

Review Article

Cultivating Healthy Smiles: Exploring Regenerative Therapy in Periodontics

Anushree Choudhary¹, Rohit Mishra², Vibhor Hazari³, Sheewali Saggar^{4*}, Manisha Choubey⁴, Anubha Shrivastava⁴

¹Associate Professor, Department of Periodontics and Implantology, Hitkarini Dental College and Hospital, Dumna Hills, Jabalpur, Madhya Pradesh, India

²Professor and Head of Department, Department of Periodontics and Implantology, Hitkarini Dental College and Hospital, Dumna Hills, Jabalpur, Madhya Pradesh, India

³Private Practitioner at Hazari Dental Clinic, India

⁴Post Graduate Resident, Department of Periodontics and Implantology, Hitkarini Dental College and Hospital, Dumna Hills, Jabalpur, Madhya Pradesh, India

*Correspondence author: Sheewali Saggar, Post Graduate Resident, Department of Periodontics and Implantology, Hitkarini Dental College and Hospital, Dumna Hills, Jabalpur, Madhya Pradesh, India; E-mail: shivalisaggar96@gmail.com

Citation: Saggar S, et al. Cultivating Healthy Smiles: Exploring Regenerative Therapy in Periodontics. J Dental Health Oral Res. 2023;4(3):1-11.

<https://doi.org/10.46889/JDHOR.2023.4303>

Received Date: 25-09-2023

Accepted Date: 16-10-2023

Published Date: 23-10-2023



Copyright: © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CCBY) license (<https://creativecommons.org/licenses/by/4.0/>).

Abstract

Regenerative therapy is a cutting-edge therapeutic strategy used in periodontics with the goal of restoring the health and functionality of the tissues that support teeth, including the periodontal ligament, bone and gums. These supporting tissues can be destroyed by periodontal disorders, including gingivitis and periodontitis, which may result in tooth loss. Regenerative therapy encourages the regeneration of missing or damaged tissues in an effort to undo or heal this damage.

Biological solutions to biological problems are emerging as a new paradigm in dentistry and medicine. Scientific discoveries in cellular, developmental and molecular biology have truly revolutionized our collective understanding of biological processes, human genetic variations, the continuity of evolution and the etiology and pathogenesis of thousands of human diseases and disorders.

There have been a number of encouraging developments in periodontics and regenerative therapy. Guided Tissue Regeneration (GTR), osseous grafting and newer techniques like Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF), stem cell therapy, growth factors and biomaterial, gene therapy, 3D-printing and tissue engineering, anti-inflammatory drugs, microbiome-based therapy and minimally invasive methods have all advanced from these earlier approaches. The current improvements in regenerative therapy for periodontics that yield superior results are contextualized in this research.

Keywords: Regeneration; Growth Factors; Biomaterials; Tissue Engineering

Introduction

Periodontitis is an inflammatory disease that causes pathological alteration in the teeth and their supporting structures, potentially leading to tooth loss. The significant burden of periodontal diseases and their impact on general health and patient quality of life point to the need for more effective management of these condition. Regenerative periodontal therapy employs specialized methods to replace tooth-supporting tissues that have been destroyed due to periodontitis or gingival damage [1]. The term "regeneration" refers to the process of regenerating damaged or destroyed tissues in a way that preserves both the original structures and their intended purposes. Procedures designed to regenerate missing periodontal tissues encourage the development of new attachments, involving the development of fresh periodontal ligaments with their fibers inserted into alveolar bone and freshly produced cementum [2]. Currently, there are five main categories of therapeutics used or in development for tissue regeneration:

- Conductive therapeutics
- Inductive therapeutics
- Cell-based therapeutics
- Gene-based therapeutics
- RNA-based therapeutics

Conventional periodontal surgical treatment modalities (surgical debridement and respective procedures) have been established as effective means of treating periodontal disease and arresting its progression [3].

GTR procedures were then developed in which barrier membranes were used to accomplish the objectives of epithelial exclusion via controlled cell/tissue repopulation of the periodontal wound, space maintenance and clot stabilization. The technique using barriers was introduced by Nyman, et al., in 1982 and the term GTR was coined by Gottlow, et al., in 1986. This method of enhancing periodontal regeneration was also referred to as selective cell repopulation or controlled tissue regeneration [4]. Bone transplants offer the structural support necessary for clot growth, maturation and bone remodeling, which leads to the production of new bone in osseous defects. Bone grafting materials also exhibit variable capacities to promote the coordinated growth of bone and periodontal ligament when injected and held in place in osseous defects. Bone loss patterns in periodontal disease can be vertical or horizontal. The regenerative techniques can be graft- associated and non-graft- associated new attachment procedures. Bone graft materials are generally evaluated based on their osteogenic, osteoinductive or osteoconductive potential. Hegedus employed bone transplants for intraosseous lesions for the first time in 1923 [5]. Objectives of bone grafts [6]

- Probing depth reduction
- Clinical Attachment Level (CAL)
- Bone fill of the osseous defect
- Regeneration of new bone, cementum and periodontal ligament

Bone grafts are classified into autogenous, allogenic, alloplastic, xenograft, syngensio grafts and orthotopic grafts based on their origin. The gold standard for alveolar bone restoration is an autologous bone graft [7].

Growth Factors

Growth factors are proteins or polypeptides that can encourage the production of deoxyribose nucleic acid and the progression of the cell cycle, triggering the proliferative process of dormant cells. They are a group of multipurpose biologic mediators that control the growth, differentiation, angiogenesis, proliferation and protein synthesis of connective tissue cells, as well as the inflammation, tissue healing and immunological response.

