# PERIODONTAL REGENERATION OF 1-, 2-, AND 3-WALLED INTRABONY DEFECTS USING ACCELL CONNEXUS<sup>®</sup> VERSUS DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT: A RANDOMIZED PARALLEL ARM CLINICAL CONTROL TRIAL

by

Teresita LaRonce Alston Lieutenant Commander, Dental Corps United States Navy

A thesis submitted to the Faculty of the Periodontics Graduate Program Naval Postgraduate Dental School Uniformed Services University of the Health Sciences in partial fulfillment of the requirements for the degree of Master of Science in Oral Biology Naval Postgraduate Dental School Uniformed Services University of the Health Sciences Bethesda, Maryland

CERTIFICATE OF APPROVAL

#### MASTER'S THESIS

This is to certify that the Master's thesis of

Teresita LaRonce Alston

has been approved by the Examining Committee for the thesis requirement for the Master of Science degree in Oral Biology at the June 2015 graduation.

Thesis Committee:

Matthew B. Miller, CDR, DC, USN Program Director, Periodontics Department

Thu Četka, CAPT, DC, USN Chairman, Periodontics Department

Jeffery Wessel, LCDR, DC, USN Assistant Program Director, Periodontics Dept

Men (

Peter Bertrand, CAPT (ret), DC, USN Research Department

Glenn Munro, CAPT, DC USN Dean, Naval Postgraduate Dental School

The author hereby certifies that the use of any copyrighted material in the thesis manuscript titled:

"PERIODONTAL REGENERATION OF 1-, 2-, AND 3-WALLED INTRABONY DEFECTS USING ACCELL CONNEXUS<sup>®</sup> VERSUS DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT: A RANDOMIZED PARALLEL ARM CLINICAL CONTROL TRIAL"

is appropriately acknowledged and, beyond brief excerpts, is with the permission of the copyright owner.

Teresita LaRonce Alston

Periodontics Graduate Program Naval Postgraduate Dental School June 2015

#### NAVAL POSTGRADUATE DENTAL SCHOOL TERESITA LARONCE ALSTON

2015

This thesis may not be re-printed without the expressed written permission of the author.

#### ABSTRACT

### PERIODONTAL REGENERATION OF 1-, 2-, AND 3-WALLED INTRABONY DEFECTS USING ACCELL CONNEXUS VERSUS® DEMINERALIZED FREEZE-DRIED BONE ALLOGRAFT: A RANDOMIZED PARALLEL ARM CLINICAL CONTROL TRIAL

#### TERESITA L. ALSTON DMD, PERIODONTICS, 2015

Thesis directed by: Peter M. Bertrand, DDS CAPT (Ret), DC, USN Professor Naval Postgraduate Dental School

Introduction: Combination therapy, in guided tissue regeneration (GTR), is often used in the treatment of intrabony defects. Particulate demineralized freeze- dried bone allograft (DFDBA) is a bone grafting materials used successfully in GTR on humans for almost 30 years. A newer form of DFDBA, Accell Connexus<sup>®</sup> (Accell), has been FDA approved for use in periodontal regeneration which is the growth of new bone, cementum and periodontal ligament on a previously diseased tooth root surface. Accell Connexus<sup>®</sup> contains 5-7 times more bone morphogenic proteins (BMP) than the traditional particulate DFDBA. This increase in BMP is thought to increase the potential of periodontal regeneration.

Methods: A total of 30 patients diagnosed with severe periodontitis having an intrabony defect with a probing depth of > 6 mm are included in this study. Customized plastic stents were fabricated to obtain standardized clinical probing depth (PD) and clinical attachment level of the defects at baseline, surgery, 6 and 12 months post-surgery. Standardized digital radiographs were taken using a customized bite-plate and a paralleling device for reproducibility of periapical radiographs at baseline and at 6 and 12 months after surgery. All participants received the same standardized surgical approach for GTR combination therapy. After defect debridement, and before root surface treatment with ethylenediaminetetraacetic acid (EDTA), the surgical team opened the sealed envelope containing the name of the bone graft material randomized to the participant's study number: DFDBA (control) or Accell (test). Fifteen patients will receive DFDBA and 15 patients Accell. Participants were re-evaluated to assess postoperative healing at weeks 1, 2, 4, 6, 8, 12, and 16, and again at 6, 9 and 12 months. After the 12 month re-evaluation, participants continued periodontal maintenance therapy with their providers. This interim data analysis compared changes in plague index, bleeding on probing, PD, CAL and radiographic bone levels at baseline, 6 and 12 months post-surgery using the Mann-Whitney U test.

Results: A total of 21 subjects have been enrolled in this study and surgery has been completed on 20. Six month results have been finalized on 14 subjects and 1 year results on 13 of the subjects. Three patients were exited. Two of the exited patients were from the Accell group and 1 from the DFDBA group. At this time there were 13 complete sets of data therefore 13 sets of 6 month and 1 year results were analyzed with 8 subjects in the DFDBA group and 5 in the Accell group for this interim analysis. No significant difference was found with respect to bleeding on probing (BOP) or plaque scores. The mean probing depth (PD) decreased from 7.6 to 3.8mm for Accell and from 8mm to 4mm for DFDBA. Mean gain of CAL was 3.4mm for Accell and 3.0mm for DFDBA. Accell and DFDBA attained positive percent radiographic bone fill; 65.79% and 59.9% respectively. The results were not statically significant.

Discussion: Definitive conclusions cannot be drawn at this time because 12 month clinical measurements have been made in less than half of the subjects in the approved sample size.

Conclusions: The data analysis at this point does not show any significant statistical difference in clinical and radiographic outcomes between DFDBA and Accell. Both bone graft materials resulted in improved clinical parameters.

# TABLE OF CONTENTS

## Page

LIST OF TABLES v			
LIST OF FIGURES			
LIST OF ABBREVIATIONS			
CHAPTER			
Ι.			
1.			
11.	REVIEW OF THE LITERATURE	3	
	a. Overview	3	
	b. The Periodontium	5	
	c. The Periodontium in Disease	6	
	d. The Etiology of Periodontitis		
e. Smoking and Periodontitis			
f. Treatment of Periodontitis			
g. Guided Tissue Regeneration			
h. Materials Used in Guided Tissue Regeneration			
i. Root Surface Conditioners			
ii. Bone Grafts		22	
ii. Barrier Membranes 1. Nonresorbable verses Resorbable -Nonresorbable		25	
		25	
		26	
	-Synthetic Resorbable	27	
- Natural Resorbable		27	
	i. Soft Tissue (Gingiva) Closure	29	
111.	MATERIALS AND METHODS	32	
IV.	RESULTS		
V.	DISCUSSION		
VI.	CONLUSIONS	53	
APPENDIX A	Raw Data A1 Baseline	55 55	

	A2 Surgical A3 6 Months Post- Surgery A4 12 Months Post-Surgery A5 Radiographic Baseline/ 6 and 12 Months Post-Surgery	56 57 58 59
APPENDIX B	Accell Connexus® Statistics	60
APPENDIX C	DFDBA Statistics	63
APPENDIX D	Mann-Whitney Statistic Tables	66
APPENDIX E	Frequency Tables	67
appendix f	Flow Diagrams F1 Flow Diagram of Study Design F2 Flow Diagram of Accell Processing	70 70 71
APPENDIX G	Patient Check/ Safety Sheets G1 Inclusion/ Exclusion Check Sheet G2 Adverse Event/ Deviation Log	72 72 73
APPENDIX H	Data Collection H1 Data Collection Sheets H2 Periodontal Charting Form	74 74 79
APPENDIX I	Example NPDS Periodontics Dept Pot-op Instructions	80

REFERENCES	 81

### LIST OF TABLES

Table		Page
1.	Collagen Resorbable Membranes	28
2.	Sample Random Sequence Generator	39

## LIST OF FIGURES

Figure		Page
1.	The Periodontium in Health	5
2.	The Periodontium with Gingivitis	7
3.	The Periodontium with Periodontitis	8
4.	Radiographic Bone Patterns	10
	a. Normal	
	b. Horizontal Bone Loss	
	c. Vertical Bone Loss	
5.	Example Clinical 3 Walled Defect	11
6.	Sample Customized Stent	36
7.	Sample Customized Radiographic Bite Plate	37
8.	Demineralized Fre zed Dry Bone Allograft	43
9.	Accell Connexus®	43
10.	Sample Case	47
	a. Radiographic Baseline	
	b. Surgical Debridement of 3- Walled Defect	
	c. Radiographic Results 6 Months Post-surgery	
	d. Radiographic Results 12 Months Post-surgery	
11.	Graph of Probing Depth Results	49
12.	Graph of Clinical Attachment Level Results	49
13.	Graph of Radiographic Bone Fill in Millimeters	50
14.	Graphic of Radiographic Bone Fill in Percentage	50

15.	Radiographic Sample Case	
	a. Case Randomized to DFDBA Baseline	
	b. Case Randomized to DFDBA 12 Month Results	
	c. Case Randomized to Accell Connexus® Baseline	

d. Case Randomized to Accell Connexus® 12 Month Results

.

### LIST OF ABBREVIATIONS

GTR		Guided Tissue Regeneration
вмр		Bone Morphogenetic Protein(s)
BOP		Bleeding on Probing
OHI		Oral Hygiene Instructions
SRP		Scaling and Root Planning
OFD	••••••	Open Flap Debridement
CAL		Clinical Attachment Level
CEJ		Cementoenamel Junction
DFDBA		Demineralized Freeze-Dried Bone Allograft
EDTA		Ethylenediaminetetraacetic acid
FDBA		Freeze-Dried Bone Allograft
GS		Gingival Sulcus
JE		Junctional Epithelium
со		Supracrestal Fibers
AC		Alveolar Crest
OE		Oral Epithelium
PD		Probing Depth
PDL		Periodontal Ligament
SE		Sulcular Epithelium
SEM		Scanning Electron Microscope
HCG		Human Chorion Gonadotropin
NPDS		Naval Postgraduate Dental School

#### **CHAPTER I: INTRODUCTION**

According to the 4<sup>th</sup> Edition of the Glossary of Periodontal terms, periodontal regeneration is the "reproduction or reconstitution of a lost or injured part" related to a diseased periodontium. The periodontium consist of the periodontal ligament, cementum and bone that surround the tooth. When these structures are destroyed due to periodontal disease the bone is lost creating a horizontal defect (flat) or a vertical intrabony defect. The potential to regenerate them is termed guided tissue regeneration (GTR). Completing GTR for regeneration of an intrabony defect is more predictable than for a horizontal defect. Over the years many specific techniques have been utilized however one GTR technique is to employ the use of a barrier membrane with a bone graft after the defect has been debrided and the root surface properly cleaned.

The purpose of the membrane is to allow for selective cell exclusion (Melcher, 1976). This means to prevent faster growing cells like the epithelium and connective tissue or collectively termed the gingival corium from rapidly growing into the site where slower growing cells; the periodontal ligament (PDL) fibroblast, cementoblast and osteoblast, would normally populate. This exclusion would allow for regeneration of the lost parts of the periodontium. Two main types of barrier membranes exist resorbable and non-resorbable. Resorbable collagen membranes prevent the need for a second surgical procedure which must be done to remove a non-resorbable membrane.

Although bone grafts are not always used in GTR procedures it has been shown that the addition of a bone graft can enhance regeneration (Bowers 1989 a, b, c). There are several types of bone grafting materials however the use of demineralized freeze dried bone allograft (DFDBA) was the first type of bone graft material to histologically

demonstrate regeneration (Bowers 1989 b, c) and is considered the gold standard for GTR with bone grafts. Newer forms of DFDBA have been formulated to include Accell Connexus<sup>®</sup>, which is believed to increase the potential of regeneration due to its ability to stay in place and its increased amount of bone morphgenic proteins (BMP).

If the combination of a membrane and a bone graft can enhance periodontial regeneration; will the combination of a non-resorbable membrane and a newer form of DFDBA, Accell Connexus<sup>®</sup>, further enhance periodontal regeneration?

#### Chapter II: Review of the Literature Overview

Techniques for the surgical treatment of intrabony defects has varied from; open flap debridement, gingivectomy, osseous therapy, guided tissue regeneration (GTR), GTR with bone graft, GTR with bone graft and membrane, laser therapy to extraction of the tooth. Although completing a simple gingivectomy to address an intrabony lesion is no longer an accepted standard of care (Schluger, 1949) all of the other surgical options are still utilized as a standard form of care for intrabony defects. Of those treatment options GTR has been employed since the early 1980's. The concept of periodontal GTR was first described in humans by Dr. Sture Nyman and colleges who found that a new connective tissue attachment could form on a previously diseased root surface (Nyman, 1982). They tested a single severe, chronic infected mandibular incisor having a clinical attachment level of 11mm and a 2mm intrabony component at which point a crestal level notch was made in the tooth. After degranulation along with scaling and root planning a Millipore filter non-resorbable membrane was properly sized to cover an area coronal to the cemental enamel junction (CEJ) to slightly beyond the bony crest. The site was sutured with the membrane slightly exposed and was allowed to heal for three months. Histologically, they found collagen fibers inserting into newly formed cementum 5mm beyond the notch and bone regenerated only to the level of the bony crest. This proved that regeneration could occur on a previously diseased root surface.

In the field of periodontics it is import to regenerate bone, cementum and the periodontal ligament (PDL) that have been lost around teeth due periodontitis. The bone, cementum and PDL are also known as the periodontal attachment or periodontium. When reconstituting these parts the process of GTR can be utilized. GTR is a procedure attempting to restore lost periodontal structures through differential tissue responses (Melcher, 1976). The

use of barrier techniques, using membranes such as polytetrafluoroethylene, expanded polytetrafluoroethylene (ePTFE), polyglactin, polylactic acid, calcium sulfate and collagen, are employed in the hope of excluding epithelium and the gingival corium from the root or existing bone surface in the belief that they interfere with regeneration. Along with membranes, bone substitutes can also be applicable in GTR. The use of both a membrane and bone grafts together is termed combination therapy. Bone replacement grafts such as autografts, allograft, isografts, xenografts and alloplast have been used (Bowers, 1989b; Bowers, 1989c; Reynolds, 2003). In addition growth factors like; transforming growth (TGF), insulin like growth factor (IGF), vascular endothelial growth factor (VEG-F), enamel matrix derivative (EMX) and platelet derived growth factor (PDGF) have been used to assist in periodontal regeneration( Giannobile 2003; Marx 2004; Chong 2006). Some clinicians apply conditioners to prepare the root surface for GTR with hopes that a chemically cleaner root surface would assist in gaining additional new periodontal attachment beyond that of scaling root planning alone (Lafferty 1993.)

The following review of the literature will address periodontitis and periodontal regeneration as it relates to 1-, 2-, and 3-walled intrabony defects utilizing the GTR technique with and without bone grafts. This literature review will also seek to find a possible difference in percentage of regenerated periodontium with Accell Connexus<sup>®</sup>, a second generation demineralized freeze-dried bone allograft product that contains 5-7 times the amount of bone morphogenetic proteins (BMP) as regular demineralized freeze-dried bone allograft (DFDBA) and compare it to traditional particulate DFDBA while employing a porcine collagen membrane, Bio-Gide, as an exclusion barrier.

#### The Periodontium

The periodontium [(periodontal attachment and the gingival tissue (gums)] refers to the tissues that support teeth in the alveolus of the maxilla and the mandible (jaws). The periodontium consists of gingiva, PDL, cementum and bone. The cementum surrounds the root surface and is attached to the alveolar housing (tooth socket) via the PDL which suspends the tooth within the alveolus. The gingival tissue is composed of epithelium (oral, sucular and junctional) and supracrestal connective tissue fibers located coronal to the level of the bone and PDL. The epithelial-lined sulcus or crevice encircles teeth while the junctional epithelium forms a hemidesomal attachment to the tooth surface (Pöllänen, Salonen, & Uitto, 2000). The gingival soft tissue also consist of gingival fibers that surrounds the tooth to assist in attaching the gingival tissue to the cementum, holding the gingival tissues firmly against the tooth and preventing deflection of the gingival tissue during mastication (Hassel, 1993).



Figure 1. The Periodontium in Health. From Page and Schroeder Model of Pathogenesis (1976). Used with permission via personal communication from author Dr. Roy Page.

Page and Schroeder's Model of Pathogenesis (1976) with images for health, gingivitis and periodontitis (Figures 1, 2 and 3) is the illustrator's model of health and disease. Three types of epithelial tissues characterize the gingiva (see figure 1): (1) the keratinized oral epithelium (OE) that comprises the visible band of gingiva around the teeth, (2) the sulcular epithelium (SE), which is the transition tissue at the edge of the tooth, and (3) the specialized non-keratinized epithelium called the junctional epithelium (JE) that lines the bottom of the gingival sulcus (GS). The JE is attached to the tooth via hemidesmosomes which are made of adhesion proteins called integrins. In health (Figure 1) the JE is the first barrier to prevent bacterial plaque from reaching the underlying connective tissue and bone. The terms gingival sulcus (GS) and gingival crevice are used interchangeably. Also in figure, 1 the image depicting "Health" shows how the intact JE, supracrestal fibers (CO) and the PDL between the alveolar bone and root surface support a tooth. The PDL fibers serve as the connective tissue support that holds the tooth in place in the bone and helps cushion the tooth from forces when we bite, chew or clench (Beertsen, McCulloch, & Sodek, 2000). The PDL contains pressure receptors that are activated by tooth contact. The impulses generated by these receptors are sent to the brain and used to help coordinate the sequencing of jaw movement (Byers & Dong, 1989).

#### The Periodontium in Disease

Gingival inflammation or gingivitis is caused by bacterial plaque that when allowed to remain in the GS for an extended period of time will cause a degree of inflammation within the gingival tissues. The amount of time to develop gingivitis

depends on the individual however the average range is 10- 21 days (Loe, Theilade & Jensen, 1965). As seen in Page and Schroeder's "Gingivitis" diagram (Figure 2), the integrity of JE is disturbed when inflammatory cells accumulate in the underlying connective tissue. In gingivitis, the early form of periodontal disease, the gingival tissue may become red, swollen and tender and often bleeds on manipulation i.e. brushing, flossing and probing. While the supracrestal gingival fibers can become irritated, the PDL attachment and the alveolar bone remain intact.



Figure 2. The periodntium with gingivitis. From Page and Schroeder Model of Pathogenesis (1976). Used with permission via personal communication from author Dr. Roy Page.

Gingivitis transitions to periodontitis when the host's immune response cannot resist bacterial plaque and the inflammatory process (Weinman, 1941; Takata & Donath, 1988). Destruction of connective tissue and alveolar bone, leading to possible tooth loss, is a consequence of the interaction between the plaque front and immune response (Waerhaug 1977; Haffajee, Socransky & Goodson, 1983). This tissue breakdown is clear in Page and Schroeder's "Periodontitis" diagram (Figure 3). With the onset of periodontitis, the gingival crevice becomes a deeper periodontal pocket, with destruction of supracrestal gingival fibers, PDL, and the breakdown of the alveolar bone. This process of connective tissue and bone destruction is called clinical attachment loss.



Figure 3. The periodntium with periodontitis. From Page and Schroeder Model of Pathogenesis (1976). Used with permission via personal communication from author Dr. Roy Page.

Clinical attachment loss is a measure of how much periodontal support has been destroyed. It is assessed by gently inserting a periodontal probe into the GS or a periodontal pocket to measure the distance from the CEJ to the base of the periodontal pocket. The University of North Carolina (UNC) 15 periodontal probe has 1 mm increments with color coding at the fifth, tenth and fifteenth millimeter. In health, insertion of the periodontal probe is resisted by the intact connective tissue and probing depths should measure 3 mm or less. When periodontal disease is present, the periodontal probe inserts more deeply into the pocket because the connective tissue has been destroyed (Fowler, Garrett, Crigger & Engelberg, 1982). In a diseased state, the probing depths will be 4 mm or greater, and the tissue may bleed upon probing

(Armitage, Svanberg & Loe, 1977). Probing depth measurements aid in the diagnosis of the severity of periodontal disease. It is not uncommon to have healthy and significantly diseased locations within the same person and on the same tooth (Haffajee & Socransky, 1986).

As the disease process continues and more connective tissue is lost, bone loss becomes evident on radiographs. Once sufficient mineral content in the bone has been destroyed (Bender, 1961). The radiograph provides a visual tool for detecting and characterizing intrabony defects (Rees, 1971). However, clinical detection of attachment loss, indicated by deeper probing depths, usually precedes radiographic evidence of bone loss by a period of six to eight months (Goodson, Haffajee & Socransky, 1984). Probing depths, clinical attachment level (CAL), and radiographs help clinicians assess extent (localized or generalized), duration (chronic or aggressive) and severity (mild, moderate or severe) of periodontal disease which will assist in rendering the appropriate treatment. Radiographs assist in determining whether bone loss is horizontal, vertical, or a combination of the two. A normal bony pattern is shown in figure 4a. Horizontal defects appear on radiographs as bone that has decreased in a parallel manner to the occlusal table (Figure 4b). Whereas in vertical defects, the bone is lost in a mode that depicts an intrabony defect or a defect which appears to have a wall or multiple walls surrounding a defects (Figure 4c). Although horizontal bone loss is often associated with slowly progressing disease both horizontal and intrabony defects can be seen in chronic forms of periodontal disease.



Figure 4a shows a normal bony pattern in which the bone level follows the cemental enamel junction (CEJ) with no clinical loss of bone. Figure 4b shows horizontal bone loss where the bone appears to recede away from the CEJ evenly. Figure 4c shows vertical bone loss on the mesial and distal of #14. Note that the bone appears to have lost a wall buccal or lingually. Used with permission by the author of this thesis, LCDR Teresita Alston.

