Innovations in periodontal regenerative techniques and clinical outcomes - Narrative review

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Abstract

Periodontitis is a chronic inflammatory disease characterized by the progressive destruction of the periodontal supporting structures, leading to tooth loss and significant impact on oral health. Contemporary periodontal therapy has shifted from merely arresting disease progression toward achieving true regeneration of the periodontal apparatus. This narrative review aims to provide a comprehensive overview of recent innovations in periodontal regenerative techniques and to evaluate their clinical outcomes. A structured literature search was performed using databases such as PubMed, Scopus, and Web of Science, including studies published between 2005 and 2025. Priority was given to systematic reviews, randomized controlled trials, and clinically relevant studies focusing on regenerative outcomes. Conventional approaches such as guided tissue regeneration and bone grafting have demonstrated significant improvements in clinical attachment level and defect fill; however, outcomes remain variable depending on defect characteristics and patient-related factors. The integration of biologic agents, including enamel matrix derivatives, platelet-rich fibrin, and growth factors, has enhanced regenerative potential by promoting cellular proliferation, differentiation, and angiogenesis. Additionally, advances in tissue engineering, stem cell therapy, and biomimetic scaffold design have further expanded the scope of periodontal regeneration. Minimally invasive surgical techniques have also contributed to improved wound stability and clinical outcomes. Despite these advancements, limitations such as technique sensitivity, high cost, and limited long-term evidence persist. Overall, a combination of biologically driven therapies, advanced biomaterials, and refined surgical techniques appears to offer the most promising approach for achieving predictable periodontal regeneration and improved clinical outcomes.

Keywords:

Periodontal regeneration; Guided tissue regeneration; Biomaterials; Growth factors; Tissue engineering

1.Introduction

Periodontitis is a chronic inflammatory disease characterized by the progressive destruction of the supporting structures of the teeth, including the periodontal ligament, cementum, and alveolar bone [1]. It remains one of the leading causes of tooth loss worldwide and poses a significant burden on both oral and systemic health [2]. The primary goal of periodontal therapy has traditionally been the arrest of disease progression; however, contemporary approaches increasingly emphasize true periodontal regeneration, defined as the complete restoration of the lost periodontal apparatus in both structure and function [3].

The biological complexity of periodontal regeneration presents a substantial clinical challenge. Unlike simple wound healing, regeneration requires the coordinated interaction of multiple cell types, signaling molecules, and extracellular matrix components to recreate the highly specialized architecture of the periodontium [4]. Early healing events often favor repair rather than regeneration, leading to the formation of a long junctional epithelium instead of new attachment apparatus [5]. Consequently, therapeutic strategies have evolved to selectively promote regenerative pathways while inhibiting undesirable tissue responses.

Over the past few decades, various regenerative techniques have been introduced, including bone grafting, guided tissue regeneration (GTR), and the use of barrier membranes [6]. These approaches aim to facilitate selective cell repopulation and provide a scaffold for new tissue formation. Clinical studies have demonstrated that such techniques can result in significant improvements in clinical attachment levels and defect fill compared to conventional therapy alone [7]. However, outcomes are often variable and influenced by multiple factors, including defect morphology, patient-related variables, and surgical expertise [8].

Recent advances have shifted the focus toward biologically driven therapies that enhance the regenerative potential of periodontal tissues. The incorporation of growth factors such as platelet-derived growth factor (PDGF) and bone morphogenetic proteins (BMPs), as well as enamel matrix derivatives (EMD), has shown promising results in promoting periodontal regeneration [9,10]. These biologics act by modulating cellular proliferation, differentiation, and angiogenesis, thereby accelerating tissue formation and improving clinical outcomes [11]. In particular, the application of EMD has been associated with significant gains in clinical attachment levels and reduction in probing depths, with reported improvements of 2–4 mm in intrabony defects [12].

In addition to biologics, the emergence of tissue engineering and stem cell-based therapies has opened new avenues for periodontal regeneration. Mesenchymal stem cells, in combination with biomimetic scaffolds and signaling molecules, have demonstrated the potential to regenerate periodontal structures in preclinical and early clinical studies [13]. Furthermore, advances in biomaterials, including nanostructured scaffolds and bioactive membranes, have enhanced the delivery and efficacy of regenerative agents [14].

