COMPARISON OF EFFECTS OF RIDGE PRESERVATION WITH AND WITHOUT BUCCAL OVERLAY GRAFTING

by

MAJ Adam R. Lincicum

Thesis submitted to the Faculty of the
US Army Advanced Education in Periodontics Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Master of Science 2017

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Adam R. Lincicum
Army Advanced Education Program in Periodontics
Uniformed Services University
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Initiator

1. USU Principal Author (Last, First, Middle Initial): Lincicum, Adam, R
2. Academic Title: Master's Degree Candidate
3. School/Department/Center: Postgraduate Dental College, US Army, Periodontics
4. Phone: 706-787-5102
5. Email: adam.r.lincicum.mil@mail.mil
6. Clearance: ☑ Paper ☐ Article ☐ Book ☐ Presentation ☐ Other
7. Title: COMPARISON OF EFFECTS OF FREEZE-DRIED BONE ALLOGRAFT HUMAN RIDGE PR
8. Intended Publication/Meeting: Master's Thesis
9. Required by: PDC
10. Date of Submission: 31 May 2017

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Name (Last, First, Middle Initial) Lancaster, Douglas D.

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ACKNOWLEDGMENTS

I would sincerely like to thank the faculty and mentors at the U.S. Army Advanced Education Program in Periodontics at Fort Gordon, Georgia for assistance in this research endeavor. Without their insight, ideas, guidance and continued support this research project would not have been possible. In particular, the insight and hard work of Dr. Brandon Coleman has been instrumental in achieving approval from the Institutional Review Board, in the day-to-day conduct of the study, and providing guidance from proposal development through thesis completion. The research proposal class of Dr. Douglas Dickinson was crucial in outlining the goals of the study and developing an effective and organized proposal. Many thanks to my co-residents, who served as surgeons and assisted in data gathering, all in the course of providing efficient and effective patient care. Without the constant support of my family, specifically my wife Julie, through this trying time in residency, none of this would be achievable. Last, but not least, I would like to my co-researcher, Dr. Ken Hussey for his cooperation, ideas, and unending work ethic in organizing and conducting our research projects in concert with each other.

ABSTRACT

Comparison of Effects of Ridge Preservation With and Without Buccal Overlay Grafting: Lincicum, MS Oral Biology, 2017

Thesis directed by: MAJ Brandon J. Coleman, Deputy Director, US Army Advanced Education in Periodontics

In this single blind, randomized clinical trial, two freeze dried bone allograft (FDBA) grafting techniques for ridge preservation were compared, one with socket grafting alone, and one with socket grafting and a buccal overlay. The goal of the study was to determine if either grafting technique is superior in minimizing ridge resorption following tooth extraction. Two different membranes are utilized for each of these techniques, Cytoplast, a dense PTFE membrane, and BioXclude, an amnion-chorion derived resorbable membrane. Following baseline data gathering, 28 patients were randomized into one of the four treatment groups based on grafting technique and membrane use: no overlay with either Cytoplast or BioXclude, and buccal overlay with both membranes. An initial small volume CBCT was taken of the extraction site, and surgery was conducted in accordance with the randomized technique. Data were gathered at surgery, 1, 2 and 4 weeks post-surgery, and a final CBCT image taken at 4 months after surgery. Three patients were removed from the study for varying reasons, and another patient had non-diagnostic CBCT scans, resulting in 24 patients available for analysis, six in each group.

Initial and final CBCT scans were compared using Dolphin 3D software and the two images aligned three dimensionally to allow direct analysis of dimensional changes.

Measurements were determined at the level of the original crest, 2mm and 4mm below the original crest.

Nearly all patients lost ridge width at all three levels. While not statistically significant given the small sample size of this exploratory study, the groups with buccal overlay grafting lost less width than those without overlay grafting at both 2mm and 4mm levels, warranting further enrollment and study.

Continuation of data collection to increase the study power is required to determine if a significant difference in grafting techniques exists.

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CHAPTER 1: Introduction

STATEMENT OF THE PROBLEM

Following extraction of a tooth, even if minimally traumatic, both vertical and horizontal alveolar ridge reduction due to bone resorption has been well documented. [1-5] This reduction can be considerable, and the majority of loss has been shown to occur within the first six months.[4,5] Vertically, a reduction in bone height is appreciated by resorption of crestal bone, and horizontally, ridge width is reduced primarily by resorption of the buccal plate.[5]

Reduction of the residual alveolar ridge can have significant deleterious restorative implications. Loss of bone width and height significantly compromises the ability of a clinician to place a successful implant in an extraction site, and can significantly impair efforts to achieve an esthetically acceptable prosthodontic outcome. The mechanisms driving this bone resorption are understood poorly.

Various clinical strategies have been developed to maximize ridge dimensions, and to reduce ridge resorption, after tooth extraction. Current techniques include using grafts of compatible materials, such as allografts with human cadaver bone, and membranes composed of various materials, both resorbable and non-resorbable. The non-resorbable membranes require a second surgery for removal, adding to the treatment required.

In order to maximize the preservation of the ridge following extraction, epithelium must be prevented from growing into and encapsulating graft materials, as this can prevent conversion of the graft material to native bone in the extraction socket.

Research by Wikesjö and colleagues has indicated that to prevent this occurring, clot stability and space maintenance must be maintained, and by doing so, epithelium will be excluded naturally.[6,7] To these ends, a membrane is typically placed over a healing socket to provide both protection and these key components to bone healing and to prevent epithelial ingrowth. Previously, many membranes utilized for ridge preservation ideally required primary closure. Without primary closure, salivary enzymes and oral contaminants quickly degrade resorbable membranes, eroding the ability to exclude epithelial growth from the socket area, provide wound stability/space maintenance, and inducing a bone-resorbing inflammatory reaction. However, achieving primary closure often requires either harvesting a tissue graft from a second site or coronally advancing a full-thickness flap, potentially reducing attached gingival width and requiring a periosteal release incision. Although this is often possible, it can require a significant increase in surgical time, clinician skill, and result in post-surgical morbidity (e.g. pain and swelling), as well as a potential reduction of the keratinized tissue around the graft site.

The advent of newer materials such as high-density PTFE, and more recently, amniotic-tissue derived membrane material, has potentially enhanced our ability to preserve bone following extraction and to reduce the morbidity associated with primary closure techniques. Uniquely, neither of these newer materials requires primary closure per the manufacturers' recommendations, making them attractive for post-extraction ridge preservation techniques.

If alveolar ridge bone is to be preserved optimally to maximize the likelihood of an excellent prosthetic outcome, the clinician must be able to determine the optimal membrane to use. However, although the ability of these membrane materials,

particularly PTFE, to exclude epithelial growth during bone maturation is well documented,[8] an evidence-based comparison of these materials for ridge preservation is lacking. Numerous small studies or case reports have been presented in the literature,[9-11] but a true, direct comparison of these membranes and grafting techniques has not been conducted.

Even with effective ridge preservation utilizing intra-socket grafting and a membrane, some resorption of the alveolar ridge still occurs.[2,3] As an alternative or supplement to the use of membranes, several small-scale human and animal studies suggest that additional grafting of the buccal surface with bone graft material may be helpful in reducing post-extraction resorption.[12-14] The use of particulate bone and various membranes has been demonstrated successfully on previously resorbed edentulous ridges, and guided bone regeneration at the time of extraction has been suggested.[15] By initially augmenting the ridge outside the buccal plate with bone, dimensional changes both horizontally and vertically may be minimized, or perhaps even increased. Additional research is needed to determine if the extra cost (and surgical complexity) of placing allograft material on the buccal surface of the extraction site, alone or in combination with the membranes, is warranted.

SIGNIFICANCE

A direct comparison of ridge preservation using buccal augmentation and traditional intra-socket grafting using advanced membranes that do not require primary closure is lacking. A knowledge of which technique more effectively preserves ridge height and width more predictably or that can maintain additional grafted bone would greatly clarify the optimal choice for the clinician. If there is a significant difference

found in the ability of the grafting techniques with the two membranes to preserve alveolar ridge bone following extraction, then practitioners will be able to implement the most effective method to maximize restorative outcomes. For the Army, maximizing initial preservation of bone will minimize the likelihood of additional surgical procedures post-extraction, decrease lost work and training time for military personnel, reduce costs, and enhance their esthetic/functional outcomes restoratively.

CHAPTER 2: Review of the Literature

INTRODUCTION

One of the most common dental procedures worldwide is tooth extraction, with over 20 million extractions in just the U.S. each year.[16] Healing of the extraction socket usually occurs without issue, but alterations in the surrounding hard and soft tissue following extraction can make restorative treatment of the area a challenge.

PHYSICAL BONE ALTERATIONS FOLLOWING EXTRACTION

Elian Classification

Trauma to the surgical site during extraction or naturally occurring osseous defects can have a profound effect on post-surgical healing. Elian, in 2007, proposed an extraction socket classification system that is widely used today to indicate the likelihood of a positive healing outcome. Type I extraction sockets indicate normal bone and soft tissue pre and post-operatively, while Type II sockets exhibit facial soft tissue with a partially missing buccal plate after extraction, indicating that further treatment is likely needed to ensure ridge preservation. Type III sockets display markedly reduced soft and hard tissue after extraction, indicating the need for significant intervention.[17] Additionally, the proper classification of sockets by this system has treatment planning implications. Elian Type I sockets can be treated effectively by either immediate or delayed (staged) implant protocols, while Type II and III sockets are best treated using delayed implant placement.

Resorption

Even with an ideal, Elian Type I extraction socket, residual ridge bone changes after extraction can be significant. Horizontal buccal bone resorption has been shown to be as high as 56%, while lingual bone resorption can approach 30% of horizontal width.[18] Human reentry studies have shown that horizontal bone loss of 29% to 63% and vertical bone loss of 11% to 22% can take place within the six months following tooth extraction.[5] Although resorption continues at varying rates over time, the most significant loss has been shown to occur in the first six months, and can approach 3-5mm horizontally.[4,19] Of interest to esthetically important and implant restored sites, bone resorption (particularly vertical loss) is generally greater on the buccal surface compared to the palatal/lingual aspect due the fact that the buccal bone is much thinner initially.[20,21]

The dramatic dimensional change following tooth extraction has been studied extensively, but the biologic reason for it and techniques for optimally preventing it remain somewhat elusive. Histologically, human and canine biopsies have been utilized to describe healing events following tooth extraction.[20,21] Described by Araújo, healing following tooth extraction progresses through three phases. Initially an inflammatory phase occurs, involving large numbers of cells mediating an inflammatory response to "clean" the extraction site before new tissue begins forming.[20] Granulation tissue is replaced by connective tissue matrix as the area becomes sterilized, leading to the proliferative phase. During this phase, fibroplasia occurs, involving rapid deposition of provisional matrix and subsequent penetration by vessels and bone-forming cells. Woven bone is then formed around the small vessels, which must be replaced by bone with significant strength and load bearing capacity (mature bone).

The third phase of healing described by Araújo consists of bone modeling and remodeling. Dimensional changes of extraction sites occur during this phase, primarily by bone modeling, defined as change in the shape and architecture of the bone.[20] Using human biopsies several weeks after tooth removal, osteoclasts can be found on the crest of both buccal and lingual walls and on inner and outer alveolar surfaces of the extraction socket site.[22] Bone modeling (leading to a change in dimensions) occurs before bone remodeling, which is defined as change in bone type/composition without a change in shape or contour.[4,22] As such, significant changes that occur during bone modeling are solidified as the conversion from bundle bone to mature bone types (bone marrow and lamellar bone) is completed.[20]

RIDGE PRESERVATION

Rationale

Historically, efforts to prevent extraction-induced ridge resorption have taken on a variety of forms. Early initiatives included retention of submerged roots or insertion of hydroxyapatite cones in an effort to maintain ridge dimensions.[23] Following issues with soft tissue infiltration and loss of the cones, particulate grafting techniques became more popular, but not without problems related to bone graft migration and particle loss.[23] Technological advances in xenograft and allograft processing as well as the arrival of barrier membranes brought new options for alveolar ridge preservation. In a pair of 1997-8 studies involving both resorbable and non-resorbable membranes, Lekovic provided proof of principle that these new membranes could be used successfully to reduce resorption following tooth extraction.[24,25] In a 2003 randomized clinical trial, Iasella et al. demonstrated significant reduction of resorption using freeze-dried bone

allograft (FDBA) with a collagen membrane compared to natural healing alone.[26] The ridge preserved group lost 1.6 mm less in width and gained 1.3 mm in height, compared to a loss of 0.9 mm for the non-preserved group. In a 2012 systematic review, Horowitz concluded that alveolar ridge preservation procedures had significant benefit.[2] Without preservation, horizontal loss will typically exceed 3mm, with 1mm or more of vertical loss. With modern preservation procedures, this loss can be reduced to slightly more than 1mm horizontally and with minimal or no loss vertically.[2,3,27]

Current Approaches to Ridge Preservation

A variety of techniques and materials have been utilized to minimize these changes after tooth extraction. Attempts at preserving the extraction socket have focused primarily on two methodologies, often used in conjunction: utilizing particulate grafts to fill the socket or augment hard tissues and using various membranes or autogenous soft tissue grafts to isolate the socket. More recently, the addition of biologic materials to promote the healing process has been introduced.