Combination defects are sometimes difficult to see radiographiclly. However a combination defect can be seen in figure 4c on the mesial of #14. Note that the tooth has lost bone in a vertical configuration however the mesial of #14 also radiographiclly presents with a difference in color contrast. The difference in contract may be a combination 1, 2, or 3 wall vertical, intrabony, defect. However one can only make an assumption using radiographs as to the type of vertical defect because vertical defects are better visualized surgically and can often be missed radiographiclly if they are less than 3mm (Paul and Trott, 1966). Below is a surgically exposed example of a 3 walled intrabony defect on a mandibular second molar.



Figure 5. This depicts a three walled defect. Used with permission from the author of this thesis, LCDR Teresita Alston.

#### The Etiology of Periodontitis

The prerequisite for developing periodontitis is gingivitis, which develops within 1-3 weeks of bacterial plaque contact with the gingival tissues (Löe, Theilade, Jensen, 1965). Although gingivitis is a must to progress to periodontitis not all individuals who develop gingivitis will progress to periodontitis. In fact, the etiology of bone loss in periodontics is due to bacterial plaque in a susceptible host (Waerhaug, 1977; Page, 1992). One can become prone to periodontitis due to systemic diseases, genetics, local factors (calculus, poorly placed restorations, tooth anatomy, root fractures), oral infections (Armitage, 1999), smoking (Haber, Wattles, Crowley, Mandell, Joshipura & Kent, 1993; Tomar& Asma, 2000) or viruses, (Contreras & Slots, 2000). The local factor, calculus, is often seen in individuals with periodontitis and calculus can assist in further destruction of bone. Within the oral cavity calculus is covered by a layer of plaque which may contain a variety of bacteria both non-pathogenic and pathogenic (Socransky, Haffajee, & Smith, 1998). Although living bacteria can be harmful it has been demonstrated in an animal model that even sterile calculus can cause a foreign body reaction (Allen & Kerr, 1965). This showed that calculus, even sterile, can cause an issue within an otherwise healthy environment. Although we know calculus can cause a reaction it is sometimes difficult to detect clinically and on radiographs. It has been shown that radiographs have a low sensitivity and a high specificity and that the detection of calculus is subjective to its thickness (Buchananan, Jenderseck, Granet, Kircos, Chambers & Robeertson, 1987). Even though calculus at times may be difficult to detect it should be removed to prevent destruction or lessen the severity of the destruction.

The level of destruction is often dependent on the type if bacterial microflora involved. The bacterial microflora exists in complexes in subgingival plaque and has been divided into five major color coded complexes (Socransky, Haffajee, & Smith, 1998). Not all complexes are associated with periodontitis however the more virulent bacteria are found in the red complex. According to Socransky, 1998 the gram negative red complex which consist of *Bacteroides forsythus, Porphyromonas gingivalis* and *Treponema denticola* are highly related to increase pocket depth and bleeding on probing. *Aggregatibacter actinomycetemcomitans,* formally, *Actinobacillus,* is found within the green complex however multiple serotypes exist (Yang, 2004). However one serotype, serotype b, though it may cause destructive periodontal disease is not within

the green spectrum. Orange complex bacteria, *Fusobacterium nucleatum, Prevotella intermedia, Prevotella nigrescens and Peptostreptococcus micros*, have also been shown populate diseased sites. Those gram negative bacteria as well as others have been found to be associated with active periodontal lesions (Kornman, 1986). Again not all gram negative bacteria are associated with active periodontal disease. In several studies, *Bacieroides intermedius.* "fusiform" *Bacteroides. Actinobacitlus aeiinomyeetemeoniitans* and *Woiinella recia. Fusobacterium nucleatum. Capnoeyiophaga gingivalis* and *Eikenella corrodens* were found in higher numbers in non-active sites (Dzink, Tanner, Haffajee & Socransky, 1985).

#### **Smoking and Periodontitis**

Smoking can increase ones risk of developing more severe periodontal disease (Haber, Wattles, Crowley, Mandell, Joshipura & Kent, 1993). In fact it is believed that smokers account for 41.9% of periodontitis cases and former smokers account for another 10.9% of periodontitis (Tomar& Asma, 2000). In the NHANES study conducted between 1988 and 1994 found that 27.9% of the U.S. populations are smokers and 23.3% are former smokers (Tomar& Asma, 2000). Smoking can increase ones risk of developing more severe periodontal disease more rapidly (Haber, Wattles, Crowley, Mandell, Joshipura & Kent, 1993; Stoltenberg, Osborn, Pihlstrom, Herzberg, Aeppli, Wolff & Fischer, 1993; Tomar& Asma, 2000). Even in those with very low levels of plaque increase their risk. According to the AAP 1999 position paper when plaque levels were adjusted for in several studies, smokers had greater probing depths, clinical attachment loss and bone loss. Bergstrom, Eliasson and Preber, 1991 completed a

study with Swedish dental hygienist and found that smokers had 1.71mm of bone loss compared to 1.45mm in non-smokers. This demonstrated that even in the presence of good oral hygiene smoking leads to greater loss of attachment.

When studying the bacteria found in the pockets of those who smoked, one study found that smokers have a greater extent of colonization of red and orange complex bacteria in pocket depths less than 4 mm (Haffajee & Socransky, 2001) however other studies determined that there was no significant difference in any combination of bacteria when they compared smokers to non-smokers (Bergstrom, Linder, 1992; Stoltenberg, Osborn, Pihlstrom, Herzberg, Aeppli, Wolff, Fischer, 1993). Nevertheless there was a difference in treatment outcome when it came to treating smokers who had periodontial disease. In a studying comparing heavy smokers (more than 19 cigarettes per day) to light smokers (less than 19 cigarettes per day), former smokers and never smokers, smokers responded less favorable to periodontal therapy (Ah, Johnson, Kaldahl, Patil & Kalkwarf, 1994; Kaldahl, Johnson, Patil, Kalkwarf, 1996). Although less favorable smokers did respond positively to treatment (Kaldahl, Johnson, Patil, Kalkwarf, 1996; Rosen, Marks, Renolds, 1996). Preber and Bergstrom (1986) attained a slight difference in probing depth reduction 1.1mm in smokers and 1.2mm in non-smokers in probing depths of 4-6mm with non-surgical therapy. When periodontal regenerative therapy using DFDBA in 110 intrabony lesions was carried out and followed for 1, 2 and 5 years it was noted that both smokers and non-smokers had an improvement in clinical attachment levels (2.7mm : 3.4mm), plaque score, and probing depths (3.0mm : 3.8mm) at one year post surgery. However smokers had significantly inferior CAL gain (smokers 29.2%: non-smokers 42.5%) when compared to

pretreatment parameters at 1, 2 and 5 years post-surgery (Rosen, Marks, Reynolds, 1996). However if smokers stopped smoking they may experience the same healing as those who never smoked (Grossi, Zambon, Machtei, Schifferle, Andeeana, Genco, Cummins & Harrap, 1997).

Although bone loss can become more severe due to certain systemic diseases, necrotizing disease, periodontial abscess, combination endodontic/ periodontic lesions or developmental/ acquired deformities (Armitage, 1999) this literature review will not cover those topics.

#### **Treatment of Periodontitis**

All periodontal patients should have a review of their medical history; head and neck exam; full mouth periodontal examination and a full mouth series of radiographs or a comparable radiographic assessment. A full mouth periodontal examination should record a minimum of PD, CAL, BOP, recession (amount of root seen clinically), furcation involvement, purulence, plaque and mobility. After the review of the medical history; the complete periodontal evaluation and review of radiographs a diagnosis can be made. Schallhorn published an article in 1977 that presented a flow for the treatment osseous defects however can be applied to other treatment. The author pointed out that once the diagnosis has been formulated the first phase of periodontal treatment can take place followed by different ways to proceed to the next phase or move among the phases of periodontal treatment. In the first phase, the patient would receive palliative care; extraction of hopeless teeth due to periodontal reasons or otherwise; oral hygiene instructions (OHI) on the proper techniques of oral hygiene

along with initial therapy; and any other procedure the clinician believes must be taken care of prior to re-evaluation. Initial therapy consists of removal the plaque and calculus accumulation both supra and subgingivally non-surgically. The removal of accretions from the root along with diseased cememtum is called scaling and root planning (SRP). Many people refer to this as a deep cleaning. Although this is call a deep cleaning the effectiveness of SRP decreases as the pocket depth becomes deeper. Stambaugh (1981) found that a PD beyond 3.73mm the efficacy of SRP is less. That study confirmed a previous study conducted on teeth that underwent SRP, by experienced hygienist, on teeth at various PD then extracted them to see the effectiveness of SRP. The study found that the deeper the site the greater the percentage of deposits are left on the root. In fact, a PD greater than 3mm left calculus behind 17% of the time; PD between 3-5mm calculus was left behind 61% of the time and PD greater than 5mm calculus was behind 89% of the time (Waerhaug, 1978). Therefore the predictability of effectively cleaning PD greater than 4mm is greatly decreased with non-surgical therapy. After a period of 4-6 weeks patients are re-evaluated to assess their response to initial therapy (Proye, 1982). If the patient has residual areas of deep probing depths (>4mm) with signs of inflammation like BOP then the clinician may decide that surgical corrective therapy may be the best option for the patient.

The goal of non-surgical periodontal therapy is to reduce the PD and gain clinical attachment which would allow for the patient to better clean their mouth; better access for professional care which would allow for a healthy oral environment. It is not different for corrective surgical treatment. Except now in order to properly clean the area the surgeon must have access to the area by reflecting a soft tissue flap. Corrective surgical

therapy may be OFD; osseous resective therapy, or regeneration. All of these forms of treatment require a flap to be reflected so that the bone and roots can be accessed. OFD implies that a flap is reflected; the defect is debrided and the roots are cleaned via SRP. The flap is then sutured back in place and allowed to heal. This may be a good surgical option for shallow defects however this would not be a good treatment decision for moderate to deep defects. Osseous resective surgery is basically the same as OFD however some of the soft tissue is remove or is apically positioned and the nonsupporting alveolar bone is plastied and ostectomy of supporting bone to allow for a positive bony architecture (Selipsky, 1976; Tibbetts L, Ochsenbein C, Loughlin D, 1976; Ochsenbein, 1986). The site is then sutured and allowed to heal with more tooth structure exposed to the oral cavity. The down side to osseous resective surgery is the possibility of sensitivity due to root exposure and esthetic concerns due both root exposure and long appearing teeth. In contrast, with periodontal regeneration the soft tissue is not usually resected however the bone may be slightly recontoured to better develop the site for graft containment. Like OFD and osseous resective therapies the defect is debrided and the roots are cleaned. The defect may now receive monotherapy: cover the defect with a membrane, GTR; bone graft placed into the defect without a membrane; or combination therapy, placement of a bone graft followed by coverage with a membrane. The site is then sutured gaining primary closure (proximation of the wound edges). Although all three forms of regeneration is effective it has been shown that combination therapy is the most effective in the long term (McClain, 1993; Luepke, 1997; Reynolds, 2003; Avila-Ortiz, 2015).

#### **Guided Tissue Regeneration**

Nyman is credited with completing the first guided tissue regeneration (GTR) procedure in 1982. Since Nyman's initial use of GTR, many dentists as well as Nyman have tried to improve techniques and materials to make completion of GTR more user friendly. However when completing GTR procedures one must consider several factors. Factors that influence how much regeneration occurs were documented in 1986 by Gottlow et al. Gottlow stated that "the degree of gingival recession that occurs during healing; the morphology of the periodontal defect, and the amount of remaining periodontum are all factors to consider when planning GTR. GTR is a procedure in which three of the four tissues of a diseased periodontum are regenerated and the fourth is excluded by a member barrier. The bone, cememtum and periodontal ligament are desired tissues for regeneration as they contain cells which form those structures. The periodontal ligament contains cells which can produce all three components (Gottlow 1982). When grafting one must always consider the three factors stated earlier by Gattlow however, morphology and remaining periodontum seem to be a bit more important.

When considering morphology the number of walls a defect has is important. It is known that a three walled defect is the most predictable followed by a two wall defect. One and zero wall defects are difficult to obtain good bone fill. The remaining periodontum goes somewhat hand in hand with morphology however it takes into account the width and depth of the defect. Deep, narrow followed by shallow, wide defects are better for grafting as blood supply would be greatest and one would likely

get regeneration up to the alveolar crest. On the other hand deep, wide defects would have less blood supply coming from the surrounding bone and thus not the best defect for grafting procedures. Overall deep, narrow, three wall defects are the most predictable and favorable sites for GTR (Becker W, Becker B; 1993). According to one study the average bone fill of intrabony defects using GTR are: three wall 95%, two wall 82% and one wall 39% (Cortellni 1993). That study also found that there was a 4.7mm reduction of the intrabony defect and that 90% of the sites gained 2mm or more of bone fill and no site lost supporting bone. The fourth tissue of the periodontum is the epithelium which is excluded in GTR. If the epithelium is not excluded then one is likely to get more epithelium than the other three structures which are important in securing the tooth. The more bone, cementum, and periodontal ligament that can be regenerated around the tooth the better or more successful the GTR procedure especially if one can achieve a long term outcome and there have been reports greater than fifteen years (Cortellini 2004).

GTR can be done without or with a bone graft (combination therapy) and with apparently the same success rate as with bone grafts (Trejo 2000). Trejo found that when comparing GTR to GTR with a bone graft that PD, CAL and recession were not statistically different. However Luepke (1997) found in a study comparing the use of a bioresorbable membrane with and without DFDBA and found that the use of a bone graft increased vertical bone height in furcations. In a different study comparing GTR to combination therapy; it was found that sites treated with a bone graft were more stable over the 5 year period. The results of that study also showed that more furcation sites

obtained complete bone fill and maintain the bone fill when compared to the site treated by GTR alone. (McClain, 1993)

Although GTR is an effective form of treatment for bony defects the long term stability of sites treated with combination therapy has better success. The ultimate fate of a bone graft is to turnover into the patient's bone and that turned over bone should be unified with the surrounding bone. Although an autograft has bone forming cells within the graft the patient may not want to have a second surgical site to obtain bone. An allograft maybe a good alternative as a second surgical site is not required. The autograft may have the osseogenic advantage over allografts specifically DFDBA in and extraction socket (Becker, 1994) however it has been shown that allografts are effective in GTR procedures. Mellonig (1984) found in a study with 32 test teeth and 15 controls, open flap debridement, having a reentry period of 6-13 months that there was greater bone repair 2.57mm and less crestal bone resorption 0.47mm than in sites not treated with a bone graft which had 1.26mm of repair and 1.26mm of crestal bone resorption. They also had a CAL gain of 2.91mm with the bone graft compared to 1.53mm in the sites not receiving a bone graft. That study also presented the data in percentage of bone fill. The sites treated with DFDBA had 78% of sites with complete or greater than 50% bone fill whereas the control had only 40% have complete or greater than 50% bone fill.

# Materials Used in Combination Therapy Root Surface Conditioners

Several types of root surface cleaners or conditioners have been used to assist cleaning the tooth's root surface in periodontal regeneration. Citric acid, tetracycline

and ethylenediaminetetraacetic acid (EDTA) are a few examples of root surfaces conditioners that have been used. According to a systematic review the use of these products to modify the root surface had no benefit with regards to improvement in the clinical outcome over scaling and root planning alone (Mariotti, 2003). However in an invitro study testing tetracycline HCL showed that tetracycline treated root surfaces increased the binding of fibronectin which in turn stimulated fibroblast attachment and growth as well as subduing epithelial attachment and growth. (Terranova et al, 1986). This study demonstrated that tetracycline HCL had a positive effect on fibroblast growth and a negative effect on the growth of epithelium. In a comparative study viewing extracted teeth under SEM showed that teeth treated with tetracycline HCL or citric acid (pH=1) for 5 minutes without burnishing showed removal of the smear layer thereby exposing the dentinal tubules and rendering a surface devoid of debris found on surfaces that had only been root planned (Lafferty, 1993). Therefore both tetracycline and citric acid had the ability to better cleanse the root surface better than root surfaces that were only scaled and root planned. 24% EDTA can provide the same results as citric acid and tetracycline according to a study completed on teeth that were SRP only, SRP and treated with EDTA or treated with EDTA only then immediately extracted and viewed under scanning electron microscope (SEM) or used to culture human PDL. fibroblast for 24 hours. In that study it was found that the SRP only teeth as well and the EDTA treated only teeth still had areas of bacterial accumulation and a failure of PDL cells to adhere to the root surface. However teeth that had been SRP followed by 4 minutes of EDTA treatment the smear layer was removed and round to oval dentinal tubules were exposed along with the observations of collagen fibrils. This group also

showed a significant increase in the number of fibroblast cell attachment (Gamal, 2003). This proved that EDTA could remove the smear layer providing a cleaner surface with a greater potential for cells to attach and grow.

#### **Bone Grafts**

In combination therapy, a bone graft is utilized and can be autografts, allografts, isografts, xenografts, or alloplast. These bone grafts may have osteogenic, osteoinductive or osteoconductive capabilities. The purpose for using the specific type of bone lies within the properties of the graft used; however, the end result of its use is always to see a clinical and or radiographic increase in bone. It has been shown in many studies that a membrane without bone grafting can increase the fill of bone in defects (Bowers 1989, Becker 1993, Cortellini 2004). However there have also been studies which found that the addition of a bone graft (DFDBA) with a membrane had no extra benefit when compared to a membrane alone (Chen 1995, Gottlow 1986). Altiere in 1979 reported that "nongrafting procedures may be more effective in generating new attachments or reattachments in human periodontal osseous defect than previously believed." All be it, a 2003 systematic review by Reynolds showed that combination therapy in general had a greater benefit due to their ability to decrease crestal bone loss and increase bone levels.

Autografts are transferred from one site to another site in the same individual (American Academy of Periodontology Glossary of Periodontal Terms 2001) and has the greatest potential for osteogenesis because it contains osteoblast from the patient.

Autografts can be taken from the maxillary tuberosity, the ramus, tori, exostoses or from a recent extraction site to name a few.

Allografts are transferred from genetically dissimilar individuals of the same species (American Academy of Periodontology Glossary of Periodontal Terms 2001). They can be osteoconductive or osteoinductive. Allografts are divided into two categories freeze dried bone allograft (FDBA) and demineralized freeze dried bone allograft (DFDBA). FDBA is only osteoconductive meaning it can only be used as a scaffold for bone to form on. DFDBA is potentially osteoinductive because it contains exposed growth factors, collagen, and BMP which can induce the surrounding tissues to produce osteoblast which produces bone. Urist, in 1975, discovered that human bone could undergo chemical extraction that would make it useful as a bone graft material. A study completed by Bowers (1989) found that intrabony defects grafted with DFDBA had an increased amount of collagen, bone and periodontal ligament and therefore enhanced new attachments apparatus formation and labeled DFDBA as osteoinductive. However, Becker in 1994 reported that the study he conducted "questions the use of DFDBA as a bone inductive graft material." Although some authors may question the use of DFDBA in GTR procedures, DFDBA has been used successfully for GTR procedures in humans for almost 30 years. (Bowers, 1989).

Now a product distributed by Keystone Dental, Accell Connexus<sup>®</sup>, is a new bone allograft material approved by the FDA for periodontal regeneration. It is contains DFBBA within a proprietary poloxamer reverse phase medium. The medium permits the material to have a putty consistency and allows the practitioner to mold and shape

the bone graft. Because it is moldable it is believed that Accell Connexus® will maintain its shape and remain in place better than particulate DFDBA. Accell Connexus<sup>®</sup> undergoes a slightly different processing from traditional DFDBA. The additional step involves splitting a large sample of DFDBA into two parts. One part is dissolved releasing growth factors and bone proteins that are isolated and extracted. That extract is then added to the other half of the DFDBA and the reverse phase medium. This process results in the increased concentration of BMP compared to traditional DFDBA allowing Accell Connexus<sup>®</sup> to have 5-7 times more BMP than the particulate DFDBA (Company information, Keystone Dental). The bone graft is then sterilized in the same manner as particulate DFDBA which has been shown to preserve growth factors.

Isografts are from genetically identical individuals, usually identical twins (American Academy of Periodontology Glossary of Periodontal Terms 2001). They are much like allografts however these grafts contain the same genetic make-up of the individual receiving the graft.

Xenografts or heterografts are from a different species (American Academy of Periodontology Glossary of Periodontal Terms 2001). These grafts are usually bovine, equine or porcine when it comes to use in humans. They are only osteoconductive .

Alloplast are synthetic or inert foreign body implanted into tissue (American Academy of Periodontology Glossary of Periodontal Terms 2001). They are materials such as bioactive glass, calcium sulfate or beta tri- calcium phosphate and are only osteoconductive.

#### **Barrier Membranes**

Biologic membranes have been used to assist in the regeneration of bone, cementum and the periodontal ligament. It is believed that if the gingiva, primarily the epithelium, is excluded regeneration of the underlying periodontium can take place. However if no barrier is present to prevent the epithelium from growing into the site of regeneration then the new attachment will more than likely be long junctional epithelial (Bunyaratavej 2001). The junctional epithelium will reattach to enamel, cementum, dentin and in some conditions calculus (Melcher 1976). Because epithelium grows at a rate of 0.5mm per day which is faster than bone, cementum and the periodontal ligament (Engler 1966) inhibiting these non-osteogenic cells from infiltrating the regeneration site seems ideal. For that reason barrier membranes were introduced into dentistry in the early 1980's. The first membranes were nonresorbable and required a second surgery for removal. Not only do non-resorbable membranes require a second surgery to be removed there were also problems associated with early membrane exposure (Schallhorn, 1994). The resorbed membranes were introduced in dentistry the late 1980's and eliminated the need for a second surgery because these membranes resorbed. However with the ability to resorb these membranes were subject to a faster resorption when exposed to the oral environment. Therefore gaining primary closure is very important to prevent a more rapid breakdown of the barrier membrane.

