BIOMATERIALS USED IN ALVEOLAR BONE REGENERATION: A NARRATIVE REVIEW

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Abstract

Objectives. Although the range of biomaterials applicable for alveolar bone regeneration has expanded considerably over the last two decades, uncertainty persists regarding the best selection from autogenous, allogeneic, xenogeneic, synthetic and composite options. This narrative review sought to critically evaluate the current evidence on the biological rationale and clinical performance of these materials, with a focus on their mechanisms of action in the context of implant-prosthetic rehabilitation. **Materials and Methods.** A structured literature search was conducted in PubMed/MEDLINE, PubMed Central, Scopus and Web of Science, covering publications from 2000 to 2025. Narrative reviews, systematic reviews, randomized controlled trials and cohort studies were included. Primary outcomes were bone volume gain, graft integration rate, implant survival in augmented sites, resorption dynamics and complication profiles. Data were synthesized narratively due to heterogeneity among included studies. **Results.** Autogenous bone is gold standard, combining osteogenesis, osteoinduction and osteoconduction within a single material, though donor site morbidity and limited harvest volume limit its use in alveolar bone grafting. Allografts and xenografts provide reliable osteoconductive scaffolds, while demineralized bone matrix preserves have osteoinductive potential. Synthetic substitutes — hydroxyapatite, beta-tricalcium phosphate, calcium sulphate, bioactive glasses and calcium phosphate cements — have the advantage of limited resorption rate. Composite materials and growth factor-enriched represent promising biomaterials for alveolar bone grafting. No currently available material fulfils all criteria of an ideal bone substitute, and outcomes remain dependent on defect morphology, residual bone quality and systemic patient factors. **Conclusions.** Material selection for alveolar bone regeneration should follow a defect-specific and patient-centred approach, in which biological augmentation is viewed as synergistic to scaffold-based strategies. Further progress requires improved clinical trial design and deeper integration of regenerative biology into routine implant-prosthetic treatment planning.

Key words: biomaterials, alveolar bone, grafting, osteoconduction, osteogenesis

INTRODUCTION

A functional and stable mandibular implant-prosthetic restoration in posterior area can be compromised on long term due to shape and orientation of the residual alveolar bone, improper sagittal intermaxillary relationships as well as the presence of mandibular inferior nerve. The enhancement of alveolar bone volume and quality is requested. However, the high density and low vascularization of the mandibular cortical bone can hinder an effective grafting on the mandible body or regeneration processes of some bone chambers [1].

A various range of bone regenerative bone have been proposed to create conditions for long term success of the implant-prosthetic restorations in mandible posterior areas (Guided Bone Regeneration, distraction osteogenesis, alveolar ridge splitting techniques, bone expansion techniques, bone grafting techniques) [2, 3].

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Every surgical technique has advantages and disadvantages, but specialists should give priority to those procedures which are easy-to-use (according to the practical experience of the clinician), less invasive, have lower risk of complications, and allow osteointegration of dental implants within the shortest post-operatory time [4]. Despite high number of studies related to the reconstruction of resorbed alveolar bone, data are controversial regarding the success rate on medium and long term due to insufficient methodological quality (inadequate sample size, lack of well-defined success criteria, insufficient follow-up) [4].

Significant changes in the volume and quality of the prosthetic field require corrective interventions involving the collaboration of prosthodontists, implantologists and oral surgeons [5]. In recent years, patient demand for complex oral rehabilitation treatments has increased, and the production of bone reconstruction and guided tissue regeneration materials has grown and diversified. In this context, the selection of guided tissue regeneration techniques, bone augmentation materials and barrier membranes, and the surgical protocol exert both a direct and indirect influence on the magnitude and distribution of future occlusal forces transmitted to the prosthetic restoration and on the mucosal-osseous support. Pre-implant surgical procedures are designed on the basis of the biological conditions required to enable bone regeneration [6].

