# Periodontal Surgery - Revolution from Resection to Regeneration : Review Article

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**Abstract**

The focus of periodontal surgery has shifted over time from a philosophy based on resection to one based on regeneration. This shift has particular significance in cases of advanced periodontitis in aesthetic zone. When severe attachment loss is present, cosmetic reconstruction can not take place until the periodontitis has been treated and the ongoing loss of attachment has been arrested. In the past, resective surgical techniques were used to treat such cases without aesthetic value. Recent advancement in regeneration techniques have potential to restore lost periodontal tissue and has aesthetic value.

## History of Periodontal Resective Surgery

In the past periodontitis had been treated by resective techniques to reduce probing depth.

The aim of resective procedure was the re-establishment of a healthy periodontium at a reduced level, accepting the destruction that has already occurred.These procedures were all designed to achieve pocket elimination or reduction by apical shift of the gingival margin.

The earliest form of resection was Gingivectomy, this procedure dates back to the Roman times, who burned the diseased tissue.

Pierre[1] Fauchard described a resective procedure in 1742 and designed specific instrumentation to remove the excessive tissue.

Another category or resective technique is Flap Surgery.This procedure was introduced in periodontics during the beginning of 20th century.Widman, Neumann, Cieszynski and others are associated with the initial description of periodontal flap surgery (1911)[2]

Neumann described his technique as the 'radical treatment of alveolar pyorrhea'[3]

Modification of Neumann's flap was presented by Widman to the Scandinevian Dental Association in 1916 and was later published by Widman in 1918.

Cieszynski had introduced reverse bevel incision in the periodontal flap operation.

During early 1950, concerns were expressed regarding the unsatisfactory outcome when pocket depth extends beyond the mucogingival line. As a result of this, new flap procedures were designed. Periosteal fenestration was among this newly developed techniques.

In 1976, after an extensive series of laboratory studies, Melcher presented the basic concept that led to the development of the clinical techniques known as GTR. He suggested that the cells that repopulate the root surface after periodontal surgery will determine the type of attachment that forms on the root surface. [6]

## Regenerative Periodontal Surgery

The ultimate goal of periodontal therapy is the complete restoration of the structure and function of diseased periodontal tissues. Periodontal regeneration is defined histologically as regeneration of the tooth supporting tissues, including alveolar bone, periodontal ligament and cementum over a previously diseased root surface. Regeneration of periodontium is considered to be an essential part of current mode of periodontal treatment approach. Several surgical techniques have been developed in attempt to regenerate periodontal tissues.

A. Root surface biomodification
B. Bone replacement grafts
C. Use of barrier materials (GTR)
D. Matrix proteins and Growth factors
E. Future of periodontal regeneration
   1) Gene therapy
   2) Use of mesenchymal stem cell

## A. Root Surface Biomodification

In periodontal diseases root surfaces are contaminated by bacterial products, especially endotoxins in the necrotized cemental surface. In vitro, study demonstrated that diseased root surfaces do not favor the attachment or growth of fibroblast but promote epithelial migration along the root surface. Secondly diseased root surface demonstrated to be hypermineralized (higher content of calcium, phosphorus magnesium and fluorides) and pathologic granules have been described in exposed cementum. These granules contained cholesterol and steroid and may represent the foci of degradation of collagen. Thirdly,the presence of imbalance between the activated metalloproteinase (MMPs) and their inhibitors leads to pathologic breakdown of the extracellular matrix in disease such as periodontitis.

Several substances have been proposed to apply on the root surface during surgical treatment.They have effect of removing smear layer and exposing the collagen matrix which may enhance the regenerative action.

i Citric acid
ii Fibronectin
iii Tetracycline
iv EDTA
v Enamel matrix proteins

Application of citric acid or Tetracycline result in demineralization. Demineralized dentin has been demonstrated to have bone inductive effect.

Register and Burdick reported that citric acid applied for 2 to 3 minutes was the most desirable for producing optimal demineralization and new attachment with no untoward side effect.

