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Bone graft material derived from extracted tooth

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Certification of the Supervisor

I certify that this project entitled "**Bone graft material derived from extracted tooth**" was prepared by **Jafar Ibrahim Jafar and Jaafar Abdulhameed Jafar** under my Supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Supervisor's name: Lecturer Dr. Nibras Hamdan Chasib

Dedication

I would like to dedicate my humble effort to:

My sweet and lovely Father & Mother their affection, love, encouragement and prays of day and night make me able to get success and honor.

Jafar Ibrahim Jafar

Jaafar Abdulhameed Jafar

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List of Abbreviations

BMPs	**Bone morphogenic proteins**
NCP	Non-collagenous proteins
OPN	Osteopontin
autoBT	Autogenous tooth bone graft material
DFDBA	Demineralized freeze-dried bone allograft
RGD	Tripeptide Arg-Gly-Asp
RANKL	Receptor activator of NF-B ligand
OPG	Osteoprotegerin
CSF	Colony-stimulating factor
rhBMP	Various recombinant human BMPs
IGF	Insulin-like growth factor
PDGF	Platelet-derived growth factor
FGF	Fibroblast growth factor
TGF	Transforming growth factor
DSP	Dentin sialoprotein
BMP	Bone morphogenic protein
IGF-II	Insulin-like growth factor-II
OC	Osteocalcin
BSP	Bone sialoprotein
XRD	X-ray diffraction analysis
HA	hydroxyl apatite
TCP	tricalcium phosphate
ACP	amorphous calcium phosphate
OCP	Octacalcium phosphate
SEM	scanning electron microscope
EDS	Energy Dispersive Spectroscopy
DDM	Demineralized dentin matrix
PDM	Partially demineralized matrix
ADDM	Autogenous demineralized dentin matrix
GBR	Guided bone regeneration
CT	Computed tomography
HDDM	Homogenous demineralized dentin matrix
LMP-1	LIM mineralization protein 1
HAM	Human amniotic membrane
PTFE	Polytetrafluoroethylene

Introduction

Tooth extraction is one of the most common procedures in dentistry, with almostall the extracted teeth being regarded as clinical wastes and hence discarded. It iswell known that the alveolar process is a structure dependent on tooth, its volumeand shape is controlled by the form, axis and inclination of the teeth **(Van der Weijden *et al*., 2009).** Evidence provided by many previous studies showed that, following tooth extraction alveolar process undergoes structural and dimensional change therebycausing ridge atrophy. Hence the restoration of the normal functionsand suitable esthetic of the patient is important, ridge augmentation with bone grafting materials is required **(DSouza, 2012)**.

In dentistry several bone grafting materials are available that helps in ridge preservation and augmentation of the defects in the alveolar process supporting the teeth **(Kumar *et al*., 2013).** These materials used in dentistry ranges from autogenous, allogeneic, xenogeneic, and synthetic or alloplastic. Three properties are required for an ideal bone graft material: osteoconduction, which provides scaffolds for bone regeneration. osteoinduction which promote formation of bone tissue by inducing differentiation of progenitorcells into osteoblasts. osteoproliferation which stimulate bone generation by inducing the cells which are present in the graft material. Therefore, autogenousbone graft is considered gold standard, since they have the property to induce osteogenesis, osteoinduction, osteoconduction **(Pandit *et al*., 2016).**

However,limited availability and rapid resorption of autogenous bone, defects of donor siteand morbidity or discomfort from distant extra-oral grafts to the patients, in case of large bone needed, hinder the use of autogenous bone **(Kim, 2016).** Allografts, xenografts and alloplasts are not amount restricted, do not create donor site morbidity and have the capacity

to carry cellular growth factors **(Ting *et al*., 2017).** Yet still, none of them exhibits all the three properties, since xenografts and alloplasts have only osteoconductive capacity and allografts fail to promote osteoproliferation **(Nampo *et al*., 2010).** These issues have spurred on researchers and clinicians to look for novel graft solutions, more specifically, the use of tooth-derived materials.

The chemical compositions of teeth, especially dentin and bones, are very similar. Enamel consists of 96% inorganic substances and 4% water, whereas dentin has 65% inorganic substances, 35% organic substances, and water. Cementum is made up of 45-50% inorganic substances, 50-55% organic substances, and water. Finally, alveolar bone has 65% inorganic and 35% organic substances **(Desoutter *et al*., 2014)**.

In organic parts, dentin and cementum include type I collagens and various growth factors such as bone morphogenic proteins (BMPs). Type I collagen occupies about 90% of the organic parts of tissues, with the rest non-collagenous proteins (NCP), biopolymers, lipid, citrate, and lactate. NCPs include phosphophoryn, sialoprotein, glycoprotein, proteoglycan, osteopontin (OPN), osteocalcin, dentin matrix protein-1, osterix, andCbfa1 (Runx2). These proteins are known to trigger the bone resorption and generation processes **(Kim *et al*., 2013).**

Based on the potentials of osteoconduction, osteoinduction, and osteogenesis through growth factors in tooth and similar histogenesis between tooth and bone, a novel bone graft material can be developed utilizing the inorganic and organic components of an extracted tooth. Indeed, Autogenous tooth bone graft material (autoBT) was developed in 2008 and has been used for guided bone regeneration tosupport implant placement. Currently, AutoBT is widely used in clinics in Korea and Japan **(Kim *et al*., 2013)**.

Aims of the study:

1. To review the evidences in literature regarding the efficacy of using teeth derived bone graft in ridge augmentation Socket preservation Maxillary sinus bone graft and implant placement.
2. To summarize the clinical procedure used for chairside preparation of tooth derived bone graft.

Chapter one: Review of literature

1.1 Types of bone graft materials

Bone substitutes have been actively used in clinics to reconstruct bony defects. There are four categories of bone graft materials: autograft, allograft, alloplast, and xenograft. With four types of graft materials available, the use of these materials depends on clinical applications, volume of deficiency, and evidence-based studies Above all, autografts are known to be the gold standard due to its osteoinductivity, osteoconductivity, and osteogenesis **(Figure 1)**. Still, autogenous bone grafts harvested from extra-oral sites have Bone grafting materials vary by their source. Autogenous bone grafts may be harvested from the patient's iliac crest, mandibular ramus or other intraoral sites. The donor site chosen is determined based on the volume of graft material required **(Zhao *et al*., 2021)**.

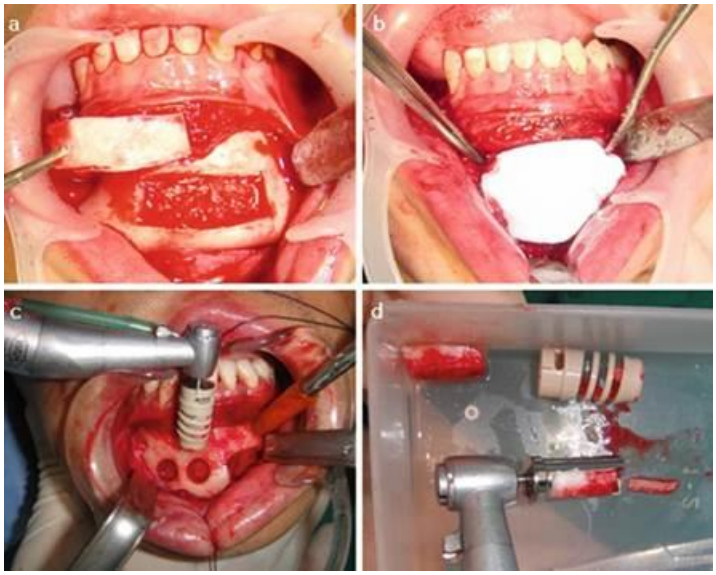

Fig. 1. Chin bone harvesting. (a) Window type block bone harvesting, (b) Barrier membrane placed for bone healing of the donor site, (c and d) Mushed particulated bone block harvesting with bone mill bur **(Sasaki et al., 2015).**

Autogenous bone heals in three phases. The first phase is osteogenesis and here the surviving cells form the osteoid. The second phase is osteoinduction and starts two weeks' post grafting. The blood vessels from

host bone invade the graft and native bone cells follow the vessels. Bone formation and resorption now is mediated by bone morphogenetic protein (BMP). The third phase occurs as the minerals from the graft act as scaffolding for native bone to from a matrix upon. The third phase is synonymous with osteoconduction. These three phases overlap and are not separate entities **(Misch *et al*., 1993)**. Disadvantages of autografts include the need for a second surgical site and the morbidity related to bone harvesting **(Giannoudis *et al*., 2005)**.

Autogenous bone may also require a longer time period for resorption than some synthetics or DFDBA mixed with calcium sulfate. This could also be a disadvantage if full graft resorption is desired in a short time frame which will not occur with autogenous cortical bone grafts. Allograft material is bone material from another individual of the same species—often cadaveric. The bone material is sterilized, processed and stored in bone (**Saima *et al*., 2016)**.

Allografts act via osteoinduction and to have osteoconductive capabilities as well on native undifferentiated mesenchymal cells. They are known to form bone via osteoconduction by a combination of resorption of the graft matrix and deposition of new bone on the residual scaffold **(Park *et al*., 2012)**. Osteogenesis is not an option for allografts as the cells are not vital. Some challenges with this type of bone is that the medical history of the donor must be cleared of infections, cancers and other problems for the recipient's safety. It has been hypothesized that bone formation is slower and may produce less volume for allografts versus autografts as allografts do not conduct osteogenesis, an example of commercially available allograft is shown in **(Figure 2) (Zhao *et al*., 2021)**.

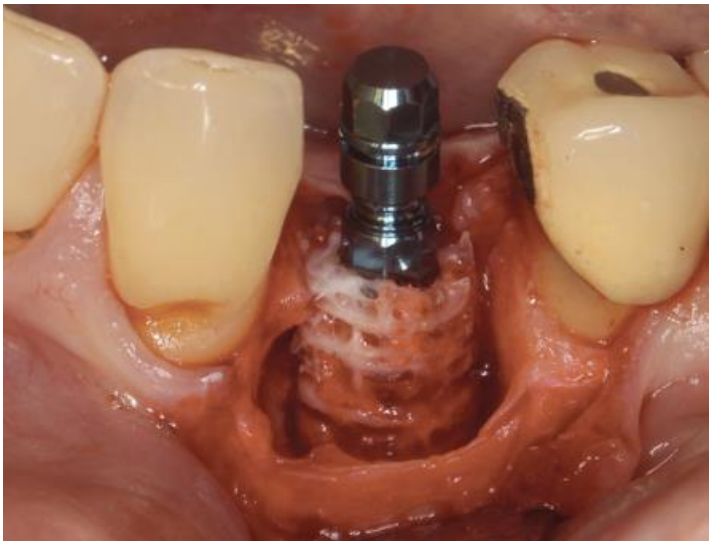

Fig. 2. Implant inserted through allograft ring **(Miller *et al*., 2019)**

Xenograft material is bone material from equine, porcine or bovine sources that is mostly deproteinized and further processed as seen in **(Figure 3)**. The organic components of these materials are removed to mitigate immune reactivity or pathogen transmission. The remaining minerals act as a scaffolding for native bone growth. They might be used in combination with growth factors or allografts to simulate the autogenous bone. Bone formation occurs mostly via osteoconduction **(Nazirkar *et al*., 2014)**.

