SPECIAL ISSUE

https://doi.org/10.5125/jkaoms.2019.45.2.51
pISSN 2234-7550 · eISSN 2234-5930

Dental alloplastic bone substitutes currently available in Korea

Jeong-Kui Ku[1,2], Inseok Hong[3], Bu-Kyu Lee[1], Pil-Young Yun[2], Jeong Keun Lee[4]

[1]*Department of Oral and Maxillofacial Surgery, Asan Medical Center, Seoul,*
[2]*Department of Oral and Maxillofacial Surgery, Section of Dentistry, Armed Forces Capital Hospital, Seongnam,*
[3]*Department of Oral and Maxillofacial Surgery, School of Dentistry and Institute of Oral Bioscience, Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, Chonbuk National University, Jeonju,*
[4]*Department of Oral and Maxillofacial Surgery, Institute of Oral Health Science, Ajou University School of Medicine, Suwon, Korea*

Abstract (J Korean Assoc Oral Maxillofac Surg 2019;45:51-67)

As dental implant surgery and bone grafts were widely operated in Korean dentist, many bone substitutes are commercially available, currently. For commercially used in Korea, all bone substitutes are firstly evaluated by the Ministry of Health and Welfare (MOHW) for safety and efficacy of the product. After being priced, classified, and registration by the Health Insurance Review and Assessment Service (HIRA), the post-application management is obligatory for the manufacturer (or representative importer) to receive a certificate of Good Manufacturing Practice by Ministry of Food and Drug Safety. Currently, bone substitutes are broadly classified into C group (bone union and fracture fixation), T group (human tissue), L group (general and dental material) and non-insurance material group in MOHW notification No. 2018-248. Among them, bone substitutes classified as dental materials (L7) are divided as xenograft and alloplastic bone graft. The purpose of this paper is to analyze alloplastic bone substitutes of 37 products in MOHW notification No. 2018-248 and to evaluate the reference level based on the ISI Web of Knowledge, PubMed, EMBASE (1980-2019), Cochrane Database, and Google Scholar using the criteria of registered or trademarked product name.

Key words: Bone substitutes, Dental implantation, Korea

[paper submitted 2019. 3. 24 / revised 2019. 3. 28, / accepted 2019. 3. 28]

I. Introduction

As dental implant surgery for edentulous patients became a gold standard, bone grafts such as guided bone regeneration and sinus lift were widely operated in Korean dentist. There has been increased in the number of bone substitute products available to the dental clinician. Still the autologous bone is considered to gold standard, because of its three properties with osteoconduction, osteoinduction and osteogenesis. Osteogenesis is, the property of autogenous graft, generation of new bone from osteogenic cells within the graft. Osteoinduction is the property of the autogenous graft, allogenic graft and intrinsic bone matrix proteins such as transforming growth factor and bone morphogenetic proteins (BMP) to recruit of host stem cells. Osteoconduction is the property of a mechanical structure with biocompatibility for the migration of osteogenetic cells[1,2].

Allograft has been widely used and is an attractive alternative as it avoids donor site morbidity. It has the following advantage: (1) donor site is not needed, (2) abundant supply, and (3) little risk of transmission of infectious diseases[3]. The ideal alloplastic bone substitutes is biologically stable and maintain its volume with allowing cell infiltration and remodeling process[4]. The alloplastic bone substitutes has various osteoconductive capabilities depending on the manufacturing methods, crystal structure, size of pores, mechanical properties, composition and absorption rate[5].

Hydroxyapatite (HA) is the main mineralized of bone tissue and it exerts an osteoconductive ability when grafted in the defect. Synthetic calcium phosphate ceramics (β-tricalcium

Jeong Keun Lee
Department of Oral and Maxillofacial Surgery, Institute of Oral Health Science, Ajou University School of Medicine, 164 WorldCup-ro, Yeongtong-gu, Suwon 16499, Korea
TEL: +82-31-219-5333 FAX: +82-31-219-5329
E-mail: arcady@ajou.ac.kr
ORCID: https://orcid.org/0000-0002-5561-6297

phosphate [β-TCP] and HA) could be altered to autogenous graft, allogenic graft and xenogenic graft and it was used as block, cement, pastes, powder, granules and putty type with carboxymethyl cellulose or hyaluronic acid[6]. In Korea, the development of implant dentistry has led to the development of many dental synthetic bone substitute in many domestic companies.

As dental implant surgery for edentulous patients became a gold standard, bone grafts such as guided bone regeneration and sinus lift were widely operated in Korean dentist. All bone substitutes used commercially in Korea are firstly evaluated by the Ministry of Health and Welfare (MOHW) for safety and efficacy of the product. They are commercialized after being priced, classified, and registration by the Health Insurance Review and Assessment Service (HIRA). The post-application management is obligatory for the manufacturer (or representative importer) to receive a certificate of Good Manufacturing Practice (GMP) by Ministry of Food and Drug Safety (MFDS).

According to Korea Food and Drug Safety (KFDS) No. 2016-156 of 'medical device manufacturing and quality control standards', after the approval of commercially use, the manufacturer or importer is required to renew the conformity certification every three years or immediately if the information of product changed[7]. If any information of the product changed, the certificate of conformity should be issued or reissued by the manufacturer or the importer. Therefore, the manufacturer or importer of registered in the MFDS could be important factors in terms of quality control of currently available bone substitutes.

However, it is difficult for clinicians to know whether the certification or the quality of product is properly managed. Therefore, the purpose of this study is to analyze ingredients, manufacturers, importers, current status and reference levels of dental synthetic bone listed in MOHW notification No. 2018-248.

II. Materials and Methods

Commercially available dental alloplastic bone substitute which was approved MOHW notification (No. 2018-248)[8] is analyzed the details of manufacturer, importer, composition, available form, Food and Drug Administration (FDA, USA) approval.

This review of literature included studies that detailed the use of bone graft substitute in dental situation, animal, *in vivo*, and *in vitro* studies. We excluded studies in the orthopedic and neurosurgery field and those not published in English or Korean. The Google Scholar, ISI Web of Knowledge, PubMed, EMBASE (1980-2019) and Cochrane Databases were searched in February 2019 using the criteria of registered or trademarked product name. The authors read the full text of the studies and classified it according to the 'level of evidence' presented by Wright et al.[9].(Table 1)

Human study level I evidence is a prospective, randomized, or splint-mouth study with definite results that support the use of alloplastic bone substitute in clinical condition. The case report was classified as level IV. Clinicial studies used alloplastic bone substitute as carrier of osteoinductive growth factors or as comparison of membrane efficacy have not been evaluated for osteoconductive capacity, but have been assigned to human study level IV as showing clinical stability. The animal, *in vivo*, and *in vivo* study were separately indicated. All authors reviewed each paper and independently assigned evidence levels. If there is a disagreement on the assigned level, discussion and resolution were made. All studied with human study level I, II, III, or IV were included to be citation[10].

III. Results

In December 2018, thirty-seven dental alloplastic substi-

Table 1. Level of evidence for research questions[9]

Type	Level	Description
Published human studies	I	Randomized controlled trial (RCT) Split-mouth study
	II	Prospective cohort[1] Systematic review with level II studies Poor-quality RCT (e.g., <80% follow-up)
	III	Case-control study[2] Retrospective cohort study[3] Systematic review with under level III studies
	IV	Case series or case report no/or historical, control group and poor designed human studies
Animal studies		
In vivo studies (cell culture)		
In vitro studies		

[1]Patients were compared with a control group of patients treated at the same time and same institution.
[2]Patients with a particular outcome ('cases') were compared with those who did not have the outcome ('controls').
[3]The study was initiated after treatment was performed.
Jeong-Kui Ku et al: Dental alloplastic bone substitutes currently available in Korea. J Korean Assoc Oral Maxillofac Surg 2019

tutes were registered in MOHW and HIRA[8]. However, there were two products (BIO-C [Cowellmedi, Busan, Korea] and OssPol-Dental [Genewel, Seongnam, Korea]) that were not commercially available and one product of DualPor COLLAGEN D-INJECTION (OssGen, Daegu, Korea) that was discontinued in the market. Of the remaining 34 alloplastic substitutes, 28 products (82.4%) could be obtained information and included in this review. To approve certificate of GMP from MOHW and MFDS, the company should submit the researches for safety and efficacy of its product, as same procedure as U.S. FDA.(Table 2) The researches, however, were not published and the authors could not include in this review. The available information regarding the delivery form, component, indications, morphology (porosity, biomechanical structure, particle size), and property are shown in Tables 3 to 8.

1. The products approved in FDA

Seven products were approved in FDA[11-17].(Table 2) Although TCP Dental (Kasios SAS, L'Union, France) was not licensed for dental indication in intended use of FDA[17]. However, the authors included TCP Dental in this category because manufacturer did not distinguish between KASIOS TCP and (KASIOS) TCP Dental.