More recent studies indicate that the use of EDTA which has less acidic Ph may expose collagen fibers, thus promoting cell attachment. Tetracycline enhance osteoblastic activity and inhibit bone resorption by inhibiting osteoblast and osteoclast derived MMPs.

Several studies have reported controversial results regarding the use of root surface conditioning. Gotlow,Nyman Karing and Lindhe examined the effect of root surface treatment on the attachment and growth of human gingival fibroblast histologically with the use of scanning electron microscopy. They concluded that the outcome of treatment based solely on the completeness of root debridement. Only roots which has been planed whether or not citric acid demineralization was used promote cell attachment and growth.[7]

## Enamel Matrix Proteins Derivatives (EMD)

Periodontal regeneration mediated by EMD is based on a different concept. It is believed that EMD used in periodontal lesion mimic the development of the tooth supporting apparatus during tooth formation. It is composed of number of proteins, 90% of which are amelogenin. Such proteins are thought to induce the formation of periodontal attachment during tooth formation.[12]

It has been approved by the US Food and Drug administration for use in achieving periodontal regeneration in angular bony defects. It is a group of enamel matrix proteins isolated from developing porcine teeth. Crude enamel material is removed from the developing teeth and proteins are extracted and purified yielding a material which is used for root conditioning.

The only commercially available product using EMD is Emdogain in viscous gel form. Cochran and Woznew published and excellent review of role of an EMD. They described that EMD, a set of matrix proteins stimulate the initial acellular cementum formation. Based on this observation, the proteins are included as a biological mediators for periodontal regeneration.[9,10]

## B. Bone Replacement Grafts

The effectiveness of bone grafting for periodontal regeneration in infrabony defect

was assessed in a systemic review which showed improved probing [5]attachment level for some biomaterials when compared to open flap deberidement. Many excellent review articles are available to compare the success rate of GTR and bone grafts.[8]

Bone graft materials are generally evaluated based on their osteogenic, osteoinductive or osteoconductive potential.

- Osteogenesis- direct transfer of viable cell to the area that will regenerate new bone.
- Osteoinduction it is a chemical process by which molecules contained in the graft (bone morphogenic proteins) stimulate the osteoprogenitor cells to differentiate into the osteoblast which in turn form new bone.
- Osteoconduction it is a physical effect by which the matrix of the graft forms a scaffold that favors outside cell to penetrate the graft to form new bone. Osteoblast from the margin of the defect that is being grafted utilize the bone graft material as a framework upon which to spread and generate new bone.

The types of graft materials used in various regenerative procedures can be broadly divided into

**a. Natural graft**

i) Autogenous graft
ii) Allograft
iii) Xenograft

**b. Synthetic grafts** (non bone graft material)which includes sclera, dura, cartilage, ceramic and coral derived materials.

**i. Autogenous Graft**

Many osseous grafting materials have been used towards the goal of obtaining periodontal regeneration of which autograft harvested from intraoral site or extraoral site is the most predictable osteogenic organic graft for osseous tissue regeneration. Autogenous grafts retain some cell viability and are considered to promote bone healing mainly through osteogenesis and/or osteoconduction

**a. Intraoral sites**

- Edentulous areas of jaws
- Healing extraction sites
- Maxillary tuberosities
- Mandibular retromolar area
- Zygomatic process of the maxilla
- Mandibular Symphysis

Generally cancellous bone is preferred as graft material but chips or shaving of cortical bone mixed whith blood and pulverized into coagulam have also been used in periodontal defect.

**b) Extraoral sites**

- Illiac crest graft provide adequate quantity of graft material.
- Fibula
- Ribs

Autogenous graft is gold standard , it is ostoinductive, osteogenic as well as osteoconductive. However, disadvantages associated is need for second surgical site to procure donor material and the frequent lack of intraoral donor sites to obtain sufficient quantities of donor bone for multiple or deep osseous defects spurred the development of bone allograft.