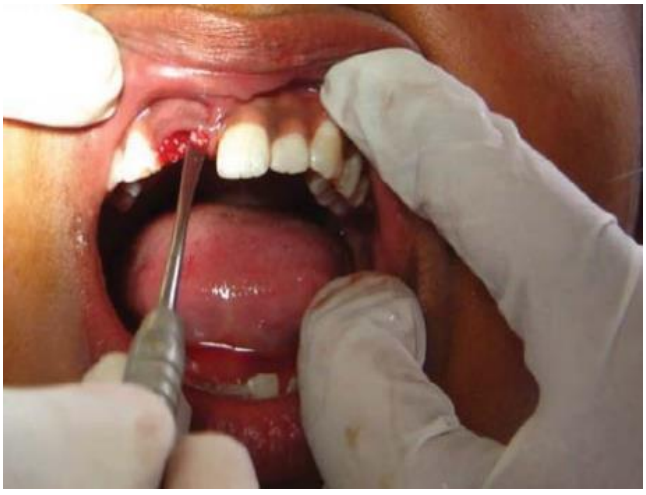

Fig. 3. Bovine bone graft along with Platelet rich fibrin **(Koyel *et al*., 2020)**

The resulting crystal structure is described to be rather similar to human cancellous bone **(Kao *et al*., 2007)**. Alloplastic material is entirely

synthetic and synthesized from non-organic sources **(Booth *et al*., 2003).** The most prevalent type of alloplasts are bioactive ceramics as shown in **(Figure 4)** such as calcium phosphate **(Saima *et al*., 2016)**. Ceramics (calcium phosphates, bioglass, calcium sulfate) can be mixed with growth factors and ions to increase bone mineral density and osteoblast proliferation. The mode of bone formation for these ceramics is osteoconduction. When transplanted, osteoid is produced directly onto the ceramic surface by native bone and later undergoes remodeling **(Ginebra *et al*., 2018)**.

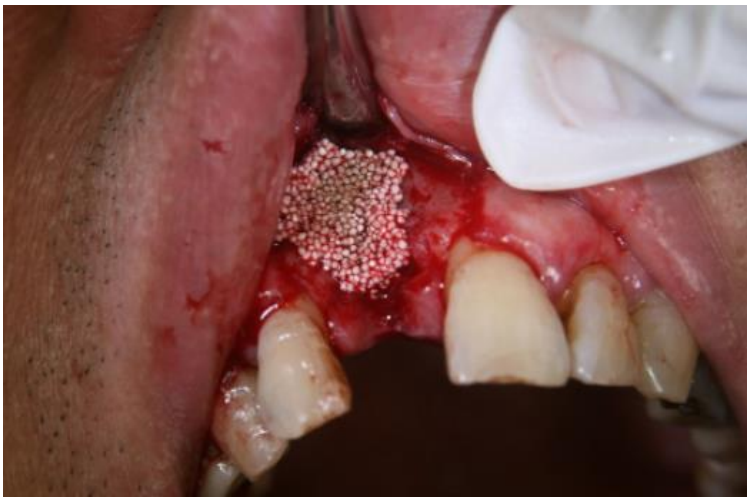

Fig. 4. Alloplast bone grafting material placed and molded to shape the area **(Stadeker *et al*., 2008).**

1.1.1 Bone Growth, Modeling, and Remodeling

Bone undergoes longitudinal and radial growth, modeling, and remodeling during life. Longitudinal and radial growth during growth and development occurs during childhood and adolescence. Longitudinal growth occurs at the growth plates, where cartilage proliferates in the epiphyseal and metaphyseal areas of long bones, before subsequently undergoing mineralization to form primary new bone **(Ubara *et al*., 2005)**.

Modeling is the process by which bones change their overall shape in response to physiologic influences or mechanical forces, leading to gradual adjustment of the skeleton to the forces that it encounters. Bones may widen or change axis by removal or addition of bone to the appropriate surfaces by

independent action of osteoblasts and osteoclasts in response to biomechanical forces **(Ubara *et al*., 2003)**.

Bones normally widen with aging in response to periosteal apposition of new bone and endosteal resorption of old bone. Wolff's law describes the observation that long bones change shape to accommodate stresses placed on them. During bone modeling, bone formation and resorption are not tightly coupled. Bone modeling is less frequent than remodeling in adults **(Kobayashi *et al*., 2003)**.

Modeling may be increased in hypoparathyroidism, renal osteodystrophy, or treatment with anabolic agents **(Lindsay *et al*., 2006)**.

Bone remodeling is the process by which bone is renewed to maintain bone strength and mineral homeostasis. Remodeling involves continuous removal of discrete packets of old bone, replacement of these packets with newly synthesized proteinaceous matrix, and subsequent mineralization of the matrix to form new bone. The remodeling process resorbs old bone and forms new bone to prevent accumulation of bone microdamage. Remodeling begins before birth and continues until death. The bone remodeling unit is composed of a tightly coupled group of osteoclasts and osteoblasts that sequentially carry out resorption of old bone and formation of new bone. Bone remodeling increases in perimenopausal and early postmenopausal women and then slows with further aging, but continues at a faster rate than in premenopausal women. Bone remodeling is thought to increase mildly in aging men **(Burr, 2002)**.

The remodeling cycle is composed of four sequential phases. Activation precedes resorption, which precedes reversal, which precedes formation. Remodeling sites may develop randomly but also are targeted to areas that require repair **(Parfitt, 2002)**.

Remodeling sites are thought to develop mostly in a random manner. Activation involves recruitment and activation of mononuclear monocyte,

macrophage osteoclast precursors from the circulation **(Roodman, 1999)**. lifting of the endosteum that contains the lining cells off the bone surface, and fusion of multiple mononuclear cells to form multinucleated preosteoclasts. Preosteoclasts bind to bone matrix via interactions between integrin receptors in their cell membranes and RGD (arginine, glycine, and asparagine)-containing peptides in matrix proteins, to form annular sealing zones around bone-resorbing compartments beneath multinucleated osteoclasts **(Boyle *et al*., 2003)**.

Osteoclast-mediated bone resorption takes only approximately 2 to 4 week during each remodeling cycle. Osteoclast formation, activation, and resorption are regulated by the ratio of receptor activator of NF-B ligand (RANKL) to osteoprotegerin (OPG) IL-1 and IL-6, colony-stimulating factor (CSF), parathyroid hormone, 1,25-dihydroxyvitamin D, and calcitonin **(Blair and Athanasou, 2004)**. Resorbing osteoclasts secrete hydrogen ions via H-ATPase proton pumps and chloride channels in their cell membranes into the resorbing compartment to lower the pH within the bone-resorbing compartment to as low as 4.5, which helps mobilize bone mineral **(Silver, 1988)**.

1.2 Components of tooth

1.2.1 Inorganic and Organic Component of dentin

1. Hydroxyapatite, inorganic component

Dentin consists of 70% hydroxyapatite in its weight volume. Hydroxyapatite in dentin is structured with low- crystalline calcium phosphate **(Kim *et al*., 2011)**, making future bone remodeling possible. Bone tissues are also mainly composed of low-crystalline apatite. In contrast, hydroxyapatite in enamel is structured as high- crystalline calcium phosphate. High crystalline contents are not easily decomposed by osteoclasts, resulting in slow resorption and consequently poor osteoconductivity **(Kim *et al*., 2011)**.

2. Bone growth factors and type I collagen

Growth factors are signaling proteins that regulate cellular growth, proliferation, and differentiation **(Karfeld-Sulzer *et al*., 2012)**. **Urist et al. (1965)** initially discovered BMPs and studied their roles in 1965. BMPs are known to exist in the bone matrix, osteosarcoma tissue, and dentin matrix, functioning to differentiate perivascular mesenchymal stem cells into cartilage and bone tissues **(Hanamura *et al*., 1980; Sampath *et al*., 1983)**. Several studies have successfully isolated BMPs from dentin, enamel, and cementum of bovine, rats, guinea pigs, and rabbit teeth, With extensive studies on BMPs, researchers have confirmed the osteoinductivity of BMPs extracted from animal teeth such as bovine, lapine, and murine teeth. Since only a limited amount of BMPs can be extracted from the teeth, however, the clinical utilization may be limited **(Chae *et al*., 1997; Oh DW et al., 1996)**.

Therefore, various recombinant human BMPs (rhBMP) have been recently manufactured by gene recombination based on mammal cells or colon bacilli Dentin and cementum contain various other growth factors besides BMPs such as insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and transforming growth factor (TGF)-β **(Finkelman *et al*., 1990)**.

Rocha reported the extraction of TGF-β, IGF-I, IGF-II from human dentin but at lower levels compared to those from human bone **(Rocha *et al*., 2002)**. About 90% of dentinal organic components are known to be type I collagens. These triple-helix structured collagens are the most abundant protein in vertebrates. Collagen- derived materials have demonstrated biocompatibility and interference in bone formation at the implanted sites **(Maki *et al*., 2000 and Nampo *et al*., 2010)**.

The rest of dentinal organic components are NCP. NCPs that contribute to mineralization are osteocalcin, osteonectin, phosphophoryn,

dentin sialoprotein (DSP), dentin-specific extracellular matrix protein, etc. Phosphophoryn in particular, bound to type I collagen, contributes to the mineralization process; it is of the largest amounts among NCPs. Previous studies discovered through the immune-histochemical study that OPN and DSP manifested 6-8 weeks after grafting the tooth graft material on alveolar bone defects in Wistar rats. OPN is known to trigger osteogenesis through the early differentiation of the osteoblasts but also leads to bone resorption by allowing adherence of osteoclasts to the bone surface. DSP has a significant role in dentin calcification **(Linde *et al*., 1989 and Ritchie *et al*., 1998)**.

1.3 Resemblance between tooth and bone

Tooth and bone exhibit similar biochemical composition, consisting mainly of organic and inorganic constituents. Alveolar bone comprised 65% inorganic and 35% organic with the percentage comparable to dentine (inorganic 65–70% and organic 30–35%) and cementum (inorganic 45–50% and organic 50–55%). Another, remarkable property of dentin and cementum is the presence type I, type III collagen and number of growth factors including bone morphogenic protein (BMP), insulin-like growth factor-II (IGF-II), and transforming growth factor-β (TGF-β), which play a major role in promoting bone remodeling **(Finkelman *et al*., 1990, Schmidt-Schultz *et al*., 2005).**

Majority of proteins found in bone like osteopontin (OPN), osteocalcin (OC), bone sialoprotein (BSP), osterix, type I collagen and Cbfa1 (Runx2) have also been identified in dentin, which could make it an effective substitute for another bone grafting materials available **(Choi *et al*., 2013, McKee et al., 2013)**.