2. Registered in MOHW and commercially available information for product name, manufacturer, importer, and component

The details of dental alloplastic bone substitute which was approved by MOHW notification No. 2018-248 were analyzed[8].(Table 3) Among them, BIO-C and OssPol-dental were officially discontinued. CollaOss (SK Bioland, Cheonan,

Table 2. Dental bone graft substitutes which Food and Drug Administration (FDA) 510(k) approved

Product name	Approved date (mo/day/yr)	Indications with FDA 510(k) approved
Cerasorb M granules	7/22/2005	Alveolar augmentation Filling of defects after root resection, apicoectomy, and cystectomy Filling of extraction sockets Elevation of the maxillary sinus floor Filling of periodontal/perio-implant defects for GTR and GBR
MBCP	12/11/2003	Bone void filler for bony voids or gaps of the skeletal system Used with autograft as a bone graft extender Osseous defects and/or from traumatic injury to the bone. Without initial mechanical properties. Therefore, rigid fixation techniques may often be recommended. Gradually resorbs and is replaced with bone.
MBCP Plus, MBCP+	7/30/2007	Periodontal/infrabony defects Ridge augmentation Extraction site (for implant) Sinus graft and cyst defect
OSTEON	7/8/2010	Periodontal/infrabony defects Ridge augmentation Extraction site (for implant) Sinus lifts Cystic cavities
OSTEON II	12/26/2011	Periodontal/infrabony defects Ridge augmentation Extraction site (implant preparation/placement) Sinus lifts Cystic cavities
OSTEON III	9/14/2016	Periodontal/infrabony defects Ridge augmentation Extraction site (implant preparation/placement) Sinus lifts Cystic cavities
TCP Dental	11/10/2004	Cystic cavities Packed into bony voids or gaps of the skeletal system (such as the extremities, spine and the pelvis). Osseous defects and/or from traumatic injury to the bone. Resorbs and is replaced with bone during the healing process. -Approved for KASIOS TCP not (KASIOS) TCP Dental

(GTR: guided tissue regeneration, GBR: guided bone regeneration)

Table 3. Dental bone graft substitutes with manufactures, importer, components and inconsistency with registered in Korean Ministry of Health and Welfare and Korean Health Insurance Review and Assessment Service

Product name	Manufacturer	Nationality	Importer name	Registered components	Remarks
OSSABASE-HA	LASAK	Czech	Mono Dent	HA	OSSABASE-HA → OssaBase-HA
OVIS BONE HA	DENTIS	Korea	DENTIS	HA	OVIS BONE HA → Ovis BONE HA
COLLAOSS (BLOCK), OOSSBONE COLLAGEN	SK Bioland	Korea	SK Bioland	HA (90%±5%)+ collagen (10%±5%)	COLLAOSS (BLOCK), OSSBONE COLLAGEN → CollaOss (BLOCK), OssBone collagen Role out xenograft
COLLAOSS (PUTTY)	SK Bioland	Korea	SK Bioland	HA (90%±5%)+ collagen (10%±5%)	COLLAOSS (PUTTY) → CollaOss (PUTTY) Role out xenograft
COLLAOSS (SYRINGE)	SK Bioland	Korea	SK Bioland	HA (90%±5%)+ collagen (10%±5%)	COLLAOSS (SYRINGE) → CollaOss (SYRINGE) Only block and putty type of CollaOss
DUALPOR COLLAGEN D-PUTTY	OssGen	Korea	OssGen	HA (60%)+bovine atelo collagen (0.3%)+ distilled water (39.7%)	DUALPOR COLLAGEN D-PUTTY → DualPor Collagen D-Putty HA (60%)+β-TCP (40%)+bovine collagen
DUALPOR COLLAGEN D-INJECTION	OssGen	Korea	OssGen	HA (60%)+bovine atelo collagen (0.3%)+ distilled water (39.7%)	DUALPOR COLLAGEN D-INJECTION → DualPor Collagen Injection NA
BONESIGMA TCP	SigmaGraft	USA	KodentTMS	β-TCP 100%	BONESIGMA TCP → BoneSigma TCP
EXCELOS INJECT	BioAlpha	Korea	BioAlpha	β-TCP etc.	EXCELOS INJECT → Excelos INJECT BioAlpha → CGbio
EXCELOS (TCPGLD)	BioAlpha	Korea	BioAlpha	β-TCP 100%	EXCELOS (TCPGLD) → Excelos (TCPGLD) BioAlpha → CGbio
EXCELOS (TCPGMD, TCPGLD)	BioAlpha	Korea	BioAlpha	β-TCP 100%	EXCELOS (TCPGMD, TCPGLD) → Excelos (TCPGMD, TCPGLD) BioAlpha → CGbio
MEGA-TCP (CGL)	CGbio	Korea	CGbio	β-TCP 100%	MEGA-TCP (CGL) → Mega-TCP CG bio → MegaGen
Mega-TCP (CGM, CGL)	CGbio	Korea	CGbio	β-TCP 100%	MEGA-TCP (CGM, CGL) → Mega-TCP NA
SORBONE	META-BIOMED	Korea	META-BIOMED	β-TCP 100%	SORBONE → Sorbone
SYNCERA	Oscotec	Korea	Oscotec	β-TCP	SYNCERA → Syncera
CERASORB	Curasan	Germany	B.ITRADING	β-TCP	Cerasorb → Cerasorb M
BIO-C	Cowellmedi	Korea	Cowellmedi	β-TCP+HA	NA
BONCELOS	BioAlpha	Korea	BioAlpha	β-TCP+HA	BONCELOS → Boncel-Os BioAlpha → CGbio
BONESIGMA BCP	SigmaGraft	USA	KODENT TMS	β-TCP (40%)+HA (60%)	BONESIGMA BCP → BoneSigma BCP
CERASORB M GRANULES	Curasan	Germany	Mono Dent	β-TCP+HA	CERASORB M GRANULES → Cerasorb M HA+β-TCP → 99% β-TCP

Table 3. Continued

Product name	Manufacturer	Nationality	Importer name	Registered components	Remarks
FRABONE DENTAL	Inobone	Korea	Inobone	β-TCP (40%±5%)+ HA (60%±5%)	FRABONE DENTAL → FRABONE
FRABONE DENTAL INJECT	Inobone	Korea	Inobone	β-TCP+HA	FRABONE DENTAL INJECT → FRABONE-Inject Hyaluronic acid addition
GENESIS-BCP	DIO	Korea	DIO	β-TCP (40%)+HA (60%)	N/S
MBCP	Biometlante	France	Purgo Biologics	β-TCP+HA	N/S
MBCP PLUS	Biometlante	France	Purgo Biologics	β-TCP+HA	MBCP PLUS → MBCP or/with syringe type
NEW BONE	GENOSS	Korea	GENOSS	β-TCP+HA	NEW BONE → Newbone
OSSPOL DENTAL	Genewel	Korea	Genewel	β-TCP (40%)+HA (60%)	OSSPOL DENTAL → OssPol
OSTEON	GENOSS	Korea	GENOSS	HA (β-TCP)	NA
OSTEON II	GENOSS	Korea	GENOSS	β-TCP+HA	N/S
OSTEON III	GENOSS	Korea	GENOSS	β-TCP+HA	N/S
OSTEON III COLLAGEN	GENOSS	Korea	GENOSS	β-TCP+porcine collagen (95%)	N/S
OSTEON SINUS	GENOSS	Korea	GENOSS	HA (β-TCP)	Only syringe type of OSTEON I, II, and III
OVIS BONE HA	DENTIS	Korea	DENTIS	β-TCP+HA	OVIS BONE HA → Ovis BONE HA
TCP Dental	Kasios SAS	France	B.IMTECH	β-TCP (95%)+HA (5%)	β-TCP (95%)+HA (5%) → β-TCP (99.9%)
Q-OSS+	OSSTEM IMPLANT	Korea	OSSTEM IMPLANT	β-TCP (80%±5%)+ HA (20%±5%)	N/S
TOPGEN-S	Toplan	Korea	Toplan	β-TCP (80%±5%)+ HA (20%±5%)	N/S
INNO CAP	Cowellmedi	Korea	Cowellmedi	Calcium phosphate (100%)	INNO CAP → INNO-CaP

(HA: hydroxyapatite, β-TCP: β-tricalcium phosphate, NA: not available, N/S: nothing special)

Jeong-Kui Ku et al: Dental alloplastic bone substitutes currently available in Korea. J Korean Assoc Oral Maxillofac Surg 2019

Korea) is registered as 60% of HA, 0.3% of bovine-derived collagen (0.3%) and 39.7% of distilled water and as block, syringe and putty types. Currently, only bock and putty type are available in the manufacturer. DualPor COLLAGEN D-PUTTY and DualPor COLLAGEN D-INJECTION is available as DualPor Collagen D-Putty and DualPor Collagen Injection, but no any information could be found.

There are seven products that do not match the manufacturer or importer registered in MOHW: (1) MBCP+ (Biometlante, Vigneux-de-Bretagne, France; sold only as MBCP and MBCP syringe type, not MBCP+), (2) Excelos Inject (BioAlpha, Seongnam, Korea; produced by CGbio, Seongnam, Korea), (3) Excelos (TCPGLD) (BioAlpha; produced by CGbio, sold exclusively by Excelos), (4) Boncel-Os (BioAlpha; produced by CGbio), (5) Mega-TCP (manufactured by CGbio; MegaGen, Seoul, Korea, sold as a single product without discrimination between CGM and CGL), (6) Cerasorb and Cerasorb M granule (sold only by Curasan, Kleinostheim, Germany: Cerasorb M, registered as importer) BI Trading currently available is not available), and (7) OSTEON Sinus (GENOSS, Suwon, Korea: sold as syringe type of OSTEON I, II, or III).(Table 3)

CollaOss is listed as a dental synthetic bone in the MOHW and HIRA data. Although it was represented as xenograft in the journal[18-21]; however, it was included in this review.(Table 3)

There are three products that do not match in the component registered in MOHW: (1) Cerasorb M granules (99% β-TCP not β-TCP combined with HA; Curasan), (2) FRABONE-Inject (Inobone, Cheonan, Korea: hyaluronic acid addition with HA+β-TCP), and (3) TCP Dental (99% β-TCP not 95% β-TCP combined with 5% HA).(Table 3)

As a result, out of the 33 dental bone substitutes that are currently registered in MOHW and HIRA, 28 products could be commercially available when considering the products that are different form registered information as below: Excelos (TCPGLD) and Excelos (TCPGMD, TCPGLD) are sold exclusively by Excelos, Mega-TCP (CGL) and Mega-

TCP (CGM, CGL) are sold only by Mega-TCP, Cerasorb and Cerasorb M granules are sold by Cerasorb M, Cerasorb M is 99% β-TCP, FRABONE-Inject is sold by adding hyaluronic acid, CollaOss is sold in putty and block form without syringe type, DualPor COLLAGEN D-INJECTION is not produced, and TCP Dental (99% β-TCP).

