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Review Article

Tissue Engineering For Periodontal Regeneration

Periodontal Tissue Engineering: A Literature Review

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Abstract: Periodontal regeneration is the formation of new cementum, periodontal ligament, and alveolar bone following periodontal surgery. It is widely believed that tissues formed during regeneration are more resistant to deterioration than those gained when healing occurs through repair, which is why regeneration is so important. The two main goals of periodontal therapy are controlling the infection and rebuilding the architecture and function of periodontal tissues. Due to the periodontium's highly hierarchical organization, which calls for a highly coordinated spatiotemporal healing response to enable regeneration, the regeneration of the periodontal apparatus with the formation of the bone-PDL-cementum complex at the same time continues to present challenges. The final goal of periodontal therapy for tissues destroyed by periodontal diseases is the regeneration of the attachment apparatus, composed of the development of new alveolar bone, periodontal ligament, and cementum. With a clear understanding of the periodontal disease process, the regeneration of the periodontium is one of the major goals of periodontal therapy. This review is an update on the current tissue engineering knowledge as a possible periodontal regeneration technique.

Keywords: Periodontal Regeneration, Tissue engineering, Stem Cells, Platelet Concentrates, Scaffolds, Cell Sheet Engineering, Review

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1. INTRODUCTION

Regeneration is the reproduction or reconstitution of a lost or injured part. Periodontal regeneration is the formation of new cementum, periodontal ligament, and alveolar bone following periodontal surgery. It is widely believed that tissues formed during regeneration are more resistant to deterioration than those gained when healing occurs through repair, which is why regeneration is so important. Repair is defined as wound healing by tissue that does not fully restore the previous architecture or function [1]. The two main goals of periodontal therapy are controlling the infection and rebuilding the architecture and function of periodontal tissues. Due to the periodontium's highly hierarchical organization, which calls for a highly coordinated spatiotemporal healing response to enable regeneration, the regeneration of the periodontal apparatus with the formation of the bone-PDL-cementum complex continues to present challenges. This challenge is currently at the forefront of periodontal practice and research. The compromised environment in which periodontal wound healing occurs, which entails a nonvascular tooth surface residing in a microbially rich oral environment that promotes biofilm formation, is another barrier to regeneration. Due to the development of a protracted junctional epithelium along the root surface, the healing response to normal periodontal surgical treatment is one of repair rather than regeneration[2]. Regeneration can lengthen the lifespan of the dentition because it is, by definition, a periodontium rebirth; yet, attaining this goal is not easy.

Tissue engineering techniques have emerged due to recent developments to overcome the problems above. The various methods that have been employed in recent years to stimulate periodontal regeneration with variable degrees of effectiveness have taught us a lot. It has become clear that the surgical or regenerative site needs to be sufficiently separated from the oral environment for the best possible regeneration. It is also obvious that certain cell types need to be removed from the area, and others need to be recruited to promote regeneration. Periodontal regeneration is a complex process that requires the differentiation of the numerous cell types involved and the synthesis of these cells in adequate numbers in the appropriate environment (Table 1 shows different patterns of Periodontal Tissue Healing and regeneration). It is also understood that molecular signalling systems primarily control choosing cells. These soluble mediators or growth factors engage the extracellular matrix and cell surface receptors in interaction. Numerous mediators and growth factors have been linked to the periodontium's regenerative and formative processes. However, there isn't a clear link between a single growth factor and periodontal regeneration, but there is some evidence that different growth factors can improve regenerative processes [3]. The current review focuses on the most recent studies on periodontal regeneration. It covers the bone, PDL, and cementum regeneration mechanisms, stem cell mobilization and transplantation, the development of absorbable, injectable, and bio-printed materials, and gene therapy for bone, PDL, and cementum regeneration.

Table 1: illustrates the different Patterns of Periodontal Tissue Healing and regeneration.

Tissue	Pattern
Periodontal Tissue Regeneration	*Regeneration of the tooth cementum, a functionally aligned PDL, Alveolar bone and Gingiva in the periodontal defect results in the healing of the periodontal defect.*
Connective tissue repair	*Collagen fibres positioned parallel or perpendicular to an instrumented root surface that has previously been exposed to periodontal disease or is otherwise devoid of its periodontal attachment ca heal periodontal defects.*
Bone or bone-like tissue repair	*Bone or bone-like tissue growth without particular PDL and/or acellular extrinsic fibre cementum regeneration can heal periodontal defects*
Long junctional epithelium healing	*Keratinocytes that migrates into the pocket from the crevicular epithelium produce a new epithelium attachment along the instrument root surface to treat the periodontal deficiency.*

Keratinocytes carry out the healing of Long junctional epithelium, while collagen fibers carry out that of connective tissue. Bone-like tissue repair and regeneration of cementum, PDL, alveolar bone, and gingiva all results in healing of periodontal healing [Ref. 11 Table 1]

