

Cadaveric Bone Allografts: Current challenges and advancements in bone regeneration

Aloinjertos Óseos Cadavéricos: desafíos actuales y avances en la regeneración ósea

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Abstract:

When endogenous bone repair is insufficient, bone allografts from cadaveric donors represent a key therapeutic alternative. These grafts are primarily indicated for multifragmentary or complex fractures, lytic lesions, and conditions involving bone resorption, nonunion, or pseudarthrosis that have failed to respond to initial treatment. Currently, allografts account for approximately one-third of all bone grafts used in North America. By definition, an allograft consists of sterilized bone tissue recovered from human cadavers for transplantation. It is commercially available in various preparations, including cortical, cancellous, and demineralized bone matrix (DBM). The rising incidence of bone-related pathologies, including infections and tumors, coupled with the global surge in orthopedic surgeries, has significantly increased the demand for bone grafts and substitutes. Bone grafting has become an essential component of modern musculoskeletal and dental practice worldwide. This expansion in clinical applications underscores the critical need for musculoskeletal tissue donation—not only for immediate surgical use but also for research and development of novel biomaterials. These advancements aim to enhance osteoinduction, osteoconduction, and osseointegration, thereby improving patient outcomes and addressing the escalating clinical need. Cadaveric donor bone allografts offer several advantages, including their diverse presentations and their inherent capacity to facilitate bone regeneration. However, clinical success remains contingent upon several factors, such as biocompatibility, processing techniques, and the host's immune response. This article synthesizes current evidence regarding the characteristics, clinical applications, and future perspectives of cadaveric allografts. By providing an updated overview, this review positions these grafts as a viable and effective alternative for enhancing bone regeneration and optimizing clinical outcomes across a wide spectrum of pathologies and surgical procedures.

Keywords:

Allograft, Autograft, Bone transplantation, Bone regeneration, Allograft processing, Clinical applications of allografts.

Resumen:

Cuando la reparación ósea es insuficiente implican el uso de injertos óseos de donantes cadavéricos, utilizados especialmente en fracturas multifragmentadas, complejas, lesiones líticas o con secuelas de resorción ósea, no unión o pseudoartrosis que no responden bien al tratamiento inicial. Actualmente, en Norteamérica, los aloinjertos representan alrededor de un tercio de los injertos óseos utilizados. El aloinjerto se refiere al hueso proveniente de cadáveres humanos, el cual se procesa de manera estéril y se trasplanta a un receptor, este se presenta en diversas formas como cortical, esponjoso, matriz ósea desmineralizada, etc. La creciente incidencia de afecciones óseas, como infecciones y tumores, junto con el aumento de las cirugías ortopédicas en todo el mundo, contribuyen significativamente a la demanda de injertos y sustitutos óseos. Estos procedimientos de injerto óseo forman parte integral de las prácticas médico-quirúrgicas y odontológicas en la actualidad en todo el mundo. El creciente número de estas técnicas, usos y procedimientos subrayan la importancia de la donación de tejido musculoesquelético, no solo para su uso clínico, sino también para

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la investigación y desarrollo de nuevos biomateriales con el objetivo de mejorar la osteoinducción, osteoconducción y osteointegración, para con ello obtener mejores resultados en los pacientes y satisfacer la creciente demanda. Los injertos óseos provenientes de donantes cadavéricos incluyen diferentes ventajas como su disponibilidad en diferentes formas y su capacidad para promover la regeneración ósea. Sin embargo, su éxito depende de distintos factores tales como la biocompatibilidad, el procesamiento y la respuesta del huésped. El presente artículo recopila información relacionada con las características, aplicaciones y perspectivas de los injertos óseos de donantes cadavéricos, proporcionando un panorama actualizado que los posiciona como una alternativa tanto eficaz como viable para potenciar la regeneración ósea y mejorar los resultados clínicos en diversas patologías y procedimientos quirúrgicos.

Palabras Clave:

Aloinjerto, Autoinjerto, Trasplante óseo, Regeneración ósea, Procesamiento de aloinjertos óseos, Aplicaciones clínicas de aloinjertos.

