Protocol Title: The Combination of BioHorizon's Striate+ membrane in conjunction with MinerOss X Plug for Providing Hard Tissue Regeneration in Socket Preservation Procedure
Principal Investigator: David M. Kim, DDS, DMSc Faculty Advisor (if PI is a student):
Description of Study Population: Patients seen in the Harvard Dental Center pre-doctoral and post-doctoral clinics.
Version Date: 1/25/2023

Key Information

The following is a short summary of this study to help you decide whether or not to participate. More detailed information is listed later on in this form.

The goal of our research project is to provide detailed comparison and evidence of new bone formation in patients undergoing socket preservation utilizing two widely accepted treatment modalities that are used to maintain ridge dimension after a tooth extraction.

Why am I being invited to take part in a research study?

We have invited you to take part in a research study because you have expressed interest in implant therapy to replace a missing tooth, but you require an extraction first which could result in an insufficient amount of bone for implant placement.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You may discuss your decision with your family, your friends and/or your doctor.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research project is to assess the capability of new regenerative products in building bone prior to implant placement. The materials used in the study include a bovine (cow) bone graft and porcine (pork/pig) collagen membrane.

How long will I take part in this research?

We expect that you will be in this research project for 6 months which will include placement of dental implant.

What will I be asked to do?

You will be asked to attend 8 study visits. The first visit includes taking x-rays and photos to collect baseline data. The second visit will be the extraction and socket preservation surgery. The next 5 visits are follow ups. The seventh visit will include taking x-rays and photos to collect post-surgical data. The last visit will include implant placement. You will then be referred to a provider who will make a crown for the implant. The study team will make sure a treatment plan is created and a dental provider is assigned to you for the implant crown before beginning the surgical treatment.

More detailed information about the study procedures can be found under the *"What can I expect if I take part in this research*?" section.

Is there any way being in this study could be bad for me?

The study is expected to have favorable results; however the results may not always be satisfactory. The bone gain may be suboptimal and require further bone grafts at the time of implant placement. It is customary to include the potential need for bone grafting at the time of implant placement in the overall treatment plan. There is no extra cost.

The study is expected to have favorable results; however the esthetics may be suboptimal. Soft tissue grafting at the time of implant placement or prior to delivery of the implant crown may be needed. It is also customary to include the potential need for soft tissue grafting in the overall treatment plan. There is no extra cost.

More detailed information about the risks of this study can be found under the *"What are the risks and possible discomforts?"* section.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from taking part in this research. However, possible benefits may include reconstruction of your bone in the area missing teeth to allow for the optimal placement of an implant. The procedures are aimed to improve chewing function.

What happens if I do not want to be in this research?

Participation in research is voluntary. You can decide to participate, not to participate, or stop participation at any time without penalty or loss of benefits to which you are otherwise entitled. Instead of being in this research study, your choices may include implant placement with no socket preservation, teeth supported bridge or no treatment.

Detailed Information

To follow, please find more detailed information about this study than already provided above.

About this consent form

Please read this form carefully. It provides important information about participating in research. You have the right to take your time in making decisions about participating in this research. If you have any questions about the research or any portion of this form, you can ask us at any time. If you decide to participate in this research you will be asked to sign this form. A copy of the signed form will be provided to you for your record.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at Harvard Dental Center by contacting (617) 432-1434.

This research has been reviewed by a Harvard Longwood Campus Institutional Review Board (IRB). If you wish to speak with someone from the IRB, you may contact the Office of Regulatory Affairs and Research Compliance (ORARC) at irb@hsph.harvard.edu or 617-432-2157 (toll-free at 1-866-606-0573) for any of the following:

- If your questions, concerns, or complaints are not being answered by the research team,
- If you cannot reach the research team,
- If you want to talk to someone besides the research team,
- If you have questions about your rights as a research participant, or
- If you want to get information or provide input about this research.

Participation is voluntary

You are invited to take part in this research because you have expressed interest in implant therapy and would benefit from socket preservation prior to implant placement. It is your choice whether or not to participate. If you choose to participate, you may change your mind and leave the study at any time. Refusal to participate or stopping your participation will involve no penalty or loss of benefits to which you are otherwise entitled.

