

Lessons Learned from the Clinical Use of Tooth as Bone Graft MaterialAnil Kumar Sharma¹, Alka Sharma²¹Associate Professor, Department of Dentistry, SMS Medical College, Jaipur²Junior Resident, Department of Orthodontics, Jaipur Dental College, Jaipur

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Abstract:

To treat osseous defects, a range of bonegrafts and their replacements have been accessible, but appropriate reconstruction by any bony defect persists as a therapeutic hurdle. The current narrative review analyses significant outcomes in patients treated with bonegrafts and bonegraft substitutes for surgical therapy of osseous defects based on peer-reviewed literature. Despite autograft, xenograft, and alloplast bonegraft substitutes being employed in a number of periodontic procedures, all of them have their own set of restrictions. Autogenous tooth bonegraft is functional in clinics due to different available forms which can be availed for different clinical challenges. Moreover, due to genetic uniformity, it fosters efficient bone regeneration by allowing osteoinduction and osteoconduction, as well as reducing foreign body reactions.

Keywords: allograft, dentin, bone graft, osseous defect.

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Introduction

In dentistry, bonegraft materials are commonly utilized to promote bone development. Among various such materials, an autologous bone graft is accepted globally as it is osteoregenerative property. However, Autogenous bone grafts have significant disadvantages, including limited availability, donor site morbidity, and a high resorption rate. For overcoming these limitations, alternative grafts like allograft, xenograft, and alloplastic bonegrafts are introduced. Despite recent progress, some limitations have been reported such as pathogen transmission and rejection by the recipient's body in case of allografts and xenografts use, and absence of osteoinductive properties & poor mechanical features of alloplastic bonegrafts.[1] Whether autograft, allograft, xenograft, or alloplast are used to fill bone deformities, each has its own set of drawbacks.

Additional procedures were required, as well as functional and esthetic issues at the donor site, as well as different degrees of graft resorption and the small amount of graft recovered, necessitating the search for an alternative. Numerous substitutes are being tried to address the relevant flaws. These substitutes should have properties of ideal bone graft which include stabilization of the blood clot, provision of a biomechanical scaffold for cell migration, proliferation, and differentiation, should contain functional proteins and peptides, having appropriate resorption, and remodeling while new bone is formed. Dentin is one such material which

may be attempted as a bone graft material. Other than the fact that dentin and bone have similar biochemical properties (80% hydroxyapatite crystals and 20% type I collagen), it also contains growth factors found in bone, such as insulin-like growth factor II (IGF-II), transforming growth factor (TGF- β), and bone morphogenic protein(BMP).[2] As dentin includes a number of proteins that are found in bone, such as osteopontin, bone sialoproteins, dentin sialoproteins, osteonin, and osteocalcin, it has been used as a bonegraft. Autogenous and allogeneous demineralized dentin matrix (DDM) are the two main kinds of DDM.[3] Extracted adult human third molars were crushed in liquid nitrogen, washed in sodium chloride, 1M (NaCl), demineralized in an acidic solution such as acetic acid or hydrochloric acid (pH = 2), rinsed in cold distilled water, and lyophilized to make the graft suitable to use.[4]

Dentin has osteoinductive properties, similar to those of bone due to which, multiple investigations have shown that dentin-derived bone substitution stimulates osteoinduction. The regenerative feature of autogenous DDM was initially demonstrated by Yeomans and Urist. BMP, which is found in DDM and bone, is a key stimulant with osteoinductive effects, according to Urist.[5] There are two types of autogenous dental bone transplant materials: block and powder. The block type of graft material possesses osteoinduction potential owing to blood wettability, as well as osteoconduction potential due

to space maintenance and creeping substitution. Different particle sizes, porosity, blood wettability, osteoconduction, osteoinduction, and creeping substitution abilities are used to determine the powder type. Both types can be employed for extraction socket preservation, cosmetic alveolar bone replacement, restoration of the perforated sinus membrane, and augmentation of early implant stabilization.

Thus, autogenous tooth bonegraft is functional in clinics due to different available forms which can be availed for different clinical situations. Furthermore, it promotes excellent bone regeneration by allowing for osteoinduction and osteoconduction, and it reduces foreign body reactions owing to genetic homogeneity.[6] Autogenous tooth bone graft material finds a lot of clinical applications. Because it is autogenous, the possibility of an immunological reaction is eliminated. It may be employed for guided tissue regeneration, tooth socket preservation, ridge augmentation, sinus bone graft and grafts in tumor resections, cyst enucleation, etc. [6] After tooth extraction, Kim et al. placed autogenous tooth bone powder and a block in the socket. After 3.5 months, they determined that the socket had healed well and was suitable for implant insertion.[7]

Objectives: The current review aimed to describe tooth as a bone grafting material based on the most recent literature.

Search Strategy

Articles on the tooth as a bone grafting material were found through electronic research using several databases. In the review process, all types of articles with data on autogenous grafts published in English were included. To provide an updated overview of this area, only research published in the last seven years was evaluated for this study.

The following keywords, combined with the Boolean term "AND", were used: "Autogenous Teeth Graft", "Bone Graft", "Tooth osteoplastation" and "Autogenous fresh demineralized tooth"

Study Selection and Data Collection Process

Two masked independent reviewers assessed eligibility; one of the review's authors gathered data from the included studies, while a second author confirmed it. Disagreements between reviewers were handled by discussions among the two authors, and if no agreement could be achieved, a third author made the final judgment.

Name of author and year of publication, the form used, and type of surgery was tabulated for all studies (Table 1) The flow chart used for this study is depicted in Figure 1.

Methodological quality appraisal

No formal assessment of the methodological quality of all included studies was undertaken in accordance with review guidelines.