**ii) Allografts**

Allogenic grafts were utilized in attempt to stimulate bone formation in infrabony defects in order to avoid the second surgical insult associated with the use of autografts. These grafts are transferred between members of the same species.

Graft procured from donor are freeze dried and treated to prevent disease transmission are available from commercial tissue banks. Two types of grafts are available.

a. Freeze dried bone graft (FDBA)
b. Demineralized freeze dried bone graft (DFDBA) responsible for osteoinduction (Meloning and Boners 1990)

- Controlled clinical trials indicate bone fill ranging from 1.3 to 2.6mm when FDBA used to treat periodontal defects.
- Human trials using DFDBA have demonstrated bone fill similar to that achieved with FDBA.

**iii) Xenograft**

Graft that are shared between different species,currently there are two available source of xenograft

- Bovine bone
- Natural corals

These grafting materials are also referred to as anorganic bone , since proprietary processes are suggested to remove all cells and proteinaceous material leaving behind an inert absorbable bone scaffolding upon which revascularization, osteoblast migration and woven bone formation occur. There is very little human clinical data supporting use of these materials for managing periodontal defects.

**b) Non Bone Graft Material**

They are synthetic material or alloplastic materials used in periodontal regeneration. They offer the advantages of unlimited quantity, no additional surgical site and no potential for disease transmission.

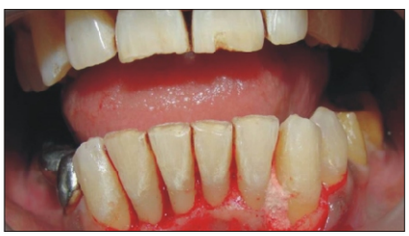
- **Bio Ceramic Materials**

i Tricalcium phosphate (partially resorbable)
i) Hydroxylapetite (non resorbable)

- Bio active glasses
- Polymer HTR

Several studies were conducted on the use of alloplast, clinical result were good but histologically these material appeared to be encapsulated by collagen. They are osteoconductive and has scaffold effect.

Use of tricalcium phosphate in combination with hydroxyapatite give both effect osteo conduction and resorbability.



**Properties of various types of bone grafts**

| | Osteoconductive | Osteoinductive | Osteogenic |
|---|---|---|---|
| Alloplast | + | - | - |
| Xenograft | + | - | - |
| Allograft | + | +/- | - |
| Autograft | + | + | + |

**C. Use of Barrier Materials (GTR)**

A Cochrane review has shown that GTR is a little more effective than open flap debridement. However it was also observed that there was a marked variability of result with GTR

**Concept of GTR**

It consists of placing barriers of different types to cover the bone and PDL thus temporarily separating them from gingival epithelium. Excluding the epithelium and gingival tissues from the root surface during the post surgical phase not only prevent the epithelial migration into the wound but also favors repopulation of the area by cells from

the PDL and the bone. PDL is the only tissue that contain progenitor cells for cementum, alveolar bone and periodontal ligament.

This method derives from the classic studies of Nyman, Lindhe, Karring and Gottlow.

### Membrane used for GTR

### a) First Generation (non resorbable)

i) Millipore filter
ii) EPTFE ( Goretex)
iii) Nucleopore membrane
iv) Rubber dam

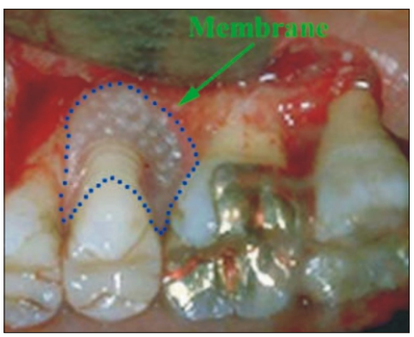
### b) Second Generation (resorbable)

**Synthetic Polymer**

i) Polylactic acid membrane (guidor)
ii) Vicryl mesh
iii) Cargile membrane
iv) Oxidized cellulose
v) Hydrolysable polyester

**Natural Biomaterials**

i) Collagen




### c) Third Generation (resorbable with growth factors)

Growth factors helps in the regeneration of periodontal tissue.