3. Analysis of dental alloplastic bone substitutes according to constituents

The main components of dental alloplastic bone substitute are tricalcium phosphate ($Ca_3(PO_4)_2$, β-TCP), calcium phosphate (CaP), and hydroxiapatitie ($Ca_{10}(PO_4)_6(OH)_2$, HA) which is crystalline form of CaP.(Table 4)

1) Dental alloplastic bone substitutes consist of hydroxyapatite

HA is an inorganic material which account for 65% of bone matrix and can be classified as dense and porous, sintered ceramic and non-ceramic, and bovine, coralline and synthetic depending on the origin. Typical characteristics are as below. (1) As large as the particle size, it remains for a long time with slow absorption. (2) The higher the porosity, the easier the penetration of new bone and the quicker absorbed. (3) The larger the crystallinity, the longer the absorption period. (4) Rigid and dense block-form products have high compressive strength but are susceptible to fracture. (5) The higher the porosity, the lower the strength[5].

Among the dental alloplastic bone substitutes allowed for use in Korea, there were four products that consisted of HA. OssaBase-HA (LASAK, Praha, Czech) has a retrospective study of guided bone regeneration in 2018, but it was obtained human study level IV due to a poor study design[22]. However, many other animal, *in vivo*, and *in vitro* studies for osteoconductivity[23-26]. No journals were found for Ovis BONE HA (DENTIS, Seoul, Korea). CollaOss consists of 90% porcine-deriven HA and 10% porcine deriven collagen. It was classified as alloplastic graft in MOHW and HIRA, on the other hands, it was introduced as xenograft in many studies[18-21]. In the manufacturer (SK Bioland), it is commercially available in plug type and putty type. In comparison with the collagenated bovine bone (Bio-Oss collagen; Geistlich Biomaterials, Woulhusen, Switzerland) into the extraction socket, it was received the human study level III because there was no difference in the efficacy[18]. Human study level IV was received in a clinical study to comprare the effects of membranes on peri-implant defect[19]. Animal studies showed osteoconductivity[20,21].(Table 4)

Table 4. Commercially available dental alloplastic bone substitutes according to components

Commercially available dental alloplastic bone substitutes	Total (n=28)
Hydroxyapatite (HA)	4
β-Tricalcium phosphate (β-TCP)	8
β-TCP+HA	15
Calcium phosphate (CaP: composition not confirmed)	1

Jeong-Kui Ku et al: Dental alloplastic bone substitutes currently available in Korea. J Korean Assoc Oral Maxillofac Surg 2019

2) Dental alloplastic bone substitutes consist of tricalcium phosphate

TCP has a composition of calcium and phosphorus in ratio of 3 and 2. It was known as partially transition into HA and absorption *in vivo*, but various absorption periods of three to 24 months have been reported depending on the products. The rate of absorption varies according to the chemical structure, porosity and particle size of the material[5]. The general characteristics suggested by the manufacturer of TCP are as follows. (1) Use with platelet-rich plasma is effective. (2) It is absorbed at the same time as new bone graft. (3) Due to the interconnection of the pores, bone fibers are rapidly penetrated and could promote the regeneration. (4) Since the particle is rounded, there is little mechanical irrigation in surrounding tissues and little inflammatory reaction. (5) High mechanical stability prevents early collapse and inhibits undesirable macrophage activity.

Of the approved products for Korean dental alloplastic bone substitute, seven products that consist with TCP were commercialization. BoneSigma TCP (SigmaGraft, Fullerton, CA, USA) has been described as one of the *in vitro* studies[27], and clinically available products[28,29] but no clinical studies have been published. Excelos is registered as β-TCP etc. in MOHW and has two types of powder and injection and registered. Injection type is a mixture of biodegradable polymers such as poloxamer and hydroxypropyl methylcellulose (HPMC) to enhance injectable property, moldability and hemostasis. A clinical study comparing putty type Excelos with extraction and using as BMP carriers received a human study level IV[30]. Excelos has animal studies for BMP carrier[31,32] and *in vivo* study for osteoconduction[33]. No journals were found for Mega-TCP. Sorbone (META-BIOMED, Cheongju, Korea) was validated and received human study level II by a split-mouth study as a control of cockle-shell bone substitute in socket preservation[34], and used as a control material for the effect of alendronate on periodontal intra-osseous defect[35].

SynCera (Oscotec, Seongnam, Korea) had animal and *in vivo* study for osteoconductivity[36,37]. Cerasorb was approved by the FDA and commercially available to Cerasorb M which reduced porosity from 80% to 65%[11]. It was received human study level I by randomized controlled trial and systematic review that was equivalent to an autogenous graft in sinus lift[38,39]. It was received human study level III in cystic lesion, periodontal defect and cleft alveolus[40]. Also, as a result of histologically sufficient alveolar bone regeneration, human study level III was obtained in extraction socket[41]. As human study level IV, it was used with an enamel matrix derivative in the periodontal defect[42,43], peri-implant defect after immediately implantation after extraction[44], every lots of animal, *in vivo*, and *in vitro* studies for osteoconduction[6,45-56]. TCP Dental was registered as 5% of HA and 95% of β-TCP in MOHW and HIRA. However, the manufacturer (Kasios SAS) and importer (B.IMTECH, Yongin, Korea) advertised as 99% of β-TCP. Many studies and FDA 510(k) also represented as β-TCP[17,57-65]. It was received human study level III by successful histologic and clinical result comparing Xenograft (BonePlus-xs; Integros, Adana, Turkey) in sinus lift[57]. Animal, *in vivo*, and *in vitro* studies for osteoconductivity[58-65].

3) Dental alloplastic bone substitutes consist with hydroxyapatite and tricalcium phosphate

The mixing ratio of HA and TCP varies from 2:8 to 7:3. It has the following characteristics. (1) It has micropore and macropore. They could induce effective tissue reaction and growth of new bone tissue. Micropores could enable ion exchange and form new contact surfaces for cell adhesion through the deposition of bone crystals. Macropores could help in angiogenesis and remodeling and growth of new bone. (2) HA acts as a mechanical support until the new bone tissue could be remolded for structural stability, and TCP could spread the adhesion surface of osteoblast by ion exchange through rapid resorption. (3) It has porosity of 70% to 90%[5].

Boncel-Os (CGbio) consists with 30% of HA and 70% of β-TCP. It was introduced as one of the clinically available products[66], and there is an animal study used as a BMP carrier[56]. BoneSigma BCP (SigmaGraft) consists with 60% of HA and 40% of β-TCP. *In vivo* study has been published that

Table 5. Dental bone graft substitutes which was consisted with hydroxyapatite (HA)

Product name	Delivery	Component	Indication	Morphology	Property	Level of evidence
OssaBase-HA	Granule	HA:CaP (1.65), $Ca_{10}(Po_4)_6(OH)_2$	Remodeling of the alveolar ridge Treatment of periodontal defects Treatment of bone defects around dental implants Sinus lift Filling of bone defects after surgical extractions to prevent alveolar atrophy Filling of bone defects after extirpation of cysts	Macro-nano bone like structure 83% interconnected porosity Narrow size ranges of available granules Enough space for bone ingrowth over large distances	Volume maintenance Low substitution rate No risk of immunological reactions or pathogen transmission	Human study level (IV: GBR[22]) Animal, *in vivo*, *in vitro* studies
Ovis BONE HA	Granule	100% HA	Periodontal bone defect Intrabony defect Extraction site Ridge augmentation Sinus lift Cystic cavity	Well-formed macro/micro porous Porosity	Osteoconductivity Biocompatibility Non toxicity Non inflammatory nature Easy manipulation	NA
CollaOss (Block), Ossbone Collagen	Plug	HA 90%±5%+ collagen 10%±5%	Periodontal bone defect Intrabony defect	Well-formed macro/micro porous Porosity	Easy manipulation and adhesion due to collagen Slow absorption and partial remodeling	Human study (III: extraction socket[18], IV: peri-implant defect[19])
CollaOss (Putty)	Granule	HA 90%±5%+ collagen 10%±5%	Periodontal bone defect Intrabony defect	Well-formed macro/micro porous Porosity	Easy manipulation and adhesion due to collagen Slow absorption and partial remodeling	Animal study

(CaP: calcium phosphate, GBR: guided bone regeneration, NA: data not available)

Jeong-Kui Ku et al: Dental alloplastic bone substitutes currently available in Korea. J Korean Assoc Oral Maxillofac Surg 2019

Table 6. Dental bone graft substitutes which was consisted with β-tricalcium phosphate (β-TCP)