Growth factors have been proposed to have a beneficial effect on periodontal regeneration when used therapeutically as topical agents. Some growth factors in periodontal regeneration include

- a) Platelet- Derived Growth Factor (PDGF)
- b) Transforming Growth Factor (TGF)
- c) Insulin- like Growth Factor (IGF)
- d) Basic Fibroblast Growth Factor (bFGF) [8]

Platelet- Derived Growth Factor

Its sources include degranulating platelets, endothelial cells, smooth muscles, macrophages, fibroblasts, osteoblasts and osteoclasts and it is also known as glioma- derived growth factor [8].

A concentration of autologous thrombocytes, Platelet- Rich Plasma (PRP), induces neoformation of blood vessels, which are essential in the process of regeneration. Its components include growth factors WBC, phagocytic cells, native fibrinogen concentration, vasoactive and chemotactic agents, high concentrations of platelets. It has been observed that using this autologous plasma, which is a rich supply of growth factors, is an efficient strategy to promote tissue repair and regeneration [9].

PRP is a novel tissue engineering application that both doctors and researchers are working to understand. Growth factors, particularly PDGF and TGF- β , which both have an impact on bone regeneration, are stored in it. Although the mechanics and growth factors at play are still not fully understood, the simplicity with which PRP may be used in a dental clinic and its positive results, such as reduced bleeding and quick healing, offer hope for future surgeries. The main benefit of using this autologous product is that it eliminates worries regarding immunogenic reactions and disease transmission [9,10].

A fibrin matrix called Platelet-Rich Fibrin (PRF) can act as a resorbable membrane by trapping platelet cytokines and cells that are released after a predetermined amount of time. Developed in France by Choukroun, et al., in 2000, the PRF production protocol attempts to accumulate platelets and releases cytokines in a fibrin clot. With streamlined processing and no artificial biochemical alteration, Platelet-Rich Fibrin (PRF) offers a significant development in the platelet gel therapeutic idea. Unlike other platelet concentrates, this method doesn't need anticoagulants or bovine thrombin (or any other gelifying agent), so it's just centrifuged natural blood without any other ingredients at 3000 rpm for 10 minutes [9,11]. Gassling, et al., have shown that PRF is a suitable scaffold for breeding human periosteal cells *in-vitro*, which may be suitable for bone tissue engineering applications [12].

Minimally Invasive Surgical Techniques

The invasiveness of surgical treatments has been drastically reduced in both medicine and dentistry and new equipment and materials have been created to prepare for the inevitable evolution of the surgical arsenal. This unusual and creative strategy has only lately been added to the field of periodontal surgery. Minimally Invasive Surgery (MIS), as advocated by Harrel and Rees¹, aims to handle the soft and hard tissues with care and leave behind a few scars [13]. By using magnifying instruments like operating microscopes and microsurgical tools and materials, smaller, more precise surgical operations are made possible and are referred to as "minimally invasive surgery". Cortellini and Tonetti recommended the use of an operational microscope in periodontal regenerative surgery, noting an improved potential for primary care due to an increased capacity to move the soft tissue wound healing and closure. According to Harrel and Rees, Minimally Invasive Surgery (MIS) strives to handle the soft and hard tissues gently and leave behind a few scars utilizing the M-MIST, a modified minimally invasive surgical approach that additionally included the concept of regeneration-friendly space. The MIS and the MIST, on the other hand were created with the goal of minimizing flap extension and mobility in order to improve blood clot and wound stability, lessen invasiveness and lower patient morbidity. A surgical advancement led to the M-MIST, where just a very small buccal flap is lifted [14]. The morbidity for the patient during surgery and in the weeks that follow is frequently associated with these therapeutic improvements being exceedingly low. Compared to more conventional surgical procedures, such a surgery requires substantially less time in the operating room. However, minimally invasive surgery is not always an option. Clinicians should be assisted in choosing the optimal course of action via a stepwise decision-making process. Periodontal regeneration could perhaps benefit from minimally invasive surgery [15].

Tissue Engineering: A Giant Leap in Periodontal Regeneration

Numerous strategies, including the use of barrier membranes and bone replacement grafts, have been tried, but none have succeeded in attaining "Restitutio ad integrum" - a fully functional link. The development of novel techniques for periodontal regeneration based on tissue engineering principles is a significant challenge for the future, given the limitations of existing treatments.

In 1993, Langer, et al., suggested, tissue engineering as a potential method for replacing missing periodontal tissues. In the interdisciplinary discipline of tissue engineering, technologies and ideas from engineering and the life sciences are used to create biological substitutes that can repair, preserve and enhance the function of organs and tissues that have been damaged. Tissue engineering aims to facilitate healing and, ideally, real regeneration of a tissue's form and function more reliably, more swiftly, less intrusively and more effectively than passive treatments previously available. When a wound heals naturally, tissue scarring or repair typically occurs. Tissue regeneration is induced by manipulating the wound healing process via tissue engineering. There are two important elements that determine whether the injured tissues heal through regeneration or repair:

- Access to the necessary cell types
- The presence or lack of cues or signals required to draw in and activate these cells

Scaffold

The scaffold offers a three-dimensional substrate on which the cells can multiply and move, generate a matrix and develop into a functioning tissue with the required shape in periodontal tissue engineering. A suitable bioactive three-dimensional scaffold is crucial to promoting cellular proliferation and differentiation. A scaffold functions as a delivery vehicle, a barrier to prevent infiltration, a framework to facilitate cellular migration into the defect, as well as physically reinforcing the defect to maintain its shape. Scaffolds used for periodontal regeneration include naturally derived ceramics like hydroxyapatite and polymers like alginate, agarose and albumin and synthetic scaffolds like synthetic polyesters such as Polyglycolic Acid (PGA), copolymers of polyethylene oxide and polypropylene oxide known as 'PLURONICS' [16].

Cells

When using tissue engineering techniques to replace missing tissues and functions, cell source is a crucial factor to take into account. A daughter stem cell that is identical to the parent stem cell and a progenitor cell that can differentiate into more mature cells are created via asymmetric mitosis from stem cells. Immature progenitor cells with multi-lineage differentiation and self-renewal capabilities are called stem cells.