INTRODUCTION

The human skeleton possesses a unique regenerative capacity, enabling it to undergo self-repair following injury. This skeletal repair process mirrors embryonic development patterns, as both rely on the recruitment and differentiation of undifferentiated mesenchymal cells (MSCs). During the bone healing cascade, specific biochemical and mechanical stimuli guide these progenitor cells along the chondro-osteogenic pathway, resulting in the formation of new bone tissue. However, several factors can impair bone healing, including genetic predispositions, as well as mechanical, vascular, nutritional, and hormonal imbalances. Although bone regeneration occurs naturally in most cases, specific clinical scenarios—such as nonunion, pseudarthrosis, avascular necrosis, extensive periosteal stripping, or bone tumors—can result in critical-sized defects where spontaneous regeneration is unlikely. In these instances, bone grafting is essential to induce or conduct regeneration, thereby restoring the damaged bone or ensuring its integration into the existing skeletal structure.^{1,2}

The clinical use of bone grafting in orthopedic procedures dates back to the 17th century, when the Dutch surgeon Job van Meekeren performed a xenograft by transplanting a fragment of canine bone into a soldier's cranial defect. This represents the first documented bone graft in history; however, the Church subsequently ordered the removal of the graft on ecclesiastical grounds. Despite this mandate, the procedure could not be completed, as the bone had already achieved complete osseointegration with the soldier's skull. Later, in 1879, Sir William MacEwan pioneered the concept of allografting by successfully replacing the proximal two-thirds of the humerus in a 4-year-old child using bone segments harvested from other patients. Today, allografts account for approximately one-third of all bone grafting procedures in North America. These grafts consist of bone tissue recovered from deceased donors, which is subsequently processed for transplantation into a recipient. Regarding the three fundamental mechanisms of bone healing, allografts exhibit both osteoconductive and osteoinductive properties. Their primary clinical advantage lies in their versatility, as they can be prepared in various shapes and sizes to ensure optimal coverage of the bone defect. Furthermore,

allografts eliminate donor site morbidity, establishing them as a viable and widely used alternative to autologous bone grafts.²⁻⁵ Bone grafting serves as a critical adjunct to surgical procedures, utilizing specialized tissue to repair, reconstruct, or stimulate local bone formation, thereby facilitating consolidation. Its application spans traumatic, orthopedic, oncologic, and dental surgeries, establishing bone as the second most frequently transplanted tissue in the human body, surpassed only by blood and blood-derived products. Annually, approximately 2 million bone grafting procedures are performed worldwide. This figure is projected to increase significantly, as these grafts are increasingly utilized in orthopedics and traumatology—spanning from the treatment of complex fractures and limb salvage procedures to intricate reconstructions and spinal surgeries. However, this rising demand has resulted in a shortage of available donor tissue, underscoring the urgent need to raise awareness within the Mexican population regarding the vital importance of organ and musculoskeletal tissue donation.^{2-4,6} Bone consolidation is a dynamic, multi-factorial cellular process. It requires a construct that provides adequate mechanical stability while preserving the integrity of the surrounding soft tissues to facilitate revascularization. This biological environment is essential to enable the orchestrated process of osteogenesis, osteoinduction, and osteoconduction. Osteogenesis refers to the biological process of new bone formation; osteoinduction involves the recruitment and stimulation of undifferentiated pluripotent cells to differentiate into bone-forming lineages; and osteoconduction describes the scaffold-like property that allows bone to grow along a surface or through pores and channels. Consequently, an ideal bone graft should possess three essential characteristics: an osteoconductive matrix, osteoinductive signaling factors, and osteogenic cells, thereby ensuring a predictable and successful bone repair process.^{3,4}

Bone grafts are primarily classified into two types: autografts and allografts. An autograft involves harvesting healthy bone tissue from a donor site within the same individual for transplantation into the target area. Regarding bone consolidation, autografts possess superior integration potential and are widely considered the “gold standard” by clinicians and researchers alike. However, significant drawbacks—including the requirement for two simultaneous surgical sites, limited

bone availability, risk of hemorrhage, prolonged operative time, and potential for infection—have driven a growing interest in a viable alternative: allografts.^{4,6}