The bone is made up of numerous Harversian's system, while dentin is complex structure consisting of dentinal tubules. When dentin is

demineralized, the tubules become broader exposing collagen fibers making it more permeable causing an outward flow of dentinal fluid with it several enzymes and growth factors **(Tjäderhane *et al*., 2009)**.

X-ray diffraction analysis (XRD) have confirmed the presence of hydroxyl apatite (HA), and also small amounts of tricalcium phosphate (TCP), amorphous calcium phosphate (ACP), and octacalcium phosphate (OCP) in different area of the tooth which are components similar to those of human bone. The previous study by **(Kim *et al*., 2011; Kim *et al*., 2013)** conducted to compare the traditional grafting materials and autogenous tooth, they also showed using XRD that the crystalline structures of an autogenous tooth had a similar pattern to autogenous bones. The use of scanning electron microscope (SEM) to examine the surface structure of autogenous tooth had also been performed in the previous studies **(Kim *et al*., 2010, kim *et al*., 2013)**.

SEM reveals that after preparation of an autogenous tooth; it is mostly homogenous with dentinal tubules and dense collagen matrix clearly visible **(Kim *et al*., 2010)**. Energy Dispersive Spectroscopy (EDS) used to study the phase of calcium phosphate apatites in tooth or Ca/P ratio, showing extensive calcium dissolution during the early phase, which is similar to autogenous bones **(kim *et al*., 2013)**.

Owning to this property the study of **Priya *et al*. (2010)** who reported that extensive dissolution of calcium phosphate releasing its ions induces the reprecipitation of the apatite onto the surfaces. **Priya *et al* (2010)** also observed that the calcium phosphate composite dissolution had rough surface and icroporous regions formation, which allowed the proliferation of both biological cells and bone growth. This desired property of biocompatible materials is the ability tocompletely absorbed in living organisms via biodegradation, since poor biodegradation prohibits natural bone growth for prolonged periods **(kim et al., 2013)**.

1.4 Demineralized Dentin Matrix

Demineralized dentin matrix (DDM), an osteoinducing bone substrate, has been used as an rhBMP-2 carrier since 1998. In addition, DDM has both microparticle and nanoparticle structures, which do not undergo remodeling, unlike bone. In vitro, DDM is a suitable carrier for BMP-2, with the continued release over 30 days at concentrations sufficient to stimulate osteogenic differentiation **(Um *et al*., 2020)**.

1.4.1 Demineralization

The demineralization process is required for freeing the various growth factors and proteins, since the release of the growth factors is sometimes blocked by the presence of hydroxyapatite crystals. Many authors observed that heterotrophic bone was induced when DDM was grafted in the lapine, porcine, and murine muscle tissues. As such, decalcification of dentin is believed to induce the release of BMP, thereby leading to osteoinduction **(Urist et al., 1971)**. Researchers use various decalcification methods. Decalcified dentin and bone using 0.6N HCl in normal solution led to the inducement of connective tissue cells and formation of endochondral bone in muscle and in skin connective tissues **(Inoue *et al*., 1986)**. Ike and Urist partially demineralized the roots of the teeth using 0.6N HCL for 24 hours, and then cut them in 0.5 g blocks to produce partially demineralized matrix (PDM) **(Ike and Urist, 1998)**. PDM was then washed in cold water and lyophilized. An alternative approach was employed by **Inoue et al. (1986)** they grafted the demineralized dentin tissues using 0.6N HCL (pH1) and 3M (9N) in the rectal abdominis muscles of Wistar rats. Inoue reported favorable chondrogenesis and osteogenesis, with the HCL-demineralized dentin showing relatively superior results. Different approaches in acid treatment protocols were used. DDM was treated using 2% HNO3. Several animal studies showed favorable results, with observed new bone Formation **(Reddi**

***et al*., 1983)**.

Some studies showed contrary results. When human partially demineralized dentin granules were grafted in the intramuscular pockets, osteoinduction was not observed **(Ike and Urist, 1998)**. Based on the quantitative analysis of proliferation and differentiation of the MG-63 cell, however, cellular adhesion and proliferation activity of the MG-63 cell on partially demineralized dentin matrix were noted **(Urist MR et al. 1968; Huggins *et al*., 1970; Reddi *et al*., 1983)**. With differently employed methods, it could be conjectured that the osteoinductive properties of dentin might depend on different acid treatment protocols.

1.4.2 Autogenous demineralized dentin matrix

Extensive studies in vitro have been conducted on Autogenous demineralized dentin matrix (ADDM) with its biocompatibility, osteoinductivity, and osteoconductivity (**Catanzaro-Guimarães *et al*., 1989)**. In animal studies, ADDM induced bone formation according to histological analysis **(Gomes *et al*., 2001; Murata *et al*., 2012)**. For instance, Gomes performed a histological evaluation of the osteoinductive property of ADDM on calvarial bone defects in rabbit. According to the study, ADDM was verified to have chemotactic properties for osteoprogenitor cells and osteoblasts, promoting the acceleration of bone repair process at the bony defect. Slices of ADDM induced direct bone formation, and they were incorporated by the newly formed bone tissue and remodeled **(Gomes *et al*., 2001)**. The mechanisms involved in the osteogenesis of ADDM include endochondral and intramembranous bone formation **(Ryu *et al*., 1996; Murata *et al*., 2012)**. Likewise, the osteogenesis of ADDM is influenced by the size and form of graft materials. The ideal sizes of graft material granules are different from author to author, ranging from 75 μm to 500 μm **(Bhaskar *et al*., 1971; Hosny *et al*., 1985)**.

Some authors reduced the inter-particulate distances by adding β-TCP due to difficulties in homogenizing the sizes. Since ADDM contains native growth factors supporting mesenchymal cell attachment and further absorbs several proteins derived from body fluid, however, some authors state that homogenizing the ADDM granule size is not critical **(Murata *et al*., 2011)**. The clinical effectiveness of ADDM was tested in pocket preservation. Wistar rat's incisors were frozen soon after extraction, and then milled with hydroxypropyl cellulose added. Consequently, early healing and bone formation in the extraction socket were observed when grafted with milled tooth. This study used the extracted tooth as a whole without decalcification, including both enamel and dental pulp. Therefore, the results indicate that osteoinductive healing may come from growth factors in dentin or dental pulp **(Miyata *et al*., 2011)**.

Another study was conducted on the human third molar socket wherein the greater homogeneity of bone radiopacity with enhanced healing process was observed **(Kim *et al*., 1999)**. Periods of radiographic observation focusing on the changes in radiopacity and in the peripheral boundary between graft material and bone and clinical observations confirmed that the graft was biocompatible and clinically easy to use. Another application of ADDM is on implant dentistry. In fact, ADDMs have been actively tested in implant osseointegration and bone remodeling capacity; thus enhancing implant primary stability **(Jeong *et al*., 2011)**.

Based on decades of research and scientific facts on tooth, some studies suggested that AutoBT is an excellent alternative to autogenous bone graft **(Jeong *et al*., 2011; Kim *et al*., 2011)**.

AutoBT was developed and has been in clinical use since 2008. With the patient's consent, the extracted teeth are sent to Tooth Bank in 75% ethyl alcohol storage container. preparation of extracted teeth for storage is shown in **(Figure 5)**. After dissection of the anatomical crown, sample root portions

are ground into powder form, with each particle measuring 400-800 μm in diameter. The remaining soft tissues and contaminants of the particulate AutoBT are removed with distilled water. Once subjected to dehydration, defatting, lyophilization, and ethylene oxide sterilization processes, AutoBT is packed. A block form of AutoBT is fabricated in the same manner as particulate bone graft excluding the grinding steps as seen in **(Figure 6) (Kim et al., 2013)**.

Fig. 5 Preparation of extracted teeth for storage A. Tooth after extraction B. Dental fragments after elimination of carious or discolored dentine, periodontal ligament and dental plaque. C. Fragments in the dentin crushing chamber **(Kim *et al*., 2013).**

Fig. 6 Extracted teeth are ready to be fabricated into autogenous tooth bone graft (AutoBT) in either powder form or block form. A. AutoBT powder. B. AutoBT crown and root powder C. AutoBT block form **(Kim et al., 2013).**

1.5 Clinical application of tooth derived bone graft

1.5.1 Guided bone regeneration

Implant placement and severe periodontitis probably develop bone dehiscence and bone fenestrations over time. In order to avoid this, guided bone regeneration (GBR) using bone graft in the peri-implant areas are becoming popular these days. A study evaluated the use of autogenous DDM

in growing bone by guided bone regeneration. They achieved 46 to 74% new bone formation in 3 to 6 months **(Kim *et al*., 2010)**. Another study said that histologically, autogenous DDM shows resorption initially and eventually shows new bone formation by osteoinduction and osteoconduction when subjected to guided bone **(Kim et al., 2011)**.

1.5.2 Maxillary sinus bone graft

Pneumatization is a process by which the floor of the maxillary sinuses descend downward in edentulous maxillary arches. This might complicate the placement of implants at a later date. In order to push the floor of the sinuses upward, surgeries called ‘sinus lift' surgeries are performed. Lee et al conducted a study to compare the efficiency of autogenous DDM and other bone graft materials used in sinus bone graft surgeries, after a 4 months healing period, all the groups showed favorable bone formation, but autogenous DDM showed a faster rate and superior quality bone formation. **(Lee *et al*., 2011; Janjua *et al*., 2022)**.

1.5.3 Socket preservation

The residual alveolar bone gets resorbed very rapidly immediately after teeth extraction. This causes difficulty in the seating of prosthesis at a later date or might also be esthetically unpleasant **(DSouza, 2012)**. Hence, alveolar bone preservation after teeth extraction is a common practice these days. Gomes et al conducted a human study in 2006 using autogenous DDM. Twenty-seven lower third molar sockets were selected. The experimental sockets were filled with autogenous DDM and were covered with PTFE membrane. After 90 days, the experimental sockets showed bone formation of the same radiopacity as the surrounding bone. Also, these sockets had shown a faster rate of bone formation as compared to the other groups (control group with no material in the socket and the third group with PTFE in the sockets). It was also proven that the experimental socket had a superior bony architecture. **(Gomes *et al*., 2006)**.

Kim used autogenous tooth bone powder and block in a socket immediately after tooth extraction. They reported good healing of the socket after 3 to 3.5 months which was then taken up for implant placement as seen in **(Figure 7) (Kim *et al*., 2013)**.

