MEDICINE AND MATERIALS

Volume 4, Issue 4, 2024: 163-168 | ISSN: 2784 – 1499 & e-ISSN: 2784 – 1537
DOI: 10.36868/MEDMATER.2024.04.04.163 | www.medicineandmaterials.com |

PROCESSED XENOGRAFTS, TOP BIOMATERIALS FOR BONE TISSUE RECONSTRUCTION

Vlad DĂNILĂ [1], Carina BALCOȘ [1,*], Adina ARMENCIA [1], Dana BACIU [1]

[1] Faculty of Dental Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi

Abstract

Xenografts, derived from animal tissues, have emerged as a valuable solution in bone tissue reconstruction due to their osteoconductive properties and wide clinical applicability. These biomaterials are extensively used in dentistry, maxillofacial surgery, and orthopedics, addressing challenges such as bone defects caused by trauma, tumors, or degenerative diseases. The processing of xenografts involves antigen removal and sterilization, ensuring biocompatibility and reducing the risk of immunological reactions. Their availability and adaptability in various forms, such as granules, blocks, and pastes, make them suitable for a range of defect sizes and locations. The advantages of xenografts include cost-effectiveness, elimination of the need for a second surgical site, and compatibility with other biomaterials, allowing for hybrid applications in complex cases. Despite their benefits, limitations exist, such as slower integration rates and potential biomechanical fragility. However, advancements in tissue engineering and the combination of xenografts with growth factors and synthetic materials hold promise for improving their clinical outcomes. This review explores the biological characteristics, clinical applications, advantages, limitations, and future perspectives of processed xenografts, emphasizing their potential to revolutionize bone tissue reconstruction and expand treatment possibilities.

Keywords: xenografts, bone reconstruction, osteoconductivity, biomaterials, tissue engineering, biocompatibility, clinical applications

Introduction

Bone reconstruction represents a significant challenge in modern medicine, being essential in the treatment of conditions such as congenital bone defects, severe trauma, infections or degenerative diseases. In these cases, the regeneration of lost bone tissue requires the use of materials that provide structural support and facilitate the healing process. The biomaterials used for these purposes range from synthetic materials to natural grafts, each with specific advantages and limitations [1,2].

Xenografts are materials derived from animal tissues used for medical purposes, including bone reconstruction. They undergo complex processing processes that remove cells and antigens to reduce the risk of immunological rejection. By preserving the mineral structure and collagen, xenografts provide a favorable osteoconductive environment for bone regeneration [2,3].

The use of xenografts has gained popularity due to their high availability, lower costs compared to autografts, and the elimination of the need for additional surgery for harvesting. These materials offer a promising alternative for treatments that require extensive bone reconstruction. However, their processing requires rigorous standards to ensure safety and efficiency, which underlines the importance of continuous research and development in this area [1-4].

Corresponding author: carina.balcos@umfiasi.com

This review aims to analyze the use of processed xenografts in bone reconstruction, focusing on processing methods, clinical applications, and their advantages and limitations. The future prospects and potential for integration of xenografts with other types of biomaterials are also discussed. This synthesis provides a comprehensive look at the role and importance of xenografts in contemporary medical practice [2-4].

Features of xenografts

Xenografts are biomaterials derived from bone tissues of animal origin, widely used in bone reconstruction. They are valued for their properties similar to human bone and for their ability to support the bone regeneration process, undergoing complex processing methods to ensure their biocompatibility and safety in clinical use [2-5].

The origin of these materials is diverse, the most common sources being cattle and pigs, due to their wide availability and structural characteristics compatible with human bone tissue. The bone tissue of these animals exhibits a mineral composition and a three-dimensional architecture that can be used effectively to provide structural support and osteoconductivity, both of which are essential for integration into the host bone [2-6].

The processing of xenografts is a critical aspect, as the raw tissues are not usable in their natural form. The first stage of processing consists of removing antigens and living cells from the tissue, thus reducing the risk of immunological rejection and minimizing inflammatory reactions. This stage involves the use of enzymes, chemical solutions, and sometimes heat treatment to completely remove the organic material. After removing the antigenic components, the tissues undergo a sterilization process to destroy any pathogenic microorganisms. Sterilization can be achieved by various methods, including gamma radiation, heat treatment, or the use of chemicals, each method having its advantages and limitations [3-7].