**Non-resorbable Membrane**

The first membrane used experimentally by Nyman's group were constructed from Millipore(cellulose acetate) filters, since these were easily available in the lab.

Commercial membrane (ePTFE) obtained in different sizes and shapes to suit the defects.

**Disadvantages**

Since the membrane is made up of non-resorbable material a second procedure is necessary to remove them. This causes additional trauma to the patient as well as healing of periodontal tissue.

**Resorbable Membrane:**

**Advantages**

No need for second surgery to remove the membrane which may disrupt the healing.

**Disadvantages**

- Early absorption is not desirable because the regenerative tissues may still be immature. Researchers have demonstrated that the critical time for healing tissue is 3-4 weeks post surgery.
- Breakdown product of the absorbable membrane may disturb the healing.
- In large defect collagen tends to collapse if it isn't supported.

Recently, titanium reinforced PTFE membrane is available. It increases the rigidity and allows for the creation and preservation of space when used with bone grafting materials and doesn't collapse.

### Comparison Between Resorbable & Non-resorbable Membrane

Although GTR using resorbable or non-resorbable membrane has revolutionized clinical practice, the results are not yet predictable.

- Primary closure is important in resorbable membrane to promote undisturbed and uninterrupted healing.
- Space creation and maintenance to facilitate space for bone in growth.
- Stability at the wound to induce blood clot formation is also important.
- Angiogenesis to provide necessary blood supply and undifferentiated mesenchymal cells.

Resorbable collagen membranes in periodontal therapy have shown promising result but are not osteo-inductive. As protein ( rhBMPs-2) is known to have an affinity for collagen, The use of this osteo-inductive agent incorporated into a membrane may act as a suitable carrier to promote periodontal regeneration.[11]

### D. Matrix Proteins and Growth Factors

Growth factors are polypeptide molecules released by cells in the inflammed area that regulates events in wound healing. These are proteins responsible for coordinating cellular repair processes.

Growth factors therapy aim to stimulate the specific progenitor cells which are responsible for the regeneration of mineralized and non mineralized tissues that comprises the periodontium. As natural biological mediators, polypeptide growth factors modulate significant cellular event in tissue repair.

- Cell proliferation
- Chemotaxis or directed migration
- Differentiation
- Matrix synthesis via binding to specific cell surface receptors

Currently the growth factors which are believed to contribute to periodontal regeneration include:

a. Platelet derived growth factor (PDGE)
b. Insulin like growth factor (IGF-I and IGF-II)
c. Fibroblast growth factor (FGF)
d. Transforming growth factor (TGF alpha and beta)
e. Bone morphogenic protein (BMP 1-12)
f. Epidermal Growth factor (EGF)

These mitogenic polypeptides attract mesenchymal cells and fibroblasts to migrate into the periodontal wound and stimulate their proliferation.[13] The continuing process of periodontal tissue repair is followed by granulation tissue as a source for future periodontal connective tissue cells such as osteoblast, PDL fibroblasts, cementoblasts.

### Bone Morphogenic Proteins

BMP is the growth factor belonging to TGF-B super family.

They are found in significant amounts in bone and they are secreted by osteoblast as well as various other cell types. BMPs were originally identified as bone matrix proteins with the ability to induce ectopic endochondral bone formation when implanted into rat muscles.(Urist 1965) This observation led to the purification, cloning and expression of Recombinant human BMPs. At least 20 BMPs have been isolated and clone. They all exert a large no. of effect on bone they stimulate cell division in undifferentiated mesenchymal cells and osteoblast precursors. Ripormonti et al. reported that BMPs in conjunction with collagenous matrix induced PDL cementum and alveolar bone regeneration in surgically created defect.[14,15,16]

### Platelet Rich Plasma (PRP)

It is an autologous source for growth factor obtained from a sample of a patient blood in dental office. Soft tissue healing is substantially improved through the application of PRP via increasing collagen content. PRP can be prepared by separating fresh anti coagulated blood by simple centrifugation which concentrates platelets upto 6 times the baseline count in whole blood.

