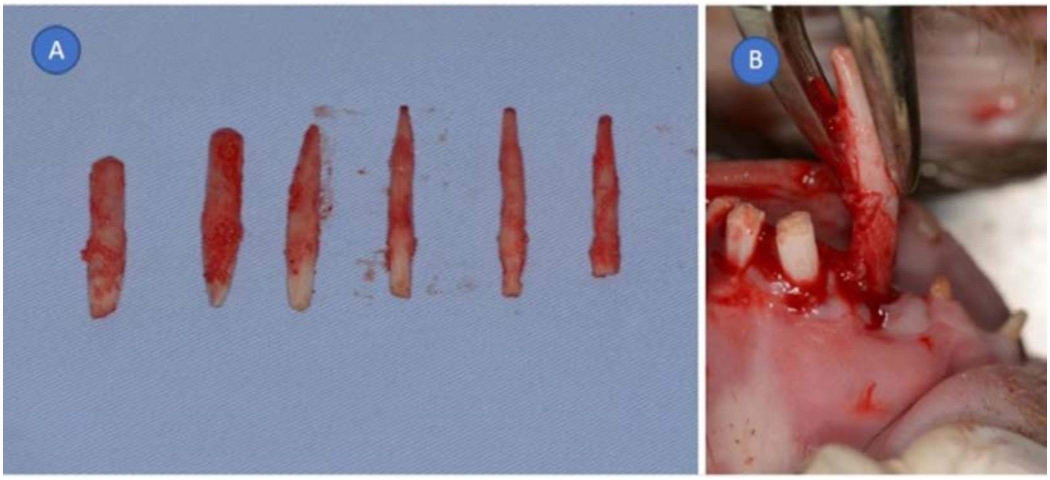

Fig. 1 – Extracted teeth (A) and extraction of the tooth in the inter-canine sector (B).

tory cooling with saline. Defects on the left side were filled with alloplastic bone substitute (Tixxu® graft, 60% hydroxyapatite – 40% tricalcium phosphate, Bredent, Germany) with granule sizes of 0.5–1.0 mm, while defects on the right side were filled with xenograft of bovine origins (D Bone®, Divinity Capital LLC) with granule sizes of 0.25–1 mm.

After augmentation, the defects were covered by placing the collagen resorptive membrane with a thickness of 0.6–0.8 mm (Angiopore, Bredent, Germany) from both vestibular and lingual sides of the defect; thus, the membrane passed over the edges of the defect for 5 mm or more, in order to prevent its collapse.

For easier identification of the augmentation site after a period of healing, fixing screws (Titan pin set, Botiss Biomaterials GmbH, Germany) were placed at a distance of 3 mm from the edges of the defect, thereby making the membrane additionally stabilized. After filling the defect and placing the membrane, the flap was repositioned and sutured with resorptive sutures (Figure 2).

The surrounding native bone was used as a control.

Postoperatively, for five days, antibiotic therapy with benzylpenicillin was ordered to experimental animals, with a dose of 12 000 IU/kg (Neo-penicillin 4 000 000 IU, FM Pharm d.o.o. Subotica).

CBCT analysis

After 12 weeks, experimental animals were sacrificed by intravenous (iv.) administration of 7.4% potassium chloride solution, which causes cardiac arrest. After sacrificing, the lower jaw was separated from the skull, and soft tissue was removed. Using a handsaw and performing a mandatory cooling with saline, the front segment of the mandible was detached and divided in the medial line area into two bone blocks. Each bone block contained an examined bone defect,