Graft Materials Utilized for Ridge Preservation

The use of grafting materials in extraction sockets leads to reduced horizontal resorption compared to non-grafted sites. Numerous grafting materials have been utilized for this purpose. In 1996, Nemcovsky described the successful use of hydroxyapatite in extraction sockets to minimize changes in ridge dimensions.[28] In the same year, Doblin described the use of demineralized, freeze-dried bone allograft in combination with expanded PTFE membranes for ridge preservation.[15] In 2008, Barone et al. demonstrated that porcine xenograft could be used to reduce horizontal resorption following extraction.[29] Wood & Mealey compared both demineralized (DFDBA) and

mineralized freeze-dried bone allografts (FDBA) in ridge preservation, and found that DFDBA provided significantly greater new bone formation.[30]

Buccal Overlay Grafting

In order to minimize or possibly prevent buccal bone resorption, placement of grafting materials on the outer buccal surface of the socket has been proposed as a method of potentially counteracting the resorption process following tooth extraction.[14] Such measures could be biologically plausible given what we know about extraction site healing and the resorptive process. Potentially, placement of a slower resorbing allograft material as a facial overlay may disrupt the process of normal bone resorption following tooth extraction.[14] Additionally, the possibility exists that while resorption of the original bundle bone of the extraction socket may be inevitable, placement of a facial overlay, protected by a membrane, may serve as a form of guided bone regeneration (GBR) to additionally grow new bone on the surface of the extraction site. GBR has been shown to be a successful method for increasing ridge width and height through grafting with a variety of materials.[31] This technique clearly results in new bone formation, and the possibility that its use on the facial surface of extraction sockets may disrupt the natural resorption process is appealing. The potential also exists that by placing a facial overlay at the time of ridge preservation, an additional surgery to regain lost width with GBR before implant placement could be avoided.

In 2004, Dr. Hom-Lay Wang and colleagues described a technique whereby deficient alveolar ridges and buccal osseous defects around dental implants could be corrected by buccal augmentation. Their technique involved placement of autograft from implant osteotomies, DFDBA and bovine hydroxyapatite to create a buccal graft where

needed, in a procedure they named the “Sandwich Bone Augmentation Technique”. By using absorbable collagen as a membrane and achieving primary wound coverage, the authors were able to achieve an average of 10.5 mm new bone coverage over buccal implant dehiscences.[13] While achieving impressive results, this case series with a study size of only five patients should be viewed as a pilot study or proof-of-principle, with the authors ultimately suggesting further research on the technique was needed.

A 2013 randomized clinical trial by Poulias et al. examined the use of bovine bone in conjunction with a polylactide absorbable membrane to determine if the loss of ridge width could be reduced by using an overlay graft. A significant reduction of bone loss was found, with 1.3 mm of buccal bone resorption being spared by the technique. Primary wound coverage was however required to prevent contamination of the polylactide membrane.[14] While this was the first randomized controlled trial to look at the concept of overlay grafting extraction sockets, the relatively small size of the study (24 total patients) and the use of a single surgeon limits the generalization of their findings.

The ability of dPTFE and amnion/chorion membrane materials to prevent infection and exclude epithelial ingrowth has been documented in the literature.[32,33,36,37] However, combining these advanced membranes with overlay grafting for ridge preservation has not been researched, and currently, the effectiveness of these advanced membranes in conjunction with overlay grafting techniques to preserve ridge dimensions following extraction has not been documented in the literature. Knowing the effectiveness of such materials and techniques would allow treating dentists to choose the optimal combination to maximize the chances of a patient having a successful restorative

outcome. A head-to-head comparison, something seldom seen in dental research literature, is needed to compare both membranes as well as bone grafting techniques.

Membrane Use in Ridge Preservation

Numerous techniques and materials have been utilized in an effort to isolate the extraction socket from infection and epithelial invasion during healing. Use of resorbable membranes as well as non-resorbable membranes such as expanded PTFE membrane has been employed in an effort to provide isolation, but both require achievement of primary coverage over the membrane material. If not, infection and loss of the graft is possible. Unfortunately, achieving primary closure is often quite difficult or impossible. As an alternative, the use of both autogenous free-gingival grafts and sub-epithelial connective tissue grafts has been advocated and demonstrated in the literature.[34,35] The requirement for a second surgical site has limited the appeal of these as an option to assure site coverage.

Newer materials do not require primary coverage to prevent infection, providing a great advantage for the surgeon. Originally developed in 1993, high-density polytetrafluoroethylene (dPTFE) membranes feature submicron (0.2 μm) pore size, eliminating the issue of bacterial penetration.[32] As such, along with their inherent biocompatibility, primary closure is not required for successful membrane use. In a large, but retrospective, non-randomized study published in 2008, Hoffman described using dPTFE membranes without primary closure or any graft material to achieve successful preservation. Taking direct measurements using a stent at extraction and 12 months, Hoffman and colleagues noted significant regeneration of socket volume. Histologic core samples of ten of these sites demonstrated that the extraction site was

mainly bone.[23] Despite the large size of this study (276 sites), a lack of a negative control limits its clinical implications.

Newer to the market, amnion-chorion derived membranes have been advocated for use in a number of dental indications, including guided tissue regeneration, ridge preservation and even root coverage procedures.[36,37] In a 2014 small, retrospective case series, Holtzclaw described the use of an amnion-chorion membrane (BioXclude) over a blended mineralized and demineralized bone allograft in 10 patients, with reported results consistent with previously published site-preservation studies.[38] In a randomized, split-mouth study presented at the 2014 American Academy of Periodontology meeting, Hassan et al. compared ridge preservation using amnion chorion membrane against dPTFE, finding that results for each material were comparable.[10]

CHAPTER 3: Purpose

The overall purpose of this study was to evaluate four ridge preservation techniques – extraction socket grafting with and without additional buccal graft augmentation using either dPTFE (Cytoplast) or amniotic-tissue derived membrane (BioXclude). The purpose of this thesis focused on determining if buccal bone graft augmentation provides superior ridge preservation following single tooth extraction over socket grafting alone in clinical patients. Following tooth extraction as part of the normal treatment plan, one of four ridge preservation techniques as used in approved clinical practice was conducted based on random sequence generation. Sockets were evaluated with and without buccal bone augmentation of 1mm and with each of the two membranes, forming the four study groups. All sites received particulate bone graft material within the extraction socket, as is performed routinely. Use of materials and technique was standardized among all surgeons. Cone-beam CT with software processing for anatomical reference and indexing was utilized before extraction and at four months post-procedure to evaluate residual ridge width and height dimensions, and changes were calculated.

CHAPTER 4: Hypothesis

HYPOTHESIS

It was hypothesized that the use of buccal bone augmentation with both dPTFE and amniotic tissue membrane would provide significantly greater retained alveolar bone at 4 months post extraction when compared to alveolar bone when either membrane is used with no buccal augmentation.

CHAPTER 5: Specific Aims

AIM #1 – BUCCAL AUGMENTATION

Determine the quantitative change in alveolar ridge width and height after extraction and placement of buccal overlay graft with either membrane. This was accomplished by measuring CBCT bone dimensions before extraction and approximately 4 months post extraction.

AIM #2 – AMNIOTIC TISSUE MEMBRANE VS DPTFE

Determine the quantitative change in alveolar ridge width and height after extraction and ridge preservation using allograft bone material along with either amniotic tissue membrane (BioXclude) or dPTFE (Cytoplast) membrane. Determine which product preserved underlying ridge dimensions better, regardless of bone grafting technique utilized. This was accomplished by measuring CBCT bone dimensions before extraction and approximately 4 months post extraction.

AIM #3 – DOLPHIN 3D SOFTWARE

Validate the use of Dolphin 3D CBCT imaging software for superimposing and measuring CBCT images from different time points. Determine if this method of data gathering and analysis proves to be a useful and reproducible method of measuring change in hard tissue dimensions.

CHAPTER 6: Protocol Development

CBCT IMAGING CAPTURE AND SOFTWARE

Of significant importance in designing this study was the integration of modern methods of imaging and the forms of data that they can provide. Previous methods of measuring alveolar ridge change following extraction involved direct measurement of ridge dimensions and were generally dependent on surgical guides or stents for measurement consistency before and after healing.

By utilizing the advanced imaging modality of cone-beam computed tomography (CBCT), high-resolution, three-dimensional images of the extraction site can be taken before extraction, as well as following healing for analysis.

Using Dolphin 3D imaging software (Dolphin Imaging and Management Solutions, Chatsworth, CA), we developed a novel and to our knowledge previously un-utilized approach and technique for comparing and analyzing initial and final CBCT images. By using a unique feature of the Dolphin 3D software called volume superimposition, images from one patient at two different time points, such as pre-extraction and post-healing (Figures 1 and 2) can be compared.

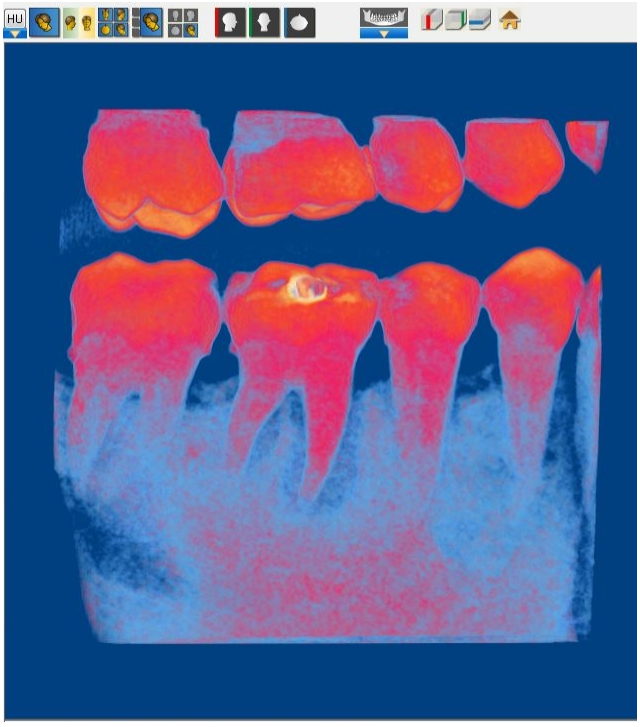

Figure 1. Pre-extraction CBCT 3D rendering (Dolphin 3D software)

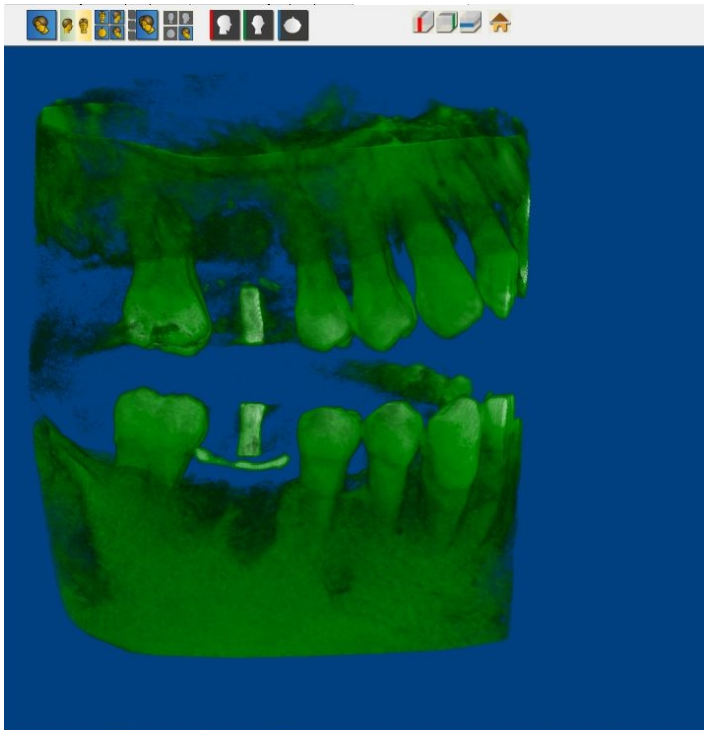

Figure 2. Post-healing CBCT 3D rendering (Dolphin 3D software)

Scans then can be imported and overlaid upon each other using common points of reference (uninvolved teeth, maxillary sinus, mandibular ramus, etc.) (Figures 3 and 4).

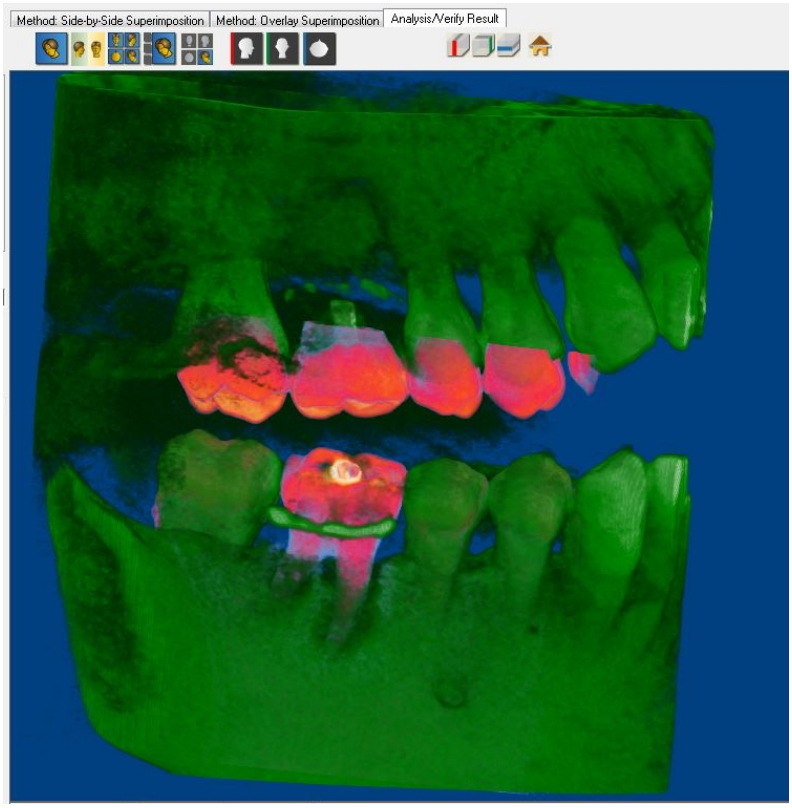

Figure 3. Overlaid 3D images from two different time points – Buccal view (Dolphin 3D software). Pink/rainbow colored objects are components of the initial scan, and green objects are components of the final scan.