The structural and biological characteristics of xenografts make them ideal for use in regenerative medicine. Due to their mineral composition similar to that of human bone, they are able to quickly integrate with host bone tissue, supporting the formation of a strong and durable bond. In addition, preserved collagen contributes to cell adhesion and supports osteoblastic activity, which accelerates the regeneration process [5-8].

Another major advantage of xenografts is their adaptability. They are available in a wide range of shapes, including granules, blocks, or pastes, allowing for customization according to the size and shape of the bone defect that needs to be reconstructed. Their versatility makes them suitable for a variety of clinical applications, from bone augmentation in implantology to the restoration of complex bone defects in orthopedic or maxillofacial surgery [5-9].

Clinical indications for the use of xenografts

Processed xenografts play an important role in various medical fields, being successfully used for bone reconstruction in complex cases. These biomaterials are valued for their osteoconductive properties and biocompatibility, and their adaptability makes them ideal for a wide range of clinical applications [7-10].

Xenografts are most commonly used in procedures that require bone tissue restoration or augmentation. In oral and maxillofacial surgery, they are used for alveolar ridge augmentation, post-extraction bone defect repair, treatment of periapical defects, and restoration of bone defects caused by cysts or tumors. In implantology, xenografts are essential for bone augmentation prior to dental implant insertion, providing adequate support for their long-term stability [8-11].

In orthopedics, xenografts are used to treat bone defects caused by trauma, tumor resections, or degenerative diseases. They are also used in spinal fusion surgeries, where they create a solid support for the vertebrae to join, supporting the healing process and reducing pain

associated with abnormal mobility. In the case of large bone defects requiring extensive reconstruction, xenografts can be combined with other biomaterials, such as autogenous bone matrix or synthetic materials, to enhance clinical outcomes [8-12].

Clinical studies demonstrate that xenografts are able to effectively integrate into the host bone tissue, supporting the regeneration process. Biological integration depends on factors such as particle size, porous structure, and the degree of purification of the material. Most processed xenografts exhibit a porous structure that allows osteogenic cells to migrate and proliferate, promoting the formation of new bone (Figure 1) [9-12].

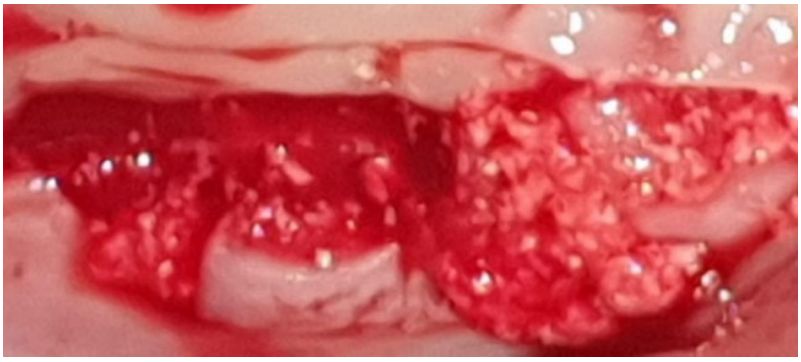

Fig. 1. Positioning of the xenograft on the resorbed bone area.

For example, in maxillary sinus augmentation, the use of bovine xenografts has shown positive clinical results, with the formation of a sufficient amount of bone for the insertion of dental implants. In vertical and lateral alveolar ridge augmentation procedures, xenografts have proven effective in restoring lost bone volume, providing a solid foundation for implants and other prosthetic restorations [9-12].

Compared to autografts, xenografts have the advantage of eliminating the need for additional surgery to harvest the bone, thus reducing patient discomfort and associated risks. They are also more accessible than allografts and easier to store and transport. Compared to synthetic biomaterials, xenografts offer a biological advantage due to their natural composition, which mimics the structure of human bone and better supports integration into the host tissue [10-13].

Although they are versatile and effective, xenografts may have limitations in certain clinical settings. In very large bone defects or in conditions of compromised healing, integration may be slower. Also, some cases may require combinations with other materials to achieve optimal results. Despite these limitations, xenografts remain a valuable option due to their multiple benefits and versatility in use [10-14].