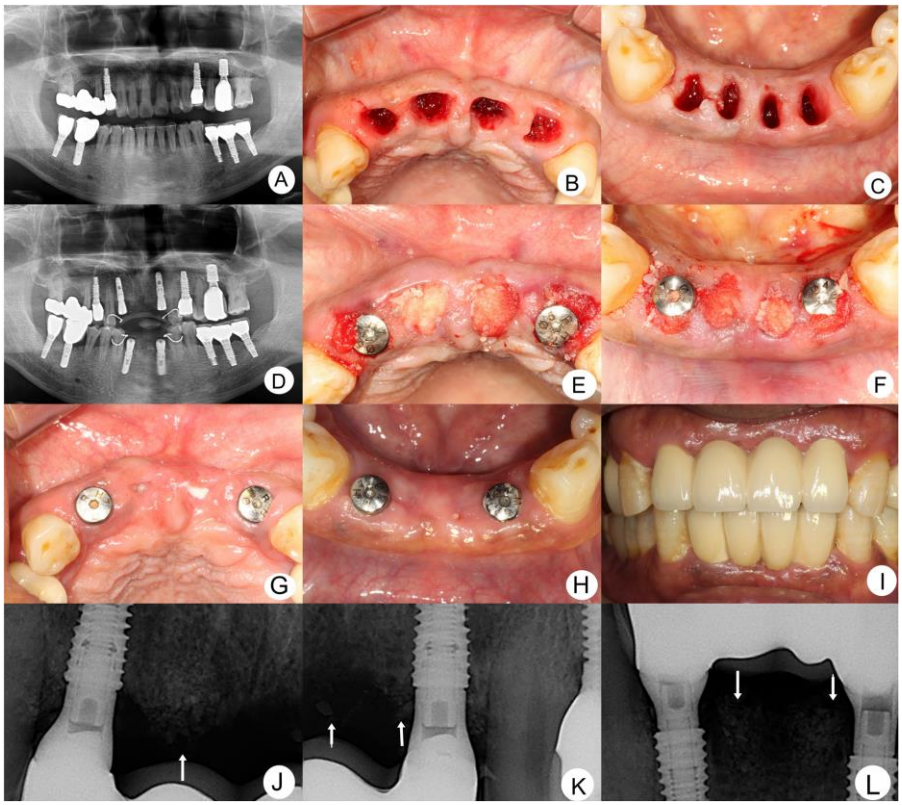

Fig. 7. Socket preservation using tooth derived bone graft. a Horizontal and vertical alveolar bone resorption were observed on upper and lower anterior teeth in panoramic view. b Extracted upper incisors sites. c Extracted lower incisors sites. d Implant installation on lateral incisors and socket preservation on extraction sites in immediate post-operative panoramic view. e Extraction sockets on #11, 21 and labial sides of implant fixation on #12, 22 were filled with powder Auto-FDT and Colla tape. f Extraction sockets on #31, 41 and labial sides of implant fixation on #32, 42 were filled with powder Auto-FDT and Colla tape. g,h Epithelial closure of socket preservation sites was achieved at 2 weeks after socket preservation. I. At 5 months after socket preservation, 4-unit fixed bridges were placed. Intro-oral photo: The final restorations were delivered. j-l Periapical x-ray views: At six months after final prosthesis placement, regenerated bone appeared to support the implant well. (white arrow: maintenance of the triangular bony structure on the mesial site of the implants) **(Kim *et al*., 2015).**

1.5.4 Ridge augmentation

This is a process of increasing the height or width of alveolar bone in cases of bony deficiency. Bone grafts are added vertically or horizontally on the upper parts or laterally on the residual alveolar ridges respectively. **Kim et al. (2011)** reported case of ridge augmentation where he used autogenous DDM as shown in **(Figure 9)**. The results were pretty acceptable. **Nilsson *et al*. (2007)** said that an appropriate carrier is needed for the BMPs and growth factors to be incorporated as bone grafts while, others opined that DDM by itself can play the role of a carrier of exogenous BMP and growth factors as well as have osteoinductive effect as seen in **(Figure 8) (Murata *et al*., 2012)**.

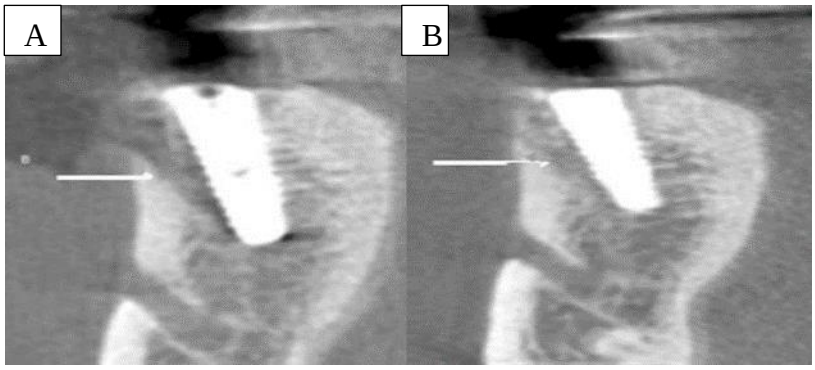

Fig. 8. After 6 months, computed tomography (CT) scan around buccal wall defect (arrow) showed more radio-opacity than the initial implantation with auto-tooth bone grafting. A. Initial CT view. B. CT view after 6 months. **(Um *et al*., 2020).**

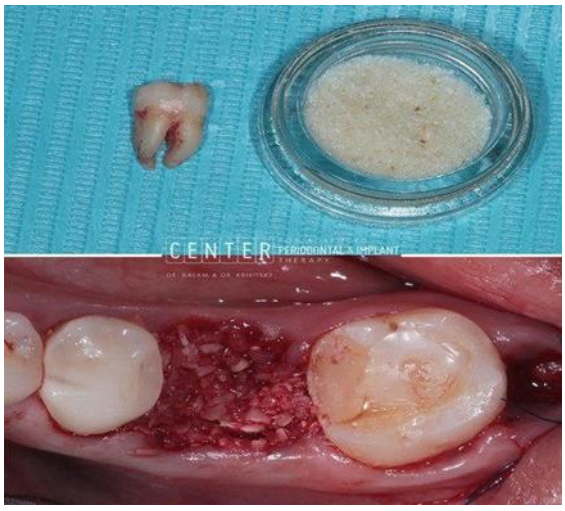

Fig. 9. Extraction socket preservation using autogenous tooth bone graft material**.**

(Advanced Periodontal & Implant Therapy, 2020)

1.6 Biocompatibility

Traditionally, roots were intentionally left for the prevention of alveolar bone resorption in removable prosthodontics or in cases of tooth extractions **(Gongloff *et al*., 1986; Fareed *et al*., 1989)**. Intentional partial odontectomy has been safely practiced when roots of impacted third molar are situated close to the inferior alveolar nerve or ankylosed since only a crown portion is dissected, leaving the roots behind **(Freedman *et al*., 1992)**. The root remnant of non-pathology involved tooth in alveolar bone does not induce any inflammatory response. Osteoclast cells appear in the pulp cavity, with the pulp replaced by bone, followed by root resorption. After all, the remaining roots completely fuse with the surrounding alveolar bone. Based on these clinical reports, alveolar bone and teeth can be inferred to have high level of affinity to each other **(Tsukamoto-Tanaka H et al., 2006; Hasegawa *et al*., 2007)**. Homogenous demineralized dentin matrix (HDDM) is as an effective biocompatible bone graft material as autogenous demineralized dentin matrix (ADDM) since it induces heterotopic bone formation with no host immune rejection **(Bang *et al*., 1967; Yeomans *et al*., 1967)**.

The demineralization process of HDDM does not denature osteopromotive properties. HDDM is a reservoir of biochemical factors that induce cellular proliferation as well as cell differentiation and chemotaxis **(Carvalho *et al*., 2004; Gomes *et al*., 2007).** In the histomorphometric analysis of HDDM in vitro, HDDM resorbs itself during the bone remodeling process **(Carvalho *et al*. 2004).**

Gomes further evaluated the bone repair process after implantation of HDDM slices in surgical defects created in the parietal bones of rabbits with

alloxan-induced diabetes. They reported that HDDM was biocompatible, stimulating bone tissue formation. In this study, HDDM is well accepted by the host and is totally incorporated into newly formed bone tissue **(Gomes *et al*., 2007)**.

1.6.1 Evidence of osteoinductivity from autogenous tooth

The prospect of inducing new bone formation of dentin has been described in many previous studies. The presence of 90% of organic matrix in the form of Collagen type I and other non-collagenous proteins as growth factors like endogenous BMP, phosphoproteins, osteocalcin, proteoglycans, osteonectin and sialoprotein in dentin is well documented **(McKee *et al*., 1996; Bessho K *et al*., 1998 and Feng *et al*., 1998)**.

The first documented evidence of regenerative potential of autogenous demineralized dentin matrix (DDM) was provided by the study of Yeomans and Urist and according to the study of Urist, BMP in DDM and bone possesses the osteoinductive property **(Yeomans *et al*., 1989)**

The study of Bessho purified BMP was homogenous and could induce bone formation when implanted in muscle pouch of wistar rats within 3 weeks. Even though the BMP derived from dentin was different to BMP from bone, the mode of action of both is identical **(Bessho *et al*., 1998).**

In other words, two types of BMP exhibit the same action in the body **(Bessho K *et al*., 1998 and Kawai *et al*., 1989; Nakashima M *et al*., 1994)**. Since BMP belongs to the family of TGF-β and are the only signaling molecules that can solely induce de novo bone formation at orthotopic and heterotopic sites, making them clinically valuable as substitutes to bone graft **(Bessho K *et al*., 1998 and Xiao *et al*., 2007)**.

LIM mineralization protein 1 (LMP-1) was first defined by the study of Boden et al, which regulates differentiation and maturation of osteoblasts and hence bone formation **(Boden *et al*., 1998)**. Later the previous study of Wang et al. identified the expression of LMP-1 mainly in predentin, odontoblasts

and the endothelial cells of blood vessels of teeth with suggestion that LMP-1 plays an important role in differentiation of odontoblast and also mineralization of dentin matrix of human teeth **(Wang *et al*., 2008)**.

The osteoinductive property of autogenous demineralized dentin matrix (ADDM) on experimental surgical bone defects in the parietal bone of rabbits using the guided bone regeneration (GBR) technique incorporating human amniotic membrane (HAM) was evaluated in the study of Gomes et al. The experimental bone defect repaired faster, and new bone formation was stimulated in groups that used ADDM slices. The ADDM slices were entirely integrated into the newly formed bone tissue, having been resorbed during the bone remodeling process **(Gomes *et al*., 2001)**. DDM granules derived from human impacted tooth by the study of Murata independently induced bone and cartilage formation in subcutaneous tissues of nude mice, showing property of bone induction **(Murata et al., 2010)**.

The previous study by Kim Kyung-Wook in 2014 showed when DDM was grafted into the muscle of nude mouse (subcutaneously) and evaluated for hard tissue induction histo-morphologically, that induced cartilage and bone independently in soft tissues Hence human DDM could be good alternative to autogenous bone graft materials **(Kim, 2014)**.

1.6.2 osteoconductivity of autogenous tooth

Besides the property of osteoinduction, BMP present in the ADDM also could act as matrix or framework for new and native bone to perpetuate and regenerate, thereby showing osteoconductivity property **(Um IW et al., 2016)**. Previous studies have investigated the osteopromotive property of ADDM. The protein substrate that exists in ADDM was found to be free from degradation and helped in socket repair **(Gomes *et al*., 2001, Catanzaro Guimarães *et al*., 1986, Carvalho *et al*., 2004)**.