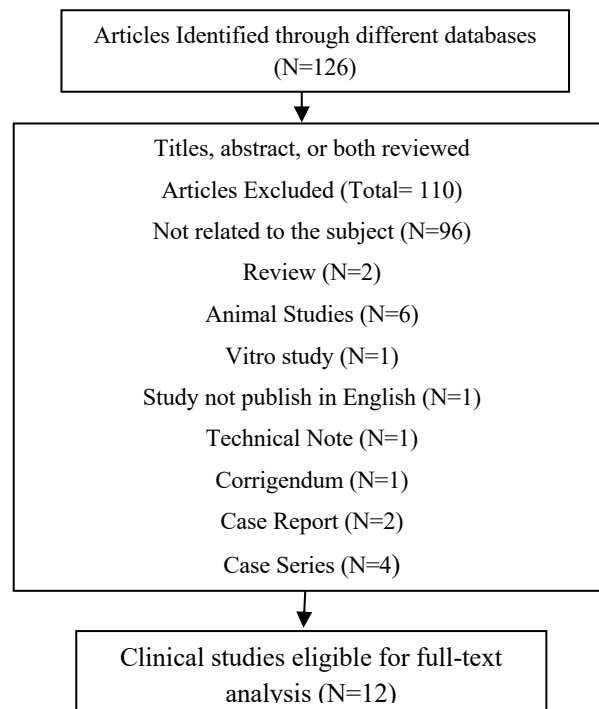


Figure 1: Literature Search

Table 2: Characteristics of included studies

Author	Form Used	Type of Surgery
Kim ES 2015(8)	Powder	During dental implant surgery, an autogenous fresh demineralized tooth graft was prepared at the chairside for alveolar bone grafting.
Joshi et al 2016(9)	Powder	For alveolar ridge preservation, autogenous tooth grafts and beta-tricalcium phosphate (β -TCP) alloplast were utilized.
Kim et al 2016(10)	Block	For maxillary sinus augmentation with simultaneous implant placement, an autogenous fresh demineralized tooth block(Auto-FDT block) containing platelet-rich plasma was used.
Pang et al 2017(11)	Powder	In post-extraction alveolar bone augmentation, autogenous tooth graft material was compared to organic bovine bone(Bio-Oss).
Pohl et al 2017(12)	Powder	In lateral alveolar ridge augmentation or for the filling of jaw deformities, chemically unaltered tooth material is used.
Lip et al 2018(13)	Powder	In guided bone regeneration(GBR) for rapid implantation in periodontal postextraction sites, autogenous demineralized dentin matrix against Bio-Oss granules were compared.
Parvini et al 2018(14)	Block	For lateral alveolar ridge augmentation, autogenous tooth roots were compared to autogenous boneblocks.
Schwarz et al 2018(15)	Block	For lateral alveolar ridge augmentation and two-stage implant insertion, compare the efficacy and safety of autogenous tooth roots and autogenous bone blocks.
Canto-Diaz et al 2019(16)	Powder	Socket preservation with autologous dental material.
Dong et al 2019(17)	Powder	The effectiveness of autogenous tooth bone grafts against xenogenic bone grafts in immediate implant placement with a bone deficiency was compared.
Shejali et al 2020(18)	Block	In order to restore the vertical and horizontal dimensions at periodontally hopeless extraction sites, autogenous tooth roots were used as a block bone transplant.
Kuperschalang et al 2020(19)	Powder	Following extraction of impacted third molars, an autogenous dentin graft is used to correct osseous defects distal to the mandibular 2nd molars.

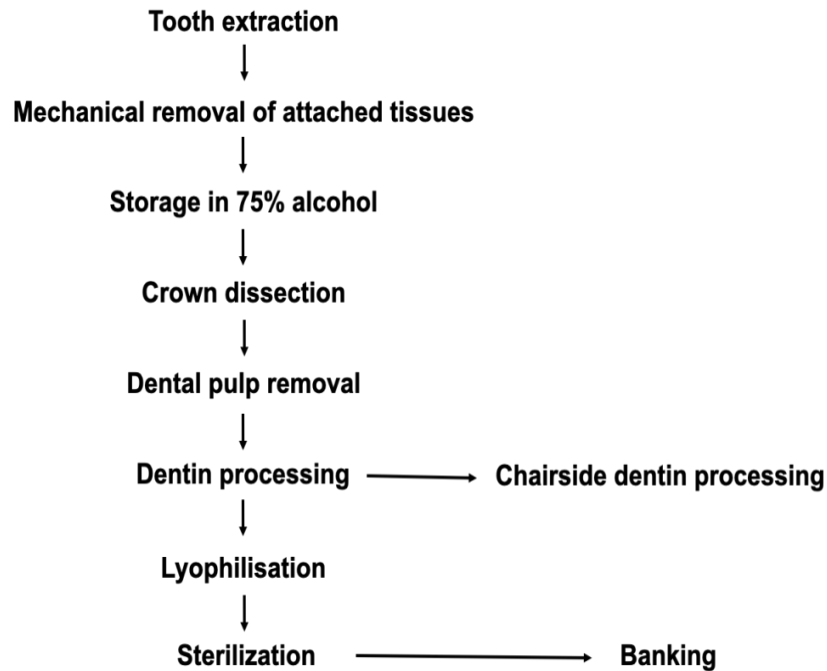


Figure 2: Flow diagram summarizing steps for tooth graft material

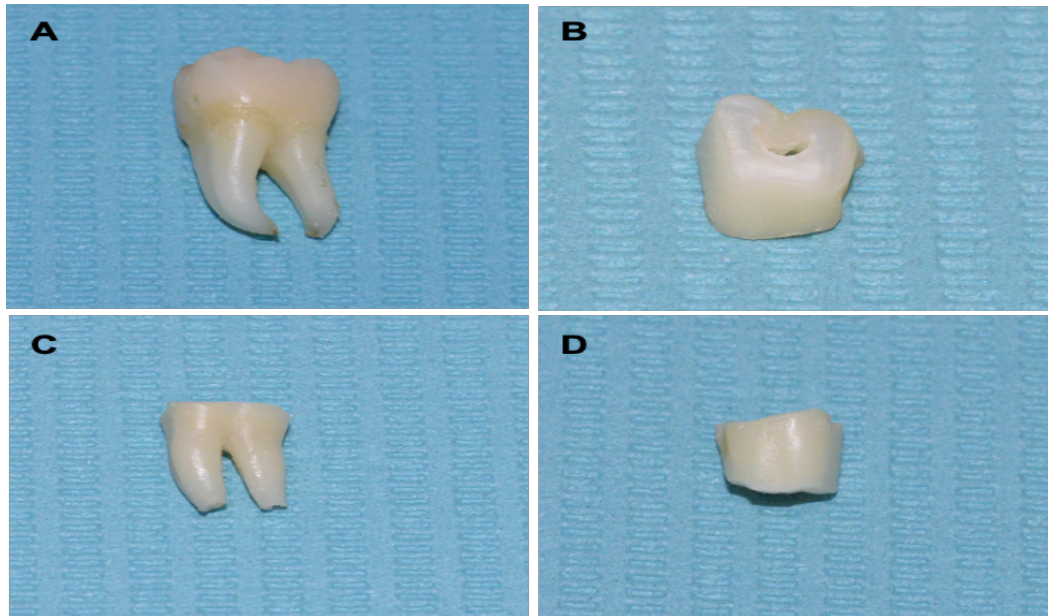


Figure 3: Pictures showing molar tooth (A), crown part (B), a tooth with form (C), and root in type (D)