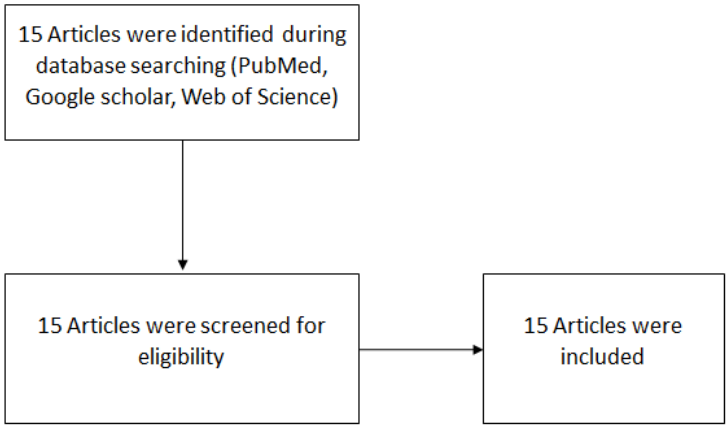


Fig:1 Flow chart of the publication assessment.

2. GUIDED TISSUE REGENERATION

Guided tissue regeneration (GTR) for the periodontium, which was first described in the 1980s, offered a pioneering biological method for periodontal tissue engineering. Although GTR was biologically feasible, clinical outcomes were frequently unsatisfactory because of the technically delicate nature of the surgery and the high rate of postoperative

complications. Despite its clinical limitations, guided periodontal regeneration has been regarded as a significant advancement in regenerative periodontal therapy. The discovery that periodontal tissues are capable of regeneration sparked additional research into the molecular and cellular biology of periodontal regeneration [3]. Fig 2 shows a schematic representation of guided tissue regeneration. For treating intrabony defects, a Systematic Review compared the use of GTR to open flap debridement alone [4]. Clinical measures such as attachment gain, reduced pocket depth, decreased gingival recession, and increased hard tissue probing at re-entry all showed improvements. It is crucial to remember from the systematic reviews that have been published thus far that GTR only produces moderate, variable, and maybe non-existent gains in the long-term aim of tooth retention [4,5]. GTR is, therefore, conceptually solid, but clinical outcomes are inconsistent and predictable regeneration is difficult to achieve in the majority of periodontal abnormalities, maybe with the exception of a few "ideal" circumstances.

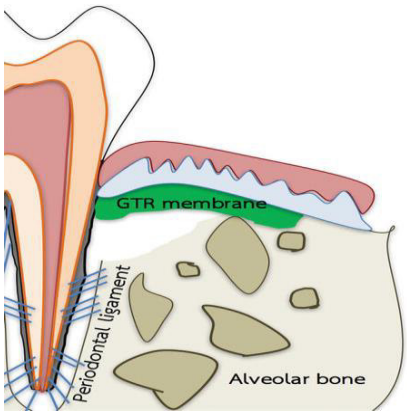


Fig 2: Schematic representation of guided tissue regeneration. Periodontal tissues can regenerate by being separated from the damaged area by a GTR membrane placed over the periodontal defect.[12]

3. TRIAD OF TISSUE ENGINEERING

Scaffolds, Cells, and Signalling molecules comprise the Triad of Tissue Engineering, as shown in Fig:3a and 3b. Each of these components of tissue engineering is further explained in this review.

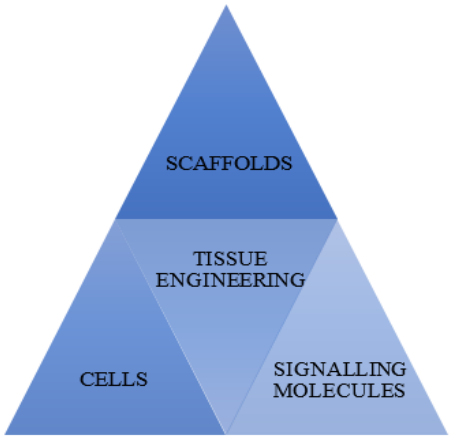


Fig 3a: Figure showing the triad of tissue engineering

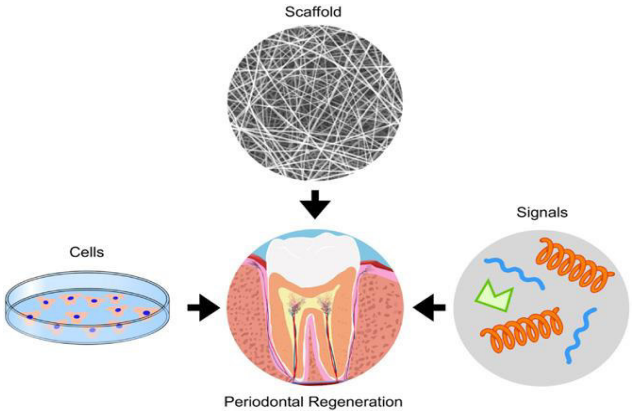


Fig 3b: Figure showing the triad of tissue engineering [14]