Product name	Delivery	Component	Indication	Morphology	Property	Level of evidence
BoneSigma TCP	Powder	β-TCP 100%	Extraction socket Horizontal and vertical augmentation Peri-implant defects Periodontal regeneration Ridge augmentation Sinus floor elevation	>95% β-TCP Interconnected macro and micro porous structure	Osteoconductive High resorption rate: rapid osseointegration and recovery in dental implants	*In vitro* study
Excelos Inject	Injectable	β-TCP 100%	Sinus lift Guided bone regeneration Socket preservation	β-TCP particle (size: 45-75 μm) with hydrogel (poloxamer, hydroxypropyl methylcellulose [HPMC])	Hemostasis and injectable by poloxamer-based hydrogel High moldability Osteoconductive High resorption rate Space maintaining for new bone formation	Human study level (IV: extraction socket[30]) Animal studies (for BMP carrier), *in vivo, in vitro* studies
Excelos (TCPGLD)	Powder	β-TCP 100%	Sinus floor elevation Alveolar bone augmentation Extraction socket preservation	100% β-TCP Average 80% macro-porosity (pore size: 100-300 μm)	Osteoconductive Faster absorption and biodegrade rate Space maintaining for new bone formation	Animal, *in vitro* studies
MEGA-TCP (CGL)	Powder	β-TCP 100%	NA	Porous structure like human cancellous bone >99% interconnectivity Average 75% macro-porosity (pore size: 100-300 μm)	Biocompatibility Biodegradable	NA
Sorbone	Powder	β-TCP 100%	Extraction socket Cystic cavities Periodontal defects Intrabony defects Ridge augmentation Sinus floor elevation	Average 55%-60% macro-porosity	Osteoconductive High resorption rate Biocompatibility Easy handling	Human study (level II, socket preservation[34] and periodontal defect[35])
SynCera	Powder	β-TCP 100%	NA	Macro- and micro-porosity	Osteoinduction >70% new bone formation	Animal, *in vivo, in vitro* studies
Cerasorb M	Powder	β-TCP 99%	Augmentation or reconstructive treatment of alveolar ridge Infrabony periodontal defects Defects after root resection, apicoectomy, and cystectomy Extraction socket Sinus lift Guided tissue regeneration Guided bone regeneration Peri-implant defect	Micro-meso-macro pore (pore size 5-500 μm) about 65% porosity with full range of pore size and interconnected porosity	99% resorption Optimal microencironment for osteoblast adhesion proliferation and Subsequent bone remodeling	Human study level (I: sinus[38,39], III: cystic lesion, periodontal defect, cleft alveolus[40], extraction socket preservation[41], IV: peri-implant defect[44], periodontal defect with enamel matrix derivative [42,43]) Animal, *in vivo, in vitro* studies
TCP Dental	Granule	β-TCP 99%	Sinus graft Bone loss correction Filling alveoli Periodontology	Interconnected macro-porosity >90% porosity (pore size: 0.2-0.5 mm) Particle size: 0.15-2.0 mm	Osteoconductive Early resobable and angiogenesis	Human study (III: sinus graft[57]) Animal, *in vivo*, *in vitro* for osteoconduction

(BMP: bone morphogenetic proteins, NA: data not available)

Table 7. Dental bone graft substitutes which was composed with hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP)

Product name	Delivery	Component	Indication	Morphology	Property	Level of evidence
Boncel-Os	Granule	β-TCP (70%)+ HA (30%)	Ridge augmentation Extraction sockets Periodontal defect Sinus lift	High porosity Interconnected porous structure	High biocompatibility Osteoconduction Excellent wettability	Animal study
BoneSigma BCP	Granule	β-TCP (40%)+ HA (60%)	Ridge augmentation Extraction sockets Cystic cavities Sinus floor elevation Periodontal defects Peri-implant defects	Micro- and macro-porosity	Osteoconductive properties Long-term volume stability	*In vivo* study
DualPor COLLAGEN D-PUTTY	Block	β-TCP (40%)+ HA (60%)+ bovine collagen (5.5%)	NA	Trabecular like structure Interconntected macro- and micro-porosity 80% of porosity	Biocompatibility Bioabsorbable Easy handling and moldable Hemostasis and anti-adhesion effect	NA
FRABONE	Granule	β-TCP (40%)+ HA (60%)	NA	Haversian canal like structure (international patent: PCT/ KR2011/005509-USA and Germany), 150-300 μm macropore Average 8.1 μm micropore 0.7 mm size of porous particles	Biocompatibility Bioactive Osteoconductivity Osteoinductivity Mechanical strength Structural feature reserves stable room and filled up with vessels and new bone material, resulting in faster regeneration	NA
FRABONE -Inject	Injection	β-TCP (40%±5%)+ HA (60%±5%)+ coated with hyaluronic acid	NA	Haversian canal like structure (international patent: PCT/ KR2011/005509-USA and Germany),100-300 μm micropore 0.7 mm size of porous particles	Highly biocompatible and bioresorbable due to hyaluronic acid Osteoconductivity Osteoinductivity High mechanical strength Structural feature Moldability Injectability	NA
GENESIS-BCP	Granule	β-TCP (40%)+ HA (60%)	NA	70% of complete interconntected porosity 75% macropore (300-700 μm) 25% micropore (<10 μm)	High mechanical strength Highly biocompatible	Human studies (level II: periodontal defect[70], level IV: horizontal augmentation[71]) Animal, *in vivo, in vitro* studies for osteoconduction
MBCP Plus	Granule	β-TCP (80%)+ HA (20%)	Sinus lift augmentation Ridge augmentation Alveolar regeneration Alveolar regeneration Intra-osseous pockets	70% porosity with 35% microporosity 1/3 micropores (<10 μm) 2/3 macropores (300-600 μm)	Permeable Resorbable Hydrophilic Bioactive Osteoconductive Regeneration	Human study (level IV: extraction socket[84]) Animal, *in vivo, in vitro* for osteoconduction

Table 7. Continued

Product name	Delivery	Component	Indication	Morphology	Property	Level of evidence
NEW BONE	Granule	β-TCP (80%)+ HA (20%)	Ridge augmentation Extraction site and osteotomy Cystic cavities Sinus lift Periodontal defect	80% porosity (pore size: 200-400 μm) 0.2-2.0 mm size of porous particles	Osteoconductive synthetic bone graft Highly resorbable due to 80% β-TCP Easy manipulation	Animal study
OSTEON	Granule/ syringe	β-TCP (30%)+ HA (70%)	Periodontal/infrabony defects Ridge augmentation Extraction site (implant preparation/placement) Sinus lift Cystic cavities	HA coated with β-TCP Interconnected porous structure similar to that of human cancellous bone 77% porosity (pore size: 300-500 μm) Irregular shaped particles of size Particle size (granule): 0.3-2.0 mm Particle size (sinus, syringe): 0.5-2.0 mm Particle size (lifting, syringe): 0.3-1.0 mm	Osteoconductive	Human study (level III: sinus lift[94]) Animal, *in vivo, in vitro* for osteoconduction
OSTEON II	Granule/ syringe	β-TCP (70%)+ HA (30%)	Periodontal/infrabony defects Ridge augmentation Extraction site (implant preparation/placement) Sinus lift Cystic cavities	Interconnected porous structure similar to that of human cancellous bone >70% porosity (pore size: 250 μm) Irregular shaped particles of size Particle size (granule): 0.2-2.0 mm Particle size (sinus, syringe): 0.5-2.0 mm Particle size (lifting, syringe): 0.2-1.0 mm	Highly resorbable due to higher β-TCP content Easy manipulation Excellent wettability Osteoconductive	Human study (level III: extraction socket[99], level IV: sinus lift[100], vertical ridge augmentation[101], ridge augmentation[102,103], periodontal defect[105]) Animal, *in vivo* for osteoconduction
OSTEON III	Granule/ syringe	β-TCP (40%)+ HA (60%)	Periodontal/infrabony defects Ridge augmentation Extraction site (implant preparation/placement) Sinus lift Cystic cavities	Interconnected macro and micro porous structure <80% porosity Particle size (granule): 0.2-2.0 mm Particle size (sinus, syringe): 0.5-2.0 mm Particle size (lifting, syringe): 0.2-1.0 mm >70% crystallinity CaP=1.59	Biocompatible Osteoconductive	Animal study (BMP carries)
OSTEON III Collagen	Cylinder	β-TCP (40%)+ HA (60%)+ type I collagen (>95% porcine tendon collagen)	Alveolar bone defect	Particle size: 0.2-1.0 mm	Easy manipulation Excellent wettability	NA
Ovis BONE BCP	Granule	β-TCP (80%)+ HA (20%)	Periodontal bone defect Intrabony defect Extraction site Ridge augmentation Sinus lift Cystic cavitiy	70% porosity (pore size: 20 μm) Particle size: 0.3-2.0 mm	Osteoconductive Excellent wettability Easy manipulation Biocompatibility and great bioactivity	NA

Table 7. Continued

Product name	Delivery	Component	Indication	Morphology	Property	Level of evidence
Q-OSS+	Granule	β-TCP (80%)+ HA (20%)	NA	Porous structure	Excellent hydrophilicity Osteoconductive Biocompatibile Bioasorbable Rapid osteogenesis rate	Cell culture
TOPGEN-S	Granule	β-TCP (80%)+ HA (20%)	NA	Interconnected macro and microporous Particle size: 1.0-2.0 mm	Excellent hydrophilicity Osteoconductive	NA