The origin of the stem cell determines whether it is totipotent, pluripotent, or multipotent. Mesenchymal stem cells were first discovered by Friedenstein and colleagues in adult bone marrow aspirates. Mesenchymal Stem Cells (MSCs), which are adult stem cells derived from bone marrow, are adherent, proliferating cells that have a high potential for autologous cell-based therapy because they can differentiate into a variety of tissues, including bone, cartilage, muscle and tendon. The possibility of allogenic use of MSCs in regenerative medicine without the need for immunosuppressive medication is another crucial quality [17].

Signals

Proteins known as signaling molecules have a variety of effects on cellular growth and function, either locally or systemically. Growth factors and morphogens, which modify cell phenotypes, are the two categories of signaling molecules that have drawn the most attention. Some of the pleiotropic actions of these cytokines include mitogenic (proliferative), chemotactic (stimulate directed cell movement) and angiogenic (stimulate new blood vessel development) effects. Growth factors signal nearby mesenchymal and epithelial cells to migrate, divide and enhance matrix synthesis by acting on the target cell's external cell membrane receptors. In both hard and soft tissue wound healing, platelet-derived growth factor has drawn the greatest interest [18-20].

Tissue Engineering Clinical Applications for Periodontal Tissue Regeneration

1. Protein-Based Approaches

The most widely used tissue engineering technique for the regeneration of periodontal tissues is the use of growth and differentiation agents. A variety of growth factors have been utilized, including: converting growth factor (Superfamily members), bone morphogenetic proteins, fundamental fibroblast growth factor and platelet-derived growth factor

2. Enamel Dentin Matrix

It has been demonstrated that emdogain, a commercially accessible type of Enamel Matrix Proteins (EMPs), encourages periodontal regeneration. A systematic review found that, biologically speaking, EMPs encourage epithelial cell, gingival fibroblast and PDL fibroblast cell adhesion. They stimulate the expression of transcription factors involved in the development of chondroblasts, osteoblasts and cementoblasts. Total protein production and extracellular matrix molecules have both been shown to be boosted [21,22]. The only challenge with using EMD has been its application and associated viscous nature, which may not provide enough support for soft tissue or flaps, thereby reducing the amount of space available for the regeneration process

3. Recombinant Protein Therapeutics

The creation and marketing of pure recombinant human growth factor matrix combinations have been made possible by advancements in recombinant technology. Clinicians and researchers are paying more and more attention to combination products, which are the next generation of tissue engineering treatments, as a way to maximize tissue regeneration.

Under strictly controlled and regulated circumstances, vast quantities of sterile proteins can be produced, concentrated, purified and packed. The ability to mix highly concentrated forms of particular signaling proteins with growth-modulating chemicals in a pure, consistent and high-concentration form IS CRUCIAL in order to improve the predictability of regenerative processes. Three recombinant growth factor products that are frequently employed:

- rh PDGF-BB (gel)
- rhPDGF-BB (with β tricalcium phosphate)
- rh BMP-2 (with type I collagen sponge) [23]

Platelet-derived growth factor (rh PDGF BB) is a recombinant protein that is more than 98% pure and was produced using conventional recombinant expression methods under rigorous conditions. In order to make them, relevant DNA sequences from a human cell are first taken out and put into a bacterial plasmid. The bacterial plasmid is then transfected into the host cells, which have the capacity for rapid growth. These are basically protein factories that generate and secrete a substantial quantity of proteins. Next, rh PDGF BB is separated utilizing cutting-edge technology [22].

Orthopaedic, craniomaxillofacial and periodontal reasons for tissue engineering employing PRP or recombinant protein therapies are all already available in the clinic. Finally, dental surgeons have access to pure recombinant tissue growth factors, which enables us to move from old passive therapies to new active ones, improving the possibility of bone and other tissue regeneration and resulting in a more predictable, quick, less invasive, less traumatic and more effective outcome for the patient.

Gene Therapy

The single administration of purified tissue growth factors has not been shown to be clinically effective in supporting the horizontal regeneration of periodontal tissue breakdown because of their short biological half-lives. Once applied, these factors are subject to proteolytic breakdown and receptor-binding problems and are dependent on the stability of the carrier system.

Gene transfer methods may circumvent many of the limitations of protein delivery to soft tissue wounds. Greater sustainability is offered by the gene transfer application of growth factors or soluble cytokine receptors than by the application of a single protein. enhanced bioavailability of growth factors in periodontal lesions due to gene therapy may result in enhanced generative potential [24]. Gene Delivery Methods Genetic engineering approaches generally consist of two modalities:

- *In-vivo* gene delivery
- *Ex-vivo* gene delivery

Vectors used in gene therapy include plasmids, Adenoviruses (Ad), lentiviruses, retroviruses, Adenoassociated Viruses (AAVs) and baculoviruses, each of which has its own advantages and disadvantages [25]. Dunn, et al., implemented the delivery of Ad-BMP-7 using a collagen matrix in a preclinical model in order to treat peri-implant osseous defects and reported that gene delivery began on day 1 and reached peak expression at day 4. Gene treatment of dental implant fixtures with Ad-BMP-7 resulted in enhanced alveolar bone defect fill, coronal new bone formation and new bone-to-implant contact [26]. A biodegradable carrier and naked DNA are the foundation of one of the most promising gene therapy strategies for periodontal regeneration. In this method, a so-called "Gene-Activated Matrix" (GAM) that can convey the bare DNA *in-vivo* is constructed using collagen or another carrier. When compared to other medicines, gene therapy has several advantages. Gene therapy may be less risky and more affordable than cell-based therapies because neither cell transplantation nor laboratory cell culture are required. Additionally, gene therapy may imitate the intricate natural process of periodontal tissue better than currently available recombinant single-protein therapies since it uses multiple genes and numerous proteins can be delivered within bone defects [27].

