8-2007

Ridge preservation comparing a flap vs. a flapless technique using a demineralized bone matrix allograft plus mineralized particulate allograft and covered with a calcium sulfate barrier.

Trever L. Siu
University of Louisville

RIDGE PRESERVATION COMPARING A FLAP VS. A FLAPLESS TECHNIQUE USING A DEMINERALIZED BONE MATRIX ALLOGRAFT PLUS MINERALIZED PARTICULATE ALLOGRAFT AND COVERED WITH A CALCIUM SULFATE BARRIER

By

Trever L. Siu
DMD, Boston University, 2004

A Thesis
Submitted to the Faculty of the
Graduate School of the University of Louisville
in Partial Fulfillment of the Requirements
for the Degree of

Master of Science

Program in Oral Biology
School of Dentistry
University of Louisville
Louisville, Kentucky

August 2007

RIDGE PRESERVATION COMPARING A FLAP VS. A FLAPLESS TECHNIQUE USING A DEMINERALIZED BONE MATRIX ALLOGRAFT PLUS MINERALIZED PARTICULATE ALLOGRAFT AND COVERED WITH A CALCIUM SULFATE BARRIER

By

Trever L. Siu

D.M.D., Boston University, 2004

A Thesis Approved on

August 3rd, 2007

By the following Thesis Committee:

_____

Thesis Director

_____

_____

DEDICATION

This manuscript is dedicated to my wife, Sheila, and to my mother and father for all the support and encouragement throughout my numerous years of education and providing me with the foundations for reaching my goals.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to the following individuals:

Dr. Henry Greenwell, Program Director of Graduate Periodontics, for his invaluable guidance and mentoring in my training as a periodontist, his help in the preparation of this thesis and for the lifelong friend I have acquired.

Dr. Margaret Hill, Assistant Program Director, for her inspiration and commitment to excellence and her caring encouragement of all the residents.

Dr. James Scheetz, Ph.D., Statistician, for his dedication to educating health professionals in the field of statistics and assistance with the analysis of the data from this study.

ABSTRACT

RIDGE PRESERVATION COMPARING A FLAP VS. A FLAPLESS TECHNIQUE USING A DEMINERALIZED BONE MATRIX ALLOGRAFT PLUS MINERALIZED PARTICULATE ALLOGRAFT AND COVERED WITH A CALCIUM SULFATE BARRIER

Trever L. Siu, DMD

August 3rd, 2007

Aims. The primary aim of this study is to compare the clinical and histologic results of a flap vs. a flapless technique of ridge preservation after 4 months of healing. Both groups received an intrasocket graft of demineralized bone matrix mixed with mineralized particulate allograft that was covered with a calcium sulfate barrier..

Methods. Twelve test patients received ridge preservation using the flapless technique while 12 positive control patients were treated with a flap technique. All sockets were grafted with a mixture of demineralized bone matrix and a mineralized particulate allograft. Following tooth extraction horizontal ridge dimensions were measured with a digital caliper and vertical ridge dimensions were measured from a stent. Each site was re-entered for implant placement at about 4 months. Prior to implant placement a 2 X 6 mm trephine core was obtained and preserved in formalin for histologic analysis.

Results. The horizontal ridge width of the flapless group at the crest decreased from 8.3 ± 1.3 mm to 7.0 ± 1.9 mm for a mean loss of 1.3 ± 0.9 mm ($p < 0.05$) while the flap group decreased from 8.5 ± 1.5 mm to 7.5 ± 1.5 mm for a mean loss of 1.0 ± 1.1 mm ($p < 0.05$). There were no statistically significance differences between the two groups ($p > 0.05$). The mean mid-buccal vertical change for the flap group was a loss of 0.9 ± 1.3 mm ($p < 0.05$) vs. a loss of 0.5 ± 0.9 mm ($p < 0.05$) for the flap group. There were no statistically significant differences between groups for vertical change ($p > 0.05$). Histologic analysis revealed 44 ± 10% vital bone for the flapless group and 35 ± 15% for the flap group. Non-vital bone was 17 ± 13% for the flapless group and 19 ± 12% for the flap group.

Conclusions. Crestal ridge width following treatment with a flapless ridge preservation procedure using a demineralized bone matrix plug allograft and a calcium sulfate barrier was not significantly different than a flap ridge preservation technique using the same materials. There was a trend toward less loss of ridge height when the flapless procedure was used, although the difference was not statistically significant ($p > 0.05$).

TABLE OF CONTENTS

PAGE

LIST OF TABLES

TABLE **PAGE**

LIST OF FIGURES

FIGURE **PAGE**

CHAPTER I

LITERATURE REVIEW

With an increasing use of dental endosseous implants as a tooth replacement option, tooth extraction has become a significant part of treatment planning in current dental practices. The events following the extraction of a tooth has been studied in both animals and humans.