(NA: data not available, CaP: calcium phosphate, BMP: bone morphogenetic proteins)
Jeong-Kui Ku et al: Dental alloplastic bone substitutes currently available in Korea. J Korean Assoc Oral Maxillofac Surg 2019

it inhibited osteoclast formation with plate-rich fibrin[67]. Dual-pore Collagen D-Putty was registered as 60% of HA, 0.3% of bovine-derived collagen, and 39.7% of distilled water by the MOHW and HIRA. On the other hand, the manufacturer (OssGen) advertised the product as 60% HA and 40% β-TCP in 94.5% of biphasic CaP, and with an additional 5.5% bovine collagen but there are no reports of any evaluations of the evaluating its information provided. In MOHW and MFDS, Inobone has registrated its products as FRABONE DENTAL and FRABONE DENTLA INJECT, but they are commercially available as FRABONE and FRABONE-Inject. FRABONE (Inobone) consists with 60% of HA and 40% of β-TCP and it was received patent in USA, Germany, and Korea as mimic the harversian canal structure[68,69]. FRABONE-Inject (Inobone) is a product of hyaluronic acid addition to FRABONE, which advertised to increase moldability and absorption rate by act as soluble granules of hyaluronic acid. However, there was no related researched were found. GENESIS-BCP (DIO, Busan, Korea) consists with 60% of HA and 40% of β-TCP. It was received human study level II by prospective controlled clinical trial which results good outcome in periodontal defect[70]. In horizontal augmentation, it was showed successful result with NanoBone (HA and silica gel matrix; Artoss GmbH, Warnemünde, Germany) in case report and it obtained human study level IV[71]. There were many animal, *in vivo*, and *in vitro* studies for osteoconductivity[72-77]. Manufacturers have the two types of MBCP as combination of HA and β-TCP as ratio as 60:40 and 20:80, and a moldable MBCP (In'Oss) made by mixing hydrogel to MBCP. However, represented importer (Purgo Biologics, Seongnam, Korea) only has granule or syringe type of MBCP+ which consists with 20% of HA and 80% of β-TCP. MBCP and MBCP+ were received in FDA 510(k) approved[12,16]. There were many clinical studies from MBCP which consists with 60% of HA and 40% of β-TCP[78-84]. On the other hand, MBCP+ was published only animal studies[85-88] and *in vitro* studies[89,90]. Although not introduced as MBCP+, a combination of 20% of HA and 80% of β-TCP was as same resorption and bone growth as combination of 60% of HA and 40% of β-TCP in retrospective clinical trial for extraction socket and it could be human study level IV[84]. Newbone (GENOSS) consists with 20% of HA and 80% of β-TCP. Although there were animal and *in vivo* studies for osteoinductivity[91-93], no clinical studies were found. Boncel-Os consists with 30% of HA and 70% of β-TCP. It was introduced as one of clinically available products[66] and used as BMP carrier in animal study[56].

OSTEON series (GENOSS) were available as vial, sinus,

Table 8. Dental bone graft substitutes which was consisted with calcium phosphate

Product name	Delivery	Component	Indication	Morphology	Property	Level of evidence
INNO-CaP	Granule	Calcium phosphate (100%)	Sinus lift Guided bone regeneration	0.41-1.4 mm of particle size	Completely resorpted and progressively replaced by normal-structured bone Biocompatibility Osteoconductivity Safety	NA

(NA: data not available)

Jeong-Kui Ku et al: Dental alloplastic bone substitutes currently available in Korea. J Korean Assoc Oral Maxillofac Surg 2019

and lift type. OSTEON, OSTEON II, and OSTEON III were received FDA 510(k) approval[13-15]. In registration of MOHW and HIRAO, OSTEON and OSTEON Sinus were separated but OSTEON Sinus is not available product to commercially use. The manufacture (GENOSS) has classified OSTEON Sinus and OSTEON Lifting according to the size of syringe. In FDA 510(k), there also received approval as same as OSTEON, OSTEON Sinus, and OSTEON Lifting[13]. OSTEON consists with 70% of HA and 30% of β-TCP. In retrospective clinical study for sinus lift, OSTEON alone could result well-developed lamellar bone as same as Xenograft (Bio-Oss; Osteohealth, Shirley, NY, USA) and it could be received human study level III[94]. There were many animal and *in vivo* studies for osteoconductivity[95-98]. OSTEON II consists with 30% of HA and 70% of β-TCP. In retrospective clinical study for extraction socket, OSTEON II and OSTEON II Collagen were significantly more effective than collagen or native defect and the histological result was shown in animal studies[99]. Therefore, it could be received human study level III in extraction socket. It was received human study level IV by retrospective study as control group for sinus lift[100], 6 months after vertical augmentation which particulated OSTEON II was showed no significantly difference on volume change and peri-implant marginal bone loss compared with autogenous block and allogenous block bone[101], successful results on clinical and histologically in ridge augmentation[102,103], successful outcome on graft after implant removal[104], and clinically effective on periodontal defect[105]. Many animal and *in vivo* studies for osteoconductivity[95-97,106,107]. OSTEON III consists with 60% of HA and 40% of β-TCP. There was animal study as BMP carrier[108]. Although there was no OSTEON III Collagen related study, OSTEON II Collagen had animal and *in vivo* studies for osteoconductivity[109,110]. Ovis BONE BCP (DENTIS) consists with 20% of HA and 80% of β-TCP. No journals were found for Ovis BONE BCP. Q-Oss+ (OSSTEM IMPLANT, Seoul, Korea) consists with 20% of HA and 80% of β-TCP. It was received human study level IV by the clinical study on peri-implant defect[111]. There were *in vivo* study for osteoconductivity[112] TOPGEN-S (Toplan, Seoul, Korea) consists 20% of HA and 80% of β-TCP and there could not be found for journals for TOPGEN-S.

4) Dental alloplastic bone substitutes consist with CaP (composition not confirmed)

INNO-CaP (Cowellmedi) was advertised that consists CaP, however, the composition was not cleary known and no relevant research were found.

IV. Discussion

Commercially available dental alloplastic bone substitute which was approved MOHW notification No. 2018-248 were broadly divided into 4 groups as C group (bone union and fixation group), L group (general materials), T group (human tissue), and non-insurance group. In the subcategory, there were C0 group (bone substitutes: xenograft, alloplastic graft), L7 group (dental material: dental xenograft, dental alloplastic graft), TB group (bone, demineralized bone matrix, bone block, bone chip, bone powder), non-insurance group (treatment material, human-derived bone, bone substitute containing bone morphogenetic protein [rhBMP-2])[8]. Among them, dental alloplastic bone substitutes in L7 of L group were included in this study.

The post-application management is obligatory for the manufacturer (or representative importer) to receive a certification of GMP by MFDS. According to FKDS No. 2016-156 of 'medical device manufacturing and quality control standards', the certification of GMP of human tissue or functional replacement product should be renewed every three years in article 9. According to article 10 of KFDS No. 2016-156, the certification of GMP should be reissued when any information for the products changed (change of the name of the importer or manufacturer, change of location of the importer or manufacturer). In article 12 and 15, the quality

control examination agency reports periodic on the compatibility of medical device to director of KFDA[7]. Therefore, the manufacturer or importer of registered in the MFDS could be important factors in terms of quality control of currently available bone substitutes.

However, nineteen products (51.4%) were different information among the 37 products registered in MOHW. Four products (10.8%) were different registered ingredients from journal or advertisement including DualPor COLLAGEN D-PUTTY (OssGen), Cerasorb M granules, FRABONE-Inject, and TCP Dental. Nine products (24.3%) were differ in product name or not available including CollaOss (Syringe), Mega-TCP (CGL), Cerasorb, Cerasorb M granules, BIO-C, Excelos (TCPGMD, TCPGLD), MBCP Plus (Biometlante), OssPol DENTAL, and OSTEON Sinus. Especially, CollaOss (Block) and CollaOss (Putty) were registered as dental alloplastic bone substitute in MOHW but they were introduced as xenograft in advertisement and journals. Five products (13.5%) had different manufacturer or importer including Excelos Inject (CGbio), Excelos (TCPGLD), Excelos (TCP-GMD, TCPGLD), Mega-TCP (CGM, CGL), Boncel-Os.

For a successful clinical outcome, it cannot be overemphasized that the quality of the materials or medical device should be constant and strictly controlled. Unfortunately, it is hard to identify the certification of GMP or to verify the quality in every clinical situation. Therefore, it is necessary to leave certificate to the government agency or the company which is responsible for the product. In addition the related dental institute or academy should to consider the security on quality of the product.

Implant dentistry has become a common treatment in Korea, many studies and development have been made on implant and bone graft materials. Among dental alloplastic bone substitutes which were registered in MOHW, twenty-nine (78.4%) products were domestically produced, of which three out of seven approved by FDA were made in Korea[11-17]. However, there are only ten products (27.0%) have been published with clinical study, of which six are Korean products. In the view of reference, the reference level could not be as directly same as the efficiency of the product, but it could be the basis of product selection for the clinician since minimal safety and efficiency can be regarded as verified. Reference level I received Cerasorb M (β-TCP 99%) as a sinus lift[38,39]. Reference level II received Sorbone (β-TCP 100%) in extraction socket and periodontal defect[34,35], GENESIS-BCP (β-TCP 40% and HA 60%) in periodontal defect[70]. Reference level III received Cerasorb M (β-TCP 99%) in cystic cavity, periodontal defect, cleft defect and extraction socket[40,41], CollaOss (HA 90% and collagen 10%) in extraction socket[18], OSTEON (β-TCP 30% and HA 70%) in sinus lift[94], OSTEON II (β-TCP 70% and HA 30%) in sinus lift[99], TCP Dental (β-TCP 99.9%) in sinus lift[57]. Reference level IV is insufficient to verify the efficiency, could be seen as a step that clinically confirms safety. Cerasorb M was in peri-implant and periodontal defect[42-44], CollaOss was in peri-implant defect[19], OssaBase-HA (HA 100%) was in guided bone regeneration[22], Excelos (β-TCP 100%) was in extraction socket[30], MBCP+ (β-TCP 80% and HA 20%) was in extraction socket[84], GENESIS-BCP was in ridge augmentation[71], OSTEON II was in sinus lift[100], ridge augmentation[101-103], periodontal defect[105] achieved for reference level IV. In addition, there were many animal, *in vivo*, and *in vitro* studies for osteoconductivity or role as carrier of osteoinductive growth factors or control material. In order to obtain MOHW and MFDS approval for commercial use in Korea, a data based on research or experiments should be required, but these data could not be included in this study because they were not publicly available. Because dental bone graft surgery has been performed in various environments such as sinus lift, ridge augmentation, cystic lesion, periodontal defect, peri-implant defect, extraction socket, it could be difficult to obtain high reference level in all dental bone grafting fields. However, it is nevertheless necessary to demonstrate the clinical level of Korean dental operation and the development level of bone graft substitutes.