Platelets are circulating in blood. They are responsible in hemostasis and regeneration of tissue from trauma. Tissue repair normally begins with clot formation and platelet degranulation which leads to release of growth factors PDGF and TGF-B. Through the application of PRP to the bone graft wound site substantially increase in the platelet count. This increases the availability for platelets to create the cascade response via PDGF and TGF-B.

It can be considered that PRP "jumpstarts" the cascade of regenerative events leading to form the mature graft site.

### E. Future of Periodontal Regeneration

The single administration of purified tissue growth factor has not been shown to be clinically effective in supporting the horizontal regeneration of periodontal tissue breakdown. This maybe caused by insufficient capabilities to maintain therapeutic protein levels at the wound site.

Periodontal tissue engineering is a contemporary area of science based on the principles of cell biology, bio-engineering,

bio-materials, bio-chemistry and bio-physics to solve clinical and surgical problems related to tissue loss and organ's function failure.[21]

### 1) Gene Therapy

Tissue engineering using mesenchymal stem cells (MSCs) is a recent therapeutic options with several advantages. This includes high quality regeneration of damaged tissues without forming fibrous tissue, minimum donor site morbidity compared to autografts, low risk of autoimmune rejection and disease transmission.

MSCs represent a valuable source for tissue engineering. They were first identified by Friedenstein et al. in 1966 from bone marrow. MSC s like populations from both dental and non dental tissues had provided exciting possibilities for the application of tissue engineering as well as gene based therapies. Findings suggest that deciduous teeth may constitute a source of stem cells.[18] In vitro biological properties of highly purified mesenchymal progenitor cells (MPCs) harvested from the PDL of deciduous and permanent are comparatively assessed. MPCs have also been isolated from the dental follicle of human 3rd molar.

It is believed that periodontal regeneration can be successfully attained through the migration of periodontal ligament stem cells and these cells subsequently differentiated into osteoblasts, cementoblasts and fibroblasts. The concept that stem cells may reside in the periodontal tissue was first proposed by Melcher.

### 2) Use of Mesenchymal Stem Cell

Gene transfer methods may circumvent many of the limitations of periodontal regeneration with protein delivery to soft tissue wounds. Gene therapy may achieve greater bio availability of growth factors within periodontal wounds which may provide greater regenerative potential.[22,23] It involves the transfer of genetic information to target cells which enables them to synthesize a protein of interest to treat disease. The challenge in gene therapy is how to get the correct genetic material to the appropriate cell.[24] According to Encyclopedia Britannica 1998 there are 3 types of delivery systems, a viral vector, a chemical method or a physical method. The most common and accurate method is viral vector. They deliver the desired gene to a target cell. Viral vectors are Retro virus, Adenovirus and non viral vectors are plasmid or DNA polymer complexes.[23]

### Summary

Over the last 3 decades the periodontal literature has been filled with reports related to periodontal regeneration. This therapeutic goal although ideal is difficult to achieve. A variety of graft materials and regenerative strategies are now available however they all have limitations. The surgical procedure can be technically demanding and when success is achieved the maintenance of positive result is highly dependent on patients' oral hygiene habits and compliance with periodontal maintenance.

Despite all these difficulties periodontal regeneration is a clinical possibility that can be offered to patients. The clinicians must carefully evaluate the various regenerative and reparative approaches.

Treatment planning in periodontics also has changed dramatically in the last decade because of the acceptance of dental implants as a viable long term option for replacing missing teeth with the increasing predictability of implants. Sometimes the best management of a periodontal defect maybe extraction when regenerative efforts have been unsuccessful. Heroic regenerative procedures would be contra-indicated and clinician has to decide and evaluate the pros and cons of the regenerative technique.

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