RNA Interference

RNAi is the name given to the RNA-mediated silencing mechanism; Fire and Mellow received the Nobel Prize in 2006. The identification of RNA interference (RNAi) has paved the way for RNA-based treatments that could be useful in the treatment of a wide range of illnesses and in tissue regeneration, including periodontal tissue regeneration. RNA interference (RNAi) functions by directing the degradation of complementary or partially complementary messenger RNA molecules (post-

transcriptional gene silencing) or interfering with the expression of specific genes at the promoter level (transcriptional gene silencing) using small RNAs, which are made up of 20 to 30 nucleotides. Today, researchers can artificially induce RNAi by introducing synthetic molecules of RNA into cells. Small linear RNAs (siRNA) or artificially generated short hairpin RNAs (shRNAs) can be directly transfected into the cells or delivered by plasmid or viral transduction. The shRNAs, or siRNAs, take part in endogenous posttranscriptional gene silencing in the cytoplasm. An endoribonuclease known as Dicer recognizes and processes the synthesized RNAs before incorporating them into the RNA-induced silencing complex. The target messenger RNA is then cut by AGO2 to silence the target gene. SiRNAs are used in the majority of RNA-based treatments now being researched because they are secure and affordable. They can be chemically manufactured and introduced into the cells without the use of viruses. The VEGF-targeted RNA for the treatment of macular degeneration of the retina was the first siRNA-based therapy tested in human clinical trials. As RNAi emerges as a promising technology for the treatment of several diseases, one may also envision RNAi as an effective tool for tissue regeneration, including periodontal regeneration. Through the silencing of genes that negatively control cell proliferation and differentiation or genes that induce inflammation or apoptosis, RNAi may favor tissue regeneration [28,29].

Regeneration Around Peri Implant Defects

Bone fill of peri-implant defects resulting from previous peri-implantitis may be achieved following anti-infective therapy and using the biological principle of Guided Tissue Regeneration (GTR) (Lehmann, et al.,). Once the primary goal of surgical intervention (i.e., a bacterium-free implant surface) has been achieved, it may be necessary to correct the anatomic conditions to improve plaque control and eliminate the favorable environment for anaerobic bacteria (i.e., deep pockets). This may be accomplished either with respective procedures (bone resection and apically repositioned flaps) or with regenerative procedures (guided bone regeneration [GBR], autologous, or Regeneration Around Peri Implant Defects 150 allogenic bone grafts). The decision-making process regarding the use of resective or regenerative procedures may be influenced by the degree and/or morphology of the peri-implant tissue destruction. If the amount of lost supporting bone is minimal, a reflexive approach may be preferable. If a major portion of the supporting bone has been resorbed, forming a crater-like defect with remaining wall structures, a regenerative technique is preferred [30,31].

Guided Bone Regeneration

Guided Bone Regeneration (GBR) is a reconstructive procedure of the alveolar ridge using membranes. This procedure is indicated when there is no sufficient bone for implantation or in the case of optimal implant installation for aesthetic or functional needs. GBR can be performed before implant placement, when there is not enough bone for initial stability of implants and less predictable outcomes (staged approach), or performed simultaneously with implantation (combined approach) [32]. GBR is based on the principles of Guided Tissue Regeneration (GTR), which are based on the principle that, specific cells contribute to the formation of specific tissues. Melcher described the concept of selective cell repopulation of defects to enhance healing. The GBR concept employed the same principles of specific tissue exclusion but was not associated with teeth. Thus, the term applied to this technique was Guided Bone Regeneration (GBR). Guided Bone Regeneration (GBR) techniques have been successfully applied in the treatment of peri-implant bone defects and for increasing the width and height of the alveolar ridge. These techniques utilize porous membranes as mechanical barriers to create a secluded space around the defects to permit bone regeneration without the competition of other tissues. The membranes most frequently employed for this purpose are non-resorbable, expanded Polytetrafluoroethylene (e-PTFE). Non-resorbable e-PTFE membranes are supposed to remain in place, completely covered by the soft tissues, for a period of time sufficient to allow bone regeneration and maturation and then they must be removed with re-entry surgery. Most of the Osseo integrated implant systems involve a two-stage surgical approach that allows easy removal of the membrane at the second-stage surgery; therefore, re-entry procedures are not considered a disadvantage in implant applications. Based on these clinical and experimental findings, it may be concluded that GBR applied to failing implants does not yet provide predictable results [30].

Alloderm

The multi-step patented method used to create Alloderm, an acellular dermal matrix made from donated human skin, removes both the epidermis and the cells that can cause tissue rejection. It has consistently produced outstanding outcomes in a wide range of soft tissue grafting techniques, including root covering, soft tissue augmentation and guided bone regeneration. Two thickness ranges are available for usage in various procedures: N0.9 to 1.6 mm; AlloDerm for soft tissue ridge augmentation,

root covering, etc. For directed bone regeneration and barrier membrane function, use N0.5 to 0.8 mm AlloDerm GBR [33]. AlloDerm has a safety history of more than a decade. Introduced in 1994 for treating burn patients, AlloDerm has proven its versatility and safety in more than a million diverse procedures in general, including orthopaedic, urogenital and dental surgeries. The proprietary processing to derive AlloDerm from donor tissue involves a series of steps: First, treatment with a buffered salt solution to separate and eliminate the epidermis; followed by a N series of washes with mild non-denaturing detergent solutions to solubilize and eliminate all cells; and finally, a freeze-drying step using patented technology that prevents damaging ice crystal formation [34]. AlloDerm is effective in augmenting thin tissue around dental implants to create more attached tissue. Dermis is processed to eliminate its cellularity and then cryoprecipitates to remove its antigenicity to create Alloderm GBR, a collagen-based barrier membrane. Its production follows the exact same steps as AlloDerm's, which supports primary closure. It is structurally comparable to alloderm, which is used to cover recessions and only differs in thickness (0.5 to 0.9 mm), it is thinner. It doesn't matter which way around an alloderm's connective tissue and basement membrane sides are [35]. It readily adapts to graft sites and can be secured with either sutures or tacks. AlloDerm has up to a 2-year shelf life when stored between 1°C - 10°C (34-50°F). The AlloDerm GBR barrier membrane really enables the body to reconstruct it into the patient's own tissue, in contrast to conventional barrier membranes that either resorb too soon or do not resorb at all. This improves soft tissue quality and appearance while producing optimal bone regeneration. AlloDerm, used as a barrier over resorbable hydroxyapatite in extraction sites, was able to preserve ridge dimensions and significantly increase the width of keratinized tissue (Fig. 1-8) [36].