In conclusion, there is not enough information about the effectiveness and safety of currently available alloplastic bone substitute in dental performance. Further clinical trials including well designed RCTs are necessary to evaluation the clinical efficacy of dental alloplastic bone substitutes in Korea. It should be aware of the limited information and developed the clinical evidences and regulations for clinicians.

ORCID

Jeong-Kui Ku, *https://orcid.org/0000-0003-1192-7066*
Inseok Hong, *https://orcid.org/0000-0003-0114-0534*
Bu-Kyu Lee, *https://orcid.org/0000-0001-8483-937X*
Pil-Young Yun, *https://orcid.org/0000-0001-6097-1229*
Jeong Keun Lee, *https://orcid.org/0000-0002-5561-6297*

Authors' Contributions

J.K.K. performed study, participated in data collection and wrote the manuscript. I.H. attributed to write the manuscript.

B.K.L. and P.Y.Y. analyzed the study, J.K.L. helped in drafting the manuscript and helped in study design. All authors read and approved the final manuscript.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Dimitriou R, Tsiridis E, Giannoudis PV. Current concepts of molecular aspects of bone healing. Injury 2005;36:1392-404.
2. Delloye C, Cornu O, Druez V, Barbier O. Bone allografts: what they can offer and what they cannot. J Bone Joint Surg Br 2007;89:574-9.
3. Dalkýz M, Ozcan A, Yapar M, Gökay N, Yüncü M. Evaluation of the effects of different biomaterials on bone defects. Implant Dent 2000;9:226-35.
4. Kim YK, Yun PY, Lim SC, Kim SG. Sinus bone graft using OSTEON® and BioOss®: histologic comparative study. Implantology 2007;11:4-18.
5. Kim YK. Systematic classification and application of alloplastic bony substitutes and autogenous teeth bone graft material. J Dent Implant Res 2009;28:77-88.
6. Tadic D, Epple M. A thorough physicochemical characterisation of 14 calcium phosphate-based bone substitution materials in comparison to natural bone. Biomaterials 2004;25:987-94.
7. Ministry of Food and Drug Safety. Medical device manufacturing and quality control standards (No. 2016-156) [Internet]. Sejong: National Law Information Center [cited 2017 Mar 1]. Available from: http://www.law.go.kr/LSW/admRulLsInfoP.do?admRulSeq=2100000073289.
8. Ministry of Health & Welfare. No. 2018-248. Medical device price list [Internet]. Wonju: Health Insurance Review & Assessment Service [cited 2018 Nov 30]. Available from: https://www.hira.or.kr/rd/insuadtcrtr/bbsView.do?pgmid=HIRAA030069000400&brdScnBltNo=4&brdBltNo=51151.
9. Wright JG, Swiontkowski MF, Heckman JD. Introducing levels of evidence to the journal. J Bone Joint Surg Am 2003;85:1-3.
10. Kurien T, Pearson RG, Scammell BE. Bone graft substitutes currently available in orthopaedic practice: the evidence for their use. Bone Joint J 2013;95:583-97.
11. U.S. Food and Drug Administration (FDA). Cerasorb: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2017 Sep 17]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf11/K113282.pdf.
12. U.S. Food and Drug Administration (FDA). MBCP+: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2007 Jul 30]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf9/K093122.pdf.
13. U.S. Food and Drug Administration (FDA). Osteon: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2010 Jul 8]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf10/K102015.pdf.
14. U.S. Food and Drug Administration (FDA). Osteon II: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2012 Jan 17]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf11/K112716.pdf.
15. U.S. Food and Drug Administration (FDA). Osteon III: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2016 Sep 14]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf15/K153676.pdf.
16. U.S. Food and Drug Administration (FDA). MBCP: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2005 May 3]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf5/K051885.pdf.
17. U.S. Food and Drug Administration (FDA). Kasios TCP: 510(k) summary [Internet]. Silver Spring (MD): FDA [cited 2004 Nov 10]. Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf4/K042340.pdf.
18. Lim HC, Jung UW, You H, Lee JS. Randomized clinical trial of ridge preservation using porcine bone/cross-linked collagen vs. bovine bone/non-cross-linked collagen: cone beam computed tomographic analysis. Clin Oral Implant Res 2017;28:1492-500.
19. Lee JH, Lee JS, Baek WS, Lim HC, Cha JK, Choi SH, et al. Assessment of dehydrothermally cross-linked collagen membrane for guided bone regeneration around peri-implant dehiscence defects: a randomized single-blinded clinical trial. J Periodontal Implant Sci 2015;45:229-37.
20. Benic GI, Joo MJ, Yoon SR, Cha JK, Jung UW. Primary ridge augmentation with collagenated xenogenic block bone substitute in combination with collagen membrane and rhBMP-2: a pilot histological investigation. Clin Oral Implants Res 2017;28:1543-52.
21. Kwak EJ, Cha IH, Nam W, Yook JI, Park YB, Kim HJ. Effects of locally administered rhBMP-2 and bisphosphonate on bone regeneration in the rat fibula. Oral Dis 2018;24:1042-56.
22. Papež J, Dostálová T, Chleborád K, Kříž P, Strnad J. Chronological age as factor influencing the dental implant osseointegration in the jaw bone. Prague Med Rep 2018;119:43-51.
23. Petrenko YA. Properties of mesenchymal stromal cells during 3D culturing within scaffolds of different origin. Probl Cryobiol 2012;22:144-7.
24. Horkavcová D, Zítková K, Rohanová D, Helebrant A, Cílová Z. The Resorption of ß-TCP and HA materials under conditions similar to those in living organisms. Ceram Silik 2010;54:398-404.
25. Strnadová M, Strnad Z, Šponer P, Jirošova J, Strnad J. In vivo behaviour of the synthetic porous hydroxyapatite prepared by low temperature microwave processing and comparison with deproteinized bovine bone. Key Eng Mater 2012;493-494:236-41.
26. Rohanová D, Horkavcová D, Helebrant A, Boccaccini AR. Assessment of in vitro testing approaches for bioactive inorganic materials. J Non-Cryst Solids 2016;432:53-9.
27. Lee DSH, Pai Y, Chang S. Effect of thermal treatment of the hydroxyapatite powders on the micropore and microstructure of porous biphasic calcium phosphate composite granules. J Biomater Nanobiotechnology 2013;4:114-8.
28. Dorozhkin SV. Calcium orthophosphate-based bioceramics and its clinical applications. In: Kaur G, ed. Clinical applications of biomaterials: state-of-the-art progress, trends, and novel approaches. Cham: Springer; 2017:123-226.
29. Dorozhkin SV. Multiphasic calcium orthophosphate (CaPO4) bioceramics and their biomedical applications. Ceram Int 2016;42:6529-54.
30. Lee SM. Clinical evaluation of efficacy and safety of NOVOSIS-inject containing bmp-2 for socket preservation after extraction of a single-rooted tooth. Clin Oral Implant Res 2018;29:318.
31. Chang AR, Cho TH, Hwang SJ. Receptor activator of nuclear factor kappa-B ligand-induced local osteoporotic canine mandible model for the evaluation of peri-implant bone regeneration. Tissue Eng Part C Methods 2017;23:781-94.
32. Song J, Kim J, Woo HM, Yoon B, Park H, Park C, et al. Repair of rabbit radial bone defects using bone morphogenetic protein-2 combined with 3D porous silk fibroin/β-tricalcium phosphate hybrid scaffolds. J Biomater Sci Polym Ed 2018;29:716-29.
33. Park HJ, Min KD, Lee MC, Kim SH, Lee OJ, Ju HW, et al. Fabrication of 3D porous SF/β-TCP hybrid scaffolds for bone tissue reconstruction. J Biomed Mater Res A 2016;104:1779-87.
34. Alharissy M, AbouSulaiman A, Manadili A, Dayoub S. Radio-