MECHANISMS OF BONE GRAFTS

The Bone Repair Process

Bone remodeling occurs through two distinct consolidation pathways: primary and secondary healing. Primary bone healing occurs when the bone fragments are in direct apposition with minimal interfragmentary gaps, requiring absolute stability. This process enables direct cortical remodeling and bone growth without the development of a fracture hematoma or subsequent callus formation. In contrast, secondary bone healing is the most prevalent mechanism and involves the initial formation of a fracture hematoma, followed by callus development. This process comprises three distinct phases: inflammation, proliferation, and remodeling. In both healing pathways, bone grafting serves as a critical adjunctive support. During the inflammatory phase, a cascade of signaling molecules and growth factors stimulates the recruitment of mesenchymal stem cells (MSCs), prompting their differentiation into osteoblasts. This culminates in the formation of a fibrocartilaginous bridge, commonly referred to as a bony callus. During the proliferative phase, angiogenesis occurs, giving rise to highly vascularized granulation tissue. Subsequently, new bone is synthesized via intramembranous ossification. Finally, the remodeling phase yields bone tissue that is both biocompatible and structurally analogous to native bone, possessing comparable porosity and mechanical strength.^{2,3} For successful fracture consolidation to occur, several coordinated biological mechanisms must be present—mechanisms that fundamentally justify the use of bone grafts, as each type of graft fulfills a specific role in the regenerative cascade.²

Osteogenesis

Osteogenesis represents the initial and most critical phase of bone repair and remodeling, as it encompasses the development and formation of new bone from specific cellular elements within the graft. Compared to other types of grafts, cancellous bone grafts exhibit excellent osteogenic potential because they contain all the necessary components to stimulate osteogenesis, including a large surface area lined with osteoblasts, thereby enhancing their capacity to generate new bone.^{2,3}

Osteoinduction

A key process in this regenerative cascade is osteoinduction, defined as the stimulation of undifferentiated mesenchymal cells to differentiate into osteoprogenitor cells capable of forming new bone. This phenomenon, first described by Marshall R. Urist in the 1960s, demonstrated that demineralized bone matrix possesses properties that can induce bone formation when implanted in extraskeletal sites.⁷ Following this discovery, Urist and his collaborators identified the specific

proteins responsible for osteoinduction, known as bone morphogenetic proteins (BMPs). These proteins belong to the larger transforming growth factor-beta (TGF- β) superfamily, with at least 15 variants identified by the mid-1990s. BMPs promote the differentiation of mesenchymal stem cells at and around the recipient site, recruiting them to differentiate into osteoblasts and chondroblasts, thereby triggering osteogenesis. Other growth factors involved in this process include platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and various interleukins (ILs). In addition to these, autologous bone grafts, bone marrow aspirate concentrate (BMAC), and platelet-rich plasma (PRP) also contribute to osteoinductive processes.^{2,3,7,8}

Osteoconduction

Osteoconduction is a fundamental biological process in bone regeneration, whereby an implanted material provides a three-dimensional scaffold that supports the migration, adhesion, and proliferation of osteogenic cells, thereby facilitating the formation of new bone tissue. This phenomenon occurs when a graft or biomaterial enables the colonization of osteoblasts and progenitor cells from the adjacent bone tissue, promoting inward bone growth and subsequent integration with the surrounding tissue. To be considered osteoconductive, a material must exhibit appropriate physicochemical properties, such as an interconnected porous structure, bioactivity, and biocompatibility. These characteristics allow for vascular infiltration, cellular proliferation, and matrix deposition, thereby supporting bone healing. Among the most frequently used osteoconductive materials in clinical applications are autologous, allogeneic, and xenogeneic bone grafts, as well as synthetic biomaterials such as hydroxyapatite, calcium phosphate, and bioactive glasses.^{2,3,9-11}

The combination of osteoconductive materials with osteoinductive agents—such as bone morphogenetic proteins (BMPs) or mesenchymal stem cells—can enhance bone regeneration and improve clinical outcomes. Recent studies have shown that the design and surface modification of biomaterials can optimize their osteoconductive capacity, promoting better cell adhesion and integration with the host bone tissue. Therefore, the development of novel strategies based on tissue engineering and nanotechnology remains a major focus in the field of regenerative medicine.¹²

