

Recent Advances in Bone Grafts in Oral and Maxillofacial Surgery

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Abstract:

Bone resorption, which is the loss of bone tissue, cannot be reversed after tooth loss. As a result, the affected area lacks sufficient bone volume for successful implant treatment. To address this issue, bone grafting is the only viable solution and is required in one out of every four dental implants. The ideal biomaterial substitute for bone repair should have osteogenic, osteoinductive, and osteoconductive properties, as well as the ability to stimulate the neo-angiogenesis process. It should also avoid any antigenic, teratogenic, or carcinogenic reactions, and prevent systemic toxicity complications. The purpose of this article is to provide an overview of the various materials used for bone grafts and biomaterial substitutes for bone repair, as well as to discuss current and future perspectives in this field.

Keywords: Bone resorption, bone grafting, osteoinductive, osteogenic, osteoconductive

Introduction:

A bone graft is living tissue that can help promote bone healing. It is transplanted into a bone defect either alone or in combination with other materials. The US Food and Drug Administration (USFDA) classifies bone grafts as Class II devices for filling bony voids and defects, and Class III devices for bone grafting that contains drugs [1].

The durability, functionality, and aesthetic appeal of dental implants have made them the preferred option for tooth replacement. However, the success of an implant placement depends largely on the amount of bone available at the implant site [2]. To ensure successful implant placement, it is necessary to have sufficient alveolar bone dimensions, which should be at least 10mm in height and 3mm to 4mm in diameter [3].

Allografts and autografts are two types of bone grafts that are commonly used. Allografts involve the transfer of grafting materials between two individuals who are not genetically related. Autografts, on the other hand, involve the transfer of grafting material from one site of the body to another within the same individual [4].

Discussion:

Dental Bone Grafts and Substitutes of Bone Repair:

Calcium phosphate-based materials are widely used for bone repair, including both natural and synthetic

options. 2

Natural bone graft and substitute materials:

Autografts:

Autografts are often taken from various sites in the same person's body, including the mandibular symphysis, mandibular ramus, external oblique ridge, iliac crest, proximal ulna, or distal radius. These sites are considered good sources of both cortical and cancellous bone. [4]. Autografts, while effective, come with downsides such as the need for a secondary surgical visit, donor site injury, and potential scarring. Compared to other options, such as histocompatibility and immunogenicity tissues, autografts have been associated with higher surgical costs and higher surgical risks [5,10].

Cancellous bone is a type of bone tissue that is commonly used for autografts. It contains osteoblasts and progenitor cells that have considerable potential for bone formation. These cells have relatively large trabecular surfaces, which make it easier for them to establish an osteoinductive environment by promoting revascularisation and incorporating into the recipient site. On the other hand, cortical bone lacks osteoblast and osteogenic cells. Instead, it provides structural mechanical support and promotes bone healing through osteoconduction. However, cortical grafts are slower to integrate when compared to cancellous grafts due to their limited potential for revascularisation [11].

In dental treatments, while other bone substitutes are commonly used for treating localized alveolar bony defects and maxillary sinus bone grafting, block autografts remain a common choice for alveolar ridge augmentation procedures. This is because autogenous block grafts can reliably improve the quality and quantity of bone, allowing for placement of implants with maximum diameter, which in turn supports long-term strength and survival [12,13].

Allografts :

Allografts can be prepared in three primary forms: fresh, frozen, or freeze-dried. However, fresh and frozen allografts are rarely used nowadays due to the higher risk of post-immunogenic response, limited shelf life, and increased risk of disease transmission. [11].

In recent decades, the use of allograft materials has become more popular because it addresses many of the concerns associated with autografting procedures, especially in cases of large bony defects. However, there are still some limitations, such as the risk of transmitting infectious diseases like HIV and hepatitis B and C [14]. These concerns can be addressed through tissue processing, such as sterilization, mechanical debridement, ultrasonic washing, and gamma radiation. [9]. Allografts have been successfully used in combination with xenografts to aid in bone regeneration in bone augmentation procedures. Allografts are compatible with the body's tissues and are available in various forms including whole bone segments, cortico-cancellous, cortical pieces, chips, wedges, pegs, power, and DBM. However, cancellous autografts and allografts have poor mechanical strength. Also, cancellous allografts exhibit inadequate healing capacity due to tissue processing techniques such as treatment with alcohol, acetic acid, or nitric acid, which reduce the materials' osteoconductive capabilities. [11].

In dental procedures, allografts are commonly used to fill defects in the periodontal, maxillary, and mandibular regions. Block allografts are typically used to correct deficiencies in alveolar ridge height or severe ridge atrophy, allowing for the necessary bone height for dental implant placement. [15-17].

