THREE-DIMENSIONAL MEASUREMENT OF SOFT TISSUE CHANGES FOLLOWING SURGICAL CORRECTION OF RECESSION DEFECTS

by

Ryan Andrew Kaye, D.M.D
Lieutenant, Dental Corps
United States Navy

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Naval Postgraduate Dental School
Uniformed Services University of the Health Sciences
Bethesda, Maryland

CERTIFICATE OF APPROVAL

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MASTER'S THESIS

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This is to certify that the Master's thesis of

Ryan Andrew Kaye, D.M.D

has been approved by the Examining Committee for the thesis requirement for the Master of Science degree in Oral Biology at the June 2019 graduation.

Research Committee:

[redacted]

Glen Imamura, D.D.S.
CAPT, DC, USN
Professor, Dental Research
Thesis Supervisor

[redacted]

John Wilson, D.M.D, M.S
CAPT, DC, USN
Chairman, Periodontics Department

[redacted]

Keith Merchant, D.D.S, M.S
CDR, DC, USN
Program Director, Periodontics Department

[redacted]

John Bissell, D.D.S, M.S
CDR, DC, USN
Faculty, Periodontics

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Ryan Andrew Kaye
Periodontics Department Graduate Program
Naval Postgraduate Dental School
May 2019

NAVAL POSTGRADUATE DENTAL SCHOOL
Ryan Andrew Kaye

May 2019

ABSTRACT

"**THREE-DIMENSIONAL MEASUREMENT OF SOFT TISSUE CHANGES FOLLOWING SURGICAL CORRECTION OF RECESSION DEFECTS**"

RYAN ANDREW KAYE, D.M.D
NPDS PERIODONTICS, 2019

Directed by: GLEN IMAMURA, D.D.S., PROFESSOR, DENTAL RESEARCH
Naval Postgraduate Dental School

Introduction: Historically, periodontal research evaluating the efficacy of root coverage procedures used the periodontal probe to obtain clinical measurements. This method has several inherent inaccuracies and does not allow for evaluating volumetric changes in the tissues. **Purpose**: Optical scanning of stone models may increase the accuracy of these measurements and provide information about volumetric tissue changes following gingival augmentation procedures. **Methods:** Thirty subjects will be consented and enrolled. A periodontal probe will be used to measure; gingival recession (GR), probing depth (PD), clinical attachment level (CAL) and width of keratinized tissue (KT) at baseline, 3 and 6 months post-operatively. At each of these visits alginate impressions will be taken to generate stone models. An optical scanner will be used to generate a stereolithography file of each model. Anatomic landmarks on the models will be used to establish digital GR measurements. Digital GR measurements will be used to calculate digital percent root coverage (RC) at 3 and 6 months. Images of baseline, 3 and 6 month models will be generated using software (3-Matic^{TM}). The 3 and 6 months images will be superimposed over the baseline image to determine volumetric changes. Finally, conventional probing measurements will be compared to the digital measurements. **Results:** To date, 2 subjects have been enrolled, and 3-month data has been obtained on a total of four surgical sites using digital analysis. The average digital percent root coverage for the four treated sites is

50.98% after 3 months. Volumetric analysis demonstrates that the tissue volume at the treated sites increased by an average of 51.7mm^3 after 3 months. **Discussion:** Data collection is ongoing.

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LIST OF ABBREVIATIONS

GR – Gingival Recession

PD – Probing Depth

CAL – Clinical Attachment Level

KT – Keratinized Tissue

FGM – Free Gingival Margin

CEJ – Cementoenamel Junction

RC – Root Coverage

3-D – Three Dimensional

WRNMMC – Walter Reed National Medical Military Center

NPDS – Naval Postgraduate Dental School

CHAPTER 1: INTRODUCTION

Mucogingival surgery is a common treatment modality used for the coverage of exposed root surfaces. Historically, research conducted on the efficacy of root coverage procedures has most commonly employed the use of a periodontal probe in order to obtain clinical measurements of recession defect size, probing depth, and clinical attachment level. This method, although used frequently, presents several inherent issues. The variability of periodontal probes, even within the same manufacturing lot, can produce measurement differences in excess of 0.5mm[1,2]. The difficulties associated with measuring steep inclines or non-linear surfaces, as well as standardization of a reference point, probe location, and probe angulation can result in significant inaccuracies[3]. In addition, the fixed reference point most commonly used is the cemento-enamel junction (CEJ). In many cases, the CEJ is difficult or impossible to detect[4]. Consequently, intra- and inter-examiner agreement is frequently insufficient, resulting in pre- and post-operative descriptions of soft tissue that are inaccurate and difficult to reproduce[5,6].

Vertical soft tissue changes measured with a periodontal probe are typically linear measurements from the free gingival margin to a fixed reference point, such as the CEJ, which can be compared over time. Tissue thickness is inherently more difficult to measure and typically involves trans-mucosal probing with endodontic instruments[7], ultrasonic devices[8], bone sounding with periodontal probes[9], direct measurement with a caliper during flap surgery[10], or subjective estimation. These methods only allow for measurement of tissue thickness at a single point, and provide little information about volumetric changes within the treated area[11]. Therefore, there is currently a lack of a standardized or reliable method for measuring changes in tissue volume.

Researchers have recently begun to utilize digital scans of three dimensional (3D) models to analyze soft tissue volumes. In 1997, Mehl et al. described the principle of the optical 3D

scanner, which uses triangulation of a light line projected onto a charge-coupled device (CCD) at a certain triangulation angle[12]. This generates a data point cloud that corresponds to the subject, which can then be used to create a three-dimensional model known as a stereolithography (STL) file in a process called reconstruction. In this study, the STL file can be used to identify the free gingival margin (FGM) and the CEJ. The distance between these two points is then measured to determine the gingival recession (Figure 1). STL files can be generated at multiple timepoints, then superimposed and automatically matched to each other, so long as 3 points which have not changed over time can be triangulated. This allows for analysis of surface changes that occur over time within a specified region of interest, such as the height of the free gingival margin (Figure 2) and changes in tissue volume (Figure 3).

