Form CT
UTHSA Clinical Trial Description

This form is not mandatory. Other documents are acceptable if equivalent information is provided.

UTHSCSA Tracking Number *(internal use only)*		**1. Original Version Date**	June 24, 2019
		1.1. Revision Date(s) *add rows as needed*	

2. Background

Briefly discuss the important literature relevant to the trial and that provides background for the trial. Include the importance of the trial and any relevant treatment issues or controversies.

Bone grafting following tooth extraction is often performed to preserve bony ridge dimensions adequate to support subsequent implant placement. Alveolar ridge resorption commonly occurs following tooth extraction, and the decrease in bone volume has the potential to make dental implant therapy impossible without surgery to reconstruct the ridge. The aim of ridge preservation grafting is to prevent or minimize this resorptive process, thereby preserving an adequate volume of bone for implant placement. Ridge preservation generally involves placement of a particulate bone graft material in the tooth socket, followed by use of a membrane or similar substance over the socket entrance to contain the bone graft.

Various grafting materials have been recommended for these ridge preservation procedures, including cortical and cancellous freeze-dried bone allograft (FDBA), demineralized freeze-dried bone allograft (DFDBA), various xenografts, alloplasts and autografts. Our research group here in the Department of Periodontics at the UT Health Science Center at San Antonio has spent several years evaluating wound healing and clinical changes in ridge dimension following ridge preservation procedures using a variety of bone grafting materials and treatment protocols.[1-9] In most of these studies, bone allografts were used for ridge preservation. For various reasons, many clinicians prefer not to use human bone graft products, recommending use of xenografts or alloplastic materials instead. Our study group has previously examined use of various bovine xenografts. [1-10]
Of interest are two composite materials that include either bovine bone or hydroxyapatite granules and sugar cross-linked collagen. These materials possess better handling properties that allow them to be used without the addition of a membrane during ridge preservation procedures. Two such composite materials are currently available in the U.S - a composite bovine xenograft with porcine collagen matrix and a hydroxyapatite graft with porcine sugar cross-linked type I collagen tendon matrix. The bovine/collagen matrix has been extensively researched for ridge preservation procedures. [11-17]
The porcine collagen in the newer hydroxyapatite-containing composite graft material is cross linked with sugar with a proprietary technology (Glymatrix®). This cross-linking technology has shown promising results in its use as a membrane. [3, 18, 19].

However, only a recent animal study presented as a poster at the 2017 Academy of Osseointegration on beagle dogs compared the two composite materials for a ridge restoration procedure. [20] The results of this animal study showed comparable healing and biocompatibility profiles, increased percentage of vital bone and a larger overall ridge restoration for the hydroxyapatite/collagen matrix.

3. Objectives and Endpoints *All data points collected in the study should support an objective or have a regulatory purpose. Complete the table – add rows as needed.*

3.1. Objective(s) *Clearly and concisely define the primary and secondary outcomes.*	**3.2. Endpoint** *Clearly define the endpoints. (endpoints are the basis for concluding that the objective has been met).*	**3.3. Justification for Endpoint** *Briefly explain why the endpoint(s) were chosen.*
Is there a difference in histologic wound healing following tooth extraction and ridge preservation between groups treated with Bio-Oss® Collagencompared to Ossix™ Bone	% vital bone formation, % residual graft material, and % "CT/other" (fibrous tissue and marrow space)	% vital bone formation shows the amount of new bone formed after the procedure. The higher this % is the better the healing of the site % residual graft material shows how much of the graft material remained intact. Ideally all the graft materials should turn over to vital bone

		% CT/other (fibrous tissue and marrow space) is the amount of tissue that is neither native bone or graft material. It may be connective tissue that will mature to osteoid and bone or marrow space that is part of the normal healing.
	Change in ridge width; Change in buccal ridge height, and Change in lingual ridge height	

4. Rationale

Briefly state the reason for conducting the clinical trial.

