RESEARCH PAPER

From Repair to Regeneration: The Integration of Growth Factors in Periodontal Bone Grafting: A Literature Review

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ABSTRACT

The primary objective of periodontal therapy extends beyond the mere maintenance of periodontal health; it should also encompass the regeneration of hard and soft tissues compromised by disease. Periodontitis, a persistent inflammatory condition, progressively damages the supporting structures of the teeth, including the alveolar bone, potentially resulting in tooth loss if not addressed. To counteract this, bone grafting procedures are employed to reconstruct the lost bone using either autogenous tissue or graft substitutes. Among these, demineralized freeze-dried bone allograft (DFDBA) has been widely used for over four decades due to its osteoinductive properties. The fundamental purpose of any grafting material is to stimulate new bone formation and restore structural integrity. In recent years, the integration of bioactive agents such as growth factors into graft materials has significantly enhanced their regenerative capabilities. These polypeptide hormones regulate vital cellular functions such as proliferation, chemotaxis, and extracellular matrix production, thereby accelerating tissue repair. Numerous commercially available graft products now incorporate various combinations of growth factors, offering improved clinical outcomes and presenting a promising approach to periodontal regeneration. This review highlights the diverse range of bone grafts and biomaterials used in regenerative periodontal therapy, emphasizing their evolving role in modern clinical practice.

Keywords: Autograft, Allograft, Biomaterial, Bone graft, Growth factors, Periodontal regeneration

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INTRODUCTION:

Periodontal disease, particularly periodontitis, is a chronic inflammatory condition that leads to the progressive destruction of the supporting structures of the teeth, including the alveolar bone. One of the most significant clinical challenges in periodontology is the management of intraosseous defects caused by this bone loss. These defects may occur as isolated lesions or in various complex combinations, depending on the extent and pattern of tissue destruction. The ultimate goal of periodontal therapy in such scenarios is not merely to halt the progression of disease, but to regenerate the lost components of the periodontium—namely, the alveolar bone, periodontal ligament (PDL), and cementum.[1]

Bone grafting has emerged as a cornerstone surgical technique in the regeneration of these lost tissues.[2] The procedure involves the placement of graft materials derived from various sources such as autografts (from the patient's own body), allografts (from human donors), xenografts (from animal sources), alloplasts (synthetic substitutes), or newer biologically enhanced alternatives. Bone tissue is unique in its ability to regenerate completely, provided that an appropriate scaffold and adequate space are maintained. As natural bone grows, it gradually replaces the graft material, resulting in a structurally and functionally integrated new bone.[3]

The foundation for bone grafting in periodontal therapy was laid as early as by **Hegedus**[4] and later

reintroduced by **Nabers and O'Leary**[5]. Initial approaches relied primarily on biologically inert materials that acted as passive scaffolds. However, while these conventional grafts—autografts, allografts, xenografts, and alloplasts—provided some structural support, they lacked the biological potential to stimulate or direct bone regeneration, particularly in cases marked by osteogenic deficiency.

To overcome these limitations, modern advancements in regenerative dentistry have ushered in what is now referred to as the "Second Technological Trend." This phase incorporates bioactive elements such as living cells, gene constructs, and most notably, growth factors (GFs) into traditional grafting materials.[6] Growth factors are naturally occurring polypeptides that regulate key cellular processes, including chemotaxis, proliferation, differentiation, and matrix synthesis. Their integration into grafts has significantly amplified the regenerative outcomes by accelerating bone formation and increasing the height, volume, and density of new bone.[7] Consequently, these growth factor-enriched bone grafts have enhanced clinical success rates, offering not only improved anatomical reconstruction but also better functional outcomes and overall quality of life for patients.

Modern bone grafts are classified into various categories based on their composition and mechanism of action. These include:

1. Autografts – harvested from the same individual,
2. Allografts – derived from human donors,
3. Xenografts – obtained from other species,
4. Alloplasts – synthetic, inorganic materials,
5. Factor-based bone grafts – enriched with biologically active molecules like growth factors,
6. Cell-based bone grafts – containing living cells that promote osteogenesis, and
7. Polymer-based bone grafts – combining structural and biofunctional elements.[8]

Periodontal regeneration has undergone a transformative evolution with the advent of bone grafts containing growth factors. Traditional bone grafting, though effective in providing a scaffold for new bone formation, often lacked the biological cues necessary for optimal tissue regeneration.[9] Modern bone graft materials have shifted from passive scaffolds to biologically active constructs—capable of stimulating and directing tissue regeneration. This leap in periodontal therapeutics is largely attributed to the integration of growth factors into grafting materials, leading to enhanced osteogenesis, angiogenesis, and ultimately, clinical outcomes.[10] These grafts are designed to be osteoconductive, osteoinductive, and in some cases, osteogenic, incorporating bioactive elements that mimic or enhance the natural regenerative environment.

Biological Basis of Growth Factor-Enhanced Bone Grafts:

To understand the effectiveness of these materials, it is crucial to appreciate the biological processes they engage:

- **Osteoconduction**: The graft material acts as a scaffold over which new bone can grow, guided by osteoblasts from the surrounding bone.
- **Osteoinduction:** The material induces differentiation of mesenchymal stem cells into osteoblasts, often facilitated by BMPs and other growth factors.
- **Osteopromotion:** Aids osteoinduction indirectly, enhancing its effects without being independently osteoinductive.
- **Osteogenesis:** Involves direct contribution of viable osteoblasts (e.g., from autografts or stem cell-based grafts) to bone formation.[11]

An ideal graft material should fulfill these characteristics while being biocompatible, predictable, clinically feasible, and minimally invasive.

