TITLE

Histological evaluation of alveolar ridge preservation using MInerOss® versus Osteogen plug® bone graft techniques: clinical study analysis part II.

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THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Main Consent Form

TITLE: Clinical Evaluation Of Soft Tissue Closure In Alveolar Ridge Preservation Procedures

PRINCIPAL INVESTIGATOR: Cimara Fortes Ferreira, DDS, MSc, PhD,MDS
University of Tennessee Health and Science Center
875 Union Ave, Memphis TN 38163

CO-INVESTIGATOR: Zacharia Kashlan, DMD
University of Tennessee Health and Science Center
875 Union Ave, Memphis TN 38163

1. KEY INFORMATION:

You are being given the opportunity to participate in this research study. The purpose of this consent form is to help you decide if you want to be in the research study.

The purpose of this study is to compare the OsteoGen® Bone Grafting Plugs, a calcium crystals and bovine (cow) collagen substance, and a cortico-cancellous bone chips mix with polytetrafluoroethylene (dPTFE) barrier membrane's ability to maintain the bone ridge in a tooth socket which could make that area more suitable for implants and removable dental appliances, after a tooth has been surgically removed.

The placement of a bone graft is the standard of care for individuals whom are found to have "too little" bone left after the tooth or teeth have been removed. This treatment is often recommended in persuit of a better treatment outcome for individuals that are considering dental implants and/or replacement appliances after a tooth or teeth have been removed. The bone grafting procedure is an optional treatment, meaning you do not have to have a graft placed because you had a tooth (teeth) surgically removed. Should you chose not to have the bone graft, you still may be able to have a dental implant placed in your mouth, or removeable dental appliances made for your mouth.

This is a Pilot study. A Pilot study is the first step of testing medical devices in humans, primarily to obtain safety and performance of the chosen materials.

The OsteoGen® Bone Grafting Plugs and Cytoplast™ GRB have been approved for use in this study.

Procedures:

Your extraction site will be randomly assigned (like the flip of a coin) to receive a one-step grafting solution (OsteoGen® Bone Grafting Plug) or a two-step titanium–reinforced high-density membrane (Cytoplast™ GRB). You have a 1 in 2 chance of receiving OsteoGen® Bone Grafting Plug or Cytoplast™ GRB. The investigator will not be the person who decides which you receive. A computer program that gives random numbers will be used to decide which you receive. It is not known whether OsteoGen® Bone Grafting Plug is as good as, better than, or worse than Cytoplast™ GRB.

Your participation in this study will last approximately 3 months. You will visit the clinic for

a total of eight (8) times, with a total time commitment of 4 and ½ hours over 3 months post-operatively after the ridge augmentation procedure.

The following procedures are being performed as standard of care and will be performed even if you are not enrolled in this study:

- Tooth extractions
- Bone ridge augmentation with bone grafting

The following procedures are being performed for research purposes only:

- Randomized to receive either Osteogen Bone Grafting Plug or Cytoplast GRB
- Recording of extraction site after 3-months
- Copying of information such as your dental and medical history
- Intra-oral photographs of the treatment site
- Use VAS10 to record pain levels
- 5 additional clinic visits

For a detailed explanation of the procedures, refer to the section of this consent form entitled, DETAILED PROCEDURES TO BE FOLLOWED.

Risks:

Some of the most common side effects from the study devices are discomfort of the gum tissue where the bone grafting plug was placed, numbness and a tingling sensation. These devices could also cause scarring of the tissue and infection at the site of the where the ridge augmentation was performed. In the OsteoGen® Bone Grafting Plug there is an occasional change of allergy to bovine collagen.

For a detailed list of the potential risks, refer to the section of this consent form entitled, RISKS ASSOCIATED WITH PARTICIPATION.

Benefits:

If you are randomized to receive Cytoplast™ GRB or OsteoGen® Bone Grafting Plug, they are likely to be as safe and effective in treating bone defects as it is when given outside the research setting. Both Cytoplast™ GRB and OsteoGen® Bone Grafting Plug are used as standard therapies for this condition. The results of this study may help people with bone defects in the future by providing a way to increase the bone in that area during active treatment.

You will benefit from this study if you receive the Osteogen plug for your treatment site as there will not be a need for a second surgical procedure; as necessary for the Cytoplast GRB for the removal of the non-resorbable membrane.

Alternatives:

You may receive Cytoplast™ GRB or OsteoGen® Bone Grafting Plug as treatment for ridge augmentation without participating in this study, as both of these materials are available and on the market for dental use.