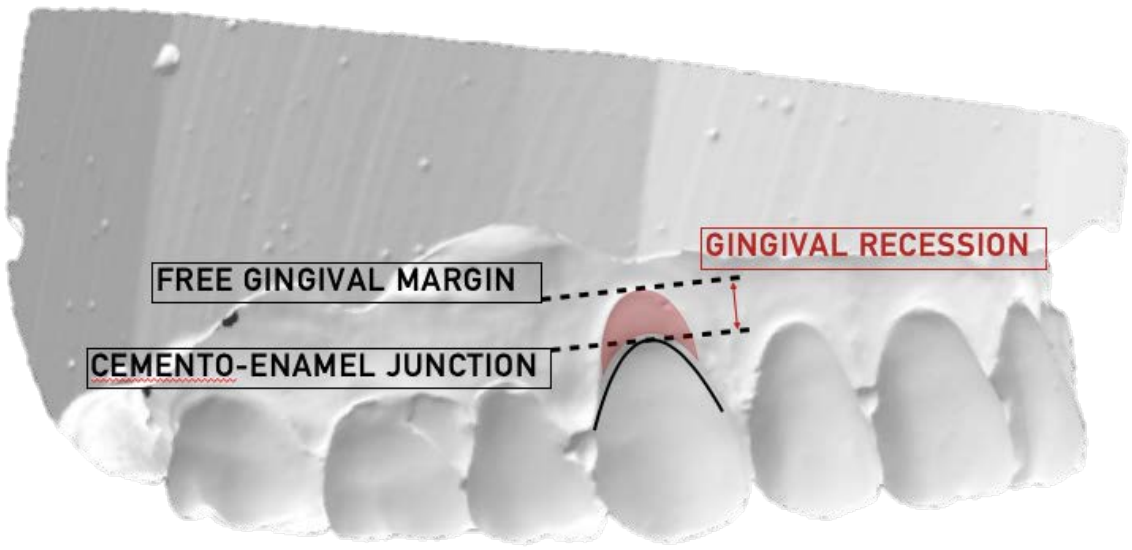


Figure 1: The free gingival margin (FGM) and cemento-enamel junction (CEJ) are identified on the STL file. Gingival recession (GR) is then measured as the distance between the FGM and CEJ.

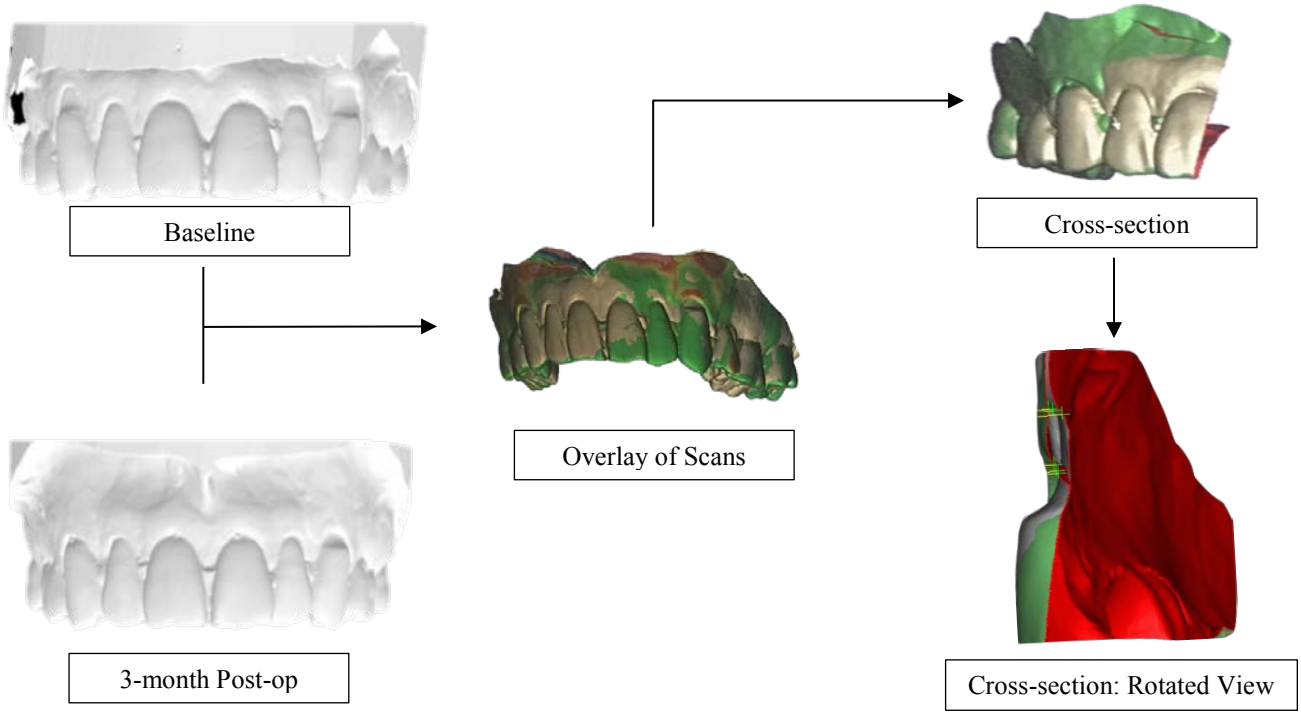


Figure 2: The baseline and 3-month post-op STL files are overlaid. The overlaid STL files are cut in cross-section and rotated, allowing for direct visualization of the pre- and post-op FGM as well as the CEJ. This allows for measurement of linear tissue height changes as well as percent root coverage.

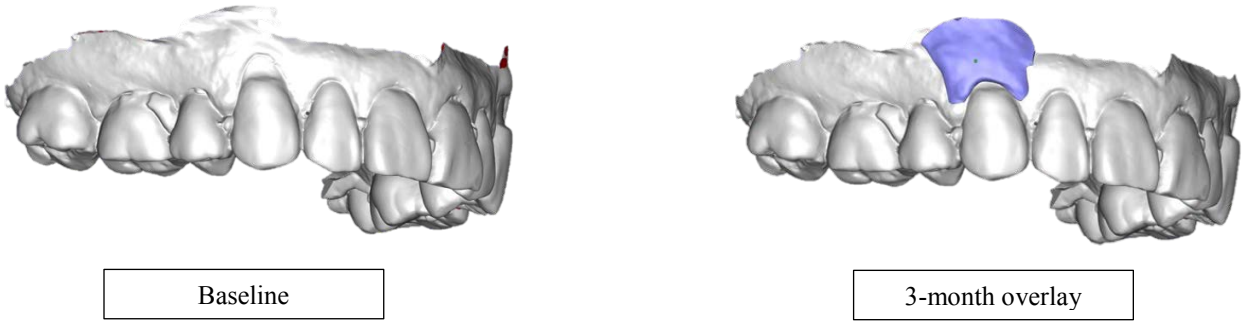


Figure 3: Volumetric analysis of soft tissue changes within a specified region of interest (blue) at pontic sites by superimposing stereolithography (STL) files at baseline and 3-months post-op.

Several studies have shown that using 3D imaging was an acceptable method to store and analyze dental study models for research purposes. Measurements made on these 3D scans are accurate and reproducible. Studer et al. made measurements of casts using a projection system to evaluate tissue volume[12]. The results of the study proved the applicability of this system for measurement of 3D soft tissue changes over time. However, the clinical applicability of the system was limited by the time required for analysis and the necessity of using complicated appliances. Windisch et al. described a promising new method of measuring soft tissue volume on edentulous ridge defects with a 3D optical system[14]. This optical system was shown to be highly accurate and yielded measurements with high reproducibility. It also allowed for analysis of soft tissue changes that were obtained after augmentation procedures. Leifert et al. confirmed the accuracy of the 3D optical system by demonstrating that the mean difference between measurements on digital models and physical casts was less than 0.5mm[15]. That same year, the clinical applicability of this method was further demonstrated in a study that applied 3D imaging to volumetrically assess alteration of the ridge contour after extraction socket preservation treatment[11]. Another study utilized a similar method to document volumetric soft tissue changes of the interdental papilla[16]. Bienz et al. described a method of overlaying stereolithography (STL) files from baseline, 5 and 10 years post-grafting at pontic sites and specifying a region of interest within which soft tissue volumetric changes could be analyzed[17].