Guided tissue regeneration involves the use of membranes as a barrier against epithelial proliferation and as a stimulatory environment for osteogenesis, allowing tissues to regenerate the bony defect by blocking invasion by unwanted cells [7]. Guided tissue regeneration techniques rely on the use of grafting materials with osteogenic, osteoinductive or osteoconductive properties, enabling the restoration of deficient alveolar areas. Rigorous sealing of these materials facilitates the formation of high-quality bone. This sealing of the bone augmentation material can be achieved using resorbable or non-resorbable membranes. This approach confers improved primary stability, facilitates implant placement into mature bone that can be clinically assessed and deemed suitable for dental implant insertion at that site. Volumetric correction of edentulous ridge atrophy using autologous, allogeneic or heterologous grafts aims to recreate a microenvironment identical to that of autogenous cortico-cancellous bone. By inserting and stabilizing materials that provide effective osteoconduction, osteogenic cells are induced to adhere to these biomaterials and form an osteogenic matrix. Bone regeneration techniques employ grafting materials — xenografts, allografts and alloplastic substitutes — which serve as a matrix for new bone tissue formation, becoming integrated into the newly formed bone and being gradually resorbed as they are progressively replaced by neoformed osseous tissue [8].

MATERIALS AND METHODS

Search Strategy

The identification of relevant studies was carried out by consulting the electronic databases PubMed/MEDLINE, PubMed Central (PMC), Scopus, and Web of Science. The literature search was performed using combinations of keywords and MeSH terms such as: „alveolar bone”,

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„resorption” „grafting” "biomaterials", „autogenous”, "alloplast", „xenografts” „allogeneic”. Search terms were used both individually and in Boolean combinations (AND/OR) to maximize retrieval of relevant records. Priority was given to studies available in full text via PMC Open Access.

Selection Criteria

Eligible designs included randomized controlled trials, prospective and retrospective observational studies, cohort and case-control designs, and clinical investigations reporting outcomes of bone augmentation procedures in patients treated with implant-prosthetic rehabilitation. Systematic reviews and meta-analyses were included when they assessed graft success or failure, implant survival in augmented sites, complication rates, or the long-term clinical behavior of bone substitute materials. Narrative reviews from guidelines and authoritative sources in oral surgery, implant dentistry, and regenerative dentistry were also considered when they provided substantive and clinically relevant insight. Studies were required to report measurable clinical outcomes — including bone volume gain, graft integration rate, implant survival, and resorption dynamics — over a defined follow-up period, with specific outcome measures such as peri-implant bone stability, resorption rates, and complication rates. Evidence that could not be linked to tangible patient outcomes was considered insufficient for inclusion.

Evidence that could not be anchored to real patient outcomes was not considered sufficient. The exclusion criteria followed the same logic in reverse. Animal studies without meaningful clinical translation, publications predating 2000, and investigations with no direct relevance to bone augmentation in the context of implant site preparation were set aside. Studies confined to laboratory work, material testing, or *in vitro* characterization were excluded if they reported no clinical outcomes. Publications addressing prosthetic performance in isolation from the regenerative phase, and those whose data were too sparse or incomplete to contribute to synthesis, were similarly excluded.

Data Extraction and Quality Assessment

Two reviewers worked independently through each included study, cross-checking their findings to reduce the risk of selective extraction or oversight. For every article, a standardized set of variables was recorded: study design and level of evidence; sample size and patient profile; type and extent of the alveolar bone defect; the category and composition of the augmentation material used; membrane type where relevant; and the length of follow-up. Clinical outcomes — bone volume gain, graft integration, implant survival in augmented sites, and resorption dynamics — were captured alongside markers of success or failure, including biological and mechanical complications, maintenance needs, and peri-implant bone stability.

LITERATURE REVIEW

1. General aspects

The selection of bone graft type is determined by the patient's systemic status, the osteogenic potential of the recipient site, and the available maturation time.

The properties of an ideal bone augmentation material are as follows [9]: biocompatibility; absence of toxicity;

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mechanical stability; uniform porous structure; uniform bone resorption; stimulation of bone tissue formation; low cost.