If you decide not to enter this study, there are other choices available. These include: not having a bone graft placed in the extraction site, or having alternative bone graft materials placed like a magnesium enriched calcium phosphate or calcium sulfate. Ask the study doctor to discuss the alternative with you. You do not need to be in this study to receive treatment for your condition

You will receive dental treatment for the bone defect whether or not you participate in the study.

Voluntary Participation:
Your participation in this research study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Deciding to not take part in this research study will not change your regular dental care in any way.

If you are a student of University of Tennessee Health Science Center, participating or not participating in this study will in no way influence your grade in any course. If you are a resident or fellow of University of Tennessee Health Science Center, participating or not participating in this study will in no way influence your academic standing. If you are an employee of University of Tennessee Health Science Center, participating or not participating in this study will not affect your employment status.

2. DETAILED PROCEDURES TO BE FOLLOWED:

Up to 20 subjects needing tooth extractions, for a combined total of 20 extraction sites will be chosen for this study. It is possible for you to receive more than 1 extraction site operated on in this study and therefore potentially receiving both treatment options in this study.

The study will take place at the University of Tennessee Health Science Center, Department of Periodontology, located at 875 Union Ave, on the 5rd floor of the Dunn Dental Building, Memphis TN 38163. This is the only site for this study.

Visit 1 (this will take an additional 30min. at your dental visit)(standard of care visit)
At this visit you will be asked to:

- Read and sign this consent form and be given a signed copy for your records
- Complete information about your race, age, and birthdate
- Complete a medical history form

Then a licensed dental professional will:

- Perform an exam of the inside of your mouth.
- Record the tooth/teeth to be taken out of your mouth
- Take one (1) intraoral digital photograph of the chewing surface of the tooth to be taken out.

Lastly, the subject will be scheduled for the tooth/teeth to be taken out and be provided pre-surgery instructions for the surgery phase of treatment.

Visit 2/(Within 1 month after initial consult) (1 hour)(standard of care visit and research visit)
At this visit you will:

- Be asked questions about your continued enrollment in the study
- Have your medical history and medications reviewed since the last time you were in the clinic

Then the principal investigator and/or a member of his research team will:

- Conduct an oral exam of the inside of your mouth
- You will be randomly assigned (like the flip of a coin) to receive Cytoplast™ GRB (standard treatment) or the OsteoGen® Bone Grafting Plug into the area where the tooth was removed. You have a 1 in 2 chance of receiving the OsteoGen® Bone Grafting Plug. The investigator will not be the person who decides which you receive. A computer program that gives random numbers will be used to decide which you receive. It is not known whether the experimental treatment is as good as, better than, or worse than the standard treatment.
- Perform the tooth removal surgery and place the device you have been randomized to receive as the bone augmentation treatment
- After that, you will have stitches placed around the tooth removal site
- Take one (1) intraoral digital photo of the chewing surface of the site where the tooth was removed.
- Be instructed on how and when to answer questions about rating the amount of pain they have after treatment. This survey will be completed on days 1, 3, 5 & 7 post-operatively using the VAS by a website access. If the subject chooses paper format, 4 VAS print-outs will be given to the patient to take home to be filled at the end of each day indicated in the study. Each form will require the subject to circle the level of pain from no pain (“0”) to maximum imagined pain (“10”) for each of the indicated time periods.

Then, you will be instructed not use over-the-counter mouthwashes, antibiotic mouthwashes, alcohol, or brush the treatment area for two (2) weeks.

Lastly, you will be given post-operative instructions, and given prescriptions for pain medications to be taken as needed, and a 3-day supply of anitibiotic medications. You will also be asked to return back to the clinic to have the stitches removed in 12-15 days.

Visit 3: (7 days) (30 mins))(standard of care visit and research visit)
At this visit a licensed dental professional will:

- Review your medical history and medications since the last time you were in the clinic
- Ask questions about your continued enrollment in the study
- Have the stitches removed from the site where the tooth was removed
- Take one (1) intraoral photo of the chewing surface of the site where the tooth was removed and the ridge augmentation was preformed

If infection occurs in any of the two proposed procedures, the site will be treated just as standard of care, which includes: removal of the regenerative material with a special instrument; profuse irrigation with saline solution; decontamination with 3% tetracycline for 1 minute; profuse irrigation with saline solution; cleaning the extraction site with a special instrument to obtain clot and replacement of the graft as chosen by the what you were initially randomized to receive in this study.

Lastly, you will be asked to return to the clinic in 2 weeks for a follow-up visit.