IMMUNOLOGY OF ALLOGRAFTS

An allogeneic bone graft is considered the primary alternative when autologous bone grafting is not feasible.¹³ Most allografts are regarded as having low immunogenic potential, as donated musculoskeletal tissues typically undergo rigorous cleansing procedures to remove cellular components or are preserved through specific processing methods. Allografts can be stored for periods ranging from weeks to years prior to use; consequently, they must be processed to preserve both safety and clinical efficacy over extended durations. In general, allograft preservation involves the use of specialized storage

media, cryopreservation, or lyophilization, enabling storage under ambient temperature, refrigeration, or freezing conditions.^{13,14}

Unlike other types of transplanted tissues, HLA (human leukocyte antigen) haplotype matching is not required for these grafts. However, it has been proposed that residual cellular material may trigger an immune response, potentially leading to suboptimal graft incorporation due to activation of major histocompatibility complex (MHC) antigens. Consequently, immunogenicity concerns must be minimized to ensure optimal biocompatibility of the allograft at the time of implantation. Different tissue types exhibit varying degrees of immunogenicity, which is primarily determined by their antigenicity. Generally, skin tissue is more immunogenic than bone or tendon tissues; the latter display lower immunogenicity that can typically be managed through standard allograft cleansing procedures.^{13,14}

PROCESSING OF ALLOGENEIC BONE GRAFTS

Tissue obtained from cadaveric donors must comply with the provisions established in the General Health Law, Title Fourteenth, Chapter I, as well as the Regulations of the General Health Law on Sanitary Control of the Disposal of Organs, Tissues, and Human Corpses, published in the Official Federal Gazette on March 16, 1987, including its current amendments, under the supervision of the Ministry of Health of the Federal Government of Mexico. Additionally, the procedure must adhere to the standards of the American Association of Tissue Banks (AATB), as outlined in its most recent technical guide. Tissue procurement is performed using aseptic surgical techniques, while both processing and packaging are conducted under strictly controlled conditions, in accordance with applicable national and international regulations.¹⁵⁻¹⁷

Reduction of Disease Transmission Risk

Tissue providers mitigate the risk of disease transmission through three primary strategies:

1. Minimizing the procurement of tissues from donors with high biological risk.

Prior to donation, a comprehensive review of the donor's clinical history is performed to identify medical conditions or pathological processes that may contraindicate tissue donation—such as malignancy or autoimmune diseases. This screening follows established protocols and criteria approved by the tissue bank's medical director. Additionally, medical and social histories are evaluated to detect high-risk behaviors to prevent transmission of infectious diseases, strictly adhering to the guidelines established by COFEPRIS, CENATRA, and international tissue banking standards.^{14,15}

Donors also undergo mandatory serological screening using samples collected prior to tissue procurement. These screenings include testing for:

- Hepatitis B surface antigen (HBsAg)
- Anti-HIV-1 and HIV-2 antibodies

- Nucleic Acid Testing (NAT) for HIV and Hepatitis C (HCV).
- Rapid Plasma Reagin (RPR) test for *Treponema pallidum* (syphilis)
- Anti-HCV antibodies.
- IgG/IgM antibodies against Hepatitis B core antigen (anti-HBc).
- IgG antibodies against *Trypanosoma cruzi* (Chagas disease)

Additionally, microbial cultures are performed to detect aerobic and anaerobic contaminants.

2. Environmental control and tissue handling practices.

Biological contamination is mitigated through strict aseptic processing techniques during tissue recovery and processing. Furthermore, microbial control assays (bioburden testing) are conducted on tissues at multiple stages, including procurement, processing, and packaging.^{15,18}

3. Reducing residual bioburden through disinfection and sterilization techniques.

The bioburden can be further diminished through tissue cleaning and disinfection; these procedures vary depending on the tissue type and may include:

- Debridement.
- Low-dose pre-irradiation (performed prior to subsequent chemical processing steps)
- Physical methods, such as washing, centrifugation, and sonication.
- Chemical methods involving substances such as antibiotics, hydrogen peroxide (H₂O₂), peracetic acid, ethanol, ethylene oxide, and other broad-spectrum biocides.