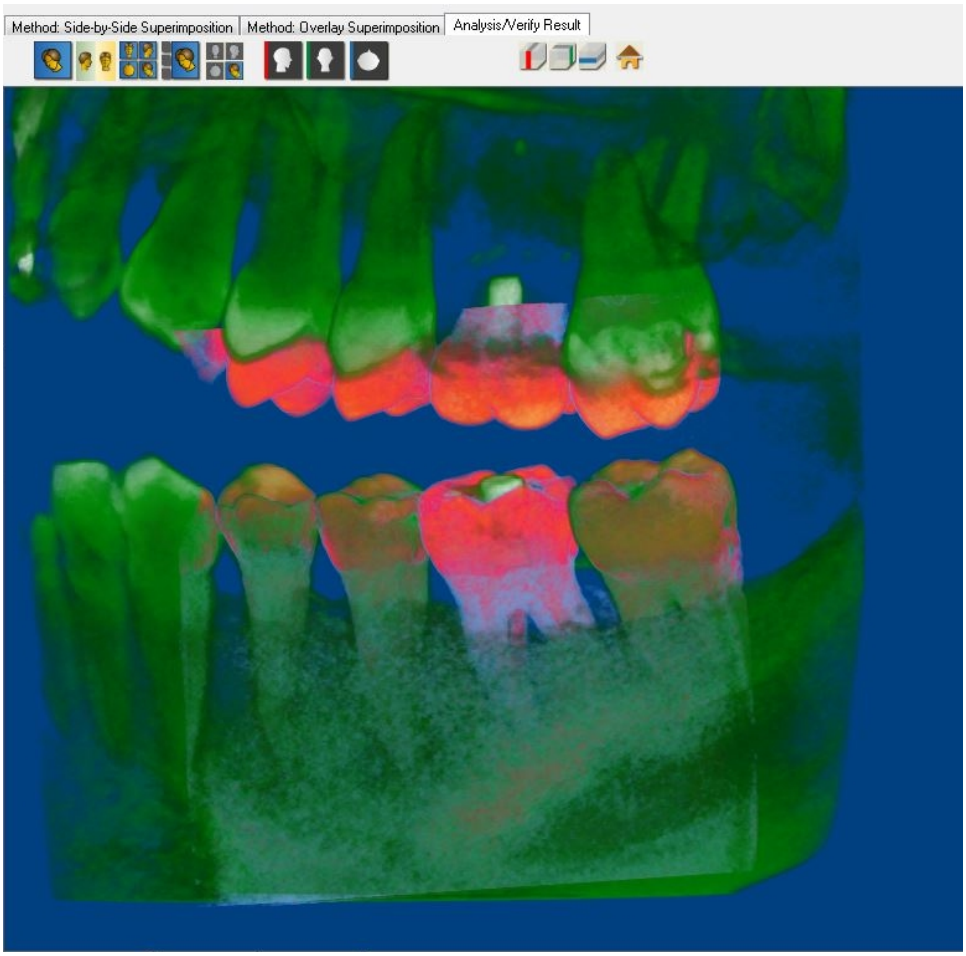

Figure 4. Overlaid 3D images from two different time points – Lingual view (Dolphin 3D software). Pink/rainbow colored objects are components of the initial scan, and green objects are components of the final scan. Mandibular arch is superimposed. Lack of alignment of the maxillary arch is due to variation in how widely the patient was opened during the two scans.

Once overlaid and oriented, measurements can be taken in any dimension at both time points, ensuring an exact calculation of dimensional change, in precisely the same plane (Figure 5).

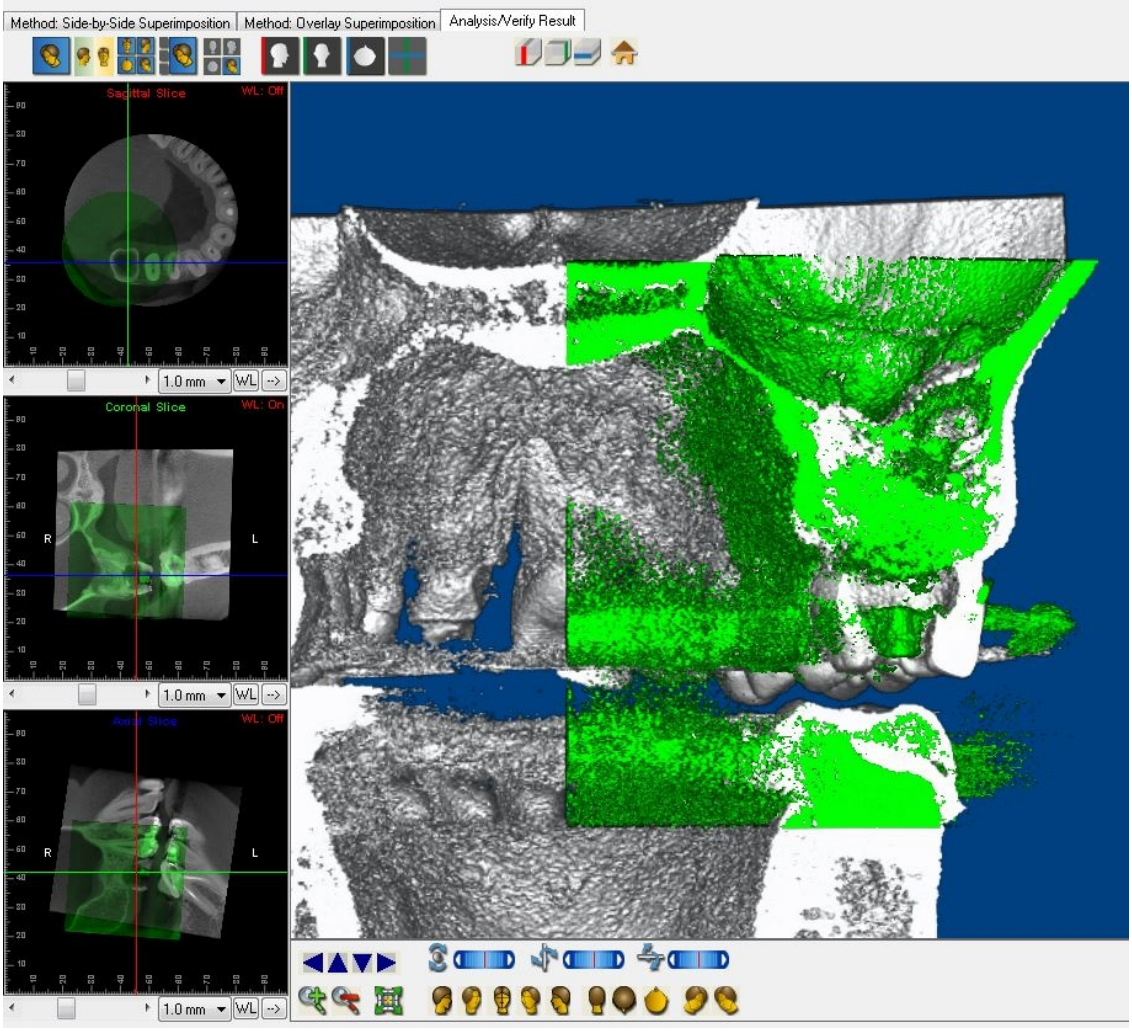

Figure 5. Overlaid CBCT 3D images from two different time points. White areas indicate bony dimensions pre-extraction. Green areas indicate bony dimensions following healing. (Dolphin 3D software)

To our knowledge the use of this type of comparative analysis of hard tissue dimensions using overlaid CBCT data at two different time points has not been done before. Developing the data gathering protocol for this study using the CBCT images along with advanced CBCT 3D software has the potential for numerous other study designs. The ability to assess non-invasively changes in alveolar contours in the exact same plane at different time points has significant potential in the study of guided bone

regeneration, sinus augmentation, guided tissue regeneration, or any other research study involving dimensional changes of hard tissues at separate time points.

CHAPTER 7: Materials and Methods

STUDY DESIGN AND CONSORT COMPLIANCE

In designing this study, every effort has been made to comply with the 2010 CONSORT Statement suggestions for reporting randomized trials. Many of these key elements are absent from previous literature on ridge preservation, particularly those dealing with buccal augmentation. By ensuring incorporation of these items into our design and reporting, we maximize the relevance and applicability of this study.

Power analysis based on the study design was conducted before initiation of the study in order to determine a sample size that would be sufficient to achieve statistically significant results. The analysis was calculated based on two different statistical estimates, in conjunction with relevant articles. The sample size for the study was estimated using G*Power with a fixed effects, special, main effects and interactions ANOVA statistical test for a power of 80% with p set to 0.05. A four-group design with the numerator degree of freedom of one (main effect or interaction) was used, with an effect size f of 0.25, considered to be a medium effect size for F-tests. This requires a total sample size of 128 subjects (32 per group). In terms of a clinical effect, this would provide a sensitive test with approximately 6% of the variance being due to the effect. A second sample size calculation was also conducted in the event that a MANOVA test would be utilized for the data. Using G*power, a MANOVA: repeated measures, between factors, effect size .15, power .80, 4 groups and 4 iterations, also gave a sample size of 128.

Interim results from the study were analyzed using data collected from 32 subjects (eight per group). This sample size would have a 78% power to detect a main effect size f=0.5 (p=0.05). If at this stage one treatment had proved significantly better than the other three, the study would have been suspended.

Estimate Required Sample Size	**128**
Estimate Participant Drop Out / Withdrawal	**22** *(15-20%)*
Total Enrollment Requirement	**150**

Table 1. Desired enrollment calculation

With eight surgeons performing the procedures, results would be more likely to be generalizable to various practitioners. Patient allocation to various treatment groups was done using an electronically randomized number assignment, and group assignment was only disclosed to the surgeons immediately before the procedure. Blinding of the data was ensured by de-identifying all documents prior to entry and analysis. CBCT measurements were conducted by two investigators with no knowledge of which preservation technique was performed, with standardization conducted to ensure accuracy of measured results. This study was conducted completely independently with absolutely no industry funding or influences whatsoever.

OVERVIEW

Single teeth that were treatment planned for extraction and ridge preservation were assessed and had a baseline CBCT taken following informed consent for both study participation and the surgical procedure itself. Teeth were extracted with minimal trauma,

attempting to leave the periosteum as intact as possible. Allograft (LifeNet FDBA 250-1,000µm particle size) bone material was placed in all extraction sockets. Patients were divided by a randomly generated number sequence into four groups based on the two variables of grafting technique and membrane choice. Buccal overlay graft with bone was assigned to half of the patient population, and the other half received no overlay graft. Half of the patients received amniotic tissue membrane (BioXclude) membrane to protect the graft, and the other half received dPTFE (Cytoplast). Any post-operative complications were reported during follow-up appointments at 1, 2 and approx. 4 weeks, and a CBCT at four months was taken to observe alveolar bone changes, just prior to implant placement.

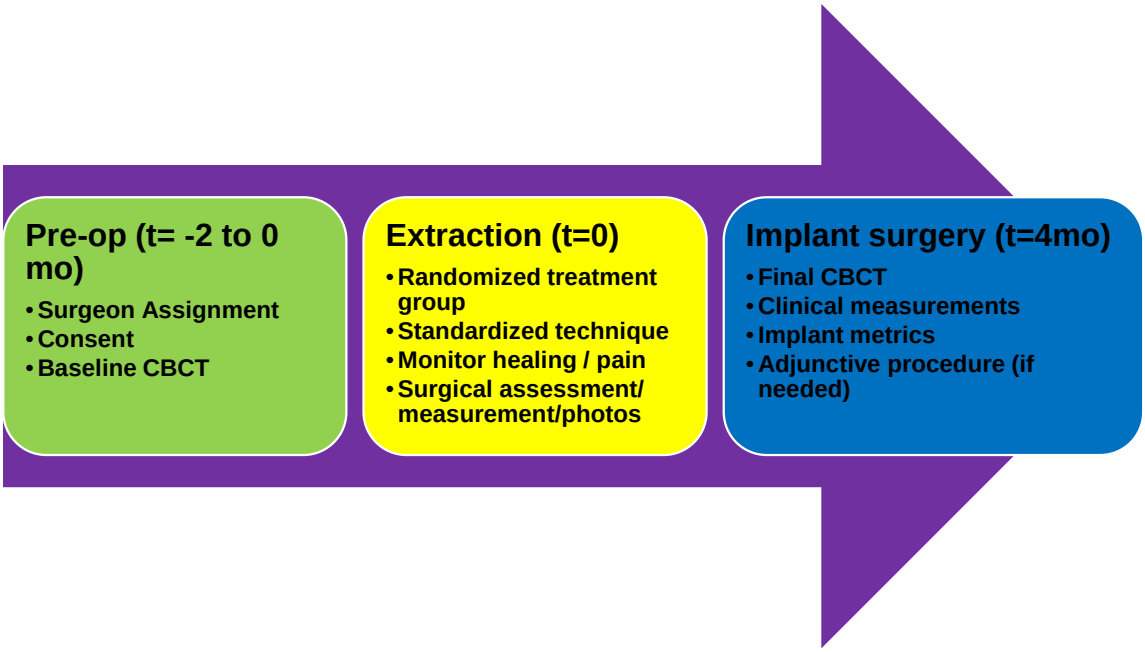

Figure 6. Experimental Design

RESTATEMENT OF THE HYPOTHESES

Hypothesis

It was hypothesized that the use of buccal bone augmentation with both dPTFE and amniotic tissue membrane would provide significantly greater retained alveolar bone at 4 months post extraction when compared to alveolar bone when either membrane is used with no buccal augmentation.

DETAILED METHODOLOGY

Patient Selection and Assessment

Hopeless teeth requiring extraction and implant placement were included in this study. All patients who met inclusion criteria during the study were asked to be included.

Inclusion criteria were as follows:

1. All patients (age 18-65) referred to Tingay Dental Clinic's periodontics department for extraction and ridge preservation of a "hopeless" tooth
2. Diagnosis of "hopeless" tooth documented and confirmed by periodontal staff
3. Eligible for extraction and ridge preservation with an implant planned for the extraction site.