How many people will take part in this research?

About 20 people will take part in this research.

People who meet the following criteria are eligible for the study:
1. Male or female, between 20-70 years of age, who requests dental implant treatment and requires socket preservation procedure.
2. People who sign the consent form, participate and return for follow-up visits.
3. People without a complex medical history and currently not on medications that might complicate the results of the study.
4. Has a single-rooted tooth (upper and lower premolars to premolars) requiring extraction with two neighboring teeth on either side of it and intact bony walls.

People who meet the following criteria are ineligible for the study:
1. People who do not meet the above criteria or who will not attend all study visits.
2. People who have had a failing implant.

3. People who require additional bone buildup procedures in the area aside from the socket preservation procedure.
4. People who have untreated gum disease, cavities, or infection in the mouth near the surgical site.
5. People who have used nicotine-containing products within 3 weeks prior to surgery.
6. People who have Type 1 diabetes or uncontrolled diabetes.
7. People who have had a history of cancer within the past 5 years.
8. People who are nursing or pregnant.
9. People who are presently taking bone medications or have bone diseases.
10. People with an autoimmune disease or an allergy to materials used in the study.
11. Anticipated difficult extraction that may disrupt/fracture the bony walls.
12. People who are taking blood thinner medications.

What can I expect if I take part in this research?
As a participant, you will be expected to complete the following:

	Study Procedures
Visit #1	Standard of care baseline clinical examination and x-rays.
Visit #2	Standard of care socket preservation procedure will include administration of local anesthesia, tooth extraction, placement of bone graft and stitches used to close site. Half of patients will receive a dissolvable membrane over the bone graft material prior to stitches being placed. Oral hygiene and post-surgery instructions will be provided. Study specific procedures will include performing clinical measurements before the extraction, but after the local anesthesia. An ultrasound will also be used to measure gum thickness. Additional clinical measurements will be taken during the procedure while the surgical area is numb.
Visit #3-6	Standard of care follow-ups will occur at 2, 4, 8, and 12 weeks.
Visit #7	Study specific post-surgery clinical examination and x-rays.
Visit #8	Standard of care implant therapy will include administration of local anesthesia, placement of implant and stitches used to close site. Study specific procedures will include performing clinical measurements before implant placement, but after the local anesthesia. An ultrasound will also be used to measure gum thickness. Additional clinical measurements will be taken during the procedure while the surgical area is numb. A bone core biopsy will be collected from the socket where the graft was placed. The biopsy will be obtained during the time of implant placement following standard of care procedures.

What are my responsibilities?

As a participant, you are responsible for cooperating with the research protocol and attending all study visits.

What are the risks and possible discomforts?
As with all oral surgery procedures, you can expect swelling, bruising, discomfort, and minor bleeding after the procedure. In addition, the risk of nerve injury is possible but with proper treatment planning and dental x-rays, the risk can be minimized. The length the study may be inconvenient for some as it will require you to attend 8 appointments. We will be collecting demographic and medical information to be stored in a secure system and the risk of a breach in confidentiality is minimal.

We will require x-rays at multiple steps throughout the procedure. This allows for proper treatment planning to provide you with the best outcome and assess for important structures in the area (i.e., nerve location). CBCT scans will be collected before and after the bone graft procedure. The use of a thyroid collar/shield can not be used when taking these scans. The exposure to radiation is minimal. The effective dose for a CBCT scan small or medium field of view is 0.011-0.674 mSv.

Additionally, bone biopsies will be collected for research purposes. The risks associated with the biopsy is similar to any other oral surgery procedure. You may expect swelling, bruising, discomfort, bleeding and infection. The biopsies will be sent to a company specializing in biopsy analysis outside of Harvard. The biopsies will not contain your direct information and the company will not be able to identify you. The biopsies will be labelled using numerical values (#01, #02…). Once the analysis is completed, the biopsies will be destroyed, and the results will not be returned to you.