Teeth structure and composition versus alveolar bone

Alveolar bone and tooth share the same origin and are derived from neural crest cells. Despite that, they are dramatically different from their morphologies and physical functions. The crown, which is covered in enamel and normally visible in the mouth, and the root, which is buried in the jaw and supports the tooth in its bone socket, are the two anatomical elements of the tooth. Root makes up approximately two-thirds of the tooth. The tooth has 3 hard tissue components: the enamel, the dentin, and the cementum. Dental enamel, the hardest tissue of the human body, comprising 96% of high crystalline apatite with a complex crystalline lattice organization, 3% water, and less than 1% of the organic matrix in weight volume. The layer underlying enamel, called dentin, contains microscopic tubules that traverse its entire thickness with nanocrystalline reinforced composite, 70% of low crystalline carbonated apatite, and ~ 20% of organic contents. Dentin has a variable water content that changes by around 20-fold from superficial to deep dentin. Cementum, a layer of connective tissue that binds the roots firmly to the jawbone, has a ratio of ~ 45% of low crystalline carbonated apatite and ~ 50% of organic contents.[20,21] The comparable chemical composition of bone and teeth inspired the notion of using autogenous tooth as a bone substitute in bone grafting procedures. The biological entity (i.e. cells) regardless, alveolar bone is made up of 65% low crystalline carbonated apatite and 25% organic component. Fibrillar type I collagen (COL-I), With dozens of additional non-collagenous macromolecules, the primary organic component of teeth accounts for over 90% of its total organic content (i.e. phosphophoryn, dentine sialoprotein,

osteonectin, osteopontin, osteocalcin, and dentin matrix protein-1) that account for the remaining 10%. These macromolecules act as linkages between collagen fibrils, securing the collagenous network in place. Teeth and bone differ however a level of collagen cross-linking. Furthermore, a small amount of type III collagen, abundantly described in connective tissues, is localized in the intertubular dentin dentinal tubule matrix. From the structural point of view, the density, the roughness, the porosity, and the homogeneity of the dentin are similar to human mandibular cortical bone. [22] Dentinal tubules have numerous branches and ramifications, providing a dense canaliculus anastomosing system near to the osteocyte lacuna in bone. [20] This network of channels spreads radially from the pulp outward to the dentin enamel junction and cementum. Density and diameter of tubules are lowest near the dentin enamel junction & rises as they get closer to the pulp. Dentin is a strong and elastic mineralized tissue constituting tooth mass and supports the enamel, compensating for its brittleness from a mechanical standpoint. Dentin has an elastic modulus of 18 GPa close to the cortical bone (14 GPa) but higher to trabecular bone (1.3 GPa).[23] The dental pulp is a soft tissue that runs from the central chamber to the root apex of the tooth. The pulp is a connective tissue made up of pulp cells, collagen fibers, nerves, and blood vessels from a structural standpoint. Among pulp cells, dental pulp stem cells (DSPCs) share the same phenotype with bone marrow-derived mesenchymal stem cells and are responsible for tissue repair and self-renewal along with the prepositioned inflammatory process.[24]

Teeth procurement: Bone graft material from autologous tooth processing is a system that treats

patients by their own extracted teeth, in a safe way as minimal immune response is induced. Up to now and to our knowledge, no specific criteria have been defined for tooth type for such application. Deciduous teeth as well as adult teeth; impacted and unimpacted third molar, were successfully used.[16] However, for the host's safety, teeth chosen were restorations and caries free, and endodontic treatment. For a practitioner, autogenous tooth presents an interesting alternative to autologous bone as they provide chairside ease of preparation. A Korean team (2009) developed a technique for creating bone transplant materials from autogenous tooth following demineralization, freezing, drying, and sterilization(Flow chart).

Therefore, The graft material can be stored at room temperature for up to five years for a patient probably requiring subsequent procedures.[7] Korea Tooth Bank claims that it can deliver tooth-based materials on demand.[22,7] When compared to allografts, autografts have the most rapid and extensive osseointegration.[25] Allografts can trigger an immunological reaction in the recipient since they are not genetically matched; nevertheless, fresh allografts are known to induce higher immunologic responses than fresh-frozen or freeze-dried allografts.[26] Thus, the Tooth Bank may also be able to provide allogeneic tooth bone graft material, which has the advantage of being available in a variety of forms and sizes. The mouth cavity, which is warm, wet, and nutrient-rich, is an ideal environment for microbe colonization, which typically takes the form of a complex structure termed biofilm, or plaque. To avoid microbial contamination that could impair osteogenesis and induce bone resorption, tooth-based material must be sterile, without microbial or microbial-product contaminants. Several procedures of decontamination upstream or downstream dental processing have been described. Therefore, following extraction, teeth are immersed in 4% hydrogen oxide, 75% basic ethyl alcohol, or chlorhexidine solution. Ethylene oxide was used downstream of dental processing and lyophilization. Ethylene oxide sterilization has the advantage of being an industry standard, second only to gamma irradiation. Although there is evidence that ethylene oxide can kill viruses in allografts, harmful residues may remain after treatment.[27]

