Periodontal Bioengineering

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ABSTRACT

Periodontal diseases, such as periodontitis and gingivitis, are prevalent oral health conditions affecting a significant portion of the global population. Traditional treatment approaches for periodontal diseases, such as scaling and root planning, have limitations in achieving complete regeneration of periodontal tissues. In recent years, bioengineering approaches have emerged as promising strategies to regenerate and restore periodontal tissues. This chapter provides an overview of the current state of periodontal bioengineering, focusing on tissue engineering, regenerative therapies, and the use of biomaterials. Furthermore, it discusses key advancements and potential future directions in this rapidly evolving field.

Keywords— Periodontits, Bioengineering, Regenerative therapies, Biomaterials

# INTRODUCTION

 Periodontal disease, is a chronic inflammatory condition that affects the tissues surrounding and supporting the teeth. It is one of the most prevalent oral health issues worldwide and is a leading cause of tooth loss in adults. Periodontal disease is influenced by various risk factors, including: Poor oral hygiene, Smoking and tobacco use, Genetics, Diabetes, Immune system disorders, Hormonal changes, Medications.

 Prevention and management of periodontal disease involve a combination of professional dental care and good oral hygiene practices at home. Regular dental check-ups and professional cleanings are essential to monitor the health of the gums and address any early signs of gum disease. Additionally, maintaining proper oral hygiene through regular brushing, flossing, and using mouthwash can help prevent plaque buildup and reduce the risk of gum disease. In severe cases of periodontitis, treatments may include scaling and root planing (deep cleaning), antibiotic therapy, and, in advanced cases, surgical procedures to repair and regenerate damaged tissues and bones around the teeth.

 Traditional periodontal treatment methods, while effective in many cases, do have some limitations. Some of the key limitations include: Invasiveness, Pain and Discomfort, Limited Tissue Regeneration, Dependency on Patient Compliance, Time-Consuming, Risk of Infection, Potential for Recurrence, Cost.Rationale for periodontal bioengineering.

# PERIODONTAL BIOENGINEERING

 Periodontal bioengineering is an emerging field that aims to apply principles of engineering and regenerative medicine to develop novel treatments for periodontal diseases. The goal is to promote the regeneration of damaged or lost periodontal tissues, including bone, ligaments, and cementum, to restore the health and function of the affected teeth and surrounding structures. This innovative approach holds great promise in overcoming some of the limitations of traditional periodontal treatment methods. Here are some key rationales for periodontal bioengineering:

1. Tissue Regeneration: Periodontal bioengineering focuses on stimulating the body's natural regenerative processes to rebuild damaged or lost periodontal tissues. By using biomaterials, growth factors, and tissue scaffolds, it aims to create an environment conducive to tissue repair and regeneration.

2. Minimally Invasive: Bioengineering techniques often aim to be minimally invasive compared to traditional surgical methods. This can lead to reduced patient discomfort, faster recovery times, and better acceptance by patients who may be anxious about invasive treatments.

3. Personalization: Bioengineering allows for personalized treatment approaches. By tailoring the biomaterials and growth factors to each patient's specific needs, the potential for successful tissue regeneration is increased.

4. Long-Term Results: The goal of periodontal bioengineering is to promote the long-term stability and health of the regenerated tissues. This can lead to more sustainable outcomes and reduce the risk of disease recurrence.

5. Preservation of Tooth Structure: In some cases, traditional periodontal treatments may involve the removal of tooth structure or require the extraction of severely affected teeth. Bioengineering techniques aim to preserve and restore natural teeth whenever possible.

6. Potential for Adjunctive Therapies: Periodontal bioengineering can complement and enhance traditional treatments. For example, bioengineered materials can be used in conjunction with surgical procedures to improve the outcomes of regenerative therapies.

## **Growth factors for Periodontal Regeneration:**

 To facilitate the sustained release of the factors for periods of time, the incorporation of bioactive molecules into scaffolding materials is obligatory. The two basic modes of incorporating bioactive molecules into the scaffolds are at the time of fabrication [1] or after the fabrication [2]. Bioactive molecules incorporated directly into bioresorbable scaffolds are typically released through a diffusion-controlled mechanism, which is governed by the scaffold's pore sizes. The different pore sizes influence the scaffold's tortuosity, thereby controlling the release of proteins [3]. The rate and type of degradation of the delivery device determines the rate of growth factor release as well as the growth factor diffusion through the scaffold's pores. The incorporation of human parathyroid hormone (PTH) into biodegradable PLGA microspheres demonstrated a controlled release of PTH [4]. The bioactivity of PTH was effectively preserved by the polymer microspheres which is evidenced by stimulation of cAMP release and raise in the serum calcium levels when injected subcutaneously into mice. An investigation by Murphy et al., showed the release of vascular endothelial growth factor (VEGF), from PLGA scaffolds which is a potent mitogen for endothelial cell over a 15-day period [5]. The vascularization is enhanced when VEGF incorporated polymers were seeded with endothelial cells and implanted in vivo [6]. After two weeks, hydrogel systems with microspheres containing IGF-1/TGF-1 and chondrocytes produced more cells and glycosaminoglycan than control gels without microspheres did [7]. Hydrogels with the RGD (arginine-glycine-aspartic acid) cell adhesive molecule motif and substrates for matrix metalloproteinases as linkers to polymer chains were recently used in a method. These biomimetic scaffolds efficiently regulated the release of BMPs, promoting the healing of craniofacial defects through cell invasion into the scaffolds [8]. However, despite these promising advancements in controlled-release delivery systems, further development is needed to create suitable bioactive molecule devices or alternative delivery methods to optimize therapeutic outcomes in regenerative medicine.