Lehmann et al. outlined a novel technique for assessing soft tissue volume in gingival recession defects with the use of a digital scanner[4]. Through repeated scans of casts obtained via silicone impressions, they were able to show that the data was highly stable and reproducible, with a standard deviation of less than 0.1mm between scans. Schmitt et al. used an optical 3D scanner to evaluate casts pre- and post-surgically of beagle dogs undergoing soft tissue grafting

procedures[18]. They concluded that their method of analysis was viable for evaluation of soft tissue volume changes; however, more research was needed in order to confirm the data obtained in the study. Rebele et al. demonstrated the successful use of optical scans to track soft tissue healing after grafting procedures by analyzing volume differences within a region between points in time[19]. Study models were optically scanned and superimposed, allowing for evaluation of healing within a region of interest at grafted sites.

A number of different optical scanners are commercially available, including both intra-oral and desktop versions. Intra-oral scanners eliminate the need for a stone model to be poured from a physical impression, while desktop scanners that employ white LED light offer increased resolution. The Degree of Freedom HD desktop scanner™ (DOF Inc.) has two high-resolution cameras that provide a single data set, increasing precision and accuracy while reducing noise (unwanted variations in brightness or surface texture in an otherwise homogenous image). The combined resolution of the dual cameras is 2 megapixels, with an accuracy of 10 micrometers[20]. Disadvantages of this technology include the cost of the scanning armamentarium and the need for dedicated training. Digital scans may provide the ability to make measurements that are more accurate than traditional probing, as the 3-matic software used in this study allows for measurements to the nearest 0.01mm. Their use in this study may provide additional information on the value of the machine within the research setting. The purpose of this study is to determine the efficacy of using digital measurements to track changes in tissue height, volume, and thickness before and after gingival grafting with a coronally advanced flap with a collagen matrix (CM) with and without enamel matrix derivative (EMD). In addition, a comparison will be made between the measurements obtained clinically in Part One to those obtained digitally in

this study in order to determine the level of correlation of digital to clinical measurements. Conventional percent root coverage (RC) and digital percent RC will also be compared.

CHAPTER II: MATERIALS & METHODS

This a is the second part of a two-part prospective, double-blinded, randomized, split-mouth study of Miller Class I, II, or predictable class III recession defects. In part one, treatment will involve paired recession defects on opposite sides of the same arch. One defect will receive CM+EMD (Experimental), while the other will receive CM (Control) alone. Clinical measurements of probing depth, recession, clinical attachment level, and width of keratinized tissue will be made intraorally with a periodontal probe. In part two, the same measurements will be made on STL files of stone models of the same patients treated in part one. The study was approved by the WRNMMC Institutional Review Board. Details of the study are as follows:

Subject Population:

All eligible beneficiaries ages 18 or older evaluated at the Naval Postgraduate Dental School Periodontics Clinic and diagnosed with bilateral gingival recession will be eligible to participate. Up to 30 subjects will be enrolled to obtain 24 evaluable subjects (estimated attrition: 20 percent) with up to 60 matching defects. This sample size is required to achieve an 80 percent likelihood of observing a statistical difference between the paired groups with an alpha=0.05, a minimally clinically significant difference of 0.5mm, and an assumed standard deviation of 0.85mm. These estimates were derived from a recent study that has tested an equivalent treatment condition of CM+CAF[21].

Study Procedures:

1. Initial Phase
    a. Subject is referred to Naval Postgraduate Dental School (NPDS) Periodontics for periodontal treatment.
    b. Staff member provides study brief during screening exam.

c. Principal investigator (PI) or associate investigator (AI) notified and introduced to subject.

d. Patient is given periodontal evaluation to determine if he/she meets inclusion/exclusion criteria for the study. Those patients meeting study criteria will be provided an informational handout about the study to read (see Appendix F: Informational Handout).

e. Full written disclosure of the study protocol including option to receive treatment without being part of the study is presented to the subject. Investigator addresses all of the subject's questions and concerns.

f. If the subject is willing to participate, consent and HIPAA forms are completed and signed. If the subject is uncertain, he/she will be permitted to take all forms home to decide.

g. Once consent is obtained, specific recession defects will be identified and subject will be given a coded subject identification number by the study PI.

2. Non-surgical Phase

a. In accordance with standard of care procedures at the Periodontics Department, subjects will be offered the option of having the surgery performed using: only local anesthesia, a combination of oral anxiolysis using triazolam and local anesthesia or a combination of intravenous moderate sedation with midazolam and fentanyl and local anesthesia. The use of sedation is standard care at NPDS Periodontics and sedation in any of these forms will not affect the surgical procedure or the parameters of this study.

3. Surgical Phase
    a. The surgical provider will be a faculty member or resident of NPDS Periodontics. All surgeries will adhere to the standard of care for the procedure, according to the protocol of the CM+EMD vs. CM only recession coverage study.
4. Post-Operative Phase
    a. Subjects will be recalled at 1, 2, 4, and 6 weeks to monitor post-operative healing and remove plaque /deposits at the surgical site.
    b. Sutures will be removed no earlier than 2 weeks
    c. At 6 weeks, patients will be instructed to resume normal hygiene using a soft toothbrush.
    d. Subjects will be recalled at the 3 and 6 month mark (each +/- 2 weeks) following surgery to continue to assess healing, remove plaque, reinforce oral hygiene and collect research data. The 3 and 6 month probing measurements (GR, PD, CAL and width of KT) will be collected by a study investigator at these appointments. Additionally, impressions for stone models will be made by study investigators at the 3 and 6 month follow-up appointments.
    e. At 6 months, the subject will be referred back to the primary provider for continuation of dental care. This will complete their participation in the study.
5. Digital Analysis phase:
    a. Stone models of the maxillary and mandibular arches will be captured at baseline (pre-operative), 3 and 6 months post-operative to assess healing. The following standardized procedure will be followed in taking impressions:

i. A tray size will be selected that is slightly larger than the arch.
ii. Room temperature water will be measured using a graduated cylinder according to the instructions on the alginate powder package, based on the number of scoops to be used (typically 2 scoops will be used).
iii. An alginate scoop will be filled with powder, leveled with a spatula, and added to the water.
iv. The alginate will be hand mixed for approximately 1 minute, until a smooth creamy consistency is achieved, loaded in the tray, and maxillary or mandibular impressions taken. The alginate will be allowed to completely set before the tray is removed.

b. Stone models will be poured from the alginate impressions within a maximum of one hour. The stone will be mixed and poured according to the following protocol:
    i. The recommended amount of cold water from the dental stone package will be measured with a graduated cylinder.
    ii. 30 mL water will be poured into the mixing bowl. 100g dental stone will be added from the package to the water. The dental stone and water will be mixed under vacuum until a thick but fluid-like consistency is achieved (20-30 seconds).
    iii. A stone vibrator will be used on the mixture at a low setting to remove any air bubbles.
    iv. The alginate impression will be placed on the dental vibrating machine. A small amount of dental stone will be added to the most

distal tooth with the metal spatula. The stone will be allowed to flow in an anterior direction through all the occlusal surfaces inside the impression while rotating the impression on the dental vibrator to remove additional air bubbles that come to the surface.

