Advances in Bone Grafting Materials for Dental Implants: A Review

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ABSTRACT

Bone grafting is a method by which bone deficient areas are built up with the use of different materials, such as autografts, allografts, alloplasts and xenografts. Bone graft materials are placed in different locations for various indications like in alveolar sockets post extraction, to refill a local bony defect due to trauma or infection, to refill a peri-implant defect due to peri-implantitis, for vertical and horizontal augmentation of the mandible and maxilla. Grafts materials acts as a filler and scaffold to help bone formation and promote wound healing. The dental implant therapy demands sufficient bone volume, biologic quality and certain dimensional properties for long term success. In many situations this makes bone grafting necessary along with the dental implant placement. Despite of the advancements in the field of bone graft materials and implants, the perfect bone reconstruction material for dental implant has not yet developed. The aim of this article is to provide a contemporary and comprehensive review of the bone graft materials that can be used in dental implants, discussing their properties, advantages, disadvantages, enlightening the present and the future perspective in the field of bone regeneration.

Keywords: Bone graft, Dental implant, Graft material.

INTRODUCTION

A bone graft is defined as a living tissue capable of promoting bone healing, transplanted into a bony defect, either alone or in combination with other materials [1,2]. A bone substitute is a natural or synthetic material, often containing only a mineralized bone matrix with no viable cells, that is able to achieve the same purpose [3]. Bone grafts and substitutes have been used in the medical field for centuries, with the first recorded use of bone grafts in 1682, where a cranial defect was successfully restored using a cranial bone graft from a deceased dog [4]. According to the US Food and Drug Administration (USFDA), bone grafts are classified as Class II devices (bone grafts filling the bony voids and defects) and Class III devices (bone graft containing drugs). The use of bone grafts and substitutes in dentistry have markedly increased in recent years due to advancements in dental implantology and the growing need for repair of craniofacial bony defects. These bony or skeletal defects may arise from trauma, periodontal disease, surgical excision, cranioplasty, infection or congenital malformations, and oral cancer.

Rationale for bone grafts:[4]
Placement of implants requires sufficient bone volume and biologic quality. This is due to the macro design of the implant, which demands certain dimensional properties for long-term success. Other factors which make bone grafting necessary are:

1. Resorption of the edentulous ridge post tooth extraction
2. Presence of bony defects due to trauma or infection
3. The need to place implants in strategic sites for functional and aesthetic success. In aesthetic areas, soft tissue requires a bony base since “soft tissue follows hard tissue”.

Characteristics of an Ideal Bone Grafting Material
The main function of bone grafts is to provide mechanical support and stimulate osteo- regeneration, with the ultimate goal of bone replacement [5]. The four fundamental biological properties of osseointegration, osteogenesis, osteoconduction, and osteoinduction, are paramount in performing this role effectively.

- The ability of a grafting material to chemically bond to the surface of the bone in the absence of an intervening fibrous tissue layer is referred to as osseointegration.
- Osteogenesis refers to the formation of new bone via osteoblasts or progenitor cells present within the grafting

material.

- Osteoconduction refers to the ability of a bone grafting material to generate a bioactive scaffold on which host cells can grow [5]. This structure enables vessels, osteoblasts and host progenitor cells to migrate into the interconnected osteomatrix. (Figure 1)
- Osteoinduction is the recruitment of host stem cells into the grafting site, where local proteins and other factors induce the differentiation of stem cells into osteoblasts. Multiple growth factors influence this process, including platelet-derived growth factors (PDGFs), fibroblast growth factors (FGFs) and transforming growth factors-β (TGFs-β). These four fundamental properties enable new bone formation which occurs in parallel to direct osseous interconnection.