Exclusion factors were as follows:

1. Pregnancy: Pregnant or breastfeeding women were excluded from participation in this study. Women of childbearing potential (WOCBP) had a negative urine pregnancy prior to enrollment. Research staff counselled WOCBP who were sexually active to report pregnancy prior to dental interventions at each visit and maybe withdrawn from the study at the PI's discretion.
2. Age <18 or >65
3. History of allergy to involved products or any of the following: sulfa drugs, bacitracin, polymyxin B sulfate, or gentamicin

4. Current acute infection at the site (i.e. purulent discharge, appreciable abscess or cellulitis, febrile)(chronic periapical lesions do not exclude the patient)
5. Elian Type 3 extraction sockets – the Elian classification system attempts to classify teeth according to the presence or absence of bone and soft tissue on the buccal surface of a tooth. For the purposes of this study, it was felt that an Elian Type 3 site, where both bone and soft tissue are absent, deviated too much from the overall intent of the procedure. Generally, these sites require supplemental GBR procedures anyway, and the inclusion of these patients might not have served the best interest of the patient in terms of overall management and treatment planning.
6. Sites not treatment planned for implant therapy (i.e. pontic sites, some second molar sites, sites with insufficient restorative space for an implant).
7. Third molar extraction sites – third molar sites never require ridge preservation as a standard of care.
8. Significant systemic illness that classified the patient as an ASAIII according to the American Society of Anesthesiologists guidelines. The residency SOP dictates that these patients cannot be sedated in our clinic, and would be referred to the Oral Surgery service. As such, these patients were excluded from this study, whether or not they were sedated or the procedures would be performed under local anesthesia.
9. Active duty who anticipated leaving the Tingay Dental Clinic area of service within 4 months.

10. Patients who were in a student status (e.g. Advanced Individual Training) while at Fort Gordon.

Patients willing to participate signed consent forms after a consent process (Appendix A), and were given a subject ID number for blinding purposes. Patients had a research note and clinical research checklist placed inside the dental record to indicate active involvement in the study (Appendix B). Randomization for treatment groups occurred via a random number table and stratification occurred across treating practitioners. The treating resident was given a sealed, opaque envelope, and did not know the procedure group until immediately before the surgery.

Baseline Data

Patients required a small volume Cone Beam CT at baseline. This would typically be done for any extraction case being considered for eventual implant placement. Dosage for each small volume, high resolution scan (40mm x 40mm size with 0.08 voxel resolution) using the 3D Accuitomo 170 CBCT machine is approximately 30 μSv,[39] roughly the dose of 1.5 digital panoramic radiographs. Previous CBCT data was utilized for the baseline scan if patients had an adequate CBCT of sufficient scope and quality in the 60 days before the surgery. The treating resident filled out a pre-operative assessment (Appendix C) using the subject ID number and submitted it to the PI for de-identification and data was stored on the network in a secured location. Clinical photos were gathered at a minimum of baseline, surgery, and all post-operative appointments.

Surgical Procedure

If sedation was used, technique and medication used were documented and were at the discretion of the treating surgeon and patient. Local anesthetic was used and teeth

were extracted with minimal trauma. All multi-rooted teeth were sectioned before extraction with all necessary restorative material removed before sectioning (Figure 7).

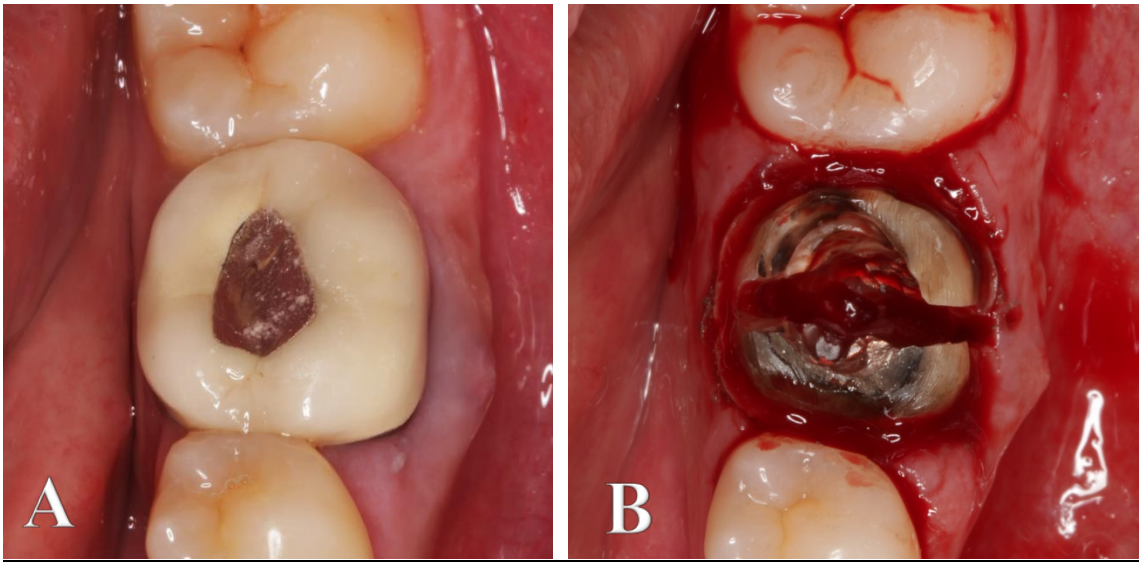

Figure 7. Restorative material removal and tooth sectioning. (A) Tooth #19 before removal of the existing porcelain-fused-to-metal crown. (B) Crown removed and #19 sectioned mesial-distally to facilitate minimally traumatic extraction.

Following successful extraction, all sockets were debrided and full thickness mucoperiosteal envelope flaps reflected to allow access at least 10mm apical on the buccal and approximately 5 mm on the lingual for membrane positioning (Figure 8).

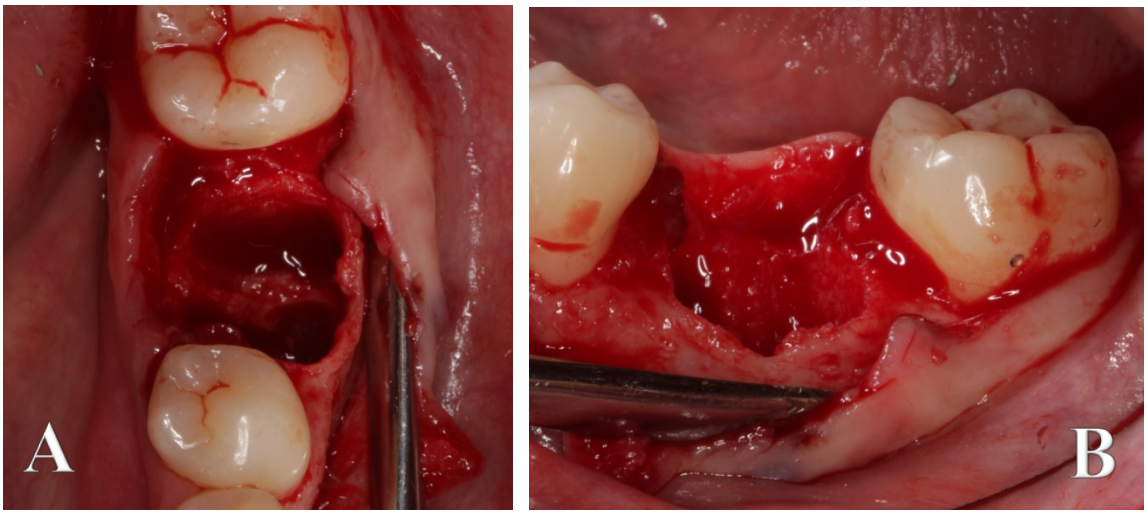

Figure 8. Minimally traumatized extraction socket and flap reflection (A) Occlusal view (B) Buccal view

If needed, any vertical releasing incisions were made at least 1 tooth away from extraction site. Freeze Dried Bone Allograft (FDBA) 250-1,000µm particle size (OraGRAFT, LifeNet Health, Virginia Beach, VA) was placed in the socket. For those receiving buccal overlay, an additional 1-2mm thick layer of FDBA was placed on the buccal surface to a depth of 5-7 mm (Figure 9).

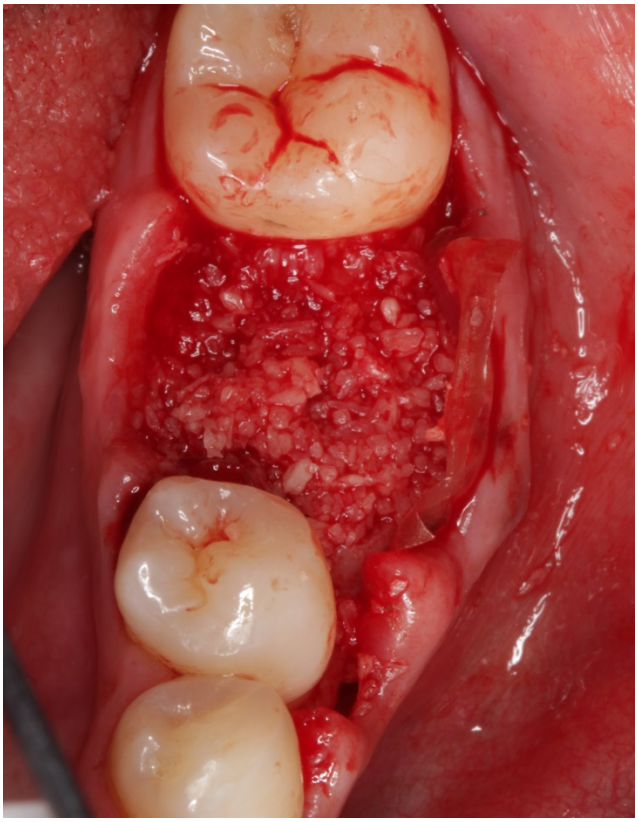

Figure 9. Grafting of extraction socket with Freeze Dried Bone Allograft (FDBA) with buccal overlay

One of the membranes was placed over bone graft material as per the randomization procedure and adapted to extend at least 10mm apically on the buccal surface and approximately 5 mm on the lingual. If using dPTFE (Cytoplast, Osteogenics

Biomedical, Lubbock, TX), membranes were trimmed to cover the socket but not encroach on adjacent teeth (Figure 10).

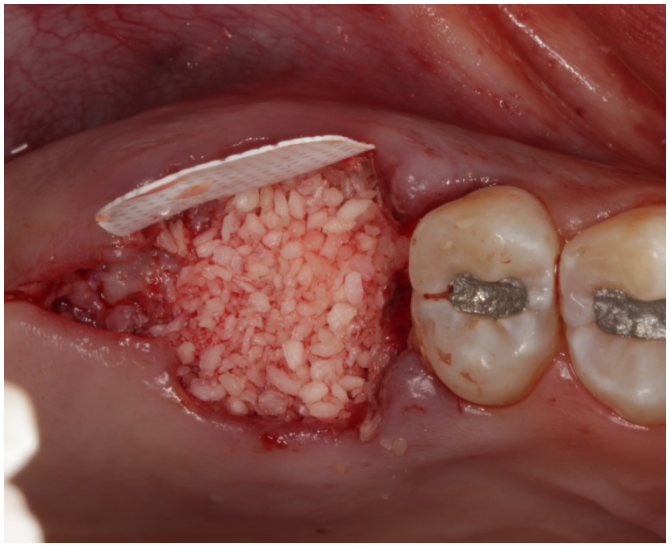

Figure 10. Cytoplast membrane placement with FDBA in place

Amniotic tissue membrane (BioXclude, Snoasis Medical, Denver, CO) was adapted and folded as needed for site coverage (Figure 11).

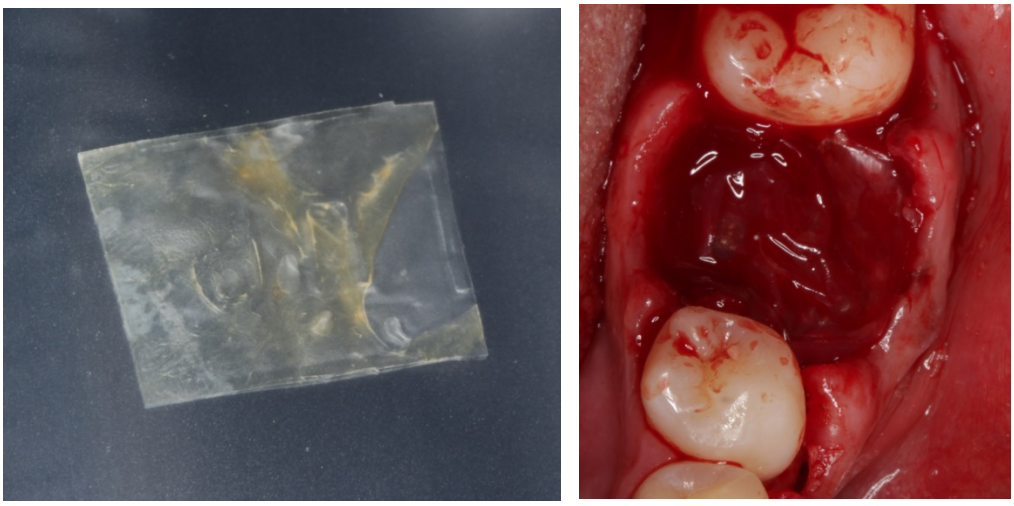

Figure 11. BioXclude membrane in extraction socket over graft material

A continuous running Gore-Tex 5.0 suture was placed for wound stability with two interrupted sutures, one each at the mesial and distal papillae with no attempt being made at primary closure (Figure 12).