4. SCAFFOLDS

In order to take advantage of the extracellular matrix's (ECM) influence on adhesion, migration, proliferation, and differentiation of resident cells, tissue-engineered scaffolds are frequently created to match the extracellular matrix of the targeted tissue. Without the use of bioprinting, early attempts to restore complete teeth and dental tissues used simple scaffolds like collagen gels that could be moulded [6]. Depending on where they came from, scaffolds can be classified as allogenic, xenogeneic, alloplastic, or living structures (when they contain cells). A new era in scaffold development has begun owing to the utilization of 3D printing and bioprinting technologies, which make it possible to build ECM with significantly improved spatial resolution. Reduced alveolar bone resorption, increased osseointegration, and decreased implant failure may result from bio-printed structures that closely resemble the material characteristics of real teeth. Recent bioprinting projects have used naturally hard and soft biomaterials that can be strengthened before use to address this therapeutic requirement and engineering difficulty [7].

4.1. Rigid biomaterials

For dental and periodontal tissue formation, rigid synthetic polymers such as ceramics, composites, and even metals have been employed as scaffolds. Rigid biomaterials have a lot of advantages for producing load-bearing tissues, even if inserting cells during scaffold construction is frequently not possible due to the conditions needed to manage these materials, which can be hazardous to cells. The most popular rigid biomaterial is polycaprolactone (PCL), which is versatile and has superior material characteristics. PCL is a matrix for composite materials that incorporate inorganic minerals and can be electro spun or 3D printed (FDM). Although it breaks down more quickly than PCL, the synthetic polymer poly (lactide-co-glycolide) acid, which has also been employed for tissue engineering scaffolds, is less usually used for dental applications [6].

4.2. Soft biomaterials

When hydrophilic polymers and a cross-linking agent are combined, soft biomaterials are produced with a high degree of flexibility and customizability. Although they are great substrates for 3D cell culture for extrusion bio printing, hydrogels have a severe drawback: they lack mechanical strength. Although a scaffold's primary goal is to duplicate the natural ECM, a hydrogel-only scaffold may not be able to maintain its shape or serve as structural support [6].

5. CELLS

Impressive outcomes have been achieved using several exogenous and endogenous cell types as tissue engineering constructs for dental applications. However, they have yet to produce a bioengineered tooth replacement that is clinically feasible [6].

5.1. Dental Derived Cells

Since collecting embryonic cells from a live patient is impossible, dental-derived cells suitable for bioprinting are isolated from both embryonic and postnatal tissue. Early studies on regenerative dentistry used mesenchymal and epithelial cells isolated from embryonic tooth germs to bioengineer teeth with 'pulp,' 'dentin,' and 'enamel' as well as 'penetrating nerve fibers' and 'blood vessels.' Fig 4 shows cell-based tissue engineering in Periodontal regeneration. According to some research, cells taken from dental pulp or the apical papilla of wisdom teeth may be viable, especially if they are fortified with signalling molecules like bone morphogenetic protein-2 and recombinant human amelogenin. Research shows postnatal tissue-derived cells are inferior to embryonic cells (BMP-2). Comparing SCAP cells to dental pulp cells extracted from the same tooth, 'dental pulp' cells showed higher cell motility and were more proliferative. They also produced more 'dentin' [6]. Recent successes using 'postnatal dental-derived cells' suggest that these cells could be successfully employed to bio print dental tissues if supported by the right scaffolds and signalling molecules.