Visit 4: (14 days) (30 mins)(research visit)
Same as Visit 3

Visit 5: (21 days) (30 mins) (research visit)
Same as Visit 4
Lastly, you will be asked to return to the clinic in 1 week for a follow-up visit.

Visit 6: (28 days) (30 mins)(research visit)
Same as Visit 5

Lastly, you will be asked to return to the clinic in 2 weeks for a follow-up visit.

Visit 7: (42 days) (30 mins) research visit)
Same as Visit 6

Lastly, you will be asked to return to the clinic in 4 weeks for a follow-up visit.

Visit 8: (56 days) (30 mins) research visit)
Same as Visit 7

Lastly, you will be given at-home instructions and dismissed from the study.

The standard of care tooth extraction and bone risdge augmentation procedures listed above would happen even if you were not enrolled in this study. However, being randomized to the standards of care treatment groups, answering questions about your participation, having information copied from your dental record, having digital photos, completing a consent form, medical history and demographic form, and reporting pain levels are all for research purposes only.

3. RISKS ASSOCIATED WITH PARTICIPATION:
All drugs can have side effects. Although not all or none of these side effects may occur, if they do occur, they may need medical attention. You must notify your study doctor about all symptoms, side effects, complaints, illnesses, or injuries which you experience during the course of the study regardless of whether or not you think these are related to the study drug. You should discuss these with your study doctor as well as your regular health care provider, if you choose.

As a result of your participation in this study, you are at risk for the following side effects.

Digital Photos

Very Rare (1%)

- Discomfort from mouth retractors used to hold back the lips

Bone grafting

Very Common (51-100%):

- Discomfort of the gum tissue where the bone grafting plug was placed
- Numbness and a tingling sensation

Very Rare (1%)

- Scarring of the tissue
- Infection at the site of the where the bone grafting plug was placed
- Failure due to infection

Cytoplast™ GRB may cause some, all, or none of the side effects listed below.

Very Common (51-100%)

- Discomfort of the gum tissue where the bone grafting plug was placed
- Numbness and a tingling sensation

Very Rare (1%)

- Scarring of the tissue
- Infection at the site of the where the bone grafting was placed (may result in graft failure)

OsteoGen® Bone Grafting Plug may cause some, all, or none of the side effects listed below.

Very Common (51-100%)

- Discomfort of the gum tissue where the bone grafting plug was placed
- Numbness and a tingling sensation

Occassional (6-20%)

- allergy to bovine collagen

Very Rare (1%)

- Scarring of the tissue
- Infection at the site of the where the bone grafting plug was placed(may result in graft failure)

There is a risk that your private identifiable information may be seen by people not involved in the research (such as if a researcher's computer is stolen or an electronic database is hacked). However, we will use very careful security measures (such as locks on file cabinets, computer passwords, etc.) to minimize the chance that any unauthorized persons might see your confidential information.

The research may involve risks to which are currently unforeseeable. You will be told about any new information that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

Surveys:
Completion of the VAS pain survey may make you feel uncomfortable or cause troublesome feelings or emotions. You may refuse to answer any of the questions and you may take a break at any time during the study.

4. CONFIDENTIALITY:

Research records
All your paper research records will be stored in locked file cabinets and will be accessible only to research personnel and those entities named below in this section, except as required by law (such as reports of child abuse, plans to commit suicide, etc.).

All your electronic research records will be computer password protected and accessible only to research personnel and those entities named below in this section, except as required by law (such as reports of child abuse, plans to commit suicide, etc.).

Your private information collected as part of this research, even if identifiers are removed, will not be used or distributed for future research studies.

Dental Records
Information about your participation in this study or the results of procedures performed in this study will be placed in your dental record.

Presentations/Publications
While individual details about your case might be provided in publications or presentations about this research, they will not be discussed in a way that would allow you to be individually identified as a participant.

Limits to Confidentiality
Information obtained during the course of the study, which in the opinion of the investigator(s) suggests that you may be at significant risk of harm to yourself or others, may be reported to a third party to protect the rights and welfare of those at potential risk.

Authorization to Use and Disclose Protected Health Information for Research Purposes
Under federal privacy regulations, you have the right to decide who can review and copy your identifiable health information (called "protected health information" or PHI). PHI collected in this study may include information such as:

- Past and present medical records
- Records about your study visits
- Records about phone calls made as part of this research
- Research records

By signing this consent form, you are giving your permission for the study doctor and the study staff to get your PHI from your doctor and/or facilities where you have received health care.

They may also share your PHI with:

- The Institutional Review Board (IRB) at the University of Tennessee Health Science Center
- The US Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) or other government agencies
- Your dental insurance provider

However, some of these organizations or institutions above do not have the same obligations to protect your PHI.