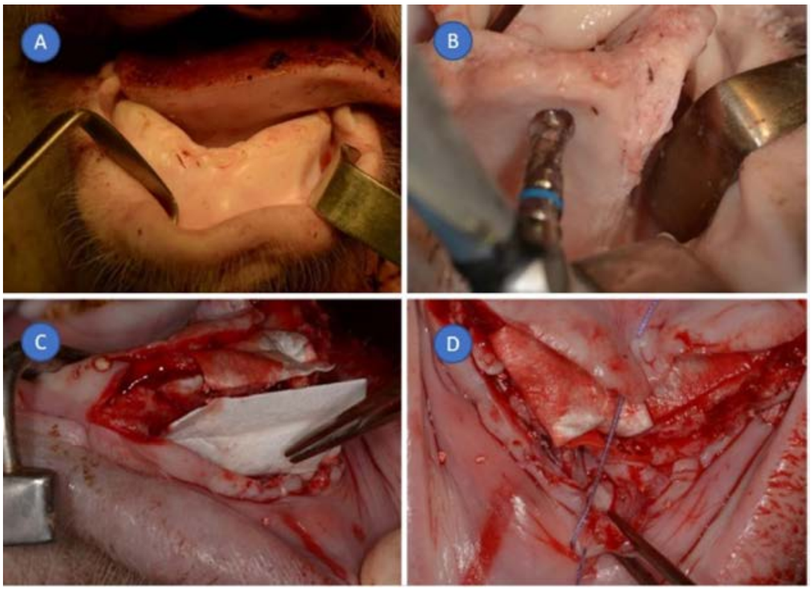

Fig. 2 –Surgical procedure: A) appearance of the toothless alveolar ridge 9 weeks after tooth extraction; B) preparation of bicortical defect after elevating the mucoperiosteal flap; C) filling a defects with a bone substitute and covering with a resorptive collagen membrane from the vestibular and lingual side; D) reposition and suturing of the flap.

clearly visible due to previously installed pins (Figure 3). Detached bone blocks were immersed in a 4% neutral formalin solution and sent for radiographic examination. The examination involved measuring the density of bone tissue in the region of examined defects, as well as in the region of surrounding native bone, expressed in the Hounsfield Unit (HU).

X-ray analysis was carried out in the V Dental Center in Podgorica (Montenegro), using the CBCT scanner PlanmecaProMax 3D and PlanmecaRomexis analysis software (Figure 4).

Statistical analysis

Descriptive methods and methods for testing statistical hypotheses were used for the analysis of data. Descriptive statistical methods included measures of central tendency (median) and measures of variability (range). Methods for testing statistical hypotheses included the Kruskal-Wallis test with Bonferroni correction. For statistical processing, the statistical software package SPSS 21 was used. Statistical hypotheses were tested at the statistical significance level of 0.05.

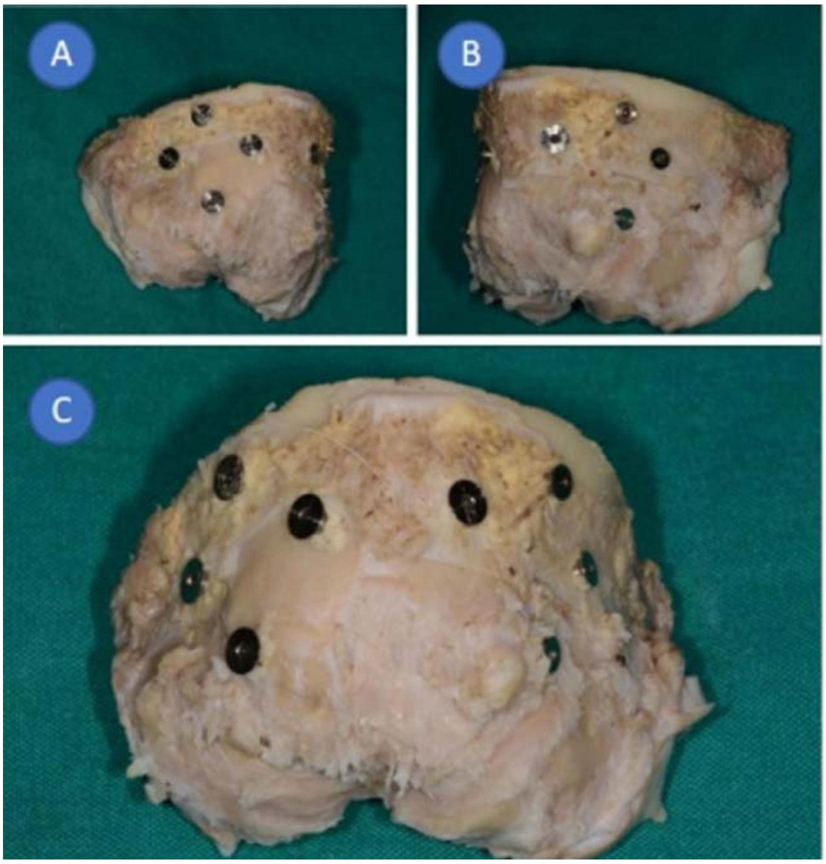

Fig. 3 – The bone defects marked with pins, prepared for cone-beam computed tomography analysis (A–C).