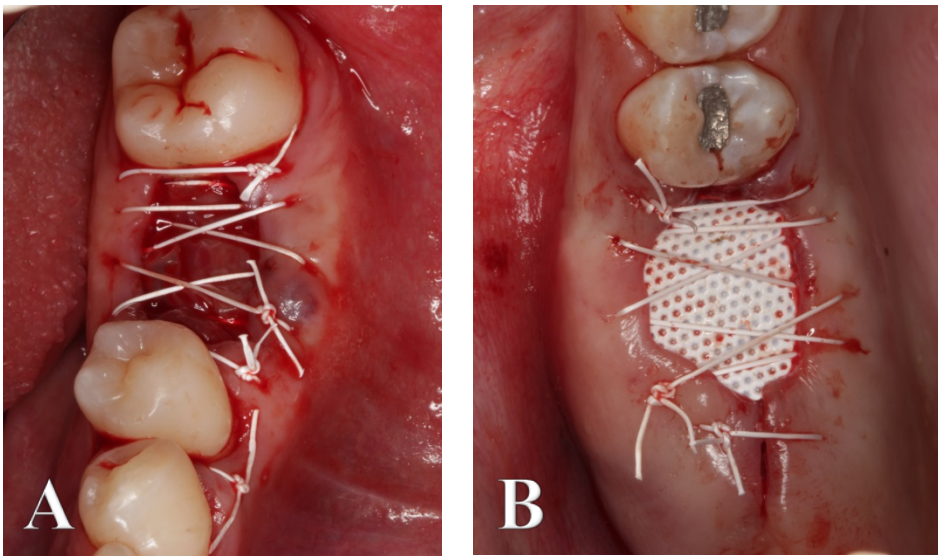

Figure 12. Ridge preservation suturing. Continuous suture over graft site and membrane, with simple interrupted suture placed at papillas. (A) BioXclude membrane; (B) Cytoplast membrane

Post-Operative Management

Post-operative medication was standardized. All patients, barring allergy or intolerance, were given amoxicillin or azithromycin, hydrocodone 5mg, and NSAIDS or APAP, and a chlorhexidine rinse. Patients were recalled at approximately 1, 2 and approximately 4 weeks, and a post-operative assessment form (Appendix C) was completed. At the one week appointment, pain perception was recorded. At the two week appointment, sutures were removed and at 4 weeks, the cytoplast membrane was removed; removal of amniotic tissue membrane (BioXclude) is not required (Figure 13).

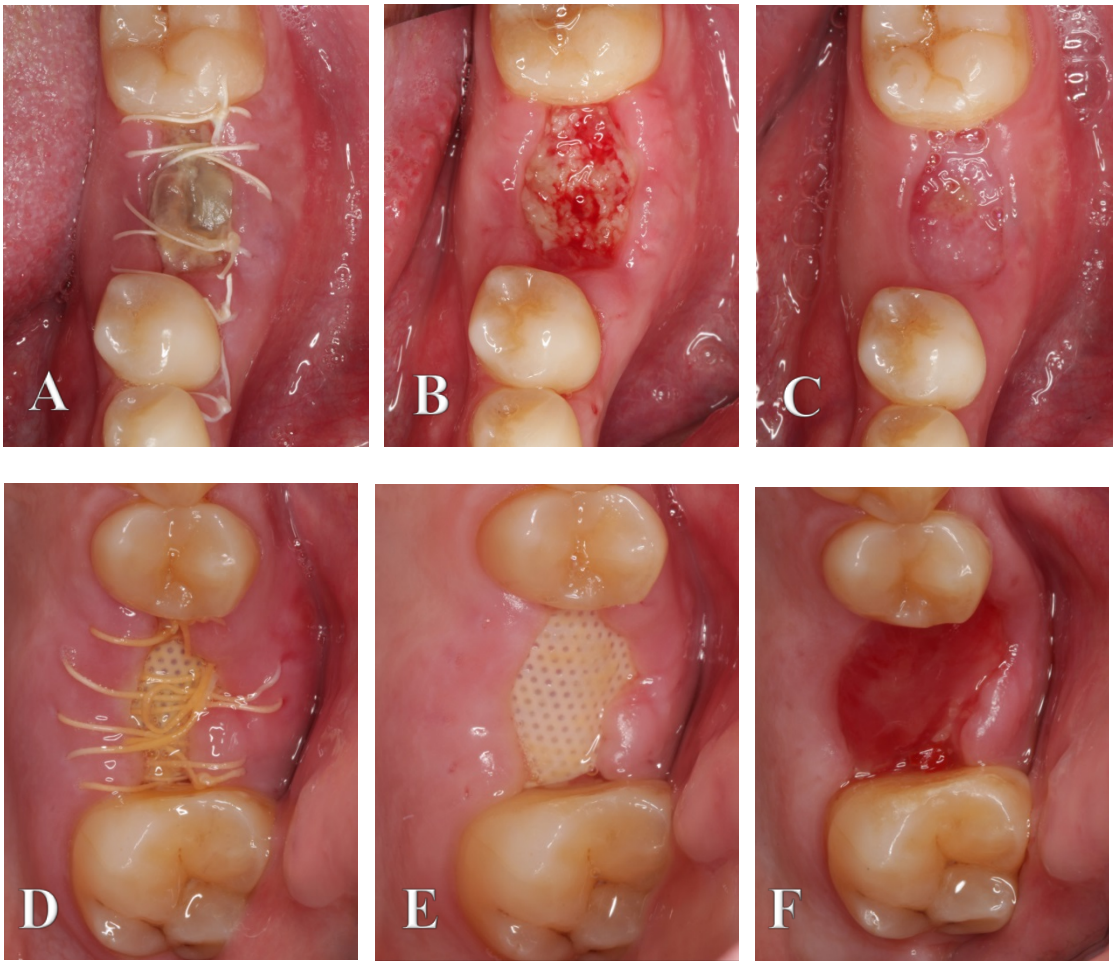

Figure 13. Preserved sites at 1,2 and 4 weeks. (A) BioXclude site at one week. (B) BioXclude site at two weeks with sutures removed. (C) BioXclude site at 4 weeks. Membrane does not require removal. (D) Cytoplast membrane site at one week. (E) Cytoplast site at two weeks with sutures removed. (F) Cytoplast site at 4 weeks following membrane removal. Note pre-osteoid type material in extraction site.

At approximately four months, or when the patient was ready for implant placement, an assessment was completed including a second small volume CBCT image to evaluate the implant site. After placement of the implant (Figure 14), the patient was followed to the time of restoration where possible to determine initial integration.

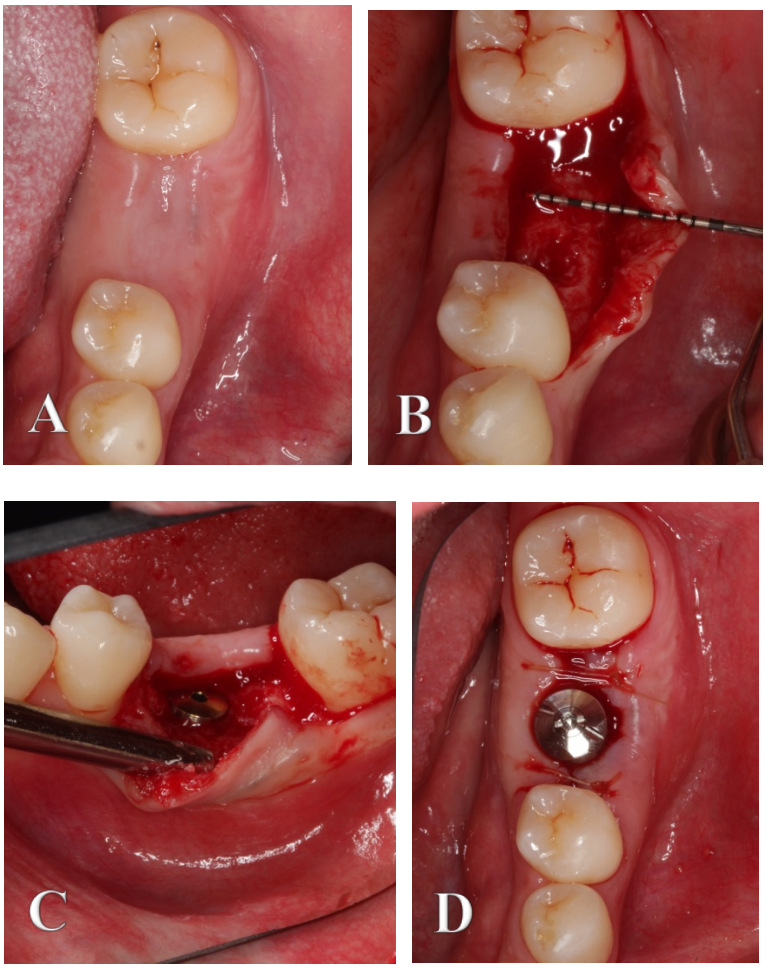

Figure 14. Implant placement at four months. (A) Extraction site at four months post-ridge preservation. (B) Exposure of ridge (C) Implant placement (D) Healing abutment placement and closure.

Assessment	Visit / Follow Up (F/U) Interval						
Study Day / period	2-8 wks Before*	1 day Before*	Treatment	F/U1 1 wk post TX**	F/U2 2 wks post TX**	F/U3 4 wks post TX**	F/U4 4 mo post TX**
Informed Consent, discuss Plan, etc.	X						
Screening	X						
Randomization	X						
Demographics, History & Physical	X						
Pregnancy test		x					
Cone Beam CT	X						x
Treatment			X				
Pain Survey				x			
Suture removal					X		
Membrane removal (dPTFE only)						x	
Post-operative care				x	X	x	x
Implant placement							x

Table 2. Patient event and appointment chronology

Final CBCT processing

As close as possible to the 4-month point after tooth extraction and ridge preservation, a final CBCT scan with the same volume specifications was taken of the extraction site. Initial and Final CBCT Digital Imaging and Communications in Medicine (DICOM) volumes were exported from the 3D Accuitomo 170 CBCT machine and imported into the Dolphin 3D Imaging Software. With this software program, initial and final CBCT images of the same site at two different time points can be overlaid upon each other. Precise superimposition was accomplished using anatomical references that were shared between the initial and final scans, but not anticipated to change following

tooth extraction (non-involved teeth, maxillary sinus anatomy, unique vascular/nerve structures, mandibular ramus, etc.) (See Figures 1-5 above).

Once accurately superimposed, images were manipulated to view a slice oriented in a facial/palatal or facial/lingual manner that was aligned with the long axis of the tooth at the mid-point of the tooth mesial/distally. A unique feature of Dolphin 3D allowed us to view only the initial image, only the final image, or a blend of the two in exactly the same plane by use of a slider bar. Once measurements from a baseline on the initial image were completed, the slider bar could be adjusted to just the final image, and final measurements taken in exactly the same plane using this feature.

To produce initial measurements, the image was rotated to set a baseline reference for the bony crest of the initial ridge. Using the calibrated ruler in Dolphin 3D, width measurements were accurately determined at the initial crest, 2mm below and 4mm below the initial crest (Figure 15).

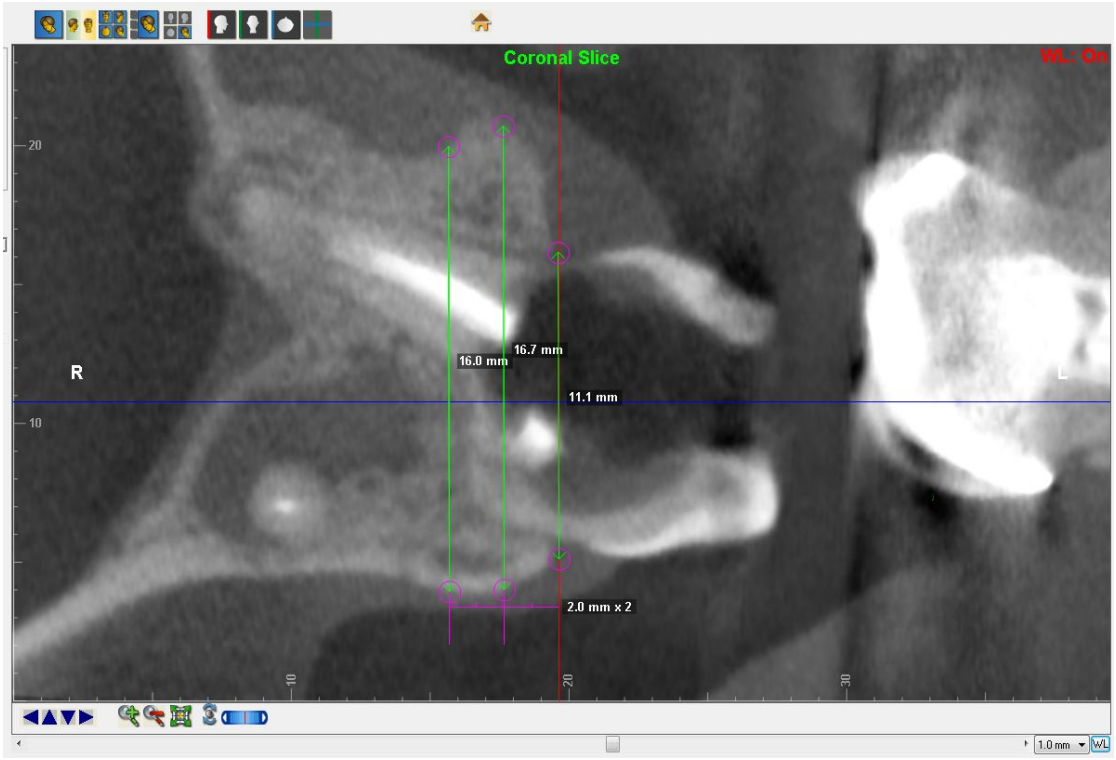

Figure 15. Initial CBCT image through middle of tooth mesial/distally and oriented down the long axis of the tooth. Baseline measurement at the initial alveolar crest is displayed by the red vertical line. Using the moveable calibrated ruler (pink), measurements (green) can be generated 2mm and 4mm below the alveolar crest

Once measurements were recorded from the initial scan image, the slider bar could then be adjusted to only display the final image. The baseline reference that was placed at the initial bony crest remained in the same exact anatomical position. We could then generate measurements of the ridge dimensions at the same baseline, 2mm and 4mm below the original crest, but on the final scan. Vertical gain or loss could also be

determined and measured referenced against the original crestal height. (Figure 16)