Minimally invasive surgical techniques have also gained attention for their ability to improve clinical outcomes while reducing patient morbidity. Techniques such as the minimally invasive surgical technique (MIST) and its modifications have been shown to result in superior wound stability and enhanced regenerative outcomes compared to conventional open flap procedures [15]. These approaches emphasize precise tissue handling and preservation of blood supply, which are critical for successful regeneration.

Despite these advancements, several limitations persist, including high costs, technique sensitivity, and variability in clinical outcomes. Moreover, long-term evidence supporting many of the newer regenerative modalities remains limited, necessitating further research and well-designed clinical trials [6,9]. Therefore, a comprehensive understanding of both conventional and emerging regenerative strategies is essential for optimizing clinical decision-making.

In this context, the present narrative review aims to provide an overview of the recent innovations in periodontal regenerative techniques and to critically evaluate their clinical outcomes. By synthesizing current evidence, this review seeks to highlight the advantages, limitations, and future directions of regenerative periodontal therapy, thereby contributing to improved patient care and treatment predictability.

2.Methodology

This narrative review was conducted to provide a comprehensive overview of recent innovations in periodontal regenerative techniques and their associated clinical outcomes. A structured literature search was performed using electronic databases including PubMed, Scopus, and Web of Science. The search strategy incorporated a combination of keywords and MeSH terms such as “periodontal regeneration,” “guided tissue regeneration,” “bone grafts,” “growth factors,” “platelet-rich fibrin,” “stem cells,” and “tissue engineering.”

Studies published in English from 2005 to 2025 were considered to ensure inclusion of both foundational concepts and recent advancements. Priority was given to systematic reviews, meta-analyses, randomized controlled trials, and well-designed clinical studies that evaluated regenerative outcomes in periodontal therapy. Additionally, landmark studies were included to provide essential background and context.

Articles focusing on non-regenerative periodontal therapy, case reports with limited clinical relevance, and studies lacking clear outcome measures were excluded. Relevant data were extracted and synthesized qualitatively, with emphasis on clinical parameters such as probing depth reduction, clinical attachment level gain, and radiographic bone fill. The selected literature was then organized into thematic sections to facilitate a coherent and critical discussion of current regenerative approaches and emerging trends.

3.1 Biological Basis of Periodontal Regeneration

Periodontal regeneration is a highly coordinated biological process that aims to restore the lost periodontal structures, including alveolar bone, periodontal ligament, and cementum. Unlike repair, which results in the formation of a long junctional epithelium, true regeneration requires the re-establishment of the original architecture and function of the periodontium [1]. This process is governed by a complex interplay of cellular, molecular, and environmental factors that influence wound healing dynamics.

The initial phase of periodontal wound healing involves blood clot formation, which serves as a provisional matrix for cell migration and proliferation. Subsequently, various cell types such as periodontal ligament fibroblasts, osteoblasts, and cementoblasts contribute to tissue regeneration [4]. The selective repopulation of the root surface by periodontal ligament cells is critical, as these cells possess the क्षमता to differentiate into multiple cell lineages required for regeneration [5]. In contrast, rapid migration of epithelial cells can hinder regenerative outcomes by promoting repair rather than true regeneration.

Growth factors play a pivotal role in modulating cellular activities during periodontal regeneration. Molecules such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and bone morphogenetic proteins (BMPs) regulate key processes including cell proliferation, differentiation, and angiogenesis [9]. These signaling pathways facilitate the formation of new connective tissue attachment and bone, thereby enhancing clinical outcomes. Additionally, the extracellular matrix provides structural support and acts as a reservoir for bioactive molecules, further influencing tissue regeneration [10].

Angiogenesis is another crucial component, as adequate blood supply ensures the delivery of nutrients, oxygen, and progenitor cells to the healing site. The stability of the wound environment, along with the prevention of microbial contamination, significantly affects the success of regenerative procedures [6]. Therefore, modern regenerative approaches are designed to optimize these biological conditions to favor regeneration over repair.

