9/10/2019

NCT03095976 Unique Protocol ID: 1608175133

Principle Investigator: Dr. Yusuke Hamada, DDS, MSD

Project title:
Amnion-Chorion Allograft Barrier Used for Root Surface and Guided Tissue Regeneration for Periodontal Intrabony Defects and Grade II Furcation Defects.

Protocol:

Patients who are referred to the Graduate Periodontics Clinic at Indiana University School of Dentistry for the treatment of severe chronic/aggressive periodontitis will be screened for possible participation in this study. Up to 20 subjects will be accepted into this study.

Written informed consent and authorization will be obtained from all participants and they will be given a copy of the signed informed consent documents.

The procedures listed below are all within standard care for a regenerative therapy around the teeth except the application of the membrane on the root surface prior to the bone grafting. No data collected for this study will be taken from sources outside of that already recorded for standard of care procedures.

Inclusion / Exclusion Criteria:

The following site inclusion criteria will be used:

1) ASA class I or II;
2) age $\geq$18 years old;
3) Non-smoker;
4) diagnosis of chronic or aggressive periodontitis previously treated with nonsurgical mechanical debridement;
5) patients have at least one two-wall intrabony defect in interproximal areas with radiographic evidence of an intrabony component of $\geq$ 4 mm, PPD $\geq$ 6 mm with 1-wall or 2-wall or combination of those defects or Glickman Grade II furcation involvement on buccal of mandibular or maxillary first or second molars without soft tissue exposure of furcation entrance;
6) tooth mobility Miller Grade $\leq$1;
7) more than 2mm of keratinized tissue with those selected teeth.

The following exclusion criteria will be used:

1) did not meet all inclusion criteria;
2) pregnancy or nursing woman;
3) subjects with active systemic or localized infection (exclude chronic periodontitis);
4) poor compliance or failure to maintain good oral hygiene as ascertained by the presence of full-mouth plaque score $\geq$ 20%;
5) restorations or caries on root surfaces or untreated endodontic infections;
6) participants received periodontal surgical treatment on the same site of this study within 2 years;
7) use of systemic or local antibiotics on the anticipated surgical sites during the past 3 months.

Clinical Measurements

A single calibrated examiner will perform clinical baseline and 6-month follow up measurements. O'Leary plaque score will be assessed. Six sites of each tooth of probing depth (PD), recession (REC) and clinical attachment level (CAL) will be recorded to the nearest millimeter with a University of North Carolina Probe (UNC Probe). For Glickman grade II furcation defects, in addition to the previous measurements, vertical probing pocket depth (VPD) and horizontal probing depth (HPD) will be measured.

Radiographic assessment will be performed with vertical bite-wing radiographs at baseline and 6-month post-surgical treatment. In order to maximize the standardization of the angulation of radiographs, bite registration will be taken prior to the first radiograph and utilized with beam-guiding device. It will be stored to be used post operatively. Sirona Dental Systems© with 7mA 60kV with 0.16s exposure time will be utilized for all radiographs. Digital #2 films manufactured by Air Techniques Inc. will be used for radiographic assessment. Bony defect (BD) will be defined as the most coronal point where the periodontal ligament space showed a continuous width. If several bony contours could be identified, the most apical one that crossed the root will be defined as the BD and the most coronal one as alveolar crest. If the cemento-enamel junction (CEJ) was destroyed by the restorative treatment, the margin of the restoration will be taken as a landmark.

Surgical Procedures:

All surgery will be rendered at the Graduate Periodontics Clinic at Indiana University School of Dentistry. All the patients will be treated under local anesthesia (2% lidocaine with 1/100,000epi or 4% articaine with 1/100,000epi). If the patient is willing to receive the surgery under intravenous or oral sedation, those services will be provided based on the necessity. After local anesthesia, intracrevicular incisions will be made and full-