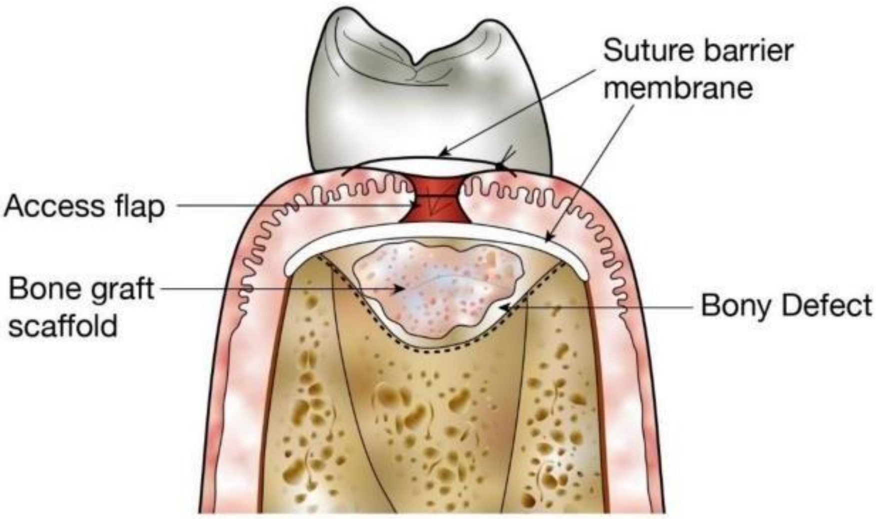

Figure 1. Use of structural scaffolds to restore bony defects. Diagram shows placement of a bone graft scaffold within a bony defect in alveolar bone following surgical generation of an access flap.

Factors required for success of bone graft

Below are the factors upon which success of bone graft depends: [6]

1. Osteoblasts: Only osteoblasts are responsible for new bone formation. For a graft to be successful, the graft matrix must contain osteoblasts. If there is an insufficient number of osteoblasts, the graft will fail.

2. Blood Supply: The bone grafting is a type of regeneration and not the repair. The term "repair" implies regaining of lost tissue; regeneration is a biologic process where not only the tissue is regained, but also its form and function. This requires a good blood supply to the graft and surrounding tissue. Blood is needed for cell viability and clot formation. The clot serves as the initial matrix where cells migrate and then serves as anchorage for the osteoblasts.

3. Graft Stabilization: Mechanical stresses on the graft during healing can lead to disruption of fibrin clot. Movement of graft material will cause fibrous tissue to fill the defect instead of bone. This is a form of repair and is not true regeneration. Fixation devices like guided bone regeneration (GBR) collagen membranes, titanium mesh and bone screws may be used.

4. No tension on the soft tissue: Bone is the slowest growing tissue. The GBR is based on the separation of grafted site from the surrounding soft tissue. This GBR membrane keeps the faster growing tissues like epithelium, fibrous tissue or gingival connective tissue out of the defect allowing controlled regeneration to occur with vital bone formation. The application of bone graft material into the defect prevents the collapse of the collagen membrane and it acts as a place holder for new regenerating bone and an osteoconductive scaffold for the in growth of blood vessels and osteoblasts.

Types of bone graft materials:[7]

Graft category	Graft type	Advantages	Disadvantages	Commercially available
Autograft Isograft	Extraoral: Cranium, Fibula, Iliac crest, Radius, Rib, Tibia Intraoral: Anterior maxillary sinus wall, Anterior nasal spine, Ascending ramus, Symphysis, Tuberosity, Palate,	- Osteogenic - Osteoinductive - Osteoconductive - No disease transfer or immunogenicity	- Donor site morbidity - Limited quantity - Possibility of general anaesthesia and hospitalization for extra-oral sites.	
Allograft	- Fresh and/or frozen bone, - FDBA - DFDBA	- Osteoinductive - Osteoconductive - Relative availability	- Possibility of disease transmission, immunogenicity - Variability of properties depending on productive method	Allogro, DBX, DynaBlast, Dynagraft, Grafton,
Xenograft	- Bovine - Porcine - Equine - Coralline - Algae	- Osteoconductive - High availability - Low cost	- Possibility of disease transmission, immunogenicity - Variability of properties depending on productive method	Algipore, Biocoral, Bio-Oss, Cerabone, Endobon, Gen-OS, Interporo 200,
Synthetic bone substitute	- $Ca_3(PO_4)_2$ - Hydroxyapatite - Calcium carbonate - Calcium sulphate - HTR Polymer - Bioactive glasses	- Osteoconductive - Availability - Low cost	- Variability of properties depending on productive method	Biogran, BonePlast, Calcibone, Cortoss, Eurobone, Perioglass,

Autograft:[7]