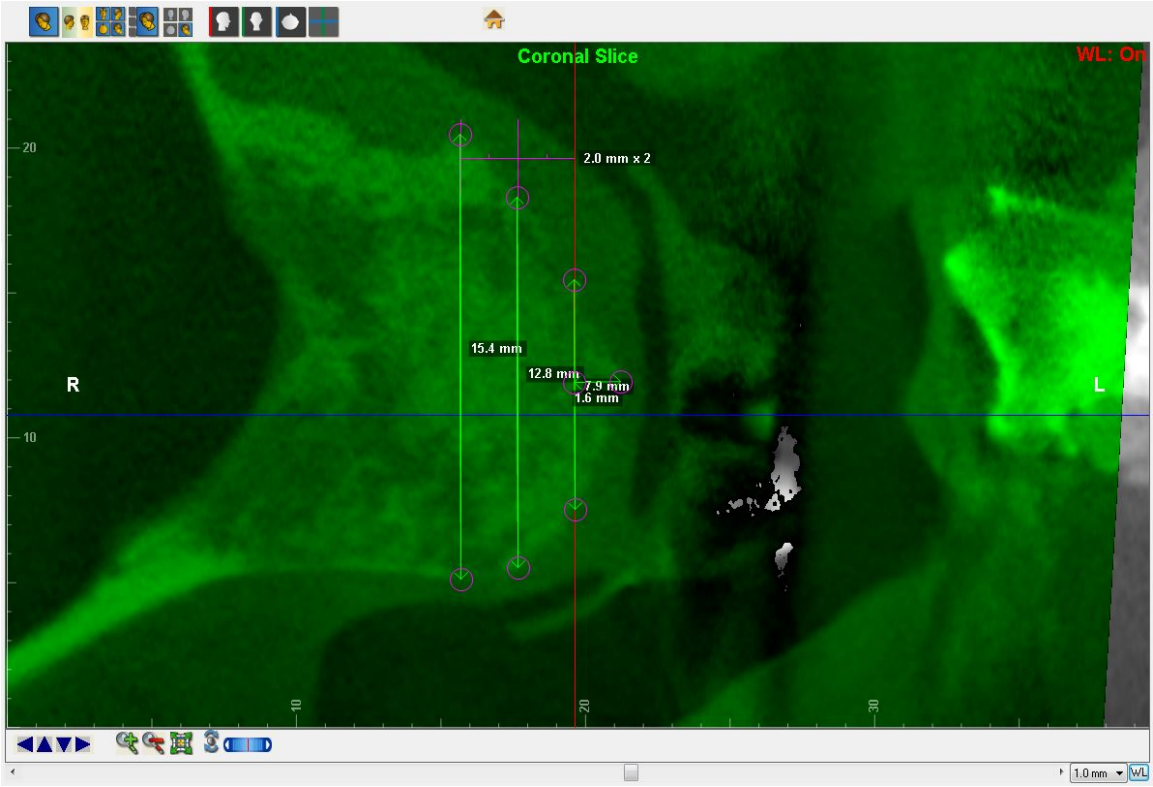

Figure 16. Final CBCT image through middle of tooth mesial/distally and oriented down the long axis of the tooth. Original baseline measurement at the initial alveolar crest is displayed by the red vertical line, in the same exact anatomical location. Using the moveable calibrated ruler (pink), measurements (green) can again be generated at the original crest height, 2mm and 4mm below the original alveolar crest. Vertical loss or gain from the original crest height can also be calculated, in this example, a gain of 1.6mm.

The images were measured and analyzed independently by both assistant investigators. For any disputed measurements, the case was reviewed and discussed and an agreed conclusion was determined. Results were recorded on CBCT Measurement Form (Appendix C), one for initial measurement, and one for final measurements.

Implant Surgery

At the time of implant surgery, the treating resident completed an Implant Surgery Assessment Form (Appendix C) with all required and pertinent data and submitted it to the primary investigator (PI). Clinical photos were gathered for the implant surgical appointment.

Data Management

All forms generated regarding each patient encounter (Appendix C) were initially turned in to the PI with the patient's name on it for identification. The PI then assigned a random number for each patient based on a secured spreadsheet that remained blinded for both assistant investigators (AIs).

The name was then removed from the top of the sheet, and the AIs were able to enter data from each sheet and patient encounter using only the randomized patient number. In this manner, both AIs remained blinded as to which patient belonged to each group until all data was gathered, solidified, and analysis had begun. Data was entered by the AIs into an electronic data tracking sheet, with each AI verifying data entered by the other AI from the data sheets to provide redundancy and to ensure no errors were made in data transfer.

Data Description

Independent Variables

There are two categorical nominal independent variables in this ongoing study: buccal augmentation, and membrane type. Each has two levels, respectively: with and without buccal augmentation (Nominal); and dPTFE (Cytoplast) and Amniotic tissue membrane (BioXclude).

Dependent Variables

Primary Variables:

1	Ridge width (from CBCT) – mm and percentage change from baseline (varying crestal levels)(Continuous)
2	Ridge height (from CBCT) – mm and percentage change from baseline (varying crestal levels)(Continuous)

Secondary Variables:

1	Post-operative pain perception at one week – visual analog scale
2	Sedation utilized – yes or no
3	Implant placement success at four months – yes or no (Categorical, Nominal)
4	Change in keratinized gingiva – mm
5	Tooth location – anterior or posterior (site number recorded)
6	Anticipated Elian Classification *(a priori)* – 1-3
7	Actual / Observed Elian classification – 1-3
8	Presence of Pre-Operative Infection (e.g. radiographic lesion present)
9	Extraction Difficulty – Routine or Complex (subjective)
10	Buccal Plate Thickness – mm
11	Initial Crest Ridge Width – mm
12	Dehiscence/ Fenestration – Yes/No (if yes, an estimated % of root surface will be measured)
13	Ease of Use – 1-5 (subjective)
14	Complications after surgery - descriptive, to include time after surgery
15	Membrane Removal (Cytoplast only) – number of days post-surgery

16	Crest Ridge Width at Implant Placement – mm
17	Implant Platform Information – Size
18	Primary Implant Stability – Ncm Torque
19	Additional Augmentation at Surgery – Yes or no (i.e. whether or not performed)
20	Graft Necessary – Yes or No (if performed, was it essential or adjunctive?)
21	Cortical Bone Thickness at Crest - mm

Table 3. Primary and Secondary Variables

DATA ANALYSIS

Statistical analysis of all data was conducted in consultation with the Department of Biostatistics and Epidemiology, Medical College of Georgia. SAS 9.4 software (SAS Institute, Cary, NC) was used for all statistical analyses. An alpha level of 0.05 was used to assess statistical significance. A preliminary analysis was done to examine the distributions and characteristics of the data. Variables for changes from baseline (for Horizontal Width at Crest, 2 mm, and 4 mm) were created, and descriptive statistics were calculated for all variables.

For each variable, a Wilcoxon Signed Rank test was used to examine whether changes from baseline were significantly different from 0, and a Wilcoxon Rank-Sum test was used to examine differences (in change from baseline) between products and techniques. A Kruskal-Wallis test was used to examine differences (in changes from baseline) between the 4 groups defined by product A and B and technique A and B.

CHAPTER 7: Results

28 patients were enrolled in the study initially, had initial CBCT taken and data gathered, and had their study tooth extracted with ridge preservation. Three patients were dis-enrolled, for a variety of reasons. One patient left active duty service unexpectedly, and another moved duty stations between having the ridge preserved and the final CBCT taken. The third patient was removed from the study due to non-compliance with the required study appointments. This drop-out rate (11%) was comparable to the drop-out rate estimate used for the study design (15-20%). The 25 remaining enrolled patients completed all data gathering with the exception of two patients who had not had their implants placed yet due to treatment planning considerations. One patient completed the study, but CBCT data from the patient was unreadable due to significant radiographic scatter on both the initial and final CBCT images, making comparison and measurement impossible.

Data from the remaining 24 patients was utilized in the analysis of results. Each of the four study groups had 6 patients, resulting in an even split of 12 patients receiving extraction and ridge preservation with buccal overlay grafting (abbreviated group BO), and 12 patients with no overlay (abbreviated group NO). (Table 4)

Treatment group	N	Technique	Product
1	6	**No Overlay (NO)**	Cytoplast
3	6	**No Overlay (NO)**	BioXclude
2	6	**Buccal Overlay (BO)**	Cytoplast
4	6	**Buccal Overlay (BO)**	BioXclude

Table 4. Treatment Groups

At the crest and 2mm below the original crest, all patients, at all levels lost horizontal width, regardless of the grafting technique assigned or membrane used. All

patients also lost ridge width at the 4mm level, with the exception of one patient who gained +0.4mm. All ridge losses were quantified with a negative number (e.g. -5.4mm) and all gains were quantified with a positive number (e.g. +4.7mm), as shown in Table 5.

Variable		Median	Mean	SD	Min	Max
Horizontal Width at Crest	Baseline	9.28	9.65	1.75	6.35	14.30
	Final	0	2.38	3.89	0.00	12.20
	Δ	**-8.18**	**-7.28**	**3.11**	**-11.50**	**-0.90**
Horizontal Width at 2 mm	Baseline	11.08	11.48	2.36	7.10	16.60
	Final	7.78	7.52	3.90	0.00	13.80
	Δ	**-2.75**	**-3.96**	**3.30**	**-11.65**	**-0.75**
Horizontal Width at 4 mm	Baseline	11.95	12.30	2.53	8.00	17.40
	Final	10.58	10.71	3.06	5.15	15.80
	Δ	**-1.05**	**-1.59**	**1.83**	**-7.65**	**0.40**
Vertical Height (Δ)		**-0.50**	**-0.05**	**1.33**	**-2.10**	**2.95**

***Δ = Change from baseline to final**

Table 5. Descriptive statistics (all patients, n = 24)

Ridge width loss for all patients at the crest ranged from -0.9mm to -11.5mm, with a median loss of -8.18mm. 16 of the 24 patients experienced complete loss of the ridge at the level of the original crest, resulting in at least some level of vertical height loss.

Width loss at 2mm below the original crest for all patients ranged from 0.75mm to -11.65mm, with a median loss of -2.75mm. Two patients had complete loss of width at 2mm below the original crest as well.

At the level of 4mm below the original crest, no patients experienced complete loss of ridge width, and no vertical loss progressed to this level. One patient gained

+0.4mm in width at this level, and losses for the rest varied to a maximum loss of -7.65mm. Median ridge width loss at the 4mm level was -1.05mm.

Vertical change for all patients varied greatly from a loss of -2.1mm to a gain of +2.95mm. Median change vertically was a loss of -0.5mm.

Due to the fact that most of the data deviated from normality, or that sample size was too small to make distribution assumptions, and other assumptions for parametric tests were not met, non-parametric tests were used to assess whether differences were significant.

Given the non-normal distribution of data, median values were used to determine if the change for each technique was statistically significantly different from zero. A Wilcoxon Rank Sum test was utilized to determine if the two techniques were significantly different from each other at each measured level, regardless of the membrane product used.

HORIZONTAL CHANGE AT CREST

For both grafting techniques, with and without a buccal overlay, median horizontal width changed (decreased) significantly at the crest from baseline measurements (P=0.0005 for each). Ridge width loss from baseline for the NO group ranged from -1.5mm to -11.5mm, with a median value of -8.25mm. Ridge width loss from baseline for the buccal overlay group (BO) ranged from -0.9mm to -11.1mm, with a median value of -8.18mm. The median decrease, however, was not significantly different between the non-overlay group (NO) compared to the buccal overlay group (BO), as displayed in Table 6 (Wilcoxon Rank Sum test, $p = 0.8865$).

For patients in the NO group, 7/12 experienced complete loss of ridge width at the crest, compared to 9/12 patients in the BO group.

Technique	Measure	Mean	SD	Min	Max	Median	p-value*
NO	Baseline	10.31	1.81	7.75	14.3	10.00	
(No Overlay)	Final	3.04	4.29	0	12.2	0.00	
	Δ	**-7.27**	**3.54**	**-11.5**	**-1.5**	**-8.25**	**0.0005**
BO	Baseline	9.00	1.49	6.35	12.05	8.85	
(Buccal Overlay)	Final	1.71	3.49	0	11.15	0.00	
	Δ	**-7.29**	**2.78**	**-11.1**	**-0.9**	**-8.18**	**0.0005**
Wilcoxon Rank Sum test, p = 0.8865 (Δ NO group vs. Δ BO group)							

*Wilcoxon Signed Rank test (**Δ = 0**)

Table 6. Horizontal Change at Crest by Technique (N = 12)

HORIZONTAL CHANGE AT 2MM BELOW CREST

For both grafting techniques, median horizontal width changed (decreased) significantly 2mm below the crest from baseline measurements (P=0.0005 for each). Ridge width loss from baseline for the NO group ranged from -0.95mm to -11.65mm, with width loss for the BO group ranging from -0.75mm to -5.6mm. Median change from baseline for the NO and BO groups were -4.45mm and -2.53 respectively. A Wilcoxon Rank Sum test comparing the two group did not reach significance (p = 0.1971) as displayed in Table 7.

2/12 patients in the NO group experienced complete loss of ridge width 2mm below the original crest, while no patients in the BO group displayed complete loss of width at this level.