thickness mucoperiosteal flaps will be raised both buccally and lingually; the surgeon will try to preserve the maximum extent of the marginal and interdental gingival tissue to obtain primary closure and membrane coverage. Vertical releasing incisions will only be used if necessary to gain access for defect debridement. The alveolar bone will be exposed at least 3 mm beyond the edges of the defect, and periosteal releasing incisions will be made to ensure complete membrane coverage at the time of suturing if necessary. All granulation tissue will be removed, the defects will be debrided, and the roots will be thoroughly scaled and root planed by hand instruments and ultrasonic devices. Following debridement, 17% EDTA solution with cotton pellet will be applied on the root surface for 2 minutes. After thorough irrigation with saline, BioXclude® (Amnion-Chorion Membrane: FDA Approved materials for intrabony defects) will be cut into two pieces. The amnion-chorion BioXclude membrane is regulated by the FDA under section 361 of the Public Health Service Act as a "Human cells, tissues, and cellular or tissue-based product" (HCT/P). The FDA does not require pre-market approval for these products like it would with drugs, biologics or devices. Therefore, this product will have no associated "investigational device exemption" (IDE) number. The FDA views using amnion chorion as a wound covering to aid in the healing of tissues throughout the body to be a "homologous use". One goes to the root surface, and coronal portion of the membrane has to be >3mm coronal of CEJ. Once applied the membrane, one drop of saline will be applied to obtain better adaptation of membrane on the root surface. Bone substitutes 0.5cc (Particle size of 0.25-0.5mm of Corticocancellous, Maxxeus®) will be hydrated for at least 10min prior to application, and applied into the defects. The bone particles will not exceed the edge of defects in order to avoid over fill. Following the bone graft will be delivered to the defect. The coronal portion of excessive membrane will be just folded over the graft materials. The other BioXclude membrane will be utilized over the grafts, and will always be placed coronal to the interproximal bone crest so that it completely covers the defect and extends 2 to 3 mm beyond the residual bone. No sutures, pins, or tacks will be used for membrane fixation or stabilization. The orientation of the membrane will not matter. Vertical or horizontal mattress sutures with 5-0 Proline (Monofilament/Nylon) will be placed in the interproximal tissues to obtain primary closure as much as possible.

Intra-surgical Clinical Measurements.

Intrabony defects: defect morphology will be measured (1 wall, 2 walls and/or those combinations) from the deepest aspect of the defect from the most coronal side of edge of the defects.

Postoperative Care and Maintenance:

All patients will receive antibiotics (875mg amoxicillin twice /day) for one week. If participants are allergic to amoxicillin, clindamycin (150mg twice/day) for one week will be prescribed. Analgesics (600mg ibuprofen three times/day) will be prescribed as needed for discomfort. Pt will be seen one, two and four weeks as a post-operative follow up. Patients will be advised to rinse twice daily with 0.12% chlorhexidine for 2 weeks after surgery. Patients will be instructed to refrain from brushing the teeth in the surgical area for 2 weeks. After that, they will be instructed to initiate brushing with an extra-soft toothbrush. Subjects will be recalled at 4-week intervals after 4weeks from surgical procedure for a period of 6 months for plaque scoring, oral hygiene instruction, and professional prophylaxis as needed. No subgingival probing or instrumentation will be performed at the experimental sites until the 6-month follow-up appointment.

Statistical Analysis:

Due to the nature of this pitot study, no sample size justification estimated were performed. Means and standard deviations for all parameters will be calculated. The paired-sample t test will be used to assess the statistical significance of the difference between the initial and the 6-month visit within group. Difference will be considered statistically significant at the $P < .05$. All data analysis will be performed using statistical software. (Microsoft Excel.)

Informed consent form:

PRINCIPAL INVESTIGATOR:	Yusuke. Hamada, DDS, MSD
ADDRESS OF STUDY SITE:	Indiana University School of Dentistry 1121 West Michigan Street Indianapolis, IN 46202
DAYTIME TELEPHONE:	(317) 274-5121
AFTER HOURS TELEPHONE:	In a study related emergency only, call (317-874-7860)

INTRODUCTION
You are being asked to volunteer for a dental research study. You were chosen as a possible subject because you are an adult attending a visit at the periodontal clinic at Indiana University (IU) School of Dentistry. Before agreeing to be in this study, you should read this consent form which describes the purpose, procedures, benefits, payment, and risks of the study. No promises or guarantees can be made as to the results of the research study. Please ask as many questions as you want so you can decide whether you want to be in the study.

This study is being conducted by Dr. Y. Hamada of the (IU) School of Dentistry. The Amnion-Chorion membranes to be used in this study were donated Snoasis Medical, LLC. All remaining funds required to conduct the study were provided by the IU School of Dentistry.

BACKGROUND AND STUDY PURPOSE
Bone allografts and membrane allografts are used in dentistry to treat bony defects due to the tooth loss and gum diseases. An Amnion-Chorion membrane allograft is used in the medical field as well as dentistry to treat a wound surface since this membrane can accelerate the wound healing. Typically in dentistry a bone graft is placed over the bone defect and is covered with a membrane allograft. In this study we will place the membrane allograft against the root surface of the defect area first and then place the bone graft over it and then cover the bone graft with an additional membrane. The purpose of this pilot study is to evaluate the use of the membrane on the root surface before placing the bone graft. We will study how much your probing depth, recession and clinical attachment level changes as a result of placing this membrane on the root from measurements taken before and after your surgery.

HOW LONG THE STUDY WILL LAST AND THE NUMBER OF SUBJECTS PARTICIPATING
This study will last about six months. Your study visits will be the same days as your treatment visits. If you agree to participate, you will be one of up to 20 adult subjects participating in this study.

