

## REVIEW ARTICLE

# Demineralized Dentin Material Sponge as a Guided Bone Regeneration

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## ABSTRACT

Reconstruction of craniofacial bone defects due to trauma, infection or tumor resection is a major problem faced by professions in dentistry, oral and maxillofacial surgery, orthopedic surgery, oncology and neurosurgery. One of the treatments that can be done for cases of bone defects is using Guided Bone Regeneration (GBR). The objective of this study is to present an evaluation of literature regarding the role of Demineralized Dentin Matrix Sponge (DDMS) as GBR. GBR procedure uses a membrane that acts as a physical barrier to invasion of connective cells and epithelial cells from the surrounding soft tissue, which also produces osteogenic cells, showing a slower migration rate, thus creating a situation conducive to bone regeneration. Demineralized Dentin Matrix (DDM) affects the release of growth factors in the type I collagen matrix which is usually involved in bone mineralization. This makes DDM more inductive than mineralized dentin. DDMS as a biomaterial has the potential for bone tissue engineering in terms of biophysics and biocompatibility, and has the potential to be used as Guided Bone Regeneration in bone tissue regeneration.

**Keywords:** Tissue engineering, Guided bone regeneration, Bone, Dentin, Sponge

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## INTRODUCTION

Facial bone defects are medical cases where there has been loss of bone tissue in the cranial and facial areas (1). These defects can occur due to trauma, tissue necrosis, infectious and degenerative diseases, abnormal bone growth or deliberate medical procedures such as craniectomy and reconstructive surgery. These defects can lead to reduced cranial bone function and anatomical changes. (2,3,4).

One of the treatments that can be done for cases of bone defects is by performing bone grafts in areas that have

lost or damaged bone tissue. Management of other bone defects includes allograft bone grafts or donors from other people, xenografts or donors from other species, for example the form of xenograft donor bone is bone taken from bovine or bovine bone or by using artificial bone substitutes. (5).

Tissue engineering consists of a combination of knowledge in the fields of stem cells, growth factors and scaffold. One of the tissue engineering techniques is the formation of bone cells through the GBR method. One of the efforts made was to carry out the craniofacial bone reconstruction procedure using membrane assistance through the GBR procedure. (6,7,8).

DDM derived from bovine dentin is a material used as a substitute for human teeth. In recent years, DDM has been widely used in dental research because it is easily obtained in large quantities of high quality with a more

uniform composition than human teeth (9,10). Dentin bovine has a composition similar to human dentin consisting of 70% inorganic material, 20% organic matter and 10% water. The dentin microstructure consists of a network of collagen fibers and contains various growth factors, such as insulin-2 growth factor (IGF-2), bone morphogenetic protein (BMP), tumor- $\alpha$  growth factor (TGF- $\alpha$ ), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF) (11,12). Research on the characteristics of the DDM material with a sponge form (13), which was then carried out in vitro testing to test the viability, attachment and osteogenic differentiation needed to be carried out in the future to test the effectiveness of DDMS as a GBR in bone tissue engineering.

## DISCUSSION

### Guided Bone Regeneration (GBR)

GBR is a technique that aims to produce enough bone volume to fill the defect. This technique is based on the phenomenon that the application of a barrier membrane creates a space to facilitate the proliferation of angiogenic and osteogenic basal bone cells to the space where bone volume is required without being affected by fibroblasts (14). To ensure the success of GBR, there are four principles that must be fulfilled, namely: the absence of epithelial and connective tissue involvement, space maintenance, fibrin clot stability and primary wound closure. GBR procedure uses a membrane that acts as a physical barrier to invasion of connective cells and epithelial cells from the surrounding soft tissue, which also produces osteogenic cells, showing a slower migration rate, thus creating a situation conducive to bone regeneration. Tissue barrier application provides the following advantages, there are augmentation bone defects, stimulates bone regeneration, increases bone graft yield, and reduces dental implant failure.(6,7)

The application of the GBR procedure has been shown to aid bone regeneration in a defect (15). However, there is still disagreement about whether the membrane in the GBR procedure should always be used to protect the region where bone graft has been applied in bone defects (16, 17). Protected bone graft by the membrane in the GBR procedure can improve the process of bone graft fusing with the host tissue (18) and improve the prognosis of bone graft life (17). The membrane in the GBR procedure also functions as a space maintainer, which allows bone regeneration in the space formed. (19,20,21)