Manufacturing of tooth graft materials

Following the excision of associated soft tissues, an anatomical tooth crown section is currently dissected, as the chemical composition of enamel. Indeed, in contrast to the low-crystalline apatite from dentin and cementum, Enamel's high crystalline apatite is difficult for osteoclasts to breakdown, resulting in delayed resorption and poor osteoconductivity.[28] In terms of elastic and

flexible qualities, enamel behaves more like metal. (elastic modulus > 100 GPa).[23] The enamel-based material was however thought to be suitable for maintaining volume rather than osseointegration (Ref). Although the dental pulp contains DSPCs with regenerative features close to bone marrow-derived mesenchymal stem cells, most protocols recommend removing this soft tissue before tooth processing. Tooth graft materials, from dentin and cementum parts, are divided into a block- and/or granule-based material.[6]

Block-based materials (BBM): The clinical application of BBM represents about 9% of the clinical application. Made from dentin, the most voluminous structural component, BBM osteoinductive properties are attributed to their blood wettability while their osteoconductive properties are mainly attributed to the space maintaining abilities.[6] Following hydration in 0.9% NaCl solution for 30 min, BBM has superior handling properties, since it can be sliced with a surgical knife by operators, firmly fixed without the use of any other tools. In dentistry, BBM with root forms is appropriate for the preservation and reconstruction of extraction socket as well as large bone defect reconstruction. In orthopaedical applications, few preclinical studies showed osseointegration of the root on types graft in femur and tibia bone defect. [29,30,31] Graft revascularization is required for graft-bone ankylosis. The blood vessels in non-vascularized grafts slowly penetrate into the graft from the recipient's bone, prolonging healing time.[30] Following implantation, the revascularization of cancellous bone grafts occurs faster than cortical bone grafts, as the large pores between trabeculae allow the capillary and vascular tissue invasion, thereby promoting osteogenesis. As the features of BBM are close to cortical bone, holes sized 0.2 mm at the surface of canal area were additionally proposed. Thus, creating artificially macropores increases the surface area and promotes vascular invasion and bone formation.[31]

Granule-based material (GBM)

With about 75% of the clinical application, GBM can be obtained from the crown and/or root grinding.[32] Clinicians can make a chairside bone graft with a particle size ranging from 300 to 1200 μ m that is disinfected and can be used in 8 minutes using a commercial tooth grinding device (i.e. Tooth transformer or dentin grinder).[33] The resulting particle volume is roughly 2–3 times that of the tooth's original volume. (i.e. tooth weighing 0.25 g produces at least 1 cm³ of particulate).[34] Clinicians prepare the desired particle size depending on the intended use. Small particles (less than 300 μ m) are thought to enable rapid bone resorption and remodeling, while larger particles

(more than 1200 m) are thought to protect against rapid bone resorption. Many studies have shown that bovine bone particles with a diameter of 300 m have superior bone formation [11], while bigger particles with a diameter of 1000 m had inferior bone growth.[11] The degree of porosity and its disposition directly influences the biological behavior of bone graft materials.[37] GBM is made up of a porous network with an average pore size of 0.431 0.213 m and a total porosity of 55%.[11] The appropriate granule absorption rate is also important for improved bone repair. The crystallinity of apatite in bone is minimal, with nanometer-scale particle sizes. Biodegradation in the human body will become impossible when crystallinity and particle size grow, lowering osteoconductivity. Because of its degradation rate, small size particles seem suitable for bone regeneration.[1]

Demineralized dentin matrix

The technique for transforming teeth into acceptable grafting material is the most important phase in the entire surgery. Studies claimed that removing any highly crystalline inorganic substances and exposing osteogenic components and collagen matrix is required for successful tooth-based graft in the bone defect.[35] To achieve that partially demineralized or totally demineralized dentin matrices have been processed using environmentally-friendly aqueous-based methods. As for demineralized bone matrix [36] and in contrast to previously described tooth-based material, demineralized dentin does not contain viable cells. Demineralized dentin is a composite of collagen, non-collagenous proteins, and growth factors, a variable percent of residual calcium phosphate mineral. The resulting dentin-derived collagen is the most highly insoluble matrix owing to its cross-linking, which could be however remodeled following enzymatical actions. The mineral part of BBM or GBM is extracted with acidic treatment (0.5–0.6 N hydrochloric acids, 2% nitric acid, 10% citric acid or 10% EDTA). The rate of demineralization depends on the size of the material and the time of incubation. Koga et al., reported that 70% demineralization of dentin takes approximately 20 minutes while a complete demineralization took around 180 minutes for 1000 µm particles.[1] As described above, several critical parameters for improving the efficiency of bone graft materials are the overall structure, including geometry and size of particles, pore shape and size, and the pore interconnection pathway. Thus, the biological and clinical justification to demineralize dentine matrix relies on the structural changes such as the exposure of organic matrix mainly type I collagen to osteogenic cells such as mesenchymal stem cells and osteoblasts, allowing their attachment and their differentiation.[37] As demineralized time rises, the surface structure of the matrix displayed

the exposure of dentinal tubules and inter-tubular & peri-tubular fiber bundles loss, provides a rough surface that is required for cell attachment.[6] Pobloth et al., demonstrated that within the channel-like pores of a scaffold provided a guiding structure for ECM alignment and progenitor cell recruitment as well as vascularization.[38] Despite an increase in dentinal tubules at the surface, their size remains too small for the cell and capillary ingrowth. To increase the porosity, demineralized dentin-BBM was perforated, creating pores (with 0.5 to 1 mm in diameter, 30 uniformly distributed holes). New bone ingrowth was seen in most perforated demineralized dentin block parts including the outer edge, the inner pulp cavity space, and the perforated macropores.[31,6] The reduction of the mineral content and the increase in tubular size are thought to favor the bioavailability of osteogenic growth factors such as TGF- α , BMP-4, BMP-2 and BMP-7 that entangled within the composite matrix [39] Ground demineralized dentin matrix results in variable particle size, geometry, and surface area. As a result, some debate about the appropriate particle size and size range for demineralized dentin matrix preparations shows that larger particles (500–1000 m) have higher osteoinductive characteristics than fine particles less than 250 µm. These letters are thought to be phagocytosed by giant cells and digested by enzymes.[40] We cannot exclude the potential role of the mechanical properties of completely demineralized dentin. Indeed, the loss of mineral content compromises its mechanical qualities, making it unsuitable for usage in stress-bearing sections of the bone.[40] Additionally, to the structural changes, the chemical composition of demineralized dentin plays an important role to improve the efficiency of the graft materials. Physicochemical characterization of partially demineralized dentin GBM or BBM contains 5%–10% or 10%–30% mineral, with amorphous calcium phosphate, beta-tricalcium phosphate (β -TCP),[1] and octacalcium phosphate phases.[23,6] The residual calcium phosphate showed excellent bioactivity. Calcium and phosphorous ions are released, causing the apatite to reprecipitate on the surfaces, increasing the osseointegration of the dentin graft material.[13]