#### Nonresorbable verse Resorbable Membranes

Both nonresorbable and resorbable membranes can be used in GTR. Some authors have reported that with nonresorbable membranes there is an increase in soft
tissue complications due to the membrane becoming exposed. Tal 2008 completed a study on crossed linked and non-cross linked collagen membranes and found that 50% of cross linked collagen membranes became exposed compared to 23.1% of non-cross linked membranes. Although collagen membranes can also become exposed it seems that resorbable membranes have become more popular. Zitzmann et al. 1997 stated that with Gor-Tex, a nonresorbable membrane, had "44% wound dehiscences and/ or premature membrane removal occurred" and that Bio-Gide, a resorbable membrane, was "a useful alternative." In a clinical comparative study between bioresorabable and non-resorbable membranes Cortellini and colleagues (1996) concluded that clinically significant CAL gains can be obtained with GTR procedures with both types of membranes however less issues were associated with the bioresorbable membranes.

### Nonresorbable Membranes

Polytetrafluroethylene (ePTFE) is comprised of a carbon chain with two fluorine atoms for every carbon atom. The complete fluorination of the carbon chain, along with the strength of the carbon-to-fluorine bonds, makes PTFE highly stable. This stability results in a synthetic polymer that is non-resorbable, biologically inert, chemically nonreactive (<u>www.osteogenics.com</u> cited 2012 October 30) and must be removed. Examples of PTFE are Gor-Tex which was the first non-resorbable membrane on the U.S. in the 1980's and Cytoplast placed on the U.S. market in 1997 (<u>www.osteogenics.com</u> cited 2012 October 30).

### Synthetic Resorbable Membranes

These membranes are made from synthetic materials such as glycolide and trimethylene carbonate copolymer fiber or glycolide and lactide copolymer (<u>www.goremedical.com</u> cited 2012 October 30). Examples are Vicryl Mesh Polyglactin 910 and Polyglycolin Acid (Resolut XT).

### **Natural Resorbable Membranes**

Collagen membranes are type I and/ or type III collagen from cows or pigs and can be either cross-linked or noncross-linked. These membranes are hydrolyzed or enzymatically degraded (Duskova et al.) therefore do not require removal. According to one author "collagen membranes have the following properties: hemostasis, stimulation of fibroblast by chemotaxis, acts as a support construction for the migration of fibroblast to periodontal ligaments, easy to shape and adapts well to root surfaces, has low antigeneicity and immunogenicity, and eliminates the need for a second surgery because they are bioabsorbable" (Duskova M, et al, 2006). A few examples are Bio-Gide porcine membranes, Biomend and Biomend Extend bovine membranes.

Name	Company	Source*	Cross Linked (C) / Noncross Linked (N)*	Resorption Rate*
Bio-Gide	Geistlich	Porcine dermis collagen type 1 and 3	N	24 weeks
Biomend	Zimmer	Bovine collagen type I	Formaldehyde	8 weeks
BioMend Extend	Zimmer	Bovine collagen type I	Formaldehyde	18 weeks

Table 1: Examples of collagen resorbable membranes. \*Company Information

Membranes are derived from human tissues have been shown to have grater biocompatibility and immunogenicity (Xenoudi 2011, Chen 2010, Park 2009, Niknejad 2008, Duskova 2006, Kubo 2001). It has also been reported that they allow for more rapid healing. One study reported, three days after surgery, the site containing a cryopreserved amniotic membrane had more epithelialization than the control site which did not contain a membrane (Valaz 2010). However that study also reported that at two weeks both the sites containing the membrane and the control were clinically equal. Dura Mater, Pericardium, and Placenta are donated human tissues that have been utilized as membrane barriers.

It seems that the use of a resorbable or nonresorbable membrane in GTR procedures is acceptable. However the clinician must use their clinical judgement as to which membrane is best for the patient.

#### Soft Tissue (Gingiva) Closure

The soft tissue covering the membrane should have primary closure and heal rapidly. Rapid healing of the soft tissue from all sides is usually desired whenever a wound occurs and there is scientific evidence that the healing of wounds occurs from all borders regardless of the type of tissue being repaired (Cutright 1969). Epithelium is one of the fastest growing tissues as reports by Engler 1966. Engler found that epithelium grows at a rate of 0.5mm per day. Although in many situations it would be highly desired to have a wound heal with epithelium, it is not the tissue surgeons consider ideal when it comes to GTR. One would rather have cells which form connective tissue, cementum and bone. Over the years many techniques have been tried to eliminate epithelial cells from infiltrating grafted sites. One method left denuded bone at the time of mucoperiosteal surgery leaving the epithelium with a longer distance to travel than the connective tissue. Because of this one would get a connective attachment ahead of a long epithelial attachment (Pfeifer 1963). As one could imagine, this procedure was reported in Pfeifer's article as painful. Therefore it is better to have bone covered during the healing process to prevent pain and possible infection.

The keratinized stratified squamous epithelium of the oral epithelium is in place to withstand the forces of brushing, flossing, food particles contacting the gingival and

etcetera. Sulcular epithelium is an extension of the oral epithelium however lacks keratinizaton. Sulcular epithelium is on average 0.69mm (Gargiulo 1961). The extension of the sulcular epithelium is the junctional epithelium and on average in a normal healthy periodontium as reported by Gargiulo 1961 is 0.97mm. The junctional epithelium often interferes with the desired healing in GTR if no barrier is in place to exclude it. In the event that the junctional epithelium grows past its normal resting place during wound healing it would then be called the long junctional epithelium. Apical to the junctional epithelium is the connective tissue attachment which contains collagen type I, III and IV. The connective tissue contains gingival fibers which hold the free gingiva up around the tooth like rubber bands which runs in different directions. The connective tissue also anchors the gingival corium to the bone via Sharpey's fibers and is the final protective barrier prior to the bone. The gingival tissue is tightly bound to the bone by its basement membrane. In an animal study completed by Hiatt et al. in 1968 found that it took 225 grams of force on silk sutures to separate a flap from the tooth and bone after two to three days of healing following mucoperiosteal flap surgery and at two weeks the tissues could be partially separated using 340 grams. However using 1,700 grams of force after four to six months of healing the sutures pulled through the tissues leaving the flap intact. This also demonstrated that "the strength of the epithelial attachment to the root is greater than the attachment between cells (Hiatt 1968). Although one would prefer a connective tissue attachment during would healing it has been demonstrated in an animal models that a long junctional epithelium may be just as effective as the connective tissue attachment to inflammation (Beaumount, 1984) and the length of the long junctional epithelium does not play a role of gingival health

(Magnusson, 1983). Although a connective tissue attachment may show no advantage over a long junctional epithelium attachment in the animal model regeneration implies that one would prefer the connective tissue attachment.

This review of the literature addressed periodontitis and periodontal regeneration as it relates to intrabony defects utilizing the GTR techniques. Because there are no published studies comparing DFDBA and Accell Connexus<sup>®</sup>, the present study will address GTR as it relates to the comparison between DFDBA and Accell. This study will attempt to find a difference in PD reduction; CAL gain, recession, as well as gain in radiographic bone fill with the use of a Bio-Gide barrier membrane. Therefore the objective of this research is to determine if Accell provides superior regeneration compared to traditional DFDBA in intrabony defects. The hypothesis is that Accell Connexus<sup>®</sup> provides periodontal regeneration that is superior to traditional DFDBA. The sites treated with Accell will have better outcomes with respect to greater clinical attachment level gain, which is the primary outcome measure, greater decrease in probing depths, and more radiographic bone fill.

# CHAPTER III MATERIALS AND METHODS

Thirty subjects diagnosed with severe periodontitis are being enrolled in the study. (Please see Appendix A1 for a flow diagram of the proposed study.) The findings of their comprehensive periodontal evaluation such as probing depths (PD), clinical attachment levels (CAL), and recession were recorded on the Navy Periodontal Chart Form - NAVMED 6660/2 (appendix B2) by the subject's provider. Patient who met the inclusion criteria (Please see Appendix \*\*\*for inclusion/ exclusion check list.) for the study, were offered the opportunity to participate. The methodology for this study is listed below in sequential order.

The inclusion and exclusion criteria for this study included the following:

### Inclusion Criteria

- a. Patient aged ≥18 years old
- b. Patient will be remaining in the Capital region for at least 12 months following the surgical procedure for follow up appointments
- c. Diagnosis of generalized or localized severe periodontitis
- Radiographic evidence of a vertical intrabony defect at one or more sites with a probing depth ≥ 6 mm
  - If the patient present with more than one defect site meeting inclusion criteria, the site with the deepest probing depth will be used in the study

### **Exclusion Criteria**

- a. Patient under the age of 18
- b. Patient will be moving from the Capital region area prior to 12 months following the surgical treatment
- c. Furcation involvement in combination with the intrabony defect determined pre-surgically

- d. Patients with restorations extending beyond the cementoenamel junction at the intrabony defect site
- e. Patients with an indiscernible cementoenamel junction either clinically or radiographically
- f. Patients with periapical pathology, unrestored caries, defective restorations, root resorption, or vertical root fracture
- g. Patients requiring restorative dental care (fillings and crown and bridge work) that cannot be completed prior to fabrication of the customized stent
- h. Female patients who are pregnant or nursing
- Patients who currently smoke tobacco or use tobacco products. Former smokers will be excluded if they quit smoking < 6 months prior to selection in the study.
- j. Patients with clinically significant systemic diseases, which may affect healing (e.g. uncontrolled diabetes).
- k. Patients allergic to chlorhexidine gluconate (Peridex).
- I. Patients allergic to tetracycline
- m. Patients with poor oral hygiene unsuitable for periodontal surgery
- n. Patients who cannot or will not sign the informed consent form
- Patients receiving immunosuppressive therapy such as chemotherapy and systemic corticosteroids not to include inhaled or topical steroids
- p. Patients with severe endocrine-induced bone diseases (e.g. hyperthyroidism, altered parathyroid function)
- q. Teeth with intrabony defect have mobility classified as Miller class 2 or greater
- r. Patients with bleeding complications (e.g. hemophilia)
- s. Patients on warfarin therapy
- t. Patient with a history of osteoporosis or taking bisphosphonate medications
- u. Patients with a history of radiation therapy in the head and neck area

#### Initial Sequence:

- 1. Patient is referred for a comprehensive periodontal evaluation.
- 2. Initial therapy in the form of scaling and root planing is accomplished by a registered hygienist, periodontist, or periodontal resident.
- 3. 4 to 6 weeks following initial periodontal therapy, the patient's initial therapy is reevaluated to assess healing and oral hygiene.
- 4. A 2<sup>nd</sup> full periodontal charting will be completed at re-evaluation; including probing depth measurements, clinical attachment level measurements, bleeding on probing, and plaque scores for each tooth.
- Based on the re-evaluation a treatment plan will be developed for each patient.
  Typical treatment plans are:
  - a. Maintenance therapy. No surgical treatment required; patient is not a candidate for the study.
  - b. Surgical treatment required, but regenerative therapy is not indicated, the patient is not a candidate for the study.
  - c. Intrabony vertical defect is present, but site has furcation involvement. The patient is not a candidate for the study.
  - d. Intrabony vertical defect is present and regenerative therapy is the treatment of choice.
    - Patient will be asked if he/she would like to participate in the study and will then be provided a one page brief about the study
      - i. If the patient consents to be in the study, the therapy will continue as stated below
      - ii. If the patient does not consent to be in the study, surgical therapy will continue as planned by the patient's surgeon.

# Following Consent:

- Maxillary and mandibular impressions using an irreversible hydrocolloid material (alginate) will be made using stock impression trays; sized small, medium, or large depending on the size of the subject's mouth. The impressions will be poured with dental stone. The stone models of the subject's jaws will be used to fabricate a customized plastic stent to allow standardized measurements of the surgical site.
  - a. Plastic stent fabrication:
    - A plastic stent for making probing depth measurements will be fabricated utilizing the methods described by Isador 84 and Deas 04.
    - A 2 mm thick co-polyester plastic dental splint material (biocryl material) will be adapted to the stone model of the subject's arch utilizing a BioStar matrix machine.
    - iii. The stent will be trimmed to end just above the height of contour of the crowns of the teeth in order to visualize the gingiva.
    - iv. A fissure bur (1169 bur) will be used to cut grooves in the interproximal areas and along the buccal and lingual aspects of the teeth being investigated. These grooves accommodate the periodontal probe and allow the investigator to probe the same location and with the same angulation at pre or post-surgical visits.
    - v. Following use the stent will be cleaned and disinfected with Dispatch spray and stored in a ziplock plastic bag labeled with the subject's study number. The bag will be locked in a secured drawer maintained by the primary examiner; and then retrieved for measurements at 6 and 12 months.



Fig 6: Example of the customized stent used for data collection Used with permission from the author of this thesis, LCDR Teresita Alston.

- A customized bite-plate registration using the paralleling radiographic technique will be fabricated for each patient to standardize radiographs at baseline and 6 and 12 months after surgery.
  - i. A Rinn film holder used for the paralleling technique will be selected based upon the size of the sensor used for the digital radiographs:
    - 1. Size 1 for individuals with smaller mouths
    - 2. Size 2 for individuals with larger mouths.
  - ii. Blu-mousse, a bite registration material, will be applied to each side of the film holder where the teeth contact the holder>
    - Subjects bite into blu-mousse until the material hardens (approximately 45 seconds).
    - 2. The film holder is removed from the mouth.
    - 3. The film holder is reinserted into the mouth and the subject bites down to confirm that the bite is reproducible.

iii. \*Following use, the film holder will be cleaned and disinfected with Dispatch spray and stored in a ziplock plastic bag labeled with the subject's study number and locked in a secured drawer maintained by the primary examiner; and then retrieved for postoperative radiographs at 6 and 12 months.



Fig 7. Sample customized holder for standardized radiographic using Blu Mousse bite registration material Used with permission from the author of this thesis, LCDR Teresita Alston.

- Prior to surgery, clinical parameters will be measured using the customized plastic stent\* and a UNC-15 periodontal probe. All clinical measurements will be made by a blinded study investigator.
  - Probing depth: measured in millimeters from the gingival margin to the base of the pocket.
  - b. Clinical attachment level: Measured from the cementoenamel junction of each tooth to the soft tissue base of the pocket.
  - c. Recession: Measured from the cementoenamel junction of the tooth to the gingival margin.
  - d. Bleeding on probing: 30 seconds following measurements of the probing depth and clinical attachment level, the area will be re-examined.
    - i. The presence or absence of bleeding will be recorded on the data collection sheet.
  - e. Plaque score: The presence or absence of plaque at the defect site will be recorded on the data collection sheet.
- 4. Prior to surgery, a standardized digital periapical radiograph will be made using the customized bite-plate and the paralleling technique.
  - a. All radiographs made at NPDS are stored on the NNMC-DDILOCAL radiographic database and are viewed using the software XrayVision DCV. This database is secured. The database can only be accessed by authorized CAC users. Radiographs are identified by the patient's full name, social security number and date image was made.

### Randomization Procedure:

- A computer program will randomly sequence each subject's study enrollment numbers (1-30) as in the example below.
  - a. A random sequence table will be generated by the research coordinator following IRB approval in order to maintain blinding of investigators.

Table 2. Sample Random Sequence Generator:

4
15
28
10
6
21
7
26
17
9
12
23
20
27
* 8

http://www.random.org/sequences/?min=1&max=30&col=2&format=html&rnd=new

Timestamp: 2012-05-31 18:54:03 UTC

- 2. Thirty envelopes marked 1 -30 will contain either a card stating DFDBA or Accell. Thereafter, the random sequence table will be placed in a sealed envelope that will not be opened until all data has been collected. Sealed envelopes (1-30) will be stored by the principal investigator in a locked drawer.
- 3. When each participant goes to surgery the investigator will provide the surgical team the envelope corresponding to that subject's enrollment number. The surgical team will open the envelope and remove a card which will state which bone graft material to place following debridement and categorization of the defect.
  - a. A surgical team member will check on the card whether the intrabony defect was ideal for bone grafting, ≥ 4mm in depth or less than ideal, < 4mm in depth, and if a furcation was evident that was not detected pre-surgically.
    - i. Please note that surgical findings sometimes differ from pre-surgical estimates of the surgical site.

One of the cards below will be sealed in each envelope (1-30).



- 4. The completed card will be returned to the numbered envelope and resealed. The study investigator will collect the sealed envelope and place it in the data collection folder for each study participant that is stored by the principal investigator in a locked drawer.
- The study investigators who make the postsurgical clinical and radiographic assessments at 6 and 12 months will be blinded to which bone graft material a given participant received.

# Surgical Procedure:

Females of child bearing age will be asked to complete a HCG (human chorionic gonadotropin) urinalysis prior to the surgical procedure. If the results of the HCG test are positive, the subject will be exited from the study.

Prior to surgical procedure, in line with standard procedure at the Periodontics Department participants will be offered the option of having the surgery performed using: 1. only local anesthesia, or 2. a combination of oral anxiolysis with Triazolam and local anesthesia, or 3. a combination of IV moderate sedation with Versed and Fentanyl and local anesthesia. The use of sedation will not affect the surgical procedure.

- The surgical provider will be either a board certified staff periodontist or a 2<sup>nd</sup> or 3<sup>rd</sup> year periodontal resident. All surgical providers will be briefed in the protocol. All surgeries will follow the same steps listed below.
  - a. Surgical set-up is standardized for all surgeries done at the Naval Postgraduate Dental School Periodontics Department.
  - b. Both the experimental (Accell) and control (DFDBA) materials will be available to the surgeon. The bone graft material used will be determined when the sealed envelope is opened by a surgical team member after the defect has been debrided and characterized.
  - c. Surgical Procedure Steps:
    - i. Placement of normal saline IV
      - 1. Administration of 8mg Dexamethasone IV
    - ii. Administration of oral anxiolysis or IV moderate sedation if patient desired and indicated
    - iii. Administration of topical and local anesthetic with any combination of 2% Lidocaine with 1:100K epinephrine, 4% Articane with 1:100K epinephrine, and 0.5% Marcaine with 1:200K epinephrine
    - iv. Sulcular incisions and full thickness reflection of the surgical flap
    - v. Debridement of the surgical site/defect to remove granulation tissue and calculus using hand instruments and cavitron ultrasonic instrument
    - vi. Characterization of the defect by a study investigator

- 1. Number of defect walls present: 1-, 2-, 3-walled defect or combination defect
- 2. Depth of defect from CEJ to the base of the bony pocket
- Depth of defect from the alveolar crest to the base of the bony pocket
- 4. Mesial-distal defect width: Measured in the mesial-distal direction from the tooth to the mesial or distal margin of the defect
- Buccal-lingual defect depth: Measured in the buccal-lingual direction from the buccal margin of the defect to the lingual margin of the defect
- 6. Following defect characterization, the investigator provides the surgical team with the sealed envelope to determine which bone graft material, Accell or DFDBA, the participant was randomized to receive, and the investigator leaves the surgical suite.
- vii. The graft material will be prepared as defined by the manufacturing instructions:
  - 1. Hydration of the graft material with sterile saline DFDBA
  - 2. Graft material dispensed from syringe Accell.
- viii. The root surface of the tooth bordering the defect site will be treated with a 24% EDTA gel f for 4 minutes. The site will then be washed with sterile saline for 1 minute.
- ix. Osteoplasty (reshaping unsupported the alveolar bone) will be performed as needed
- Intramarrow penetration of the bone within the defect using a ¼ surgical round bur to induce bleeding in the defect site
- xi. Graft material (determined from the sealed envelope) placed into the defect up to the level of the alveolar crest
- xii. Bio-Gide membrane trimmed and positioned to cover grafted defect
- xiii. Primary flap closure achieved using a non-resorbable monofilament suture (ie. Gore-tex)
- xiv. Gauze pressure will be held on the site for 5 minutes to achieve

hemostasis and reduce the size of the fibrin clot formed.