v. Once the occlusal surfaces have been carefully covered, additional stone will be added to fill the impression. The impression will be placed on the vibrator for 2 to 3 seconds to ensure the dental stone is evenly distributed in the alginate impression.

vi. The stone models will be left undisturbed for 45 to 60 minutes until the material completely sets.

vii. The stone models will be digitally scanned within 3 days of pouring the model.

c. A Degree of Freedom™ (DOF) scanner will be used to scan subjects stone models obtained at baseline (pre-operative), 3 months, and 6 months (post-operative). The coded STL image files will be uploaded and opened in 3-Matic™ software. Digital GR measurements at baseline (pre-operative), 3 months, and 6 months (post- operative) will be made in an analogous manner to clinical GR measurements. Distances from the cementoenamel junction to free gingival margin will be measured on the uploaded image files using the software measurement tool. The data will be entered onto data collection sheet.

d. At the end of the data collection phase, the study PI will unmask each subject's data to identify which tooth in the pair received CM and which received CM + EMD.

Statistical Analysis

Significance for all independent analyses will be set at a global alpha = 0.05. The coded STL image files obtained from scanning each of the stone models obtained at baseline, 3 and 6 months post-operatively will be matched and overlaid using 3-Matic software. Changes in vertical height of the FGM, as well as volumetric soft tissue changes, will be analyzed within the region of interest corresponding to the surgically treated teeth. The following calculations will be made:

a. A digital percent RC, calculated using the following formula:
    i. Digital % RC = (digital post-operative GR - digital pre-operative GR / digital pre-operative GR
b. Volumetric soft tissue changes from:
    i. Baseline to 3 months
    ii. Baseline to 6 months
    iii. 3 months to 6 months
c. A comparison will be made between conventional percent RC and digital percent RC, calculated as follows:
    i. The difference between percent RC and digital percent RC will be plotted over time, and linear regression will be used to quantify the relationship and will be reported as R^2.

Data will be reported to the nearest 0.01mm.

CHAPTER III: RESULTS

Thus far, 2 patients have been enrolled in the study and completed surgical treatment. Four sites have been treated in total, consisting of two maxillary canines and two mandibular premolars. 3-month data have been obtained for all treated sites. The baseline recession depth was similar for all patients (Table 1).

Table 1: Baseline Recession Depth

	Right Side	**Left Side**
Subject 1	3.12mm	3.10mm
Subject 2	2.91mm	3.02mm

For the four treated sites, the average digital percent root coverage measured is 50.98%, with a range of 15.9% to 95.0% (Table 2). There was a notable difference between the root coverage in the two patients, with the root coverage on subject one being dramatically lower.

Table 2: Linear Change in Vertical Tissue Height at the Free Gingival Margin

	Right Side	**Left Side**
Subject 1	0.50mm	0.62mm
Subject 2	2.12mm	2.87mm
Average (all sites)	1.53mm	

Table 3: Digital Percent Root Coverage at 3 months

	Right Side	**Left Side**
Subject 1	15.9%	20.1%
Subject 2	72.9%	95.0%
Average (all sites)	50.98%	

Volumetric analysis demonstrated a significant increase in volume at all treated sites. The average gain was 51.65mm^3, with a range of 34.31mm^3 to 69.01mm^3 (Table 3).

Table 4: Tissue Volume Gain

	Right Side	**Left Side**
Subject 1	45.95mm^3	57.35mm^3
Subject 2	34.31mm^3	69.01mm^3
Average (all sites)	51.65mm^3	

CHAPTER IV: DISCUSSION

With the limited data obtained thus far, this study has demonstrated that digital analysis is a viable method for measurement of recession defect size, changes in gingival margin height over time, and volumetric changes in soft tissue. It appears that based on these results, digital analysis is a more accurate method for measuring soft tissue defects and changes. This is in part due to the fact that digital measurements are reported to the nearest μm, while in Part One of the study, the measurements obtained with a UNC-15 periodontal probe are reported only to the nearest 0.5mm. To the author's knowledge, this is also the first study that has demonstrated the possibility of measuring volumetric changes in soft tissue after gingival augmentation.

Digital analysis may have significant impact on periodontal research in the future, as data that may ultimately influence clinical decision making would be far more accurate. This technique also allows for volumetric analysis, which previously would have been difficult or even impossible to perform with clinical evaluation alone. The primary disadvantage to this technique is that it takes more to time to overlay the STL files and perform digital analysis than to take intraoral measurements with a periodontal probe.

Four sites were treated in two patients. The average digital percent root coverage was found to be 50.98%, while in Part One of this study, the reported average percent root coverage was 60%. This seems to indicate that the root coverage was slightly overestimated in Part One; however, this data did not reach statistical significance due to the small N. As more data is collected over the course of this study, it will remain to be seen whether this trend continues. There was a notable difference between the root coverage in the two patients, with the root coverage on subject one being dramatically lower. This was likely due to the fact that both of the treated teeth in subject one were adjacent to dental implants, which lack an interproximal

connective tissue attachment[22]. The data obtained from this patient are expected to be outliers in the final data set. Moving forward, the exclusion criteria will be modified to include adjacent dental implants.

