

# Bone Repair Materials Used in Guided Tissue Regeneration - Advantages and Disadvantages

Mariya Miteva, Tsvetalina Gerova

Department of Periodontology and Dental Implantology, Faculty of Dental Medicine, Medical University of Varna, Bulgaria

**Abstract:** *Depending on their origin, there are several groups of bone repair materials: autogenous, allogeneic, xenogeneic, and alloplastic bone substitutes. Autogenous, allogeneic and xenogeneic grafts are of natural origin, while alloplastic grafts are synthetic materials.*

**Keywords:** guided tissue regeneration, autograft, allograft, xenograft, alloplastic

## 1. Introduction

Bone graft materials are a tissue, a biomaterial or a combination of the following, placed in a receiving lodge to assist tissue regeneration in order to maintain or restore their volume and quality. Respectively, bone repair materials are used to maintain or restore bone quality and / or volume.

Depending on their origin, there are several groups of bone repair materials: autogenous, allogeneic, xenogeneic, and alloplastic bone substitutes. Autogenous, allogeneic and xenogeneic grafts are of natural origin, while alloplastic grafts are synthetic materials [1]. An autogenous bone substitute is a bone material harvested in a situation where the donor and the recipient beds belong to the same individual. Allogeneic bone substitute is a bone material of genetically different organisms to the same species. Xenogeneic bone substitute is a material of biological origin from a different species. The alloplastic bone substitute is an inorganic synthetic material.

## 2. Aim

The purpose of this study is to describe and review the types of bone repair materials used in periodontology and implantology.

## 3. Materials and Methods

Articles related to the subject were searched in PubMed and Google Scholar databases. Articles in English only, published from 1974 to 2019, were included. The search was performed using a combination of different keywords such as: "guided tissue regeneration", "periodontal regeneration", "autograft", "allograft", "xenograft", "alloplast".

## 4. Results and Discussion

Tissue materials provide one or more of the following phenomena, which contribute to the repair processes in the intraosseous defects: Osteogenesis - bone growth carried out through vital cells transmitted via an autograft - autogenous bone. Osteoinduction - bone formation occurring after the differentiation of mesenchymes into osteoprogenitor cells, under the influence of one or more

inducing factors, originating from the bone matrix. Osteoconduction - Bone growth through adjacent bone apposition [2, 3, 4].

Bone replacement materials must be biocompatible, they must also integrate well with the surrounding bone, have adequate mechanical properties with an ideal degree of substitution, and be predictable with a good level of acceptance from the recipient bed [5, 6, 7].

- Autogenous bone repair materials

Transplants harvested in a situation where the donor and recipient beds belong to the same individual. Autogenous bone is defined as the gold standard for regenerative procedures because it has osteogenic, osteoinductive and osteoconductive properties. There are numerous histological findings from case reports that confirm the potential of autotransplants [2, 8, 9, 10]. However, one of the most significant disadvantages of this type of transplant is the limited amount of tissue that can be taken from the donor site [1, 11]. Other disadvantages are the lack of volumetric stability due to the rapid remodeling of the autograph and the need for a second operating field [2].

Autogenous bone repair materials can be of intraoral or extraoral origin. The intraoral sites from which autogenous bone can be taken from are the area of the mentum [12], linea obliqua mandibulae, tuber maxillae, crista zygomaticoalveolaris and bone exostoses [13, 14]. The extraoral areas from which autogenous bone can be taken from are the area of the calvaria, spina iliaca, crista iliaca and others. [15, 16, 17, 18].

Autogenous bone repair materials can be cortical or spongy. Cortical grafts have very high strength, but about 6 months after transplantation, they are found to be 50% weaker than normal bone tissue [19]. Initially, the spongy graft's strength is less due to their porous structure, but over time they become stronger. Another significant feature is that spongy grafts revascularize earlier (approximately on the 5th day after transplantation) because of their structure [4].