- xv. Periodontal dressing may be placed over the surgical site.
- xvi. Surgical team checks appropriate findings on randomization card, reseals card in envelope, and envelope collected by investigator.
  - 1. Envelopes will not be re-opened until after data analysis



Figure 8. Hydrated DFDBA



## Figure 9. Accell Connexus®

# **Post-operative Care:**

- 1. All participants receive the following post-operative regimen:
  - a. Pain medication consisting of any of the following alone or in combination:
    - i. Ibuprofen 800 mg , Take 1 tab PO q6-8h for moderate pain
    - ii. Hydrocodone/Acetaminophen 5/325 mg, Take 1-2 tab PO q6h prn severe/breakthrough pain
    - iii. Oxycodone/Acetaminophen 5/325mg, Take 1-2 tab PO q6h prn severe/breakthrough pain

- b. Pain medication for patients who cannot take NSAIDS will be prescribed any of the following alone or in combinations:
  - i. Acetaminophen 325 mg, Take 1-2 tabs PO q4h for moderate pain
  - ii. Oxycodone 5mg, Take 1 tab PO q4h prn severe/breakthrough pain
- c. Antibiotics consisting of either of the following:
  - i. Amoxicilin 500mg, Take 1 tab PO q8h for 10 days
  - ii. Clindamycin 300 mg, Take 1 tab PO q8h for 10 days
- d. 0. 12% Chlorhexidine, 1 bottle, Rinse and spit bid with 1 TBSP as directed on the bottle
- All patients are provided with the standard post-operative instructions (See appendix B3 for an example of the standard postoperative care instruction form).
- 3. Patients are recalled at 1 week to assess post-operative healing and remove plaque/deposits on the surgical site.
- 4. Patients recalled at 2 weeks post-operative to assess healing, remove plaque, and remove sutures at the surgical site.
- 5. Patients recalled at weeks 4, 6, 8, 12, and 16 to assess healing, remove plaque, and reinforce oral hygiene.
- 6. Patients recalled at 6 months following the surgical procedure to assess healing, remove plaque, and reinforce oral hygiene.
  - a. A study investigator blinded to the graft material used will evaluate the periodontal parameters using the customized stent and take a periapical radiograph using the customized bite-plate and paralleling technique.
    - i. Same methods as in pre-surgical evaluation
    - ii. If the customized stent is not stable on the patient's teeth at the follow-up appointment, the clinical data will not be used in the analysis. The radiographic data will still be collected.
  - 7. Patients recalled at 9 months for periodontal maintenance therapy
  - 8. Patient recalled at 12 months following the surgical procedure to assess healing, remove plaque, and reinforce oral hygiene.
    - a. A study investigator blinded to the graft material used (other

than the surgeon or the staff member on the surgical case) will evaluate the periodontal parameters using the customized stent and take a periapical radiograph using the customized bite-plate and paralleling technique.

- i. Same methods as in pre-surgical evaluation
- ii. If the customized stent is not stable on the patient's teeth at the follow-up appointment, the clinical data will not be used in the analysis. The radiographic data will still be collected.
- 9. Patient will be exited from the study and followed by their primary provider for periodontal maintenance therapy.

### Analysis of Data:

- 1. Periodontal parameters assessed at 6 months and 12 months will be compared to the baseline measurements to determine change in clinical attachment level and probing depth.
  - a. A comprehensive periodontal charting (probing depths, attachment levels, bleeding on probing, plaque score) for all teeth present in the mouth will be done at the 12 months visit as well.
- Two reviewers, board certified periodontist(s) and/or a board certified oral radiologist, blinded to which bone graft material subjects received will access the NNMC-DDILOCAL database, and use the Xray Vision software used for viewing to measure bone levels before surgery and at 6 months and 12 months.
  - a. Radiographic analysis will be completed following data collection
  - b. To access the radiographs, the examiners will be provided with a submaster list containing the study number, name, and last four of the social security number.
  - c. The examiners will access the patient's radiographic record on the NNMC-DDILOCAL database using the patient's name and last four.
  - d. The standardized radiographs taken at baseline, 6 months following

surgery and 12 months following surgery will be obtained.

- e. Using the digital radiograph software, measurements will be made and recorded on the data collection sheet for radiographs.
- f. The sub-master list will be destroyed following all measurements.
- 3. If subtraction radiography becomes available at NPDS, the same radiographs will be used to assess changes in bone volume from baseline to 6 and 12 months postoperatively.
- 4. Statistical analysis will assess pre and post-test differences.

#### CHAPTER IV: RESULTS

A total of 21 subjects meeting the enrollment criteria between December 2012 and May 2015 were enrolled. There were 14 males and 7 females with and age range of 22-74. As of May 26, 2015 twenty subjects had surgery completed by a second or third year resident or a board certified periodontist. Of the 20 subjects 19 completed combination therapy and 1 had osseous resective therapy due to having a non-graftable defect. Three subjects were exited from the study; one due to lack oral hygiene compliance, one due to a permanent change of station, and the other due to a nongraftable defect. Probing depth (PD), relative clinical attachment level (CAL), plaque, bleeding on probing (BOP), surgical intrabony defect type and radiographic percent bone fill were assessed. Clinical and radiographic assessments were completed by two board certified periodontitis.



Figure 10: This is an example of a patient randomized to DFDBA. Figure 10a shows the radiographic defect at baseline. 10b shows the 3 walled defect after debridement. 10c is the 6 months post-surgical results. 10d 12 months post combination therapy. Used with permission from the author of this thesis, LCDR Teresita Alston.

Due to the enrollment status and number of exited patients 6 month and one year results were completed on 13 subjects; 7 males and 6 females with an age range of 22-67 years (mean 40.6 years). Two subjects were exited from the Accell group and 1 from the DFDBA group. Therefore 13 sets of 6month and 1 year results were analyzed with 8 subjects in the DFDBA group and 5 in the Accell group for this interim analysis.

No significant difference was found with respect to bleeding on probing (BOP) or plaque scores. The mean probing depth (PD) decreased from 7.6 (range 5.0-14.0mm) to 3.8mm (range 3.0 - 5.0mm) for Accell and from 8mm (7.0-11.0mm) to 4mm (3.0-5.0mm) for DFDBA. The mean gain of CAL was 3.4mm for Accell and 3.0mm for DFDBA. Accell and DFDBA attained positive percent radiographic bone fill; 65.79% and 59.9% respectively. The results were not statically significant.





months post treatment.







Figure 15: 15a and c are baseline radiographics of sites randomized to DFDBA and Accell respectively. 15b and 15d are the results of combination therapy at 12 months post treatment. Used with permission from the author of this thesis, LCDR Teresita Alston.

#### **CHAPTER V: DISCUSSION**

Definitive conclusions cannot be drawn at this time because 12 month clinical measurements have been made in less than half of the subjects in the approved sample size. However clinically it does appear that Accell does offer the clinical ability to allow bone apposition above the residual bony crest radiographicIly. It also appears that sites grafted with Accell are less radiopaque than sites grafted with DFDBA at the 12 months evaluation period. The makers of Accell claim that Accell is designed to release BMP immediately and over an extended period. With the extended release of those growth factors it may take longer for Accell to mature radiographicIly which may imply that 12 months is too soon to effectively evaluate the radiographic and possibly the clinical results of Accell.

The assertion is that Accell is easier to place and mold within the defect. It seems to the author that the claim is true as the material is easily placed and remained in the site. However not all providers using Accell, in this study, found Accell easy to work with. Some providers felt that the material was too soft and felt as if they could not pack the material into the defect properly.

# **CHAPTER VI: CONCLUSION**

The data analysis at this point does not show any significant statistical difference in clinical and radiographic outcomes between DFDBA and Accell Connexus<sup>®</sup>. Both bone graft materials resulted in improved clinical parameters. Longer term follow up needs to be conducted on Accell for both clinical and radiographic results.

Appendix

Treatment Group	SubjectID	Baseline Date	Gender	Age	Tooth	Location	Baseline_ Probing Depth Buccal mm	Baseline_ Probing Depth Lingual mm	Baseline_ CAL Buccal	Baseline_ CAL Lingual	Baseline_ Recession Buccal	Baseline_ Recession Lingual		Baseline_ Plaque Lingual	Baseline_ BOP Buccal	Baseline, BOP Lingual
Accell Connexus		17-Jan-2013	Male	22	18	Distal	6	4	11	8	0	0	No	No	Yes	Yes
DFDBA	1	9-May-2013	Female	53	4	Distal	6	1	1	10	0	05	No	No	Yes	Yes
Accell Connexus	3	5-Mar-2013	Male	39	19	Distal	6	5	10	9	0	1	No	No	Yes	Yes
DFDBA	4	15-Apr-2013	Female	25	19	Mesial	6	1	11	13	0	0	No	Yes	Yes	Yes
Accell Connexus	68 <b>5</b> (10)	15-Apr-2013	Female	45	26	Distal	7	6		11	0	D	Yes	Yes	Yes	Yes
DFDBA	6	24-0ct-2013	Male	47	31	Distal	1	5	11	8	0	0	Yes	No	Yes	Yes
DFDBA	<b>1</b>	15-May-2013	Male	32	3	Mesial	3	1	9	12	0	0	No	No	No	Yes
DF <b>D</b> BA	8	23-Sep-2013	Male	40	18	Distal	1	4	15	88 <b>7</b> /2	0	O	No	No	Yes	No
Accell Connexus	9 Exit															
DFDBA	10	21-Oct-2013	Female	67	- 30	Mesial	5	1	5	1	0	0	No	No	Yes	No
Accell Connexus	_11	2-May-2014	Male	54	30	Distal	5	5	9	9	0	0	No	Yes	Yes	No
DFDBA	12	24-Mar-2013	Male	41	18	Distal	8	10	11	1	0		Yes	No	Yes	Yes
DFDBA	13	4-Mar-2014	Female	25	18	Distal	<b>Set S</b>	8	8	8	0	-3	No	No	Yes	Yes
Accell Connexus	14 Exit															
Accell Connexus	15	12-May-2014	Female	38	27	Distal	14	1	19	15	0	0	Yes	Yes	Yes	Yes

Treatment Group	SubjectID	Surgery Date	Surgical_ Defect Class Buccal	Surgical_ Defect Class Lingual	Surgical_ CEJ-Base Buccal	Surgical_ CEJ-Base Lingual	Surgical_ Depth Buccal	Surgical_ Depth Lingual	Surgical_ M-D Width Buccal		Surgical_ B-L Width Buccal	Surgical_B L Width Lingual
Accell Connexus	1	17-Jan-2013	3	3	6	5	4	4	3	3	7	7
DFDBA	2	9-May-2013	3	3	13	14	10	9	2	2	9	9
Accell Connexus	3	5-Mar-2013	3	3	6	7	5	4	3	3	7	7
DFDBA	4	15-Apr-2013	1	3	10	9	7	4	4	4	9	9
Accell Connexus	5	15-Apr-2013	2	2	6	8	3	5	3	3	7	7
DFDBA	6	24-0ct-2013	3	3	6	6	5	4	5	6	13	13
DFDBA	<b>:7</b>	15-May-2013	2	3	6	8	4	5	2	3	9	9
DFDBA	8	23-Sep-2013	3	3	11	10	9	8	4	3	9	9
Accell Connexus	9 Exit											
DFDBA	10	21-0ct-2013	3	3	5	6	3	4	1	1	6	6
Accell Connexus	11.55	2-May-2014	3	3	7	8	5	5	2	3	7	7
DFDBA	12	24-Mar-2014	3	3	7	9	5	7	6	6	11	11
DFDBA		4-Mar-2014	3	3	6	7	4	5	3	3	8	8
Accell Connexus	14 Exit											
Accell Connexus	15	12-May-2014	3	3	14	14	9	10	13	4	8	8

Treatment Group	Subjectl	SixMonth Date	SixMonth_ Probing Depth	SixMonth_ Probing Depth Lingual mm	SixMonth_ CAL Buccal	SixMonth_ CAL Lingual	1008063636439601956	SixMonth_ Recession Lingual	AND	SixMonth_ Plaque Lingual	SixMonth_ BOP Buccal	SixMonth BOP Lingual
Accell Connexus	1	18-Jul-2013	4	5	7	5	0	0	No	Yes	No	Yes
DFDBA	2	4-Dec-2013	4	5	8	9	0	1	No	Yes	No	Yes
Accell Connexus	3	24-Sep-2013	3	4	8	7	1	2	No	No	Yes	Yes
DFDBA	4	16-0ct-2013	2	4	3	4	1.000	0	. No	No	No	Yes
Accell Connexus	5	18-0ct-2013	3	3	5	5	2	2	No	No	No	No
DFDBA	6	5-May-2014	4	5	8	9	0	0	No	No	No	Yes
DFDBA	<b>1</b>	21-Nov-2013	3	4	9	10	2	1	Yes	Yes	Yes	No
DFDBA	8	18-Mar-2014	6	4	9	7	0	-1	Yes	Yes	Yes	Yes
Accell Connexus	9 Exit											
DFDBA	10	22-Apr-2014	2	4	7	8	1	1	No	No	No	No
Accell Connexus	11	3-Dec-2014	4	4	8	9	0	0	No	No	No	No
DFDBA	12	26-Sep-2014	3	3	7	6	0	-1	No	No	No	No
DFDBA	13	4-Sep-2014	7	7	10	10	-4	-4	Yes	Yes	No	Yes
Accell Connexus	14 Exit											
Accell Connexus	15	9-Dec-2014	3	3	7	7	0	2	No	Yes	No	No

Treatment Group	Subjecti D	TwelveMonth Date	TwelveMo nth_Probin g Depth Buccal mm	Lingual		TwelveMo nth_CAL Lingual	TwelveMo nth_Reces sion Buccal	TwelveMo nth_Reces sion Lingual		TwelveMo nth_Plaqu e Lingual	TweiveMo nth_BOP Buccal	TwelveMo nth_BOP Lingual
Accell Connexus	1	16-Jan-2014	3	5	9	7	1	0	Yes	Yes	Yes	No
DFDBA	2	21-May-2014	4	3	<b>7</b> 7	8	1	2	No	No	No	Yes
Accell Connexus	3	19-Mar-2014	4	4	9	8	0	0	No	Yes	Yes	No
DFDBA	4	4-Apr-2014	3	5	9	11	1	1	No	No	Yes	Yes
Accell Connexus	5	18-Jun-2014	2	3	10	9	2	3	No	No	No	No
DFDBA	. 6	12-Nov-2014	3	5	6	8	0	0	No	Yes	No	Yes
DFDBA	7	28-May-2014	3	3	9	8	1	1	No	No	Yes	No
DFDBA	8	24-Sep-2014	4	2	9	7	0	0	Yes	Yes	Yes	Yes
Accell Connexus	9 Exit											
DFDBA	10	5-Nov-2014	2	4	207	9		0	Yes	No	Yes	No
Accell Connexus	11	14-May-2015	4	3	146 <b>8</b> 449	<b>8</b>	<b>.</b>	1	No	Yes	No	No
DFDBA	12	25-Mar-2015	3	3	6	7	0	0	No	No	Yes	Yes
DFDBA	13	16-Mar-2015	4	4	2	3	0	0	No	Yes	No	Yes
Accell Connexus	14 Exit											
Accell Connexus	្រទ	13-May-2015	2	3	<b>7</b> 2	<b>7</b>	0	2	No	No	No	No

.

.

Treatment Group	Subjecti D	Radio_Base line_CEI- Base	Radio_Base line_CEJ- Apex	-	ine per ja⊡ stat	Radio_Six Month_CEI- Apex	∎ Bageria∏ isag		Radio_Twelve Month_CEI- Apex	Radio_Twelve Month_CEJ- Alveolar
Accell Connexus	1	4.51	11.6	0.74	3.08	11.57	0.96	3	11.67	0.78
DFDBA	2	9.96	13.28	1.18	5.76		2.64	5.91		2.04
Accell Connexus	3	5.43	14.34	1.89	4.57	13.48	2.65	3.48	12.83	1.94
DFDBA	4	5.25	16.66	2.15	3.83		1.48	5.02		1.54
Accell Connexus	5	7.9	18,41	3.5	0	19.68	6.21	0	16.46	4.37
DFDBA	6	5.07	13.27	2.18	3.81	12.13	0.51	1.59	12.34	0.4
DFDBA	7	4.99	15.28	1.75	2.45	11.4	1.97	4.05	13.55	2.59
DFDBA	8	9.32	11,48	1.79	3.26	15.41	1.13	0	12.58	1.53
Accell Connexus	9 Exit				a set a set a		میں میں ایک ایک ایک ایک ایک میں محمد میں معاہد میں ایک ایک			
DFDBA	10	4.81	21.89	1.47	2.75	15.72	0.72	0	15.37	0.24
Accell Connexus	11	5.69	13.41	3.6	2.8	12.16	2 <b>2</b> 99	2.91	12.56	1.9
DFDBA	12	6.27	14.21	1.53	3.49	13.95	1.78	2,07	13.97	1.11
DFDBA	13	3.62	15.17	0.37	1.8	15.82		1.11	15.01	0.28
Accell Connexus	14 Exit					an a a a stat				
Accell Connexus	15	12.4	16.5	5.16	3.2	16.3	3.2	2.9	15.6	2.9

surgery Appendix A5: Raw data at radiographic baseline and 6 and 12 months post-

.

3	Minimum	Maximum	Median	Percentil e 25	Percentil e 75	Mean	Standard Deviation	Valid
MAX Baseline ProbingDepth	5.00	14.00	6.00	6.00	7.00	7.60	3.65	5
MAX Baseline CAL	9.00	19.00	11.00	10.00	11.00	12.00	4.00	5
MAX Baseline Recession	.00	1.00	.00	.00	.00	.20	.45	5
MAX_Surgical_DefectClass	2.00	3.00	3.00	3.00	3.00	2.80	.45	5
MAX Surgical CEJBase	6.00	14.00	8.00	7.00	8.00	8.60	3.13	5
MAX Surgical Depth	4.00	10.00	5.00	5.00	5.00	5.80	2.39	5
MAX_Surgical_MDWidth	3.00	13.00	3.00	3.00	3.00	5.00	4.47	5
MAX Surgical BLWidth	7.00	8.00	7.00	7.00	7.00	7.20	.45	5
MAX_SixMonth_ProbingDepth	3.00	5.00	4.00	3.00	4.00	3.80	.84	5
MAX SixMonth CAL	5.00	9.00	7.00	7.00	8.00	7.20	1.48	5
MAX SixMonth Recession	.00	2.00	2.00	.00	2.00	1.20	1.10	5
MAX TwelveMonth ProbingDepth	3.00	5.00	4.00	3.00	4.00	3.80	.84	5
MAX TwelveMonth CAL	7.00	10.00	9.00	8.00	9.00	8.60	1.14	5
MAX TwelveMonth Recession	.00	3.00	1.00	1.00	2.00	1.40	1.14	5
Change6moProbingDepth_MAX	-11.00	-1.00	-2.00	-4.00	-1.00	-3.80	4.21	5
PChange6moProbingDepth_MAX	-78.57	-16.67	-33.33	-57.14	-20.00	-41.14	26.29	5
Change12moProbingDepth_MAX	-11.00	-1.00	-2.00	-4.00	-1.00	-3.80	4.21	5
PChange12moProbingDepth_MAX	-78.57	-16.67	-33.33	-57.14	-20.00	-41.14	26.29	5
Change6moCAL_MAX	-12.00	.00	-4.00	-6.00	-2.00	-4.80	4.60	5
PChange6moCAL_MAX	-63.16	.00	-36.36	-54.55	-20.00	-34.81	25.63	5
Change12moCAL_MAX	-12.00	-1.00	-1.00	-2.00	-1.00	-3.40	4.83	5
PChange12moCAL_MAX	-63.16	-9.09	-11.11	-18.18	-10.00	-22.31	23.12	5
Change6moRecession_MAX	.00	2.00	1.00	.00	2.00	1.00	1.00	5
Change12moRecession_MAX	-1.00	3.00	1.00	1.00	2.00	1.20	1.48	5

# TreatmentGroup\_num = Accell Connexus

TreatmentGroup_num = Accell	Minimum	Maximum	Median	Percentile 25	Percentile 75	Mean
Age	22.0	54.0	39.0	38.0	45.0	39.6
Baseline_ProbingDepthBuccalmm	5.0	14.0	6.0	6.0	7.0	7.6
Baseline_ProbingDepthLingualmm	4.0	11.0	5.0	5.0	6.0	6.2
Baseline CALBuccal	9.0	19.0	11.0	10.0	11.0	12.0
Baseline CALLingual	8.0	15.0	9.0	9.0	11.0	10.4
Baseline_RecessionBuccal	.0	.0	.0	.0	.0	.0
Baseline_RecessionLingual	.0	1.0	.0	.0	.0	.2
Surgical DefectClassBuccal	2.0	3.0	3.0	3.0	3.0	2.8
Surgical DefectClassLingual	2.0	3.0	3.0	3.0	3.0	2.8
Surgical CEJBaseBuccal	6.0	14.0	6.0	6.0	7.0	7.8
Surgical CEJBaseLingual	5.0	14.0	8.0	7.0	8.0	8.4
Surgical_DepthBuccal	3.0	9.0	5.0	4.0	5.0	5.2
Surgical_DepthLingual	4.0	10.0	5.0	4.0	5.0	5.6
Surgical_MDWidthBuccal	2.0	13.0	3.0	3.0	3.0	4.8
Surgical MDWidthLingual	3.0	4.0	3.0	3.0	3.0	3.2
Surgical BLWidthBuccal	7.0	8.0	7.0	7.0	7.0	7.2
Surgical_BLWidthLingual	7.0	8.0	7.0	7.0	7.0	7.2
SixMonth_ProbingDepthBuccalmm	3.0	4.0	3.0	3.0	4.0	3.4
SixMonth_ProbingDepthLingualmm	3.0	5.0	4.0	3.0	4.0	3.8
SixMonth CALBuccal	5.0	8.0	7.0	7.0	8.0	7.0
SixMonth CALLingual	5.0	9.0	7.0	5.0	7.0	6.6
SixMonth_RecessionBuccal	.0	2.0	.0	.0	1.0	.6
SixMonth RecessionLingual	.0	2.0	2.0	.0	2.0	1.2
TwelveMonth_ProbingDepthBuccaimm	2.0	5.0	4.0	2.0	4.0	3.4
TwelveMonth_ProbingDepthLingualmm	3.0	4.0	3.0	3.0	3.0	3.2
TwelveMonth CALBuccal	7.0	10.0	9.0	8.0	9.0	8.6
TwelveMonth_CALLingual	7.0	9.0	8.0	7.0	8.0	7.8
TwelveMonth_RecessionBuccal	.0	2.0	.0	.0	1.0	.6
TwelveMonth RecessionLingual	.0	3.0	1.0	.0	2.0	1.2
Radio_Baseline_CEJBase	4.51	12.40	5.69	5.43	7.90	7.19
Radio Baseline CEJApex	11.60	18.41	14.34	13.41	16.50	14.85
Radio_Baseline_CEJAlveolar	.74	5.16	3.50	1.89	3.60	2.98
Radio SixMonth CEJBase	.00	4.57	3.08	2.80	3.20	2.73
Radio_SixMonth_CEJApex	11.57	19.68	13.48	12.16	16.30	14.64
Radio SixMonth CEJAlveolar	.96	6.21	2.65	2.00	3.20	3.00
Radio TwelveMonth CEJBase	.00	3.48	2.91	2.90	3.00	2.46
Radio_TwelveMonth_CEJApex	11.67	16.46	12.83	12.56	15.60	13.82
Radio_TwelveMonth_CEJAlveolar	.78	4.37	1.94	1.90	2.90	2.38
Change6moProbingDepthBuccalmm	-11.00	-1.00	-3.00	-4.00	-2.00	-4.20
PChange6moProbingDepthBuccalmm	-78.57	-20.00	-50.00	-57.14	-33.33	-47.81
Change12moProbingDepthBuccaimm	-12.00	-1.00	-2.00	-5.00	-1.00	-4.20
PChange12moProbingDepthBuccalmm	-85.71	-16.67	-33.33	-71.43	-20.00	-45.43
Change6moProbingDepthLingualmm	-8.00	1.00	-1.00	-3.00	-1.00	-2.40
PChange6moProbingDepthLingualmm	-72.73	25.00	-20.00	-50.00	-20.00	-27.55
Change12moProbingDepthLingualmm	-8.00	-1.00	-2.00	-3.00	-1.00	-3.00
PChange12moProbingDepthLingualmm	-72.73	-20.00	-40.00	-50.00	-25.00	-41.55
Change6moCALBuccal	-12.00	-1.00	-4.00	-6.00	-2.00	-5.00
PChange6moCALBuccal	-63.16	-11.11	-36.36	-54.55	-2.00	-37.04
Change12moCALBuccal	-12.00	-1.00	-1.00	-2.00	-1.00	-37.04
PChange12moCALBuccal	-63.16	-9.09	-11.11	-18.18	-10.00	-22.31
Change6moCALL ingual	-8.00	-0.00	-3.00	-6.00	2.00	-3.80