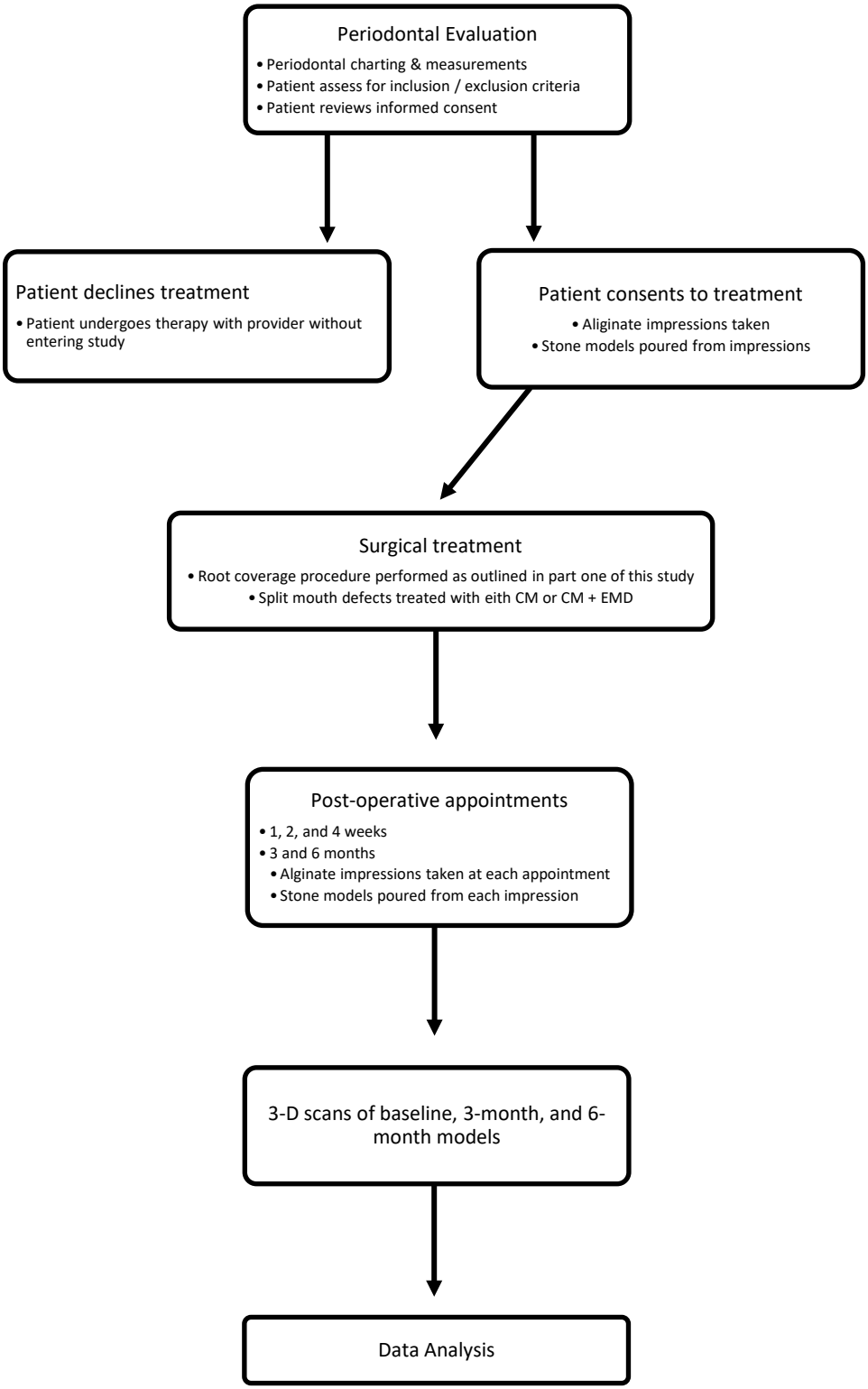
The average gain in soft tissue volume was 51.65mm^3. An increase in soft tissue volume was noted at all treated sites, even those in subject one which demonstrated a low percentage of root coverage. Evaluating changes in tissue volume may have a myriad of applications in addition to soft tissue grafting, including guided bone regeneration and tooth extraction.

In this study, STL files were obtained by scanning stone models with a desktop scanner. The stone models were poured from alginate impressions. Alginate has a lower degree of accuracy than other impression media[23]. The rationale for choosing alginate is that at the Naval Postgraduate Dental school, the standard of care is to take an alginate impression for each patient. In the future, this study may be repeated using an intra-oral scanner to directly obtain an STL file clinically. Intra-oral scanners are less accurate than desktop scanners[24], but acquiring the scan intra-orally would eliminate any inaccuracies introduced by the alginate impression material or in the stone model.

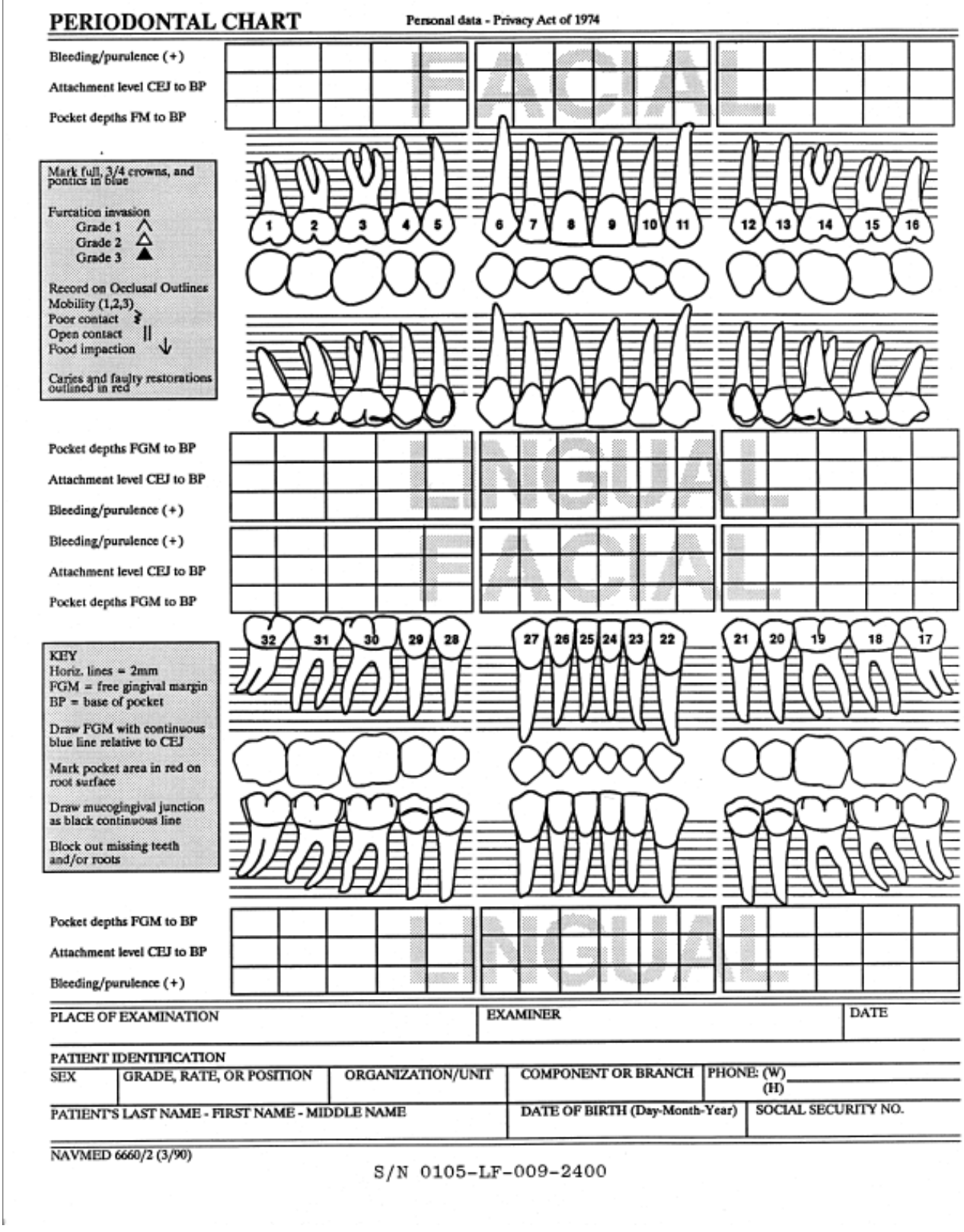
CHAPTER V: CONCLUSIONS

Measurement of soft tissue changes with three-dimensional analysis is a viable option, allowing for direct measurement of changes in the free gingival margin pre- and post-operatively, as well as for measuring changes in tissue volume. In addition, digital analysis allows for measurements that are more accurate than those made with a periodontal probe.