A recent animal study presented as a poster at the 2017 Academy of Osseointegration on beagle dogs compared the two composite materials for a ridge restoration procedure. (20) The results of this animal study showed comparable healing and biocompatibility profiles, increased percentage of vital bone and a larger overall ridge restoration for the hydroxyapatite/collagen matrix. The proposed study will assess the histologic healing of this material in humans and compare it to a similar material that is well researched.

5. Study Design

5.1. Number of Groups/Arms	2	**Group name(s)**	Active control group – Bio-Oss® Collagen Test group – Ossix™ Bone

5.2. Overall Design

Select all applicable

☒	**Randomization**	☐	**Cluster Randomized**		
☐	**Group-Sequential**	☐	**Adaptive Design**		
☒	**Parallel Design**	☐	**Placebo-Controlled**		
☐	**Superiority**	☐	**Equivalence**	☐	**Non-inferiority**
Device ☐	Pilot	☐	Pivotal	☐	Post-Approval

Drug/Biologic	☐	Phase 1	☐	Phase 1/2	☐	Phase 2	☐	Phase 2/3	☐	Phase 3	☒	Phase 4

☐	**Dose escalation**	*If yes, details →*	
☐	**Dose ranging**	*If yes, details →*	
☐	**Sub-studies**	*If yes, details →*	

5.3. Other Design Details:

6. Study Population

6.1. Study Population(s) Label/Name *To add more populations – select a row, copy & paste*	**6.2. Identify the criteria for inclusion** *The criteria that every potential participant must satisfy, to qualify for study entry.* All individuals in this study population must meet all of the inclusion criteria in order to be eligible to participate in the study	**6.3. Identify the criteria for exclusion** *The characteristics that make an individual ineligible for study participation.* All individuals in this study population meeting any of the exclusion criteria at baseline will be excluded from study participation.
Dental patients needing extraction	• One tooth, excluding molars, that has been identified by dental	• Will not cooperate with the follow-up schedule.

	faculty as requiring a single tooth extraction • A dental implant is indicated and treatment planned to replace the missing tooth • Have adequate restorative space for a dental implant-retained restoration • Have at least 10mm of alveolar bone height, without impinging on the maxillary sinus or inferior alveolar canal. • Have a dehiscence of the buccal or lingual bony plate of the tooth socket extending no more than 50% of the total depth of the socket. • Female patients who have undergone a hysterectomy, tubal ligation, or menopause, and non-pregnant women of child-bearing potential. • Are nonsmokers or former smokers. Current smokers may be included if they smoke ≤10 cigarettes per day	• Patients will not be entered who are mentally incompetent, prisoners, or pregnant. • Pregnant women or women intending to become pregnant during the study period (as confirmed verbally; an over the counter pregnancy test will be provided if pregnancy status us unknown or suspected). • Patients who become pregnant during the study will be withdrawn and standard care will be delivered. • Smokers who smoke >10 cigarettes per day • Clinical and/or radiographic determinations which will preclude inclusion in this study are: Active infection other than periodontitis; Inadequate bone dimensions or restorative space for a dental implant; Presence of a disease entity, condition or therapeutic regimen which decreases probability of soft tissue and bony healing, e.g., poorly controlled diabetes, chemotherapeutic and immunosuppressive agents, autoimmune diseases, history of bisphosphonate use or long-term steroid therapy; Positive medical history of endocarditis following oral or dental surgery.
6.4. **Will screen failures be allowed to <u>re-screen</u> at a later date?**	☐ **No** ☒ **Yes** *If yes, describe criteria below ↓* Subjects who do not meet inclusion criteria initially may be re-screened and included in the study if inclusion criteria is met at a later date	

7. Study Intervention(s) being tested or evaluated

This can include prevention, diagnostic or therapeutic interventions (e.g., drug or device) or educational, health services or basic science interventions (e.g., educational program, health care delivery model, or examining basic physiology)

1) Active Control Group: Bio-Oss® Collagen, (Geistlich, Inc.), 90% bovine derived xenograft granules and 10% porcine collagen.
2) Test Group: Ossix™ Bone (Datum Dental Ltd), a resorbable sponge-like matrix of 80% hydroxyapatite and 20% sugar cross-linked porcine collagen.