Stand

Devia

11.7 3.6

2.8 4.0

2.8 .0 .4 .4

.4

3.5

3.4

2.3

2.5

4.6

.4

.4 .4

.5 .8

1.2

<u>1.7</u> .9

<u>1.1</u> 1.3

.4 1.1

.8

.9

1.3

3.17 2.66

1.70 1.67

3.36

1.98

1.39

2.08

1.34

3.96

22.48

4.66

31.30

3.44

36.81

2.92

21.12

4.36

22.09

4.83

23.12

3.19

22.92

3.05

18.17

-3.80

-2.60

-33.52

-21.25

#### TreatmentGroup\_num = Accell Connexus

Change6moCALLingual

PChange6moCALLingual

Change12moCALLingual

PChange12moCALLingual

.00

.00

-1.00

-11.11

-3.00

-1.00

-12.50

-37.50

-6.00

-2.00

-18.18

-53.33

-2.00

-1.00

-11.11

-22.22

-8.00

-54.55

-8.00

-53.33
Change6moRecessionBuccal	.00	2.00	.00	.00	1.00	.60	.89
Change12moRecessionBuccal	.00	2.00	.00	.00	1.00	.60	.89
Change6moRecessionLingual	.00	2.00	1.00	.00	2.00	1.00	1.00
Change12moRecessionLingual	-1.00	3.00	1.00	.00	2.00	1.00	1.58
Change6moRadio_Baseline_CEJBase	-9.20	86	-2.89	-7.90	-1.43	-4.46	3.84
PChange6moRadio_Baseline_CEJBase	-100.00	-15.84	-50.79	-74.19	-31.71	-54.51	33.49
Change12moRadio_Baseline_CEJBase	-9.50	-1.51	-2.78	-7.90	-1.95	-4.73	3.70
PChange12moRadio_Baseline_CEJBase	-100.00	-33.48	-48.86	-76.61	-35.91	-58.97	28.63
Change6moRadio_Baseline_CEJApex	-1.25	1.27	20	86	03	21	.97
PChange6moRadio_Baseline_CEJApex	-9.32	6.90	-1.21	-6.00	26	-1.98	6.17
Change12moRadio_Baseline_CEJApex	-1.95	.07	90	-1.51	85	-1.03	.76
PChange12moRadio_Baseline_CEJApex	-10.59	.60	-6.34	-10.53	-5.45	-6.46	4.60
Change6moRadio_Baseline_CEJAlveolar	-1.96	2.71	.22	-1.60	.76	.03	1.90
PChange6moRadio_Baseline_CEJAlveolar	-44.44	77.43	29.73	-37.98	40.21	12.99	52.61
Change12moRadio_Baseline_CEJAlveolar	-2.26	.87	.04	-1.70	.05	60	1.32
PChange12moRadio_Baseline_CEJAlveolar	-47.22	24.86	2.65	-43.80	5.41	-11.62	32.12
a. TreatmentGroup_num = Accell Connexus							

## TreatmentGroup\_num = DFDBA

<b>a</b>	Minimum	Maximum	Median	Percenti le 25	Percentil e 75	Mean	Standard Deviation	Valio N
MAX_Baseline_ProbingDepth	7.00	11.00	7.00	7.00	9.00	8.00	1.60	8
MAX_Baseline_CAL	7.00	15.00	11.00	9.50	12.50	11.00	2.56	8
MAX_Baseline_Recession	.00	.50	.00	.00	.00	.06	.18	8
MAX_Surgical_DefectClass	3.00	3.00	3.00	3.00	3.00	3.00	.00	8
MAX_Surgical_CEJBase	6.00	14.00	8.50	6.50	10.50	8.88	2.75	8
MAX_Surgical_Depth	4.00	10.00	6.00	5.00	8.00	6.50	2.14	8
MAX_Surgical_MDWidth	1.00	6.00	3.50	2.50	5.00	3.63	1.77	8
MAX_Surgical_BLWidth	6.00	13.00	9.00	8.50	10.00	9.25	2.05	8
MAX_SixMonth_ProbingDepth	3.00	7.00	4.50	4.00	5.50	4.75	1.28	8
MAX_SixMonth_CAL	4.00	10.00	9.00	7.50	9.50	8.25	1.98	8
MAX SixMonth Recession	-4.00	2.00	.50	.00	1.00	.13	1.81	8
MAX TwelveMonth ProbingDepth	3.00	5.00	4.00	3.50	4.50	4.00	.76	8
MAX_TwelveMonth_CAL	3.00	11.00	8.50	7.50	9.00	8.00	2.33	8
MAX_TwelveMonth_Recession	.00	2.00	.50	.00	1.00	.63	.74	8
Change6moProbingDepth_MAX	-7.00	-1.00	-3.00	-4.00	-2.00	-3.25	1.91	8
PChange6moProbingDepth_MAX	-70.00	-12.50	-42.86	-44.16	-28.57	-39.21	16.76	8
Change12moProbingDepth_MAX	-7.00	-2.00	-3.50	-5.50	-2.50	-4.00	2.00	8
PChange12moProbingDepth_MAX	-70.00	-28.57	-46.43	-60.39	-35.71	-47.95	15.23	8
Change6moCAL_MAX	-9.00	2.00	-2.00	-5.00	50	-2.75	3.58	8
PChange6moCAL_MAX	-69.23	25.00	-18.18	-38.18	-1.19	-19.92	30.02	8
Change12moCAL_MAX	-6.00	2.00	-3.00	-4.50	-2.50	-3.00	2.39	8
PChange12moCAL_MAX	-62.50	28.57	-27.27	-38.18	-20.19	-25.65	25.99	8
Change6moRecession_MAX	-4.00	2.00	.25	.00	1.00	.06	1.78	8
Change12moRecession_MAX	.00	1.50	.50	.00	1.00	.56	.62	8

# TreatmentGroup\_num = DFDBA

,

	Minimum	Maximum	Median	Percentile 25	Percentile 75	Mean	Stanc Devia
Age	25.0	67.0	40.5	28.5	50.0	41.3	14.4
Baseline_ProbingDepthBuccalmm	3.0	11.0	6.0	5.0	7.5	6.4	2.4
Baseline_ProbingDepthLingualmm	4.0	10.0	7.0	6.0	7.5	6.9	1.8
Baseline_CALBuccal	5.0	15.0	11.0	8.5	11.0	10.1	2.9
Baseline_CALLingual	7.0	13.0	9.0	7.5	11.5	9.5	2.3
Baseline_RecessionBuccal	.0	.0	.0	.0	.0	.0	.0
Baseline_RecessionLingual	-3.0	.5	.0	.0	.0	3	1.1
Surgical_DefectClassBuccal	1.0	3.0	3.0	2.5	3.0	2.6	.7
Surgical_DefectClassLingual	3.0	3.0	3.0	3.0	3.0	3.0	.0
Surgical_CEJBaseBuccal	5.0	13.0	6.5	6.0	10.5	8.0	2.9
Surgical_CEJBaseLingual	6.0	14.0	8.5	6.5	9.5	8.6	2.6
Surgical_DepthBuccal	3.0	10.0	5.0	4.0	8.0	5.9	2.5
Surgical_DepthLingual	4.0	9.0	5.0	4.0	7.5	5.8	2.0
Surgical_MDWidthBuccal	1.0	6.0	3.5	2.0	4.5	3.4	1.7
Surgical_MDWidthLingual	1.0	6.0	3.0	2.5	5.0	3.5	1.8
Surgical_BLWidthBuccal	6.0	13.0	9.0	8.5	10.0	9.3	2.1
Surgical_BLWidthLingual	6.0	13.0	9.0	8.5	10.0	9.3	2.1
SixMonth_ProbingDepthBuccalmm	2.0	7.0	3.5	2.5	5.0	3.9	1.8
SixMonth_ProbingDepthLingualmm	3.0	7.0	4.0	4.0	5.0	4.5	1.2
SixMonth_CALBuccal	3.0	10.0	8.0	7.0	9.0	7.6	2.1
SixMonth_CALLingual	4.0	10.0	8.5	6.5	9.5	7.9	2.1
SixMonth_RecessionBuccal	-4.0	2.0	.0	.0	1.0	.0	1.8
SixMonth_RecessionLingual	-4.0	1.0	.0	-1.0	1.0	4	1.7
TwelveMonth_ProbingDepthBuccalmm	2.0	4.0	3.0	3.0	4.0	3.3	.7
TwelveMonth_ProbingDepthLingualmm	2.0	5.0	3.5	3.0	4.5	3.6	1.1
TwelveMonth_CALBuccal	2.0	9.0	7.0	6.0	9.0	6.9	2.4
TwelveMonth_CALLingual	3.0	11.0	8.0	7.0	8.5	7.6	2.3
TwelveMonth RecessionBuccal	.0	1.0	.5	.0	1.0	.5	.5
TwelveMonth_RecessionLingual	.0	2.0	.0	.0	1.0	.5	.8
Radio Baseline_CEJBase	3.62	9.96	5.16	4.90	7.80	6.16	2.27
Radio Baseline CEJApex	11.48	21.89	14.69	13.28	15.97	15.16	3.14
Radio_Baseline_CEJAlveolar	.37	2.18	1.64	1.33	1.97	1.55	.58
Radio SixMonth CEJBase	1.80	5.76	3.38	2.61	3.82	3.40	1.18
Radio_SixMonth_CEJApex	11.40	15.82	14.68	12.13	15.72	14.07	1.92
Radio SixMonth CEJAlveolar	.00	2.64	1.31	.62	1.88	1.28	.86
Radio_TwelveMonth_CEJBase	.00	5.91	1.83	.56	4.54	2.47	2.26
Radio TwelveMonth CEJApex	12.34	15.37	13.76	12.58	15.01	13.80	1.24
Radio TwelveMonth CEJAlveolar	.24	2.59	1.32	.34	1.79	1.22	.87
Change6moProbingDepthBuccalmm	-5.00	2.00	-3.00	-4.50	-1.00	-2.50	2.45
PChange6moProbingDepthBuccalmm	-66.67	40.00	-44.16	-61.25	-16.67	-33.85	36.64
Change12moProbingDepthBuccalmm	-7.00	.00	-3.00	-4.50	-1.50	-3.13	2.23
PChange12moProbingDepthBuccalmm	-63.64	.00	-53.57	-61.25	-26.67	-43.33	23.34
Change6moProbingDepthLingualmm	-7.00	.00	-2.50	-3.00	50	-2.38	2.26
PChange6moProbingDepthLingualmm	-70.00	.00	-35.71	-42.86	-6.25	-29.96	24.51
Change12moProbingDepthLingualmm	-7.00	.00	-3.50	-4.00	-2.00	-3.25	2.05
PChange12moProbingDepthLingualmm	-70.00	.00	-50.00	-57.14	-35.71	-44.46	21.60
Change6moCALBuccal	-8.00	2.00	-3.00	-5.00	1.00	-2.50	3.63
PChange6moCALBuccal	-72.73	40.00	-27.27	-38.18	12.50	-17.33	36.88
Change12moCALBuccal	-6.00	2.00	-4.50	-5.50	-1.00	-3.25	2.96
PChange12moCALBuccal	-75.00	40.00	-38.18	-45.45	-9.09	-27.56	34.92
Change6moCALLingual	-9.00	2.00	50	-45.45	1.00	-1.63	3.70
	-69.23	25.00	-5.00	-31.06	13.39	-11.20	32.11
PChange6moCALLingual Change12moCALLingual	-5.00	25.00	-2.00	-4.00	.00	-1.88	2.42
PChange12moCALLingual	-62.50	28.57	-17.69	-34.85	.00	-17.38	27.72
		1 /0 31/	1 - 17 024	1 - 14 (12)		1 - 17,00	1 21.12

	y						
Change12moRecessionBuccal	.00	1.00	.50	.00	1.00	.50	.53
Change6moRecessionLingual	-1.00	1.00	.00	-1.00	.75	06	.86
Change12moRecessionLingual	.00	3.00	.50	.00	1.25	.81	1.07
Change6moRadio_Baseline_CEJBase	-6.06	-1.26	-2.30	-3.49	-1.62	-2.77	1.62
PChange6moRadio_Baseline_CEJBase	-65.02	-24.85	-43.58	-50.49	-34.61	-43.40	13.00
Change12moRadio_Baseline_CEJBase	-9.32	23	-3.77	-4.51	-1.73	-3.69	2.79
PChange12moRadio_Baseline_CEJBase	-100.00	-4.38	-67.81	-84.67	-29.75	-58.61	34.96
Change6moRadio_Baseline_CEJApex	-6.17	3.93	70	-3.88	.65	-1.15	3.54
PChange6moRadio Baseline_CEJApex	-28.19	34.23	-5.21	-25.39	4.28	-4.25	22.80
Change12moRadio_Baseline_CEJApex	-6.52	1.10	59	-1.73	16	-1.41	2.67
PChange12moRadio_Baseline_CEJApex	-29.79	9.58	-4.35	-11.32	-1.05	-6.88	13.24
Change6moRadio_Baseline_CEJAlveolar	-1.67	1.46	52	71	.24	27	.93
PChange6moRadio_Baseline_CEJAlveolar	-100.00	123.73	-34.02	-63.81	14.46	-17.88	69.67
Change12moRadio_Baseline_CEJAlveolar	-1.78	.86	34	92	.38	34	.91
PChange12moRadio_Baseline_CEJAlveolar	-83.67	72.88	-25.89	-55.01	16.74	-17.39	55.07
a. TreatmentGroup_num = DFDBA	-	-	-				• • •

# Appendix D: Mann Whitney

Test Statistics <sup>a</sup>	• •			-				
	MAX_Baseline	MAX_Baseli	MAX_Baseli	MAX_Surgi	MAX_Surgi	MAX_Surg	MAX_Surg	MAX_Surgi
	ProbingDept	ne_CAL	ne_Recessi	cal_DefectC	cal_CEJBase	ical_Depth	ical_MDW	cal_BLWidt
	h		on	lass			idth	h
Mann-Whitney U	10.500	19.000	18.000	16.000	18.000	15.500	20.000	5.500
Wilcoxon W	25.500	34.000	54.000	31.000	33.000	30.500	56.000	20.500
Z	-1.465	151	465	-1.265	297	696	.000	-2.187
Asymp. Sig. (2-tailed)	.143	.880	.642	.206	.767	.486	1.000	.029
Exact Sig. [2*(1-tailed Sig.)]	.171 <sup>b</sup>	.943 <sup>b</sup>	.833 <sup>b</sup>	.622 <sup>b</sup>	.833 <sup>b</sup>	.524 <sup>b</sup>	1.000 <sup>b</sup>	.030 <sup>b</sup>
Exact Sig. (2-tailed)	.155	.937	.744	.385	.811	.550	1.000	.023
Exact Sig. (1-tailed)	.077	.469	.385	.385	.404	.290	.516	.009
Point Probability	.005	.055	.256	.385	.033	.081	.024	.002

a. Grouping Variable: TreatmentGroup\_num b. Not corrected for ties.

#### Test Statistics<sup>a</sup>

	MAX_SixMon th_ProbingDe pth		h_Recession	-	_	MAX_TwelveM onth_Recessio n
Mann-Whitney U	11.000	11.000	12.500	17.000	17.500	11.500
Wilcoxon W	26.000	26.000	48.500	32.000	53.500	47.500
Z	-1.371	-1.347	-1.153	472	379	-1.321
Asymp. Sig. (2-tailed)	.170	.178	.249	.637	.705	.187
Exact Sig. [2*(1-tailed Sig.)]	.222 <sup>₺</sup>	.222 <sup>b</sup>	.284 <sup>b</sup>	.724 <sup>b</sup>	.724 <sup>b</sup>	.222 <sup>b</sup>
Exact Sig. (2-tailed)	.236	.221	.287	.678	.726	.249
Exact Sig. (1-tailed)	.134	.120	.178	.422	.379	.140
Point Probability	.084	.042	.031	.210	.059	.085

a. Grouping Variable: TreatmentGroup\_num

b. Not corrected for ties.

#### Test Statistics<sup>a</sup>

	moProbi	oProbingDe	oProbingDe pth_MAX	•	moCAL_	6moCAL_		moCAL_MA		Change12mc ion_MAX
Mann-Whitney U		20.000			14.500	13.500	12.500	13.000	14.000	13.000
Wilcoxon W	53.000	56.000	50.000	51.500	29.500	28.500	48.500	49.000	50.000	49.000
Z	447	.000	892	661	819	954 、	-1.112	-1.026	914	-1.070
Asymp. Sig. (2-tailed)	.655	1.000	.372	.508	.413	.340	.266	.305	.361	.285
Exact Sig. [2*(1-tailed Sig.)]	.724 <sup>b</sup>	1.000 <sup>b</sup>	.435 <sup>6</sup>	.524 <sup>b</sup>	.435 <sup>b</sup>	.354 <sup>b</sup>	.284 <sup>b</sup>	.354 <sup>b</sup>	.435 <sup>b</sup>	.354 <sup>b</sup>
Exact Sig. (2-tailed)	.714	1.000	.399	.540	.452	.370	.293	.335	.427	.324
Exact Sig. (1-tailed)	.352	.512	.193	.267	.228	.185	.152	.168	.247	.168
Point Probability	.042	.026	.017	.016	.031	.017	.030	.018	.116	.008

a. Grouping Variable: TreatmentGroup\_num

b. Not corrected for ties.

## Appendix E: Frequency Tables

Gender	Gender										
		Frequency			Cumulative Percent						
	Female	6		46.2	46.2						
Valid	Male	7	53.8	53.8	100.0						
	Total	13	100.0	100.0							

		Frequency	Percent	Valid Percent	Cumulative Percent
	3.0	1	7.7	7.7	7.7
	4.0	1	7.7	7.7	15.4
	18.0	4	30.8	30.8	46.2
	19.0	2	15.4	15.4	61.5
Valid	26.0	1	7.7	7.7	69.2
	27.0	1	7.7	7.7	76.9
	30.0	2	15.4	15.4	92.3
	31.0	1	7.7	7.7	100.0
	Total	13	100.0	100.0	

#### Location

		Frequency	Percent	Valid Percent	Cumulative Percent
	Distal	10	76.9	76.9	76.9
Valid	Mesial	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

### Baseline\_PlaqueBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	9	69.2	69.2 <sup>-</sup>	69.2
Valid	Yes	4	30.8	30.8	100.0
	Total	13	100.0	100.0	

### Baseline\_PlaqueLingual

		B		Valid Percent	Cumulative Percent
	No	9	69.2	69.2	69.2
Valid	Yes	4	30.8	30.8	100.0
	Total	13	100.0	100.0	

### Baseline\_BOPBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	1	7.7	7.7	7.7
Valid	Yes	12	92.3	92.3	100.0
	Total	13	100.0	100.0	

### Baseline\_BOPLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	3	23.1	23.1	23.1
Valid	Yes	10	76.9	76.9	100.0
: . 	Total	13	100.0	100.0	

#### SixMonth\_PlaqueBuccal

		_	Percent	Valid Percent	Cumulative Percent
	No	10	76.9	76.9	76.9
Valid	Yes	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

### SixMonth\_PlaqueLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	7	53.8	53.8	53.8
Valid	Yes	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

### SixMonth\_BOPBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	10	76.9	76.9	76.9
Valid	Yes	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

### SixMonth\_BOPLingual

		Frequency		Valid Percent	Cumulative Percent
	No ·	6	46.2	46.2	46.2
Valid	Yes	7	53.8	53.8	100.0
	Total	13	100.0	100.0	

### TwelveMonth\_PlaqueBuccal

		Frequency	Percent		Cumulative Percent
	No	10	76.9	76.9	76.9
Valid	Yes	3	23.1	23.1	100.0
	Total	13	100.0	100.0	

### TwelveMonth\_PlaqueLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	7	53.8	53.8	53.8
Valid	Yes	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

#### TwelveMonth\_BOPBuccal

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	6	46.2	46.2	46.2
Valid	Yes	7	53.8	53.8	100.0
	Total	13	100.0	100.0	

### TwelveMonth\_BOPLingual

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	7	53.8	53.8	53.8
Valid	Yes	6	46.2	46.2	100.0
	Total	13	100.0	100.0	

.