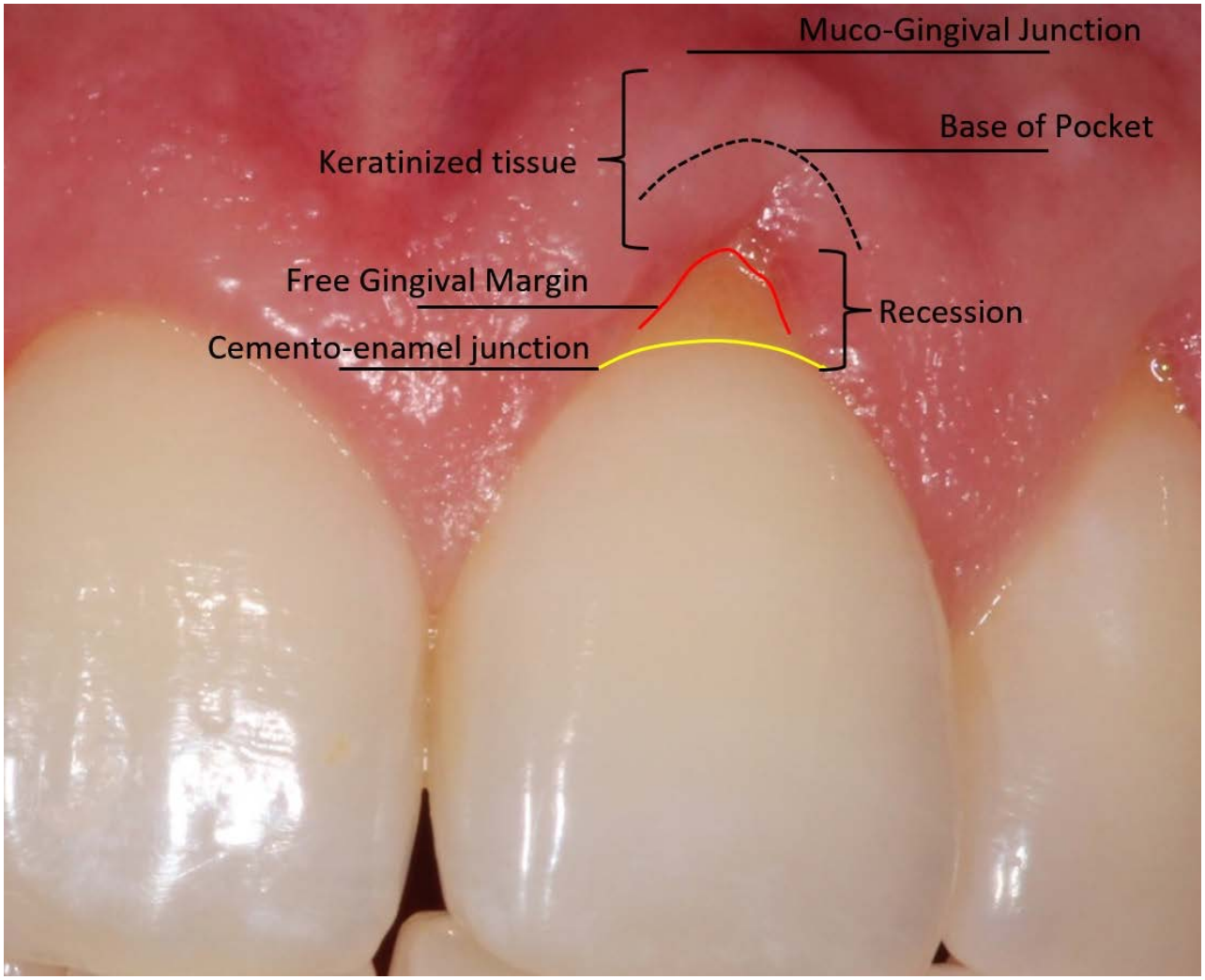
APPENDIX A: STUDY DESIGN



APPENDIX B: PERIODONTAL CHARTING FORM



APPENDIX C: MEASUREMENT LANDMARKS



Measurements:

Amount of Recession = Cemento-enamel Junction to Free Gingival Margin

Probing depth = Free Gingival Margin to Base of Pocket

Clinical Attachment Level = Cemento-enamel Junction to Base of Pocket

Width of Keratinized Tissue = Free Gingival Margin to Mucogingival Junction

APPENDIX D: STL DATA COLLECTION SHEET

Subject ID	
Date	
Provider	

Measurements: Reference point to FGM (to nearest 0.01 mm)	**Tooth#**	**Tooth#**
Baseline		
2 months		
3 months		
6 months		

Reference point:

_____Incisal edge

_____CEJ

APPENDIX E: MASTER DATA LIST

Research Master List: CM vs CM + EMD

Code	Name	Phone #	Email	Last 4 of SSN	Meet Incl / Excl Criteria?	EMD on left / right?	Withdrawn from study?
1							
2							
3							
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APPENDIX F: INFORMATIONAL HANDOUT

Study on Surgical Correction of Gingival Recession
Informational Handout

The Periodontics Dept. at the Naval Postgraduate Dental School is conducting a research study evaluating the correction of gingival recession (also called gum recession) defects using tissue grafting procedures. Autografts consist of tissue taken from the palate (roof of the mouth) to serve as the grafting material to correct the defect. Autografting has been the gold standard for treating gum recession. A xenograft is graft material taken from an animal. Xenografting has gained popularity because it avoids having to take tissue from the patient's palate. NPDS uses Mucograft®, a xenograft derived from pigs. It has demonstrated success similar to autografts. The collagen in Mucograft® has been tested to be free of disease and it is further processed to be free of biologic contaminants. It is considered extremely safe. It employs the same surgical technique used for autografts. Emdogain®, a liquid biologic material, is also derived from pigs. Emdogain® used alone has also shown success in grafting procedures. Our goal is to evaluate whether adding Emdogain® to Mucograft® makes a difference in the treatment of gum recession.

You have been asked to participate in this study because you have 2 teeth requiring gum recession treatment. If you decide to participate, Mucograft® will be saturated with Emdogain® and used as the graft material for one tooth. Mucograft® *without* Emdogain® will be used as the graft material for the other tooth. Treatment for gingival recession normally requires 7 appointments; 2 pre-operative appointments, 1 surgical date, and 4 follow-up appointments (1, 2, 4 and 6 weeks) to monitor your healing by taking measurements. A study participant will be required to return to the clinic for 2 additional appointments at 3 and 6 months following surgery to monitor healing and take measurements. If you do not wish to participate in the study, you can still to receive grafts for your gum defects at the Periodontics Clinic.

This is the first study to independently assess Mucograft® in combination with Emdogain®. Both products have been approved by the Food and Drug Administration in treating gum recession defects. If you are interested in participating, a study investigator will meet with you to more thoroughly explain the study. Your participation is voluntary. Meeting an investigator does not obligate you. If you have any further questions, you can contact the principal investigator, LT Ryan Kaye at 301-295-2127. Thank you for your consideration.