Deproteinized dentin matrix

Deproteinization aims to abolish all protein content, preventing the host's immune and inflammatory response with maintenance of surface morphology and mechanical integrity of the remaining tooth structure. Thermal and/or chemical treatments are commonly used procedures for this proposal. Heated deproteinization broke down the hydrogen bond of a polypeptide chain. Thermogravimetric analysis-differential thermal analysis of heated tooth showed that the decomposition of organic matrix ranged from 300 to 550°C.[41] After, annealing at

temperatures above 1000°C, the tooth became bioceramic-like material.[44] Although the heated-deproteinization technique is simple and quick, the low-temperature thermal treatment (500°C) was not able to entirely eliminate the protein content.[41] To achieve a complete deproteinization a dual thermal and chemical deproteinization procedure was proposed. The chemical deproteinization by using sodium hydroxide and hydrogen peroxide alters pH and results in protein precipitation. The two-step deproteinization took longer and resulted in increased discolouration of the teeth particles.[41] Heat/sodium hydroxide dual treatment showed a higher deproteinization rate in comparison with heat/hydrogen peroxide dual treatment. While both dual treatments revealed a wider dentinal tubule (diameter 1–2µm) than in untreated dentin, heat/sodium hydroxide treatment results in a rough dentin surface. Thermal and heat/hydrogen peroxide dual treatments kept the smooth dentin surface.[41] The elemental analysis of deproteinized GBM revealed that the Ca:P ratio ranges 1.5–1.8; similar to Ca:P ratio of cortical bone and cancellous bone. But the calcium and phosphate drop to 10–20 % in weight volume, suggesting a decrease in the bioactive ability of GBM to directly bond to the bone.[41]

In vitro evaluation

The initial step in the screening of tooth-derived material biocompatibility was to conduct cytotoxicity tests using cell culture-based methodologies.[42] Although almost all studies did not relate a cytotoxic effect of tooth-derived material in culture, Tabatabaei et al., observed a cytotoxic effect dose-dependent. Therefore, a concentration of 20 mg/mL of GBM was found as no cytotoxic regarding human dental pulp stromal cells, while 40 mg/mL decrease significantly the cell viability after 48h of culture.[43] Bone biomaterials should provide a platform to support osteogenic cells' adhesion and function that are conditioned by their intrinsic features such as structural, mechanical, and physicochemical features. As described above demineralization of dentin affects deeply the structural and physicochemical characteristics of dentin. In comparison with demineralized or totally demineralized dentin, the partially demineralized dentin matrix showed a higher bone regenerative activity.[1] Demineralization allows the enlargement of dentinal tubules but the size of the resulting pores remains too small for cell infiltration and ingrowth. In contrast, the loosening of the collagen network, following demineralization, provides surface microroughness or micro-texture in favour of cell adhesion and proliferation. The demineralization process aids proteins and growth factors release from the organic matrix.

The reduction of the mineral content and the increase in tubules size are thought to favor the bioavailability of osteogenic growth factors.[39] ELIZA experiments showed that demineralized dentin releases and activates the stored growth factors such as BMPs, IGF, FGF, TGF- α . [23,32] Few studies have found that protein components in teeth cause strong inflammatory reactions, which affect tissue repair and new bone production directly.[23,44] Thermal and/or chemical treatments are proposed as successful protocols for the effective deproteinization of a tooth. The evaluation of the direct and indirect cytotoxicity of annealed tooth powder did not show a cytotoxic effect on human alveolar bone marrow stem cells.[41] MC3T3-E1 osteoblasts cell line adheres and proliferates to the surface of chemical (sodium hydroxide) and thermal treated tooth powder and forms a multilayered and dense cell sheet accumulated after 7 days of culture.[41] Several researchers claimed that deproteinization of tooth-derived materials decreases its immunogenicity and prevents the host's immune following implantation. However, to the best of our knowledge, any in vitro evaluation of the inflammatory and immune cell response to deproteinized GBM or BBM was found in the literature.

In vivo and preclinical evaluations

Human, rodent, and bovine tooth-based material have researched upon for efficacy as bone substitutes (Table 1). Whatever studied species, the site of implantation (calvaria, mandible versus femur and tibia), the form (granular versus block), and the process (undemineralized, demineralized, thermal treatment, chemical treatment), the tooth based materials showed, in the most of studies good biocompatibility with a minimal inflammatory reaction.

Bonegraft materials should be kept in place and reabsorbed over time until new bone growth occurs. Several studies that looked at the influence of dentin demineralization on bone formation found that as the amount of graft demineralization increased, the rate of graft resorption increased, as long as there was a limited inflammatory reaction surrounding the dentin graft.[47] Grafting dentin caused fibrous encapsulation, which hampered bone repair. This is most likely owing to micromovements generated by the dentin graft's non-fixation during the bone healing phase.[45]

Regarding the definition of the osteoinduction and of the osteoconduction established by Glowacki & Mulliken [46] the in vivo studies revealed that demineralized tooth matrix set high standards for both osteoinduction and osteoconduction validations. The standard in vivo biological assay for bone induction in mice ectopic site showed that demineralized GBM induced independently bone

and cartilage formation after 4 weeks of implantation [3,23] versus 8 weeks for demineralized GBM.[7]

In comparison with totally demineralized GBM, partially demineralized particles induced a higher osteoid formation following implantation in calvaria bone defect.[1] Osteocyte of the newly formed tissue in contact with partially demineralized particles formed a network connected by their cellular processes.[47] Other researchers discovered that when human demineralized dentin is inserted in the marrow space of a rabbit tibia, near-native bone, it encourages new bone formation, implying that the osteoconductive qualities of dentin play a larger role during graft healing than the osteoinductive properties.[48]