Your PHI will only be used and/or given to others:

- To do the research
- To study the results
- To see if the research was done correctly

Your PHI will be used until the study is completed.

You may withdraw or take away your permission to use and disclose your PHI at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you may not be able to stay in the study.

When you withdraw your permission, no new PHI will be gathered after that date. However, information that has already been gathered may still be used and given to others. The federal regulations allow you to review or copy your PHI that is used in this study.

However, in order to complete the research, your access to this PHI may be temporarily suspended while the research is in progress. Once the study is over, your right to review and copy your PHI will be reinstated.

5. COMPENSATION AND TREATMENT FOR INJURY:

You are not waiving any legal rights or releasing the University of Tennessee or its agents from liability for negligence. In the event of physical injury resulting from research procedures, the University of Tennessee does not have funds budgeted for compensation for medical treatment. Therefore, the University of Tennessee does not provide for treatment or reimbursement for such injuries.

If you are injured or get sick as a result of being in this study, call the study doctor immediately. The study doctor will provide acute medical treatment, and will provide you with a subsequent referral to appropriate health care facilities.

If you are injured or get sick as a result of being in this study, you and/or your insurance will be billed for the costs associated with this medical treatment.

No compensation will be available to you for any extra expenses that you may have as the result of research-related physical injuries, such as additional hospital bills, lost wages, travel expenses, etc.

No compensation will be available to you for any non-physical injuries that you may have as a result of research participation, such as legal problems, problems with your finances or job, or damage to your reputation.

6. QUESTIONS:

Contact Dr.Cimara Ferreira at (901) 448-4494 (office) if you have questions about your participation in this study, or if you have questions, concerns, or complaints about the research.

If you feel you have had a research-related injury or a reaction to the study devices, contact Dr. Cimara Ferreira at 954-579-9545 (cell phone)(24-hour/7-day telephone number).

You may contact Cameron Barclay, MSA, UTHSC IRB Director, at 901-448-4824, or visit the IRB website at http://www.uthsc.edu/research/compliance/irb/ if you have any questions about your rights as a research subject, or if you have questions, concerns, or complaints about the research.

7. PAYMENT FOR PARTICIPATION:

You will not be paid for participation in this research study.

8. COSTS OF PARTICIPATION:

You or your insurance company will be billed for:

- Tooth extractions

- Bone augentation and use of Cytoplast GRB

The cost for your participation will not exceed what you would normally incur with the standard of care treatment. If randomizized to receive the Osteogen plug, this will not be billed to you or your insurance.

You may want to talk with your insurance company about its payment policy for dental care or procedures performed as part of a research study. If your insurance company does not pay, you may be billed for those charges.

9. FUTURE CONTACT:

If we lose contact with you during the study for any reason (your phone number changes; your physical or email address changes; you are not responding to our attempts to contact you about your continued participation; etc.), we will attempt to find you or make contact with you in the following ways:

- The phone number(s) you provided to us will be called, but if you are not the person who answers, we will not say the title of the study or the fact that you are/were participating in a study.
- An email will be sent to the email address(es) you provided to us, you will be blind copied and the title of the study or the fact that you are/were participating in a study will not be listed in the subject heading.

Put your initials on <u>one</u> of the lines below:

_____We CAN attempt to find/contact you in the above ways.

_____We MAY NOT attempt to find/contact you in the above ways.

Please note that if we lose contact with you and there is new information about your participation in the study that could affect your safety, we will attempt to find you or make contact with you in any way possible.

Sometimes we wish to keep your contact information, medical diagnosis, and other health information in order to contact you in the future and tell you about other studies in which you might be eligible to participate.

Put your initials on <u>one</u> of the lines below:

_____We CAN keep your contact information and health information to ask you about participating in future studies.

_____We MAY NOT keep your contact information and health information to ask you about participating in future studies.

Main Consent Form

10. CONSENT OF SUBJECT:

You have read or have had read to you a description of the research study as outlined above. The investigator or his/her representative has explained the study to you and has answered all the questions you have at this time. You knowingly and freely choose to participate in the study. A copy of this consent form will be given to you for your records.

Signature of Research Subject (18 years +)	**Date**	**Time**

Printed Name of Adult Research Subject

Signature of Person Obtaining Consent	**Date**	**Time**

Printed Name of Person Obtaining Consent

In my judgment, the subject has voluntarily and knowingly given informed consent and possesses the legal capacity to give informed consent to participate in this research study.

Signature of Investigator	**Date**	**Time**