Alveolar bone addition biomaterials are classified into [10]:

- Autologous bone tissue (autografts) — graft harvested and transplanted from the same patient; possesses osteogenic, osteoconductive and osteoinductive properties.
- Homologous bone tissue (allografts) — processed human bone that can be stored in bone banks; the bone may be freeze-dried and demineralized (Demineralized Freeze-Dried Bone, DFDB) or freeze-dried only (FDB).
- Heterologous bone tissue (xenografts) — processed from one species and applied to another (bovine, porcine bone, etc.); collagenated porcine grafts exhibit high porosity, and the collagen component promotes mineral deposition and neovascularization; current data have demonstrated that this biomaterial is compatible with human bone and, once transplanted, exhibits osteoconductive integration properties without signs of adverse reactions (animal studies) [11].
- Synthetic alloplastic grafts:
    - Hydroxyapatite — enhanced osseointegration capacity;
    - Tricalcium phosphate $Ca_3(PO_4)_2$ — releases Ca and Mg ions into bone tissue during resorption, with inductive activity for alkaline phosphatase production;
    - Bioactive glass — osteoconductive properties.

A classification of grafting biomaterials with potential use in alveolar bone rehabilitation is shown in Table 1 [9].

Table 1. Classification of Bone Graft Materials [9]

No.	Category	Subcategory / Type	Examples / Products
1	Natural Bone Bone Substitute Materials	Autogenous Bone	Harvested from the same patient (iliac crest, chin, mandibular ramus)
		Allograft Materials	Demineralized bone matrix (DFDB, FDBA)
		Xenograft Materials	Bovine bone, porcine bone, chitosan, silk
		Phytogenic Materials	Coral- or marine algae-based materials
2	Synthetic Bone Substitutes	Hydroxyapatite	Synthetic HA, natural HA (Cerabone, Bio-Oss)

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No.	Category	Subcategory / Type	Examples / Products
		Beta-tricalcium phosphate ceramic (beta-TCP)	Cerasorb, ChronOS
		Calcium Sulphate	Osteoset, Allomatrix
		Polymers	Biodegradable and non-degradable polymers; Healos (collagen + HA)
		Bioactive Glasses	Bioglass, Cortoss
		Calcium Phosphate Cements	BoneSource, Calcibon, Norian SRS
		Metals	Titanium, metal alloys for reconstruction
3	Composite Bone Substitutes	NanoBone	HA nanoparticles in a bioactive glass matrix
		Fortoss Vital	Combination of bioactive glass + beta-TCP
		SmartBone	Bovine bone + resorbable polymers + collagen
4	Bone Substitutes with Vital Osteogenic Cell Infusion	Osteotransplant Dent	Bone matrix with live autologous osteogenic cells
		Bioseed-Oral Bone	Autologous osteogenic stem cells on scaffold
5	Bone Substitutes with Growth Factors	BMP (Bone Morphogenetic Proteins) and derivatives	Osigraft (OP-1/BMP-7), Augment (rhPDGF-BB), Infuse (rhBMP-2)

Source: Zhao R, Yang R, Cooper PR, Khurshid Z, Shavandi A, Ratnayake J. Bone Grafts and Substitutes in Dentistry: A Review of Current Trends and Developments. Molecules. 2021;26(10):3007.

2. Mechanisms of Action and Properties of Bone Augmentation Materials

The mechanisms of action of bone augmentation materials are based on four properties [12]: osteoconduction; osteoinduction; osteopromotion; osteogenesis.

Osteoconduction refers to the property of supporting new bone tissue formation within the structure of the grafting material. Osteoblasts located at the periphery of the graft utilize the graft structure as a matrix that enables bone tissue formation [12].

Osteoinduction refers to the capacity of the material to stimulate the differentiation of precursor cells into osteoblasts and the formation of new bone tissue. The most well-known cellular mediator is bone morphogenetic protein (BMP), which is incorporated into certain bone augmentation materials [13]. Augmentation materials that also exhibit osteoconduction support a superior rate of bone regeneration compared to materials based exclusively on osteoconduction [12].

Osteopromotion is the capacity of the material to stimulate osteoinduction —

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that is, the differentiation of new osteoblasts — without itself possessing osteoinductive properties. Enamel matrix derivative products are introduced in combination with demineralized bone-derived materials to enhance their osteoinductive properties [12, 13].

Osteogenesis is the property characteristic of autogenous materials, which incorporate vital osteoblasts within their structure and thereby accelerate new bone tissue formation [12].