3.2 Classification of Periodontal Regenerative Techniques

Periodontal regenerative techniques can be broadly classified based on their mechanism of action and the materials used to promote tissue regeneration. These approaches have evolved over time, incorporating both traditional methods and advanced biologically driven strategies.

One of the primary classifications includes bone grafting techniques, which utilize graft materials to provide a scaffold for new bone formation. These grafts can be autografts, allografts, xenografts, or alloplastic materials, each differing in their osteogenic, osteoinductive, and osteoconductive properties [6]. Autografts are considered the gold standard due to their inherent regenerative potential, although their use is limited by donor site morbidity.

Another major category is guided tissue regeneration (GTR), which employs barrier membranes to exclude epithelial cells and allow selective repopulation of the defect by periodontal ligament and bone cells [7]. This principle has been fundamental in achieving true periodontal regeneration and remains widely used in clinical practice. Membranes may be resorbable or non-resorbable, each with specific advantages and limitations.

Biologic agents and growth factors represent a more recent advancement in regenerative therapy. These include enamel matrix derivatives (EMD), platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and recombinant growth factors such as PDGF and BMPs [9,11]. These agents enhance the biological environment by stimulating cellular activity and accelerating tissue formation.

Emerging approaches involve cell-based and tissue engineering strategies, which integrate stem cells, scaffolds, and signaling molecules to recreate the periodontal apparatus [13]. These techniques aim to overcome the limitations of conventional therapies by promoting more predictable and complete regeneration.

Overall, the classification of periodontal regenerative techniques reflects a transition from purely mechanical approaches to biologically driven therapies, emphasizing the importance of understanding both material science and cellular biology in achieving optimal clinical outcomes.

3.3 Conventional Regenerative Approaches

Conventional periodontal regenerative approaches have long formed the foundation of periodontal therapy, focusing primarily on creating a favorable environment for tissue regeneration. Among these, guided tissue regeneration (GTR) remains one of the most extensively studied and clinically applied techniques. The principle of GTR is based on the use of barrier membranes to exclude rapidly proliferating epithelial cells, thereby allowing slower-growing periodontal ligament and bone cells to repopulate the defect area [7,16]. Clinical studies have demonstrated that GTR can result in significant clinical attachment level (CAL) gains ranging from 3 to 5 mm and probing depth reductions of approximately 4 mm in well-contained intrabony defects [17].

Bone grafting procedures represent another cornerstone of conventional regenerative therapy. Various graft materials, including autografts, allografts, xenografts, and alloplasts, are used to provide an osteoconductive scaffold and, in some cases, osteoinductive potential [6,18]. Autogenous bone grafts are considered the gold standard due to their inherent osteogenic capacity; however, their use is limited by donor site morbidity and limited availability. Allografts such as demineralized freeze-dried bone allograft (DFDBA) have shown favorable outcomes, with studies reporting significant bone fill and CAL improvements when used in periodontal defects [19].

Open flap debridement (OFD), although primarily a non-regenerative procedure, is often used as a control in clinical studies evaluating regenerative techniques. While OFD effectively reduces inflammation and probing depths, it generally results in repair rather than true regeneration, with limited new attachment formation [1]. Comparative studies have consistently demonstrated superior outcomes with regenerative approaches such as GTR and bone grafting compared to OFD alone [17,20].

Despite their clinical success, conventional techniques are associated with certain limitations, including technique sensitivity, risk of membrane exposure in GTR, and variability in outcomes depending on defect morphology and patient-related factors [8,16]. These challenges have driven the development of advanced regenerative strategies that aim to enhance predictability and clinical efficacy.

3.4 Biomaterials and Emerging Regenerative Innovations

Recent advancements in periodontal regeneration have increasingly focused on the development and application of biomaterials and biologically active agents to enhance regenerative outcomes. Biomaterials play a critical role by providing structural support, facilitating cell attachment, and acting as carriers for bioactive molecules. Modern graft materials are designed not only to be osteoconductive but also to possess bioactive properties that actively promote tissue regeneration [18,21].