### Demineralized Dentin Material Sponge (DDMS)

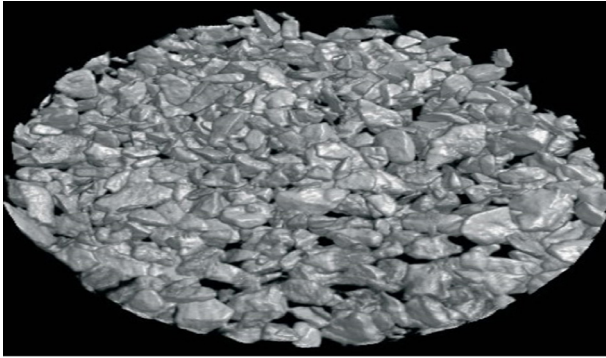
Bone and dentin are mineralized tissues with a similar chemical composition. Its composition consists of 18% collagen, 2% non-collagen protein (NCP), 70% hydroxyapatite (HA) and 10% body fluids (percentage indicates weight / volume). Dentin consists of Type I collagen fibers. The remaining organic components

consist of non-collagen proteins, phosphorylated and nonphosphorylated proteins. The matrix is a storage area for growth factors, including Bone Morphogenetic Protein (BMP), Platelet Derived Growth Factors (PDGF), Transforming Growth Factor-B (TGF- $\beta$ ) and basic Fibroblast Growth Factor (bFGF), known to be present in non-protein fractions. -phosphorylated. Some NCPs, such as osteocalcin (OCN) and osteopontin (OPN) are abundant in bone and dentin, while dentin phosphoprotein is an NCP found specifically in dentin. (12,13)

Autogenous demineralized dentin matrix (Auto-DDM) has been widely used in implant dentistry in Korea since 2008 for socket preservation, alveolar ridge augmentation, sinus augmentation, and guided bone regeneration (GBR) associated with dental implants (22,28). Auto-DDM has shown promising clinical and histological results as an alternative to autogenous bone grafts without the limitations of donor availability, risk of infection at the donor site, and marked resorption rates of  $\geq 50\%$  (23). The Auto-DDM has some limitations. Primarily, it is time-consuming because of the inevitable surgical extraction and the external manufacturing process required to prepare the material. Following, the amount of Auto-DDM obtained is unpredictable as it depends on several clinical conditions, such as dental caries, restorations, and prostheses in the harvested teeth. (24).

The application of allogeneic DDM (Allo-DDM) has been proposed to overcome the shortcomings of Auto-DDM. Kim et al. reported that the use of Allo-DDM for alveolar bone augmentation in 18 patients did not elicit an immune response or antigenicity and showed clinical results similar to those of Auto-DDM [20]. In 2017, the first randomized, controlled, prospective, a clinical pilot study on comparative alveolar ridge preservation using allogeneous tooth graft versus allogeneous free-dried bone graft in 15 patients was reported in India [21]. This study showed that the mineralized whole tooth allograft (WTA) consistently indicated superior results, demonstrating the least reduction in the alveolar crest height. Histological analysis also confirmed the new bone formation at the WTA sites. (25,26).

DDM is more inductive than mineralized dentin which is mainly due to the release of growth factors in the type I collagen matrix such as BMP as well as osteocalcin, osteonectin and dentin phosphoproteins which involved in bone regeneration (12). Dentin, including DDM, contain many dentinal tubules, which are unique spatial structures. The dentinal tubules run radially from the pulp to the dentinal enamel borders and are involved in the stimulation mechanism of the tooth. Odontoblasts and interstitial fluid that enter the tubules form and maintain dentin. Bone morphogenetic protein in dentin and bone is the main stimulant with osteoconductive properties (27). DDM can increase alkaline phosphatase (ALP) activity,



**Figure 1. The shape of DDM scaffold particles in 3D images of  $\mu$ -CT. (24 p.197)**

mineralize nodules and induce in vitro odontoblastic differentiation (9). Bone morphogenic protein is found in the bone matrix, osteosarcoma tissue and the dentin matrix. In recent years DDM studies have focused on particle size, production and processing methods that result in more efficient bone formation (27). The particle sizes of DDM scaffolds obtained were between 355  $\mu$ m and 710  $\mu$ m (Figure 1), while the ideal particle size for bone graft material is 500  $\mu$ m. (29).

DDM has a higher osteoinductive efficiency and simultaneously induces bone growth. DDM can be considered as type I collagen complex (COL-I) and growth factor which has lost bound mineral crystals, which are released from the matrix; it has significant osteoinductive and osteoconductive biological effects. Demineralized dentin, autologous and xenogenous materials have been used to treat bone injuries and bone damage (9). DDM is a collagen agent with less antigenicity for releasing growth factors such as bone morphogenic proteins (BMPs), clinically applied as a bone filling agent in the maxillofacial region. Common production methods for DDM involve crushing and demineralizing dentin, including cementum and removing enamel. DDM transplant therapy developed by several studies by Urist and other researchers showed that demineralized bone and dentin transplantation trigger bone formation. (27)

Pang et al. (28) conducted a study of AutoBT (autogenous human DDM, Korea Tooth Bank, Seoul, Korea) to compare bovine and inorganic bone in socket extraction augmentation. Bovine inorganic bone was effective as a vertical dimensional augmentation that histologically confirmed new bone formation. The results of this study showed that graft is a viable for alveolar bone augmentation after tooth extraction (12). In vivo studies have shown that DDM is a more effective bone-strengthening matrix than calcified dentin matrix (CDM), because CDM granules induce the formation of only a small amount of bone after a latency period of 8-12 weeks. The inductive nature of CDM may be related to the inhibition of BMP release by apatite

crystals. (13)

## CONCLUSION

DDM has the potential biomaterial for bone regeneration in terms of biophysics and biocompatibility, and has the potential to be used as Guided Bone Regeneration in bone tissue regeneration.

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