graphic alternations in alveolar bone dimensions following socket preservation using two bone substitutes. J Int Dent Med Res 2018;11:906-10.
35. Naineni R, Ravi V, Subbaraya DK, Prasanna JS, Panthula VR, Koduganti RR. Effect of alendronate with β - TCP bone substitute in surgical therapy of periodontal intra-osseous defects: a randomized controlled clinical trial. J Clin Diagn Res 2016;10:ZC113-7.
36. Miramond T, Borget P, Baroth S, Guy D. Comparative critical study of commercial calcium phosphate bone substitutes in terms of physic-chemical properties. Key Eng Mater 2014;587:63-8.
37. Jang CH, Cho YB, Yang HC, Kim JS, Choi CH, Jang SJ, et al. Effect of piperacillin-tazobactam coated β-tricalcium phosphate for mastoid obliteration in otitis media. Int J Pediatr Otorhinolaryngol 2011;75:631-4.
38. Zijderveld SA, Zerbo IR, van den Bergh JP, Schulten EA, ten Bruggenkate CM. Maxillary sinus floor augmentation using a beta-tricalcium phosphate (Cerasorb) alone compared to autogenous bone grafts. Int J Oral Maxillofac Implants 2005;20:432-40.
39. Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P. The efficacy of horizontal and vertical bone augmentation procedures for dental implants - a Cochrane systematic review. Eur J Oral Implantol 2009;2:167-84.
40. Horch HH, Sader R, Pautke C, Neff A, Deppe H, Kolk A. Synthetic, pure-phase beta-tricalcium phosphate ceramic granules (Cerasorb) for bone regeneration in the reconstructive surgery of the jaws. Int J Oral Maxillofac Surg 2006;35:708-13.
41. Horowitz RA, Mazor Z, Miller RJ, Krauser J, Prasad HS, Rohrer MD. Clinical evaluation alveolar ridge preservation with a beta-tricalcium phosphate socket graft. Compend Contin Educ Dent 2009;30:588-90, 592, 594 passim; quiz 604, 606.
42. Döri F, Arweiler N, Gera I, Sculean A. Clinical evaluation of an enamel matrix protein derivative combined with either a natural bone mineral or beta-tricalcium phosphate. J Periodontol 2005;76:2236-43.
43. Bokan I, Bill JS, Schlagenhauf U. Primary flap closure combined with Emdogain alone or Emdogain and Cerasorb in the treatment of intra-bony defects. J Clin Periodontol 2006;33:885-93.
44. Harel N, Moses O, Palti A, Ormianer Z. Long-term results of implants immediately placed into extraction sockets grafted with β-tricalcium phosphate: a retrospective study. J Oral Maxillofac Surg 2013;71:e63-8.
45. Klein M, Goetz H, Pazen S, Al-Nawas B, Wagner W, Duschner H. Pore characteristics of bone substitute materials assessed by microcomputed tomography. Clin Oral Implants Res 2009;20:67-74.
46. Neamat A, Gawish A, Gamal-Eldeen AM. beta-Tricalcium phosphate promotes cell proliferation, osteogenesis and bone regeneration in intrabony defects in dogs. Arch Oral Biol 2009;54:1083-90.
47. Kasten P, Beyen I, Niemeyer P, Luginbühl R, Bohner M, Richter W. Porosity and pore size of beta-tricalcium phosphate scaffold can influence protein production and osteogenic differentiation of human mesenchymal stem cells: an in vitro and in vivo study. Acta Biomater 2008;4:1904-15.
48. Bernhardt A, Lode A, Peters F, Gelinsky M. Novel ceramic bone replacement material Osbone® in a comparative in vitro study with osteoblasts. Clin Oral Implants Res 2011;22:651-7.
49. Bernhardt A, Dittrich R, Lode A, Despang F, Gelinsky M. Nanocrystalline spherical hydroxyapatite granules for bone repair: in vitro evaluation with osteoblast-like cells and osteoclasts. J Mater Sci Mater Med 2013;24:1755-66.
50. Klein MO, Kämmerer PW, Scholz T, Moergel M, Kirchmaier CM, Al-Nawas B. Modulation of platelet activation and initial cytokine release by alloplastic bone substitute materials. Clin Oral Implants Res 2010;21:336-45.
51. Bernhardt A, Lode A, Peters F, Gelinsky M. Comparative evaluation of different calcium phosphate-based bone graft granules - an in vitro study with osteoblast-like cells. Clin Oral Implants Res 2013;24:441-9.
52. Ghanaati S, Barbeck M, Orth C, Willershausen I, Thimm BW, Hoffmann C, et al. Influence of β-tricalcium phosphate granule size and morphology on tissue reaction in vivo. Acta Biomater 2010;6:4476-87.
53. Handschel J, Berr K, Depprich R, Naujoks C, Kübler NR, Meyer U, et al. Compatibility of embryonic stem cells with biomaterials. J Biomater Appl 2009;23:549-60.
54. Zheng H, Bai Y, Shih MS, Hoffmann C, Peters F, Waldner C, et al. Effect of a β-TCP collagen composite bone substitute on healing of drilled bone voids in the distal femoral condyle of rabbits. J Biomed Mater Res B Appl Biomater 2014;102:376-83.
55. Bizenjima T, Takeuchi T, Seshima F, Saito A. Effect of poly (lactide-co-glycolide) (PLGA)-coated beta-tricalcium phosphate on the healing of rat calvarial bone defects: a comparative study with pure-phase beta-tricalcium phosphate. Clin Oral Implants Res 2016;27:1360-7.
56. Bernhardt A, Lode A, Peters F, Gelinsky M. Optimization of culture conditions for osteogenically-induced mesenchymal stem cells in β-tricalcium phosphate ceramics with large interconnected channels. J Tissue Eng Regen Med 2011;5:444-53.
57. Kurkcu M, Benlidayi ME, Cam B, Sertdemir Y. Anorganic bovine-derived hydroxyapatite vs β-tricalcium phosphate in sinus augmentation: a comparative histomorphometric study. J Oral Implantol 2012;38:519-26.
58. Khojasteh A, Eslaminejad MB, Nazarian H. Mesenchymal stem cells enhance bone regeneration in rat calvarial critical size defects more than platelete-rich plasma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:356-62; discussion 363.
59. Badwelan M, Alkindi M, Ramalingam S, Nooh N, Al Hezaimi K. The efficacy of recombinant platelet-derived growth factor on beta-tricalcium phosphate to regenerate femoral critical sized segmental defects: longitudinal in vivo micro-CT study in a rat model. J Invest Surg 2018. doi: 10.1080/08941939.2018.1519048. [Epub ahead of print]
60. Giuliani A, Manescu A, Larsson E, Tromba G, Luongo G, Piattelli A, et al. In vivo regenerative properties of coralline-derived (biocoral) scaffold grafts in human maxillary defects: demonstrative and comparative study with beta-tricalcium phosphate and biphasic calcium phosphate by synchrotron radiation x-ray microtomography. Clin Implant Dent Relat Res 2014;16:736-50.
61. Arbez B, Kün-Darbois JD, Convert T, Guillaume B, Mercier P, Hubert L, et al. Biomaterial granules used for filling bone defects constitute 3D scaffolds: porosity, microarchitecture and molecular composition analyzed by microCT and Raman microspectroscopy. J Biomed Mater Res B Appl Biomater 2019;107:415-23.
62. Emanuel N, Rosenfeld Y, Cohen O, Applbaum YH, Segal D, Barenholz Y. A lipid-and-polymer-based novel local drug delivery system--BonyPid™: from physicochemical aspects to therapy of bacterially infected bones. J Control Release 2012;160:353-61.
63. Catros S, Zwetyenga N, Bareille R, Brouillaud B, Renard M, Amédée J, et al. Subcutaneous-induced membranes have no osteoinductive effect on macroporous HA-TCP in vivo. J Orthop Res 2009;27:155-61.
64. Salim AS, Al Hijazi A. Evaluation of the effect of synthetic biomaterial (calcium phosphate ceramic) on healing of extracted tooth socket. J Baghdad College Dent 2010;22:57-61.
65. Kursun-Çakmak ES, Akbulut N, Öztas DD. Comparative evaluation of the radiopacity of bone graft materials used in dentistry. J Contemp Dent 2017;7:150-5.
66. You H, Yoon SR, Lim HC, Lee JS, Jung UW, Choi SH. Bone regenerative efficacy of limited-dose escherichia coli-derived rh-BMP-2 with biphasic calcium phosphate carrier in rabbit calvarial defect model. Implant Dent 2016;25:16-23.
67. Kumar A, Mahendra J, Samuel S, Govindraj J, Loganathan T, Vashum Y, et al. Platelet-rich fibrin/biphasic calcium phosphate impairs osteoclast differentiation and promotes apoptosis by the intrinsic mitochondrial pathway in chronic periodontitis. J Periodon-

