

## Successful Ridge Augmentation: The Challenge of Periodontal Tissue Engineering

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Dental implants for tooth replacement are the current standard of care for the replacement of missing teeth [1]. This is the result of 50 years of ongoing and continual research and development of new and improved surgical techniques and armamentarium. The long-term success of dental implants depends upon the degree of osseointegration that can be achieved [2-4], which is largely determined by the volume and quality of bone available at the time of surgery and the minimization of mechanical forces on the bone over the life span of the prosthesis. Bone height and volume is often diminished in patients due to the extended time after tooth loss prior to implant placement or due to periodontal disease and or trauma [5,6]. This lack of sufficient bone height and volume is the major limitation impacting long term dental implant treatment success [5,7].

Several surgical techniques and biomaterials have been developed for dental implant site development in the resorbed alveolar jaw [7-9]. Some of the commonly used surgical techniques used are (i) Osteoperiosteal flap (OPF); (ii) Distraction osteogenesis (DO); (iii) Block grafting; (iv) Guided bone regeneration (GBR) using membranes; and (v) Subperiosteal tunneling for minimally invasive approach to GBR. The material options used for bone augmentation are divided into natural transplants (autografts, allograft and xenografts) and synthetic materials (alloplasts) [8,10,11]. These grafting materials are used for clinical applications because they are osteogenic, osteoinductive, osteoconductive or possess a combination of these properties [7,8].

Although preclinical experiments using various surgical techniques in combination with the available bone replacement graft materials have reported promising results, vertical ridge augmentation procedures still experience a high rate of failure in clinical dental practice [12,13]. The main reason for failure is the soft tissue enclavation and graft shrinkage due to poor blood supply [7]. Difficulty in creation and maintenance of space in the defect area where bone regeneration is intended also proves to be detrimental. Bone loss often generates non self-containing defects covered by soft tissues which ultimately collapse onto a grafting site if not supported [7,14]. Also, epithelial cells have a higher turnover rate than bone tissue, resulting in the defect space being filled with soft tissue if barriers (membranes) are not used [14,15]. Hence, in larger defects, barrier membranes are used in combination with graft materials to allow for migration of osteoblasts and ingrowth of blood vessels from adjacent osteogenic tissues [7,14]. Tenting screws, titanium-reinforced membranes or titanium meshes are and can also be used in conjunction with graft materials to increase mechanical support [16,17].

A requirement for bone regeneration is the presence or recruitment of osteoblast precursors and growth factors at sites of augmentation. Osteoblast precursors can be provided by the graft material (cancellous autogenous bone) or by the recipient bed [8]. Growth factors can come from the graft, recipient bed and vasculature and it is believed that intra-marrow penetration of the recipient bed favors both cellular and growth factor migration into the sites where bone is required to be regenerated [18,19]. Host osteoprogenitor cells infiltrate the graft within 7 days and the early phase of bone regeneration at grafted sites is dominated by active bone resorption and formation throughout the graft [7]. The latter phase of incorporation is characterized by osteoconduction and a process known as creeping substitution [20]. Many of the bone graft materials used today are able to contribute to new bone formation through this biological process [21]. The osteoclast precursors differentiate into mature osteoblasts under the influence of osteoinductors and synthesize new

bone during the first weeks. Growth factors involved in bone formation act on fibroblast and osteoblast proliferation, extracellular matrix deposition, mesenchymal cell differentiation and vascular proliferation [22].

Bone augmentation and regeneration related research is currently focused on molecular, cellular and gene therapeutics [23]. Bone morphogenetic proteins (BMPs) are differentiation factors and have the ability to differentiate osteoprogenitor cells into mineral forming osteoblasts and stimulate vascular proliferation [24]. BMPs have shown promise for intraoral applications such as ridge preservation and sinus augmentation [25,27]. Platelet derived growth factor (PDGF) has also shown potential for use in bone regenerative applications [28]. However, optimal dosage and carriers for PDGF are still to be determined and extensive preclinical and clinical trials are required in future. A new approach to achieve bone augmentation is the addition of platelet rich plasma (PRP) from the patient blood to graft materials [29]. Initial results have shown more and denser bone compared to autografts used alone for ridge augmentation procedures [8]. The seeding of constructs with mesenchymal stem cells also holds great promise and merits further in-depth investigation [30,31].

In conclusion, there are many surgical techniques with various combinations of natural and synthetic graft materials that are currently used by periodontists and oral surgeons in an attempt to successfully achieve ridge augmentation in the vertical dimension. However, there exists no single ideal technique or graft material which consistently provides reproducible results in all cases types. There is a need to develop treatment modalities that involve less invasive vertical ridge augmentation procedures that provide reproducible results. The existing biomaterials require the addition of supplemental pharmacotherapeutics that are able to promote improved bone quality in the resulting grafted site, thereby leading to a more predictable long term result for the dental implant placed into that newly developed bone. The development of these new chemical modulators of bone development will facilitate the fine-tuning of the physico-chemical properties of the bone graft materials and should improve the predictability of bone regeneration therapeutics.

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