The bone remodelling cycle involves osteoclast activation, resorption and bone formation. Understanding these mechanisms enables the clinician to make an appropriate selection for the optimal therapeutic approach.

Bone graft integration occurs through the following three biological mechanisms:

- Osteogenesis — the intrinsic bone synthesis property of the graft;
- Osteoinduction — enables new bone formation from mesenchymal cells through a complex of growth factors and hormones present in the extracellular matrix, which migrate successively to the new site where differentiation into osteoblast cells occurs;
- Osteoconduction — provides exclusively a structural support for the formation of neoformed bone tissue.

The major factors that may affect bone graft healing are the following:

- Type of graft material;
- Local biological factors (quality of vascularization);
- Local infectious factors;
- Local mechanical factors (stability and biomechanical loading);
- Systemic factors (nutritional status, medication, systemic conditions, smoking).

The factors influencing the rate and volume of post-grafting resorption are the following:

- Bone graft volume;
- Quality of the grafting material;
- Quality of the recipient bone bed;
- Biomechanical properties;
- Adhesion.

3. Autogenous Materials

Autogenous materials consist of bone harvested from an osseous donor site of the same patient and transferred to the implant site. Autogenous bone harvesting is the only means of delivering osteogenic cells directly to the recipient site and is considered the gold standard in guided bone regeneration techniques [8]. According to their structure, bone grafts are classified as: cortical (chin, mandibular body); cancellous (iliac crest); and cortico-cancellous (iliac crest). Cortico-cancellous bone grafts are frequently employed in edentulous ridge reconstruction owing to the resistance conferred by the cortical layer. They may be used for the reconstruction of bone defects of up to 5 cm, but require rigid fixation to the recipient bone to ensure optimal healing [4]. Harvesting from the iliac crest offers the following advantages [14]: increased bone marrow volume; osteogenic properties; graft volume; enhanced accessibility.

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Autogenous bone grafts harvested from the mandibular ramus have the advantage of a reduced morbidity rate, although the available bone volume for grafting is significantly smaller [15]. The principal mechanisms of action in guided tissue regeneration techniques employing autogenous bone grafts are the following:

- Osteogenesis — in the presence of undifferentiated stem cells;
- Osteoinduction — transformation of undifferentiated stem cells into osteoblasts;
- Osteoconduction — physical matrix that stimulates the deposition of neoformed bone tissue from adjacent bone and the adhesion of mesenchymal cells to the graft surface.

The general disadvantages of autogenous bone grafts are the following [8]: occasionally insufficient available bone volume; unpredictable bone resorption; requirement for a second surgical intervention; complications at the donor site.

4. Allograft Materials

Allograft materials are bone grafts harvested from another individual of the same species and used in a different patient. They are sourced from bone banks that store materials harvested from cadavers and consist of demineralized or mineralized bone matrix. These materials are characterized by a complex of growth factors, proteins and bioactive agents that stimulate both osteoinduction and osteogenesis. To release growth factors and bioactive agents from mineralized tissues, the materials are demineralized using hydrochloric acid. Following degradation of the inorganic structure, bioactive agents are retained within the demineralized bone matrix [12]. Three types of allogeneic materials exist [12]:

-Fresh-frozen bone;
-FDBA (Freeze-Dried Bone Allograft) — freeze-dried and demineralized bone;
-DFDBA (Demineralized Freeze-Dried Bone Allograft) — freeze-dried bone.

Allograft materials have been proposed for stimulating bone formation on the basis of two properties: osteoconductive properties (containing vital cells); and osteoinductive properties. The advantages of allografts in guided tissue regeneration techniques are as follows [8]:

-Avoidance of a secondary surgical site, thereby reducing the risk of complications;
-Allows obtaining a larger volume of bone graft;
-The use of allotransplants is associated with a minimal risk of antigenic reactions and infection transmission [16];
-Low failure rate at 4–9 months postoperatively [17];
-Allows achieving a mean bone gain of 2 mm in height and 4.79 mm in width [18, 19].

The limitations of allogeneic bone grafts in guided tissue regeneration techniques are[8]:

-Frequent requirement for sterilization;
-May require protein inactivation;
-Longer period of new bone tissue formation;
-Reduced rate of bone regeneration;
-High resorption rate.