The sponsors will cover the cost of materials and procedures. The tooth extraction, socket preservation surgery, bone graft material and dissolvable membrane will be covered by BioHorizons Implant Systems. The first CBCT scan will be covered by Oral Reconstruction Foundation. The second CBCT scan will be waived. The dental implant, abutment and crown will be charged to you.

You will receive compensation at the end of the study. You will be given a $300 Amazon gift card, provided by funding through BioHorizons. If you withdraw before the end of the study, you will not receive compensation.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. You remain responsible for all deductibles, co-pays, and balances under your insurance. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay. A member of the study team can talk to you about what procedures would be considered standard care and the coverage of those costs.

Are there any benefits from being in this research study?
You are likely to benefit from this study as the treatment provided is standard of care. The objective is to build bone to allow for implant placement providing you with improved function.

What happens if I say yes, but I change my mind later?
You can leave the research at any time it will not be held against you. If you decide to leave the research, contact the research team so that continued care can be arranged with a dentist.
If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Can I still get medical care at Harvard Dental Center if I choose not to participate in this research*?* Yes, you may still get medical care at Harvard Dental Center if you choose not to participate in this study. Your decision will not change the care you receive now or in the future. Taking part in this research is your choice. If you decide to take part in this study, you may leave/stop the study at any time. There will be no penalty to you and your medical care will not be affected. If you would like to stop participating in this research you should let us know. We will make sure that you stop the study safely.

It is possible that the investigator may ask you to stop the study before it is finished. If this happens we will tell you why and arrange for other care for you if needed.

Will I be compensated for participating in this research?
The participants will not receive payment nor reimbursement during the study. The participants will not be compensated.

What will I have to pay for if I participate in this research?
The sponsors will cover the cost of materials and procedures. The tooth extraction, socket preservation surgery, bone graft material and dissolvable membrane will be covered by BioHorizons. The first CBCT scan will be covered by Oral Reconstruction Foundation. The second CBCT scan will be waived.

The dental implant, abutment and crown will be charged to you.

Outpatient Care Procedures	Estimated Dollar Amount	Covered by study	Patient responsibility	Source of Support
Tooth extraction (D7210)	$250	Yes		BioHorizons Implant Systems
1st CBCT scan (D0360)	$384	Yes		Oral Reconstruction Foundation
Socket preservation surgery (D7953)	$185	Yes		BioHorizons Implant Systems
Resorbable collagen membrane (D4266)	$324	Yes		BioHorizons Implant Systems
2nd CBCT scan	waived	Yes		
Dental implant placement (D6010)	$1278	No	Varies depending on insurance coverage	
Prefabricated abutment (D6056)	$654	No	Varies depending on insurance coverage	
Implant crown (D6065)	$1141	No	Varies depending on insurance coverage	

Costs that participants may also incur during the study:
- Transportation costs (i.e. parking, gas, public transportation)
- Opportunity costs (i.e. time in dental clinic will be forfeit where you might normally be at work)

What happens if I am injured as a result of participating in this research study?
If physical injury resulting from participation in this research should occur, although Harvard's policy is not to provide compensation, medical treatment will be available including first aid, emergency treatment and follow-up care as needed, and your insurance carrier may be billed for the cost of such treatment. In

making such medical treatment available, or providing it, the persons conducting this research project are not admitting that your injury was their fault.

For nerve injuries resulting in temporary or permanent loss of feeling in the treatment area, you will be referred to an oral surgeon at Mass General Hospital (55 Fruit Street, Wang Ambulatory Building, Suite 230, Boston, MA 02114, Phone: 617-726-2740). You are is responsible for financial charges associated with nerve repair. The risk of nerve damage can occur in any dental mandibular procedure, including local anesthesia and extractions.

If I take part in this research, how will my privacy be protected? What happens to the information you collect?

During this study, demographic, medical and dental information may be collected on Axium, a secure software, and recorded on paper. At the end of the study period, the paper documentation will be moved to an off-site storage facility which will then be destroyed after 10 years unless otherwise instructed. Data will not be used in the future. Information recorded on Axium is accessible only to the patient's treating dentists and research team members. These data are stored for life.