8. Protocol-Directed procedures, items, services or tests

List all procedures directed by the study plan - including items or services provided as part of routine or conventional care and those needed to diagnosis or treat research related complications.

Important Note – The protocol directed procedures listed must match those in the <u>Schedule of Activities (attachment)</u>

8.1. Drugs *(trade and generic, dosage, route of administration)*

Either Amoxicillin 500mg three times per day for 7 days, or if they are allergic to penicillin/amoxicillin they will be prescribed Clindamycin 300mg three times per day for 7 days. Antibiotics will be used for an approved indication and are routinely prescribed as part of routine care.

8.2. Devices

Bio-Oss® Collagen and Ossix™ Bone are both classified as devices by the FDA. Both will be used for an approved indication (in accordance with approved labeling).

8.3. Biologics

N/A

8.4. Laboratory Tests

If needed: An over-the-counter urine pregnancy test will be provided to female subjects and self-administered in the graduate periodontics clinic of UTHSCSA. A negative result is required to enter the study.
Histology of the core bone biopsy

8.5. Imaging Procedures

8.6. Other Research Procedures *(e.g., other safety and efficacy assessments.)*

1) Impressions of the arch with tooth to be extracted; 2) fabrication of a ridge measurement stent; 3) tooth extraction & ridge preservation; 4) dental implant placement & core bone biopsy; 6) bone quality determination (Lekholm and Zarb classification);

8.7 Attach a Schedule of Activities (SOA) Excel File [Download the Template here: *Schedule of Activities*]	*Check to indicate that the SOA Excel File is attached →*	☒
8.8 Description of Methods (or include in separate document)	*Check to indicate that the Methods are described in an attached file→*	☐

Each extraction socket will receive one 5 X 5 X 8mm or 5 X 5 X 10mm graft cube (research) with no attempt to fill the entire socket. No wound dressing or membrane will be used to cover the bone graft material as both materials can be used alone. All extraction sockets will be sutured with Vicryl 4.0 mattress suture which will be removed approximately 2 weeks (± 1 week) after the procedure as per standard of care. All patients will be prescribed an oral antibiotic after the procedure either Amoxicillin 500mg three times per day for 7 days, or if they are allergic to penicillin/amoxicillin they will be prescribed Clindamycin 300mg three times per day for 7 days as per standard of care.

In keeping with the protocol our study group has used several times before, the plan will be to extract non-molar teeth and graft with the test/control materials. Each subject will provide a single non-molar tooth site for study treatment. Following approx. 14 weeks of healing, we will harvest a core biopsy at the time of implant placement. The core biopsy will then be evaluated for the primary outcomes: % vital bone formation, % residual graft material, and % "CT/other" (fibrous tissue and marrow space). We will also evaluate the following secondary outcomes using a custom measuring stent for each subject: change in ridge width; change in buccal ridge height, and change in lingual ridge height. During the 14-week healing period, subjects will be followed up with biweekly and monthly visits as per standard of care, to evaluate healing.

A detailed visit by visit outline is provided below:

Step-by-Step Methods: All the procedures are routinely performed in the graduate periodontics clinic as part of standard care. The methodology is the same previous studies of our group HSC20130470H, HSC20150708H, HSC20170339H, HSC20170267H, among others.

Visit 1 - Screening examination:
If a patient presents at a consultation appointment at the graduate periodontics clinic with a non-molar tooth (incisors, canines, premolars) that needs to be extracted and replaced with a dental implant, the treating doctor will provide:

- Explanation to the patient of the purposes of the study and the planned procedures related to the study.
- Explanation to the patient of the risks, benefits and possible complications of participation in the study.
- Notification to the patient that inclusion in the study is voluntary and conditional upon satisfying the inclusion and exclusion criteria.

Patient will be given the opportunity during the appointment to ask any question that he/she may have. Following an informational discussion with the prospective subject, consent will be obtained within 2 weeks. This is up to the discretion of the patient. If the patient would like to become a subject for entry into the study, he or she can do so immediately, or can consider it for up to 2 weeks (must be prior to extraction).