### 



Appendix F 2: Accell Brochure provided by Keystone Dental

Permission to use Accell Connexus<sup>®</sup> graphic was provided by the company, Keystone Dental. This image is published on all brochures relating to the product Accell.

#### Appendix G1: Inclusion/ Exclusion Check Sheet

### Periodontal Regeneration of 1-, 2-, and 3-Walled Intrabony Defects Using Accell Connexus® versus Demineralized Freeze-Dried Bone Allograft: A Randomized Parallel Arm Clinical Control Trial

#### Inclusion/ Exclusion Check List Subject #

	Inclusion	Yes(√)/ No (X)
a.	Aged ≥18 years old	
b.	Remaining in the Capital region for at least 12 months following the surgical	
	procedure for follow up appointments	
с.	Diagnosis of generalized or localized severe periodontitis	
d.	Radiographic evidence of a vertical intrabony defect at one or more sites with a probing depth $\ge 6$ mm	
	Exclusion	
а.	Under the age of 18	
b.	Moving from the Capital region area prior to 12 months following the surgical treatment	
с.	Furcation involvement in combination with the intrabony defect determined pre-surgically	
d.	Restorations extending beyond the CEJ at the intrabony defect site	
e.	Indiscernible CEJ either clinically or radiographically	
f.	Periapical pathology, unrestored caries, defective restorations, root resorption, or vertical root fracture	
g.	Requiring restorative dental care (fillings and crown and bridge work) that cannot be completed prior to fabrication of the customized stent	
h.	Female patients who are pregnant or nursing	
i.	Currently smoke tobacco or use tobacco products. Former smokers will be	
	excluded if they quit smoking < 6 months prior to selection in the study.	
j.	Clinically significant systemic diseases, which may affect healing (e.g. uncontrolled diabetes).	
k.	Allergic to chlorhexidine gluconate (Peridex).	
I.	Allergic to tetracycline	
m.	Poor oral hygiene unsuitable for periodontal surgery	
n.	Cannot or will not sign the informed consent form	
0.	Receiving immunosuppressive therapy such as chemotherapy and systemic corticosteroids not to include inhaled or topical steroids	
р.	Severe endocrine-induced bone diseases (e.g. hyper-	
•	thyroidism, altered parathyroid function)	
q.	Teeth with intrabony defect have mobility classified as Miller class 2 or greater	
г.	Bleeding complications (e.g. hemophilia)	
5.	On warfarin therapy	
t.	History of osteoporosis or taking bisphosphonate medications	
u.	History of radiation therapy in the head and neck area	

A no (X) response in the inclusions criteria block or a yes ( $\checkmark$ ) response in the exclusion criteria disqualifies the patient from participating in this study.

,

Appendix G2: Adverse Event/ Deviation Log

.

Periodontal Regeneration of 1-, 2-, and 3-Walled Intrabony Defects Using Accell Connexus® versus Demineralized Freeze-Dried Bone Allograft: A Randomized Parallel Arm Clinical Control Trial

**Adverse Event/Deviation Log** 

Subject # \_\_\_\_\_

Date of AE or Deviation from Protocol:

,

\_\_\_\_\_

1. Was this an Adverse Event or a Deviation from the protocol? (Please circle one.)

2. What occurred?

What action was taken?

### Appendix H1: Data Collection Sheets

A master list will associate participant's name with the last 4 numbers of their social security number, telephone number and email address. Each of the following boxes (data collection sheets) will be printed on separate pieces of paper.

			Rando	mized Pa	arallel Ar	m Clinic	al Triai			
Date Subject ID # Gender Age										
Clinical Measu	rements	:								
Tooth #:			1				1		1	
	Probin Depth	-	Clinica Attach Level (	ment	Recess (mm)	sion	Plaque (+/-)	e Sc <b>o</b> re	BOP (·	+/-)
	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L	M/D-B	M/D-L
Baseline		1			1					

Date					
Subject ID #					
Gender					
Age	. <u></u>				
Clinical Measu	rements:				
Tooth #:					
	Probing Depth (mm)	Clinical Attachment Level (mm)	Recession (mm)	Plaque Score (+/-)	BOP (+/-)
	M/D-B M/D-L	M/D-B M/D-L	M/D-B M/D-L	M/D-B M/D-L	M/D-B M/D-L

e vject ID # nder					
2					
Clinical Me	asurements:				
Tooth #:					
	Probing Depth (mm)	Clinical Attachment	Rece <b>s</b> sion (mm)	Plaque Score (+/-)	BOP (+/-)
	-			_	BOP (+/-)

Date					
Subject ID #					
Gender _					
Age _					
Surgical Measure	monte (Character	vization of Dofo	.+).		
Surgical Measure	ments (Character	ization of Delet			
Tooth #:					
	Y				и
		CEJ-Base of	Depth of	Width of	Width of Defe
	Defect	Defect (mm)	Defect:	Defect: M-D	B-L Width (m
	Classification		Alveolar	Width (mm)	
	(1,2,3-walled				
	or		Crest-Base of		
	combination)		Defect (mm)		
	M/D-B M/D-L		M/D-B M/D-L		
		M/D-B M/D-L		M/D-B M/D-L	M/D-B M/D-
		W/D-D W/D-C			

	· · · · · · · · · · · · · · · · · · ·			
-Base of	CEJ-A	pex of	CEJ-Al	veolar
ect (mm)		-	Crest	(mm)
) M/D	M/D	M/D	M/D	M/D
(	-Base of ect (mm) D M/D	ect (mm) Tooth	ect (mm) Tooth (mm)	ect (mm) Tooth (mm) Crest