These cleaning processes can effectively remove bone marrow components, lipids, and low-molecular-weight proteins, thereby reducing both the graft's potential immunogenicity and the risk of bacterial, viral, and fungal contamination.^{14,18,19}

Sterilization by irradiation

This method offers superior penetrative capacity compared to alternative sterilization techniques. Irradiation protocols rely on ionizing radiation—a term encompassing high-energy radiation such as X-rays, gamma rays, and high-speed electrons—capable of inducing ionization cascades within the treated matter.

The effectiveness of ionizing radiation as a sterilization method resides in its exceptional penetrability and high efficacy in inactivating pathogenic microorganisms, avoiding complications associated with heat exchange, pressure gradients, or diffusion barriers. Gamma irradiation is the most frequently employed sterilization technique for bone allografts and is also widely utilized for processed tendons, serving either as a terminal sterilization step or as an intermediate process.

Ionizing radiation induces only a minimal thermal impact, which is manageable for temperature-sensitive biological materials, and remains effective at ambient or even subzero

temperatures. Furthermore, ionizing radiation allows for the sterilization of materials within hermetically sealed packaging, thereby preventing recontamination during storage or handling prior to clinical implantation.^{18,19}

TYPES OF ALLOGRAFTS AND THEIR CLINICAL APPLICATIONS

Allografts are available in fresh, frozen, or lyophilized (freeze-dried) forms and may consist of cortical or cortico-cancellous bone tissue. Clinicians determine the most appropriate configuration for each patient based on the specific clinical condition. These grafts are provided in various presentations –including whole bone segments, cancellous bone chips, or even powder– depending on the requirements of the surgical procedure to be performed.^{19,20}

A review of the available literature reveals certain discrepancies arising from ambiguous classification systems used to describe the various allograft types.

Scientific publications frequently reference mineralized bone allografts (MBA), fresh-frozen bone allografts (FFBA), freeze-dried bone allografts (FDBA), demineralized bone matrix (DBM), and decellularized extracellular matrix (dECM). In practice, FDBA and MFDBA (mineralized freeze-dried bone allograft) often refer to the same material under different nomenclatures, as both are essentially MBA subjected to lyophilization. Similarly, the terms DFDBA (demineralized freeze-dried bone allograft) and DBM have been used interchangeably in various clinical and research contexts.²⁰

Broadly speaking, MBA, DBM, AAA Allograft, and dECM may be considered distinct derivatives of allograft tissue. Consequently, for the purposes of this review, they will be classified accordingly (see **Figure 1**).²⁰

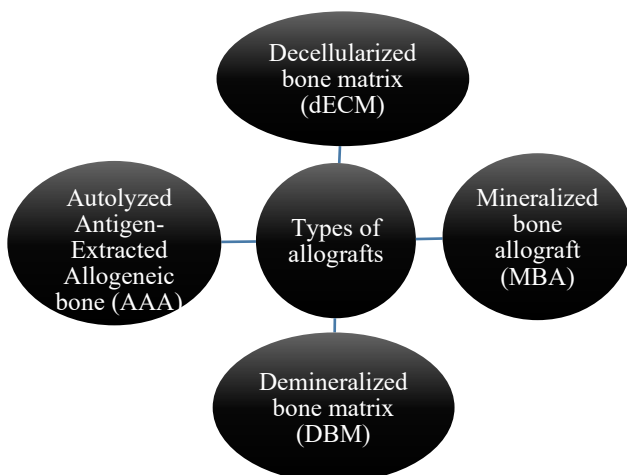


Figure 1. Classification of bone allograft types and their derivatives.²⁰

Mineralized Bone Allograft (MBA)

The most fundamental form of an allogeneic graft is the fresh, unprocessed bone block, which can be cryopreserved (fresh-frozen bone, FFB), lyophilized (freeze-dried bone allograft, FDBA or MFDBA), or implanted in its fresh state. Since processing techniques inevitably diminish mechanical strength, unprocessed allografts retain superior mechanical properties compared to their processed counterparts. However, due to the substantial risk of disease transmission and the host’s immunogenic response, the use of fresh, unprocessed allografts is rare in contemporary clinical practice.^{2,20}