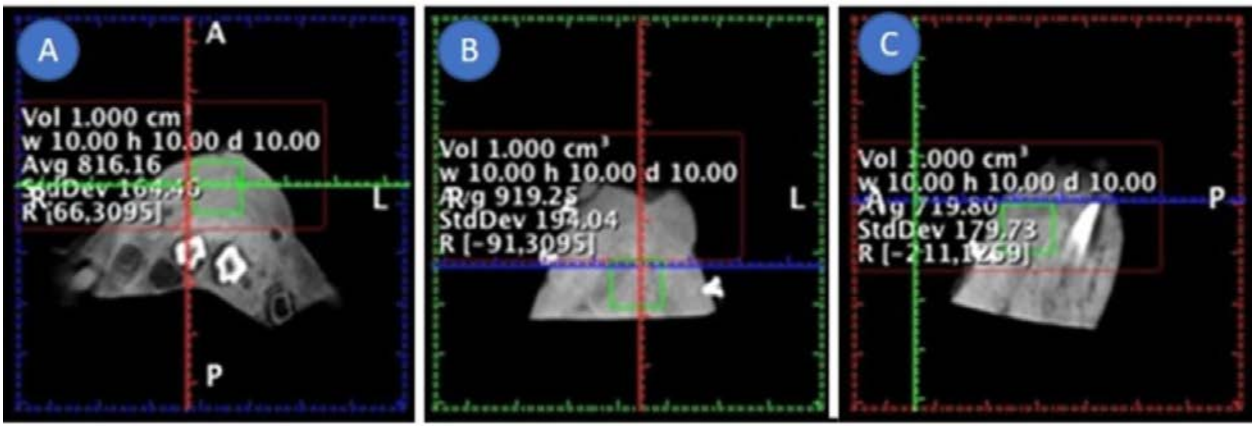

Fig. 4 – Analysis of bone density of defects filled with alloplastic substitute (A), xenogeneic substitutes (C) and bone density of surrounding native bone tissue (B).

Results

During the follow-up period, there were no postoperative complications in any animal.

Radiographic analysis of the examined defects revealed a full bone healing of all defects, whether it was filled with xenograft or with an alloplastic bone substitute.

Analysis of bone tissue density in the examined defects, as well as of surrounding native bone, expressed in Hounsfield units (HU), showed a statistically significant difference in all three examined samples (Table 1). The highest density was found in the area of the surrounding native bone (945.2 HU). The density of the defects treated with alloplastic bone substitute was substantially closer to the density values of the surrounding native bone than in the case of defects treated with xenograft, and it ranged from 773.5 to 895.8, with an average value of 829.7 HU. Values of the measured density in the defects treated with xenogeneic bone substituent were 649.7 HU.

Table 1

Bone density values of the examined defects

Bone substitute	Bone density (HU), median (range)	*p*
Allograft	829.7 (773.5–895.8)	
Xenograft	649.7 (586.4–723.5)	< 0.001
Native bone (control)	945.2 (925.7–963.5)	

HU – Hounsfield Unit.

After applying Bonferroni correction, the difference was statistically significant among all samples (Table 2).

Table 2

***p*-values after Bonferroni correction**

Difference in bone density	*p* (adjusted)
Xenogeneic substitute – alloplastic substitute	0.032
Xenogeneic substitute – native bone	< 0.001
Alloplastic substitute – native bone	0.032

Discussion

Tissue regeneration is defined as a reproduction of a lost, injured, or surgically removed part, so that the architecture and function of the lost, injured, or removed tissues could be completely restored [13]. Therefore, the bone tissue regeneration process in bicortical jaw defects can be significantly deranged as a result of periosteal damage. The periosteum is primarily a basic source of osteoprogenitor cells, necessary for the regeneration process. It also plays the role of a barrier that prevents penetration of gingival epithelium into the bone healing region. In the case of bicortical defects, the periosteum may be destroyed as a result of the infectious process that caused the appearance of bone defects. Its damage can also occur as a result of simple flap elevation, where the process in bone destroyed both cortexes completely [14]. Such damage can be the cause of incomplete bone healing or even fibrous healing, which makes possible future implant-prosthetic rehabilitation impossible in the defect area.

Numerous studies indicated a fact that guided tissue or bone regeneration can provide many benefits in terms of achieving a more predictable process of defect healing. Taschieri et al. [2, 3] emphasized that the use of guided bone regeneration increases the possibility of successful bone healing in bicortical defects. Similar results were pointed out by Pecora et al. [14]. The use of barrier membranes in such lesions improved possibility of regenerative processes, excluding the unwanted expansion of gingival connective tissue or migration of oral epithelium into the defect, which allowed the formation of the trabecular bone [15]. Moreover, concerning guided bone regeneration, many authors emphasize the importance of proper maintenance of the area below the membrane in terms of providing support for the membrane and stabilizing the blood clot by applying bone substitutes [16, 17].