#### Appendix H2: Comprehensive Periodontal Charting Form



S/N 0105-LF-009-2400

ł

#### APPENDIX L: EXAMPLE OF NPDS PERIODONTICS DEPARTMENT POST-OPERATIVE INSTRUCTIONS

You may have been given one or more of these medioalions: PAIN MEDICATIONS: Molifs 800 mg: //sobiet every 6 hours. Do not double up on dorage. Norco \$1325 mg: //sobiet every 6 hours for poin control. R can be taken in addition to beprofen. This medicine can analy you droway. Therefore, do not drive or operate machinery while taking this dreg. Additionally, do not take with alcoholic bereaver; the alcohol will make you steepler, but will not decrease your confort. ANTIBIOTICS: Dosynetting to may if stability takes of surgery, then fielded every day for 50 days. Clasharacia 300 mg: / stability takes of surgery, then fielded every day for 50 days. RINSES: Perfect (Perfect peed of the day for 10 days.			DUATE DENTAL SCHOOL
You may have been given one or more of these medications: PAIN MEDICATIONS: Morifs 800 as: Horoo \$725 arc) Hor		Bethe	sda, Maryland
PAIN MEDICATIONS:       Motth 800 p.s:       //ddd every & Aerr./or point coated: It can be taken in addition to the prove analytic restrict on the set of the s			
PAIN MEDICATIONS:       Motifs 600 pp: Norce 51325 pp: //ddd/every 6 Aeer/Ar point control is to the takes in addition to operate analytic with takes to a decime. A control is a take in addition to operate analytic with takes to a decime, do not take with indexholes bereraceys: the skoled will make you decime, do not take with indexholes bereraceys: the skoled will make you decime, but will not decime over confort.         ANTIBIOTICS:       Doveredite 100 mod 2 Hobbit decime of a readyn, dise Hobbit every day for 30 days.         RIHSES:       Peridex [Periodyn dd / Hobbit decime of a readyn, dise Hobbit every day for 30 days.         RIHSES:       Peridex [Periodyn dd / Hobbit decime of a point of the Mobbit every day for 30 days.         RIHSES:       Peridex [Periodyn dd / Hobbit decime of a point of the Mobbit edim days in the statistic of the days of the day for t	For best healing and a mini	mum of complications, plea	se read and follow these instructions carefully
PAIN MEDICATIONS:       Motth 800 p.s:       //ddd every & Aerr./or point coated: It can be taken in addition to the prove analytic restrict on the set of the s			
PAIN MEDICATIONS:       Motifs 600 ns:       //odd/every Ø Aexr/Lor Do set dotble up on dorage.         Norco 5925 nc:       Norco 5925 nc:       //odd/every Ø Aexr/Lor Do set dotble up on dorage.         ANTIBIOTICS:       Dorgerdise 100 nc: 2 Exhibits the status on discost dot correspondent of the status on discost dotage.         ANTIBIOTICS:       Dorgerdise 100 nc: 2 Exhibits the dor of records, the scaled every day for 30 dors.         RIHSES:       Peridex [Periogram / Jobits for of records, the scaled every day for 30 dors.         RIHSES:       Peridex [Periogram / Jobits for dors.         Peridex [Periogram / Jobits for dors.       Sector of the dord for strating the scale intersceled to do so         ANTIBIOTICS:       Dorgerdise 100 nc: 2 Exhibits for dors.         Peridex [Periogram / Jobits for scale or deprint for 10 dords.       Bere scale intersceled to do so         ANTIBIOTICS:       Model Dore Pack: Take a directed on the package, statile to dord, status the left of fract or of bobits (first siz tablets) to day.         The following are a list of post-operative considerations during healing:       The scale of the scale of a day soft scale or an exampter of the dord for the scale of a day soft scale or dord scale or the scale of the scale or the	You may have been olven (	one or more of these medios	i i i i i i i i i i i i i i i i i i i
Norce SP325 ncr         I Adde every 6 Access for pair control. It is not taken to additions to hoper starting white taking this date, a bot of their of operate marking white taking this date. A most the whit is decide between service taken of the starts provide the taken on operate marking white taking this date. I additionably, do not take white is decide the starts of the start of the start of the start of the start of the start per confort.           ANTIBIOTICS:         Dosycerdites too and 'S defined the day of starting the start of the start of the start per confort.           Citady marks to and the start of the start per confort.         Dosycerdites too and the start of the start of the start per confort.           ANTI-INFLAMMATION:         Medrel Dose Peck: Take as directed on at the package, starting takes instructed to do as anti-influence of taken as the start of the start of the start of the start per confort.           BLEEDING:         These only the start of the start of the start of the start per consider at the start of the start as a black of possible start of the start of the start of the start of the start as a black of possible start of the start of the start of the start of the start of the start astart of the start of the start as a black of the start of the start as a black of the start of the start as a black of the start of the start of the start of the start as a black of the start of the start as a black of the start of the start of the start of the start of the start as a start			
Ibsprofer. The medicine can make year drown. Therefore, do not the will actor	PAIN MEDICATIONS:		
ANTIBIOTICS: Doryceflas No mai. 2 Ashket die day of secony, the flobbe envy day for 30 days. Another and the second distance of the day of secony, the flobbe envy day for 30 days. Another and the second distance of the days of secony, the flobbe envy day for 30 days. Another and the second distance of the days. RINSES: Peridex Pleicouver / Month, flob discusses of the second of the boltk, stocking the day flobben ANTI-INFLAMMATION: Medical Doce Pack: Takes a flot to day the second of the boltk, stocking the day flobben ANTI-INFLAMMATION: Medical Doce Pack: Takes a flot to day the second of the boltk, stocking the day flobben ANTI-INFLAMMATION: Medical Doce Pack: Takes a flot to day the second of the boltk, stocking the day flobben BLEEDING: There may be stable blecking from the second of the bolts (first six tableta) to days. BLEEDING: There may be stable blecking from the second of the bolts (first six tableta) to days. BLEEDING: There may be stable blecking from the second of the bolts (first six tableta) to days. BLEEDING: There may be stable blecking from the second of the bolt of stores and take the fell protection and the second of the bolt of the second of the bolt of stores and the failer. BLEEDING: There may be stable blecking from the second of the bolt of stores and the failer. BLEEDING: There may be stable blecking from the second of the bolt of stores and the failer. BLEEDING: There may be stable blecking from the second of the bolt of stores and the failer of the second of the failer stores and the second of the bolt (first six tableta) to days. BLEEDING: There may be stableta (first six tableta) the failer to be second of the bolt (first six tableta) the stores and the second of the failer stores and take the failer of the second of the bolt (first six tableta) to days. BLEEDING: There may be stableta (first six tableta) the second of tableta (first six tableta) to days. BLEEDING: There may be stableta (first six tableta) the second of tableta (first six tableta) to days. BLEED			ibuprofes. This medicine cas make you drowsy. Therefore, do not drive or
ANTIBIDITICS:         Dorsey disk to Mark 2 Ablets (the day of surgery, the leablet every day low 30 days. Anothering 300 mg <sup>-1</sup> (Jabbet (de days of surgery, the leablet every day low 30 days. Chadrwards 300 mg <sup>-1</sup> (Jabbet (de days of the fabret) de days.           RIHSES:         Parket (Perloquer)         De not break of flos at the parket do days.           ANTI-INFLAMMATION:         Medical Dose Pack: Take as directed on the package, starting to days.           BIEEEDING:         There may be effect blaceding from the surgical file and take black at the full frast row of tablets [files siz tableta] to days.           BIEEEDING:         There may be effect blaceding from the surgical for 12 days ofter ewagers. Your sthra may appear stickly reddish. Table is common. If your mosh. There may have to be neared take leaf at first row of tablets [files siz tableta] to days.           BIEEEDING:         There may be effect blaceding from the surgical for 12 days ofter ewagers. Your sthra may appear stickly reddish. Table is common. If your mosh. There may have to be neared to the feature. Prices blace a stick as at disk of the other days of the surgical starts. Its blace for your condroit. U it fulls on b for byour first foort, days difficit for therest a with a to be the starts is our condroit. U it fulls on b for byour first foort, days difficit for a therest a with a to be are a possible on the cold opposite the sergery. This is not the time to start a dist. Plase and flos of these at the cold opposite the sergery. This is not the surgical she was difficated prease contract at the regular diffication, you will not start foor a they divided or undersomistical. Place do not dath start a starts - model as the bardet control a prease sinsthe oure condue they divide opposite the sergery. This is not t			
Amount min 500 ms; 1 Anohol Constances of your Fice NC days. Chaldwards 300 ms; 1 Anohol Constances of your Fice NC days. RIHSES: Purdex (Perioqued 1 Abortlo, rises of the or to NC and the Anthy Anterling the opy following are a list of post-operative considerations during heating: The so discreted on the package, statilize to day. Be sure and take the full first row of tablets (first six tablets) to days. The following are a list of post-operative considerations during heating: BLEEDING: There may be effort blecding from the surgical for 12 days after surgers. Your sites may appear slightly reddish. This is connece. If your solite an accesse in blecding please context us. BLEEDING: There may be effort blecding from the surgical for 12 days after surgers. Your sites may appear slightly reddish. This is connece. If your solite an accesse in blecding please context us. BLEEDING: There may be effort blecding from the surgical for 12 days after surgers. Your sites may appear slightly reddish. This is connece. If your solite an accesse in blecding please context us. BLEEDING: There may be effort the structure of the			
Classing is 000 mol 1//bit/ for there's divisor for Flor Roder,           Perides (Perioqued I Dorder, Price States and State Roder, Classing Lines is attracted to dose ANTI-INFLAMMATION:           Medical Dore Prets:         Take as directed as the package, statistical site subjects is attracted to dose ANTI-INFLAMMATION:           Medical Dore Prets:         Take as directed as the package, statistical today. Be sure and take the full first row of tablets [first site tablets] today.           BILEEDING:         There are to effekt blecding from the sengical for 12 days ofter sengers. Your sites may spacer slightly reddish. This is connool. Two sould as a hieraces is blecding please context re.           SUTURESISTITCHES:         You may here consider allons during healing:           Differences:         There are to effekt blecding from the sengical for 12 days ofter sengers. Your sites may spacer slightly reddish. This is connool. Two subtes an increase is blecding please context re.           BUTURESISTITCHES:         You may here consider all more than the sengicial site.         Research and the feature. Please here the conformation and the sender state is a space of the sender state.           DIET:         Or first for chick philing and the fide is a site to a space is a set to sender. You will be the sender state as a possible and the fide table of the sender state.           DIET:         It is rery important to its bar and first the sender state as a possible and the fide table as a space state.         Research and the sender state and the sender state.           DIET:         It is rery important to the ther to cist at date	ANTIBIOTICS:		
RINSES:       Peridex previous of Jocuts rises referes solvers and decode between the sequences of the sequence of the sequence of the sequences of the s			
ANTI-INFLAMMATION:       Medrol Dose Pack: Take as directed as the package, statuing to day. Be serie and take the fell If stat row of tablets (first siz tablets) to day.         The following are a list of post-operative considerations during healing:       EleEDING:         BLEEDING:       There may be slight ble diag from the sergical for 1-2 days after surgers. Your stima may appear slightly redds. This is common. If you notice as herease in bleeding please context w.         BUTURES/BTTCHES:       To way by first size placed is your moult. There may have be control in the feture. Please leave the catteres all is and ble strong to be strong to be strong to be control by. It is fails to our confort. If it fails on the following are a list of post-operative context me.         DRESSINGS:       There may by first size barrend to be strong to be strong to the fails to our confort. If it fails on the following the control to the fails to control to the fails to our confort. If it fails on the following the strong the confortable at the fails control to the fails to our confort. If it fails on the following the control to the fails to our confortable, the fails to our confortable at the fail to our confortable at the fails to our confortable at the fails to our confortable at the fails to our confortable at the state of the constant to the fails to be strong to the fails to our confortable at the fails to our confortable at the top our confortable at the state will fail of the may be stated for our confortable at the top our participal mode the fails at the fails to our confortable at the fails to our confortable at the fails to our confortable at the fails to	RINSES:		thottic, these twice a day as directed on the bottle, starting the day following
Ifest row of tablets (first siz tablets) to day.         The following are a list of post-operative considerations during healing:         BLEEDING:       There may be effect blacking from the surgical for 12 days ofter surgery. Your stirs may appear slightly reddle. This is common. Wy romanities an interest in blacking please contact w.         SUTURES/STITCHES:       You may have registed for 12 days ofter surgery. Your stirs may appear slightly reddle. This is common. They may have be for other the single large and the form of the start or your control. If it falls on both the start for your control. If it falls on both to be accorder to be a social start be active a control to a surgery affect to associal profile basil of a word wold file the dates. Please accust at a surgery affect to associal profile basil of a word wold file the dates. Please accust at a surgery affect to associal profile basil of a word wold file the dates. Please accust at a surgery affect to a start as the to easy a control to a profile basil of a word wold file basil of a word and file base context the surgery start and so a base to a surgery start and so a surgery start and the surgery start and the surgery start and so a surgery start and so a surgery start and the start and the start and the surgery start and so a surgery start and the start and the surgery start and the start and the surgery start and the start and the surgery start and so a surgery start and the start and the surgery start and the start and the surgery start and a so the surgery start and so a control start and the surgery start and a so a start and the surgery start and a so the surgery start and a so the surgery start and a so a sort of the surgery start and a so the surgery start and the start and the surgery start and the start and the start and the s			swary. Do not bresh or floss at the swajcal site valess instructed to do so.
The following are a list of post-operative considerations during healing:         BLEEDING:         There may be effect blecding from the surgical for 12 days after surgerer. Your saftra may appear slightly         tridich. This is common. If you may have to be consort in.         SUTURES/STITCHES:         SUTURES/STITCHES:         You may have subje of gain a lange for the surgical for 12 days after surgerer. Your saftra may appear slightly         tridicin. This is common. If you may have to be for solar surgerer. Your saftra may appear slightly         reduces allow a sole of set of the surgery because the surgers of the surgery state.         There may be effect ble successful for the solar sure. It is firs to its bars. It is there for your confort. If falls         or bofor floring for the surgery because the surgery far and the surgery for the surgery far and the surgery for the surgery. This is not the surgery far and the surgery far a surger control to the surgery         There may be effect ble successful reports and instance Rout. If the         surgery barser solution to the surgery far and the surgery far and the surgery         The surgery monortant and to breach or flores the surgery far and the surgery         add flores the proceeding content control and flores the surgery.         The breact instance and the surgery. To here bacterin under control apprecess instructions. Normal breachag         and flores the surgery. To here bacterin under control and proceeding content surgers         and flores the surgery. To here bacterin under control and proceeding content surgers         and flores the surgery. To here bacterin under control apprecession. Normal breachag         and flores the surgery. To here bacterin under control and there and proceeding content surgers         and flores the surgery. To here bactery the unon the surgery sheet and there a surgery shee	ANTI-INFLAMMATION:		
BLEEDING:       There may be effekt biteding from the surgical for 1-2 days after surgery. Your safirs may appear slightly reddes. This is common. If you notice as herease in biteding please context w.         SUTURES/STITCHES:       You may have for strings placed in your mouth. They may have for box conored in the feture. Please leave the catures all the as added, splease for the surgical for 1-2 days after strings. There may have for the feture. Please leave the catures all the as added, splease for the surgical area. It is there for your condort. If it is not interest for the surgical for the surgical area. It is there for your condort. If it is not interest for the surgical area. It is there for your condort. If it is not interest for the surgical area. It is there for your condort. If it is not interest for the surgical area. It is there for your condort. If it is not interest for the surgical for its contact me.         DIET:       It is reary important to maintain \$3000 files that the descelling repriced please contact me.         DIET:       It is reary important to maintain \$3000 files the surgical site well given express instructions. Normal breaking and florsing proceedures can travmating the lissee and import hereing. You may bursh and flors those areas on at pre-synchold literels. You will not how the surgical site well given express instructions. Normal breaking and florsing proceedures can travmating the lissee and import hereing. Normal breaking and different flore the surgical site well. Given any the subscence on the surgical flore to a subscence on the surgical site well. The surgery site of the surgery. To keep betary addres control a prescription month incertaing and displayed program is no subscence on the surgery site of the surgery site of the surgery site of the su			
BLEEDING:       There may be effekt biteding from the surgical for 1-2 days after surgery. Your safirs may appear slightly reddes. This is common. If you notice as herease in biteding please context w.         SUTURES/STITCHES:       You may have for strings placed in your mouth. They may have for box conored in the feture. Please leave the catures all the as added, splease for the surgical for 1-2 days after strings. There may have for the feture. Please leave the catures all the as added, splease for the surgical area. It is there for your condort. If it is not interest for the surgical for the surgical area. It is there for your condort. If it is not interest for the surgical area. It is there for your condort. If it is not interest for the surgical area. It is there for your condort. If it is not interest for the surgical area. It is there for your condort. If it is not interest for the surgical for its contact me.         DIET:       It is reary important to maintain \$3000 files that the descelling repriced please contact me.         DIET:       It is reary important to maintain \$3000 files the surgical site well given express instructions. Normal breaking and florsing proceedures can travmating the lissee and import hereing. You may bursh and flors those areas on at pre-synchold literels. You will not how the surgical site well given express instructions. Normal breaking and florsing proceedures can travmating the lissee and import hereing. Normal breaking and different flore the surgical site well. Given any the subscence on the surgical flore to a subscence on the surgical site well. The surgery site of the surgery. To keep betary addres control a prescription month incertaing and displayed program is no subscence on the surgery site of the surgery site of the surgery site of the su	The fellowing are a Rebef f	ast anarathis consideration	e during has Fag.
BUTURES/STITCHES:       Products of provide sphere control is an interact in bleeding please control in the fature. Please leave the cature subject of the sphere control in the fature. Please leave the cature subject from subject of the sphere control into the fature. Please leave the cature subject for first for control for the sphere control into the sphere control into the set of the sphere control into the set of the sphere control into the set of the set of the sphere control into the set of the set	The following are a list of h	O20-Obstative consideration	≥ uni ∎n' llagæid:
SUTURES/STITCHES:       You may higher privace placed in your monk. They may hapefood be cranored in the feiture. Please larve the catures allow as an eld-off possible. This provide the food of sources any impair larve the catures allow as an eld-off possible. This provide the food of sources any impair larve. It is fails on the food of sources any impair larve allow as an eld-off possible. This provide the impairs and the figure are called the sources and the source and the sources are called the sources and the sources are concerned to the sources and the sources are and the sources and the sources are the sources are the sources are the sources and the sources are the sources are the sources are the sources and the source and the sources are the sources and the source and the source and the sources are the sources are the sources are the source and the source and the source and the sources are the sources and the sources are the sources are the sources and the	BLEEDING:		
DRESSINGS:       There may be a ginum appeor if the residual creates the series and a more console. If it fulls one before the series and non-the series and the series of t	SITTIDES/STITCHES-		
<ul> <li>Ore befor fivor first fiber: dis oblighting displantmast and you fire control table, it is fine to leave R out. If the register is second of table and you would like the dressing replaced please control table.</li> <li>DIET: It is wrey important to maintain a Wolf fibe the dressing replaced please control and the iske is at pre-yengleal lerels. You will not it is at a week. Cheve as much as possible on the iske is at pre-yengleal lerels. You will not it is at a week. Cheve as much as possible on the iske is at pre-yengleal lerels. You will not it is at a week. Cheve as much as possible on the iske is at pre-yengleal lerels. You will not it is at a week. Cheve as much as possible on the iske is at pre-yengleal lerels. You will not it is at a week. Cheve as much as possible on the iske do not dulk using a strow.</li> <li>ORAL HYGIENE: It is erre important not to bresh or floss the sweiger is the surgers. To keep bacterin under control a pre-scription month rises has been written for you. Ikilithy, see the mouthwash to so rinse. Loter you may bresh and floss those areas not affected by the surgery. To keep bacterin under control a perscription mouth rise has been written for you. Ikilithy, see the mouthwash to so rinse. Loter you may be instructed to use a cotica dipped applexitor, dipped in the mouthwash, to swab along the surgery areas and a saft lossible as a capital (15ml) of the mouthwash twice a day, monthing a so trest of the best head likes at the set of error and the stable and the subjective and as a set of the the mouthwash. The is not person will be ended at the scaling a port follow up positiments. Please do not use a vitaer-PR or other itrigator raless instructed to ob so.</li> <li>PHYBIGAL ACTIVITY: Avoid strates some aveeling. There is no another set as the flore the site of a strate stable and a sort and the set at a strate of the site of and any safe and the site of the set and a strate at a strate of the site for the flist 3 - 4 bows after strate and pro-se income and st</li></ul>	2	setures alone as mich as possi	ble. Ewig femoral or the loss of setures may impak heated.
DIET: It is very important to maintain \$7000 World Site the dressing replaced places contact me. It is very important to maintain \$7000 dist for at least a weak. Chew so much as possible on the side opposite the surgery. This is not the time to start a dist. Place maintain your caloric and find intake is at pre-surgical iteris. You will not hear a dist. Place maintain your caloric and find intake is at pre-surgical iteris. You will not hear an effect of a structure of the start and find intake is at pre-surgical iteris. You will not hear an effect of a structure of the start and finds therein and flossing procedures can transmitte the tissue and impair hearing. You may bresh and floss those areas not affected by the surgery. To keep bacteris under control a pre-scription mouth three has been written for you. Initially, see the mouthwosh as a stars. Lost you may bresh and floss those areas not affected by the surgery. To keep bacteris under control a pre-scription mouth three has been written for you. Initially, see the mouthwosh so a stars. Lost you may be instructed to use a cotical iffeld of the mouthwash twice a day, moraling and bedtine, after breathard/flossing you non-surgically treated teeth. You may notice a mid tooth staking as a reset of the mouthwash. This is not permanent; the stals will be removed with scaling/opeillacticity (to include ranshing and hearing and hearing and bearing and whete the order of the inclustor with scaling/opeillacticity (to include ranshing and hearing the site of structury will negatively affect hearing splitting, riasing, or speaking (refling). Forcefail morem unto at the site of structury. There is four you should appear to see a structure to access and with parks at 2-3 days alter encerery. FOR SIMUK LIFT SURGE You may should be think on the site of the flux of an apply ise to the site for the flux of a hoore structure and appears to increase and structure and park econereed. Smoking is obotter scenchouse to access that third day, or if you are concre	DRESSINGS:	There may be a gramy type of	Bressing Support over the singlest area. It is there for your confort. If it falls
DIET:       It is revery important to maintain \$7507 diet for at least a week. Drawse mack as possible on the side opposite the sorgery. This is not the time to start a diet. Plasse maintain your colorities and find inste as at pre-surgical iterial. You will not have and diet prove maintain your colorities. Here, and find inste as at pre-surgical iterial. You will not have a diary our ad daydaited or wedetsourished. Plasse do not dials using a straw.         ORAL HYGIENE:       It is rever important not to bresh or floss the surgical site wall given express instructions. Hornal breshing and flossing proceedires can tryamatise the tissee and imput herbing. You may bresh and floss those areas not affected by the surgery. To keep bectain under control a prescription month rises harb bece written for you. Inihiby, use the mouthwork as a rise. Later you may be instructed to use a cotton-tipped appleator, dipped in the mouthwork as a rise. Later you may be instructed to use a cotton-tipped the mouthwork twice a day, morning and beciting, after breshballforsing your convictably treated teeth. You may notice mild toolt stabling as a reset of the mouthwork. This is not permanent; the stals will be removed with scaling/poEkibing at your follow-up appointments. Plasse do not use a Water-PR or other irrightor valess instructed to do no.         PHYBICAL ACTIVITY:       Avoid streavous playking refiliant. Forceful more much as the site of surgery mile appointers. Additionally, so vigorout opplicing a possible after sweets.         BWELLING:       You may experise some sweets a streame to ato and surph peaks at 2-3 days after creary. Phases call if the rowelling appears to lacenses after the third day, or if you are concerned.         BMOKING       Smobling and backing appears to lacelease stere the third day, or if you aredin about and your modica		succession and a succession of the	ad to word the the dressing replaced please contact me.
<ul> <li>as at pre-strajcal lerels. You will not best will if you are dubydrated or undernownisked. Please do not duba using a struw.</li> <li>ORAL HYGIENE:</li> <li>It is vers important not to bresh or floss the sergical site usill given express instructions. Normal breshing and flossing procedures can trymanitise the tissee and imput hershing. You may bresh and floss those areas not affected by the surgery. To keep beterin under control a prescription month rises hav been written for you. Initially, use the monthwork to sure a so rinse. Lot you may be instructed to use a cottoa dipped appleatorin under sort to a prescription month rise hav been written for you. Initially, use the monthwork to sure a beattin under control a prescription month rise to a copiel (15m) of the monthworks twice a day, morning and bedtine, after breakhalflossing your non-yourically treated teeth. You may notice mild tooth stakling as a strest of the monthwork. This is not permanent; the stala will be removed with scaling/poleShing at your (folsor up suppolatanests. Please do not use a Vater-PRI or other Irrightor valess instructed to aco.</li> <li>PHYBICAL ACTIVITY:</li> <li>Avoid straneyos playical activity to include ranking and heavy Efflag) for 12 howrs. Additionally, so vigorow to polationals. Please do not use a Vater-PRI or other Irrightor valess instructed to see a view to acompt press st 42-3 days affect heaving splayical activity to include ranking and also of group or any possible affect or the site for the first 3-4 hows after swater, appears to lacenses after the third day, or if you are concerated.</li> <li>BMOKING</li> <li>BMOKING</li> <li>BOD You and to barbe, we dottor if importe as a discustion ad also in prove sect extene discust as a discide on the set extenedications as directed press. Playes also are specified as at discuste and spray. Playes exect exect exect with your mostic or it you are oble as the present and a babefine or you acoustic as a biddecode and the barbe and also in</li></ul>	DIET:		
diak vsing a straw.         diak vsing a straw.         ti is very important not to bresh or floss the surgical site wall given express instructions. Normal breshing and flossing procedures can tramatise the tissee and impair healing. You may bresh and floss those areas not affected by the surgery. To keep bacterin under control a prescription month flose has been written for yon. Initially, see the monthwish as o mise. Lotry you many bresh and floss those areas not affected by the surgery. To keep bacterin under control a prescription month flose has been written for yon. Initially, see the monthwish as o mise. Lotry you may be instructed to use a cotoa dipped applexistor, dipped in the nonthwish, to woob along the pure many be instructed to use a cotoa dipped in proceeding on the surgery site. Use a capital (15ml) of the monthwish the intervent of tools a capital flossing your non-surgically treated teeth. You may backee and it both staklas as a vessel of the monthwish. This is not permanent; the stake will be removed with scaling/poExhing at your follow-up appointments. Please do not use a vister-PR or other irrightor naless inclused in colin. For cerim morea most at 2-3 days after currenty. If the stake is a coprary will negatively affect heather. You may be presented after developed. You may experience some swelling. The is common and a studies the 3-3 days after currenty. There is the regular due to the site for the flux 3-4 hours after sweater. Phose call the sweater on the sole of our our set on store sole apply ice to the site for the flux 3-4 hours about to be been wells as a day one store sole apply ice to the site for the flux 3-4 hours and the sweater wells are not sole apply ice to the site for the flux 3-4 hours and the sweater wells are about to be shead for sole approximating apply ice to the site for the flux 3-4 hours and the sweater potential keshaa and alo innore aloreal perioduatise heads.			
<ul> <li>ad florsing procedures can transmithe the lisse and imput herding. You may barsh and flors those areas not affected by the surgery. To keep bacturis under control a prescription month rise has been written for you. hildiby, see the mouthwosh as a nice. Loter you may be instructed to use a cotion-tipped appErstor, dipped in the mosthwarsh, to surbe also the surgery site. Use a cotion-tipped the monthwarsh twice also provide and the day in the surgery site. Use a cotion-tipped the monthwarsh twice also also provide and the surgery site. Use a cotion-tipped the monthwarsh twice also also, more also disclute at the backload grow can surgically used to each the monthwarsh. This is not permanent; the stain will be removed with scaling/poExhing at your follow-up populateness. Please do not use a Water-PR or other irrigator ruless instructed to do so.</li> <li>PHY BIGAL ACTIVITY invoid stransport physical scinity (to include ranshing and heavy fielding) for 12 hours. Additionally, so tigorous oppopulations rules a whete-PR or other irrigator ruless instructed to do so.</li> <li>PHY BIGAL ACTIVITY invoid stransport physical scinity (to include ranshing and heavy fielding) for 12 hours. Additionally, so tigorous optimical instance, or population rules a whete-PR or other irrigator rules a physical scinity (to include ranshing and heavy fielding) for 12 hours. Additionally, so tigorous optimical instance, or population and so rules a water server. There after you should expect to see a return to aormal. To decrease swelling you can apply ice to the site for the first 3-4 hours after sweating appears to lacrease after the third day, or if you are concerted. Smoking is obstrate created as a disclustion and prove your overall periodoatil health.</li> <li>FOR SIMUS LIFT SURGE You may also have received as a discount of so to see sections as directed rate of concerted as a discount of your addition and prove rules are state with your modicatin so in the your modication as of if your modication as a dis</li></ul>		dela's using a straw.	
not affected by the surgery. To keep bacteris under controls prescription month rinse has been written for yon. InRibly, was the monthwash as mane. Later you may be instructed to use a cotton-tipped applicator, dipped in the monthwash, to save a head the quantiles of the surgery site. Use a capital [15m] of the monthwash twice a day, morning and backline, after breakhollossing your con-surgically treated teeth. You may notice a mild tools tashing as a rest of the monthwash. This is not permanent; the state with be removed with scaling/poExhing at your follow-up papolatments. Please do not use a Water-Pit or other irrigator reless instructed to do so.         PHYBICAL AGTIVITY: Avoid streassoss physical activity (to include remaining and heavy Efflag) for 12 hours. Additionably, so vigorour opiting, itazing, or speaking (to include remaining and heavy Efflag) for 12 hours. Additionably, so vigorour opiting, itazing, or speaking (felling). For cellin more much at the site of streatury will negatively affect health of the your should expect to see a relaw to all strong packs at 2-3 days after everyety. There is all the swelling, a poers to bace as east to a born. To dicrease swelling you can apply ice to the site for the first 3-4 hours after sweary. Phese cell if the swelling appears to bacenese after the third day, or if you are concerted. Smoking is deleterious to healton, we adrise your osto providing for as long as possible after everyety. Stopping snoking will improve potential healts and sport, your over all period active health opter. Please cell as addition, avoid blowing your soes. If you acte to cate as elease modications as directed proCEDURES or if you notice as pleaded or director from your nover nose.         Your hyve appeal hours block as a biochear your nover nove nover an inhibited with your medications or if you notice as pleaded are acted inclustor for nover nose.	ORAL HYGIENE:		
sppEcstor, dipped is the mosthwash, to swob along the qualities of the swarery site. Use a capital (ISai) of the mowhwash twice a day, norming and beduine, after breakbad/lossing your non-surgically treated teeth. You may notice a mild tooth stabled as a preset of the monthwash. This is not permanent; the stah will be removed with scallsophoEshing at your follow-up appointments. Picese do not use a Water-Pit or other irrightor values instructed to do so. PHY SIGAL ACTIVITY: Avoid streamous physical activity (is include reaching and kenny liftlag) for 12 hours. Additionally, so vigorou ophtling, risping, or speaking (reliand). For colly more much set the site of streamy will negatively affect healthon specifies of streamous physical activity (is include reaching and kenny liftlag) for 12 hours. Additionally, so vigorou ophtling, risping, or speaking (reliand). For colly more much set the site of streamy will negatively affect healthon specifies of streamous physical activity (is include reaching and kenny liftlag) for 12 hours. Additionally, so vigorou ophtling, risping, or speaking (reliand). For colly more much set the site of streamy will negatively affect healthon the specifies of the synding appears to increase and struty packs at 2-3 dys shafter correspit. There after you should expect to see a return to normal. To decrease swelling you can apply ico to the site for the flux 3-4 hours after sweary. Phese call if the swelling appears to increase after the third day, or if you are concerned. Smoking is delisterious to besting. We adrise you to stop smoking for as long as possible after sweary. FOR SINUS LIFT SURGE You may also have received assai decongettat tablets and spray. Please use these medications as a directed on the package, in addition, avoid blowing your score. If you need to concere, please flow or mosth open. Please calls best endored for or develop size use can ead to checes please secces with your mostical or if you notice any bleeding or discharge from your nose. If you have easy problems or			
<ul> <li>It is monthwest twice a deg, norshiq and bedites, after breakbollossing your non-survices treated teeth. You may notice a mild tooth staking as a reset of the monthwesh. This is not permanent; the stain will be removed with scaling/poExhiq at your follow-up appointnests. Pheres do not use a Water-Pit or other irrigator reless instructed to do so.</li> <li>PHYSICAL ACTIVITY: Avoid streavess phereical activity (to include reached and heavy fifting) for 12 hours. Additionally, so vigorou spitting, rinsing, or specifical activity (to include reached and heavy fifting) for 12 hours. Additionally, so vigorou spitting, rinsing, or specifical activity (to include reached and heavy fifting) for 2 hours. Additionally, so vigorou spitting, rinsing, or specifical activity (to include reached and heavy fifting) for 2 hours. Additionally, so vigorou spitting, rinsing, or specifical activity (to include reached and heavy fifting) for 2 hours. Additionally, so vigorou spitting, rinsing, or specifical activity (to include reached and heavy fifting) for 2 hours. Additionally, so vigorou spitting, rinsing, or specifical activity to active to access and any point access and any point access and the second access and access and provide active to see a term to access any fifting of a sign and poly site to the site for the first 3-4 hours after swaqers.</li> <li>FOR SINUS LIFT SURGE You may also have accessed acceleratest tablied and spin, Presse we there and first heaving and also inprove your over all periodoatal health.</li> <li>FOR SINUS LIFT SURGE You may also have accessed active table and also inprove your overall periodoatal health.</li> <li>PROCEDURES on the package, in addition, wold blowing your acce. If you access to a table on acces, please secces with your mosth open. Please inform your doctor if you accessed to an acces, please secces with your modications or if you accessed from sole.</li> <li>V you have easy problems or gesclices, please do not keeka at disclargo prow sole.</li>     &lt;</ul>			
<ul> <li>You may notice in midi tools stabling as a reset of the monthwesh. Table is not permanent; the stale will be removed with scaling/points/in a space of the monthwesh. Table is not permanent; the stale will be removed with scaling/points/point</li></ul>		the most wash twice a day, no	awasa, to swop stong the gam the of the swidery site. Use a copial (simil of Maing and bedtime, after brashing/flossing your non-surgically treated teeth.
Initiator reless instructed to do so.         PHYSICAL ACTIVITY:         Avoid streasous plasical activity (to include reacing and keary fiding) for 12 hours. Additionally, so vigorou optimization, rissing, or speciag (reliag). Forceful movem unders the site of stratury will acquirely affect keather stream and the stream and the site of stratury will acquirely affect keather stream and strature stream and str		You may notice a mild tooth st	taking as a result of the monthwash. This is not permanent; the stain will be
PHYSIGAL AGTIVITY:       Avoid streamous physical activity (to include ranking and kenny fiding) for 72 hours. Additionably, so vigorou ophiling, flazing, or specifica (selfand). Forceful moven turks at the site of surgery will negatively affect heading         8WELLING:       You may experises concerned with the source of moven turks at the site of surgery will negatively affect heading         8WELLING:       You may experises concerned with the source of moven turks at the site of surgery will negatively affect heading         8WELLING:       The sequences swelling.         1. You may experises concerned with the source of the site of the site of the site of the first 3-4 hours with results at 2-3 days ability experises of the site for the first 3-4 hours with results at 2-3 days ability experises of the site of the site of the first 3-4 hours with results at 2-3 days ability experises of the site of the site of the first 3-4 hours with results at 2-3 days ability experises ability of the source of the site of the first 3-4 hours with results a possible after surgery.         8MOKING       Shopking a souching will importe potential having a day also improve your overall periodoats health.         FOR SINUS LIFT SURGE       You may also have received assol deconsectat tablets and spray. Please we these medications as directed on the package. In addition, world houring your score. If you weed to succes a please invert mover moves and even positive comparison that your moves and score any block asy blocked any direct assol.         PROCEDURES       In addition, world blowing your score. If you weed to score a please score with your moves a score any blocked asy blocked any dover moves.         V you have say proble			
BWELLING:         You may experience some sureling. This is common and usually peaks at 2-3 days after curgery. There of the you should expect to see a return to normal. To decrease availing you can apply ice to the site for the first 3-4 shours after surgery.           BWOKING         Phases call if the swelling appears to increase after the third say, or if you are concerned.           BMOKING         Smoking is deleterious to beating. We advise you to stop smoking for as long as possible after surgery.           Stopping smoking will importe potential kesting and also improve your concerned.         Stopping smoking will improve potential kesting and also improve your orall periodoatal health.           FOR SIMUS LIFT SURGE You may also have received as all decongentiats tablets and spray. Please use these medications as directed on the package. In addition, avoid bloming your scone. If you acid to sneeze, please succes with your mowth opper. Please inform your model of the you enclose asy bleeding or discharge from your scone.           You have say problems or gessilons, please do not besider or discharge from your nose.           V you have say problems or gessilons, please do not besidered to call be atter discharge or discharge from your nose.           V you have say problems or gessilons will be given after discharge from your nose.           V you have say problems or gessilons will be given after in discharge from your nose.		Avold streavous physical activ	rity (to include running and heavy fifting) for 72 hours. Additionally, no vigorous
In there your schoold expect to see a return to normal. To decrease swelling you can apply ice to the site for the first 3-4 hours after sweary. Phases call if the swelling appears to increase after the third day, or if you are concerned. SMOKING Shooling is deleterious to be they, we adrise you to stop smoking for as long as possible after sweary. Stopping smoking will improve potential heading and also improve your over all period statishealth. FOR SINUS LIFT SURGE You may also have incerived assist decongestant tablets and sport. Please call to exceed to serve an over all period statishealth. FOR SINUS LIFT SURGE and the server of our over a set to be the model of the set of the se	PHYSICAL ACTIVITY:		
If use 3-4 hows with: swaters,         Pieze call if the swaters,         Pieze call if the swaters,         Pieze call if the swaters,         Bmoking is dictorious to better,         We adrise you to stop snaking for as long as possible after swaters,         Stopping snaking will improve potential kesking and also improve your overall periodostal hashin.         FOR \$INU\$ LIFT SURGE You may it to bare necessariast tablets and spray. Piezes we there are indicated as a discomparing your overall periodostal hashin.         PROCEDURES         On the package, is addition, word blowing your nose. If you need to saters exerces with your mosth open. Piezes lators we doctor if you develop sizes concerns tablets to bar indicate and spray. Piezes necessaries tablets on the package will have blowed on the package.         V you have any problems or gessilons, plezse do not kesize to call me at 301-225-0011. If there is an emergency you may page your doctor is through an actionated system. Instructions will be given after disting 1-800-159-8688. The PINB for your doctor is		1 1 0/2 Book Statiscie Some Such	
SIMOKING         Smoking is deleterious to kerken.         We adrise you to stop smoking for as long as possible after strugty.           FOR SIMUS LIFT SURGE         You may also have received assid decongestant tablets and spray. Presse we there medications as directed           FOR SIMUS LIFT SURGE         In addition, avoid blowing your sose. If you accel to states medications as directed           PROCEDURES         In addition, avoid blowing your sose. If you accel to states medications or well pour mosth           opta. Please inform your doctor if you develop size concestion that is not minimized with your medications or of states are been well as to be packed or discharge from your asse.           V you have easy problems or gessiloes, please do not besitive to call me at 301-235-0017. If there is as emergency you may page your doctor is to be altomated system. Issued as the pack well as a to make a state at a date of state.			a return to normal. To decrease swelling you can apply ice to the site for the
Stopplag stacking will improve potential keskag and also improve your overall periodoutal health. FOR SINUS LIFT SURGE You may also have received assal decongestant tablets and sprave. Piesze we these medications as directed PROCEDURES on the partsque, in addition, avoid blowing your nose. If you need to concer, please exectes with your mosth open. Please laform your doctor if you develop sizes congestion that is not minimized with your medications or if you notice asy bleeding or discharge from your nose. If you have any problems or geestices, please do not besitate to call me at 301-235-0017. If there is an emergency you may page your doctor through an astomated system, instructions will be given after disting 1-800-159-8888. The PINB for your doctor is		after you should expect to see first 3-4 hours after surgery.	
PROCEDURES On the package, in addition, avoid blowing year nose. If you wated to entere, please secese with your mosth open Please lalour your doctor if you develop sixus concertion that is not minimised with your medications or if you notice any bleeding or discharge from your nose. If you have any problems or geestions, please do not kesitate to call me at 301-235-0011. If there is an emergency you may page your doctor through an actionated opstem, instructions will be given after disting 1-800-159-8688. The PINB for your doctor is	8WELLING:	ofter you should expect to see first 3-4 hours after swater. Please call if the swelling appe	ars to lacrease after the third day, or if you are concerned.
open. Please laform your doctor if you develop sixes 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 geesticnes, please do not besitate to call me at 301-235-0017. If there is an emergency you may page your doctor through an astomated system, instructions will be given after diating 1-800-159-8888. The PBVB for your doctor is	SWELLING:	after you should expect to see first 3-4 hows after sweers. Please call if the swelling appe Smoking is deleterious to heat Stopping smoking will improve	ans to lacrease after the third day, or if poo are concerned. Ing. We adrise you to stop snoking for as long as possible after surgery. E potential hesting and also improve your overall periodontal health.
or if you notice any bliceding or discharge from your nose. If you have any problems or gesticas, plaze do not besitate to call me at 301-235-0017. If there is an emergency you may page your doctor through an actemated system, lastractions will be given after disting 1-800-159-8888. The PINB for your doctor is	SWELLING: SMOKING FOR SINUS LIFT SURGI	after you should expect to see first 3-4 hows after swarry. Please call if the swelling appe Smoking is deleterious to heat Stopplag smoking will improve Stopplag smoking will improve To a may also have received as	ans to locrease after the third day, or if you are concerned. Ion, We advise you to stop smoking for as long as possible after surgery. e potential heafing and also improve your overall periodontal heafth. Is id decongestant tablets and spray. Please ese these medications as directed.
through as automated system. Instructions will be given after dialing 1-800-159-8888. The PINB for your doctor is	SWELLING: SMOKING FOR SINUS LIFT SURGI	ofter you should expect to see first 3-6 hours after swarm. Please call if the swelling appe Smoking is deleterious to heal Stopping smoking will improve E You may also have received as on the package. In addition, at	ars to lacrease after the third day, or if you are concerned. Son, We adrise you to stop snoking for as long as possible after surgery, e potential hesting and also improve your overall periodoxial insith. sail decongestant tablets and spray. Please use these meditaisath directed rold blowing over noos. If you need to sneese, please success with your nooth
through as automated system. Instructions will be given after dialing 1-800-159-8888. The PINB for your doctor is	SWELLING: SMOKING FOR SINUS LIFT SURGI	siter you should expect to see first 3-4 hours after sweeting Please call if the sweeting appe Smoking is deleteriows to best Stopplag smoking will improve You may also have received as on the package. In addition, an open, Please inform your doct	ans to lacrease after the third day, or if you are concerned. Iou. We adrise you to stop smoking for as long as possible after surgery. I potential healing and also improve your overall periodontal health. I decongestant tablets and pray. Please yet these medications as directed rold blowing your nose. If you need to eneces, please sacese with your motik to if you develop sizes congestion that is not inlainised with your modications
through as automated system. Instructions will be given after dialing 1-800-159-8888. The PINB for your doctor is	SWELLING: SMOKING FOR SINUS LIFT SURG	siter you should expect to see first 3-4 hours after sweeting Please call if the sweeting appe Smoking is deleteriows to best Stopplag smoking will improve You may also have received as on the package. In addition, an open, Please inform your doct	ans to lacresse after the third day, or if you are concerned. Iou. We adrise you to stop smoking for as long as possible after surgery. I potential heshing and also improve your overall periodontal heshin. I decongestant tablets and pray. Please you these medications as directed rold blowing your nose. If you need to sneeze, please sacese with your motifu
	SWELLING: SMOKING FOR SINUS LIFT SURGI PHOCEDURES	ofter you should expect to see fue 3 4 hours after swarn. Plesse call the swelling appe Smoking is deleterious to heat Stopping snoking will impore You may also have receired as on the package. In addition, an open Plesse inform your dock or if you notice any bleeding o sections, plesse do not beckage	ars to lacresse after the third day, or if you are concerned. Inc. We admise you to stop smoking for as long as possible after surgery, a potential hesting and also improve your overall periodozzał leszth. sal decongestast tablets and spray. Please use these medications as directed or if your develop sizes congestion that is not minimized with your model or if spon develop sizes congestion that is not minimized with your medications r discharge from your nose.
	SWELLING: SMOKING FOR SINUS LIFT SURGI PHOCEDURES	ofter you should expect to see fue 3 4 hours after swarn. Plesse call the swelling appe Smoking is deleterious to heat Stopping snoking will impore You may also have receired as on the package. In addition, an open Plesse inform your dock or if you notice any bleeding o sections, plesse do not beckage	ars to lacresse after the third day, or if you are concerned. Inc. We admise you to stop smoking for as long as possible after surgery, a potential hesting and also improve your overall periodozzał leszth. sal decongestast tablets and spray. Please use these medications as directed or if your develop sizes congestion that is not minimized with your model or if spon develop sizes congestion that is not minimized with your medications r discharge from your nose.