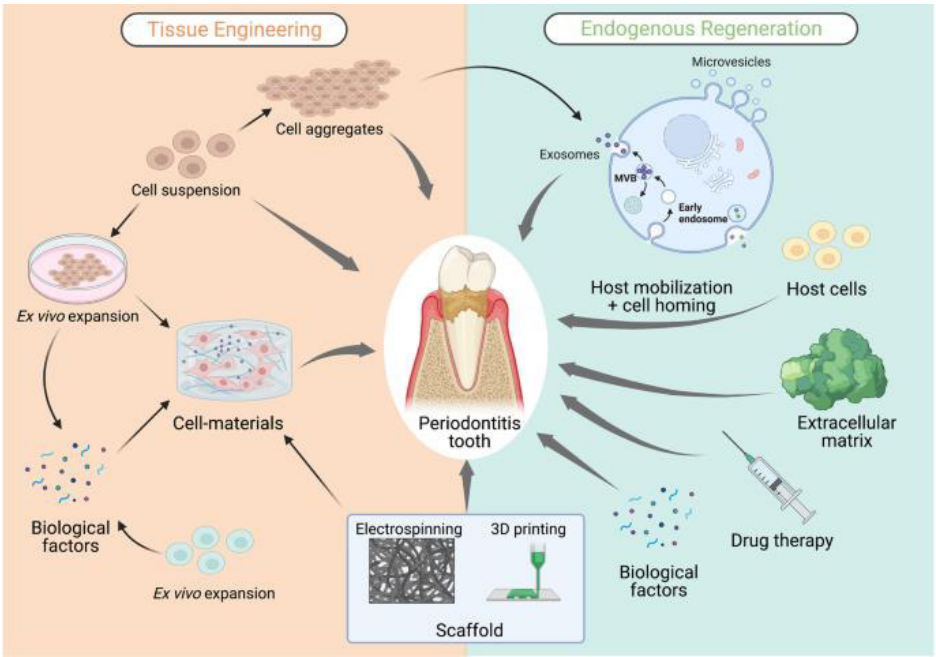


Fig 4: Cell-based tissue engineering and cell-free endogenous regeneration in periodontal regeneration.[13]

5.2. *Stem Cells*

Stem cells are defined as 'undifferentiated cells' which can self-renewal and differentiate to produce 'mature progeny cells.' Precursor or progenitor cells, which are what stem cells are known as are the intermediary cell types that stem cells produce before reaching their fully differentiated state. There are two major types of Stem Cells; Embryonic and Adult stem cells [8]. Mammalian blastocytes are the source of 'Embryonic stem cells,' which can produce various cell types from all three germ layers. However, the isolation and use of human embryonic SCs are difficult and ethically controversial. 'Adult stem cells (postnatal)' are assumed to be committed, tissue-specific progenitors that can only give rise to a few cell lineages. They can be found in several body organs that are tissue-specific, accessible, and less morally dubious. They are of two types; 'Hematopoietic' and 'Mesenchymal' stem cells. While mesenchymal stem cells are defined as a population of postnatal cells hierarchically organized with the ability to differentiate into specialized cells of at least one mesenchymal lineage, such as bone, cartilage, fat, muscle, or neuronal cells', Hematopoietic stem cells can differentiate into almost all blood cell lineage cell types. Periodontal regeneration has been successfully treated with cytotherapies using 'alveolar periosteal cells' (APCs), 'bone marrow mesenchymal stromal cells' (BMMSCs), and 'periodontal ligament cells' (PDLCs). PDL tissue, in particular, comprises multipotent stem cell populations and aids in the regeneration of 'alveolar bone,' 'cementum,' and 'periodontal ligament.' According to reports, BMMSCs can differentiate into PDL, and their implantation has promoted periodontal regeneration. Additionally, it has also been claimed that APCs enhance periodontal regeneration [8].

5.3. *Cell Sheet Engineering*

Although it is challenging to manage the placement and differentiation of transplanted cells, cell delivery for periodontal regeneration is typically accomplished using a combination of cells and scaffolds. An alternative technique for cell transplantation utilizing temperature-responsive culture dishes, known as "cell sheet engineering," has been created in contrast to methods that employ scaffolds. A thermoresponsive polymer known as Poly (N-isopropyl acrylamide) (PIPAAm) has found extensive use in cutting-edge biological applications. A PIPAAm grafted surface is a smart bio interface that allows temperature changes to manage cell adhesion and dissociation easily. Using this technology, confluently cultivated cells can now be recovered as "cell sheets," including keratinocytes, corneal epithelial cell sheets, and oral mucosal epithelial cells [9]. Fig 5 shows temperature-responsive three-dimensional (3D) vascularized cell sheet constructs for tissue regeneration.

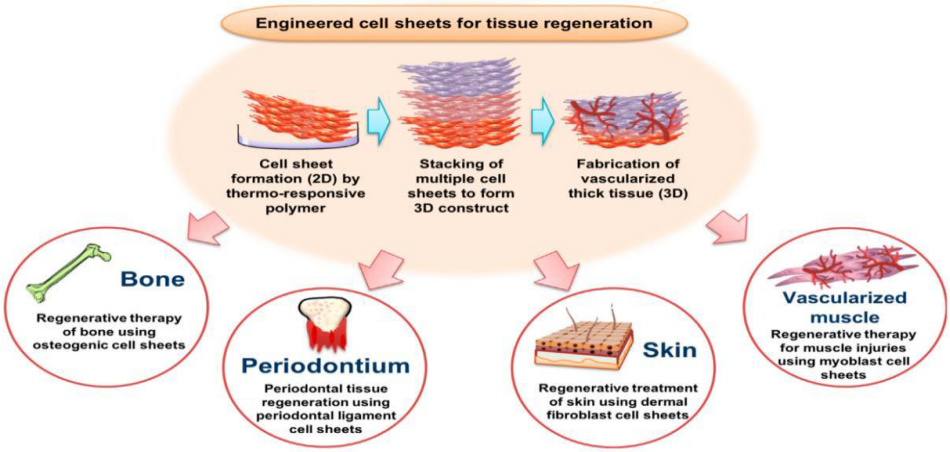


Fig 5: Schematic illustrations of temperature-responsive three-dimensional (3D) vascularized cell sheet constructs for tissue regeneration. [15]