Furthermore, Gomes et al. also observed an increase in the osteogenic cells after implantation of ADDM in wounds **(Gomes *et al*., 2001)**. Similarly, the

study of Carvalho 5 mm defect at buccal bone of mandibular molar area in 36 rabbits and dividing them into four groups as control group (untreated defect), polytetrafluoroethylene (PTFE) barrier group, PTFE + ADDM group and experimental group (ADDM). The experimental group had normal bone formation with less inflammation postoperatively and ADDM was completely incorporated in the newly formed bone tissue and was resorbed during bone remodeling **(Carvalho *et al*., 2004)**. The previous study of Nampo suggested that material prepared from extracted teeth may have the potential as bone grafting material for jawbone formation since it is more predictable and show less resorption **(Nampo et al., 2010)**.

Several proteins are common to bone, dentin and cementum such as OPN and DSP, BSP, osteocalcin, DMP-1, osterix and Runx2, and these are reportedly involved in bone formation and resorption **(McKee M et al., 1996; Bessho et al., 1991; Kawai et al., 1989)**.

It is commonly acknowledged that these NCPs play key biological roles in the formation of bone and dentin. Apart from these, the previous article of de Oliveira et al. immunostaining of BMP-2 and BMP-4 in osteoblasts during the upper second molar sockets wound healing of Holtzmann rats when filled with human DDM showed DDM acting as a scaffold for osteoblast differentiation and actively producing new bone. The effects of human DDM in the healing process of tooth sockets were, in some part, owed to matrix degradation, resulting from controlled delivery of BMP-2 and BMP-4 since the immuno-reactivity of both proteins were increased in extraction sockets at 10 days when almost entire DDM was degraded **(de Oliveira et al 2013)**.

The animal model from cranium of mini pig and sinus of porcine showed excellent osteo- conductive healing capacity of human DDM when placed in bony defects, which could be attributed to minerals present in DDM, such as low-crystallinity HA and TCP **(Kim JY *et al*., 2012; Lee DH**

***et al*., 2013)**. A study conducted in New Zealand rabbit calvarium with 3 circular defects, the CT- scans after one and six weeks of defects filled the dentin had a higher mineral (density) content showing a higher density than the autologous bone and incorporated in the bone without inflammation and gradually resorbed and replaced by new bone **(Hussain *et al*., 2013)**. Similar result was seen in bony defect (5 mm) in femur of New Zealand White rabbits, when autogenous dentin treated with liquid nitrogen at −196 °C for 20 min was used **(Atiya *et al*., 2014)**.

Clinical procedure

Tooth extraction: Local anaesthesia (2% lidocaine) followed by atraumatic extraction of the tooth using Periotomes, and careful curettage of the socket to remove any granulation tissue **(El-Said *et al*., 2017).**

Graft preparation: any restorations, caries, cementum, periodontal ligament and pulp tissue were removed. 0.3 mm holes were made along the entire tooth surface using 330 bur. The tooth should be grinded for 3 to 10 seconds using Pulverize grinder (Laymax grinder China) as seen in **(Figure 10) (El-Said *et al*., 2017)**

Other available grinders use disposable grinding chamber and stock pre-packed defatting and sterilization chemicals which require refill our technique proves to be more cost effective. Smart dentine grinder® combine grinding and sieving process together to save time but it produces calcified autogenous dentine graft as it lacks demineralization phase essential to expose the organic dentine matrix and growth factors to stimulate bone formation which will result in longer bone healing time **(Binderman *et al*., 2014).**

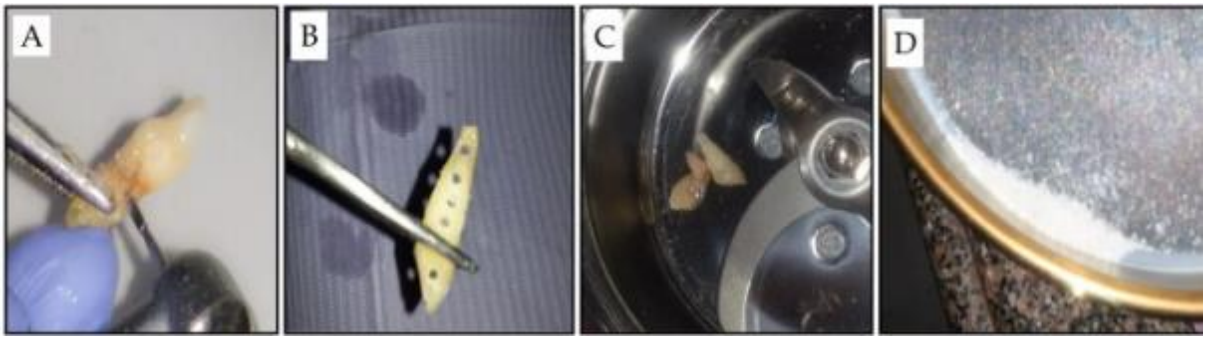

Fig. 10: Cleaning and preparation of extracted teeth (A) Removal of decay and cementum of upper left central incisor. (B) Under mining upper left central incisor using 330 bur.(C) Grinding of upper left & right central incisors. (D) Sieving of tooth particles **(El-Said *et al*., 2017)**

Tooth particles should be sieved (Gilson stainless steel wire sieve made in U.S.A) to particles size 300 to 1200 microns. The sorted particles were immersed in 70 % ethanol (El-Gomhouria CO. Egypt) and 5% Peracetic acid (El-Gomhouria CO. Egypt) in a sterile container for 10 minutes to remove any soft tissue remnants, bacteria and smear layer (defatting and sterilization). The use of Peracetic acid inhibits the bacterial growth in the autogenus fresh demineralize tooth graft due to the its strong oxidizing action which will oxidize the outer cell membranes of microorganisms **(Williams and Wilkins, 2001)**. The oxidation mechanism will denature proteins, disrupt cell wall permeability, and oxidize sulfhydral and sulfur bonds in proteins, enzymes, and other metabolites causing rapid deactivation of microorganisms. In the presence of organic matter peracetic acid will inactivate gram-positive and gram-negative bacteria, fungi, and yeasts **(Middleton *et al*., 1997)**.

Tooth particles were demineralized using 2% HNO3 (El-Gomhouria CO. Egypt) for 20 minutes to expose the dentine organic matrix. The bacteria-free particulate dentin was washed with phosphate buffered saline (El-Gomhouria CO. Egypt) twice for 5 minutes to restore the pH balance to 7.4. In the same setting, chips of autogenous demineralized dentine graft were used to reconstruct the ridge defects as shown in **(Figure 11) (El-Said *et al*.,**

2017)

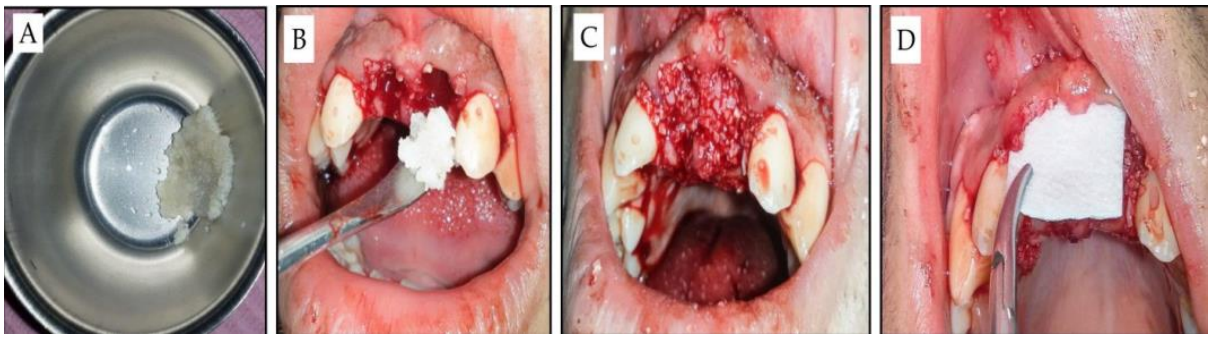

Fig. 11: Clinical procedure of grafting with tooth derived bone graft (A) The tooth derived graft is ready to use. (b) Grafting the extraction site. (C) Extraction site after grafting. (D) Resorbable collagen membrane application **(El-Said *et al*., 2017).**

Resorbable collagen Membrane (Dentium collagen membrane, Korea) with slow resorption rate over six months period, size 15 x 20 mm. and 0.3 mm thickness, was used to cover the graft site and it was fixed in place using absorbable Coated polyglactin Suture (VICRYL® Ethicon, Inc USA) **(Proussaefs *et al*., 2003)**.

Releasing incision was made to allow wound edges approximation and it was closed with 000 silk Non absorbable sutures.

Implant placement: Two pieces, titanium implants (Dentium super line implants Korea.) are placed after 3 months. Elevation of a full thickness mucoperiosteal flap allow full exposer of the graft site duo to the sensitivity of bone sample collection technique and the risk of undermining the buccal plate of bone during the procedure as seen in (Figure 6) **(El-Said *et al*., 2017)**

Dentium bone trephine with inner diameter of 2.3 mm and outer diameter of 3 mm used to perform initial osteotomy and collect a bone sample from graft site. Final drill of 3.2 mm. used to reach the desired implant length of 12 mm and allow the 3.6 mm implant to achieve high primary stability from both the lateral walls and the apical part of the osteotomy. Implants are placed to reach the alveolar bone level **(Cacaci *et al*., 2016).**

Resonance frequency analysis device (OSSTELL) used at the time of

implant placement to determine the primary stability as seen in **(Figure 12)** Immediate nonfunctional loading protocol can be used to restore patient's esthetics, photonics and allow better soft tissue healing around provisional restoration to create natural emergence profile for the final restorations **(El-Said *et al*., 2017)**.