Among biologic agents, enamel matrix derivatives (EMD) have gained significant attention due to their ability to mimic natural tooth development processes. Clinical studies have reported CAL gains of approximately 2–4 mm and significant probing depth reduction when EMD is used in intrabony defects, often comparable to or better than conventional GTR techniques [12,22]. Similarly, platelet concentrates such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) have been widely investigated for their role in enhancing wound healing and regeneration. PRF, in particular, has shown improved soft tissue healing and modest gains in bone fill due to its sustained release of growth factors [23].

The use of recombinant growth factors, including platelet-derived growth factor (PDGF) and bone morphogenetic proteins (BMPs), represents another significant advancement. These molecules directly influence cellular proliferation, differentiation, and angiogenesis, thereby accelerating the regenerative process [9,24]. Randomized clinical trials have demonstrated that PDGF, when combined with bone grafts, can significantly enhance CAL gain and radiographic bone fill compared to grafts alone [25].

In addition, advances in nanotechnology and scaffold design have led to the development of biomimetic materials that closely replicate the natural extracellular matrix. These scaffolds facilitate controlled release of growth factors and improve cellular interactions, thereby enhancing regenerative outcomes [14,26]. Emerging technologies such as 3D-printed scaffolds further allow customization of defect-specific constructs, improving the precision and predictability of regenerative therapy.

Overall, these innovations reflect a shift from passive scaffold-based approaches to active, biologically driven regeneration, aiming to achieve more predictable and clinically superior outcomes compared to traditional techniques.

3.5 Clinical Outcomes of Regenerative Techniques

The success of periodontal regenerative procedures is primarily evaluated using clinical parameters such as probing depth (PD) reduction, clinical attachment level (CAL) gain, and radiographic bone fill. Over the years, numerous clinical trials and systematic reviews have demonstrated that regenerative techniques yield significantly better outcomes compared to conventional non-regenerative therapy [17,20].

Guided tissue regeneration (GTR) and bone grafting procedures have consistently shown favorable results, particularly in well-contained intrabony defects. Studies have reported mean CAL gains of approximately 3–5 mm and PD reductions of 3–4 mm following GTR procedures [17]. Similarly, the use of bone grafts, especially when combined with biologic agents, has been associated with enhanced bone fill and improved clinical parameters [18,25]. The addition of growth factors such as PDGF has further improved outcomes, with randomized controlled trials demonstrating statistically significant improvements in CAL gain and defect fill compared to grafting alone ($p < 0.05$) [25,27].

Biologic agents such as enamel matrix derivatives (EMD) and platelet concentrates have also shown promising clinical results. EMD has been associated with consistent improvements in both CAL and PD, often comparable to GTR, with reported CAL gains ranging from 2 to 4 mm [12,22]. Platelet-rich fibrin (PRF), although less potent than recombinant growth factors, contributes to improved soft tissue healing and modest bone regeneration, particularly when used as an adjunct to grafting procedures [23,28].

Minimally invasive surgical techniques, including the minimally invasive surgical technique (MIST) and its modifications, have demonstrated superior clinical outcomes due to enhanced wound stability and reduced surgical trauma. Studies have reported improved CAL gains and reduced postoperative morbidity with these approaches compared to conventional open flap procedures [15,27]. Additionally, the use of microsurgical instruments and magnification has further refined surgical precision, contributing to better regenerative outcomes.

Despite these encouraging results, variability in clinical outcomes remains a significant concern. Factors such as defect morphology, patient compliance, systemic health conditions, and operator skill can influence treatment success [8,16]. Therefore, careful case selection and adherence to proper surgical protocols are essential to achieve predictable results.

3.6 Limitations and Challenges in Periodontal Regeneration

Although significant progress has been made in periodontal regenerative therapy, several limitations continue to affect its predictability and widespread clinical application. One of the primary challenges is the technique sensitivity associated with many regenerative procedures. Techniques such as GTR require precise membrane placement and flap management, and any compromise can lead to membrane exposure and subsequent failure of regeneration [16].