Autografts are considered the 'gold standard' among the various available grafting materials due to their osteogenic properties, maintaining viable cells from the donor to the recipient site as well as osteo-inductive characteristics since a variety of growth factors contribute to the differentiation of mesenchymal stem cells into osteoblasts. Autologous or autogenous bone grafting involves utilizing bone obtained from same individual receiving the graft. Sources of bone include iliac crest, mandibular symphysis, anterior mandibular ramus (coronoid process) and bone removed during osteoplasty and ostectomy. Whenever block graft will be performed, autogenous bone is the most preferred because there is less risk of graft rejection as the graft is originated from the patient's body. It would be osteoinductive, osteo-conductive as well as osteogenic. Disadvantage of autologous grafts is that additional surgical site is required, another potential location for post- operative pain and complications. Types of autografts include osseous coagulum, bone blend, cancellous bone marrow transplant and bone swaging.

Allograft: [7]

Allograft is derived from humans. The difference is that allograft is harvested from an individual other than the one receiving the graft. Allograft bone is taken from cadavers that have donated their bone so that it can be used for living people who are in need of it; it is typically sourced from a bone bank.3 They are available as cortical, cancellous or cortico-cancellous grafts, in various shapes and sizes. There are three types of bone allograft available:

Fresh or fresh-frozen bone: This is frozen at minus 80 degree centigrade to avoid degradation by enzymes, without further irradiation, lyophilization or demineralization process. It is acellular, possessing the highest osteo-inductive and osteo-conductive properties due to the presence of BMPs. However, this is not used anymore due to disease transmission and high immune response.

FDBA: This allograft undergoes dehydration and freezing without demineralization, leading to decreased antigenicity. It has only osteo- conductive potential.

DFDBA: This allograft undergoes dehydration, freezing and inorganic part of the bone is eliminated, leaving only the organic part that contains BMPs. These materials exhibit osteo-conductive and inductive features.

The use of allografts for bone repair often requires sterilization and deactivation of proteins which are normally found in healthy bone. The extracellular matrix of bone tissue contains bone growth factors, proteins and other bioactive materials necessary for osteo-induction and successful bone healing. The desired factors and proteins are removed from the mineralized tissue by using a demineralizing agent such as hydrochloric acid. The mineral content of the bone is degraded and the osteo-inductive agents remain in a demineralized bone matrix (DBM).

The advantages of allografts include availability in adequate quantities, sizes and shapes, predictable results and elimination of an additional donor site surgery. On the other hand, disease transmission from the donor to the recipient, although extremely small, cannot be totally excluded and additional testing for HIV, Hepatitis B virus, Hepatitis C virus and Treponema serologic markers should be performed. Higher absorption rate, immunogenic response and less revascularization compared to autologous grafts has been reported among the disadvantages of this grafting category.

Xenografts: [7]
These materials derive from donors of a different species relative to the recipient, usually possess osteoconductive features with limited resorptive. The disadvantages are the difference in bone characteristics of graft compared to humans, their processing procedure might affect their physico–chemical properties as in the case of allografts, the possibility of disease transmission and stimulation of immunogenicity. Two illustrations of xenografts used in dentistry are (i) coral- derived bone substitutes having geometry similar to that of human cancellous bone interconnected macropores (200-600 μm) and (ii) demineralized bovine bone grafts, biocompatible and osteoconductive.

1. **Coral substitutes:** Coral bone grafts have been also applied in jaw defects, exhibiting osteoconductive properties and functioning as carriers for growth factors, improving bone formation. They present initial poor mechanical strength, favourable to blood supply of recipient cite and fast resorption rate. Several studies have reported the ability to implement this material in dentoalveolar reconstruction with encouraging results.

2. **Bovine substitutes:** Bovine origin bone substitutes were the first xenografts applied to patients. They are commercially available in a wide range of products and is considered among the most documented materials of this category. They have osteoconductive properties, being deproteinized and lyophilized, causing no immune response. However, granules of these materials are considered to be subjected to poor or slow absorption23. Processing at high temperatures to avoid immune reactions, allergies and infectious diseases such as spongiform encephalopathy is considered responsible further reduced absorption potential.