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organizations involved in this research.

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

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

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

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include failure to show up for study visits, changes in medical condition that might alter wound healing, or severe infection in the treatment area. You would then be referred for continued care to your existing dentist or if you do not have a dentist, then you will be referred to a provider located in the same clinic for a seamless transition. We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know? *[Include for sponsored research. Otherwise delete.]*
Instead of being in this research study, your choices may include: implant placement with no socket preservation, teeth supported bridge or no treatment. The important risks and possible benefits of these alternatives include: accept natural bone healing post-extraction that may result in bony defects, placement of a bridge requires treatment to adjacent teeth, and no treatment is acceptance of your current condition with no improvement in function.

Federal law provides additional protections of your medical records and related health information. These are described below.

Authorization to Use and/or Share Your Protected Health Information (PHI)
Federal law requires Harvard Dental Center to protect the privacy of health information that identifies you. This information is called Protected Health Information. In the rest of this section, we refer to this simply as "health information."

If you decide to take part in this research study, your health information may be used within Harvard Dental Center and may be shared with others outside of Harvard Dental Center.

We have marked with a ☒ how we plan to use and share your health information. If a box is not checked ☐, it means that type of use or sharing is not planned for this research study.

- **Health information about you that might be used or shared during this research**
  ☒ Information from your hospital/clinic records within this institution or elsewhere, that may be reasonably related to the conduct and oversight of the research study. If health information is needed from your doctors or hospitals outside this institution, you will be asked to give permission for these records to be sent to researcher(s) conducting this study.
  ☒ New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

- **Why health information about you might be used or shared with others**
  The reasons we might use or share your health information are:
  - To do the research described above
  - To make sure we do the research according to certain standards – standards set by ethics and law, and by quality groups
  - For public health and safety – for example, if we learn new health information that could mean harm to you or others, we may need to report this to a public health or a public safety authority
  - For treatment, payment, or health card operations

- **People and groups that may use or share your health information**
  1. **People or groups within this institution**
     ☒ Researchers and the staff involved in this research study
     ☒ Harvard review board that oversees the research
     ☐ Staff within this institution who need the information to do their jobs (such as billing, or for overseeing quality of care or research)

2. **People or groups outside the institution**
   - ☐ People or groups that we hire to do certain work for us, such as data storage companies, our insurers, or our lawyers
   - ☐ Federal and state agencies such as the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protection, and other U.S. or foreign government bodies, if required by law or involved in overseeing the research
   - ☐ Organizations that made sure hospital/clinic standards are met
   - ☐ The sponsor(s) of the research study, and people or groups it hires to help perform this research study
   - ☐ Other researchers and medical centers that are part of this research study
   - ☐ A group that oversees the data (study information) and safety of this research study
   - ☐ Other:

- **Time period during which your health information might be used or shared with others**
  Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

Your Privacy Rights

- You have the right <u>not</u> to sign this form permitting us to use and share your private information for research. If you <u>do not</u> sign this form you cannot take part in this research study. This is because we need the private information of everyone who takes part.

- You have the right to withdraw your permission for us to use or share your private information for this research study. If you would like to withdraw your permission, you must notify the person in charge of this research study in writing.

- If you withdraw your permission, we will not be able to take back any information that has already been used or shared with others. This includes information used or shared to carry out the research study or to be sure the research is safe and of high quality.

- If you withdraw your permission you cannot continue to take part in this research study.

- You have the right to see and get a copy of your private information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study.

Permission to Take Part in a Human Research Study

Statement of Consent
I have read the information in this consent form including risks and possible benefits. All my questions about the research have been answered to my satisfaction. I understand that I am free to withdraw at any time without penalty or loss of benefits to which I am otherwise entitled. I understand that if I am returning this form electronically or remotely that all pages must be sent back to the researchers.

I consent to participate in the study.

SIGNATURE

Your signature below indicates your permission to take part in this research.

Printed name of participant	
Signature of participant	Date
Signature of person obtaining consent	Date
Printed name of person obtaining consent	