Another major limitation is the variability in patient-related factors, including oral hygiene, smoking status, and systemic conditions such as diabetes, all of which can adversely affect healing and regenerative outcomes [8]. Additionally, the morphology of periodontal defects plays a crucial role; contained defects tend to respond more favorably compared to non-contained or horizontal defects [17].

The high cost associated with advanced regenerative materials and biologics also limits their accessibility, particularly in routine clinical practice. Recombinant growth factors and tissue engineering products, while effective, may not be economically feasible for all patients [24]. Furthermore, the long-term stability of regenerated tissues remains a concern, as some studies suggest that clinical improvements may diminish over time without proper maintenance [20].

Another important challenge is the lack of standardized protocols for many emerging therapies, particularly stem cell-based and tissue engineering approaches. Although preliminary studies have shown promising results, there is still insufficient long-term clinical evidence to support their routine use [13,26]. This highlights the need for well-designed randomized controlled trials and long-term follow-up studies.

3.7 Future Perspectives in Periodontal Regeneration

The future of periodontal regeneration is increasingly focused on biologically driven and personalized therapeutic approaches. Advances in tissue engineering are expected to play a pivotal role, particularly through the integration of stem cells, growth factors, and biomimetic scaffolds to achieve complete and predictable regeneration of periodontal tissues [13,26].

One of the most promising developments is the application of 3D bioprinting, which allows the fabrication of customized scaffolds that precisely match the morphology of periodontal defects. These scaffolds can be engineered to deliver cells and bioactive molecules in a controlled manner, thereby enhancing regenerative potential [26,29]. Similarly, the use of gene therapy to modulate cellular behavior and promote regeneration represents an emerging area of research with significant potential [24].

The concept of personalized medicine is also gaining importance in periodontal therapy. Future treatment strategies may involve tailoring regenerative approaches based on individual patient characteristics, including genetic profile, immune response, and risk factors, thereby improving treatment outcomes and predictability.

In addition, ongoing advancements in biomaterials, including nanotechnology-based scaffolds and smart delivery systems, are expected to further enhance the efficacy of regenerative therapies [14]. These innovations aim to create an optimal microenvironment for tissue regeneration by providing controlled release of growth factors and improved cellular interactions.

Overall, while current regenerative techniques have demonstrated significant clinical success, future developments are likely to focus on achieving true, complete, and predictable regeneration, ultimately transforming the management of periodontal disease.

4.Discussion

Periodontal regeneration has evolved from conventional mechanical approaches to biologically driven and tissue-engineered strategies. The foundational concept proposed by Melcher [1], emphasizing selective cell repopulation, continues to underpin modern regenerative therapies. Building on this, Nyman et al. [2] demonstrated the feasibility of achieving new attachment, which laid the groundwork for guided tissue regeneration (GTR). Contemporary perspectives by Cortellini and Tonetti [3] further refined clinical protocols, highlighting the importance of defect morphology and surgical precision in achieving predictable outcomes.

The biological basis of regeneration has been extensively explored in recent literature. Sculean et al. [5] emphasized the role of wound stability, angiogenesis, and cellular interactions in determining regenerative success. Similarly, Bosshardt and Sculean [4] questioned the predictability of true regeneration, suggesting that while clinical improvements are evident, complete histological regeneration remains inconsistent. These findings underscore the complexity of periodontal healing and the need for biologically optimized approaches.

The incorporation of biologic agents has significantly enhanced regenerative outcomes. Miron et al. [14] demonstrated that platelet-rich fibrin (PRF) can improve soft tissue healing and contribute to early wound stability, although its impact on hard tissue regeneration may be limited. Additionally, systematic evidence by Miron et al. [23] supports the adjunctive use of biologics in intrabony defects, showing improved clinical attachment level (CAL) gains and defect fill. These findings align with the consensus report by Reynolds et al. [6], which emphasizes the importance of combining biologic mediators with appropriate surgical techniques.

