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Review Article

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Bone Allografts: Products and Clinical Applications in Iran

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Abstract

Bone allografts have become an accepted technology to replace bone loss due to common diseases, such as tumor resection, trauma, and failed total joint arthroplasty. This study briefly reviews a branch of regenerative medicine related to bone allografts and its related aspects. As new allografts stimulate an immune rejection response, bone grafts are usually prepared by freezing or freeze-drying to decrease the immune system responses. The notable biological events of associations, such as hemorrhage and inflammation, osteogenesis, osteoinduction, osteoconduction, and impressive remodeling, result in a load-bearing structure. Generally, cancellous allografts are effectively incorporated, while cortical grafts remain an admixture of viable regenerated bone and old necrotic bone for a prolonged duration. Massive bone allografts used in reconstructing tumor resection have a long-term successful outcome in about 80 percent of the procedures. Similar success has been reported for its use in total joint revision surgery and other clinical applications. The significant complications reported for grafting procedures are infection, bone graft fracture, nonunion at the graft-host juncture, and rare massive allograft resorption. Although bone allografting is a successful therapeutic approach, emerging technologies will introduce more efficient bones by mobilizing the adjunctive growth factors, cell and gene-based therapies, and tissue engineering techniques. The primary and applicable knowledge of bone allografts is essential; however, continual investigations are necessary.

***Keywords*:** Bone Allografts, Bone Regeneration, Regenerative Medicine, Orthopedic Surgery, Dentistry

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Introduction

Regenerative medicine is the branch of modern medicine that reveals approaches to regenerate, repair, or replace damaged or diseased cells, organs, or tissues of the body. This field presents novel gene, cell, and tissue-based therapeutics to treat different diseases, especially tissues and organs such as bone, skin, eye, etc. (1–3). Given that suitable cell sources, biological factors, and biomaterials create the main regenerative medicine tools(4–6), allografts as natural materials play an essential role in related branches of this field. A bone graft is a surgical approach to repair or reassemble bones by transplantation of bone extracellular compounds. Bone grafts have been used to treat bone defects, slowed union or nonunion, and complex bone fracture fusion in orthopedic clinically for some time, notwithstanding the

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emergence of different biomaterials and artificial bone graft substitutes. Indeed, bone grafts play a scaffolding role for migration, homing, differentiation, and proliferation of neighboring cells of the target tissue. Different cells begin to adhesion to the target injured zone after migration to the target injured zone based on nich condition. Stem cells and producer cells are the primary migrated cells to the grafted bone. Hence, the mixture of bone graft is vital for developing new bone tissue's healing and regeneration process. Generally, bone grafts include autografts (a graft of tissue from one locality to another of the same individual's body) and allografts (a graft of tissue from one person to another). Autograft bone is the gold standard bone grafting procedure; however, allograft bones have been recommended due to equipment limitations and the invasivity of autograft bone harvesting. Since the autogenous bone graft might cause complications related to harvesting and its restriction regarding graft amount from the patient, the allograft has been used as an alternative. The benefit of bone allograft includes no donor-site morbidity, unlimited use of material, and the availability in mechanical support with various shapes and sizes. The freeze-drying process and vacuum-packing often preserve the bone allograft. However, the matter that the mechanical property of bone allograft decrease and living osteogenic cells are removed in sterilization and storage outweighs the allograft. (7). Following allograft incorporation, the bone union rate might be low because the allograft has no osteogenesis and weak osteoinductivity and the process of sterilization and storage affects osteoconductivity and osteoinductivity (8). Allogeneic bone is accessible in many preparations, including morselized and cancellous, cortico-cancellous, cortical graft, osteochondral, hole bone segment, and demineralized bone matrix. In most clinical cases, allogenic cancellous bone repairs the partial bone defect rather than a segmental bone defect or whole bone defect because the allo-cancellous bone has no mechanical stability (9). Recently, different allograft bone types are prepared and employed in the clinical application (Figure1). This study briefly reviews a branch of regenerative medicine related to bone allografts and its related aspects.