During the freeze-drying process, most of the tissue’s water content is removed, which reduces mechanical strength and destroys osteogenic cells, as well as Class I Major Histocompatibility Complex (MHC) molecules located on the osteoblast surface. A primary advantage of this process is the significant reduction in both immunogenicity and the risk of disease transmission. The characteristics of mineralized allografts vary depending on their composition—whether cortical, cancellous, or a combination of both. In general, there is a consensus in the literature that both cortical and cancellous allografts exhibit osteoconductive properties (*Table 1*).^{2,20}

Cortical Allograft

Cortical allografts possess higher density, greater structural integrity, and superior mechanical properties compared to cancellous allografts. While they provide a stable osteoconductive framework, vascular ingrowth and new bone formation occur primarily through the interstitial spaces between particles or segments. These grafts remodel slowly and exhibit slower resorption rates, yet they offer the highest long-term volumetric stability among all allograft types. Consequently, they are indicated for structural or load-bearing applications and the management of large defects, typically in the form of whole bone segments, blocks, or struts.^{5,20,21}

Cancellous Allograft

Cancellous bone allografts are derived from the processed trabecular component of donated bone. While they lack the structural integrity required for load-bearing clinical applications, their trabecular porosity provides an expansive surface area for cellular infiltration, angiogenesis, extracellular matrix deposition, and new bone formation. Consequently, cancellous allografts are indicated for scenarios requiring accelerated bone healing, as the large intertrabecular spaces facilitate rapid and comprehensive graft incorporation. These grafts are typically available in various configurations, including chips, wedges, dowels, or powder.^{5,20-22}

Cortico–Cancellous Bone Allograft

Since neither cortical nor cancellous bone independently possesses osteogenic properties, cortico-cancellous bone blocks

are frequently utilized to leverage the combined benefits of both tissue types. The compressible cancellous layer facilitates a precise anatomical fit, while the cortical component provides essential mechanical strength and protection during the initial stages of the healing process. These grafts are commonly employed for the reconstruction of small bone segments, requiring meticulous shaping to ensure optimal mechanical support. Key clinical applications include prosthetic revision

surgeries, corrective osteotomies, and vertebral body replacements.^{4,19,22}

Table 1. Different clinical applications of mineralized bone allografts. Adapted from references.^{23,24}

	Cancellous bone	Processed Wedges	Processed Strips
Source	Any section of cancellous (spongy) tissue.	Fibula, ulna, radius, femur, tibia, and humerus.	Femur, tibia, and fibula
Clinical Uses	Spinal fractures, spinal fusion, hip prosthesis revision, total knee replacement, filling of bone voids or resorption defects, maxillofacial surgery, and oncology.	Spinal fractures, scoliosis correction, spondylolisthesis, spinal fusion, internal fixation of fractures with bone loss or malunion, and maxillofacial surgery.	Spinal fractures, lumbar/thoracic fusion, scoliosis correction, spondylolisthesis, fracture repair with bone loss or malunion, maxillofacial surgery, total knee replacement, and internal fracture fixation.
Types & Characteristics	Bone chips: High concentrations of osteoblasts and osteocytes confer superior osteogenic potential; the large trabecular surface promotes revascularization and graft integration.		
	Bone powder: Provides a scaffold matrix that stimulates bone formation via highly efficient osteoconduction. Its natural architecture facilitates cell attachment, proliferation, and vascular ingrowth within the surgical site		
Additional Properties			Processed from cancellous or cortico-cancellous bone. These mineralized matrices provide a biocompatible osteoconductive scaffold. The product is non-hemolytic, compatible with blood cells, and suitable for seeding stem cells and pre-osteoblasts.