6. SIGNALLING MOLECULES

This review will discuss recent research that combined established and novel technologies with biological signals to create bio-printed dental structures. In printed structures, bioactive signals improve cell function, encourage proliferation, induce differentiation, or affect the host tissue. Studies of potentially effective tissue-engineered dental constructs resulted in tissues that were malformed or disorganized in the absence of bioactive stimuli. As a result, careful utilization of bioactive signals may be necessary for the production of therapeutically relevant bio-printed dental structures [6].

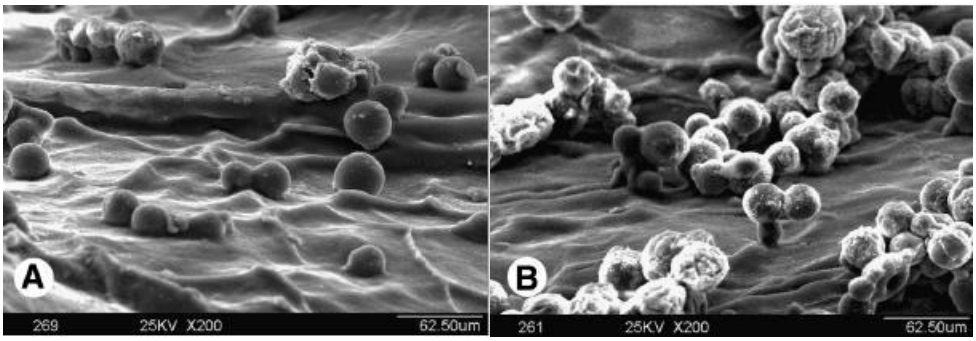
7. BIOLOGY-BASED REGENERATION

7.1. *Enamel matrix derivative*

Proteins from the amelogenin family, which is the hydrophobic component of enamel matrix proteins, are present in enamel matrix derivatives. EMD mimics the natural process of tooth formation by encouraging osteoblasts and periodontal ligament cells to proliferate and migrate, which boosts cementogenesis. The EMD also acts as a scaffold to encourage fibroblast, blood vessel, and epithelial repopulation from surrounding tissues. This matrix's therapeutic effects on augmenting keratinized gingiva and simulating the surrounding tissue are effective and predictable. Blending allografts and autografts (CAF, CTG, FGG, etc.) with EMD may produce better clinical outcomes. It is likely because the graft material's scaffolding capabilities strengthen the wound's integrity and preserve the space required for periodontal regeneration. Although the use of ECM-based scaffolds as alternatives to autogenous grafts has been suggested, the literature lacks clinical considerations on their stability and handling characteristics compared to free gingival grafts and CTG. Some examples of EMD are a) DynaMatrix, a 3D structure porcine-derived matrix from the submucosa of the small intestine in a cell-free procurement. b) Emdogain (Institut Straumann AG, Basel, Switzerland) [7].

7.2. *Volume-stable collagen matrix*

Recently, a novel porous porcine 'CM (Fibrogide®)' was unveiled for the regeneration of soft tissues. Since maintaining good volume stability is one of its key benefits, as it is made of collagen and undergoes cross-linking, this graft is also known as a 'volume-stable collagen matrix (VCMX).' VCMX is formed of collagen and goes through a cross-linking process to provide both volume stability and some flexibility. It has just one layer of porosity, which encourages angiogenesis, fibroblast infiltration, matrix formation, and tissue integration. Unlike CM, which has also been employed in an open setting, VCMX calls for a submerged healing process. To support these preliminary findings, more research with longer follow-up is required [10]. Fig 6 shows an example of Guided tissue and bone regeneration membranes obtained from collagen-based biomaterials.



A: Unloaded microparticles **B: Protein-loaded microparticles**

Fig 6: Guided tissue and bone regeneration membranes obtained from collagen-based biomaterials [Image from the same batch of scaffolds as shown][11]

7.3. *Platelet Concentrates*

Platelet concentrates (PCs) have been used as scaffold matrices and wound-healing accelerators in multiple fields of medicine. Patient blood has been centrifuged to concentrate platelets to boost the density of growth factors and accelerate wound healing. The initial generation of platelet concentrates is thought to comprise platelet-rich plasma (PRP) and plasma rich in growth factor (PRGF). The growth factor (GF) composition of autogenous platelet concentrates is biologically limited because it is orders of magnitude lower than possible with recombinant GFs like PDGFs and FGFs. Without anticoagulants, blood is centrifuged to create the second generation of platelet concentrates. Based on the processing time and speed, platelet-rich fibrin (PRF) is categorized into 'A-PRF,' 'L-PRF,' and titanium-prepared PRF (T-PRF). The release of growth factors, including PDGF, vascular endothelial growth factors (VEGF), TGF-1, and insulin-link growth factors, is one of its advantages (IGF-1) [7]. Fig 7 shows Sequential events that depict the bone regeneration after PRF application.