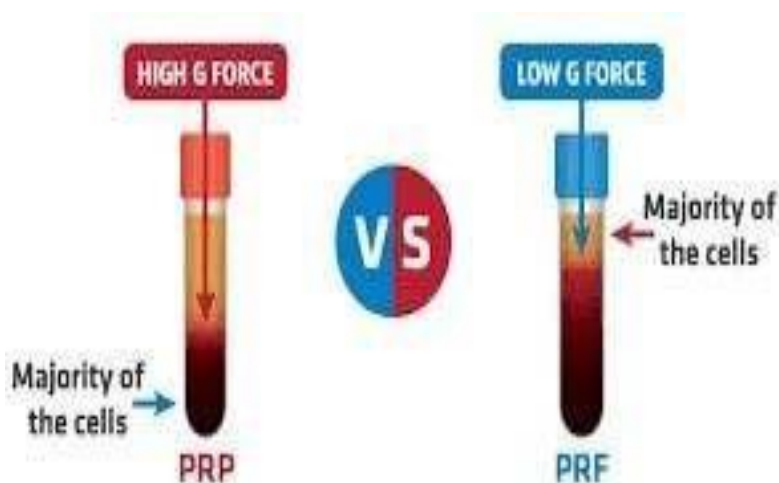


Figure 1: Difference in presence of cells in platelet rich plasma and platelet rich fibrin.

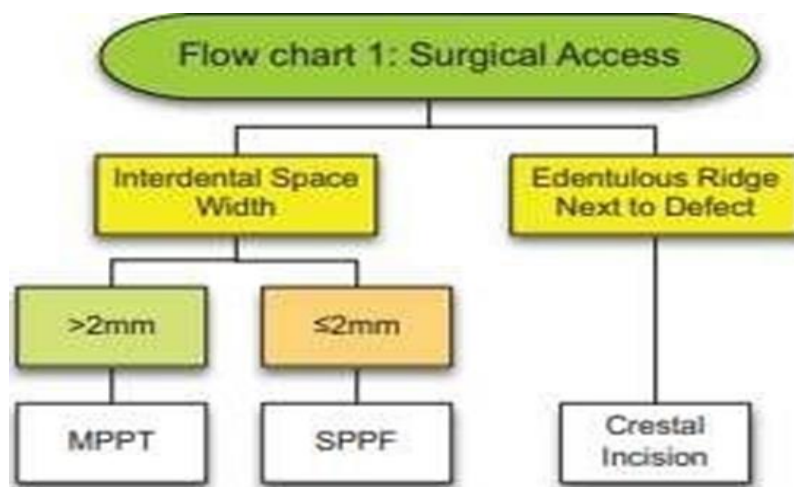


Figure 2: Surgical access in minimally invasive surgery; Modified Papilla Preservation Technique (MPPT), Simplified Papilla Preservation technique (SPPF).

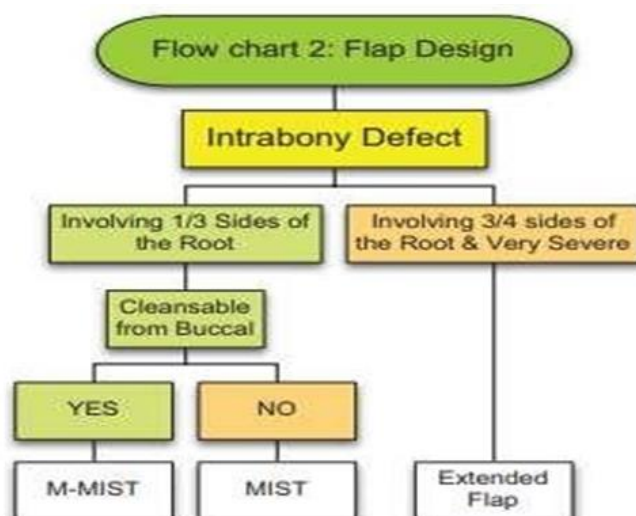


Figure 3: Flap design in minimally invasive surgery, Modified Minimally Invasive Surgical Technique (M-MIST), Minimally Invasive Surgical Technique (MIST).