Current trends in particulate bone grafting

1. Sticky Bone

Sticky bone represents a pioneering step in periodontal regeneration, where injectable platelet-rich fibrin (i-PRF) is combined with particulate bone grafts to form a cohesive, moldable matrix rich in concentrated growth factors (CGFs). These include:

- Platelet-Derived Growth Factor (PDGF)
- Transforming Growth Factor (TGF)
- Vascular Endothelial Growth Factor (VEGF)
- Epidermal Growth Factor (EGF)
- Insulin-like Growth Factor (IGF)

The fibrin matrix provides mechanical integrity and prolongs the release of growth factors, leading to enhanced cell migration and proliferation, greater vascularization, reduced graft migration, minimized

resorption during healing.[12]
Sticky bone's autologous nature and ease of preparation make it an excellent candidate for wide clinical adoption.

2. Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) containing bone graft

Infuse® Bone Graft consists of rhBMP-2 delivered on an absorbable collagen sponge. FDA-approved since 2007 for sinus and ridge augmentations, it promotes osteoinduction through MSC recruitment and differentiation, enhanced bone volume in challenging defect sites. Despite some adverse effects (e.g., inflammation, ectopic bone formation), rhBMP-2 remains a critical option, especially in patients with impaired healing capacity, such as smokers or diabetics.[13]

3. Platelet-Derived Growth Factor-BB (PDGF-BB) containing bone graft

PDGF-BB is a potent mitogen and chemoattractant that influences fibroblasts, mesenchymal stem cells, and osteoblasts. It also promotes angiogenesis, crucial for bone regeneration.

Key products include: **Gem 21S®:** A combination of rhPDGF-BB and β-Tricalcium Phosphate (β-TCP), approved by the FDA for periodontal and peri-implant defects. **Augment®** Bone Graft: Similar composition with β-TCP scaffold that prevents tissue collapse and enhances defect fill. These grafts exhibit rapid bone formation, stable tissue integration, and minimal immunogenicity.[14]

4. Allogeneic Morphogenetic Proteins : OsteoAMP®

OsteoAMP® preserves native human growth factors (up to 23 types), including BMP- 2, BMP-7, TGF-β1, VEGF, FGF, Angiopoietin-1. Unlike recombinant options, OsteoAMP® retains natural extracellular matrix components, reducing the need for synthetic carriers. Its formulation into mineralized cortical-cancellous chips adds structural strength to support functional load-bearing.[15]

5. Vascular Endothelial Growth Factor (VEGF) containing bone graft

VEGF plays a dual role—enhancing blood vessel formation and stimulating osteogenesis. **BIO4™** is the only cellular allograft to incorporate VEGF, PDGF, and basic FGF (bFGF), leading to faster vascularization, improved graft integration, enhanced new bone formation. such biologically active constructs significantly shorten healing time and increase treatment predictability.[16,17]

6. Bone Morphogenetic Proteins in Biomimetic Products

Emdogain® (Straumann) contains enamel matrix derivatives (EMDs) from porcine sources. These derivatives stimulate regeneration by mimicking embryonic tooth development and contain TGF-β and BMP-like proteins. When used with grafts, Emdogain enhances soft and hard tissue regeneration, improves clinical attachment level, reduces post-operative inflammation. Although not directly osteoinductive, it potentiates other regenerative materials—a prime example of osteopromotion.[18,19]

Growth Factor Dynamics and Mechanisms

Growth factors regulate bone healing through complex intracellular signaling. Once bound to surface receptors, they activate intracellular kinases, which trigger mRNA transcription, protein synthesis, cellular proliferation and differentiation
Crucial bone-related GFs include:

- TGF-β: Stimulates MSC differentiation
- BMPs: Directly induce osteoblastic lineage
- PDGF: Encourages cell recruitment and angiogenesis
- IGF: Promotes collagen synthesis and osteoblast activity

These elements function synergistically in growth factor-enhanced grafts, ensuring efficient and sustained tissue regeneration.[20,21]
Stem cells derived from bone marrow or adipose tissue are cultured with osteoinductive additives like dexamethasone, ascorbic acid, and BMPs. These cells are seeded onto bioactive scaffolds, creating living grafts capable of differentiation into osteoblasts and active bone matrix formation.[22,23]

CONCLUSION:

Bone grafts enriched with growth factors have transformed the scope and efficacy of periodontal regenerative therapy. While autografts remain the gold standard due to their inherent osteogenic properties, limitations in supply and donor site morbidity have

accelerated the development of growth factor-enhanced alternatives.

Technological advances have led to grafts that not only provide structural support (osteoconduction) but also actively induce and promote new bone formation (osteoinduction, osteopromotion). The integration of bioengineered molecules, naturally derived growth factors, and stem cells into grafting systems marks a paradigm shift in periodontal healing strategies.

As material science, biotechnology, and clinical periodontics continue to intersect, growth factor-enriched bone grafts will likely become the standard of care, offering predictable, accelerated, and functionally superior outcomes for periodontal regeneration.

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