- Allogeneic bone repair materials

Allotransplant is the transplantation of tissues to a recipient from a genetically non-identical donor of the same species. The transplant is called an allograft.) The allogeneic bone restorative materials are of human origin and can be from both living and deceased donor. In 2017 Reynolds et al. summarize that allogeneic bone repair materials are the most commonly used alternative to autogenous bone in the United States. Allogeneic grafts not only have osteoconductive properties, but also have some osteoinductive potential due to the presence of proteins (e.g bone morphogenetic proteins - BMP) [3, 20].

At this point in the literature, there is no evidence of a disease transmission during the 30-year history of the use of freeze-dried allogeneic bone repair materials in periodontal therapy [21]. Allogeneic bone repair materials are processed by a variety of methods. They may be - fresh frozen allograft, lyophilized allograft or demineralized allograft [22].

- ✓ Fresh-frozen bone allografts, FFB

They have the highest osteoconductive and osteoinductive potential, among all allogeneic transplants available for use [23, 24]. However, due to the risk of disease transmission, they are no longer used [3].

- ✓ Freeze-dried bone allografts (FDBA)

They are usually derived from living organisms. After anamnesis, explantation and serological examination (HBV, HCV, HIV, Lues), the process includes mechanical treatment, ultrasonic bath, ethanol / diethyl ether treatment, H<sub>2</sub>O<sub>2</sub> treatment, lyophilization (drying at low temperature and pressure, leaving water in tissue sublimates - goes from solid to gaseous, packaging and gamma-sterilization.

The lyophilization of allogeneic grafts is intended to disrupt the 3D presentation of human leukocyte antigens located on the surface of allogeneic particles and thereby interfere with immune recognition [25, 26].

The FDBA has higher mechanical properties and a certain osteoconductive activity due mainly to the mineral component [2, 3]. It has been found that FDBAs can be combined with autogenous grafts to enhance their osteogenic potential [27, 28].

- ✓ Demineralized freeze-dried bone allografts, DFDBA

DFDBA treatment is identical to FDBA treatment, but allogeneic bone is also subjected to demineralization. DFDBAs are demineralized to a level of about 2% residual calcium, which results in low mechanical strength and a deficiency of osteoconductive potential (FDBA has greater mechanical strength and osteoconductive activity). Demineralization, on the other hand, provides maximum osteoinductive potential, compared to FDBA (due to exposure to bone morphogenetic proteins and growth factors) [2, 3, 29, 30]. When DFDBA is derived from the decrease of younger individuals, it has been found that

there is a higher osteogenic potential [31, 32]. The DFDBA is used alone or in combination with FDBA and auto-grafts. The DFDBA has been found to be rapidly absorbed [33, 34].

- Xenogeneic bone repair materials:

They are a transplant derived from a different species than the species of the recipient. Xenografts have osteoconductive properties and have limited resorption potential [35, 36]. There can be a deproteinized bovine bone material, a coral exoskeleton mineral, and demineralized animal bone matrix (taken from pigs and horses) [3].

- ✓ Deproteinized bovine bone mineral (DBBM)

It is a bone material of bovine origin that has been specially processed to produce a natural bone mineral with no organic elements [37]. After thermal and chemical treatment, the mineral component, which mainly includes hydroxylapatite, retains the structure of the bone remains [38]. Although the treatment of one of the most commercially available Bio-Oss products (Geistlich-Germany) eliminates a large amount of organic matter (nearly 97%), it does not completely eliminate the potential risk of disease transmission and graft rejection [39, 40].

- ✓ Demineralized animal bone matrix (pigs)

Porcine bone graft is a porous inorganic bone graft consisting predominantly of calcium phosphate (Gen-Os®). It has a granular form and is obtained by removing the organic component from porcine bones [41, 42]. The inorganic mineral component has an interconnected macro- and microscopic porous structure [43].

- ✓ Mineral from coral exoskeleton

These materials are manufactured by subjecting the corals to high temperature under pressure in the presence of aqueous phosphate solutions. Thus, corals are converted to calcium hydroxylapatite, preserving their porous structure [44].