**B. Scaffold and extracellular matrix**

The extracellular matrix (ECM), a dynamic tissue made up of a complex mixture of macromolecules, not only supports the structure of an organism but also has a significant impact on its many cellular functions [9]. Cell adhesion, migration, proliferation, and differentiation are some of these processes that are impacted by the nature and structural layout of the ECM around them [10]. Especially in craniofacial morphogenesis and regeneration, where interactions with the ECM are contact-mediated, BMPs (bone morphogenetic proteins) play a crucial role in bone induction [11]. The ECM includes substances such heparan sulfate, heparin, type II procollagen, fibrillins, proteoglycans, noggin, chordin, DAN, and types I and IV collagen. When rhBMPs are administered to wounds, they bind to these substances. For active morphogens, these contacts result in the best conformation possible, facilitating contact-mediated reactions. The rate of material deterioration must be carefully taken into account when designing scaffolds that resemble the ECM since it has a substantial impact on tissue replacement for manufactured structures. The scaffold's growth factor release rate has a significant impact on the outcomes [13].

 Furthermore, the behavior of BMPs in bones, periodontium, and teeth may be different from how they behave when incorporated into biomaterials like collagen and hydroxyapatite [14]. This variation is attributable to BMP retention at the implantation site, which is influenced by the morphogens' isoelectric point and charge properties [15]. For specific applications, improving the efficiency of BMPs in stimulating tissue regeneration and bone formation requires an understanding of these parameters.

**Angiogenic factors for periodontal repair:**

 Three main blood vessels supply the periodontium, a highly vascularized tissue: supraperiosteal arterioles along the alveolar bone's surface, vessels in the periodontal ligament (PDL) region, and arterioles from the interdental septum extending into the gingival and sulcus area [16]. The blood supply is essential for nourishing newly created tissues in addition to preserving local homeostasis and providing enough host defense by delivering cells and defensins to the gingival crevice [17]. Targeting angiogenesis to an avascular tooth root surface, however, is one of the major difficulties in periodontal regeneration. Following an injury, capillaries invading a fibrin clot deliver nutrition, inflammatory cells, and oxygen to the wound site, promoting the early development of granulation tissue [18]. Moreover, newly formed blood vessels Additionally, newly created blood vessels foster the cell migration, proliferation, differentiation, and production of extracellular matrix, all crucial elements of early periodontal healing [19].

 FGF-2, also known as basic fibroblast growth factor (bFGF), was shown to have strong angiogenic properties [20] and the ability to stimulate the development of immature PDL cells [21]. Additionally, it has been discovered that FGF-2 stimulation increases the mRNA expression of laminin, a protein crucial for angiogenesis, in PDL cells [22]. Additionally, recent studies have looked at how enamel matrix derivative (EMD) affects the angiogenesis of periodontal wounds, indicating that it may has the ability to speed up the regeneration of periodontal tissues [23].

 However, the rapid initial healing that EMD generated might not have been the only factor in it. Additional mechanisms are most likely to blame for this acceleration. It has been demonstrated that growth factors like as TGF-b1, IL-6, and PDGF-AB that PDL cells exposed to EMD may release expedite periodontal wound repair by promoting PDL cell proliferation in particular [24]. Additionally, studies have shown that EMD has no detrimental effects on the normal flora and can inhibit the bacterial expansion of periodontal pathogens during the healing of periodontal wounds [25].

 Vasculature tissue engineering poses a number of technological difficulties [26]. It is essential to choose the right vascular cells and scaffold materials. This frequently entails in vitro growing bone marrow or smooth muscle cells with a collagen-based matrix to create tubular structures, which then permit endothelial cells to adhere to the arterial wall. The mechanical qualities of scaffolds must be similar to those of native arteries in order for them to sustain fluid shear stress, strain, and physiological blood pressures and promote the appropriate development of vascular tissue. Further consideration must be given to potential conflicts between native blood vessels and synthetic manufactured grafts.

 Growth factors are essential for facilitating tissue regeneration because they stimulate angiogenesis and give cells oxygen and nutrients. However, because of their variable in vivo stability, drug delivery mechanisms must be used. To encourage the creation of new vessels, it may be necessary to include angiogenic growth factors directly into scaffolds or use gene therapy for targeted delivery [27]. Angiogenesis is enhanced, blood vessel maturation is induced, and mature vascular networks can be formed quickly using a dual growth factor delivery method using PDGF + VEGF [28].