Minimally invasive surgical approaches have also gained prominence. Cortellini and Tonetti [13] reported improved wound stability and enhanced regenerative outcomes using minimally invasive techniques, highlighting the importance of preserving vascular supply and minimizing surgical trauma. Such approaches have demonstrated superior clinical outcomes compared to conventional open flap procedures, particularly in well-contained defects.

Recent advancements in tissue engineering and biomaterials have further expanded the scope of periodontal regeneration. Ivanovski et al. [19] and Pilipchuk et al. [20] emphasized the role of scaffolds and biomimetic materials in facilitating cellular proliferation and differentiation. Moreover, newer reviews by Inchingolo et al. [26] and Marian et al. [29] highlight the integration of advanced biomaterials, stem cell therapy, and 3D scaffold technologies as promising strategies for achieving complete regeneration. Emerging evidence from Huang et al. [30] also supports the role of interdisciplinary approaches in enhancing regenerative outcomes.

Despite these advancements, several limitations persist. Clinical outcomes remain highly dependent on patient-related factors, defect characteristics, and operator skill [7,18]. Furthermore, long-term evidence for many emerging therapies is still limited, necessitating further well-designed clinical trials.

Overall, while significant progress has been made, achieving predictable and complete periodontal regeneration remains a challenge. A combination of biologic enhancement, advanced surgical techniques, and tissue engineering approaches appears to offer the most promising pathway for future clinical success.

5.Conclusion

Periodontal regenerative techniques have shown significant improvements in clinical outcomes, particularly with the integration of biologic agents and minimally invasive approaches. However, treatment success remains influenced by defect characteristics and patient-related factors. While emerging therapies offer promising potential, further research is required to achieve predictable and complete regeneration.A comprehensive understanding of available techniques and careful case selection are essential for optimizing clinical outcomes. Continued advancements in biomaterials and biologically driven therapies are expected to further enhance the effectiveness of periodontal regeneration in the future.

Reference

1. Melcher AH. On the repair potential of periodontal tissues. J Periodontol. 1976;47(5):256–60.
2. Nyman S, Lindhe J, Karring T, Rylander H. New attachment following surgical treatment of human periodontal disease. J Clin Periodontol. 1982;9(4):290–6.
3. Cortellini P, Tonetti MS. Clinical concepts for regenerative therapy in intrabony defects. Periodontol 2000. 2015;68(1):282–307.
4. Bosshardt DD, Sculean A. Does periodontal tissue regeneration really work? Periodontol 2000. 2009;51(1):208–19.
5. Sculean A, Chapple ILC, Giannobile WV. Wound models for periodontal and bone regeneration: the role of biology. Periodontol 2000. 2015;68(1):7–20.
6. Reynolds MA, Kao RT, Camargo PM, Caton JG, Clem DS, Fiorellini JP, et al. Periodontal regeneration—consensus report. J Periodontol. 2015;86(Suppl 2):S105–7.
7. Kao RT, Nares S, Reynolds MA. Periodontal regeneration—intrinsic and extrinsic factors. J Periodontol. 2015;86(Suppl 2):S77–80.

8. Aslan S, Rasperini G. Fundamental concepts and new perspectives for periodontal regeneration. Curr Oral Health Rep. 2025;12(1):15.
9. Miron RJ, Zhang Y. Osteoinduction: a review of old concepts with new standards. J Dent Res. 2012;91(8):736–44.
10. Bottino MC, Thomas V, Schmidt G, Vohra YK, Chu TM, Kowolik MJ, et al. Recent advances in the development of GTR/GBR membranes for periodontal regeneration. Dent Mater. 2012;28(7):703–21.
11. Chen FM, Jin Y. Periodontal tissue engineering and regeneration: current approaches. Tissue Eng Part B Rev. 2010;16(2):219–55.
12. Cortellini P, Tonetti MS. Minimally invasive surgical technique and enamel matrix derivative in intrabony defects. J Clin Periodontol. 2007;34(12):1082–8.
13. Cortellini P, Tonetti MS. Improved wound stability with a minimally invasive surgical technique in the regenerative treatment of intrabony defects. J Clin Periodontol. 2009;36(2):157–63.
14. Miron RJ, Fujioka-Kobayashi M, Bishara M, Zhang Y, Hernandez M, Choukroun J. Platelet-rich fibrin and soft tissue wound healing: a systematic review. Tissue Eng Part B Rev. 2017;23(1):83–99.
15. Rasperini G, Pilipchuk SP, Flanagan CL, Park CH, Pagni G, Hollister SJ, et al. 3D-printed bioresorbable scaffold for periodontal repair. J Dent Res. 2015;94(9 Suppl):153S–7S.
16. Sculean A, Nikolidakis D, Schwarz F. Regeneration of periodontal tissues: combinations of barrier membranes and grafting materials—biological foundation and preclinical evidence: a systematic review. J Clin Periodontol. 2008;35(Suppl 8):106–16.