tol 2019;90:61-71.
68. Fabrication method of a novel artificial cortical bone using a multi-pass extrusion process. KR101241642B1 [Internet]. Daejeon: Korean Intellectual Property Office [cited 2012 Feb 6]. Available from: http://kpat.kipris.or.kr/kpat/1020100072191.pdf?method=fullText&applno=1020100072191&pub_reg=P.
69. (WO2012015226) Fabrication method of a novel artificial cortical bone using a multi-pass extrusion process [Internet]. Geneva: World Intellectual Property Organization [cited 2012 Feb 2]. Available from: https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2012015226.
70. Lee MJ, Kim BO, Yu SJ. Clinical evaluation of a biphasic calcium phosphate grafting material in the treatment of human periodontal intrabony defects. J Periodontal Implant Sci 2012;42:127-35.
71. Alagl AS, Madi M. Localized ridge augmentation in the anterior maxilla using titanium mesh, an alloplast, and a nano-bone graft: a case report. J Int Med Res 2018;46:2001-7.
72. Kim BS, Yang SS, You HK, Shin HI, Lee J. Fucoidan-induced osteogenic differentiation promotes angiogenesis by inducing vascular endothelial growth factor secretion and accelerates bone repair. J Tissue Eng Regen Med 2018;12:e1311-24.
73. Yang DH, Park HN, Bae MS, Lee JB, Heo DN, Lee WJ, et al. Evaluation of GENESIS-BCP™ scaffold composed of hydroxyapatite and β-tricalcium phosphate on bone formation. Macromol Res 2012;20:627-33.
74. Kim BS, Lee J. Enhanced bone healing by improved fibrin-clot formation via fibrinogen adsorption on biphasic calcium phosphate granules. Clin Oral Implants Res 2015;26:1203-10.
75. Seok H, Lee SK, Kim SG, Kang TY, Lee MJ, Chae WS. Migration of alloplastic bone graft material in infected conditions: a case study and animal experiment. J Oral Maxillofac Surg 2014;72:1093.e1-11.
76. Kim BS, Yang SS, Lee J. Precoating of biphasic calcium phosphate bone substitute with atelocollagen enhances bone regeneration through stimulation of osteoclast activation and angiogenesis. J Biomed Mater Res A 2017;105:1446-56.
77. Lee SH, Kim SW, Lee JI, Yoon HJ. The effect of platelet-rich fibrin on bone regeneration and angiogenesis in rabbit cranial defects. Tissue Eng Regen Med 2015;12:362-70.
78. Kim MS, Lee JH, Jung UW, Kim CS, Choi SH, Cho KS. A cumulative survival rate of implants installed on posterior maxilla augmented using MBCP after 2 years of loading: a retrospective clinical study. J Korean Acad Periodontol 2008;38:669-78.
79. Lee JH, Jung UW, Kim CS, Choi SH, Cho KS. Maxillary sinus augmentation using Macroporous Biphasic Calcium Phosphate (MBCP™): three case report with histologic evaluation. J Korean Acad Periodontol 2006;36:567-77.
80. Le Guehennec L, Goyenvalle E, Aguado E, Pilet P, Bagot D'Arc M, Bilban M, et al. MBCP biphasic calcium phosphate granules and tissucol fibrin sealant in rabbit femoral defects: the effect of fibrin on bone ingrowth. J Mater Sci Mater Med 2005;16:29-35.
81. Lee JH, Jung UW, Kim CS, Choi SH, Cho KS. Histologic and clinical evaluation for maxillary sinus augmentation using macroporous biphasic calcium phosphate in human. Clin Oral Implants Res 2008;19:767-71.
82. Wagner W, Wiltfang J, Pistner H, Yildirim M, Ploder B, Chapman M, et al. Bone formation with a biphasic calcium phosphate combined with fibrin sealant in maxillary sinus floor elevation for delayed dental implant. Clin Oral Implants Res 2012;23:1112-7.
83. Kim CS, Kim SC, Claire D, Elodie S, Daculsi G. Eight-year clinical follow-up of sinus grafts with micro-macroporous biphasic calcium phosphate granules. Key Eng Mater 2014;587:321-4.
84. Rodríguez C, Jean A, Mitja S, Daculsi G. Five years clinical follow up bone regeneration with CaP bioceramics. Key Eng Mater 2008;361-363:1339-42.
85. Jégoux F, Goyenvalle E, Cognet R, Malard O, Moreau F, Daculsi G, et al. Reconstruction of irradiated bone segmental defects with a biomaterial associating MBCP+(R), microstructured collagen membrane and total bone marrow grafting: an experimental study in rabbits. J Biomed Mater Res A 2009;91:1160-9.
86. Miramond T, Aguado E, Goyenvalle E, Moreau F, Borget P, Daculsi G. Osteopromotion of biphasic calcium phosphate granules in critical size defects after osteonecrosis induced by focal heating insults. IRBM 2013;34:337-41.
87. Pereira RC, Benelli R, Canciani B, Scaranari M, Daculsi G, Cancedda R, et al. Beta tricalcium phosphate ceramic triggers fast and robust bone formation by human mesenchymal stem cells. J Tissue Eng Regen Med 2019. doi: 10.1002/term.2848. [Epub ahead of print]
88. Miramond T, Corre P, Borget P, Moreau F, Guicheux J, Daculsi G, et al. Osteoinduction of biphasic calcium phosphate scaffolds in a nude mouse model. J Biomater Appl 2014;29:595-604.
89. Houshmand B, Tabibzadeh Z, Motamedian SR, Kouhestani F. Effect of metformin on dental pulp stem cells attachment, proliferation and differentiation cultured on biphasic bone substitutes. Arch Oral Biol 2018;95:44-50.
90. Miramond T, Borget P, Baroth S, Daculsi G. Comparative critical study of commercial calcium phosphate bone substitutes in terms of physic-chemical properties. Key Eng Mater 2014;587:63-8.
91. Kim KI, Park S, Im GI. Osteogenic differentiation and angiogenesis with cocultured adipose-derived stromal cells and bone marrow stromal cells. Biomaterials 2014;35:4792-804.
92. Wang W, Yeung KWK. Bone grafts and biomaterials substitutes for bone defect repair: a review. Bioact Mater 2017;2:224-47.
93. Habibovic P, Kruyt MC, Juhl MV, Clyens S, Martinetti R, Dolcini L, et al. Comparative in vivo study of six hydroxyapatite-based bone graft substitutes. J Orthop Res 2008;26:1363-70.
94. Kim YK, Yun PY, Kim SG, Lim SC. Analysis of the healing process in sinus bone grafting using various grafting materials. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:204-11.
95. Lim HC, Kim KT, Lee JS, Jung UW, Choi SH. In vivo comparative investigation of three synthetic graft materials with varying compositions processed using different methods. Int J Oral Maxillofac Implants 2015;30:1280-6.
96. Lim HC, Zhang ML, Lee JS, Jung UW, Choi SH. Effect of different hydroxyapatite:β-tricalcium phosphate ratios on the osteoconductivity of biphasic calcium phosphate in the rabbit sinus model. Int J Oral Maxillofac Implants 2015;30:65-72.
97. Kim DM, Nevins ML, Lin Z, Fateh A, Kim SW, Schupbach P, et al. The clinical and histologic outcome of dental implant in large ridge defect regenerated with alloplast: a randomized controlled preclinical trial. J Oral Implantol 2013;39:148-53.
98. Lim HC, Hong JY, Lee JS, Jung UW, Choi SH. Late-term healing in an augmented sinus with different ratios of biphasic calcium phosphate: a pilot study using a rabbit sinus model. J Periodontal Implant Sci 2016;46:57-69.
99. Abdulghani MM, Farha LS. Clinical and experimental study to evaluate the effect of biphasic calcium phosphate collagen composite (cpcc) on healing of bone defects after oral surgical procedures. Al-Kindy College Med J 2017;13:11-20.
100. Hussein LA, Hassan TAL. The effectiveness of oxidized regenerated cellulose as a graft material in transalveolar osteotome sinus lift procedure. J Craniofac Surg 2017;28:1766-71.
101. Park YH, Choi SH, Cho KS, Lee JS. Dimensional alterations following vertical ridge augmentation using collagen membrane and three types of bone grafting materials: a retrospective observational study. Clin Implant Dent Relat Res 2017;19:742-9.
102. Kim DM, Camelo M, Nevins M, Fateh A, Schupbach P, Nevins M. Alveolar ridge reconstruction with a composite alloplastic biomaterial. Int J Periodontics Restorative Dent 2012;32:e204-9.
103. Chee YD, Seon HK. Increase of the width of peri-implant keratinized tissue using apically positioned flap: case report. J Dent Rehabil Appl Sci 2013;29:407-17.
104. Lee JB. Selectable implant removal methods due to mechanical

and biological failures. Case Rep Dent 2017;2017:9640517.
105. Badiea RA. Evaluation of treatment of intra-bony defects with a mixture of β-tricalcium phosphate - hydroxyapatite granules and oily calcium hydroxide suspension. J Baghdad College Dent 2013;25:103-9.
106. Seo GY, Thoma DS, Jung UW, Lee JS. Increasing the tissue thickness at implant sites using guided bone regeneration and an additional collagen matrix: histologic observations in beagle dogs. J Biomed Mater Res B Appl Biomater 2019;107:741-9.
107. Bucchi C, Borie E, Arias A, Dias FJ, Fuentes R. Radiopacity of alloplastic bone grafts measured with cone beam computed tomography: an analysis in rabbit calvaria. Bosn J Basic Med Sci 2016;17:61-6.
108. Chung SM, Jung IK, Yoon BH, Choi BR, Kim DM, Jang JS. Evaluation of different combinations of biphasic calcium phosphate and growth factors for bone formation in calvarial defects in a rabbit model. Int J Periodontics Restorative Dent 2016;36 Suppl:s49-59.
109. Al Mukhtar YH, Abid WK. Effect of Osteon II collagen with hyaluronic acid and collagen membrane on bone healing process in rabbits: a radiograghical study. Int J Enhanc Res Sci Tech Eng 2016;5:36-46.
110. Khojasteh A, Motamedian SR, Rad MR, Shahriari MH, Nadjmi N. Polymeric vs hydroxyapatite-based scaffolds on dental pulp stem cell proliferation and differentiation. World J Stem Cells 2015;7:1215-21.
111. Tallarico M, Xhanari E, Cocchi F, Canullo L, Schipani F, Meloni SM. Accuracy of computer-assisted template-based implant placement using a conventional impression and scan model or digital impression: a preliminary report from a randomized controlled trial. J Oral Sci Rehabil 2017;3:8-16.
112. Kang KJ, Lee MS, Moon CW, Lee JH, Yang HS, Jang YJ. In vitro and in vivo dentinogenic efficacy of human dental pulp-derived cells induced by demineralized dentin matrix and HA-TCP. Stem Cells Int 2017;2017:2416254.