**D. Gene therapy for periodontal engineering**

 Traditional surgical methods for periodontal regeneration are limited by the short half-lives of growth factors in the body, which necessitate high growth factor concentrations [29]. Gene therapy provides a promising answer to this problem by delivering particular genes into cells, either directly or indirectly through a matrix, in order to produce the desired biological impact. Gene therapy can be used to replace dysfunctional mutant alleles with functional ones, or it can be utilized to improve the host's reaction to the mutant. Using vectors or direct delivery techniques for transfection, cells can be specifically targeted for gene therapy.

In order to promote the regeneration of alveolar bone, tooth root cementum, and the periodontal ligament (PDL), Jin et al., used an ex vivo method of periodontal repair. They implanted syngeneic dermal fibroblasts into significant alveolar bone defects after transducing them with Ad-BMP-7 or its antagonist, Ad-noggin. With fast chondrogenesis, followed by osteogenesis, cementogenesis, and predicted bridging of the bone defect, this method successfully repaired periodontal defects. However, noggin gene transfer prevented periodontal bone and cementum recovery in tissue-engineered cementum as well as periodontal defects [30].In numerous wound healing models, PDGF has demonstrated a strong potential for encouraging gingival, alveolar bone [31], and cementum regeneration. Adenovirus encoding PDGF-B was used to treat periodontal problems, and there was significant bone and cementum regeneration over and above what was seen with control vectors, with almost four-fold increases in bridging bone and six-fold increases in tooth-lining cement repair [32]. Additionally, the periodontal lesions retained the localized production of the luciferase reporter gene for up to 21 days following gene transfer. The potential of gene therapy as a successful and long-lasting way to encourage periodontal tissue regeneration is highlighted by this [33].

**Challenges and future directions:**

The currently available treatments, which are based on the “damage to heal approaches,” have had only limited success in periodontal medicine. With an increasing aging population, tissue-engineering strategies provide important cures and hope for the treatment of periodontal disease, and they have set the stage for successful regeneration of many other tissues. The development of biological transplants for reconstructive therapies has considerably improved the currently available treatment options for periodontal repair. Particularly, the accelerated pace of research in the stem-cell field and the accumulated body of knowledge has spurred interest in the potential clinical use of stem cells [34]. This developing area is attracting increasing attention from both the private and government sectors because of its considerable economic and therapeutic potential. However, there are critical steps in moving the field toward human clinical utility [35]. In particular, the events following cell transplantation are poorly understood, underscoring the considerable need for robust preclinical modeling for the evaluation of the safety and efficacy of stem cells. Although the clinical application of stem cells to the regeneration of periodontal tissue has begun, the risks of stem-cell therapies should not be ignored or underestimated by clinicians and researchers.

In periodontal medicine, the currently used therapies, which are based on "damage to heal approaches," have had only patchy effectiveness. Tissue-engineering techniques have paved the way for the successful regeneration of numerous different tissues, offering significant solutions and hope for the treatment of periodontal disease in the face of an aging population. The currently available therapy options for periodontal repair have been greatly enhanced by the discovery of biological transplants for reconstructive therapies. Interest in the potential clinical application of stem cells has been sparked, in part, by the quickening speed of research in the field of stem cells and the growing volume of knowledge [34]. Because of its significant economic and therapeutic potential, both the corporate and public sectors are paying greater attention to this emerging subject. The field is heading toward human therapeutic utility, however there are important measures to take [35]. Particularly, there is a lack of understanding of what happens after cell transplantation, which emphasizes the critical need for reliable preclinical modeling to assess the safety and effectiveness of stem cells. Researchers and clinicians should be aware of the potential side effects of stem-cell therapies even if the clinical use of stem cells for the regeneration of periodontal tissue has already started.

 There are two key requirements for effective tissue engineering. First and foremost, it is essential to understand technical principles related to scaffold biomechanics, architectural geometry, and space maintenance. In order to distribute cells and factors, biomaterials that resemble in vivo stem cell habitats are being developed. But it's possible that the intricacy of natural stem cell regulation mechanisms is not adequately captured by existing techniques. Second, effective differentiation and tissue regeneration depend on the biological functions of the engineered construct, including cell recruitment, proliferation, survival, neovascularization, and growth factor supply. Controlling stem cell behavior in a complicated in vivo environment, however, is still a difficult task.

 Periodontal therapy is being revolutionized by tissue engineering, and human patient clinical studies using stem cell transplantation have already started or are almost set to get started. A novel therapeutic paradigm for usage in clinical settings is being investigated by researchers who also want to improve and direct the healing of periodontal wounds. Host modulation therapies are essential for managing periodontal disorders and encouraging tissue reengineering, and it is necessary to understand that tissue regeneration alone might not be sufficient for long-term stable therapy.

 Investigating engineering techniques in polluted or infectious wound beds brought on by periodontitis is becoming more and more important in the field of periodontal tissue engineering. It is extremely difficult to maximize treatment effectiveness in passive or permissive settings with few biological signals. Critical issues that need to be addressed include selecting the best cell sources, figuring out therapeutically useful cell quantities, discovering efficient delivery techniques, incorporating new cells into preexisting tissue matrices, and achieving functional qualities using a variety of biomaterials.

 A major barrier that needs careful study is the clinical implementation of tissue engineering technologies' practical, safety, and regulatory considerations.

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