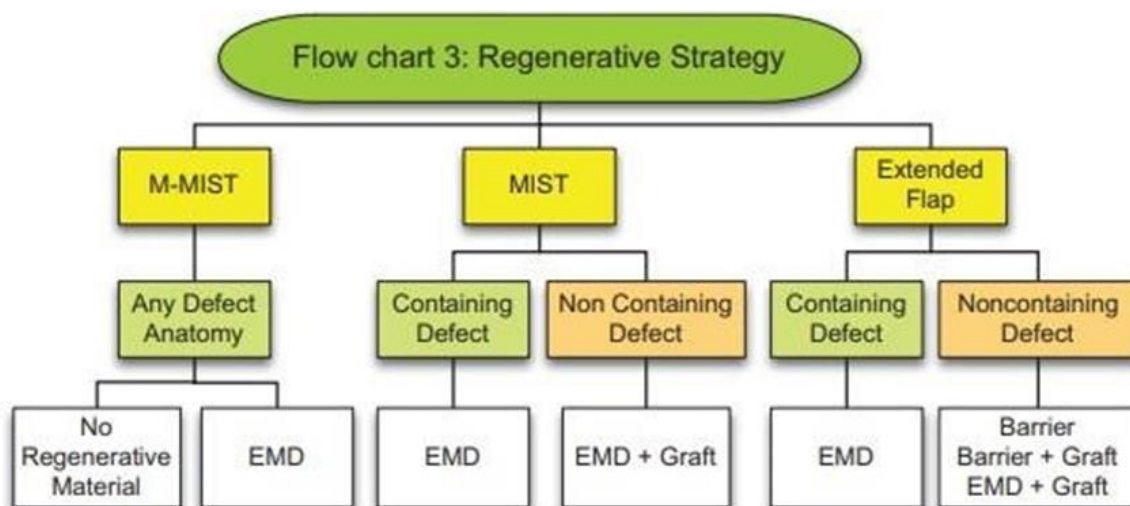


Figure 4: Regenerative therapy by using grafts, barrier and Enamel Matrix Derivative (EMD) with Modified Minimally Invasive Surgical Technique (M-MIST), Minimally Invasive Surgical Technique (MIST).

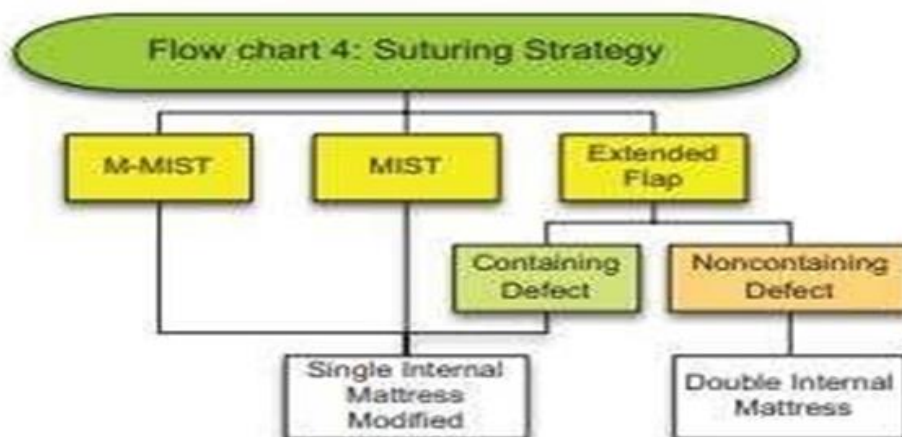


Figure 5: Suturing strategy in minimally invasive surgical approach.

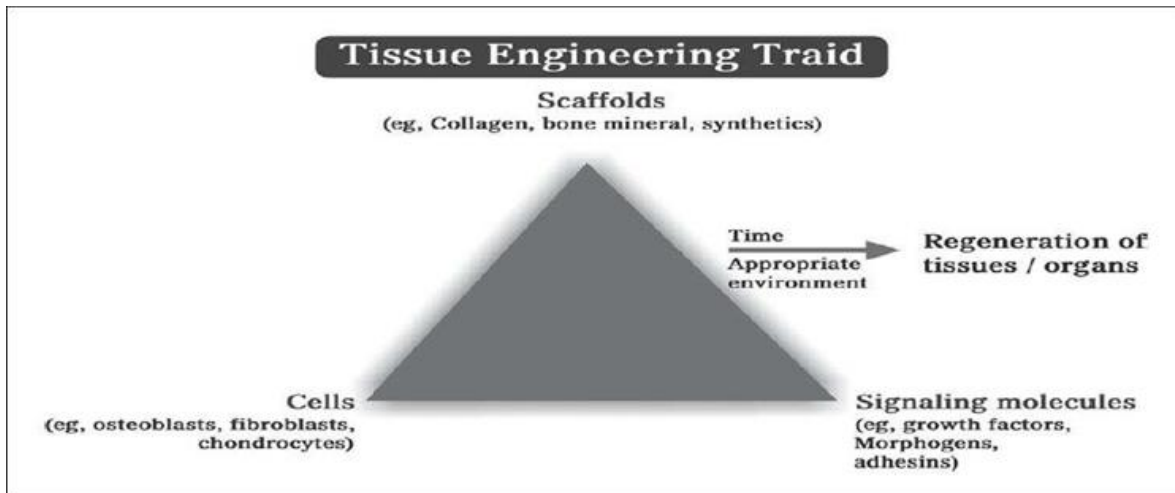


Figure 6: Key elements of tissue engineering: the tissue engineering triad.

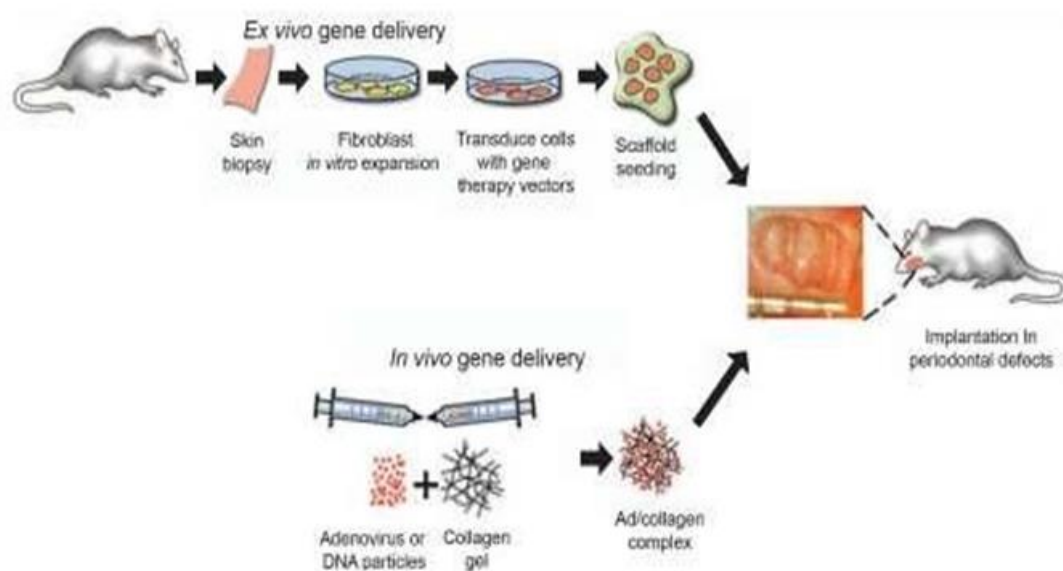


Figure 7: Gene transfer approaches for periodontal regeneration, *ex-vivo* and *in-vivo* gene delivery.