Alloplastic materials/Synthetic variants: [7]
These biomimetic materials characterized by osteoconductive, with no osteoinductive or osteogenic potential on their own. They act as a three-dimensional scaffold to support cell growth and bone formation, increase cell adhesion and proliferation. Flexible hydrogel- hydroxyapatite (HA) composite which has a mineral to organic matrix ratio, approximating that of human bone. Artificial bone can be created from ceramics such as calcium phosphates (e.g., HA and tricalcium phosphate), bio-glass and calcium sulphate as they are biologically active depending on solubility in physiological environment.26 These materials combine with growth factors, ions such as strontium or mixed with bone marrow aspirate to increase biological activity. The presence of elements such as strontium can result in higher bone mineral density (BMD) and enhanced osteoblast proliferation.

Calcium phosphate: These materials have gained special interest due to their composition similarity with natural bone. Hydroxyapatite (HA) and tricalcium phosphate (TCP) are the most important players of this category, further classified into ceramics and cements. The ceramics are subjected to heat treatment called sintering, further driving to a porous and solid material. Cements are produced in the form of paste which hardens after application within the bone defect site. [8,9]

Tricalcium phosphate (TCP): exhibits good biocompatibility and osteo- conductivity, but lacks osteogenic or osteoinductive properties. Its porous composition permits phagocytosis, absorption, vascularization and bone regeneration. In accordance to other calcium phosphate preparations, it has been found to be brittle and weak under tension and shear, but resistant to compressive loads. Compared to HA, TCP is more quickly resorbable and less mechanically stable.

HA, representing the main structural inorganic component of bones and teeth has excellent biocompatibility with the human body and can therefore be used as a bone graft. HA crystals possess mainly osteo-conductive properties and low resorption rate while they are brittle and fracture prone on shock loading. This bone implant has been established as an excellent carrier of osteoinductive growth factors and osteogenic cell populations.[10]

Biphasic calcium phosphate (BCP): results from the mixing of TCP and HA in various concentrations in order to attain desired mechanical properties and absorption rate. Calcium sulphate: Calcium sulphate, commonly known as Paris gypsum, was first used as a bone substitute in 1892 for the filling of long bones tubular cavities. It is provided in the form of cement or granules, both products exhibiting biocompatibility, bioactivity, tolerability, carrier material capability, osteo-conductivity, easy handling and low cost. Rapid absorption of the material has been noted than the rate of bone formation. In the field of dentistry, it has been extensively applied in periodontal, dentoalveolar and tooth extraction defects.[10]

Hard tissue replacement (HTR) polymeric substitutes: The most important of the polymers used in bone augmentation is polymethyl methacrylate, a porous biomaterial exhibiting osteoconductive properties, compressive strength and elasticity similar to cortical bone, but not resorbable. The high temperature which is developed during the polymerization, depending on the exact cement composition may create thermal bone necrosis, damage of blood circulation and membrane formation between bone cement interfaces.

Bioactive glass: Bioactive glass material composed of active silicate-based glass; this implant exhibits significantly greater strength compared to calcium phosphates.

It is capable of forming a strong bond between the glass and the host bone through hydroxyapatite crystals, a phenomenon called bioactivity. The resorption of bioactive glass is variable, based upon the relative amounts of components like sodium oxide, calcium oxide, silicon dioxide and phosphorous present.

Composite Grafts: [11]
Composite grafts are a combination of different bone graft materials, often mixing autografts or allografts with synthetic or xenograft materials. These grafts aim to provide both the structural support of natural bone and the osteoinductive properties of autografts or allografts.

Guided bone regeneration in implant dentistry: [12,13]
Guided Bone Regeneration (GBR) is a surgical technique commonly employed in implant dentistry to augment and regenerate bone in areas where it is insufficient for implant placement. GBR is an essential part of implant treatment planning, as a stable and sufficient bone foundation is crucial for the long-term success of dental implants.

Purpose of GBR:
GBR is primarily used to create a stable and suitable environment for dental implant placement when there is inadequate bone volume or when the available bone is compromised due to factors such as periodontal disease, trauma, or atrophy (Figure 2).