The bone induction sequence was comparable to that of the demineralized bone matrix.[4] For a better osteoinduction, few authors recommended the use of dentin particles ranging from 250 to 500 μm in size in bone site defect.[49] A complete resorption of demineralized dentin granules (less than 250 μm in size) occurred before the initiation of bone formation.[1] Dentin–bone ankylosis and new bone formation were reported at 4 to 8 weeks post-implantation. To improve the blood vessel ingrowth within BBM, artificial macropores (holes of 250 μm in diameters) were performed. [31] Compared to the TCP (Chronos), perforated dentin slices showed complete peripheral angiogenesis up to 14 days post-implantation in calvaria defect.[50]

Other strategies have been employed to increase the bone regenerative capabilities of the dentin. Kamal et al. improved surgical handling of dentin granules during graft insertion into alveolar clefts by creating a composite putty -TCP/HA and dentin granule mixture, limiting dentin graft mobility and improving graft stability in the defect. 8 weeks after implantation, Putty β -TCP/HA/ dentin granule mixture had a statistically larger bone volume fraction, bone mineral density, and % residual graft volume in comparison with putty β -TCP/HA.[53]

The use of demineralized dentin matrix as a carrier for recombinant human BMP-2(rhBMP-2) has been proposed.[31] The incorporation of rhBMP-2 in demineralized dentin was achieved by physical adsorption or by physical entrapment within nanoporous dentinal tubules. 4 Demineralized matrix/rhBMP-2 showed a mature bone with bone marrow at 2 weeks in mice and 4 weeks for rabbit.[47]

Discussion

Essentially, it's hard to evaluate radiographic and clinical effectiveness with different forms of bone grafts for osseous defects, owing to variety of abnormalities and their locations observed in clinics, as well as comparison research paucity. Regardless,

there are a few broad generalizations that can be derived from the body of literature on this subject. The iliac crest is the most popular site for autologous bone grafting, owing to the simplicity with which the graft material can be obtained. Autografts are desirable because of their complete integration, rapid healing pace, and natural biocompatibility. Autologous bone, on the other hand, is undoubtedly a poor choice for osseous defect repair due to the frequency and severity of harvest site morbidity, especially when all other bone grafting options are devoid of this possible consequence.[51]

Clinical Applications of Autogenous demineralized dentin matrix

Many clinical trials on GBR, socket preservation, and ridge augmentation revealed that new bone was generated by osteoinduction and/or osteoconduction, with crystal bone resorption averaging 0.29 mm (0–3.0 mm) during the follow-up period.[7] The average bone loss 8 months after prosthetic loading in the GBR group (14 implants) was 0.29 mm, whereas the average bone loss 7.6 months after prosthetic loading in the sinus graft group (14 implants) was 0.66 mm. 0.47 mm crestal bone loss was found in a GBR case series research with 15 patients and a 31-month follow-up period.[23] Another case series research of extraction socket preservation found that after 22.5 months (12–34 months) of functional loading, the average amount of crestal bone loss around the implant was 0.05 mm. Because of its osteoconductivity and bone remodeling capabilities, the 3-month specimen showed newly created tissues.[23] A prospective, randomized clinical investigation comparing the clinical efficacy and histological outcomes of autogenous DDM with inorganic bovine bone in postextraction alveolar bone augmentation (BioOss, Geistlich, Switzerland) found that autogenous DDM was just as successful as inorganic bovine bone.[11]

Demineralized dentin matrix blocks

In 12 patients, the first clinical report using autogenous DDM blocks for socket preservation revealed excellent bone growth and strong DDM block integration into the recipient bone. During the early phases, the alveolar bone volume was well maintained both vertically and horizontally, and the produced bone was not resorbed. Aponeurotic fusions between the gingiva and the DDM block, osteocytic embedding, osteoclastic resorption, and vascular invasion into the DDM block were all seen on histological evaluation.

A case series study based on 22 patients who received a single implant with a DDM block in the posterior area of the maxilla (12 patients) or the mandible (10 patients) was performed with an average follow-up period of 44 months to evaluate

the fate of DDM blocks during long-term follow-up observations. The results were comparable with those of earlier short-term investigations, indicating that DDM blocks can reconstruct continuously under a functional load while maintaining proper volume.[53]

Sinus bone graft of demineralized dentin matrix powder

Dr. Murata presented the first clinical instance of a sinus lifting treatment employing autogenous DDM at the 2003 IADR Congress.[3] Lee et al.[54] compared the efficiency of DDM to that of various other scaffolds in the sinus in a histomorphometric analysis. All groups had new bone formation around the transplant material and implant in the sinus after 4 months.

In patients treated with DDM or synthetic materials (11 patients/group), the quantity of bone resorption in the sinus was assessed using the crestal approach. The average bone resorption height was 0.76 mm in DDM and 0.53 mm in synthetic materials 1 year after the graft, demonstrating that DDM is a good alternative material to synthetic bone graft for bone augmented sinus lift.[55]

Conclusion

Auto tooth bonegraft is suitable to replace allograft, xenograft, and alloplastic bone grafts. There are no hereditary or infectious hazards with auto tooth bone graft material. Having good strength, it can bring about regeneration through its properties of osteoconduction and osteoinduction. Apart from that this graft is convenient for both clinicians and patients, as well as, it is very reasonable cost-wise. It seems to be a graft material and should be researched further to confirm its osteogenic effects and biological safety.