Technique	Measure	Mean	SD	Min	Max	Median	p-value*
NO	Baseline	12.18	2.51	8.55	16.6	11.48	
(No Overlay)	Final	6.78	4.68	0	13.4	7.03	
	Δ	**-5.40**	**4.10**	**-11.65**	**-0.95**	**-4.45**	**0.0005**
BO	Baseline	10.78	2.08	7.1	14.55	10.73	
(Buccal Overlay)	Final	8.25	2.95	4.4	13.8	7.78	
	Δ	**-2.53**	**1.25**	**-5.6**	**-0.75**	**-2.53**	**0.0005**
Wilcoxon Rank Sum test, p = 0.1971 (Δ NO group vs. Δ BO group)							

*Wilcoxon Signed Rank test (**Δ = 0)**

Table 7. Horizontal Change at 2mm by Technique (N = 12)

HORIZONTAL CHANGE AT 4MM BELOW CREST

At 4mm, both grafting techniques had median horizontal width values that decreased significantly from baseline measurements (P=0.0005 for each NO and 0.0029 for BO). Ridge width loss from baseline for the NO group ranged from -0.2mm to -7.65mm, with ridge change for the BO group ranging from +0.4mm to -2.2mm. Median change from baseline for the NO and BO groups were -1.18mm and -0.88mm respectively as displayed in Table 8. A Wilcoxon Rank Sum test comparing the two group did not reach significance (p = 0.2483).

No patients experienced complete loss of ridge width in either group at 4mm below the original crest.

Technique	Measure	Mean	SD	Min	Max	Median	p-value*
NO	Baseline	12.96	2.65	8.7	17.4	12.38	
(No Overlay)	Final	10.70	3.52	5.15	15.8	10.53	
	Δ	**-2.26**	**2.34**	**-7.65**	**-0.2**	**-1.18**	**0.0005**
BO	Baseline	11.65	2.34	8	15.4	11.80	
(Buccal Overlay)	Final	10.73	2.68	6.6	14.7	10.68	
	Δ	**-0.93**	**0.76**	**-2.2**	**0.4**	**-0.88**	**0.0029**

Wilcoxon Rank Sum test, p = 0.2483 (Δ NO group vs. Δ BO group)

*Wilcoxon Signed Rank test (**Δ = 0**)

Table 8. Horizontal Change at 4mm by Technique (N = 12)

VERTICAL CHANGE.

For both grafting techniques, the median vertical height change from baseline was not significantly different from zero. Additionally, the median vertical height change for the two techniques compared to each other was not significantly different as seen in Table 9 (Wilcoxon Rank Sum test, p = 0.7972). Vertical change from baseline for the NO group ranged from -2.1mm to +2.95mm, while the BO group experienced vertical change from -1.3mm to +2.35mm. Median vertical changes for NO and BO groups were -0.23mm and -0.60mm respectively.

Technique	Measure	Mean	SD	Min	Max	Median	p-value*
NO	Δ	0.01	1.53	-2.1	2.95	-0.23	0.9658
BO	Δ	-0.11	1.15	-1.3	2.35	-0.60	0.5820
Wilcoxon Rank Sum test, p = 0.7972 (Δ NO group vs. Δ BO group)							

*Wilcoxon Signed Rank test (**Δ = 0**)

Table 9. Vertical Change by Technique (N = 12)

CHAPTER 7: Discussion

It has been well established in the literature that resorption following tooth extraction is a common occurrence, and likely an inevitable result of the procedure. The extent to which interventions at the time of extraction can affect these dimensional changes is much less clear. In this study, we sought to examine buccal augmentation to determine if this intervention can prevent or minimize these changes with the goal of maximizing esthetic and functional outcomes while minimizing further surgical intervention. The current work represents the analysis of the initial set of patients recruited to an ongoing clinical study. One purpose of this initial study was to determine if any procedure had a substantial adverse or beneficial effect that would warrant cessation of the study.

In interpreting the results of this initial study, several things must be kept in mind. Overall, the group sizes for each of the four groups was relatively small (N=6), while just comparing NO vs. BO groups yielded a N = 12 in each group. Due to the small sample sizes, the likelihood of finding significant, but not dramatic, differences among groups at this point was small. As more data is gathered, and the sample sizes grow, detecting any significant differences between the groups that exists becomes more likely.

Despite the small sample size and lack of statistical significance, some potentially important clinical differences may be gleaned from the data. Minimal difference was seen between the two groups at the original crestal height. Both groups had a large number of patients that lost all of their ridge at this level, and the range of percentage of width lost for the other patients ranged from 7.4% to 72.9%. This amount of loss was statistically significant. In placing and restoring implants, the restorative endpoint for

this procedure, retaining the bone at the original crestal level is not nearly as important as at the 2mm and 4mm levels. Seldom do we want to place the implant platform at the level of the original crest, as this would not afford adequate height for restoration between the implant platform and the occlusal table. Often, the implant platform is placed approximately 3mm apical to the adjacent cementoenamel junctions (CEJs), which provides at least 7mm of vertical restorative height. Thus, the residual ridge at 2mm or 4mm below the original crest becomes much more important that the crestal bone, and some level of vertical loss is acceptable, since bone would otherwise need to be removed during implant placement anyway.

At 2mm below the ridge, buccal augmentation resulted in less width loss compared to no augmentation, though it did not reach statistical significance with such a small sample size. Median ridge losses at this level were -4.45mm and -2.53mm for NO and BO groups respectively. Looking at mean loss instead of median, an even greater difference is displayed, -5.40mm vs. -2.53mm. This average difference of nearly 3mm, if persistent with growing sample sizes, could lead to a significant reduction in the number of sites that need additional augmentation before or at the time of placement to ensure 2mm of bone circumferentially around the implant.

At the 4mm level, the buccal augmentation group also had less resorption, but also was not statistically significant given the small sample size associated with this initial study. Mean ridge losses demonstrated a larger difference that median numbers, with the NO group losing -2.26mm vs -0.93 for the BO group. Whether this difference continues and ultimately become statistically significant with an increased sample size and study power will remain to be seen.

If these trends of reduced horizontal resorption with the use of a buccal overlay continue as the study continues to grow, significant clinical implications could be realized. Previous research on the effect of buccal overlays on extraction induced ridge resorption is scant and significantly under-powered. Evidence that buccal overlays assist with preserving ridge width could justify the expenditure on additional graft material, particularly in cases where the ridge is particularly thin to begin with or a facial undercut is present initially.

Due to the current limitations on the sample sizes included in this initial portion of the ongoing study, statistically significant conclusions about techniques cannot be drawn at this time. Based on our initial power analysis conducted during the design portion of this project, it is anticipated that 128 participant's data would be needed to allow sufficient data for effective determination of differences. The fact that no significant differences can be detected so far is not surprising, and is expected at this point in the study. The perpetuation of this study will allow increased discrimination of the data, but will allow meaningful analysis of the multitude of secondary outcome measurements and their impact on the primary outcomes to determine the most effective treatment possible for our patients.

Additional uses of the data gathered during the initial portion of this study have been theorized. After developing our standardized way of measuring CBCT dimensional changes, the calculation of the change in cross-sectional area is additionally possible in Dolphin 3d software. Utilizing this software capability with the images captured could allow a more thorough analysis of ridge alteration.

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APPENDICES

APPENDIX A – CONSENT FORMS

Version # 1, Date: 1 MAY 2015

United States Army Dental Command
Fort Gordon DENTAC, Tingay Dental Clinic

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH

You are being asked for permission to use or disclose your protected health information for research purposes in the research study entitled "Comparison of Two Different Alveolar Ridge Preservation Techniques."

Protected health information is defined as individually identifiable health information.

The Health Insurance Portability & Accountability Act of 1996, Public Law 104-109 (also known as HIPAA), establishes privacy standards to protect your health information. This law requires the researchers to obtain your authorization (by signing this form) before they use or disclose your protected health information for research purposes in the study listed above.

Your protected health information that may be used and disclosed in this study includes:

• Name • Social security number (SSN) • Date of extraction • Phone numbers • Unique ID number assigned to you while you are part of the study.	Heath information collected from you or your medical record: • Laboratory results (if applicable) • Imaging results (X-ray, CBCT, intra-oral photos) • Pain survey

Your protected health information will be used for:

Your personal information will be gathered and stored securely. Your name, phone number, and social security number are collected or used to maintain your research records. This information is not used in the research itself. Radiographs and photographs are routinely taken as part of clinical care at Tingay Dental Clinic. If photographs are taken as part of this care, they will be reviewed in order to better answer research questions. Any imaging data collected for clinical care or the research study will used to answer the research questions. The health information mentioned above will collected from your medical records for the purpose of this research study. A

study ID number will be used when recording research related information to further protect your confidentiality.

The disclosure of your protected health information is necessary in order to be able to conduct the research project described. Records of your participation in this study may only be disclosed in accordance with state and federal law, including the Privacy Act (5 U.S.C. 552a) and the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (45 CFR 160 & 164). Note: Protected health information of military service members may be used or disclosed for activities deemed necessary by appropriate military command authorities to ensure the proper execution of the military mission.

By signing this authorization, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.

The Principal Investigator may use and share your health information with:

- The BAMC Institutional Review Board
- BAMC or Department of Defense representatives
- State and Federal Government representatives, when required by law
- Department of Periodontics Residents and staff who are members of the research team

The researchers and those listed above agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and federal law.

You need to be aware that some parties receiving your protected health information may not have the same obligations to protect your protected health information and may re-disclose your protected health information to parties not named here. If your protected health information is re-disclosed, it may no longer be protected by state or federal privacy laws.

You do not have to sign this Authorization. If you decide not to sign the Authorization:

- It will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.
- You will not be allowed to participate in the research study.

After signing the Authorization, you can change your mind and:

- Notify the researcher that you have withdrawn your permission to disclose or use your protected health information (revoke the Authorization).
- If you revoke the Authorization, you will send a written letter to MAJ Brandon Coleman, Tingay Dental Clinic BLDG 320, 228 E, Hospital Road, Fort Gordon, GA, 30905 to inform him of your decision.
- If you revoke this Authorization, researchers may only use and disclose the protected health information already collected for this research study.
- If you revoke this Authorization your protected health information may still be used and disclosed should you have an adverse event (a bad effect).
- If you withdraw the Authorization, you will not be allowed to continue to participate in the study.

During your participation in this study, you will not be able to access your research records. This is done to ensure the study results are reliable. After the completion of the study, you have the right to see or copy your research records related to the study listed above. A Request for Access must be made in writing to MAJ Brandon Coleman, Tingay Dental Clinic BLDG 320, 228 E, Hospital Road, Fort Gordon, GA, 30905.

If you have not already received a copy of the brochure entitled "Military Health System Notice of Privacy Practices," you may request one. DD Form 2005, Privacy Act Statement - Military Health Records (located on your medical records jacket), contains the Privacy Act Statement for the records. If you have any questions or concerns about your privacy rights, you should contact the Fort Gordon DENTAC Privacy Officer at phone number (706) 787-6927.

This Authorization does not have an expiration date.

You are the subject and have read this information. You will receive a copy of this form after it is signed.

SIGNATURE OF PARTICIPANT

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

Tingay Dental Clinic, Fort Gordon DENTAC

INFORMED CONSENT DOCUMENT

PROTOCOL TITLE: Comparison of Two Different Alveolar Ridge Preservation Techniques

PRINCIPAL INVESTIGATOR: Brandon Coleman MAJ,DC

If you choose not to participate in this research study, your decision will not affect your eligibility for care or any other benefits to which you are entitled.

DESCRIPTION/PURPOSE OF RESEARCH:

You are being asked to consider participation in this research study. The purpose of this study is to compare four different ways to preserve the bone after a tooth (ridge preservation) is removed. When a tooth is taken out and nothing else is done, your bone heals but some bone is lost overall. Studies have shown that ridge preservation can limit the amount of bone that is lost. In many cases, ridge preservation procedures save enough bone to allow an implant to be placed without the need for additional bone graft procedures. The ridge preservation procedure has been shown to save bone, but no one knows which products or techniques work the best. In addition, no one knows if overfilling the socket with bone graft is better than filling the socket with bone graft. A few small studies have shown that overfilling might add some value.

This study will enroll approximately 150 subjects at Tingay Dental Clinic (DC) over a period of 2 years.

As part of your dental care and as part of your participation in this study, you will be asked to make approximately 6 total outpatient visits with a periodontics resident or staff (1 evaluation appointment, 2 surgical procedures, and 3 or more follow-ups). It may be necessary for you to return to Tingay DC at 1,2, and 4 weeks, as you would for all surgical procedures at Tingay DC. You will also have a procedure to place the implant about 4 months after the tooth is taken out. You will have the same number of appointments whether or not you are involved in the study.

You have been selected to participate in this study because you have a tooth that has been determined to be hopeless by at least 2 dentists and needs to be removed. You are also being considered for a dental implant to replace the missing tooth.

All of the products and materials used in this study are approved by the Food & Drug Administration for the ridge preservation procedure.

PROCEDURES:

As a participant in this study you will be randomly assigned to one of four treatment plans to preserve the bone in your socket after tooth extraction. Randomization is a process like flipping a coin and means you will have a chance of being assigned to any of the plans. One group receives Cytoplast and normal bone filling, one group receives Cytoplast and overfilling, one group receives BioXclude and normal bone filling, and the last group receives BioXclude with overfilling. All 4 groups are considered the standard of care at Tingay Dental Clinic, but no one knows which group is the best. This study is a single blind study, which means that you will not know what treatment group you are in.

After your tooth is removed, the socket will be cleaned and filled with a bone graft material. As part of standard dental care, some patients will have additional bone added outside of the socket itself. The bone graft will be covered by one of two barrier devices: dense polytetrafluoroethylene (Cytoplast) or human amniotic-tissue derived membrane (BioXclude). Stitches will then be placed to hold the tissue together over the barrier device. You will be given medications for post-operative management (an antibiotic, a mouth rinse, and pain medication). You will then follow up with your doctor at 1,2, and 4 weeks as you would normally. If you receive Cytoplast, it will be removed at your 4 week appointment after surgery. This procedure is very quick and easy, but may occasionally require numbing up the area.

At four months, you will return to the clinic. At that visit, a second CBCT will be conducted as part of the research study and an implant will be placed at a second surgical procedure. Placement of your new tooth in the implant will occur at a separate visit. The study is considered complete when the implant is placed and any remaining treatment is not considered research.