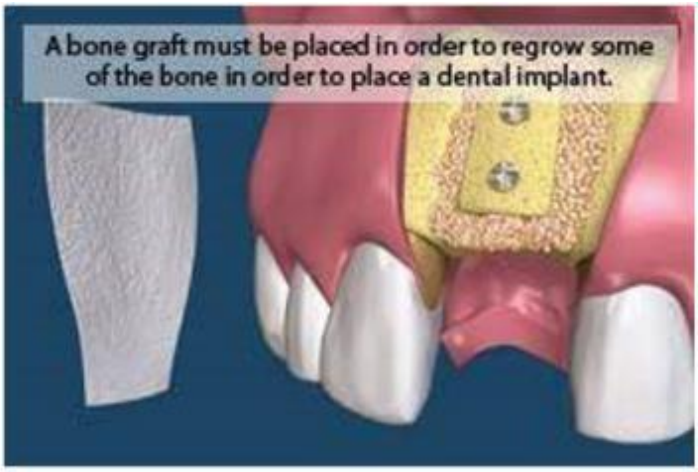

Figure 2: Guided bone regeneration in implant dentistry

Key Components of GBR:
Barrier Membrane: A barrier membrane is placed over the surgical site to protect it from soft tissue invasion and promote undisturbed bone regeneration. Membranes can be resorbable or non-resorbable, and the choice depends on the specific case and surgeon's preference. Bone Graft Material: Various types of bone graft materials, such as autografts, allografts, xenografts, and synthetic materials, are used to fill the bony defect and stimulate new bone formation. Sutures: Sutures are used to secure the barrier membrane and graft material in place.

GBR Procedure:
The surgical procedure begins with an incision to access the underlying bone, followed by careful reflection of the soft tissues. The bony defect or area requiring augmentation is prepared, often involving debridement and cleaning. The bone graft material is placed in the defect area to support new bone formation. Depending on the case, this may involve bone chips, granules, or blocks. A barrier membrane is positioned over the graft material to isolate the site from the overlying soft tissues. The soft tissues are then sutured in place to ensure closure and healing.

Healing and Integration:
Over the following months, bone regeneration takes place. The membrane prevents soft tissue interference while allowing new bone to form. Once adequate bone volume is achieved, the area is considered ready for dental implant

placement.

Future Prospects: [14]

1. Advancements in Biomaterials: Continued research in biomaterials is likely to lead to the development of more advanced and biocompatible graft materials. These materials may enhance bone regeneration and reduce complications associated with traditional grafting materials.

2. 3D Printing and Customization: The use of 3D printing technology to create custom bone grafts and implants is a growing area of interest. Customized grafts can improve the precision of graft placement and the integration of dental implants.

3. Regenerative Therapies: Emerging regenerative therapies, such as growth factors and gene therapy, have the potential to accelerate and enhance bone regeneration. These therapies may become more widely used to improve grafting outcomes.

4. Minimally Invasive Techniques: Advances in minimally invasive surgical techniques may reduce patient discomfort and recovery time, making bone grafting for dental implants more accessible and convenient.

5. Digital Technologies: The integration of digital technologies, such as computer- guided surgery and virtual planning, will continue to improve the accuracy and predictability of bone grafting procedures.

Challenges:[15]

Patient-Specific Variability: Each patient's bone quality and quantity vary, making it challenging to predict and ensure the optimal grafting outcomes in every case.

Graft Resorption: Resorption of graft material can occur over time, potentially affecting implant stability. Research is ongoing to develop graft materials with reduced resorption rates.

Infection and Complications: There is a risk of infection and other complications following bone grafting procedures, which can impact the success of dental implant placement.

Cost and Accessibility: High-quality graft materials and advanced technologies can be costly, making treatment less accessible for some patients. Reducing costs while maintaining quality remains a challenge.

Biological Compatibility: Achieving optimal biological compatibility with graft materials is an ongoing challenge. Compatibility issues can lead to graft rejection or complications.

Regulatory Hurdles: Developing and implementing new graft materials, especially those derived from innovative sources, may face regulatory hurdles and require rigorous testing and approval.

Education and Training: Dentists and oral surgeons must continually update their knowledge and skills to keep up with the evolving field. Education and training programs need to adapt to include the latest techniques and technologies.

CONCLUSION

In summary, the field of bone grafting for dental implants holds great promise with ongoing advancements in biomaterials, regenerative therapies, and digital technologies. However, addressing the challenges related to patient variability, graft resorption, complications, cost, and regulatory requirements will be crucial for the continued growth and success of this field. Moreover, ensuring that education and training programs keep pace with these advancements will be essential for providing the best care to patients.

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