The clinical applicability of xenografts is vast, and their success in dental, maxillofacial and orthopedic procedures demonstrates their potential to become a standard in bone reconstruction. Their adaptability, availability, and efficiency make them an indispensable tool for clinicians, providing viable solutions for a wide range of medical conditions and needs [11-15].

Advantages of xenografts

Xenografts offer numerous benefits that make them a valuable choice in bone reconstruction. These advantages are evident in various clinical fields, due to their biological characteristics, high availability and ease of use (Table 1) [10-18].

Table 1. Advantages of xenografts [10-18].

Category	Description	Clinical examples/applications	Impact
Availability and accessibility	Xenografts are sourced from widely available animal tissues, such as bovine and porcine, without requiring harvesting from the patient's body.	Bone augmentation in dental implantology. Spinal fusion in orthopedics.	Reduced costs, shorter preparation time for surgery, suitable for patients with limited resources.
Avoidance of a second surgical procedure	Does not involve harvesting bone from the donor site of the patient, eliminating the risks of post-operative complications.	Bone reconstruction after tumor resections. Sinus augmentation for implant placement.	Reduction of pain and infection risk, beneficial for elderly patients or those with multiple comorbidities.
Favorable biological properties	Mineral composition (hydroxyapatite) similar to human bone ensures osteoconductivity and biocompatibility. Porous structure facilitates vascularization.	Augmentation of large or small bone defects. Repair of post-traumatic bone defects.	Rapid integration with host tissue, acceleration of new bone formation, long-term stability for implants.
Safety and advanced processing	Antigen removal and rigorous sterilization reduce the risk of immunological rejection and infectious complications.	Dental and orthopedic procedures where biocompatibility is crucial.	Increased confidence in clinical use of the material, with a low rate of complications.
Flexibility in use	Available in various forms: granules, blocks, and pastes. Can be adapted to different sizes and locations of bone defects.	Bone reconstruction in maxillofacial and orthopedic surgery.	Allows personalized treatments, improving clinical outcomes based on specific patient needs.
Lower costs compared to other options	More affordable than autografts or allografts, as they do not require additional procedures and the sources are easily available.	Treatment of bone defects in patients from diverse economic backgrounds.	Improved accessibility to treatments, especially in regions with limited resources or for patients with low budgets.
Compatibility with other biomaterials	Can be combined with synthetic materials, allografts, or autografts to enhance osteoconductive and osteoinductive properties.	Complex reconstructions requiring hybrid materials for stability and extensive bone regeneration.	Enhanced efficiency and adaptability in complex treatments, expanding clinical indications.

Xenografts offer multiple advantages that make them an attractive option in bone reconstruction. Availability, favorable biological properties, safety and low costs are just some of the reasons why these biomaterials are increasingly used in clinical practice. By eliminating some limitations associated with other types of grafts, xenografts contribute to improving clinical outcomes and increasing patients' quality of life [18-23].

Conclusions

Xenografts are a valuable solution in bone reconstruction, due to their availability, favorable biological properties and adaptability in various clinical applications. These biomaterials provide excellent osteoconductive support and integrate effectively with host bone tissue, supporting bone regeneration in complex procedures such as bone augmentation in

implantology or reconstruction after tumor resections. In addition, by eliminating the need for a second surgery, xenografts reduce patient discomfort and associated risks.

However, their limitations, including the residual risk of immune reactions, mechanical fragility in some cases, and slower pace of integration, underscore the need for continuous improvement.

Emerging technologies, such as tissue engineering, and combinations with synthetic materials and growth factors offer significant opportunities for optimizing these biomaterials.

Xenografts play a critical role in regenerative medicine, and recent advances and future research will help expand clinical indications and maximize their effectiveness. By balancing the benefits and limitations, these biomaterials can become a standard in bone reconstruction, improving patients' quality of life and long-term outcomes.