Visit 2 – Extraction with ridge preservation using either 90% bovine derived xenograft granules and 10% porcine collagen (Bio-Oss® Collagen, Geistlich, Inc.) or a resorbable sponge-like matrix of 80% hydroxyapatite and 20% sugar ross-linked porcine collagen (Ossix™ Bone, Datum Dental Ltd).

The patient will be assigned to either group by simple randomization with a 1:1 ratio

If the patient has agreed to participate in the study, informed consent will be obtained and documented on a written consent form. If not, standard care treatment will be provided to the patient, but the patient would not be included in the study.

On the day of the planned extraction, the medical history will be updated.

Pregnant women or women intending to become pregnant during the study period: Prior to dental surgery, females of child-bearing age are asked verbally if there is any possibility that they are pregnant. If not, we proceed with surgery and no pregnancy test is done. If the woman states that there is a possibility that she is pregnant, an over the counter urine pregnancy test to rule pregnancy in or out will be provided. Use of the urine pregnancy test is only done if she says she may be pregnant. [If needed: Urine pregnancy test will be provided to female subjects in the graduate periodontics clinic of UTHSCSA and a negative result is required to enter the study.]

Impressions of the arch with the tooth to be extracted in place will be taken prior to extraction and poured in stone to obtain initial study casts (research). If the tooth to be extracted is fractured, a wax-up of the tooth will be made before the stent is fabricated (research).

One measurement stent will be fabricated to facilitate clinical ridge measurements. A clear suck-down resin measuring stent will be fabricated in the laboratory to allow standardization of the location of clinical measurements of ridge width and height through small holes that will be placed in the stent at the time of tooth extraction.

The width of keratinized tissue will be recorded clinically to the nearest 0.5mm using a periodontal probe at the mid-buccal and mid-lingual sites of the tooth to be extracted.

A pre-operative periapical radiographic image will be taken before the extraction as per standard of care (if not already available).

At the time of surgery, local anesthesia will be administered. Conscious sedation will be administered according to patient need and investigator preference, per standard care. Buccal and lingual flaps will be minimally reflected to a point up to 3mm apical to the bony crest.

Prior to tooth extraction, the clinical measuring stent will be placed and measurements of ridge width and ridge height will be taken and recorded to the nearest 0.5mm. Ridge width will be measured to the nearest 0.5mm using a ridge caliper at a point approximately 4mm apical to the facial and lingual bony crest through small holes created in the stent at those locations. Ridge height will be measured to the nearest 0.5mm through two holes in the occlusal aspect of the stent – one hole directly above the facial bony crest and another hole directly above the lingual bony crest. This stent will be retained for use during the subsequent implant placement surgery.

Tooth extraction will be performed as atraumatically as possible. Following tooth extraction, a final determination of enrollment into the study will be conducted based on the integrity of the buccal bone wall plate at the extraction site. If the buccal plate is intact, defined as no bony dehiscence greater than 50% of the socket depth, the patient will remain enrolled in the study. Conversely, if the buccal plate integrity has not been maintained (bony dehiscence >50%) the patient will be exited from the study and standard care therapy will be delivered to the patient.

After extraction, the number of bony walls in each socket will be recorded along with the presence of any bony dehiscences or fenestrations. Buccal and lingual flap elevation will be minimized and will extend no more than 2-3mm beyond the bony crest on the facial and lingual surfaces. The buccal plate thickness will be measured using an Iwanson gauge positioned perpendicular to the inner wall of the extraction socket. One beak of the gauge will be placed within the extraction socket 1.0mm apical to the alveolar bone crest. The other beak will be placed on the external bone surface. This buccal plate thickness measurement will be recorded to the nearest 0.1 mm.

The socket will be thoroughly debrided, a 5 X 5 X 8 mm or 5 X 5 X 10 mm bone graft cube of either 90% bovine derived xenograft granules and 10% porcine collagen (Bio-Oss® Collagen, Geistlich, Inc.) or a resorbable sponge-like matrix of 80% hydroxyapatite and 20% sugar cross-linked porcine collagen (Ossix™ Bone, Datum Dental Ltd) will be soaked in patient's blood and inserted in the socket. No attempt will be made to completely fill the socket as the materials expand after they contact fluids. No membrane or wound barrier will be placed over the graft in either group. Vicryl 4.0 sutures will be placed over the graft material to secure it in place as part of standard of care. Primary closure will not be attempted.