The final restorations are loaded 3 months after implant placement in the form of screw retained porcelain fused to metal crowns to facilitate the follow-up procedures **(Eyckmans *et al*., 2010)**

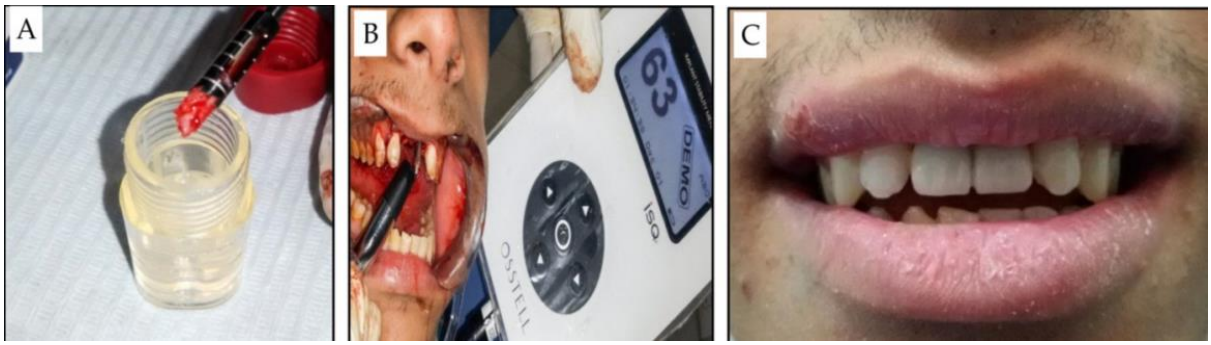

Fig. 12: Implant placement and specimen collection (A) Preserving bone specimen for histological analysis. (B) Recording osstell reading. (C) Provisional restoration **(El-Said *et al*., 2017).**

Comparison between different types of bone graft is shown in **(Table 1)**

Table 1: Comparison between different types of bone graft

Type	source	Advantages	Disadvantages
Tooth derived bone graft	patient	Biocompatible Osteoinductive Osteoconductive Used in alveolar ridge augmentation, tooth socket preservation and sinus lifts	Limited indications availability Different preparation protocols
Autografts	Patient	True osteogenic living cells Growth factors Osteoinduction Osteoconductive No disease transmission	Pain Infection Complex surgery Limited supply
Allografts	Other human	Osteoinduction Osteoconductive	Risk of disease transmission
Xenografts	Other species (Mostly bovine)	HA: Similar to human volume stability Collagen:Accelerates bone formation	Osteoconductive only
Alloplast	synthetic	No risk of disease transformation	Osteoconductive only
	Hydroxyapatite	Resorbs slowly (Preserves volune) Good growth factor carrier	
	TCP	Resorbs quickly (replaced by new bone	
	Biolglass	Bioactive (Accelerates bone formation) Resorbs quickly (replaced by bone)	

Chapter two: Discussion

The use of extracted teeth, which is considered as biomedical waste and hence disposed, unlocks the simple and readily available bone substitution material. The different and various preparation methods of extracted tooth provide their potential use as bone substitutes. The demineralized dentin matrix is exceedingly biocompatible with the property of both osteoinductive and osteoconductive. Currently, there are various bone graft materials; in particular, auto tooth bone graft material has been studied aggressively as a material to overcome the disadvantages of allograft, xenograft, and synthetic graft without losing bone regeneration capacity like autogenous bone. Auto tooth bone graft material does not have genetic and infectious risks; it is as strong as other graft materials, providing good bone generation through osteoinduction and osteoconduction as well as excellent initial bone remodeling capacity **(Wongsirichat and Natthamet, 2018)**.

Kim et al have conducted large number of studies and was successful in finding out that autogenous demineralized dentin matrix can be used for alveolar ridge augmentation, tooth socket preservation and sinus lifts. Gomes et al had pointed out that autogenous DDM had osteoconductive properties, and produce radiopaque bone. **(Gomes et al., 2006; Gomes et al., 2002)**. Lastly, an amazing work by Jiang et al have showed that autogenous DDM may prosper in the future endodontic world as an apexification material and as a permanent root canal filling material as well **(Jiang et al., 2003)**. Autogenous DDM was further suggested to be an ideal scaffold for stem cells and bone growth factors, and endodontic and tooth restorative material **(Kim et al., 2013)**. Therefore, autogenous tooth could be recycled as the innovative biomaterial **(Murata M et al., 2015)** Quick in forming bone (6–8 weeks) as compared to the conventional bone graft, this material is a boon to the dental world in this era **(Nampo *et al*., 2010)**.

Many previous studies suggested the need for a faster way of transforming extracted in to ready to use bone grafting materials. Hence the recent publications are more focused on chairside tooth preparation that could be employed in a clinical setting. The particle size efficient as the use for tooth derived bone grafting is also currently been discussed and pioneering research work of many previous researchers have shown that size ranging from 300 to 1200 µm is ideal for new bone formation **(Itzhak *et al*., 2018; Minamizato *et al*., 2018)**. However, the presence of variety of different sizes in dentistry is because diversity of human oral cavity, where some sizes could be suitable for some maxillary defects might not be appropriate for mandible and vice versa **(Klüppel *et al*., 2014)**. Another drawbacks when using tooth derived bone grafts is its availability, limited indications and as mentioned earlier issues associated to preparation **(Minamizato et al., 2018)**.

Chapter three: Conclusion and Suggestions

3.1 Conclusion

1. Tooth derives bone graft has high affinity to soft tissue and osteogenic activity on an extracted socket, periodontal defect and sinus graft without infection.

2. Autogenous tooth bone graft can induce rigid bone regeneration on a sinus graft and periodontal augmentation.

3. Successful bone formation around immediate temporalization can be achieved and autogenous tooth bone graft is a suitable bone substitute for digital bone graft.

4. Drawbacks when using tooth derived bone grafts is its availability, limited indications and some issues associated to preparation like particle size of the produced graft.

3.2 Suggestions

1. More research is needed to standardize the preparation technique for tooth derived bone graft to achieve the best prognosis.

2. More clinical studies are needed to evaluate the effectiveness of this graft in different sites of implant placement.

References

(A)

Anderson HC. (2003). Matrix vesicles and calcification. Curr Rheumatol Rep, 5, 222–226.

Atiya BK, Shanmuhasuntharam P, Huat S, Abdulrazzak S, Ha O. Liquid nitrogentreated autogenous dentin as bone substitute: an experimental study in a rabbitmodel. Int J Oral Maxillofac Implants 2014;29(2): e165±70.

(B)

Bang G, Urist MR. Bone induction in excavation chambers in matrix of decalcified dentin. Arch Surg 1967; 94:781-9.

Bang G. Induction of heterotopic bone formation by demineralized dentin in guinea pigs: antigenicity of the dentin matrix. J Oral Pathol 1972; 1:172-85.

Bang G. Induction of heterotopic bone formation by demineralized dentin: an experimental model in guinea pigs. Scand J Dent Res 1973; 81:240-50.

Bessho K, Tagawa T, Murata M. Comparison of bone matrix-derived bone morphogenetic proteins from various animals. J Oral Maxillofac Surg 1992; 50:496-501.

Bessho K, Tagawa T, Murata M. Purification of rabbit bone morphogenetic protein derived from bone, dentin, and wound tissue after tooth extraction. J Oral Maxillofac Surg 1990; 48:162-9

Bessho K, Tanaka N, Matsumoto J, Tagawa T, Murata M. Human dentin matrix derived bone morphogenetic protein. J Dent Res 1991;70(3):171±5.

Bhaskar SN, Cutright DE, Knapp MJ, Beasley JD, Perez B, Driskell TD. Tissue reaction to intrabony ceramic implants. Oral Surg Oral Med Oral Pathol 1971; 31:282-9.

Bhattacharjya C, Gadicherla S, Taranath Kamath A, Smriti K, Pentapati K. Tooth derived bone graft material. World J Dent 2016;7(1):32±5.

Bishop RC, Moore KA, Hadley MN. (1996). Anterior cervical interbody fusion using autogeneic and allogeneic bone graft substrate: a prospective comparative analysis. J Neurosurg, 85,206–210.

Blair HC, Athanasou NA. (2004). Recent advances in osteoclast biology and pathological bone resorption. Histol Histopathol ,19, 189 –199.

Boden SD, Liu Y, Hair GA, Helms JA, Hu D, Racine M, et al. LMP-1, a LIM-domain protein, mediates BMP-6 effects on bone formation. Endocrinology 1998;139(12):5125±34.

Boden SD, Schimandle JH, Hutton WC. (1995). An experimental intertransverse process spinal fusion model. Radiographic, histologic, and biomechanical healing characteristics. Spine ,20, 412–420.

Booth PW, Ward-Booth P, Eppley B, Schmelzeisen R. Maxillofacial trauma and esthetic facial reconstruction. Edinburgh: Churchill Livingstone; July 11, 2003:132±143chap 8.

Boyle WJ, Simonet WS, Lacey DL. (2003). Osteoclast differentiation and activation. Nature. 423, 337–342.

Burger EH, Klein-Nuland J, Smit TH. (2003). Strain-derived canalicular fluid flow regulates osteoclast activity in a remodeling osteon: A proposal. J Biomech, 36, 1452–1459.

Burr DB. (2002). Targeted and nontargeted remodeling. Bone 30, 2– 4.

Butler WT, Mikulski A, Urist MR, Bridges G, Uyeno S. Noncolla-genous proteins of a rat dentin matrix possessing bone morphogenetic activity. J Dent Res 1977; 56:228-32.

(C)

Carvalho VA, Tosello Dde O, Salgado MA, Gomes MF. Histomorphometric analysis of homogenous demineralized dentin matrix as osteopromotive material in rabbit mandibles. Int J Oral Maxillofac Implants 2004; 19:679-86.

Carvalho VAP, Tosello DO, de Castillo Salgado MA, Gomes MF. Histomorphometric analysis of homogenous demineralized dentin matrix as osteopromotive material in rabbit mandibles. Int J Oral Maxillofac Implants 2004;19(5):679±86.

Catanzaro Guimarães SA, Catanzaro BPN, Garcia GRB, Alle N. Osteogenic potential of autogenic demineralized dentin implanted in bony defects in dogs. Int J Oral Maxillofac Surg 1986;15(2):160±9.

Chae YP, Lee JH, Kim SK, Yeo HH. A histologic study on the repair of rat calvarial critical size defect with bovine bone morphogenetic protein (bBMP). J Korean Assoc Oral Maxillofacial Surg 1997; 23:290-303.

Choi YS, Lee JY, Suh JS, Lee G, Chung CP, Park YJ. The mineralization inducing peptide derived from dentin sialophosphoprotein for bone regeneration. J Biomed Mater Res A 2013;101(2):590±8.

Chung PH. Tooth protein extracted from extracted tooth and method for using the same. Korea intellectual property rights information service. Patent. Application No. 10-2004-0 051812.

Clarke, B., 2008. Normal Bone Anatomy and Physiology. Clinical Journal of the American Society of Nephrology, 3(Supplement 3), pp. S131-S139.

Conover MA, Urist MR. Dentin matrix morphogenetic protein. In: The chemistry and biology of mineralized connective tissues: Proceedings of the First International Conference on the Chemistry and Biology of Mineralized Connective Tissues. 3-7 May 1981, Northwestern University Dental School, Chicago, IL, USA. New York: Elsevier-North Holland Inc; 1981:597-606.

(D)

de Oliveira GS, Miziara 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(3):326±32.

Delaisse JM, Andersen TL, Engsig MT, Henriksen K, Troen T, Blavier L. (2003). Matrix metalloproteinases (MMP) and cathepsin K contribute differently to osteoclast activities. Microsc Res Tech,61,504 –513.

Dobnig H, Turner RT. (1995). Evidence that intermittent treatment with parathyroid hormone increases bone formation in adult rats by activation of bone lining cells. Endocrinology, 136, 3632–3638.