References

- Koga T, Minamizato T, Kawai Y, Miura K, I T, Nakatani Y, Sumita Y, Asahina I. Bone Regeneration Using Dentin Matrix Depends on the Degree of Demineralization and Particle Size. *PLoS One*. 2016 Jan 21; 11(1):e0147235.
- Smith AJ. The vitality of the dentin-pulp complex in health and disease: growth factors as key mediators. *J Dent Educ* 2003; 67:678-689.
- Murata M, Sato D, Akazawa T, Taira T, Sasaki T, Arisue M. Bone and cartilage induction in nude mice using demineralized dentin matrix. *J Hard Tissue Biol* 2003; 11:110-114.
- Murata. Bone engineering using human demineralized dentin matrix and recombinant human BMP-2. *J Hard Tissue Biol* 2005; 14:80-81.
- Yeomans JD, Urist MR. Bone induction by decalcified dentine implanted into oral, osseous, and muscle tissues. *Arch Oral Biol* 1967; 12:999-1008.
- Park SM, Um IW, Kim YK, Kim WK. Clinical application of auto-tooth bone graft material. *J Korean Assoc Oral Maxillofac Surg* 2012; 38:2-8.
- Kim YK, Kim SG, Kim KW, Um IW. Extraction socket preservation and reconstruction using autogenous tooth bone graft. *J Korean Assoc Maxillofac Plast Reconstr Surg* 2011; 33:264-269.
- Kim, Eun-Seok. "Autogenous fresh demineralized tooth graft prepared at chairside for a dental implant." *Maxillofacial Plastic and reconstructive surgery* 18 Feb. 2015.;37:1:8.
- Joshi CP, Dani NH, Khedkar SU. Alveolar ridge preservation using autogenous tooth graft versus beta-tricalcium phosphate alloplast: A randomized, controlled, prospective, clinical pilot study. *J Indian Soc Periodontol*. 2016; 20(4):429-434.
- Kim YK, Lee JH, Um IW, Cho WJ. Guided bone regeneration using demineralized dentin matrix: Long-term follow-up. *J Oral Maxillofac Surg*. 2016; 74:515.
- Pohl V, Pohl S, Sulzbacher I, Fuerhauser R, Mailath-Pokorny G, Haas R. Alveolar Ridge Augmentation Using Dystopic Autogenous Tooth: 2-Year Results of an Open Prospective Study. *Int J Oral Maxillofac Implants*. 2017 July/August; 32(4):870-879.
- Pang KM, Um IW, Kim YK, Woo JM, Kim SM, Lee JH, et al. Autogenous demineralized dentin matrix from extracted tooth for the augmentation of alveolar bone defect: A prospective randomized clinical trial in comparison with anorganic bovine bone? *Clin Oral Implants Res*. 2016
- Li P, Zhu H, Huang D. Autogenous DDM versus Bio-Oss granules in GBR for immediate implantation in periodontal postextraction sites: A prospective clinical study. *Clin Implant Dent Relat Res*. 2018 Dec; 20(6):923-928.
- Parvini, P., Sader, R., Sahin, D. et al. Radiographic outcomes following lateral alveolar ridge augmentation using autogenous tooth roots. *Int J Implant Dent* 4, 31 (2018).
- Schwarz F, Hazar D, Becker K, Sader R, Becker J. Efficacy of autogenous tooth roots for lateral alveolar ridge augmentation and staged implant placement. A prospective controlled clinical study. *J Clin Periodontol*. 2018 Aug; 45(8):996-1004.
- Del Canto-Díaz A, de Elío-Oliveros J, Del Canto-Díaz M, Alobera-Gracia MA, Del Canto-Pingarrón M, Martínez-González JM. Use of autologous tooth-derived graft material in the post-extraction dental socket. Pilot study. *Med Oral Patol Oral Cir Bucal*. 2019 Jan 1; 24(1):e53-e60.

17. Wu, Dong & Zhou, Lin & Lin, Jichao & Chen, Jiang & Huang, Wenxiu & Chen, Yonghui. (2019). Immediate implant placement in anterior teeth with grafting material of autogenous tooth bone vs xenogenic bone. *BMC Oral Health*. 19.
18. Shejali J, Thomas R, Kumar T, Shah R, Mehta DS, Gayathri GV. Immediate Ridge Augmentation Using Autogenous Tooth Root as a Block Graft in a Periodontally Hopeless Extraction Site: A Pilot Study. *J Oral Implantol*. 2020 Feb 1; 46(1):41-49.
19. Kuperschlag A, Keršytė G, Kurtzman GM, Horowitz RA. Autogenous Dentin Grafting of Osseous Defects Distal to Mandibular Second Molars After Extraction of Impacted Third Molars. *Compend Contin Educ Dent*. 2020 Feb;41(2):76-82; quiz 83.
20. L. Tjäderhane, M. R. Carrilho, L. Breschi, F. R. Tay, and D. H. Pashley, "Dentin basic structure and composition-an overview," *Endodontic Topics*, 2009; 20(1): 3–29.
21. Pashley DH. Dynamics of the pulpo-dentin complex. *Crit Rev Oral Biol Med*. 1996; 7(2):104-33.
22. Kim YK, Kim SG, Yun PY, et al. Autogenous teeth used for bone grafting: a comparison to traditional grafting materials. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2014; 117:e39-45.
23. Zhang, Ling & Wang, Dan-yang & Fan, Jing & Li, Fang & Chen, Yu-jiang & Chen, Ji-Hua. (2014). Stability of bonds made to superficial vs. deep dentin, before and after thermocycling. *Dental Materials*. 30.
24. Potdar PD, Jethmalani YD. Human dental pulp stem cells: Applications in future regenerative medicine. *World J Stem Cells*. 2015;7(5):839-851.
25. Oryan A, Alidadi S, Moshiri A, Maffulli N. Bone regenerative medicine: classic options, novel strategies, and future directions. *J Orthop Surg Res*. 2014; 9(1):18. Published 2014 Mar 17.
26. Titsinides S, Agrogiannis G, Karatzas T. Bone grafting materials in dentoalveolar reconstruction: A comprehensive review. *Jpn Dent Sci Rev*. 2019; 55(1):26-32.
27. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards*. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 2015.
28. Bono N, Tarsini P, Candiani G. Demineralized dentin and enamel matrices as suitable substrates for bone regeneration. *J Appl Biomater Funct Mater*. 2017 Jul 27;15(3)
29. Moharamzadeh K, Freeman C, Blackwood K. Processed bovine dentine as a bone substitute. *Br J Oral Maxillofac Surg*. 2008; 46:110–3.
30. Andersson L, Ramzi A, Joseph B. Studies on dentin grafts to bone defects in rabbit tibia and mandible; development of an experimental model. *Dent Traumatol*. 2009; 25:78–83.
31. Kabir MA, Murata M, Akazawa T, Kusano K, Yamada K, Ito M. Evaluation of perforated demineralized dentin scaffold on bone regeneration in critical-size sheep iliac defects? *Clin Oral Implants Res*. 2017.
32. Kim YK, Lee JH, Kim KW, Um IW, Murata M, Ito K. Analysis of organic components and osteoinductivity in autogenous tooth bone graft material. *J Korean Assoc Maxillofac Plast Reconstr Surg*. 2013;35:353–9
33. Canullo L, Rossi-Fedele G, Camodeca F, Menini M, Pesce P A Pilot Retrospective Study on the Effect of Bone Grafting after Wisdom Teeth Extraction. *Materials (Basel)*, 14(11), 26 May 2021
34. Ahn GJ, Kim YK, Um IW, Kim JY. Evaluation of prognosis of autogenous tooth bone graft material according to the condition of donor tooth. *J Dent Implant Res*.2015; 341:7–11.
35. Inoue T, Deporter DA, Melcher AH. Induction of cartilage and bone by dentin demineralized in citric acid. *J Periodontal Res*. 1986; 21:243–55.
36. Gruskin E, Doll BA, Futrell FW, Schmitz JP, Hollinger JO. Demineralized bone matrix in bone repair: history and use. *Adv Drug Deliv Rev*. 2012 Sep; 64(12):1063-77.
37. Murata M, Sato D, Hino J, Akazawa T, Tazaki J, Ito K, et al. Acid-insoluble human dentin as carrier material for recombinant human BMP-2. *J Biomed Mater Res A* 2012; 100:571-7.
38. Pobloth AM, Checa S, Razi H, Petersen A, Weaver JC, Schmidt-Bleek K, Windolf M, Tatai AA, Roth CP, Schaser KD, Duda GN, Schwabe P. Mechanobiologically optimized 3D titanium-mesh scaffolds enhance bone regeneration in critical segmental defects in sheep. *Sci Transl Med*. 2018 Jan 10; 10(423): eaam8828.
39. de Oliveira GS, Mizziara MN, Silva ER, Ferreira EL, Biulchi AP, Alves JB. Enhanced bone formation during healing process of tooth sockets filled with demineralized human dentine matrix. *Aust Dent J*. 2013; 58:326–32.
40. Murata M, Akazawa T, Takahata M, Ito M, Tazaki J, Hino J, et al. Bone induction of human tooth and bone crushed by newly developed automatic mill. *J Ceram Soc Jpn*. 2010; 118:434–7.
41. Tanwatana S, Kiewjurat A, Suttapreyasri S. Chemical and thermal deproteinization of human demineralized tooth matrix: Physicochemical characterization and osteoblast cell biocompatibility. *J Biomater Appl*. 2019 Nov; 34(5):651-663.
42. Moharamzadeh K, Brook IM, Van Noort R. Biocompatibility of Resin-based Dental