### REFERENCES

AAP Glossary of Periodontal Terms. American Academy of Periodontology. 2001.

AAP position Paper: Tobacco use and the periodontal patient, Science and Therapy Committee of the American Academy of Periodontology. Journal of Clinical Periodontology 2004;70(11): 1419-1427.

Allen DL, Kerr DA. Tissue response in the guinea pig to sterile and non-sterile calculus. Journal of Periodontology 1965; 36: 121-126.

Ah MK, Johnson GK, Kaldahl WB, Patil KD, Kalkwarf KL. The effect of smoking on the response to periodontal therapy. Journal of Clinical Periodontology 1994; 21 (2): 91-97.

Armitage GC, Svanberg GK, Loe H. Microscopic evaluation of clinical measurements of connective tissue attachment levels. Journal of Clinical Periodontology 1977; 4(3): 173-190.

Armitage GC. Development of a classification system for periodontal diseases and conditions. Annuals of Periodontology 1999; 4(1): 1-6.

Avila-Ortiz G, De Buitrago JG, Reddy MS. Periodontal regeneration furcation defects: A systematic review from the AAP Regeneration Workshop. Journal of Periodontology 2015;86(Suppl. 2):S108-S130.

Baab DA, Oberg PA. The effect of cigarette smoking on gingival blood flow in humans. Journal of Clinical Periodontology 1987; 14 (7): 418-24.

Beaumount RH, O'Leary TJ, Kafrawy AH. Relative resistance of long junctional epithelial adhesions and connective tissue attachments to plaque-induced inflammation. Journal of Periodontology 1983; 55 (4): 213-223.

Becker W, Becker BE. Treatment of mandibular 3-wall intrabony defects by flap debridement and expanded polytetrafluoroethylene barrier membranes: Long-term evaluation of 32 treated patients. Journal of Periodontology. 1993; 64 (11):1138-1144.

Beertsen W, McCulloch CA, Sodek J. The periodontal ligament: a unique, multifunctional connective tissue. Periodontology 2000; 13 (1): 20-40.

Bender IB, Seltzer S. Roentgenographic and direct observation of experimental lesion ion bone: I. Journal of the American Dental Association 1961, 62: 152-160.

Bergstrom J, Eliasson S, Preber H. Cigarette smoking and periodontal bone loss. Journal of Periodontalogy 1991; 62 (4): 242-246.

Bergstrom, P., Linder, L., (1992). Occurrence of periopathogens in smoker and nonsmoker patients. Journal of Clinical Periodontology, 19 (9), 667-671.

Bowers GM, Chadroff B, Carnevale R, Mellonig J, Corio R, Emerson J, Stevens M, Romberg, E. Histologic evaluation of new attachment apparatus formation in humans: Part I. Journal of Periodontology 1989; 60 (12): 664-674.

Bowers GM, Chadroff B, Carnevale R, Mellonig J, Corio R, Emerson J, Stevens M, Romberg, E. Histologic evaluation of new attachment apparatus formation in humans: Part II. Journal of Periodontology 1989; 60 (12): 675-682.

Bowers GM, Chadroff B, Carnevale R, Mellonig J, Corio R, Emerson J, Stevens M, Romberg, E. Histologic evaluation of new attachment apparatus formation in humans: Part III. Journal of Periodontology 1989; 60 (12): 683-693.

Buchananan SA, Jenderseck RS, Granet MA, Kircos LT, Chambers DW, Robertson PB. Radiographic detection of dental calculus. Journal of periodontology1987; 58 (11): 747-751.

Byers, M., Dong , W., (1989). Comparison of trigeminal receptor location and structure in the periodontal ligament of different types of teeth from the rat, cat, and monkey. Journal of Comparative Neurology, 279 (1), 117-127.

Canis MF, Kramer GM, Pameijer CM. Calculus attachment: Review of the literature and new findings. Journal of Periodontology 1979; 50 (8): 406-415.

Chong CH, Carnes DL, Moritz AJ, Oates T, Ryu OH, Simmer J, Cochran DL. Human periodontal fibroblast response to enamel matrix derivative, amelogenin, and plateletderived growth factor-BB. Journal of Periodontology 2006; 77:1242-52.

Contreras, A., Slots, J., (2000). Herpesviruses in human periodontal disease. Journal of Periodontal Research, 35 (1), 3-16.

Deas DE, Moritz AJ, McDonnell HT, Powell CA, Mealey BL. Osseous Surgery for Crown Lengthening: A 6-Month Clinical Study. Journal of Periodontology 2004; 75;1288-1294.

Duskova M, Leamerova E, Sosna B, Gojis O. Guided tissue regeneration, barrier membranes and reconstruction of the cleft maxillary alveolus. Journal of Craniofacaial Surgery 2006; 17(6): 1153-60.

Dzink JL, Tanner AC, Haffajee AD, Socransky SS. Gram negative species associated with active destructive periodontal lesions. Journal of Clinical Periodontology 1985, 12 (8): 648-659.

FowlerC, Garrett S, Crigger M, Engelberg J. Histologic probe position in treated and untreated human periodontal tissues. Journal of Clinical Periodontology 1982; 9(5): 373-385.

Gamal AY, Mailhot JM. The effects of EDTA gel conditioning exposure time on periodontitis-affected human root surfaces: surface topography and PDL cell adhesion. Journal of the International Academy of Periodontology 2003; 5:11-22.

Giannobile WV, Somerman MJ. Growth and amelogenin-like factors in periodontal wound healing. A systematic review. Annuals of Periodontology 2003;8:193-204.

Goodson JM, Haffajee AD, Socransky SS. The relationship between attachment level and alveolar bone loss. Journal of Clinical Periodontology 1984; 11(5): 348-359.

Grossi SG, Zambon J, Machtei EE, Schifferle R, Andreana S, Genco RJ, Cummins D, Harrap G. Effects of smoking cessation on healing after mechanical periodontal therapy. The Journal of the American Dental Association 1997; 128 (5): 599-607.

Haber J, Wattles J, Crowley M, Mandell R, Joshipura K, Kent R. Evidence for cigarette smoking as a major risk factor for periodontitis. Journal of Periodontology 1993;D 64(1): 16-23.

Haffajee AD, Socransky SS. Attachment levels changes in destructive periodontal disease. Journal of Clinical Periodontology 1986; 13 (5): 461-472.

Haffajee AD, Socransky SS, Goodson JM. Clinical parameters as predictors of destructive periodontal disease activity. Journal of Clinical Periodontology 1983; 10 (3): 257-265.

Haffajee AD, Socransk, SS. Relationship of cigarette smoking to the subgingival microbiota. Journal of Clinical Periodontology 2001; 28 (4): 377-288.

Hassell, TM. Tissues and cells of the periodontium. Periodontology 2000 1993; 3: 9-38.

Isidor F, Karring T. Reproducibility of pocket depth and attachment level measurements when using a flexible splint. Journal of Clinical Periodontology 1984; 11:662-668.

Kaldahl WB, Johnson GK, Patil KD, Kalkwarf KL. Levels of cigarette comption and response to periodontal therapy. Journal of Periodontology 1996; 67 (7): 675-681.

Khorsand A, Rasouli Ghahroudi AA, Motahhari P, Rezaei Rad M, Soleimani Shayesteh Y. Histological evaluation of Accell Connexus<sup>®</sup> and Bio-Oss on quality and rate of bone healing: a single blind experimental study on rabbit's calvarium. Journal of Dentistry 2012; 9(2): 116-127.

Kornman KS. The role of supragingival plaque in the prevention and treatment of periodontal disease. Journal of Periodontal Research Supplement 1986; 21(s16): 5-22.

Löe H, Theilade E, Jensen S. Experimental gingivitis in man. Journal of Periodontology 1965; 36(3): 177-187.

Lafferty TA, Gher ME, Gray JL. Comparative SEM study on the effect of acid etching with tetracycline HCL or citric acid on instrumented periodontally-involved human root surfaces. Journal of Periodontology 1993;64:689 693.

Magnusson I, Runstad L, Nyman S, Lindhe J. A long junctional epithelium- a locus minoris resistentiae in plaque infection? Journal of Clinical Periodontology 1983; 10: 333-340.

Mariotti, A. Efficacy of chemical root surface modifiers in the treatment of periodontal disease. A systematic review. Annuals of Periodontology 2003; 8 (1): 202-226.

Marx, RE. Platelet-rich plasma: evidence to support its use. Journal of Oral Maxillofacial Surgery 2004;62: 489-496.

McClain PK, Schallhorn RG. Long-term assessment of combined osseous composite grafting, root conditioning, and guided tissue regeneration. International Journal of Periodontal Restorative Dentistry 1993; 13(1): 9-27.

Newman M, Takei H, Klokkevold P. Carranza's Clinical Periodontology. 10<sup>th</sup> Edition. Elsevier 2006.

Ochsenbein C, A primer for osseous surgery. The International Journal of Periodontics and Restorative Dentistry 1986; 6: 8-47.

Page RC. Host Response Tests for Diagnosing Periodontal Diseases. Journal of Clinical Periodontology 1992; 63(4): 356-366.

Pauls, V., Trott, J., (1966). A radiological study of experimentally produced lesions in bone. Dental Practice Dental Research, 16 (7), 254-258.

Pöllänen MT, Salonen JI, Uitto V. Structure and function of the tooth-epithelial interface in health and disease. Periodontology 2000; 31 (1): 12-31.

Preber H, Bergstrom J. The effect of non-surgical treatment on periodontal pockets in smokers and non- smokers. Journal of Clinical Periodontology 1986; 13 (4): 319-323.

Proye M, Canton J, Polson A. Initial healing of periodontal pockets after a single episode ofroot planning monitored by controlled probing forces. Journal of Periodontology 1982; 53(5): 296-301.

Rees TD, Biggs NL, Collings CK. Radiographic interpretation of periodontal osseous lesions. Oral Surgery 1971; 32 (1): 141-153.

Reynolds MA, Aichelmann-Reidy ME, Branch-Mays GL, Gunsolley JC. The Efficacy of Bone Replacement Grafts in the Treatment of Periodontal Osseous Defects. A Systematic Review. Annuals of Periodontology 2003;8:227-265.

Rosen PS, Marks MH, Reynolds MA. Influence of smoking of long-term clinical results of intrabonydefects treated with regenerative therapy. Journal of Periodontology 1996; 67 (11): 1159-1163.

Schallhorn RG, McClain PK. Clinical and radiographic healing pattern observations with combined regenerative techniques. International Journal of Periodontal Restorative Dentisrty 1994; 14 (5): 391-403.

Schallhorn RG. Present status of osseous grafting procedures. Journal of Periodontology 1977; 48 (9): 570-576.

Schluger S. Osseous resection – a basic principle in periodontal surgery. Oral Surgery 1949; 2:316-325.

Selipsky H. Osseous surgery. How much need we compromise? *Dental Clinics of North America.* 1976;20:79-106.

Socransky SS, Haffajee AD, Cugini MA, Smith C, Kent RL. Microbial complexes in subgingival plaque. Journal of Clinical Periodontology 1998; 25 (2): 134-144.

Stambaugh RV, Dragoo M, Smith DM, Carasali L. The Limits of Subgingival Scaling. International Journal of Periodontics and Restorative Dentistry. 1981; 1:30-41.

Takata T, Donath K. The mechanism of pocket formation. A light microscopic study on undecalcified human material. Journal of Periodontology 1998; 59(4): 215-21.

Terranova VP, Franzetti LC, Hic S, DiFlorio RM, Lyal, RM. A biochemical approach to periodontal regeneration: Tetracycline treatment of dentin promotes fibroblast adhesion and growth. Journal of Periodontal Research 1986; 21:330-337.

Tibbetts L, Ochsenbein C, Loughlin D. Rationale for the lingual approach to mandibular osseous surgery. Dental Clinics of North America 1976; 20 (1): 61-78.

Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: finding from NHANES III. Journal of Periodontology 2000; 71 (5): 743-751.

Waerhaug J. Subgingival plaque and loss of attachment in periodontosis as evaluated on extracted teeth. Journal of Periodontology 1977; 48(3): 125-30.

Waerhaug J. Healing of the dento-epithelial junction following subgingival plaque controlll: as observed on extracted teeth. Journal of Periodontology 1978; 49(3): 119-134.

Weinmann JP. Progress of gingival inflammation into the supporting structures of the teeth. Journal of Periodontology 1941; 12:71-82.

Yang HW, Relationship of actinobacillus actinomycetemcomitans serotype to aggressive periodontitis. Journal of Periodontology. 2004; 75: 592-599.