WHAT WILL HAPPEN DURING THE STUDY
You will be given a treatment plan for your periodontal care. What will be identified on the treatment plan will be procedures and measurements considered “standard of care”, meaning they are procedures that would be performed regardless of whether or not you are in a research study. What will not be standard of care will be the placement of the membrane over the root surface before placing the bone graft during surgery. There are published studies that show the use of this membrane on the root surface for to treat gum recession, but this is not considered standard of care at the IU School of Dentistry. All data collected for this study will come from procedures and measurement associated with your recommended treatment plan. By being in this research study you are agreeing that we can place the membrane over the root surface and use data we collect as a part of your visits for this research study. You are not being asked to do anything in addition to what is written here or have any extra procedures performed that would not be done anyway as a part of your treatment.

POSSIBLE SIDE EFFECTS AND RISKS OF THE TREATMENT
There are risks associated with the treatment and surgery. These risks will be explained to you in your treatment consent. There could be unknown risks associated with the membrane being placed over your root surface during surgery. This risk is believed to be low since there are published articles of other dentists who have performed this procedure and because this member is used in medicine and dentistry to stimulate bone growth in various parts of the body.

Potential loss of confidentiality of research records is also a risk. To reduce this risk, all study records and data will be stored in locked cabinets and encrypted, password protected computer files that only study personnel can access. With the exception of the forms you sign, a unique study number is what will identify your study records.

POSSIBLE BENEFITS OF THE STUDY
There are no additional health benefits to participating in this study beyond what you will receive by undergoing your periodontal treatment. This study could help us better understand the use of this membrane on the root which could help others in the future.

ALTERNATIVES TO TAKING PART IN THE STUDY
You do not have to be in this research study to have periodontal treatment. You may choose to have the standard of care periodontal treatment (the membrane would not be placed over the root surface before placing the bone graft during surgery) at the IU School of Dentistry without being in this study or to seek standard of care periodontal treatment from a private practice outside of Indiana University.

LEGAL RIGHTS
You will not lose any of your legal rights as a research subject by signing this consent form.

RELEASE OF YOUR MEDICAL RECORDS, DISCLOSURE OF INFORMATION AND PRIVACY
Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Your identity will be held in confidence in reports in which the study may be published and databases in which results may be stored. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study sponsor, study investigator and his research associates, the Indiana University Institutional Review Board or its designees and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP).

PAYMENT FOR INJURY RELATED TO THE STUDY
In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled. If you are participating in research that is not conducted at a medical facility, you will be responsible for seeking medical care and for the expenses associated with any care received.

WHOM TO CONTACT
For questions about the study or a research related injury, please call Dr. Hamada or his staff at (317) 278-1087. For emergencies that you feel may be related to this study that fall after regular business hours, call our emergency answering service at (317)-274-7297. One of the researchers will be contacted and will call you back as soon as possible. If you want to reach the researcher during regular business hours (8:00 am–5:00 pm weekdays) but can't, call the Indiana University (IU) Human Subjects Office at (317) 278-3458 or toll free at (800) 696-2949.

For questions about your rights as a research participant or to discuss problems, complaints or concerns about a research study, or to obtain information or offer input, call the IU Human Subjects Office at (317) 278-3458 or (800) 696-2949.

PAYMENT FOR BEING IN THE STUDY
You will not receive a cash payment for your participation. However, if you decide to participate in the study, your bone graft and membrane procedures will be covered by the study funds. The estimated value of this is $454.00.

YOUR PARTICIPATION IN THE STUDY
You may refuse to be in this study, or you may leave the study at any time, without punishment or loss of benefits to which you are entitled and without affecting your future relationship with Indiana University. The study dentist may take you out of the study without your permission at any time for the following reasons:

- if it is discovered that you do not meet the study requirements
- if the study is canceled
- if it appears to be medically harmful to you

ADDITIONAL COSTS
There is no cost to you for participating in this study.

AGREEMENT TO BE IN THE STUDY
Please do not sign this form until a study person has reviewed the form with you. After the review, in signing the consent form you are agreeing to the following statements:

- I have had time to read all pages of this Informed Consent Document.
- The content and meaning of this information has been fully explained to me.
- I have been offered a chance to ask questions.
- I am satisfied with the answers to all of my questions.
- I understand that if I do not take part in the study, I will not be penalized or lose any benefits to which I am otherwise entitled.
- I agree to voluntarily participate in this study.
- I understand that I may withdraw my consent to be in the study at any time.
- I certify that all information I will give, including my medical history, is true and correct to the best of my knowledge.
- I know that it is my responsibility to tell the study doctor about all changes in my physical or mental health during the study.
- I acknowledge that I will get a copy of this signed and dated Informed Consent Document for my records.

Printed Name of Study Subject

Signature of Study Subject **Date and Time**

Printed Name of Person Explaining Informed Consent

Signature of Person Explaining Informed Consent **Date and Time**