(E)

El-Said, M.M., Sharara, A.A., Melek, L.F. and Khalil, N.M., 2017. EVALUATION OF AUTOGENOUS FRESH DEMINERALIZED TOOTH GRAFT PREPARED AT CHAIRSIDE FOR DENTAL IMPLANT (CLINICAL AND HISTOLOGICAL STUDY). Alexandria Dental Journal, 42(1), pp.47-55

Eriksen EF. (1986). Normal and pathological remodeling of human trabecular bone: Three-dimensional reconstruction of the remodeling sequence in normals and metabolic bone disease. Endocr Rev, 7, 379 – 408.

(F)

Fareed K, Khayat R, Salins P. Vital root retention: a clinical procedure. J Prosthet Dent 1989; 62:430-4.

Feng JQ, Luan X, Wallace J, Jing D, Ohshima T, Kulkarni AB, et al. Genomic organization, chromosomal mapping, and promoter analysis of the mouse dentinsialophosphoprotein (Dspp) gene, which codes for both dentin sialoprotein and dentin phosphoprotein. J Biol Chem 1998;273(16):9457± 64.

Finkelman RD, Mohan S, Jennings JC, Taylor AK, Jepsen S, Baylink DJ.Quantitation of growth factors IGF-I, SGF/IGF-II, and TGF-beta in human dentin. JBone Miner Res 1990;5(7):717±23.

Freedman GL. Intentional partial odontectomy: report of case. J Oral Maxillofac Surg 1992; 50:419-21.

(G)

Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: An update. Injury. 2005;36(3): S20±S27.

Gomes MF, Abreu PP, Morosolli AR, Araújo MM, Goulart Md. Densitometric analysis of the autogenous demineralized dentin matrix on the dental socket wound healing process in humans. Braz Oral Res 2006; 20:324- 330.

Gomes MF, Banzi EC, Destro MF, Lavinicki V, Goulart MD. Homogenous demineralized dentin matrix for application in cranioplasty of rabbits with alloxan-induced diabetes: histomorphometric analysis. Int J Oral Maxillofac Implants 2007; 22:939-47

Gomes MF, Da Silva Dos Anjos MJ, de Oliveira Nogueira T, Guimarães SAC.Histologic evaluation of the osteoinductive property of autogenous demineralized dentin matrix on surgical bone defects in rabbit skulls using human

amniotic membrane for guided bone regeneration. Int J Oral Maxillofac Implants 2001;16(4):563±71.

Gomes MF, dos Anjos MJ, Nogueira Tde O, Catanzaro Guimarães SA. Autogenous demineralized dentin matrix for tissue engineering applications: radiographic and histomorphometric studies. Int J Oral Maxillofac Implants 2002; 17:488-497.

Gomes MF, dos Anjos MJ, Nogueira TO, Guimarães SA. Histologic evaluation of the osteoinductive property of autogenous demineralized dentin matrix on surgical bone defects in rabbit skulls using human amniotic membrane for guided bone regeneration. Int J Oral Maxillofac Implants 2001; 16:563-71.

(H)

Hanamura H, Higuchi Y, Nakagawa M, Iwata H, Nogami H, Urist MR. Solubilized bone morphogenetic protein (BMP) from mouse osteosarcoma and rat demineralized bone matrix. Clin Orthop Relat Res 1980;(148):281- 90.

Handschin AE, Egermann M, Trentz O, Wanner GA, Kock HJ, Zünd G, et al. Cbfa-1 (Runx-2) and osteocalcin expression by human osteoblasts in heparin osteoporosis in vitro. Clin Appl Thromb Hemost 2006; 12:465-72.

Hasegawa T, Suzuki H, Yoshie H, Ohshima H. Influence of extended operation time and of occlusal force on determination of pulpal healing pattern in replanted mouse molars. Cell Tissue Res 2007; 329:259-72.

Hauge EM, Qvesel D, Eriksen EF, Mosekilde L, Melsen F. (2001). Cancellous bone remodeling occurs in specialized compartments lined by cells expressing osteoblastic markers. J Bone Miner Res, 16, 1575–1582.

Heppner LH, Secreto F, Jensen ED, Li X, Kahler RA, Westendorf JJ. Runx2 and bone morphogenetic protein 2 regulate the expression of an alternative Lef1 transcript during osteoblast maturation. J Cell Physiol 2009; 221:480-9.

Hosny M, Sharawy M. Osteoinduction in young and old rats using demineralized bone powder allografts. J Oral Maxillofac Surg1985;43:925- 31.

Huggins CB, Urist MR. Dentin matrix transformation: rapid induction of alkaline phosphatase and cartilage. Science 1970; 167:896-8.

Hussain I, Moharamzadeh K, Brook IM, de Oliveira Neto PJ, Salata LA. Evaluation of osteoconductive and osteogenic potential of a dentin-based bone substitute using a calvarial defect model. Int J Dent 2012; 2012:396316.

(J)

Jiang Y, Sun M, Wu D. Clinical studies on apexification with demineralized dentin matrix. West China J Stomatol 2003; 21:460-462.

(K)

KALFAS, I., (2001). Principles of bone healing. Neurosurg. Focus, 10 (4), p.3.

Kao S, Scott S. A Review of Bone Substitutes. Oral and Maxillofacial Surgery Clinics. 2007;19(4):513±521.

Karfeld-Sulzer LS, Weber FE. Biomaterial development for oral and maxillofacial bone regeneration. J Korean Assoc Oral Maxillofac Surg 2012; 38:264-70.

Kawai T, Urist M. Bovine tooth-derived bone morphogenetic protein. J Dent Res 1989; 68:1069±74.

Kim BR, Lee JH, Kim JW. Comparison of bone inducing process of porcine bone matrix-derived bmp combined with the following, freeze-dried allogeneic bone,

surface demineralized allogeneic bone, and demineralized allogeneic bone powder in rats. J Korean Assoc Oral Maxillofac Surg 1998; 24:380-95.

Kim ES. Autogenous fresh demineralized tooth graft prepared at chairside for dental implant. Maxillofac Plast Reconstr Surg2015;37(1):8. x Kim GW, Yeo IS, Kim SG, Um IW, Kim YK. Analysis of crystalline structure of autogenous tooth bone graft material: X-Ray diffraction analysis. J Korean Assoc Oral Maxillofac Surg 2011; 37:225-8.

Kim JY, Kim KW, Um IW, Kim YK, Lee JK. Bone healing capacity of demineralized dentin matrix materials in a mini-pig cranium defect. J Korean Dent Sci 2012;5(1):21±8.

Kim KW. Bone induction by demineralized dentin matrix in nude mouse muscles. Maxillofac Plast Reconstr Surg 2014;36(2(March)):50±6.

Kim SG, Yeo HH, Kim YK. Grafting of large defects of the jaws with a particulate dentin-plaster of paris combination. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999; 88:22-5.

Kim YK, Kim SG, Byeon JH, Lee HJ, Um IU, Lim SC, et al. Development of a novel bone grafting material using autogenous teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109(4):496±503.

Kim YK, Kim SG, Yun PY, Yeo IS, Jin SC, Oh JS, et al. Autogenous teeth used for bone grafting: a comparison with traditional grafting materials. Oral Surg Oral Med Oral Pathol Oral Radiol 2014;117(1): e39±45.

Kim YK, Lee HJ, Kim KW, Kim SG, Um IW. Guided bone regeneration using autogenous teeth: case reports. J Korean Assoc Maxillofac Surg 2011; 37:142-147.

Kim YK, Lee J, Kim KW, Um IW, Murata M, Ito K. Analysis of organic components and osteoinductivity in autogenous tooth bone graft material. J Korean Oral Maxillofac Surg 2013;35(6):353±9. x Kim YK, Lee J, Um IW, et al. Tooth-derived bone graft material. J Korean Assoc Oral Maxillofac Surg 2013; 393:103-111.

Kim YK, Lee J, Um IW, Kim KW, Murata M, Akazawa T, et al. Tooth derived bone graft material. J Korean Assoc Oral Maxillofac Surg 2013;39(3):103 ±11.

Kim YK, Yi YJ. Horizontal ridge augmentation using ridge expansion and autogenous tooth bone graft: a case report. J Dent Rehabil Appl Sci 2011; 27:109-115.

Kim, Young-Kyun & Lee, Junho & Um, In-Woong & Kim, Kyung-Wook & Murata, Masaru & Akazawa, Toshiyuki & Mitsugi, Masaharu. (2013). Tooth-derived bone graft material. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 39. 103-111.

Kobayashi, S., Takahashi, HE., Ito, A., Saito, N., Nawata, M., Horiuchi, H., Ohta, H., Ito, A., Iorio, R., Yamamoto, N., Takaoka, K. (2003). Trabecular minimodeling in human iliac bone. Bone 32, 163–169.

(L)

Lee DH, Yang KY, Lee JK. Porcine study on the efficacy of autogenous tooth bone in the maxillary sinus. J Korean Assoc Oral Maxillofac Surg 2013;39(3):120±6.

Lee HJ. Quantitative analysis of proliferation and differentiation of MG-63 cell line on the bone grafting material using human tooth [PhD thesis]. Seoul: School of Dentistry, Seoul National University; 2011. Linde A. Dentin matrix proteins: composition and possible functions in calcification. Anat Rec 1989; 224:154-66.

Lindsay R, Cosman F, Zhou H, Bostrom M, Shen V, Cruz J, Nieves JW, Dempster DW. (2006). A novel tetracycline labeling schedule for longitudinal evaluation of the short-term effects of anabolic therapy with a single iliac crest biopsy: Early actions of teriparatide. J Bone Miner Res ,21, 366 –373.

Locklin RM, Oreffo RO, Triffitt JT. (1999). Effects of TGFbeta and bFGF on the differentiation of human bone marrow stromal fibroblasts. Cell Biol Int ,23, 185–194.

(M)

Maki F, Murata M, Kitajo H, Sato D, Taira H, Arisue M. Bone healing in large mandibular defects without periosteum in adult rabbits: a new application of collagenous sponge for bone regeneration. J Hard Tissue Biol 2000; 9:56-62.

Martin TJ, Sims NA. (2005). Osteoclast-derived activity in the coupling of bone formation to resorption. Trends Mol Med ,11,76 – 81.

McKee M, Zalzal S, Nanci A. Extracellular matrix in tooth cementum and mantle dentin: localization of osteopontin and other noncollagenous proteins, plasma proteins, and glycoconjugates by electron microscopy. Anat Record 1996;245(2):293±312.

Miller, R. J., Korn, R., & Miller, R. J. (2019). Use of the Straumann® AlloGraft Ring with Simultaneous Implant Placement: A Novel Approach. *Compendium*, *38*.

Misch CE, Dietsh F. Bone grafting materials in implant dentistry. Implant Dentistry. 1993;2(3):205.

Miyata Y, Ozawa S, Kojima N, Kondo Y, Matuskawa R, Tanaka Y. An experimental study of bone grafting using rat milled tooth. Int J Oral Maxillofac

Implants 2011; 26:1210-6. x Murata M, Akazawa T, Mitsugi M, et al. Autograft of Dentin Materials for Bone Regeneration.