These grafts have shown the potential for good filling of periodontal bone defects and are not subjected to fibrous encapsulation [45, 46, 47].

- ✓ Alloplastic materials:

They are biomaterials of artificial or synthetic origin. Alloplasts are biocompatible, inorganic synthetic materials. Alloplastic materials used in regenerative procedures of the periodontium are separated into two main groups - ceramics and polymers. The composition, morphology and surface topography of alloplastic materials determine their osteoconductive potential. They do not have any osteogenic or osteoinductive potential. Alloplastic materials have no risk of disease transmission. The most routinely used alloplastic materials are calcium

phosphate ceramics for periodontal regeneration [42, 48]. They can also be used in implantology. [49]

#### ✓ Biphasic calcium phosphate ceramics

Calcium phosphate ceramics are of great interest in relation to periodontal regenerative therapy as they have a similar mineral bone composition. They are osteoconductive and form a very strong bond between bone and calcium phosphate [5, 6].

#### ✓ Hydroxylapatite (HA)

A biomaterial that has a composition and structure similar to the basic mineral constituent of natural bone - hydroxylapatite [50]. Hydroxylapatite grafts show a slow and limited absorption potential and therefore offer high volumetric stability [51, 52].

#### ✓ Tricalcium phosphate (TCP)

In recent years, this material has been extensively researched as a bone repair material. It has two polymorphic forms  $\alpha$ -TCP and  $\beta$ -TCP [53].  $\alpha$ -TCP is a more soluble and rapidly absorbable form and this is the reason why  $\beta$ -TCP is mainly used as a bone repair material in this group. This form shows good biocompatibility.  $\beta$ -TCP has osteoconductive properties [54]. In terms of bone regenerative potential,  $\beta$ -TCP grafts are similar to autogenous bone, FDBA and DFDBA [55].

#### ✓ Bioactive glasses

They consist of silica, calcium oxide, sodium oxide and phosphorus pentoxide [56]. After implantation of bioactive glass on a bioactive ceramic surface, a silicone gel is formed, with the outer layer serving as a binding surface for osteogenic cells and collagen fibers [57, 58]. It was proven in a 2012 that bioactive glass nanoparticles induce cementoblasts to proliferate in vivo [59].

## 5. Conclusion

The study presented shows that there are many different types of bone repair materials used to accelerate the healing process of periodontal defects. According to the literature, the guided tissue regeneration has shown different long-term results depending on the type of bone repair material. The factors that favor the success of the method are still under discussion. Bone repair materials should be biocompatible, allow new bone formation and bone remodeling to occur, have adequate mechanical properties with an ideal degree of substitution, and be predictable with a good level of acceptance from the recipient bed.

## References

[1] Sheikh Z, Hamdan N, Ikeda Y, Grynypas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review. *Biomater Res.* 2017 Jun 5;21:9. doi: 10.1186/s40824-017-0095-5. eCollection 2017.