Bibliography

1. Schlickewei C.W., Kleinertz H., Thiesen D.M., Mader K., Priemel M., Frosch K.H., Keller J. *Current and Future Concepts for the Treatment of Impaired Fracture Healing*. **Int. J. Mol. Sci.** 2019. 20, 5805. doi: 10.3390/ijms20225805.
2. Tang D., Tare R.S., Yang L.Y., Williams D.F., Ou K.L., Oreffo R.O. *Biofabrication of bone tissue: Approaches, challenges and translation for bone regeneration*. **Biomaterials**. 2016. 83, 363–382. doi: 10.1016/j.biomaterials.2016.01.024.
3. Barbeck M., Udeabor S., Lorenz J., Schlee M., Holthaus M.G., Raetscho N., Choukroun J., Sader R., Kirkpatrick C.J., Ghanaati S. *High-Temperature Sintering of Xenogeneic Bone Substitutes Leads to Increased Multinucleated Giant Cell Formation: In Vivo and Preliminary Clinical Results.* **J. Oral Implantol**. 2015. 41, e212–e222. doi: 10.1563/aaid-joi-D-14-00168.
4. Mardas N., Chadha V., Donos N. *Alveolar ridge preservation with guided bone regeneration and a synthetic bone substitute or a bovine-derived xenograft: A randomized, controlled clinical trial.* **Clin. Oral Implants Res**. 2010. 21, 688–698. doi: 10.1111/j.1600-0501.2010.01918.x.
5. Bracey D.N., Cignetti N.E., Jinnah A.H., Stone A.V., Gyr B.M., Whitlock P.W., Scott A.T. *Bone xenotransplantation: A review of the history, orthopedic clinical literature, and a single-center case series*. **Xenotransplantation**. 2020. 27, e12600. doi: 10.1111/xen.12600.
6. Lai V.J., Michalek J.E., Liu Q.Q., Mealey B.L. *Ridge preservation following tooth extraction using bovine xenograft compared with porcine xenograft: A randomized controlled clinical trial***. J. Periodontol**. 2020. 91, 361–368. doi: 10.1002/JPER.19-0211.
7. Dos Santos F.R., Minto B.W., da Silva S.W.G., Coelho L.D., Rossignoli P.P., Costa J.S., Taba M., Dias L.G.G.G. *Caprine demineralized bone matrix (DBMc) in the repair of non-critical bone defects in rabbit tibias. A new bone xenograft*. **Acta Cir. Bras**. 2020. 35, e202000801. doi: 10.1590/s0102-865020200080000001.
8. Gashtasbi F., Hasannia S., Hasannia S., Mahdi Dehghan M., Sarkarat F., Shali A. *Comparative study of impact of animal source on physical, structural, and biological properties of bone xenograft.* **Xenotransplantation**. 2020. 27, e12628. doi: 10.1111/xen.12628.
9. Tawil G., Barbeck M., Unger R., Tawil P., Witte F. *Sinus Floor Elevation Using the Lateral Approach and Window Repositioning and a Xenogeneic Bone Substitute as a Grafting Material: A Histologic, Histomorphometric, and Radiographic Analysis*. **Int. J. Oral Maxillofac. Implant.** 2018. 33, 1089–1096. doi: 10.11607/jomi.6226.
10. Cook D.C., Mealey B.L. *Histologic comparison of healing following tooth extraction with ridge preservation using two different xenograft protocols*. **J. Periodontol**. 2013. 84, 585–594. doi: 10.1902/jop.2012.120219.
11. Tovar N., Jimbo R., Gangolli R., Perez L., Manne L., Yoo D., Lorenzoni F., Witek L., Coelho P.G. *Evaluation of bone response to various anorganic bovine bone xenografts:*