During the study, we will also be reviewing and collecting information about your dental care from your dental records.

A separate surgical consent form will be given to you that describes the risks related to dental surgery.

RISKS OR DISCOMFORTS:

The risks for all four possible treatment groups are similar, both to each other, and to all periodontal surgical procedures. Some pain, swelling, and bleeding are expected 100% of the time. On rare occasion (<5%), the site may become infected or the nearby teeth or tissues can be damaged during the extraction process. On very rare occasions (<1%), you may develop an allergy to one of the products. Allergies and infections are generally mild, but could become life-threatening in some cases.

One out of 10 patients may have a Cytoplast membrane become irritating or become loose. In both cases, the membrane may be removed earlier than four weeks without any long-term consequences to your surgery site. There are currently no reported problems/potential risks with BioXclude.

This research study involves exposure to radiation from two Cone Beam CT scans. The second scan is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study can be up to 100 mrem (1000 µSv) which is well below the guideline of 5 rem (or 0.5 rem in children) per year allowed for radiation workers. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil so the dose you will receive in this research study is about the same amount you would normally receive in four months from these natural sources.

There is no direct evidence that the small amount of exposure received from participating in this study is harmful but any amount of radiation exposure may produce an insignificant, yet non-zero, increase in the risk of cancer.

As a FEMALE OF CHILD BEARING POTENTIAL wishing to volunteer for this project, you must understand that this ridge preservation procedure and/or the drugs prescribed to you might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding. Therefore, you may not be pregnant and should take a pregnancy test before you participate in this study. You must also agree to take precautions to prevent pregnancy during the course of this study due to the possible severe harm the drug/procedure may cause your unborn child. The only completely reliable methods of birth control are total abstinence or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products are not totally effective in preventing pregnancy. Also, you may not breast-feed and participate in this study.

If you become pregnant or feel you might be pregnant, contact your provider and the study investigator listed in the voluntary participation section.

There may also be unforeseen risks associated with this study.

Studies evaluating the capability of the medication under investigation to produce birth defects in an unborn child have not been completed/conducted.

Every effort is made to protect your privacy, however, any research has some risk that your confidential information may be accidentally revealed. Standard laws and procedures minimize this risk. You will be notified if a breach occurs.

BENEFITS:

There are no benefits to you for taking part in this research study. You will receive the same care as you would have received if you were not enrolled in the study. However, The results from this study may benefit future patients by leading to improvements in the dental care.

PAYMENT (COMPENSATION):

You will not receive any compensation (payment) for participating in this study.

ALTERNATIVES TO PARTICIPATION:

Choosing not to participate in this study is your alternative to volunteering for the study.

If you do not want the socket preservation and implant therapy performed, there are other treatment alternatives to you (a bridge, a removable partial denture, or leaving an empty space). Talk with your dental care provider about these other options.

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

CONFIDENTIALITY OF RECORDS OF STUDY PARTICIPATION:

Records of your participation in this study may only be disclosed in accordance with federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing

regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records.

By signing this consent document, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.

Your records may be reviewed by the U.S. Food & Drug Administration (FDA), other U.S. government agencies, the BAMC Institutional Review Board, and by the Fort Gordon DENTAC.

Complete confidentiality cannot be promised, particularly for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities. Additionally, although efforts are made to protect your study records, it is possible that your confidentiality may be breached by unplanned loss of your records.

ENTITLEMENT TO CARE:

In the event of injury resulting from this study, the extent of medical care provided is limited and will be within the scope authorized for Department of Defense (DoD) health care beneficiaries.

Your entitlement to medical and dental care and/or compensation in the event of injury is governed by federal laws and regulations, and if you have questions about your rights as a research subject or if you believe you have received a research-related injury, you may contact the Brooke Army Medical Center Institutional Review Board at, (210) 916-2598. You may also contact DDEAMC Judge Advocate General, (706) 787-7235.

BLOOD & TISSUE SAMPLES:

No blood or tissue samples will be taken as part of this study.

VOLUNTARY PARTICIPATION:

The decision to participate in this study is completely voluntary on your part. No one has coerced or intimidated you into participating in this project. You are participating because you want to. The Principal Investigator or one of his associates has adequately answered any and all questions you have about this study, your

participation, and the procedures involved. If significant new findings develop during the course of this study that may relate to your decision to continue participation, you will be informed.

You may withdraw this consent at any time and discontinue further participation in this study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must notify one of the department staff. If you would like to withdraw from the treatment as well, you will need to schedule an appointment to have the Cytoplast device removed (where applicable). Routine follow-up appointments may be needed to make sure you heal properly.

The investigator of this study may terminate your participation in this study at any time if he feels this to be in your best interest.

CONTACT INFORMATION:

Principal Investigator (PI)
The Principal Investigator or a member of the US Army, Advanced Education Program in Periodontics staff will be available to answer any questions concerning procedures throughout this study.

Principal Investigator: Brandon Coleman MAJ,DC
Phone: (210) 326-0547

Your consent to participate in this study is given on a voluntary basis. All oral and written information and discussions about this study have been in English, a language in which you are fluent.

A signed and dated copy of this form will be given to you.

SIGNATURE OF PARTICIPANT

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF CONSENTING INDIVIDUAL
(Can only be signed by an investigator or staff whose name is listed in the protocol and approved to consent)

_____
Printed Name of Consenting Individual

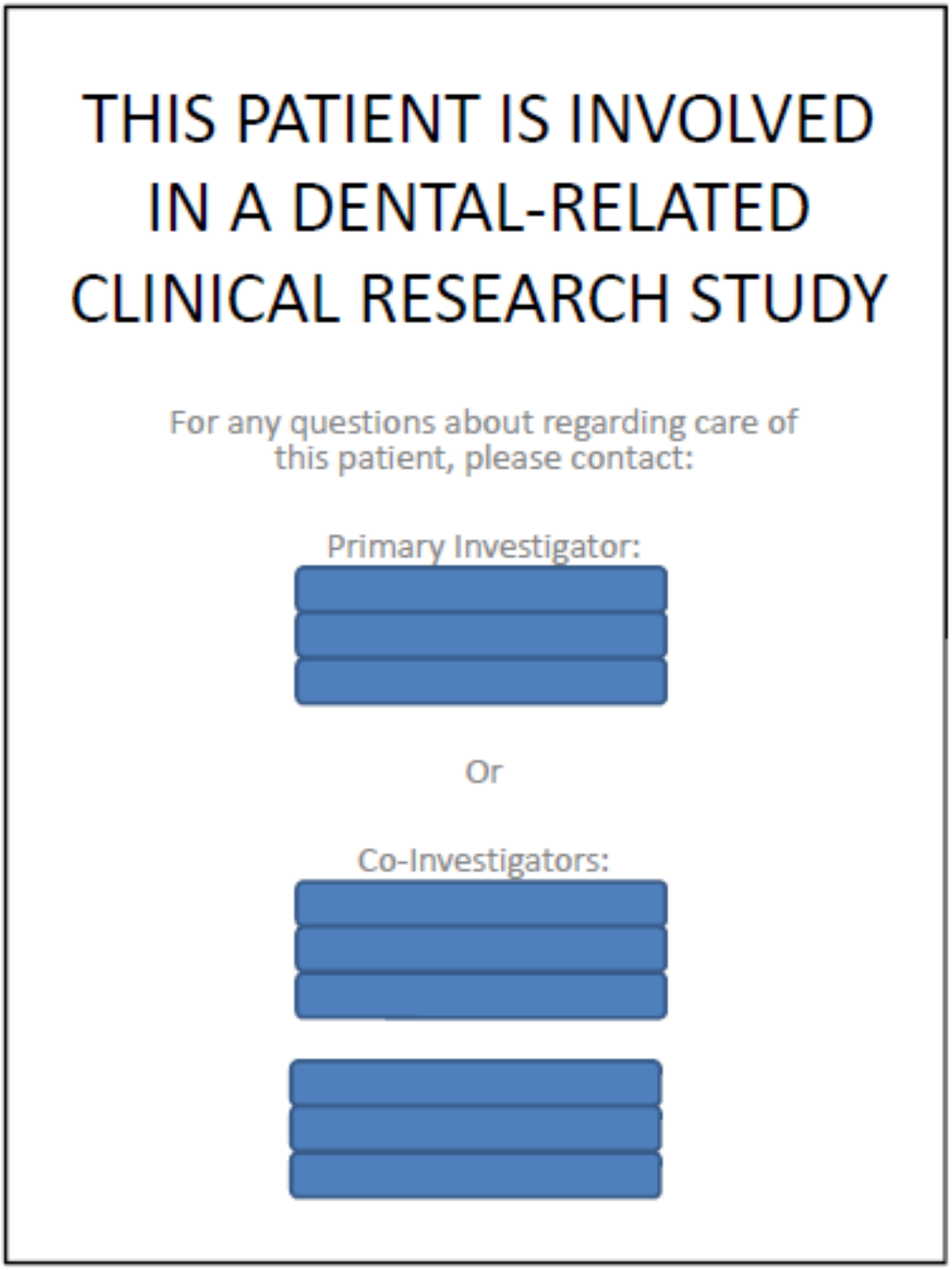
_____ _____
Signature of Consenting Individual Date

SIGNATURE OF WITNESS TO THE CONSENT/ASSENT PROCESS
I certify that the above signed research participant has freely and voluntarily provided written consent to participate in this research study.

_____
Printed Name of Witness

_____ _____
Signature of Witnessing Individual Date

APPENDIX B – CHART FORM



CLINICAL RESEARCH CHECKLIST

- ☐ **Informed Consent Form – Give to MAJ Coleman**
- ☐ **HIPAA Form – Give to MAJ Coleman**
- ☐ **Initial CBCT – Let Lincicum/Hussey know when complete**
  - **Highest Resolution/Smallest appropriate field (40x40mm)**
  - **Place cotton rolls adjacent to site for tissue separation**
  - **Label with patients full name**
- ☐ **Fill out Baseline portion of <u>Baseline and Surgical Assessment Form</u> (up to "Difficulty of Extraction") and retain**
- ☆ **Day of Surgery**
  - ☐ **Receive randomized group envelope from MAJ Coleman**
  - ☐ **Take clinical photos as usual, particularly photo of exposed buccal plate**
  - ☐ **Complete <u>Baseline and Surgical Assessment Form</u> – Give to MAJ Coleman**
- ☐ **1 Week F/U – Complete <u>Post-op Assessment Form</u> including pain perception markings – Give to MAJ Coleman**
- ☐ **2 Week F/U/Suture removal – <u>Post-op Assessment Form</u> – Give to MAJ Coleman**
- ☐ **4 Week F/U/Membrane removal (Cytoplast) – <u>Post-op Assessment Form</u> – Give to MAJ Coleman**
- ☐ **4 Months CBCT – Let Lincicum/Hussey know when complete**
  - **Highest Resolution/Smallest appropriate field**
  - **Place cotton rolls adjacent to site for tissue separation**
  - **Label with patients full name**
- ☆ **Implant surgery – complete <u>Implant Surgery Assessment Form</u> – Give to MAJ Coleman**

<u>Please ensure all forms are given to MAJ Coleman ASAP after completion!!!</u>

APPENDIX C – DATA COLLECTION SHEETS

Patient Name: _____ Rank: _____ Last4: _____

Subject ID: _____ *(to be filled in by the PI later)*

Baseline & Surgical Assessment Form

Tooth Number: _____

Keratinized Gingiva: _____ mm

Biotype: _____ (thick / thin)

Reason for extraction: _____ (be brief)

Presence or Absence of active local infection? Yes or No

Anticipated Elian classification: _____ (I II or III)

Difficulty of extraction: _____ (routine or complex)

Would GBR be required regardless of socket preservation? _____

Residual buccal plate thickness at crest: _____ mm (estimate with probe @ mid-ext site)

Residual ridge width at crest: _____ mm (estimate with probe @ mid-ext site)

Dehiscence or fenestrations? _____ (yes or no, if yes then how severe (% of buccal plate)?)

De facto Elian classification at closure: _____ (I II or III)

Ease of use of product: (very easy) 1 2 3 4 5 (very hard)

Patient Name: _____ Rank: _____ Last4: _____

Subject ID: _____ *(to be filled in by the PI later)*

Post-Operative Assessment Form

Time since surgery: _____ (days or weeks)

(1 week POT only) Please have patient place a mark along the scale indicating pain level:

Patient's report of most significant pain:

No pain _____ Extreme Pain

Patient's report of average pain experience:

No pain _____ Extreme Pain

Complications: _____ (substantial pain, graft failure, infection, etc)

Membrane removal: _____ yes or no *(this appointment only)*

This form is required at the one week post-op appointment AND for any complication or membrane removal appointment

Version 1, 18 MAR 2015

Patient Name: _____ Rank: _____ Last4: _____

Subject ID: _____ *(to be filled in by the PI later)*

CBCT Assessment Form

Tooth number: _____

Date of Scan: _____

Is this scan pre-op or post-op? _____

If post-op, how long from time of surgery? _____

Was a reference marker used? _____

B-L ridge width as measured at mid-extraction socket (or using reference point):

At crest: _____

2mm below crest: _____

4mm below crest: _____

Cortical bone thickness:

At crest: _____

2mm below crest: _____

4mm below crest: _____

Patient Name: _____ Rank: _____ Last4: _____

Subject ID: _____ *(to be filled in by the PI later)*

Implant Surgery Assessment Form

Tooth Number: _____

Keratinized Gingiva: _____ mm

Residual ridge width at crest: _____ mm (estimate with probe @ mid-ext site)

If you were not able to place the implant today, please state why: _____

If you were able to place the implant:

Implant platform placed: _____

Primary stability: _____

Was the implant size the intended implant or did you have to use a smaller implant? _____

Were any additional augmentation procedures performed? _____

If so, were these entirely necessary to place the implant IAW with prosth guidelines and have 2mm of buccal bone on the implant? Or was augmentation performed for MRB/CYA? _____

If so, was GBR going to be required from the beginning? _____