- [2] Reynolds MA, Aichelmann-Reidy ME, Branch-Mays GL. Regeneration of periodontal tissue: bone replacement grafts. *Dent Clin North Am.* 2010 Jan;54(1):55-71.
- [3] Sheikh Z, Hamdan N, Ikeda Y, Grynypas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review. *Biomater Res.* 2017 Jun 5;21:9
- [4] Sheikh ZA, A. Javaid, MA. Abdallah, MN. Bone replacement graft materials in dentistry. In: Khurshid Z SZ, editor. *Dental biomaterials (Principle and its Application)*. 2nd ed: Paramount Publishing Enterprise; 2013.
- [5] Sheikh Z, Najeeb S, Khurshid Z, Verma V, Rashid H, Glogauer M. Biodegradable materials for bone repair and tissue engineering applications. *Materials.* 2015;8:5744–94.
- [6] Sheikh Z, Abdallah M-N, Hanafi AA, Misbahuddin S, Rashid H, Glogauer M. Mechanisms of in vivo degradation and resorption of calcium phosphate based biomaterials. *Materials.* 2015;8:7913–25.
- [7] Sheikh Z, Brooks PJ, Barzilay O, Fine N, Glogauer M. Macrophages, foreign body giant cells and their response to implantable biomaterials. *Materials.* 2015;8:5671–701.
- [8] Hiatt WH, Schallhorn RG, Aaronian AJ. The induction of new bone and cementum formation. IV. Microscopic examination of the periodontium following human bone and marrow allograft, autograft and nongraft periodontal regenerative procedures. *J Periodontol* 1978;49:495
- [9] Ross SE, Cohen DW. The fate of a free osseous tissue autograft. A clinical and histologic case report. *Periodontics* 1968;6:145.
- [10] Misch CM. Autogenous bone: is it still the gold standard? *Implant Dent.* 2010;19:361.
- [11] McAllister BS, Haghghat K. Bone augmentation techniques. *J Periodontol.* 2007;78:377–96.
- [12] Peev S, Sabeva E. Bone Block Augmentation – A Long Term Follow-Up. *Scripta Scientifica Medicinæ Dentalis, [S.I.]*, v. 4, n. 2, p. 29-35, feb. 2019. ISSN 2367-7244. doi:http://dx.doi.org/10.14748/ssmd.v4i2.5652
- [13] Draenert FG, Huetzen D, Neff A, Mueller WE. Vertical bone augmentation procedures: basics and techniques in dental implantology. *J Biomed Mater Res A.* 2014;102:1605–13.
- [14] Gellrich NC, Bormann KH, Tehranchian S, Kokemuller H, Suarez-Cunqueiro MM. Containment and contouring (CoCoon) technique: a biologically adequate approach to less invasive autogenous preimplant augmentation of bone. *Br J Oral Maxillofac Surg.* 2013 Dec; 51 (8): 880-6.
- [15] Cypher TJ, Grossman JP. Biological principles of bone graft healing. *J Foot Ankle Surg.* 1996;35:413–7.
- [16] Simion M, Fontana F. Autogenous and xenogeneic bone grafts for the bone regeneration. A literature review. *Minerva Stomatol.* 2004;53:191–206.