5.Xenografts

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Xenografts are widely used materials in guided tissue regeneration techniques. Xenograft materials are obtained from bovine and porcine bone that undergone processing to remove all organic matter but preserve the mineral scaffold. Xenografts have a composition that is very similar to human bone, structurally and chemically compatible with the host bone. The deproteinization process removes antigenic constituents and decreases the chances of cross-species immunogenicity. Xenografts have an irregularly porous, osteoconductive matrix, which allows for cell attachment and ingrowth of vessels complemented with new bone formation. The most widely known xenograft materials are natural hydroxyapatite and anorganic bone matrix-based materials (Cerabone, Bio-Oss), which serve as a matrix for neoformed bone tissue, becoming integrated into human bone tissue and being gradually replaced by newly formed bone [8]. Other sources, highly biocompatible and biodegradable have been incorporated into xenogeneic-derived biomaterials, such as chitosan, a polysaccharide derived from crustacean shells [12]. Their advantages derive from the superior bone quality they provide compared to autogenous bone [20-26] or allograft materials [27-31].

6. Alloplastic Materials

Alloplastic bone substitute materials are synthetically derived. Alloplastic materials include: calcium carbonate; calcium sulphate; bioactive glass polymers; synthetic hydroxyapatite; and tricalcium phosphate. The most frequently used are synthetic hydroxyapatite, calcium phosphate-based ceramic materials and bioactive glass.

Synthetic hydroxyapatite is osteoconductive, biocompatible, resistant and inert, and is considered an excellent matrix for incorporating growth factors and osteogenic cells. Its disadvantages include a higher percentage of residual material compared to tricalcium phosphate-based materials, which may impair healing processes [32]. However, guided bone regeneration techniques using natural hydroxyapatite demonstrate consistently high success rates [32, 33].

Tricalcium phosphate-based materials have a porous structure with a resorption rate that allows simultaneous resorption and new bone tissue formation. In bone reconstruction procedures, their integration rate and stability are comparable to those of autogenous bone grafts. A study demonstrated superior osteoconductive capacity and greater volumes of newly formed alveolar bone tissue for tricalcium phosphate-based alloplastic materials when compared to bovine bone xenografts [34, 35].

Numerous alloplastic augmentation materials combine ceramics with calcium sulphate, bioactive glass, tricalcium phosphate and hydroxyapatite. These materials are osteoconductive and, when combined with growth factors, acquire osteoinduction properties [36, 37].

Polymer-based materials are classified as biodegradable and non-degradable. This category includes ceramic polymer composites combined with collagen fibres, as well as resin-based materials. Degradable polymers offer the advantage of complete resorption and the absence of foreign bodies, with very low rates of postoperative complications. The limitations and disadvantages of alloplastic bone grafts in guided tissue regeneration

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techniques are as follows [36, 37]: longer period of new bone tissue formation; reduced rate of bone regeneration; higher resorption rate compared to autogenous bone grafts; allow proteins and growth factors to adhere to the graft surface; mechanical stability; available volume; dimensional stability; absence of immunological reactions. A significant advantage of alloplastic materials is the absence of infections and rejection reactions [38].

CONCLUSIONS

The outcome of any regenerative procedure is shaped by the interplay of defect morphology, surgical technique, and the individual patient's biological regenerative capacity, as well as the selected grafting biomaterial. Autogenous bone fulfils the three essential requirements of bone regeneration — osteogenesis, osteoinduction, and osteoconduction. Allogeneic and xenogeneic grafts have established themselves as dependable osteoconductive scaffolds, while synthetic alloplastic substitutes offer the additional advantages of reproducible physicochemical behaviour and complete elimination of disease transmission risk. However, no currently available material can replicate the biological complexity of alveolar bone. Finding an ideal bone substitute that combines osteogenicity, low resorption, mechanical stability, and ease of handling, remains an active area for future research. Emerging strategies such as composite biomaterials, cell-based therapies, and growth factor delivery systems will close these gaps and may expand the range of biomaterials available for alveolar bone regeneration. Understanding the mechanisms, properties, and clinical indications of each material class remains indispensable for material selection tailored to the specific demands of each patient and alveolar bone defect configuration.

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