APPENDIX G: POST-OPERATIVE INSTRUCTIONS

PERIODONTICS DEPARTMENT
NAVAL POSTGRADUATE DENTAL SCHOOL
Bethesda, Maryland

For best healing and a minimum of complications, please read and follow these instructions carefully

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You may have been given one or more of these medications:

PAIN MEDICATIONS:	_____ Motrin 800 mg:	*1 tablet every 8 hours.* Do not double up on dosage.
	_____ Norco 5/325 mg:	*1 tablet every 6 hours for pain control.* It can be taken in addition to ibuprofen. This medicine can make you drowsy. Therefore, do not drive or operate machinery while taking this drug. Additionally, do not take with alcoholic beverages; the alcohol will make you sleepier, but will not decrease your comfort.
ANTIBIOTICS:	_____ Doxycycline 100 mg:	*2 tablets the day of surgery, then 1 tablet every day for 30 days.*
	_____ Amoxicillin 500 mg:	*1 tablet four times a day for 7 to 10 days.*
	_____ Clindamycin 300 mg:	*1 tablet four times a day for 7 to 10 days.*
RINSES:	_____ Peridex (Perioguard):	*1 bottle, rinse twice-a-day as directed on the bottle, starting the day following surgery.* Do not brush or floss at the surgical site unless instructed to do so.
ANTI-INFLAMMATION:	_____ Medrol Dose Pack:	Take as directed on the package, starting today. Be sure and take the full first row of tablets (first six tablets) today.

The following are a list of post-operative considerations during healing:

BLEEDING:	There may be slight bleeding from the surgical for 1-2 days after surgery. Your saliva may appear slightly reddish. This is common. If you notice an increase in bleeding please contact us.
SUTURES/STITCHES:	You may have sutures placed in your mouth. They may have to be removed in the future. Please leave the sutures alone as much as possible. Early removal or the loss of sutures may impair healing.
DRESSINGS:	There may be a gummy type of dressing or pack over the surgical area. It is there for your comfort. If it falls out before your first post-operative appointment and you are comfortable, it is fine to leave it out. If the surgical site is uncomfortable and you would like the dressing replaced please contact me.
DIET:	It is very important to maintain a soft diet for at least a week. Chew as much as possible on the side opposite the surgery. This is not the time to start a diet. Please maintain your caloric and fluid intake as at pre-surgical levels. You will not heal well if you are dehydrated or undernourished. Please do not drink using a straw.
ORAL HYGIENE:	It is very important not to brush or floss the surgical site until given express instructions. Normal brushing and flossing procedures can traumatize the tissue and impair healing. You may brush and floss those areas not affected by the surgery. To keep bacteria under control a prescription mouth rinse has been written for you. Initially, use the mouthwash as a rinse. Later you may be instructed to use a cotton-tipped applicator, dipped in the mouthwash, to swab along the gum line of the surgery site. Use a capful (15ml) of the mouthwash twice a day, morning and bedtime, after brushing/flossing your non-surgically treated teeth. You may notice a mild tooth staining as a result of the mouthwash. This is not permanent; the stain will be removed with scaling/polishing at your follow-up appointments. Please do not use a Water-Pik or other irrigator unless instructed to do so.
PHYSICAL ACTIVITY:	Avoid strenuous physical activity (to include running and heavy lifting) for 72 hours. Additionally, no vigorous spitting, rinsing, or speaking (yelling). Forceful movements at the site of surgery will negatively affect healing.
SWELLING:	You may experience some swelling. This is common and usually peaks at 2-3 days after surgery. Thereafter you should expect to see a return to normal. To decrease swelling you can apply ice to the site for the first 3-4 hours after surgery. Please call if the swelling appears to increase after the third day, or if you are concerned.
SMOKING	Smoking is deleterious to healing. We advise you to stop smoking for as long as possible after surgery. Stopping smoking will improve potential healing and also improve your overall periodontal health.
FOR SINUS LIFT SURGERY PROCEDURES	You may also have received nasal decongestant tablets and spray. Please use these medications as directed on the package. In addition, avoid blowing your nose. If you need to sneeze, please sneeze with your mouth open. Please inform your doctor if you develop sinus congestion that is not minimized with your medications or if you notice any bleeding or discharge from your nose.

If you have any problems or questions, please do not hesitate to call me at 301-295-0077. If there is an emergency you may page your doctor through an automated system. Instructions will be given after dialing 1-800-759-8888. The PIN# for your doctor is: _____

Your follow up appointment is scheduled for: _____ _____

NPDS, Bethesda

APPENDIX H: IRB REVIEW SUBMISSION APPROVAL

WALTER REED NATIONAL MILITARY MEDICAL CENTER
INSTITUTIONAL REVIEW BOARD
8901 WISCONSIN AVENUE
BETHESDA MARYLAND 20889-5600

DATE: March 23, 2018

FROM: WRNMMC IRB
TO: Ryan A Kaye, DMD

SUBJECT: WRNMMC IRB REVIEW OF Initial Review Submission Form

PROJECT TITLE:	Porcine Collagen Matrix With and Without Enamel Matrix Derivative for the Treatment of Gingival Recession Defects (GME)
IRB #	WRNMMC-2017-0123
REFERENCE #:	879875
ACTION:	Approved
APPROVAL DATE:	03/23/2018
EXPIRATION DATE:	03/22/2019
REVIEW TYPE:	Administrative Review
RISK LEVEL:	Minimal Risk 32 CFR 219 / 21 CFR 56

The above referenced human subject research project has been approved by the Walter Reed National Military Medical Center Institutional Review Board (IRB) with modifications required to secure approval on 02/15/2018. An administrative review of the modifications has been completed and approval has been secured on 03/23/2018. This approval is limited to the activities described in the approved protocol and supplemental documents.

The IRB complies with all U.S. regulatory requirements related to the protection of human research participants. Specifically, the IRB complies with 32 CFR 219, 45 CFR 46 with applicable subparts (if applicable), 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812, and 45 CFR 164.508-514. In addition, the IRB complies with International Conference on Harmonization (ICH) E6, Good Clinical Practice (GCP) guidelines, to the extent required by the U.S. Food and Drug Administration and Department of Defense Instruction 3216.02.

Submission Components Reviewed:

Submission Components			
Form Name	Version		Outcome
Review Response Submission Form	Version 4.0		Approved
Initial Review Submission Form	Version 1.1		Approved
EIRB Protocol Template	Version 1.4		Approved
Study Document			
Title	Version #	Version Date	Outcome
Emdogain FDA Approval	Version 1.0	01/12/2018	Acknowledged

Mucograft FDA approval	Version 1.0	01/12/2018	Acknowledged
Scientific Review	Version 1.0	12/14/2017	Acknowledged
Signature Sheet	Version 1.0	12/14/2017	Acknowledged
Data Collection Sheet	Version 1.0	12/14/2017	Acknowledged
Informational Handout	Version 1.0	12/05/2017	Approved
Master List	Version 1.0	12/05/2017	Acknowledged
Study team education/training			Acknowledged
Post OP Instructions	Version 1.0	11/27/2017	Acknowledged
Study Consent Form			
Title	Version #	Version Date	Outcome
Revised Consent with HIPAA	Version 1.4	01/08/2017	Stamped Approved

Notes:

All future research must be conducted in accordance with this approved submission. You are required to do the following:

- This is an IRB approval only. You may not begin your research until you have received a Command Start Letter from COL Peter J. Weina, MC, USA, Chief, Department of Research Programs. Please contact COL Weina at (301) 400-1239 or peter.j.weina.mil@mail.mil.