- [17] Jackson IT, Helden G, Marx R. Skull bone grafts in maxillofacial and craniofacial surgery. *J Oral Maxillofac Surg.* 1986;44:949–55.
- [18] Nkenke E, Weisbach V, Winckler E, Kessler P, Schultze-Mosgau S, Wiltfang J, et al. Morbidity of harvesting of bone grafts from the iliac crest for preprosthetic augmentation procedures: a prospective study. *Int J Oral Maxillofac Surg.* 2004;33:157–63.
- [19] Wilk R. Bony reconstruction of the jaws. In: M M, editor. *Peterson's principles of oral and maxillofacial surgery.* 2nd ed. Hamilton: B C Decker; 2004. p. 785–7.
- [20] Reddi AH, Wientroub S, Muthukumaran N. Biologic principles of bone induction. *Orthop Clin North Am.* 1987;18:207–12.
- [21] Centers for Disease Control and Prevention: Bone allografts. What is the risk of disease transmission with bone allografts? In: Department of Health and Human Services. Available at: <http://www.cd.gov/OralHealth/Infectioncontrol/faq/allografts.htm>. Accessed September 30, 2009.
- [22] Eppley BL, Pietrzak WS, Blanton MW. Allograft and alloplastic bone substitutes: a review of science and technology for the craniomaxillofacial surgeon. *J Craniofac Surg.* 2005;16:981–9.
- [23] Dias RR, Sehn FP, de Santana Santos T, Silva ER, Chaushu G, Xavier SP. Corticocancellous fresh-frozen allograft bone blocks for augmenting atrophied posterior mandibles in humans. *Clin Oral Implants Res.* 2014;27: 39–46.
- [24] Macedo LG, Mazzucchelli-Cosmo LA, Macedo NL, Monteiro AS, Sendyk WR. Fresh-frozen human bone allograft in vertical ridge augmentation: clinical and tomographic evaluation of bone formation and resorption. *Cell Tissue Bank.* 2012;13:577–86.
- [25] Quattlebaum JB, Mellonig JT, Hensel NF. Antigenicity of freeze-dried cortical bone allograft in human periodontal osseous defects. *J Periodontol.* 1988; 59:394–7.
- [26] Friedlaender GE, Strong DM, Sell KW. Studies on the antigenicity of bone. I. Freeze-dried and deep-frozen bone allografts in rabbits. *J Bone Joint Surg Am.* 1976;58:854–8.
- [27] Committee on Research S. Tissue banking of bone allografts used in periodontal regeneration. *J Periodontol.* 2001;72:834.
- [28] Mellonig JT. Human histologic evaluation of a bovine-derived bone xenograft in the treatment of periodontal osseous defects. *Int J Periodontics Restorative Dent.* 2000;20:19–29.
- [29] Mellonig JT, Bowers GM, Bailey RC. Comparison of bone graft materials. Part I. New bone formation with autografts and allografts determined by Strontium-85. *J Periodontol.* 1981;52:291–6.
- [30] Urist MR. Bone: formation by autoinduction. *Science* 1965;150:893.
- [31] Dodson SA, Bernard GW, Kenney EB, Carranza FA. In vitro comparison of aged and young osteogenic and hemopoietic bone marrow stem cells and their derivative colonies. *J Periodontol.* 1996;67:184–96.
- [32] Jergesen HE, Chua J, Kao RT, Kaban LB. Age effects on bone induction by demineralized bone powder. *Clin Orthop Relat Res.* 1991:253–9.
- [33] Russell J, Scarborough N, Chesmel K. Ability of commercial demineralized freeze-dried bone allograft to induce new bone formation. *J Periodontol.* 1997;68:804–6.
- [34] Hopp SG, Dahners LE, Gilbert JA. A study of the mechanical strength of long bone defects treated with various bone autograft substitutes: an experimental investigation in the rabbit. *J Orthop Res.* 1989;7:579–84.
- [35] McAllister BS, Margolin MD, Cogan AG, Buck D, Hollinger JO, Lynch SE. Eighteen-month radiographic and histologic evaluation of sinus grafting with anorganic bovine bone in the chimpanzee. *Int J Oral Maxillofac Implants.* 1999;14:361–8.
- [36] Thaller SR, Hoyt J, Borjeson K, Dart A, Tesluk H. Reconstruction of calvarial defects with anorganic bovine bone mineral (Bio-Oss) in a rabbit model. *J Craniofac Surg.* 1993;4:79–84.
- [37] Liu X, Li Q, Wang F, Wang Z. Maxillary sinus floor augmentation and dental implant placement using dentin matrix protein-1 gene-modified bone marrow stromal cells mixed with deproteinized bovine bone: a comparative study in beagles. *Arch Oral Biol.* 2016;64:102–8.
- [38] Jarcho M. Calcium phosphate ceramics as hard tissue prosthetics. *Clin Orthop Relat Res.* 1981:259–78.
- [39] Sogal A, Tofe AJ. Risk assessment of bovine spongiform encephalopathy transmission through bone graft material derived from bovine bone used for dental applications. *J Periodontol.* 1999;70:1053–63.
- [40] Wenz B, Oesch B, Horst M. Analysis of the risk of transmitting bovine spongiform encephalopathy through bone grafts derived from bovine bone. *Biomaterials.* 2001;22:1599–606.
- [41] Sabeva, Elitsa. Comparison between the influence of implant diameter and implant length on the primary stability. *Scripta Scientifica Medicinæ Dentalis, [S.I.]*, v4, n. 2, p. 36-41, dec.2018. ISSN 2367-7244. doi:<http://dx.doi.org/10.14748/ssmd.v4i2.5635>.
- [42] Nannmark U, Sennerby L. The bone tissue responses to prehydrated and collagenated cortico-cancellous porcine bone grafts: a study in rabbit maxillary defects. *Clin Implant Dent Relat Res.* 2008;10:264–70.
- [43] Pearce A, Richards R, Milz S, Schneider E, Pearce S. Animal models for implant biomaterial research in bone: a review. *Eur Cell Mater.* 2007;13:1–10.
- [44] Roy DM, Linnehan SK. Hydroxyapatite formed from coral skeletal carbonate by hydrothermal exchange. 1974.
- [45] Piattelli A, Podda G, Scarano A. Clinical and histological results in alveolar ridge enlargement using coralline calcium carbonate. *Biomaterials.* 1997;18:623–7.
- [46] Gao TJ, Tuominen TK, Lindholm TS, Kommonen B, Lindholm TC. Morphological and biomechanical difference in healing in segmental tibial defects implanted with Biocoral or tricalcium phosphate cylinders. *Biomaterials.* 1997;18:219–23.
- [47] Kim CK, Choi EJ, Cho KS, Chai JK, Wikesjo UM. Periodontal repair in intrabony defects treated with a calcium carbonate implant and guided tissue regeneration. *J Periodontol.* 1996;67:1301–6.