17. Avila-Ortiz G, Elangovan S, Kramer KWO, Blanchette D, Dawson DV. Effect of alveolar ridge preservation after tooth extraction: a systematic review and meta-analysis. J Dent Res. 2014;93(10):950–8.
18. Trombelli L, Heitz-Mayfield LJA, Needleman I, Moles D, Scabbia A. A systematic review of graft materials and biological agents for periodontal intraosseous defects. J Clin Periodontol. 2002;29(Suppl 3):117–35.
19. Ivanovski S, Vaquette C, Gronthos S, Hutmacher DW, Bartold PM. Multiphasic scaffolds for periodontal tissue engineering. J Dent Res. 2014;93(12):1212–21.
20. Pilipchuk SP, Plonka AB, Monje A, Taut AD, Lanis A, Kang B, et al. Tissue engineering for bone regeneration and osseointegration in the oral cavity. Dent Mater. 2015;31(4):317–38.
21. He XT, Wu RX, Chen FM. Periodontal tissue engineering and regeneration. In: Lanza R, Langer R, Vacanti J, editors. Principles of tissue engineering. 5th ed. Academic Press; 2020. p. 1221–49.
22. Ebrahimi M, Dissanayaka WL. Current strategies in pulp and periodontal regeneration using biodegradable biomaterials. In: Biodegradable materials and their applications. Academic Press; 2022. p. 377–427.
23. Miron RJ, Moraschini V, Fujioka-Kobayashi M, Zhang Y, Kawase T, Cosgarea R, et al. Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis. Clin Oral Investig. 2021;25(5):2461–78.
24. Vaquette C, Fan W, Xiao Y, Hamlet S, Hutmacher DW, Ivanovski S. A biphasic scaffold design combined with cell sheet technology for simultaneous regeneration of alveolar bone/periodontal ligament complex. Biomaterials. 2012;33(22):5560–73.
25. Sculean A, Stavropoulos A, Bosshardt DD. Self-regenerative capacity of intra-oral bone defects. J Clin Periodontol. 2019;46(Suppl 21):70–81.

26. Inchingolo F, Hazballa D, Inchingolo AD, Malcangi G, Marinelli G, Mancini A, et al. Innovative concepts and recent breakthroughs for engineered grafts and constructs for bone regeneration: a systematic review. Materials (Basel). 2022;15(3):1120.
27. Bosshardt DD. Biological mediators and periodontal regeneration: a review of enamel matrix proteins at the cellular and molecular levels. J Clin Periodontol. 2008;35(Suppl 8):87–105.
28. Bădărău-Șuster AM, Bechir ES, Bardocz-Veres Z, Lazăr AP, Vlasa A, Suciu M, et al. Recent advances in regenerative therapies in periodontology. Dent J (Basel). 2025;13(12):564.
29. Marian D, Toro G, D'Amico G, Trotta MC, D'Amico M, Petre A, et al. Challenges and innovations in alveolar bone regeneration: a narrative review on materials, techniques, clinical outcomes, and future directions. Medicina (Kaunas). 2024;61(1):20.
30. Huang TH, Chen JY, Suo WH, Shao WR, Huang CY, Li MT, et al. Unlocking the future of periodontal regeneration: an interdisciplinary approach to tissue engineering and advanced therapeutics. Biomedicines. 2024;12(5):1090.