Visit 3 - Post-operative visit

The post-operative visit after extraction/ridge preservation will be scheduled approximately 3 weeks (±1 week) after the procedure. If needed, an optional POT visit may be scheduled before this visit, per standard care and as determined by patient need.

Visit 4 - Pre-implantation:
Approximately 3 months after the extraction (± 2 weeks) a CBCT of the prospective implant site may be taken as needed per standard care. The implant surgery will ensue within 2 weeks (± 2 weeks). The CBCT is not part of the study but rather standard of care.
Prior to surgery, pregnancy status will be confirmed verbally. An over the counter pregnancy test will be provided if pregnancy status us unknown or suspected (research). A negative result is required to continue being in the study.

Visit 5 - Implant placement:
Prior to surgery, pregnancy status will be confirmed verbally. An over the counter pregnancy test will be provided if pregnancy status us unknown or suspected (research). A negative result is required to continue being in the study.
Approximately 16 weeks (±2 weeks) after the extraction, implant surgery will be performed (standard of care). The width of keratinized tissue will be measured at the prospective implant site. A piece of floss will be run over the keratinized tissue and cut to the width of keratinized tissue, i.e. from the mucogingival junction (MGJ) on the buccal to the MGJ on the lingual. The floss will be then measured with a ruler to the closest 0.5mm.
After local anesthesia (and conscious sedation if requested), the patient will undergo implant placement surgery at the previously extracted tooth site and if required simultaneous guided bone regeneration (GBR) will be performed as per standard care. First, the individual subject's measuring stent and caliper will be used to determine the ridge width and ridge height at the same locations as done in the tooth extraction/grafting surgery visit. During the implant bed preparation, a hollow drill will be used to allow retrieval of a bone core which will be collected and stored in formalin and subsequently examined histologically and outcomes including percentages of new bone formation, residual graft and connective tissue/other will be recorded.

- During the implant placement procedure, the following data will be recorded per standard care:
- Bone quality according Lekholm and Zarb (1985) classification
- Absence/Presence of bone defect, including dehiscence or crater like defect. If present, at what site(s) (Buccal, Mesial, Lingual, Distal) and what are the respective depth and width of these defects.
- Absence/Presence of bone fenestration. If present what is the size of the fenestration in height and width.
- Was additional bone grafting needed in case of thin bone or dehiscence of threads? Yes/No

Subject participation ends at the time of implant placement. However, standard care post-operative visits will be provided after implant placement. Generally, one or two post-operative visits will be provided during the first month after implant surgery to insure adequate healing.

9. Preparation/Handling/ Storage/Accountability of Investigational Drug, Biologic, or Device

☒ *N/A - This study does not include any investigational products (e.g. drugs, devices or biologics)*

☐ *N/A - An Investigator Brochure is attached*

☐ *N/A - A Drug/Device Manual is attached*

9.1. Acquisition and accountability

State how the study intervention and control product will be provided to the investigator. Describe plans about how and by whom the study intervention will be distributed, including participation of a drug repository or pharmacy, and plans for disposal of expired or return of unused product.

9.2. Formulation, Appearance, Packaging, and Labeling

Describe the formulation, appearance, packaging, and labeling of the study intervention and control product, as supplied. Information in this section can usually be obtained from the IB or the package insert, or device labeling. This section should include the name of the manufacturer of the study intervention and control product.

9.3. Product Storage and Stability

Describe storage and stability requirements (e.g., protection from light, temperature, humidity) for the study intervention and control product. For studies in which multi-dose vials are utilized, provide additional information regarding stability and expiration time after initial use (e.g., the seal is broken).

9.4. Preparation

Describe the preparation of the study intervention and control product, including any preparation required by study staff and/or study participants. Include thawing, diluting, mixing, and reconstitution/preparation instructions in this section. For devices, include any relevant assembly or use instructions.