Demineralized Bone Matrix (DBM)

DBM was first isolated from human tissue in 1975. The original freeze-dried formulations were challenging to handle, due to their lack of cohesiveness and moldability, as well as their tendency to disperse in hemorrhagic environments. This prompted researchers to combine DBM with various biocompatible carriers such as glycerol, starch, hyaluronic acid, collagen, or saline solution. These combinations significantly improve the consistency and handling characteristics of DBM,

enabling the composite to maintain its shape and enhancing its clinical utility in surgical settings.^{20,23}

DBM is produced through the acid extraction of allograft bone, which theoretically facilitates osteogenesis by increasing the surface area available for both osteoconductive and osteoinductive cellular attachment. However, the osteoinductive potential of individual DBM batches can vary significantly based on donor-specific characteristics. The manufacturing protocol involves pulverizing the allograft bone to a fine particle size (74–420 μm), followed by

demineralization using 0.5 N HCl at a specific milliequivalent-to-gram ratio for a duration of three hours. Residual acid is subsequently removed through sequential rinses with sterile water, ethanol, and ethyl ether. This process, exposes the Type I collagen within the cortical bone matrix and enhances the bioavailability of non-collagenous proteins, including essential osteoinductive growth factors such as bone morphogenetic proteins (BMPs), transforming growth factor (TGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). Consequently, DBM exhibits superior osteoinductive properties compared to mineralized allografts, regardless of their cortical or cancellous origin. However, DBM lacks inherent structural integrity and is therefore frequently combined with other allograft types or synthetic grafting materials to provide mechanical support.^{20,23}

While DBM shows significant clinical promise, current evidence supporting its efficacy as a standalone bone substitute remains limited. Its performance is markedly enhanced when combined with cancellous allograft or autologous bone marrow aspirate. Historically, the most successful clinical outcomes have been achieved by mixing DBM with autogenous bone grafts and implementing stable internal fixation. To accommodate diverse surgical needs, DBM is commercially available in various formulations, including putty, paste, blocks, particles, and powder (Table 2).^{20,23}

Table 2. Clinical applications of Demineralized Bone Matrix (DBM). Adapted from references ^{23,24}

POWDER DMB	
A demineralized bone matrix derived from human cortical bone, characterized by its high osteoinductive potential.	
Formulation	Lyophilized (freeze-dried) powder
Clinical Uses	Modality: Can be prepared as a gel or putty, to meet specific surgical requirements and optimize delivery. Oncology: Bone tumors resulting in cavitary defects or voids requiring structural filling. Trauma: Comminuted fractures or injuries involving significant loss of bone tissue. Maxillofacial Reconstruction: Repair of mandibular or maxillary defects and restoration of lost bone volume. Oral Surgery: Management of alveolar defects in the maxilla or mandible requiring supplemental bone support for stabilization.

Autolyzed Antigen-Extracted Allogeneic Bone (AAA)

AAA bone is an allograft derivative produced by incubating demineralized bone matrix in phosphate-buffered neutral solutions, a process that induces the autolytic digestion of cellular components. This enzymatic degradation yields a

scaffold with high osteoinductive potential, suitable for bone regeneration and structural repair. However, clinical observations often report significant postoperative resorption, and its overall osteogenic efficacy is frequently regarded as suboptimal compared to other advanced biomaterials. Bone tissue is highly vascularized; its regeneration involves an interplay between osteogenesis and angiogenesis, resulting in bone formation and tissue repair. Enhanced vascularization promotes bone regeneration throughout the repair process. Although literature on AAA bone remains limited, some studies have explored different repair strategies for bone defects using AAA combined with vascular endothelial growth factor (VEGF), aiming to provide new insights and practical methods for the clinical application of allogeneic bone grafts.^{20,25}

Decellularized Extracellular Matrix (dECM)

Decellularized extracellular matrix (dECM) refers to allogeneic biomaterials derived from human or animal tissues following the removal of cellular components that would otherwise elicit undesirable immune responses. Broadly defined, decellularization aims to eliminate all cellular and nuclear material from tissue while preserving the composition, biological activity, and mechanical integrity of the native extracellular matrix (ECM). Tissue engineering has emerged as a promising alternative to current treatment options through the development of structures designed to restore or enhance damaged tissues and organs. Entire organs such as the lungs and the heart have been successfully decellularized for future transplantation, this technology has also been effectively applied to bone tissue.^{20,26,27}