Murata M, Akazawa T, Mitsugi M, Um IW, Kim KW, Kim YK. Human dentin as novel biomaterial for bone regeneration. In: Pignatello R, ed. Biomaterials-physics and chemistry. Croatia: InTech; 2011:127-40.

Murata M, Kawai T, Kawakami T, Akazawa T, Tazaki J, Ito K, et al. Human acid-insoluble dentin with BMP-2 accelerates boneinduction in subcutaneous and intramuscular tissues. J Ceram Soc Jpn 2010; 118:438-41. x Murata M, Sato D, Hino J, Akazawa T, Tazaki J, Ito K, Arisue M. Acid insoluble human dentin as carrier material for recombinant human BMP-2. J Biomed Mater Res A 2012; 100:571-577.

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.

(N)

Nakashima M. Induction of dentin formation on canine amputated pulp by recombinant human bone morphogenetic proteins (BMP)-2 and-4. J Dent Res1994;73(9):1515±22.

Nampo T, Watahiki J, Enomoto A, et al. A new method for alveolar bone repair using extracted teeth for the graft material. J Periodontol 2010; 81:1264-1272.

Nampo T, Watahiki J, Enomoto A, Taguchi T, Ono M, Nakano H, et al. A new method for alveolar bone repair using extracted teeth for the graft material. J Periodontol 2010;81(9):1264±72.

Nazirkar G, Singh S, Dole V, Nikam A. Effortless Effort in Bone Regeneration: A Review. J Int Oral Health. 2014;6(3):120±124.

Nilsson, Ola, et al. "Gradients in bone morphogenetic protein-related gene expression across the growth plate." Journal of Endocrinology 193.1 (2007): 75-84.

(O)

Oh DW, Lee SH, Shin HI. Histologic evaluation of the ectopic bone formation induced by partially purified BMP-fibrous glass membrane complex. J Korean Assoc Oral Maxillofac Surg 1996; 22:86-100.

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.

(P)

Pandit N, Pandit I. Autogenous bone grafts in periodontal practice: a literature review. J Int Clin Dent Res Org 2016;8(1):27.

Parfitt AM. (2002). Targeted and nontargeted bone remodeling: Relationship to basic multicellular unit origination and progression. Bone 30, 5–7.

Parfitt AM. (2003). Osteonal and hemiosteonal remodeling: The spatial and temporal framework for signal traffic in adult bone. J Cell Biochem, 55, 273–276.

Park SM, Um IW, Kim YK, Kim KW. Clinical application of auto-tooth bone graft material. J Korean Assoc Oral Maxillofac Surg 2012;38(1):2±8.

Priya A, Nath S, Biswas K, Basu B. In vitro dissolution of calcium phosphate-mullite composite in simulated body fluid. J Mater Sci Mater Med 2010;21(6):1817±28.

Prolo DJ. (1990). Biology of bone fusion. Clin Neurosurg ,36, 135–146.

Proussaefs, P., & Lozada, J. (2003). The use of resorbable collagen membrane in conjunction with autogenous bone graft and inorganic bovine mineral for buccal/labial alveolar ridge augmentation: a pilot study. The Journal of prosthetic dentistry, 90(6), 530–538.

(Q)

Qin C, Brunn JC, Jones J, George A, Ramachandran A, Gorski JP, et al. A comparative study of sialic acidǴrich proteins in rat bone and dentin. Eur J Oral Sci 2001;109(2):133±41.

(R)

Reddi AH, Anderson WA. Collagenous bone matrix-induced endochondral ossification hemopoiesis. J Cell Biol 1976; 69:557-72

Reddy SV. (2004). Regulatory mechanisms operative in osteoclasts. Crit Rev Eukaryot Gene Expr, 14, 255–270.

Riebel ED, Boden SD, Whitesides TE. (1995). The effect of nicotine on incorporation of cancellous bone graft in an animal model. Spine ,20,2198–2202.

Ritchie HH, Ritchie DG, Wang LH. Six decades of dentinogenesis research. Historical and prospective views on phosphophoryn and dentin sialoprotein. Eur J Oral Sci 1998;106(Suppl 1):211-20.

Ritchie HH, Ritchie DG, Wang LH. Six decades of dentinogenesis research. Historical and prospective views on phosphophoryn and dentin sialoprotein. Eur J Oral Sci 1998;106(Suppl 1):211-20.

Ritchie HH, Ritchie DG, Wang LH. Six decades of dentinogenesis research. Eur J Oral Sci 1998;106(S1):211±20.

Rocha LB, Goissis G, Rossi MA. Biocompatibility of anionic collagen matrix as scaffold for bone healing. Biomaterials 2002; 23:449-56.

Roodman GD. (1999). Cell biology of the osteoclast. Exp Hematol ,27, 1229 – 1241.

Rosa FP, Lia RC, de Souza KO, Goissis G, Marcantonio E Jr. Tissue response to polyanionic collagen: elastin matrices implanted in rat calvaria. Biomaterials 2003; 24:207-12.

Rosa FP, Lia RC, de Souza KO, Goissis G, Marcantonio E Jr. Tissue response to polyanionic collagen: elastin matrices implanted in rat calvaria. Biomaterials 2003; 24:207-12.

Ryu SY, Park SI, Kim SH. Effects of demineralized dentin matrix on osseointegration of implants in dogs. J Korean Assoc Oral Maxillofac Surg 1996; 22:15-27.

(S)

Saima S, Jan S, Shah A, Yousuf A, Batra M. Bone Grafts and Bone Substitutes in Dentistry. Journal of Oral Research & Review. 2016;8(1):36± 38.

Sampath TK, Reddi AH. Homology of bone-inductive proteins from human, monkey, bovine, and rat extracellular matrix. Proc Natl Acad Sci U S A 1983; 80:6591-5.

Schmidt-Schultz TH, Schultz M. Intact growth factors are conserved in the extra-cellular matrix of ancient human bone and teeth: a storehouse for the study of human evolution in health and disease. Biol Chem 2005;386(8):767±76.

Seth J, Aeran H, Sharma A. Bone Augmentation Materials: A Literature Review. Journal of Dentofacial Sciences. 2013;2(3):1±6.

Shah A, Saima S, Jan S, Yousuf A, Batra M. Bone grafts and bone substitutes in dentistry. J Oral Res Rev 2016;8(1):36.

Shapoff CA, Bowers GM, Levy B, Mellonig JT, Yukna RA. The effect of particle size on the osteogenic activity of composite grafts of allogeneic freeze-dried bone and autogenous marrow. J Periodontol 1980; 51:625-30.

Silver IA, Murrills RJ, Etherington DJ.(1988). Microelectrode studies on the acid microenvironment beneath adherent macrophages and osteoclasts. Exp Cell Res, 175, 266 –276.

Smit TH, Burger EH, Huyghe JM. (2002). A case for strain-induced fluid flow as a regulator of BMU-coupling and osteonal alignment. J Bone Miner Res, 17, 2021–2029.

Smit TH, Burger EH, Huyghe JM. (2002). Is BMU-coupling a strain-regulated phenomenon? A finite element analysis. J Bone Miner Res ,15, 301–307.

(T)

Takamori Y, Suzuki H, Nakakura-Ohshima K, Cai J, Cho SW, Jung HS, et al. Capacity of dental pulp differentiation in mouse molars as demonstrated by allogenic tooth transplantation. J Histochem Cytochem 2008; 56:1075-86.

Tazaki J, Murata M, Yusa T, Akazawa T, Ito K, Hino J, et al. Autograft of human tooth and demineralized dentin matrices for bone augmentation. J Ceram Soc Jpn 2010; 118:442-5.

Teitelbaum SL, Ross FP. (2003). Genetic regulation of osteoclast development and function. Nat Rev Genet, 4, 638 – 649.

Ting M, Rice JG, Braid SM, Lee CYS, Suzuki JB. Maxillary Sinus Augmentation for Dental Implant Rehabilitation of the Edentulous Ridge: A Comprehensive Overview of Systematic Reviews. Implant Dent. 2017 Jun;26(3):438-464.

Tjäderhane L, Carrilho MR, Breschi L, Tay FR, Pashley DH. Dentin basic structure and composition-an overview. Endodontic Topics 2009;20(1):3± 29.

Tsukamoto-Tanaka H, Ikegame M, Takagi R, Harada H, Ohshima H. Histochemical and immunocytochemical study of hard tissue formation in dental pulp during the healing process in rat molars after tooth replantation. Cell Tissue Res 2006; 325:219-29.

(U)

Ubara, Y., Fushimi, T., Tagami, T., Sawa, N., Hoshino, J., Yokota, M., Kaitori, H., Takemoto, F., Hara, S. (2003). Histomorphometric features of bone in patients with primary and secondary hyperparathyroidism. Kidney Int ,63, 1809 –1816.

Ubara, Y., Tagami, T., Nakanishi, S., Sawa, N., Hoshino, J., Suwabe, T., Kaitori, H., Takemoto, F., Hara, S., Takaichi, K. (2005). Significance of minimodeling in dialysis patients with adynamic bone disease. Kidney Int ,68, 833– 839.

Um IW, Hwang SH, Kim YK, Kim MY, Jun SH, Ryu JJ, et al. Demineralized dentin matrix combined with recombinant human bone morphogenetic protein-2 in rabbit calvarial defects. J Korean Assoc Oral Maxillofac Surg 2016;42(2):90±8.

Um IW, Kim YK, Mitsugi M. Demineralized dentin matrix scaffolds for alveolar boneengineering. J Indian Prosthodont Soc 2017;17(2):120±7.

Urist MR, DeLange RJ, Finerman GA. Bone cell differentiation and growth factors. Science 1983; 220:6806.

Urist MR, Dowell TA, Hay PH, Strates BS. Inductive substrates for bone formation. Clin Orthop Relat Res 1968; 59:59-96.

Urist MR, Strates BS. Bone morphogenetic protein. J Dent Res1971; 50:1392-406.

Urist MR. Bone histogenesis and morphogenesis in implants of demineralized enamel and dentin. J Oral Surg 1971; 29:88-102.

Urist MR. Bone: formation by autoinduction. Science 1965; 150:893-9.

(W)

Wang X, Zhang Q, Chen Z, Zhang L. Immunohistochemical localization of LIM mineralization protein 1 in pulp-dentin complex of human teeth with normal and pathologic conditions. J Endod 2008;34(2):143±7.

(X)

Xiao YT, Xiang LX, Shao JZ. Bone morphogenetic protein. Biochem Biophys ResCommun 2007;362(3):550±3.

(Y)

Ye L, MacDougall M, Zhang S, Xie Y, Zhang J, Li Z, et al. Deletion of dentin matrix protein-1 leads to a partial failure of maturation of predentin into dentin, hypomineralization, and expanded cavities of pulp and root canal during postnatal tooth development. J Biol Chem 2004; 279:19141-8.

Yeomans JD, Urist MR. Bone induction by decalcified dentine implanted into oral, osseous and muscle tissues. Arch Oral Biol 1967; 12:999-1008.