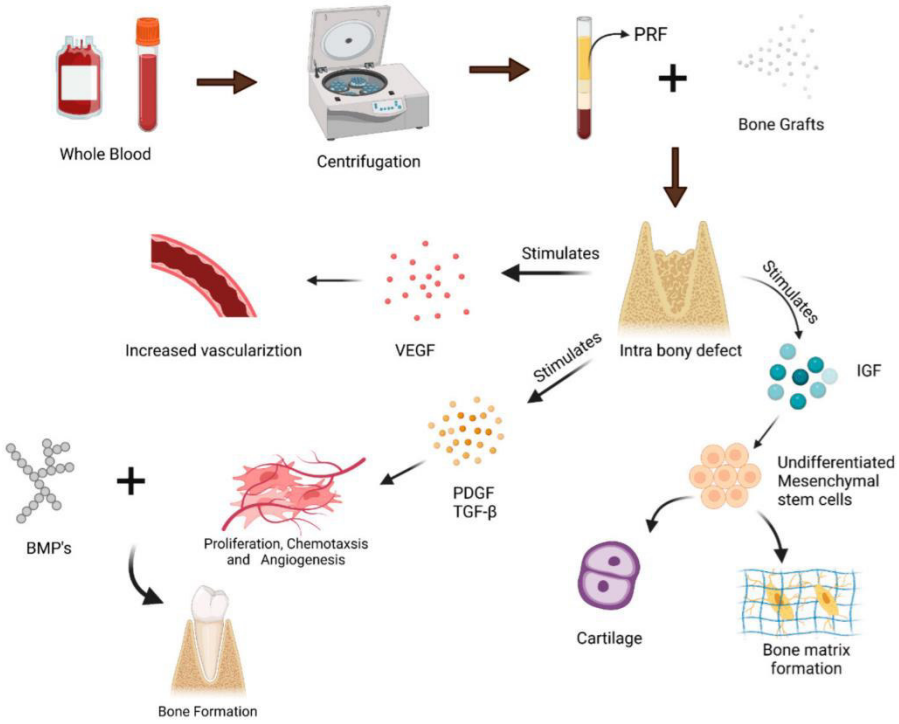


Fig 7: Sequential events that depict the bone regeneration after PRF application.[16]

7.4. Platelet-derived growth factor-BB

After periodontal therapy, the wound site develops a blood coagulum that releases tissue growth factors locally, including platelet-derived growth factor and transforming growth factor beta from degranulating platelets. These mitogenic polypeptides draw fibroblast and mesenchymal cells to the periodontal wound, where they promote their proliferation. Granulation tissue, a source of future periodontal connective tissue cells such as osteoblasts, PDL fibroblasts, and cementoblasts, forms after the ongoing process of periodontal tissue healing. Evaluation of the effects of growth factor treatments on periodontal tissue regeneration has been a prominent area of periodontal research attention. Since its original introduction in the late 1980s, platelet-derived growth factor-BB (PDGF) has gained the greatest research attention in periodontal tissue engineering. It has been established that PDL and alveolar bone cells have a variety of PDGF receptors, which promotes chemotaxis and cell proliferation in both tissues. In a case series using connective tissue grafts (CTG) as controls, 'McGuire' and 'Scheyer' were the first to look at the use of 'rhPDGF-BB' for treating GRs [7].

7.5. Fibroblast growth Factor-2

Heparin-biding cytokine fibroblast growth factor-2 (FGF-2) can make many cell types more active in the angiogenic and osteogenic processes. Due to its effective wound-healing abilities, FGF-2 has been extensively researched in periodontal and bone regeneration alone or in combination with scaffolding matrices. Mesenchymal cells can multiply and migrate more quickly in the PDL when FGF-2 is present. FGF-2-treated sites showed the improved formation of new bone and cementum, and the extent of root coverage utilizing FGF-2 is increased by including a collagen matrix scaffold. In a four-female beagle dog model with experimentally produced partial abnormalities, Sato et al. (2004) investigated the effects of basic fibroblast growth factor (bFGF) on cementum and periodontal ligament regeneration. In teeth treated with 1 g of FGF, 8 weeks after surgery, the production of thick fibers attached to the alveolar bone and freshly synthesized cementum was seen, according to histological examinations. These findings imply that a collagen gel containing fibroblast growth factor is an effective growth factor and carrier material combination for treating PDL deficiencies and may pave the way for easily implementable techniques for treating periodontal disorders [7].