Bone-derived scaffolding materials from decellularized tissue have been extensively investigated for bone repair strategies. Bone-derived dECM is obtained from living or cadaveric human or animal donors via the decellularization process. Multiple studies have demonstrated the osteoinductive capacity of dECM matrices, which can induce osteogenic differentiation and bone formation both *in vitro* and *in vivo*. These matrices retain tissue-specific memory, thereby promoting targeted cellular differentiation towards the osteogenic lineage.^{18,23,24}

Regarding preparation, dECM is subjected to various physical, chemical, and enzymatic treatments configured to completely remove cellular components without compromising the structural integrity of biological properties of the native bone ECM. Following decellularization, post-processing is essential to eliminate toxic residues and enhance biocompatibility. Sterilization and disinfection protocols include gamma irradiation, electron beam sterilization, ethylene oxide gas, antibiotic treatment, and peracetic acid washing. Once sterilized, dECM scaffolds may be recellularized with host-derived stem cells. In bone tissue engineering, mesenchymal stem

cells (MSCs) –which possess the capacity to differentiate into osteoblasts– show particular promise. The ability to seed immunocompatible stem cells onto dECM bone scaffolds offers a significant clinical perspective, enabling clinicians and patients to benefit not only from the scaffold's osteoconductive and osteoinductive properties but also from its acquired osteogenic potential. Additionally, dECM is frequently combined with collagen, hydroxyapatite, BMPs, and other relevant growth factors to enhance osteogenesis and facilitate bone formation. Notably, studies have indicated that bone matrix derived from elderly donors may provide superior support for the osteogenic differentiation of stem cells; conversely, mesenchymal stem cells (MSCs) harvested from younger donors exhibit significantly greater differentiation potential.^{20,26,27}

TISSUE BANKING

Tissue and bone banking initiatives in Mexico date back to the period between 1940 and 1952, with early establishments operating in institutions such as Hospital Juárez, the Central Military Hospital, and Clínica Primavera. Since then, tissue banking has experienced steady growth across the country. As of 2024, the National Transplant Center (CENATRA) reported 602 active donation-related facilities. Among these, 457 are licensed for procurement, 435 for transplantation, and 48 are formally registered as tissue banks.^{28,29}

Organ and tissue transplantation, alongside the development of advanced biomedical therapies –such as those discussed in this review– currently represent some of the most impactful therapeutic options for restoring physiological function and improving patient quality of life. In Mexico, the rapid advancement and increasing complexity of musculoskeletal tissue banking are strictly paralleled by ongoing updates to the national regulatory framework.^{22,28,29}

The primary functions of tissue banks include rigorous quality control and the implementation of either conservative or chemical processing protocols to obtain human-derived graft materials –such as bone chips, demineralized bone matrix (DBM), ceramics, and other tissue derivatives– thereby ensuring the safety, biological health, and clinical efficacy of these products. In Mexico, the regulation of musculoskeletal tissues as health supplies falls under the Health Supplies Regulation, enforced by the Federal Commission for the Protection Against Sanitary Risks (COFEPRIS). This classification is due to the extensive manufacturing processes these materials undergo, which necessitate strict sanitary oversight.^{22,29}

CONCLUSIONS

Allografts, derived from cadaveric sources, have proven to be an essential tool in modern medicine, playing a pivotal role in specialties such as traumatology, orthopedics, reconstructive surgery, and dentistry. Through the application of these grafts, thousands of patients have been able to regain mobility,

alleviate chronic pain, and significantly improve their quality of life following severe fractures, bone defects, or the progression of degenerative diseases. However, despite their well-documented benefits, the availability of these materials remains a significant challenge, as it depends directly on tissue donation –a subject that has yet to receive the attention and recognition it deserves, both globally and within the Mexican population. Unlike organ donation, which has been extensively promoted both nationally and globally through public health campaigns, tissue donation –particularly regarding musculoskeletal tissue– remains largely unrecognized by the general population. Beyond the challenge of availability, another critical factor in the clinical application of cadaveric bone grafts is safety. The safety of these grafts is ensured through rigorous protocols, such as decellularization and radiation sterilization. Simultaneously, research in tissue engineering is advancing through the integration of stem cells, growth factors, and specialized biomaterials. These innovations aim to accelerate graft integration, reduce patient recovery time, and minimize postoperative complications, representing significant progress in regenerative medicine and the management of complex bone injuries.

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