Fig 1: Summary of different types of bone allografts in clinical application

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Brief view to the biology of bone regeneration:

Consolidation of grafts into the host bone tissue occurs through the mediation of three biological phenomena: osteogenesis, osteoinduction, and osteoconduction(10). Osteogenesis is taken to be the potential of live cells (especially osteoblasts and precursor cells) to support the generation of osteoid substances, which may only occur with autologous grafts(11). Osteoinduction is the differentiation of multipotent cells in the host tissues into osteoblasts through a series of physiological pathways in which a cascade of growth factors plays a crucial role(12). However, osteoconduction is the process in which the canaliculi of the transplanted bone act as a guide for the growth of osteoblast bridges of new bone tissue coming from the host. A large number of homologous grafts and bone substitutes are exclusively osteoconductive(13).

Tissue harvesting:

The harvesting teams need to be appropriately registered with the transplantation centers to have legal backing and receive notifications regarding donors, not only in their hospitals but also in other institutions, often outside of their city or state. There are two types of the donor of homologous tissues: live donors, consisting mainly of donations of femoral heads after total hip arthroplasty procedures, which have the advantage that the donor patients can be called back for new tests in suspected cases; and cadaver donors, from which much more significant quantities of tissues can be harvested, from practically any segment of the skeleton, as well as generally being young donors with better quality bone tissue than seen in live donors.

Storage:

The tissues are generally kept in freezers at a temperature of 85 ℃ below zero. The freezers have a temperature control displayer connected to the hospital's generator as a precaution against possible power cuts. They also have an alarm and a supply of liquid CO_2 for additional security. Under ideal conditions and at a constant temperature, the tissues can be stored for five years, according to the norms of Anvisa (Brazilian National Sanitary Surveillance Agency) and AATB (American Association of Tissue Banks).

Allografts and their types:

Tissue transplanted between genetically non-identical members of the same species (either from living or cadaverine donor) is called allograft. It replaces the old term Homograft. Depending on the site of its placement in the recipient, allograft may be divided into: a) Orthopedic, b) Heterotopic, c) Ectopic.

a) Orthopedic: Transplanted into the same site in the recipient that it occupied in the donor, e.g., Proximal femur to the proximal donor.

b) Heterotopic: Transplanted to a different site but occupied by the same tissue as in the donor, e.g., Fibula to spine.

c) Ectopic: Transplanted to a site generally occupied by a different type of tissue. e.g., Fascia lata as a tendon graft.

Commonly orthopedic/heterotopic allografts have been wildly used. Ectopic sites for grafting have been used mainly for investigation.

Classification of Allografts:

Allografts can be classified based on the graft anatomy, processing methods, sterilization, and handling properties.

A) Graft anatomy: Cortical, Cancellous, Osteochondral, and Soft tissue allografts.
B) Graft processing: Fresh frozen, Freeze-dried, and Demineralized bone matrix.
C) Graft sterilization: Sterile processed, Irradiated, Ethylene oxide.
D) Handling properties: Powder, Particulate, Gel, Putty, Chips, Stripe, and Blocks, Massive.

Massive allograft means extensive intercalary grafts, big allograft with the joints. This is mainly useful in the reconstruction of the tumor defects and massive traumatic loss of bone. All other types like powder and particulate forms are mainly used in osteosynthesis sites and autografts for better results.

The classification of bone allograft products is divided into two major categories based on clinical application: orthopedic and dentistry.

Orthopedic and spine products:

Frozen Bone Allograft: It is used in orthopedics to replace the central part of a bone prone to bone

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amputation for reasons such as bone cancer or severe bone tissue damage, spinal fusions, repairing maxillar atrophy, and reconstructive surgery.

Mineralized Fibula, Tibia & Femur Shaft Bone: It is used for renewal or filling bone defects in orthopedic and reconstructive surgery (specifically for diaphyseal long bones).

MBA Matchstick: Mineralized bone allograft (MBA) matchstick is processed from cancellous or cortical – cancellous bone. Mineralized bone matrices provide a biocompatible osteoconductive matrix that supports new bone formation. This product is non-hemolytic and is compatible with surrounding blood cells. It is pH balanced (identical pH to human blood, 7.2) and is suitable for stem cell and preosteoblast seeding. Clinical application of Matchstick is spinal fusion, oral and maxillofacial reconstruction, and general orthopedic reconstruction.

MBA Cube: This product is cancellous bone. Its high concentrations of osteoblasts and osteocytes give it superior osteogenic potential. Additionally, its sizeable trabecular surface area encourages revascularization and incorporation at the recipient site. It is used for bone augmentation in orthopedics, spinal, maxillofacial, neurosurgery, plastic, and reconstructive surgery(14).