- [48] Lee M-J, Kim B-O, Yu S-J. Clinical evaluation of a biphasic calcium phosphate grafting material in the treatment of human periodontal intrabony defects. *J Periodontal Implant Sci.* 2012;42:127–35.
- [49] Peev S., Gusiyska A., Sabeva E., Guided Bone Regeneration and Simultaneous Implant Placement, *International Journal of Science and Research*, 2016, 5(2), 1529-1530
- [50] Wang H, Li Y, Zuo Y, Li J, Ma S, Cheng L. Biocompatibility and osteogenesis of biomimetic nano-hydroxyapatite/polyamide composite scaffolds for bone tissue engineering. *Biomaterials.* 2007;28:3338–48.
- [51] Jarcho M. Calcium phosphate ceramics as hard tissue prosthetics. *Clin Orthop Relat R.* 1981;157:259–78.
- [52] De Groot K. Bioceramics consisting of calcium phosphate salts. *Biomaterials.* 1980;1:47–50.
- [53] Tamimi F, Sheikh Z, Barralet J. Dicalcium phosphate cements: brushite and monetite. *Acta Biomater.* 2012;8:474–87.
- [54] Shetty V, Han TJ. Alloplastic materials in reconstructive periodontal surgery. *Dent Clin N Am.* 1991;35:521–30.
- [55] Nakajima Y, Fiorellini JP, Kim DM, Weber HP, Dent M. Regeneration of standardized mandibular bone defects using expanded polytetrafluoroethylene membrane and various bone fillers. *Int J Periodontics Restorative Dent.* 2007;27:151.
- [56] Shue L, Yufeng Z, Mony U. Biomaterials for periodontal regeneration: a review of ceramics and polymers. *Biomater.* 2012;2:271–7.
- [57] Hall EE, Meffert RM, Hermann JS, Mellonig JT, Cochran DL. Comparison of bioactive glass to demineralized freeze-dried bone allograft in the treatment of intrabony defects around implants in the canine mandible. *J Periodontol.* 1999;70:526–35.
- [58] Xynos ID, Edgar AJ, Buttery LD, Hench LL, Polak JM. Gene-expression profiling of human osteoblasts following treatment with the ionic products of Bioglass® 45S5 dissolution. *J Biomed Mater Res A.* 2001;55:151–7.
- [59] Carvalho SM, Oliveira AA, Jardim CA, Melo C, Gomes DA, Leite M, et al. Characterization and induction of cementoblast cell proliferation by bioactive glass nanoparticles. *J Tissue Eng Regen Med.* 2012;6:813–21.