Guided tissue regeneration membranes
Non-resorbable
Expanded PTFE – GoreTex®
High-density PTFE – Cytoplast TXT-200®
Titanium enforced high-density PTFE – Cytoplast Ti-250®
Resorbable, synthetic
Poly DL-lactic/co-glycolic acid
Polyglactin 910
Poly DL-lactide and solvent (*N*-methylpyrrolidone)
Resorbable – collagen-based
Cadaveric human skin type I collagen
Porcine skin collage type I
Bovine tendon collagen type I
Bovine tendon type I collagen
Bone grafting materials
Alloplasts
Beta tricalcium phosphate
Hydroxyapatitie
Calcium sulfate
Calcium phosphate
Bioactive glass
Autografts
Endogenous bone grafts
Allografts
Demineralized freeze dried bone allograft
Freeze dried bone allograft
Xenografts
Anorganic bovine bone xenograft
Bovine-derived xenograft and type I collagen
Growth factors and biologicals studied for periodontal regeneration
Bone morphogenetic proteins-2, -3, -4, -6, -7 and -12
Cell-binding peptide P-15
Fibroblast growth factor-2
Growth/differentiation factor-5
Insulin-like growth factor-1
Matrix factors (fibronectin, amelogenins, thrombospondin)
Platelet-derived growth factor
Platelet-rich plasma
Vascular endothelial growth factor
Enamel matrix derivative

Fig 8: Examples of currently available periodontal regeneration materials (Ref 3 Table:1)

8. SUMMARY

The rapidly evolving scientific area of tissue engineering aims to create methods for creating new tissues to replace damaged tissues. A biomaterial to serve as a scaffold or matrix to contain the cells, biological signalling molecules instructing the cells to build the desired tissue type, and implanted and cultured cells to produce the new tissue are all necessary elements for successful tissue engineering [6]. Since the periodontium includes three separate tissue types, control over tissue formation is at a premium [11]. Regeneration of tissue for larger defects requires a vascular supply for the developing tissue, and thus the inclusion of angiogenic factors into the scaffold may be necessary. Defects involving multiple tissue types (e.g., pdl, cementum, and alveolar bone) may require the application of cell-based tissue engineering methods. The capacity of various bone transplant types to induce bone growth has also been researched. To achieve periodontal regeneration, a different strategy called guided-tissue regeneration has been created [3,4,5]. It is based on the idea that the PDL contains all the progenitor cells necessary for the production of bone, cementum, and PDL and uses barrier membranes to direct and train the specialized cellular components of the periodontium. Integrating the right amount of responsive progenitor cells and bioactive levels of regulatory signals within the appropriate ECM or carrier construct are the key prerequisites for tissue engineering [6]. Periodontally injured teeth require intensive, regenerative treatment. The goal of periodontal tissue engineering research is to develop a new clinical technology that will enable the management of periodontal disorders in addition to the current methods, mainly focused on infection control [11]. Recent developments in the field have combined to usher in a promising new era, where it's feasible that biological methods will increasingly be applied to improve the reconstruction of the tooth-supporting apparatus [17,18]. Although there are still few reported human clinical trials in the current literature, periodontal clinicians and, most definitely, periodontitis patients have high expectations for regenerative medicine or tissue engineering. The field of periodontal regeneration therapy is developing and maturing steadily [11]. However, a lot of challenges remain. Despite the obstacles and challenges, tissue engineering has increased the potential for periodontal regeneration. Most importantly, compared to five years ago, we are much closer to realizing the engineering of a tissue or an organ with complex architecture. This review is an update on the current tissue engineering knowledge as a possible periodontal regeneration technique.

9. CONCLUSION

The final goal of periodontal therapy for tissues destroyed by periodontal diseases is the regeneration of the attachment apparatus, composed of the development of new alveolar bone, periodontal ligament, and cementum. With a clear understanding of the periodontal disease process, the regeneration of the periodontium is one of the major goals of periodontal therapy. The combination of conductive, inductive, and cell-based methods could lead to the engineering of replacements for large-scale defects that require multiple tissue types. This general strategy holds the promise of controllably and predictably guiding the development of specific tissues and offers a new level of precision in tissue engineering.

10. AUTHORS CONTRIBUTION STATEMENT

Dr. Shrishti Salian conceptualized and gathered the data with regard to this work. Dr. Prasad Dhadse analyzed this data, and necessary inputs were given. Dr. Ruchita Patil contributed to data gathering.

11. CONFLICT OF INTEREST

Conflict of interest declared none.