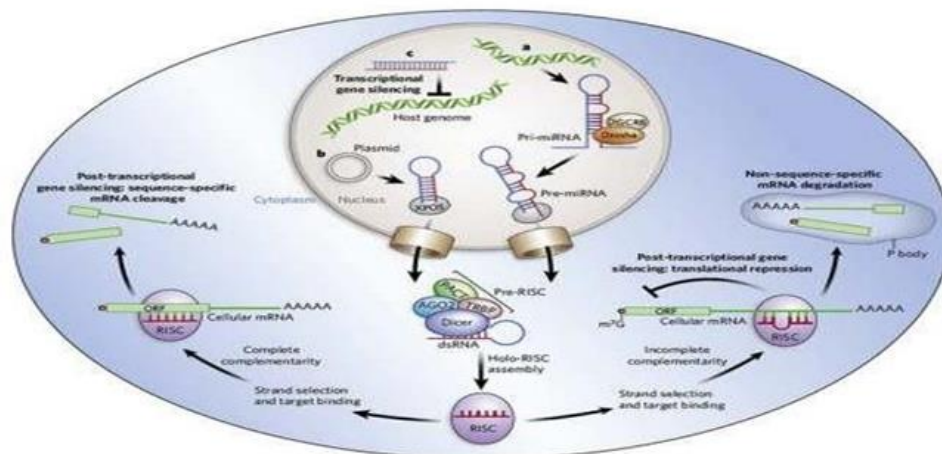


Figure 8: (a) mechanism of the posttranscriptional RNA- mediated gene silencing; (b) mechanism of artificially induced posttranscriptional gene silencing; (c) mechanism of transcriptional gene silencing.

Conclusion

A promising and ever-evolving method of treating gum disease and regaining dental health in periodontics is regenerative treatment. Clinicians have the ability to stop the progression of periodontal disease as well as regenerate lost periodontal tissues by using a variety of regenerative techniques and has experienced considerable breakthroughs and excellent outcomes in many instances. Despite the various difficulties, regenerative therapy gives patients the chance to keep their original teeth and improves both their general dental health and quality of life. Future regenerative therapy in periodontics presents the possibility of more effective, minimally invasive and patient-friendly treatments as research continues to unearth fresh methodologies and technologies. In order to give their patients, the best treatment options for periodontal disease, dental professionals must stay current on the most recent research in this area and think about adding regenerative treatments to their treatment plans where appropriate.

Conflict of Interest

The authors have no conflict of interest to declare.

References

1. Shin SY, Rios HF, Giannobile WV, Oh TJ. Periodontal regeneration: Current therapies. *Stem Cell Biology and Tissue Engineering in Dental Sci.* 2015;459-69.
2. Mancini L, Fratini A, Marchetti E. Periodontal regeneration. *Encyclopedia.* 2021;1(1):87-98.
3. Liang Y, Luan X, Liu X. Recent advances in periodontal regeneration: A biomaterial perspective. *Bioactive Materials.* 2020;5(2):297-308.
4. Bee SL, Hamid ZA. Asymmetric resorbable-based dental barrier membrane for periodontal guided tissue regeneration and guided bone regeneration: A review. *J Biomedical Materials Research Part B: Applied Biomaterials.* 2022;110(9):2157-82.
5. Sohn HS, Oh JK. Review of bone graft and bone substitutes with an emphasis on fracture surgeries. *Biomaterial's Research.* 2019;23(1):1-7.
6. Newmann C. Clinical periodontology, third south Asia edition, periodontal regeneration and reconstructive surgery. 2019.
7. Pryor ME, Polimeni G, Koo KT, Hartman MJ, Gross H, April M, et al. Analysis of rat calvaria defects implanted with a platelet rich plasma preapartion: Histological and histometric observations. *J Clin Periodontol.* 2005;32:966-72.
8. Atarbashi-Moghadam F, Rad MR, Sijanivandi S, Khodayari P, Mahmoud M. Growth factors in periodontal complex regeneration. *Chin J Dent Res.* 2022;25(2):85-92.
9. Mohan SP, Jaishangar N, Devy S, Narayanan A, Cherian D, Madhavan SS. Platelet-rich plasma and platelet-rich fibrin in periodontal regeneration: a review. *J Pharmacy Bioallied Sci.* 2019;11(Suppl 2):S126.
10. Xu J, Gou L, Zhang P, Li H, Qiu S. Platelet-rich plasma and regenerative dentistry. *Australian Dent J.* 2020;65(2):131-42.
11. Madi M, Elakel AM. The clinical implications of platelet-rich fibrin on periodontal regeneration: A systematic review. *The Saudi Dental J.* 2021;33(2):55-62.
12. Gupta V, Bains VK, Singh GP, Mathur A, Bains R. Regenerative potential of platelet rich fibrin in dentistry: Literature review. *Asian J Oral Health Allied Sci.* 2011;1:23-8.
13. Sultan N, Jafri Z, Sawai M, Bhardwaj A. Minimally invasive periodontal therapy. *J Oral Biol Craniofacial Res.* 2020;10(2):161-5.
14. Barbato L, Selvaggi F, Kalemaj Z, Buti J, Bendinelli E, Marca ML, et al. Clinical efficacy of Minimally Invasive Surgical (MIS) and non-surgical (MINST) treatments of periodontal intra-bony defect. A systematic review and network meta-analysis of RCT's. *Clin Oral Invest.* 2020;24:1125-35.
15. Imamura K, Suzuki E, Takeuchi T, Saito A. Clinical outcomes of periodontal regenerative therapy using rhFGF-2 with a modified minimally invasive surgical technique for intrabony defects: case series with a 12-month follow-up. *Int J Periodontics Restorative Dentistry.* 2022;42(4).
16. Pandit N, Malik R, Philips D. Tissue engineering: A new vista in periodontal regeneration. *J Ind Soc Periodontol.* 2011;15(4):328-37.
17. He XT, Wu RX, Chen FM. Periodontal tissue engineering and regeneration. In *Principles of Tissue Engineering.* 2020;1221-49.
18. Bottino MC, Thomas V. Membranes for periodontal regeneration-a materials perspective. *Biomaterials for Oral and*