- Prior to initiating your research study, the PI must ensure all applicable agreements have been reviewed and approved by the Department of Research Programs to comply with WRNMMC requirements.

- The IRB approved, stamped consent/HIPAA authorization form(s) must be duplicated and used to enroll subjects. Keep the signed, original consent forms in your project file; give each subject a signed copy of the consent form.

- If the collection and/or analysis of data for your project are to continue beyond one year, you must submit a report for continuation. In order for ongoing human subject research projects to be reviewed, approved and processed by the IRB within this time constraint, you may be sent an automatic reminder approximately 60 days prior to your review date. You are reminded that it is also your responsibility to maintain your research files in a secured, locked location.

- You are reminded to provide all amendments, unanticipated problems involving risk to subjects or others, deviations, and any other relevant information to the Department of Research Programs (DRP) via the EIRB system at https://dmrncac.dhhq.health.mil for reporting to the IRB.

- You are reminded that any presentations or publications regarding this project must be appropriately cleared through the publication clearance process.

- Per IAW DoDD 8910 and DoDI 1100.13, you are reminded that information collection forms (i.e. surveys) must be reviewed by the designated Information Management Control Officer for WRNMMC prior to distribution.

APPENDIX I: COMMAND START LETTER

25 April 2018

From: CHIEF, DEPARTMENT OF RESEARCH PROGRAMS, WALTER REED NATIONAL MILITARY MEDICAL CENTER, BETHESDA, MD 20889

To: LT Ryan A Kaye, DMD

Subject: Command Start Letter for Research Project IRB# WRNMMC-2017-0123, title of: *"Porcine Collagen Matrix With and Without Enamel Matrix Derivative for the Treatment of Gingival Recession Defects (GME)"*

1. Congratulations! You have been granted approval to conduct your research project at Walter Reed National Military Medical Center, Bethesda (WRNMMC).

2. Your research protocol was approved after administrative, scientific, and ethical review by the Department of Research Programs (DRP) WRNMMC Institutional Review Board (IRB) or by an Exempt Determinations Officer. Study-specific agreements and IRB committee stipulations have been met, or have been determined to be unnecessary based on your study review.

3. You, as the study Principal Investigator (PI) are ultimately responsible for the development, conduct, and management of all aspects of the research study, to include submitting annual Continuing Review documents no less than 45 days prior to study expiration date (included in your IRB approval) and submitting modifications to your protocol through the electronic IRB (EIRB) system to the Office of the IRB. It is also your responsibility to ensure all members of the research study team (associate investigators, research coordinators and assistants, collaborators, consultants, mentors, etc.) are technically competent, have been properly trained, and are appropriately qualified to perform the procedures described in the research, and that they understand their roles and responsibilities according to the study protocol. The IRB must approve all modifications to the study protocol prior to implementation unless there is an immediate risk to research subject safety. Immediate communication with the Office of the IRB is expected when this exception occurs. Examples of modifications to the protocol requiring prior approval from the IRB include, but are not limited to, a change to the onsite PI or addition of study team members, an increase in sample size, addition of other data points or data collection sites, sources of outside funding, or changes in the inclusion or exclusion criteria for study participation. All amendments, deviations, adverse events, or any other pertinent information must be submitted to DRP using the Electronic IRB System (EIRB) as a new submission within this protocol.

4. If applicable for your research, the IRB-approved, stamped consent form is to be duplicated and used to enroll study participants into your research study. Keep the signed, original consent form(s) in your project file and provide a copy of the signed consent form to each participant enrolled in your study for their records. Assurance of the quality of each participant's consent must be done in accordance with current Federal regulations. This includes ensuring that any "designee" who obtains consent on the PI's behalf is completely familiar with the protocol and is qualified to perform this responsibility. Such designees who are involved in the conduct of the research, but not included as a study team member on your research protocol, should be documented in a Delegation of Authority Log, with the designee's role clearly identified.

5. If the collection and/or analysis of data for your project are to continue beyond your project expiration date of one year, you must submit a report for continuation (Continuing Review). Otherwise, your project will expire as outlined in your IRB Notification Letter. If your study expires prior to obtaining approval of your Continuing Review (CR) by the IRB, all research-related activities must stop immediately. Please allow adequate time (minimum of 45 days) for review and approval of your CR to avoid expiration of your study. Ensure you replace the study informed consent document with the new IRB-stamped version of the informed consent document at the time of Continuing Review.
6. You may be sent an automatic reminder from the EIRB system or a DRP staff member approximately 90 and/or 60 days before your CR is due. This is a courtesy email; ultimately it is your responsibility as the study PI to maintain your research files and know how and when your submissions are due to the IRB. All study-related materials should be maintained in a secured, locked location or within password protected computer files with access only by study team members.
7. Promptly report all unanticipated problems involving risks to subjects or others (UPIRSO), related serious adverse events (SAE), or any protocol deviations that affect subjects' safety or rights and/or the integrity of the study to the Director of the Office of the IRB, Robert Roogow and/or Human Protections Administrator, Dr. Sanjur Brooks.
8. If you are deployed or leave WRNMMC, you must transfer the research records to a new PI and submit the modification to change to do so PRIOR to leaving WRNMMC. Custody of all original data must be retained by the research division in which they were generated. An investigator who moves to another institution may submit a written request to the Director, WRNMMC, to remove copies of the data from WRNMMC. This request must contain an itemized description of the data and must specify where the data will be located in the future. These requests will be submitted through DRP.
9. All products of dissemination, including publications, abstracts, manuscripts, case reports, presentations, and book chapters that report on the results or conduct of a WRNMMC approved protocol; include WRNMMC-assigned personnel or patients as subjects; or reports citing WRNMMC in the title or byline) or in any way reflect a WRNMMC affiliation must be submitted for WRNMMC publication clearance and approval before publication or presentation.
10. If your research involves standardized information gathering, such as a survey, you may be subject to DoDD 8910 (Information Collection and Reporting) as well as DoDI 1100.13 (Surveys of DoD Beneficiaries). You as the PI have the responsibility to comply with any applicable rules or clearance procedures to assure your approval for doing research is not rescinded by higher level review. (A survey is defined as a systematic data collections, using personal or telephonic interviews, or self-administered questionnaires, in paper or digital format, from a sample or census of 10 or more persons as individuals or representatives of agencies that elicit attitudes, opinions, behavior, and related demographic, social, and economic data to identical questions that are to be used for statistical compilations for research or policy assessment purposes.)
11. Please do not hesitate to contact DRP for assistance or the undersigned at (301) 400-1239 or peter.j.weina.mil@mail.mil with questions or concerns.

PETER J. WEINA
COL, MC, USA
CHIEF, DEPARTMENT OF RESEARCH PROGRAMS

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