Demineralized bone matrix is an allograft derivative that has been treated with acid to remove the mineral content. [6,9,11]. The osteoinductivity of DBM is adversely affected by tissue preparation techniques like alcohol, lactic acid, acetic acid, and nitric acid treatment. As a result, its osteoconductive potential is highly

dependent on these factors. [5,11]. One of the earliest commercially available forms of DBM is freeze-dried DBM. In recent years, Demineralized bone matrix (DBM) has been increasingly used in dental applications along with added excipients, such as glycerol, starch, hyaluronic acid, collagen, and saline, that act as transport vehicles. This preparation allows for improved handling and adaptability due to the hardening of the mixture and its components. An additional benefit of Freeze-dried DBM is the slow release of Bone Morphogenetic Proteins (BMPs), which have been shown to possess the ability to induce bone regeneration, thereby increasing the osteoinductive potential. [9,19]. Human DBM in the form of putty has been successfully used to preserve and restore alveolar bone height and thickness after tooth extraction. This leads to the formation of mineralized and mature bone within six months after grafting [20,21].

Xenografts:

Xenografts are materials used for grafting that come from a species unrelated to the host. In dentistry, the most commonly used source of xenograft material is Bio-Oss, which is made from deproteinized bovine bone tissue. Bovine bone xenografts are widely used for maxillary sinus floor lifting and implant support due to their low immunogenicity and superior stability. [23,24].

Bio-Oss has proven to be a valuable bone replacement material in clinical use. It provides good-quality newly formed bone structures and promising rates of long-term survival of dental implants inserted with it [25]. Chitosan, which is a polymer derived from crustacean exoskeletons, has shown promising results as a xenograft material in recent studies. It has the ability to stimulate bone regeneration by providing a structural skeleton that supports osteoblastic activity, mineralisation of the bone matrix, and the induction of mesenchymal cell differentiation into osteoblasts. [26].

Phytogenic material:

Phytogenic materials are materials derived from plants that are used to augment bones. In the field of tissue engineering, plant-derived compounds or extracts can be easily incorporated as biomaterials [27].

Corals have similar chemical and structural characteristics to human spongy bone, making them a promising material for bone augmentation. They possess porous structures of varying sizes, good compressive strength, and low immunogenicity. Furthermore, they bond well with bone tissue. However, their tensile strength is relatively low, they are brittle, and their resorption pattern may not be ideal. [28]. *FriosAlgiPore's* product is a type of seaweed hydroxyapatite that has been used as a bone augmentation material since 1988 [29].

Bone Graft Material Derived from Extracted Tooth used in Dentistry:

Bones, dentin, and enamel share a similar composition with hydroxyapatite in the inorganic component, along with type 1 collagen and other proteins in the organic component, but the percentage of these components differs. [30,31]. The demineralization of autologous extracted teeth's dentin enhances bone augmentation by increasing the availability of bone morphogenic proteins. [32].

Synthetic bone substitute materials:

Calcium Phosphate Ceramics (CaP Ceramics):

Hydroxyapatite (HA) is a popular ceramic material used for bone augmentation as it has a similar chemical composition and crystalline structure to bone. Its bioactivity is due to its osteoconductive properties, which enable osteoblasts to attach and migrate to the surface of the material. [35-36]. HA has been successfully used in dentistry and orthopaedics, alone or in combination with auto-/allo-/xenografts, to support bone regeneration. [37].

Tricalcium phosphate (TCP) exists in two crystallographic forms, namely α -TCP and β -TCP. The latter form, β -TCP, has been widely used as a bone replacement material for many years. The use of β -TCP as a bone substitute is limited due to its poor mechanical strength, but it can be used in combination with other materials, especially hydroxyapatite. [39].

Calcium Phosphate Cements (CPCs):

Calcium Phosphate Cements are usually composed of two or three components. These components include an aqueous component and a powder component containing sintered CP material like α -TCP and HA. When the components are mixed together, a paste is formed that can be worked with. This mixture hardens in place in a self-setting manner, forming HA nanocrystals at room temperature. [40,41].

The advantages of CPCs include their ability to self-set, shape the paste into the defect site, high biocompatibility, availability in different forms for different types of bony defects and their osteoconductive properties. [6,20,41]. CPC lacks a macroporous structure, which limits cell adhesion speed, fluid exchange, and restorability. [9,41].

Calcium Sulfates:

Calcium sulfate is produced by heating gypsum to form a powder. This powder can then form a crystalline structure known as alpha-hemihydrate[5]. When mixed with water, it can be molded into various shapes and sizes to fill bony defects. Once the paste hardens, it sets itself, making it an ideal material for medical applications[42].

In dental applications, the use of calcium sulfates has been limited due to the presence of saliva and bleeding, which makes it difficult for the material to harden. However, recent research has led to the development of a biphasic form of calcium sulfate, which contains approximately 33% hydroxyapatite. This new form of the material has the ability to harden even in the presence of bodily fluids, making it more suitable for use in dental procedures. [43]. These advancements have enabled the application of use of calcium sulfate materials in a wide range of dental applications such as surgical defects, maintaining alveolar ridge height, furcation defects and as a bone void filler[44].