- Craniomaxillofacial Applications. 2015;17:90-100.
19. Guan N, Liu Z, Zhao Y, Li Q, Wang Y. Engineered biomaterial strategies for controlling growth factors in tissue engineering. *Drug Delivery*. 2020;27(1):1438-51.
 20. Carmagnola D, Pellegrini G, Dellavia C, Rimondini L, Varoni E. Tissue engineering in periodontology: Biological mediators for periodontal regeneration. *The Intl J Artificial Organs*. 2019;42(5):241-57.
 21. Lang NP, Wilson TG, Corbet EF. Biological complications with dental implants: their prevention, diagnosis and treatment. *Clin Oral Impl Res*. 2000;11(Suppl.):146-55.
 22. Galli M, Yao Y, Giannobile WV, Wang HL. Current and future trends in periodontal tissue engineering and bone regeneration. *Plastic and Aesthetic Res*. 2021;8.
 23. Vaquette C, Pilipchuk SP, Bartold PM, Huttmacher DW, Giannobile WV, Ivanovski S. Tissue engineered constructs for periodontal regeneration: current status and future perspectives. *Adv Healthc Mater*. 2018;7:e1800457.
 24. Dunn CA, Jin Q, Taba M, Franceschi RT, Bruce Rutherford R, Giannobile WV. BMP gene delivery for alveolar bone engineering at dental implant defects. *Mol Ther*. 2005;11:294-9.
 25. Goker F, Larsson L, Del Fabbro M, Asa'ad F. Gene delivery therapeutics in the treatment of periodontitis and peri-implantitis: a state-of-the-art review. *Int J Molecular Sciences*. 2019;20(14):3551.
 26. Laird NZ, Acri TM, Tingle K, Salem AK. Gene-and RNAi-activated scaffolds for bone tissue engineering: Current progress and future directions. *Advanced Drug Delivery Reviews*. 2021;174:613-27.
 27. Liu Y, Guo L, Li X, Liu S, Du J, Xu J, et al. Challenges and tissue engineering strategies of periodontal-guided tissue regeneration. *Tissue Engineering Part C: Methods*. 2022;28(8):405-19.
 28. Urban IA, Monje A. Guided bone regeneration in alveolar bone reconstruction. *Oral and Maxillofacial Surgery Clinics*. 2019;31(2):331-8.
 29. Schwarz F, Ramanauskaite A. It is all about peri-implant tissue health. *Periodontology 2000*. 2022;88(1):9-12.
 30. Kim YK, Ku JK. Guided bone regeneration. *J Korean Association of Oral and Maxillofacial Surg*. 2020;46(5):361-6.
 31. Wang J, Wang L, Zhou Z, Lai H, Xu P, Liao L, et al. Biodegradable polymer membranes applied in guided bone/tissue regeneration: a review. *Polymers*. 2016;8(4):115.
 32. Luo D, Yao C, Zhang R, Zhao R, Iqbal MZ, Mushtaq A, et al. Silk fibroin/collagen blended membrane fabricated via a green papermaking method for potential guided bone regeneration application: *In-vitro* and *in-vivo* evaluation. *ACS Biomaterials Sci Engineer*. 2021;7(12):5788-97.
 33. Tavelli L, McGuire MK, Zucchelli G, Rasperini G, Feinberg SE, Wang HL, et al. Extracellular matrix-based scaffolding technologies for periodontal and peri-implant soft tissue regeneration. *J Periodontol*. 2020;91(1):17-25.
 34. Barootchi S, Tavelli L, Gianfilippo RD, Eber R, Stefanini M, Zucchelli G, et al. Acellular dermal matrix for root coverage procedures: 9-year assessment of treated isolated gingival recessions and their adjacent untreated sites. *J Periodontol*. 2021;92(2):254-62.
 35. Anton D, Sufaru IG, Martu MA, Laza G. Types of barrier-membrane in periodontal therapy of guided tissue regeneration. *Romanian J Med Dental Education*. 2019;8(10).
 36. Reisie BH, Farhad SZ, Sadeh SA. Evaluation and comparison number of gingival fibroblast and osteosarcoma cell (MG-63 cell line) adhesive to mocugraft, alloderm and collagen membrane with or without advanced platelet-rich fibrin. *Dental Res J*. 2021;18.

Journal of Dental Health and Oral Research



Publish your work in this journal

Journal of Dental Health and Oral Research is an international, peer-reviewed, open access journal publishing original research, reports, editorials, reviews and commentaries. All aspects of dental health maintenance, preventative measures and disease treatment interventions are addressed within the journal. Dental experts and other related researchers are invited to submit their work in the journal. The manuscript submission system is online and journal follows a fair peer-review practices.

Submit your manuscript here: <https://athenaeumpub.com/submit-manuscript/>