Allograft Bone Wedges: Bone wedges are involved in three types of anatomical regions of bones, including patellar, tibial, and iliac crest wedges. For instance, the tricortical iliac crest wedge has been designed to provide urgent structural support and restore segmental bone loss. Clinical applications of these wedges are cervical fusion, discectomy, high tibial osteotomies, osteotomies foot and ankle osteotomies, fracture management, glenoid reconstruction, and corpectomy.

MBA Chips and Crushed: Chips and Crushed allografts are processed from cancellous or cortical–cancellous bone. Mineralized bone matrices provide a biocompatible osteoconductive matrix that supports new bone formation. It is used for renewal or filling bone defects in dentistry and periodontology (socket preservation), spinal fusions (repairing discectomies, arthrodesis, etc.), oral and maxillofacial surgery (sinus elevation and jaw abnormalities fixation), and reconstructive surgery. The particle size of chips and crushed, respectively, is 1-3 mm and 3-8 mm.

Dentistry and Maxillofacial products:

MBA Granule: mineralized freeze-dried bone granule allograft is processed from the cortical-cancellous bone. The particle size of MBA granules is 1000-2000 µm. Mineralized bone matrices provide a biocompatible osteoconductive matrix that supports new bone formation. It is used for bone augmentation in orthopedics, periodontics, oral and maxillofacial surgeries, neurosurgery, ENT, plastic and reconstructive surgeries.

MBA Powders: It is used for reconstruction or filling bone defects in dentistry, periodontology, oral and maxillofacial surgery, reconstructive surgery. The particle size of MBA powders is 150-1000 µm.

DBM Powder: Demineralized Bone Matrix (DBM) was first extracted from the human body in 1975(15). It was presented in orthopedics in 1980. DBM is made by a standardized process initially described by Urist et al. (16,17). In which allobone® is pulverized to a minute particle size (74 to 420 µm) followed by demineralization in 0.5 N HCL mEq/g for 3 hours. The remaining acid is removed by rinsing in sterile water, ethanol, and ethyl ether. Through this process, type I collagen in cortical bone matrix and non-collagen proteins, including bone-inducing growth factors, such as Bone Morphogenetic Proteins (BMP), Transforming Growth Factor (TGF), Insulin Growth Factor (IGF), and Fibroblast Growth Factor (FGF), remain, but there is lack of mechanical support.

Nevertheless, thanks to the extraction of these growth factors, DBM mainly acts as an osteoinductive material and possibly as an osteoinductive material compared with an available allograft, such as cancellous or cortical graft. Although bone minerals are eliminated from allogenic bone, DBM can provide a 3-dimensional scaffold because the fibrous collagen structure of original tissues remains. Since DBM is quickly diluted and does not provide a mechanical packing effect for a bone defect lesion, its single-use is limited. DBM is manufactured with various transmitters, including glycerol, hyaluronic acid, and calcium sulfate(18). DBM

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also has a potential risk of transmitted viral infection because it is an allogenic material(19).

MBA & DBM Powder: Powder mixed of Mineralized and Demineralized Freeze-Dried Bone allograft is processed from the cortical-cancellous bone. This Mineralized/Demineralized blend combines 65% of MBA and 35% of DBM particles. Mineralized bone matrices provide a biocompatible osteoconductive matrix, and demineralized bone matrices provide an osteoinductive effect that supports new bone formation.

Conclusion

The primary purposes of this mini-review are to address the ordinary administration of bone allografts in clinical application. Bone allografts and their derived therapeutic materials are essential for regenerative medicine and tissue engineering remodeling and regeneration approaches. These grafts and their derivations provide an osteoconductive scaffold for new bone formation similar to the natural framework in the physiological condition. Bone allografts harvested from cadavers are manipulated based on target application with the different processes like ethylene oxide treatment, or γ-radiation, and freeze-drying. Orthopedics and dentistry are the eminent medical branches in which bone allografts are continuously used. Although utilization of bone allografts is continually arranged in clinical application, it faces some limitations, such as the risk of disease transmission and insufficient sources**.** The clinical outcomes had been beneficial in improving support storing the clinical application with a suitable grafting material with all components of bone formation. Looking to the future, allografts should serve a valuable role still as intact structures, partially deconstructed, or repaired grafts. However, progress will frequently drive tissue as regenerated or biologically integrative products using protein isolation and reconstitution methods, genetic modifications, in situ cell seeding, and other advances. However, investigations are going to develop combined advanced grafts.