10. Study Intervention Additional Details

10.1. Measures to Minimize Bias: Randomization and Blinding

This section should contain a description of randomization and blinding procedures (if applicable to the study design). It should include a description or a table that describes how study participants will be assigned to study groups, without being so specific that blinding or randomization might be compromised. Plans for the maintenance of trial randomization codes and appropriate blinding for the study should be discussed. The timing and procedures for planned and unplanned breaking of randomization codes should be included. Include a statement regarding when unblinding may occur and who may unblind. Provide the criteria for breaking the study blind or participant code. Discuss the circumstances in which the blind would be broken for an individual or for all participants (e.g., for serious adverse evets (SAEs)). Indicate to whom the intentional and unintentional breaking of the blind should be reported.

22 envelopes will be prepared for each arm in a simple randomization 1:1 ratio, sealed and shuffled. The faculty staffing the procedure will draw an envelope from the stack prior to the surgical procedure appointment. Since the outcome of the study is the histologic healing, blinding of the surgeon is not necessary.

10.2. Study Intervention Compliance

Define how adherence to the protocol (e.g., administration of study intervention, use of device,) will be assessed, and verified (if applicable, e.g., plasma assays, electronic monitoring devices, daily diaries).

Patients will need to be present at each scheduled visit. Failure to attend any of the visits will result in exit from the study. All providers placing test and control materials as part of the study intervention will be trained and provided with detailed instructions to ensure methods are consistent and in compliance with the protocol. All faculty staffing residents are familiar with the study protocol and are able to verify the results of the procedure and measurements taken.

10.3. Permitted Concomitant Therapy

This section should be consistent with the medication restrictions in the inclusion/exclusion criteria previously listed. Describe how allowed concomitant therapy might affect the outcome (e.g., drug-drug interaction, direct effects on the study endpoints).

N/A

10.4. Rescue Medicine

List all medications, treatments, and/or procedures that may be provided during the study for "rescue therapy" and relevant instructions.

☒ *N/A, no rescue medicine*

11. Study Intervention Discontinuation

11.1. Discontinuation of Study Intervention

Describe the criteria for discontinuing the study intervention (e.g., halting rules), including any monitoring test(s) and associated clinical decision point(s). Include reasons for temporary discontinuation of the study intervention (e.g., type and quantity of adverse events), clearly stating the length of time, if applicable, and describe the data to be collected at the time of study intervention discontinuation and approaches for restarting administration of or re-challenging with study intervention.

Study will be discontinued if more than 5% of subjects present an adverse reaction such as infection or material recall. Such a reaction would be extremely rare as the study material is FDA approved and in the US market since 2016.

11.2. Continued Follow-up Discontinuation of Study Intervention

Describe efforts that will be made to continue follow-up of participants who discontinue the study intervention, but remain in the study for follow-up, especially for safety and efficacy study endpoints (if applicable). Reasonable efforts must be made to undertake protocol-specified safety follow-up procedures to capture adverse events (AE), serious adverse events (SAE), and unanticipated problems involving risks to subjects or others (UPIRSOs).

All patients that participate in the study, including those discontinued due to adverse reactions, will be followed until completion of the study or resolution of the adverse reaction (unless consent has been withdrawn).

12. Statistical Considerations

12.1. Statistical Hypotheses

State the formal and testable null and alternative hypotheses for primary and key secondary endpoints, specifying the type of comparison (e.g., superiority, equivalence or non-inferiority, dose response) and time period for which each endpoint will be analyzed.

Hypotheses: a.) No difference in % vital bone, % residual graft and % connective /other tissues between BioOss Collagen and Ossix Bone groups. b.) No dimensional differences in alveolar ridge after ridge preservation with BioOss Collagen or Ossix Bone.

12.2. Sample Size Determination

Include number of participants to recruit, screen, and enroll to have adequate power to test the key hypotheses for the study. Provide all information needed to validate your calculations and judge the feasibility of enrolling and following the necessary number of participants.