In this study we determined the presence of bone healing of bicortical defects under resorptive membrane which covered two bone substitutes that augmented the defects. Biphasic calcium phosphate with a lower ratio of hydroxyapatite and β-tricalcium phosphate (60% : 40%), and bovine bone graft were used as materials for guided bone regeneration.

Xenograft is a bone substitute originating from different phenotypes, usually pigs, cattle, horses, or alternative natural sources, such as calcified corals [18] or algae [19, 20]. Although originating from living individuals, xenograft loses cells and bioactive molecules during the production process, so that it has only osteoconductive properties. Jensen et al. [21] and Buser et al. [22] indicate a slow rate of resorption of this graft, wherefore the newly formed bones in bone defects augmented with the xenograft show a slightly smaller volume than in the case of some more resorptive material or autotransplants; this is partly explained by the fact that limited resorption leaves less space for the formation of new bone.

The combination of hydroxyapatite and β-tricalcium phosphate enables the use of positive properties of each of them. Isolated β-tricalcium phosphate shows a high degree of resorption, creating a space for the ingrowth of blood vessels and the formation of new bone tissue in the region of resorbed granules [23]. Graft also releases calcium and phosphate ions, stimulating bone healing [24]. However, if accelerated resorption of this graft is not accompanied by simultaneous bone tissue formation, the ultimate effect may be a bone healing disorder [25]. A supplement of hydroxyapatite showing a low level of resorption [26, 27] provides good mechanical support and graft stability. Also, Jensen et al. [21, 28, 29] point out that such a low ratio of these bone substituents, as it was used in the study, allows a faster and larger formation of bone tissue compared to pure β-tricalcium phosphate, biphasic calcium phosphate with higher hydroxyapatitr/tricalcium phosphate (HA/TCP) ratios and demineralized bovine bone substitute. Although xenograft is widely used today and represents the best documented type of bone substitute, the study indicates that alloplastic material in the form of a combination of hydroxyapatite and β-tricalcium phosphate might serve as an adequate alternative, not only to xenograft but also to other types of bone substitutes. In the literature, results can be found which indicate that these materials, in addition to their osteoconductive effect, can promote osteoinduction, which is another advantage [30]. Their use may also reduce the risk of transmissible diseases if allograft and xenograft were used, particularly the transmission of prion-induced infections after the use of a substitute with bovine origins [31, 32].

Analysis of the results obtained in our study indicates that both types of bone substitutes can be used for the treatment of bicortical bone defects in order to obtain predictable bone healing. The study presented a statistically significantly higher density of the newly formed bone in defects where an alloplastic material was applied compared to defects where xenograft was applied. Obtained density values were also closer to the density of the surrounding native bone. Having in mind the Misch classification [33], we estimated that the bone in the bicortical defects treated with alloplastic material had the D2 type density according to this classification, and in defects, with a bovine substitute, it had the D3 type.

Having in mind the requirements of dental implantation, bone density is a very important parameter of bone quality assessment, which can significantly affect the success of implantation itself. The D2 is a type of bone tissue built from a solid cortical bone on the surface and a dense trabecular bone in the central part. It is better vascularized than the D1 type, allowing bleeding during the preparation of an implant bed, which prevents overheating, and also has a high healing capacity after implantation and a very predictable osteointegration [34, 35]. The D3 type is composed of a thin, porous, compact, and loose spongy bone. It is characterized by good vascularization, but also with inferior mechanical properties in comparison to the D2 bone type. Assessing the mechanical properties of the trabecular bone of the mandible, according to the Misch bone density classification [33], Misch et al. [35] concluded that the D2 bone type has a 47% to 68% higher resistance to pressure than the bone with the D3 density, and a 50% higher hardness. This has a significant effect on the primary stability of implant built into such region, which is one of the basic predictive factors of implantation success. In terms of the elastic modulus, the bone type D2 has a much higher elastic modulus and is closer to the elastic modulus of titanium, compared to the D3 and D4 bone types, which enables a higher degree of implants survival. The study of Misch [35] further indicated that bone-implant contact, after the initial healing phase, was significantly higher in the bone type D2 than D3, which is another important factor for successful implantation.

Conclusion

We can conclude that both bone substitutes used in the study showed good osteoconductive properties in terms of the formation of new bone tissue and the treatment of bicortical defects by the process of guided bone regeneration. Bone tissue density in defects filled with alloplastic bone substitute was statistically significantly higher than that in defects filled with the xenogeneic substitute. Moreover, the density of the new bone in these defects was substantially closer to the density of the surrounding native bone.

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Received on July 31, 2019
Revised on April 9, 2020
Accepted April 13, 2020
Online First April, 2020