Composite Bone Substitute Materials:

Composite bone substitute materials are designed to enhance the mechanical properties of the resulting material by combining different materials such as bioglass and polymers, which have osteoconductive properties. These are often mixed with bone marrow or combined with BMPs to improve their osteoconductive and osteoinductive properties. The primary aim is to increase the usefulness of autograft products. [5,40].

NanoBoneTM is a composite bone substitute made of 76% w/w nanocrystalline HA and 24% w/w silicone dioxide[40].

When used with platelet-rich-fibrin, it can accelerate bone regeneration and improve the quality and quantity of newly formed bone following the excision of mandibular cysts[45,46]. *Fortoss VitalTM* is a biphasic alloplastic material composed of β -TCP within a calcium sulfate matrix, which is commonly used as a resorbable composite bone substitute product in dentistry. [40,47]. In dental procedures, *Fortoss VitalTM* has been successfully used for alveolar bone augmentation, implant rehabilitation, and socket preservation. These procedures result in significant bone regeneration following grafting with *Fortoss VitalTM*[47].

Growth Factor Based Bone Substitutes (GFBSs):

Growth factors such as BMPs, PDGFs, and IGFs have osteoinductive properties, promoting bone regeneration. [1]. The dental field has been making use of bioactivated materials with growth factors to

accelerate bone healing in patients with bisphosphonate-related osteonecrosis of the jaw (BROJN). This is done by using plasma rich in growth factors (PGRF), platelet-rich plasma (PRP), and plasma rich in fibrin (PRF) [48,49].

Sticky bone is a recent concept that uses a bone graft matrix enriched with growth factors and autologous fibrin glue. [50,51]. The usage of sticky bone is helpful in stabilizing the bone graft material in bony defects, which leads to faster bone regeneration and minimizes bone loss. This material has several advantages such as good moldability, structural stability, selectivity for osteogenic progenitor, and prevention of soft tissue cell migration through fibrin interconnections. Additionally, the fibrin network allows for rapid cell adhesion and accelerated healing. A study on atrophic alveolar ridge concluded that the use of sticky bone resulted in favourable three-dimensional ridge over augmentation over 4 months. [50].

Bone Substitutes with Infused Living Osteogenic Cells:

Viable osteogenic progenitor cells, such as MSCs, can be used by themselves or in combination with other materials, such as cytokines, growth factors, and scaffolding carriers, including DBM, to stimulate new bone formation. This process enhances bone healing through osteoconduction and osteogenesis. MSCs are non-hematopoietic multipotent cells that are routinely derived from bone marrow. [1]. When used with a scaffolding carrier, they can regenerate large bone defects by differentiating into osteogenic cells. [52,53]. Several studies have demonstrated that the use of bone substitute materials that are bioengineered with MSCs (mesenchymal stem cells) can significantly enhance bone healing and reconstruction, when compared to using MSCs alone or a bone substitute material without MSCs. This leads to the formation of new bone with improved biomechanical performance, which can improve the success rates of dental implant placement [7].

Future of Bone Substitute Materials in Dentistry:

Although criteria have defined ideal bone grafting materials for decades, autografts remain the only material possessing all four biological properties [53]. There has been a shift towards using alternative grafting materials and developing novel synthetic bone substitutes due to the limited availability and associated limitations of traditional grafting materials. [40].

Developing a material with a mechanically strong and interconnected porous structure that allows for optimal osseointegration and vascularization has been identified as the main challenge in bone substitute development. However, current synthetic bone substitutes only possess osteoconductive properties, which means that bone regeneration is limited to the outer surface layer [53].

In recent times, there is a growing interest in using osteoinductive growth factors and/or MSCs along with a structural scaffold to enhance the bone regenerative potential of the material, and prevent adverse inflammatory responses in the recipient. Another approach that is gaining popularity is the controlled time-release delivery of growth factors, which helps to maintain their bioactivity throughout the therapeutic window. The development of new grafting materials should prioritize incorporating as many ideal biological parameters as possible. At the same time, it is important to ensure that these materials are readily available, cost-effective, and supported by clinical evidence. However, these newer materials are often based on case reports or experimental animal models, which can raise questions about their reliability. To better understand the clinical viability and benefits of each material, more standardized preclinical and clinical studies need to be conducted and documented. This will enable the introduction of more commercially available products. [1]

Conclusion:

In summary, the future of using bone grafts for dental implants looks promising as advancements in biomaterials, regenerative therapies, and digital technologies continue. However, it is important to address the challenges related to patient diversity, graft resorption, complications, cost, and regulatory requirements to ensure the growth and success of the field.

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