*An experimental calvaria defect study***. Int. J. Oral Maxillofac. Surg**. 2014. 43, 251–260. doi: 10.1016/j.ijom.2013.07.005.
12. Djordjevic F., Mihailovic B., Mladenovic R., Dubovina D., Kostic M., Stanisic J., Vlahovic Z. *CBCT analysis of bone density in bicortical defects after augmentation with alloplastic and xenogeneic bone substitutes—A study on domestic pigs*. **Vojnosanit. Pregl.** 2021. 78, 1200–1206. doi: 10.2298/VSP190731040D.
13. Mendoza-Azpur G., de la Fuente A., Chavez E., Valdivia E., Khouly I. *Horizontal ridge augmentation with guided bone regeneration using particulate xenogenic bone substitutes with or without autogenous block grafts: A randomized controlled trial*. **Clin. Implant. Dent. Relat. Res**. 2019. 21, 521–530. doi: 10.1111/cid.12740.
14. Alayan J., Ivanovski S. *A prospective controlled trial comparing xenograft/autogenous bone and collagen-stabilized xenograft for maxillary sinus augmentation-Complications, patient-reported outcomes and volumetric analysis*. **Clin. Oral Implant. Res**. 2018. 29, 248–262. doi: 10.1111/clr.13107.
15. Peric Kacarevic Z., Kavehei F., Houshmand A., Franke J., Smeets R., Rimashevskiy D., Wenisch S., Schnettler R., Jung O., Barbeck M. *Purification processes of xenogeneic bone substitutes and their impact on tissue reactions and regeneration*. **Int. J. Artif. Organs**. 2018. 41, 789–800. doi: 10.1177/0391398818771530.
16. Pan Q.X., Gao C.Y., Wang Y.Y., Wang Y.L., Mao C., Wang Q., Economidou S.N., Douroumis D., Wen F., Tan L.P., et al. *Investigation of bone reconstruction using an attenuated immunogenicity xenogenic composite scaffold fabricated by 3D printing*. **Bio-Des. Manuf.** 2020. 3, 396–409. doi: 10.1007/s42242-020-00086-4.
17. Bracey D.N., Seyler T.M., Jinnah A.H., Smith T.L., Ornelles D.A., Deora R., Parks G.D., van Dyke M.E., Whitlock P.W. *A porcine xenograft-derived bone scaffold is a biocompatible bone graft substitute: An assessment of cytocompatibility and the alpha-Gal epitope.* **Xenotransplantation**. 2019. 26, e12534. doi: 10.1111/xen.12534.
18. Bracey D.N., Seyler T.M., Jinnah A.H., Lively M.O., Willey J.S., Smith T.L., van Dyke M.E., Whitlock P.W. *A Decellularized Porcine Xenograft-Derived Bone Scaffold for Clinical Use as a Bone Graft Substitute: A Critical Evaluation of Processing and Structure.* **J. Funct. Biomater.** 2018. 9, 45. doi: 10.3390/jfb9030045.
19. Chen Y.W., Chen M.Y., Hsieh D.J., Periasamy S., Yen K.C., Chuang C.T., Wang H.C., Tseng F.W., Kuo J.C., Chien H.H. *Evaluating the bone-regenerative role of the decellularized porcine bone xenograft in a canine extraction socket model***. Clin. Exp. Dent.** Res. 2021. 7, 409–418. doi: 10.1002/cre2.361.
20. Martinez E.F., Oliveira R.D.E., Aloise A.C., Ferreira L.M. *Adipose Mesenchymal Stem Cells Associated with Xenograft in a Guided Bone Regeneration Model: A Histomorphometric Study in Rabbit Calvaria.* **Int. J. Oral Max Impl**. 2015. 30, 1415–1422. doi: 10.11607/jomi.4164.
21. Bienz S.P., Payer M., Hjerppe J., Husler J., Jakse N., Schmidlin P.R., Hammerle C.H.F., Jung R.E., Thoma D.S. *Primary bone augmentation leads to equally stable marginal tissue conditions comparing the use of xenograft blocks infused with BMP-2 and autogenous bone blocks: A 3D analysis after 3 years*. **Clin. Oral Implant. Res**. 2021. 32, 1433–1443. doi: 10.1111/clr.13843.
22. Lim H.C., Paeng K.W., Jung U.W., Benic G.I. *Effectiveness of xenogeneic and synthetic bone-block substitute materials with/without recombinant human bone morphogenetic protein-2: A preclinical study using a rabbit calvarium model***. J. Clin. Periodontol**. 2021. 48, 1126–1136. doi: 10.1111/jcpe.13480.
23. Yashwant V.A., Balu P., Kumar R.S., Ammayappan P., Murugaboopathy V. *Effectiveness of platelet rich fibrin versus demineralized bone xenograft in periodontally accelerated osteogenic orthodontics*. **Angle Orthod.** 2022. 92, 180-188. doi: 10.2319/030821-184.1.

Received: July 11, 2024
Accepted: November 16, 2024