Disclosure

The authors declare that they have no conflicts of interest.

Conflict of interest

The authors have no conflict of interest in this study.

References

1. Golchin A, Shams F, Kangari P, Azari A, Hosseinzadeh S. Regenerative Medicine: Injectable Cell-Based Therapeutics and Approved Products. Adv Exp Med Biol 2020;1237:75-95.
2. Golchin A, Chatziparasidou A, Ranjbarvan P, Niknam Z, Ardeshirylajimi A. Embryonic Stem Cells in Clinical Trials: Current Overview of Developments and Challenges.. Adv Exp Med Biol 2020:1–19.
3. Hashemi S, Amirabad LM, Nazhvani FD, Zarrintaj P, Namazi H, Saadatfar A, et al. Bilayer Scaffolds for Interface Tissue Engineering and Regenerative Medicine: A Systematic Reviews. Adv Exp Med Biol 2021.
4. Ardeshirylajimi A, Golchin A, Khojasteh A, Bandehpour M. Increased osteogenic differentiation potential of MSCs cultured on nanofibrous structure through activation of Wnt/β-catenin signalling by inorganic polyphosphate. Artif Cells Nanomed Biotechnol 2018;46(sup3):S943-S949.
5. Golchin A, Shams F, Karami F. Advancing Mesenchymal Stem Cell Therapy with CRISPR/Cas9 for Clinical Trial Studies. Adv Exp Med Biol 2020;1247:89-100.
7. Manyalich M, Navarro A, Koller J, Loty B, de Guerra A, Cornu O, et al. European quality system for tissue banking. Transplant Proc 2009;41(6):2035-43.
8. An HS, Simpson JM, Glover JM, Stephany J. Comparison between allograft plus demineralized bone matrix versus autograft in anterior cervical fusion. A prospective multicenter study. Spine (Phila Pa 1976) 1995;20(20):2211-6.
9. Enneking WF, Campanacci DA. Retrieved human allografts : a clinicopathological study. J Bone Joint Surg Am 2001;83(7):971-86.
10. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. Eur Spine J 2001;

[DOI: 10.52547/rabms.7.2.94]

Suppl 2(Suppl 2):S96-101.

11. Niknam Z, Golchin A, Rezaei–Tavirani M, Ranjbarvan P, Zali H, Omidi M, et al. Osteogenic Differentiation Potential of Adipose-Derived Mesenchymal Stem Cells Cultured on Magnesium Oxide/Polycaprolactone Nanofibrous Scaffolds for Improving Bone Tissue Reconstruction. Adv Pharm Bull 2020:.
12. Golchin A, Farzaneh S, Porjabbar B, Sadegian F, Estaji M, Ranjbarvan P, et al. Regenerative Medicine Under the Control of 3D Scaffolds: Current State and Progress of Tissue Scaffolds. Curr Stem Cell Res Ther 2020 ;16(2):209–29.
13. Bauer TW, Muschler GF. Bone graft materials. An overview of the basic science. Clin Orthop Relat Res 2000;(371):10-27.
14. Gross TP, Jinnah RH, Clarke HJ, Cox QG. The biology of bone grafting. Orthopedics 1991;14(5):563-8.
15. Urist MR, Mikulski A, Boyd SD. A chemosterilized antigen-extracted autodigested alloimplant for bone banks. Arch Surg 1975;110(4):416-28.
16. Urist MR, Dawson E. Intertransverse process fusion with the aid of chemosterilized autolyzed antigen-extracted allogeneic (AAA) bone. Clin Orthop Relat Res 1981 ;(154):97-113.
17. Urist MR, Silverman BF, Büring K, Dubuc FL, Rosenberg JM. The bone induction principle. Clin Orthop Relat Res 1967;53:243–83.
18. Lane JM. Bone morphogenic protein science and studies. J Orthop Trauma 2005;19(10 Suppl):S17-22.
19. Sohn HS, Oh JK. Review of bone graft and bone substitutes with an emphasis on fracture surgeries. Biomater Res 2019;23:9.

[DOI: 10.52547/rabms.7.2.94]