12. REFERENCES

1. American Academy of Periodontology. Current Terminology for Periodontics and Insurance Reporting Manual. 6th ed. Chicago: American Academy of Periodontology; 1991. p. 22.
2. Vaquette C, Saifzadeh S, Farag A, Hutmacher DW, Ivanovski S. Periodontal tissue engineering with a multiphasic construct and cell sheets. J Dent Res. 2019;98(6):673-81. doi: 10.1177/0022034519837967, PMID 30971166.
3. Bartold PM, Gronthos S, Ivanovski S, Fisher A, Hutmacher DW. Tissue-engineered periodontal products. J Periodont Res. 2016;51(1):1-15. doi: 10.1111/jre.12275, PMID 25900048.
4. Needleman IG, Worthington HV, Giedrys-Leeper E, Tucker RJ. Guided tissue regeneration for periodontal infra-bony defects. Cochrane Database Syst Rev. 2006:CD00172. doi: 10.1002/14651858.CD001724.pub2.
5. Jepsen S, Eberhard J, Herrera D, Needleman I. A systematic review of guided tissue regeneration for periodontal furcation defects. What is the effect of guided tissue regeneration compared with surgical debridement in the treatment of furcation defects? J Clin Periodontol. 2002;29;Suppl 3:103-16; discussion 160. doi: 10.1034/j.1600-051x.29.s3.6.x, PMID 12787212.
6. Morrison DG, Tomlinson RE. Leveraging advancements in tissue engineering for bioprinting dental tissues. Bioprinting. 2021;23:e00153. doi: 10.1016/j.bprint.2021.e00153, PMID 34268456.
7. Tavelli. L et al. Biology-based regenerative technologies for periodontal soft tissue engineering. J Periodontol. 2019;00:1-8.
8. Gronthos S, Akintoye SO, Wang CY, Shi S. Bone marrow stromal stem cells for tissue engineering. Periodontol 2000. 2006;41:188-95. doi: 10.1111/j.1600-0757.2006.00154.x, PMID 16686934.
9. Vaquette C, Saifzadeh S, Farag A, Hutmacher DW, Ivanovski SC.Vaquette et al. Periodontal tissue engineering with a multiphasic construct and cell sheets. J Dent Res. 2019;98(6):1-9; International & American Associations for Dental Research. doi: 10.1177/0022034519837967, PMID 30971166.
10. Tavelli. L et al. Extracellular matrix-based scaffolding technologies for periodontal jm and peri-implant soft tissue regeneration. J Periodontol. 2019;0:1-9.
11. Chen FM, Jin Y. Periodontal tissue engineering and regeneration: current approaches and expanding

opportunities. Tissue Eng Part B Rev. 2010;16(2):219-55. doi: 10.1089/ten.TEB.2009.0562, PMID 19860551.
12. Osathanon T, Chanjavanakul P, Kongdecha P, Clayhan P, Huynh NCN. Polycaprolactone-based biomaterials for guided tissue regeneration membrane [Internet]. Periodontitis - A Useful Reference; 2017. InTech.
13. Wang X, Chen J, Tian W. Strategies of cell and cell-free therapies for periodontal regeneration: the state of the art. Stem Cell Res Ther. 2022;13(1):536. doi: 10.1186/s13287-022-03225-z, PMID 36575471.
14. Yogesh, Chu, Tien-Min, Kowolik, Michael, Janowski et al.Bottino, Marco & Thomas, Vinoy & Schmidt, Gudrun & Vohra. Recent advances in the development of GTR/GBR membranes for periodontal regeneration-A materials perspective. Dent Mater Off Publ Acad Dent Mater. 2012;28:703-21. doi: 10.1016/j.dental.2012.04.022.
15. Kim H, Kim Y, Park J, Hwang NS, Lee YK, Hwang Y. Recent advances in engineered stem cell-derived cell sheets for tissue regeneration. Polymers. 2019;11(2):209. doi: 10.3390/polym11020209, PMID 30960193.
16. Varghese J, Rajagopal A, Shanmugasundaram S. Role of biomaterials used for periodontal tissue regeneration—A concise evidence-based review. Polymers. 2022;14(15):3038. doi: 10.3390/polym14153038, PMID 35956553.
17. Zhang W, Abukawa H, Troulis MJ, Kaban LB, Vacanti JP, Yelick PC. Tissue engineered hybrid tooth-bone constructs. Methods. 2009;47(2):122-8. doi: 10.1016/j.ymeth.2008.09.004, PMID 18845257.
18. Abukawa H, Zhang W, Young CS, Asrican R, Vacanti JP, Kaban LB et al. Reconstructing mandibular defects using autologous tissue-engineered tooth and bone constructs. J Oral Maxillofac Surg. 2009;67(2):335-47. doi: 10.1016/j.joms.2008.09.002, PMID 19138608.