- Materials. *Materials* (Basel). 2009; 2(2):514-548. Published 2009 Apr 28.
43. Fatemeh Sadat Tabatabaei Mirakabad, Abolfazl Akbarzadeh, Morteza Milani, Nosratollah Zarghami, Mortaza Taheri-Anganeh, Vahideh Zeighamian, Fariba Badrzadeh & Mohammad Rahmati-Yamchi. A Comparison between the cytotoxic effects of pure curcumin and curcumin-loaded PLGA-PEG nanoparticles on the MCF-7 human breast cancer cell line, *Artificial Cells, Nanomedicine, and Biotechnology*, 2016;44:1, 423-430.
 44. Roberts TT, Rosenbaum AJ. Bone grafts, bone substitutes and orthobiologics: the bridge between basic science and clinical advancements in fracture healing. *Organogenesis*. 2012;8(4):114-124.
 45. Mulliken JB, Glowacki J. Induced osteogenesis for repair and construction in the craniofacial region. *Plast Reconstr Surg*. 1980; 65:553-60.
 46. Tanoue, R., Ohta, K., Miyazono, Y. et al. Three-dimensional ultrastructural analysis of the interface between an implanted demineralized dentin matrix and the surrounding newly formed bone. *Sci Rep*. 2018; 8: 2858.
 47. Al-Asfour A, Farzad P, Al-Musawi A, Dahlin C, Andersson L. Demineralized Xenogenic Dentin and Autogenous Bone as Onlay Grafts to Rabbit Tibia. *Implant Dent*. 2017 Apr; 26(2):232-237.
 48. Um IW, Kim YK, Mitsugi M. Demineralized dentin matrix scaffolds for alveolar bone engineering. *J Indian Prosthodont Soc*. 2017; 17(2):120-127.
 49. Bormann KH, Suarez-Cunqueiro MM, Sinikovic B, Kampmann A, von See C, Tavassol F, et al. Dentin as a suitable bone substitute comparable to β -TCP – An experimental study in mice. *Microvasc Res* 2012; 84:116-22.
 50. Kamal M, Andersson L, Tolba R, et al. Bone regeneration using composite non-demineralized xenogenic dentin with beta-tricalcium phosphate in experimental alveolar cleft repair in a rabbit model. *J Transl Med*. 2017; 15(1):263. Published 2017 Dec 23.
 51. Pape HC, Evans A, Kobbe P. Autologous bone graft: properties and techniques. *J Orthop Trauma*. 2010; 24 Suppl 1:S36-S40.
 52. Kim YK, Pang KM, Yun PY, Leem DH, Um IW. Long-term follow-up of autogenous tooth bone graft blocks with dental implants. *Clin Case Rep* 2017; 5:108-18.
 53. Jeong KI, Kim SG, Kim YK, Oh JS, Jeong MA, Park JJ. Clinical study of graft materials using autogenous teeth in maxillary sinus augmentation. *Implant Dent* 2011; 20:471-5.
 54. Lee. Histomorphometric study of sinus bone graft using various graft material. *J Dent Rehabil Appl Sci* 2011; 27:141-7.
 55. Kim YK, Lee J, Yun JY, Yun PY, Um IW. Comparison of autogenous tooth bone graft and synthetic bone graft materials used for bone resorption around implants after crestal approach sinus lifting: A retrospective study. *J Periodontal Implant Sci* 2014; 44:216-21.