Power analysis revealed a sample size of 14 patients per group was enough to detect a mean difference in percentage of new bone formation of 1 SD by Mann-Whitney U test at the 0.05level with a power of 88.5%. Anticipating a potential 30% dropout rate and needing 14 fully compliant patient per treatment group, 22 patients will be enrolled in each group.

12.3. Populations for Analyses

Clearly identify and describe the analysis datasets (e.g., which participants will be included in each).

All study participants who complete the study intervention will be included in the analysis for all outcome measures.

12.4. Statistical Analyses

Include analysis of primary efficacy endpoints, secondary endpoints, safety analyses, and any planned interim analyses

The outcomes of the histologic and clinical parameters will be summarized with the sample size, mean, standard deviation, median, minimum and maximum. The significance of variation in the mean with group BioOss collagen or Ossix Bone will be assessed with two-sample *t*-testing. The significance of variation in the group effect with another variable will be assessed with an interaction term in a linear model. All statistical testing will be two-sided with a significance level of 5%. Spearman rank and Pearson correlations between clinical parameters and histologic parameters will be analyzed as well. All statistical analyses will be done with statistical software.

References:

1. Beck TM, Mealey BL. Histologic analysis of healing after tooth extraction with ridge preservation using mineralized human bone allograft. J Periodontol. 2010;81(12):1765-72.
2. Borg TD, Mealey BL. Histologic healing following tooth extraction with ridge preservation using mineralized versus combined mineralized-demineralized freeze-dried bone allograft: a randomized controlled clinical trial. J Periodontol. 2015;86(3):348-55.
3. Cook DC, Mealey BL. Histologic comparison of healing following tooth extraction with ridge preservation using two different xenograft protocols. J Periodontol. 2013;84(5):585-94.
4. Coomes AM, Mealey BL, Huynh-Ba G, Barboza-Arguello C, Moore WS, Cochran DL. Buccal bone formation after flapless extraction: a randomized, controlled clinical trial comparing recombinant human bone morphogenetic protein 2/absorbable collagen carrier and collagen sponge alone. J Periodontol. 2014;85(4):525-35.
5. Eskow AJ, Mealey BL. Evaluation of healing following tooth extraction with ridge preservation using cortical versus cancellous freeze-dried bone allograft. J Periodontol. 2014;85(4):514-24.
6. Hoang TN, Mealey BL. Histologic comparison of healing after ridge preservation using human demineralized bone matrix putty with one versus two different-sized bone particles. J Periodontol. 2012;83(2):174-81.
7. Whetman J, Mealey BL. Effect of Healing Time on New Bone Formation After Tooth Extraction and Ridge Preservation With Demineralized Freeze-Dried Bone Allograft: A Randomized Controlled Clinical Trial. J Periodontol. 2016;87(9):1022-9.
8. Wood RA, Mealey BL. Histologic comparison of healing after tooth extraction with ridge preservation using mineralized versus demineralized freeze-dried bone allograft. J Periodontol. 2012;83(3):329-36.
9. Frost NA BA, Galloway PB, Huynh-Ba G, Mealey BL. . The Decision-Making Process for Ridge Preservation Procedures Following Tooth Extraction. Clinical Advances in Periodontics 2014;4:56-63.
10. Corning PJ, Mealey BL. Ridge preservation following tooth extraction using mineralized freeze-dried bone allograft compared to mineralized solvent-dehydrated bone allograft: A randomized controlled clinical trial. J Periodontol. 2019;90(2):126-33.
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12. Araujo MG, Liljenberg B, Lindhe J. Dynamics of Bio-Oss Collagen incorporation in fresh extraction wounds: an experimental study in the dog. Clin Oral Implants Res. 2010;21(1):55-64.
13. Araujo MG, Lindhe J. Ridge preservation with the use of Bio-Oss collagen: A 6-month study in the dog. Clin Oral Implants Res. 2009;20(5):433-40.
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15. Hartman GA, Arnold RM, Mills MP, Cochran DL, Mellonig JT. Clinical and histologic evaluation of anorganic bovine bone collagen with or without a collagen barrier. Int J Periodontics Restorative Dent. 2004;24(2):127-35.
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