Animal Extraction Socket Healing Sequence

Most of the information about animal socket healing had been studied using the dog model. The earliest animal studies date back to 1936. Clafin (1936) examined the histologic healing of extraction sockets up to 31 days in dogs (Table 1). He noted that healing began with clot formation at day 1, followed by infiltration with osteoclasts at day 3, followed by bone formation around day 5-7. Complete epithelialization over the clot occurred around day 7-9 and complete socket fill by day 31. However, despite complete socket fill, osteoclasts were still present, indicating that healing was not complete at day 31. In a more recent study by Cardaropoli et al. (2003), the histologic healing sequence in beagle dogs was expanded over a period of 180 days (Table 2). Similar to Clafin, Cardaropoli and collaborators reported that socket healing in the dog

began with the formation of a blood clot at day 1. Subsequent to that, they noted that neovascularization played a significant role up to day 14 when new bone was formed along the socket walls. By day 30, in concurrence with Clafin, they observed that the socket was completely filled with bone. However, according to Cardaropoli and coworkers, the bone at day 30 was immature. It is not until day 90 that this woven (immature) bone had remodeled to become lamellar (mature) bone. By day 180, the lamellar bone had undergone further remodeling and showed a slight decrease in mineralization due to the replacement of lamellar bone with bone marrow. Araujo and collaborators (2005) also examined the histologic socket healing in the dog model using 12 sockets in 12 mongrel dogs over a period of 8 weeks (Table 3). At 1 week, the internal portion of the socket was occupied by coagulum, which was confined to the central portion of the socket. At the apical portions of the socket, islands of newly formed woven bone were noted adjacent to the bundle bone. At 2 weeks, large amounts of newly formed woven bone were found in the apical and lateral portions of the socket.

Table 1

Animal Extraction Socket Healing 31 Days (Clafin 1936)

Time	Event
Day 1	Blood Clot formation
Day 3	Osteoclast appear at crest of bone and fibroblast emerge form socket walls
Day 5 to 7	First Bone formation
Day 7 to 9	Epithelialization over clot completed
Day 11 to 15	New bone reaching the alveolar crest
Day 28 to 31	Socket filled with new bone, with osteoclasts still present

Table 2

Animal Extraction Socket Healing 180 Days (Cardaropoli et al. 2003)

Time	Event
Day 1	Blood clot formation comprising mostly of erythrocytes and platelets
Day 3	Lyses of erythrocytes and clot being replaced by vascularized tissue
Day 7	New blood vessel formation
Day 14	New bone formation on socket walls
Day 30	Socket filled with new bone
Day 90	Woven bone replaced by lamellar bone
Day 180	Some lamellar bone being replaced by bone marrow spaces

The surface of the woven bone was lined with densely packed osteoblasts and included a primitive bone marrow. At 4 weeks, at the crestal region, all bundle bone had been lost, and a large portion of the lamellar crestal bone was replaced with woven bone. Apical to the crestal region, a multitude of osteoclasts were observed on the outer surfaces of the buccal and lingual walls. By 8 weeks, the lingual wall had become wider than and positioned 2 mm coronal to the buccal wall. A zone of mineralized tissue which consisted of a mixture of woven and lamellar bone had formed between the buccal and lingual walls. This bridge of mineralized tissue traveled in an oblique direction. The two major findings of this study were: 1) the bundle bone began to disappear as early as 2 weeks post-extraction, and 2) the buccal wall undergoes a significantly greater amount of resorption that the lingual wall.

Table 3

Animal Extraction Socket Healing 56 Days (Araujo et al. 2005)

Time	Event
Day 7 (1 week)	- internal portion of the socket occupied by coagulum - apical portion showed islands of newly formed woven bone adjacent to the bundle bone.
Day 14 (2 weeks)	- apical & lateral portions showed large amounts of newly formed woven bone - surface of the woven bone was lined with densely packed osteoblasts - primitive bone marrow.
Day 28 (4 weeks)	- at the crestal region, all bundle bone had been lost - crestal lamellar crestal bone replaced with woven bone. - apical to the crestal region, a multitude of osteoclasts were observed on the outer surfaces of the buccal and lingual walls.
Day 56 (8 weeks)	- lingual wall wider than buccal wall - lingual wall positioned 2 mm coronal to buccal wall - zone of mineralized tissue which consist of a mixture of woven and lamellar bone had formed between the buccal and lingual walls traveling in an oblique direction.

Aside from studies that examined the socket healing with extraction alone, Lindhe and coworkers in Göteborg examined socket healing with the placement of an immediate implant. Berglundh and coworkers (1994) examined the vascular supply around Branemark implants in beagle dogs. It was observed that the blood vessels of the peri-implant mucosa were found to be terminal branches of larger vessels from the periosteum of the bone of the implant site. The peri-implant supracrestal connective tissue, in contrast to a tooth, was almost devoid of vascular supply. Carmagnola and coworkers (2000) examined the histologic healing around implants placed in sites previously grafted with BioOss. They utilized 16 surgically-created defects in 4 beagle dogs. They reported that osseointegration failed to occur at the implant surfaces, and a well-defined connective tissue capsule was present between the implant surface, as well as, a deep

vertical bone defect frequently present along the lingual surface of the implant. Botticelli and coworkers (2004) examined the effects of 3 different surgically-created defect configurations on bone healing around the implant. They observed that the 4-wall defects fully resolved following implant placement. In contrast, the other 2 defects with the buccal plates intentionally removed, incomplete healing was present. Botticelli and coworkers (2005) in a follow-up study, examined the effects of implant surface, implant position, and the presence of a combined horizontal and vertical residual peri-implant defect on osseointegration in Labrador dogs. After 4 months of healing, regardless of whether the implant was placed in a submerged or nonsubmerged position, a substantial amount of bone fill and a high degree of osseointegration was noted around roughened implants compared to machined implants. The results of this study suggest that implant surface characteristics played an important role in the amount of hard tissue fill and level of osseointegration. Araujo and coworkers (2005) studied the effects of immediate implant placement on the dimensional alterations of the alveolar ridge in the beagle dog model. They compared sites, which received an immediate implant to a contralateral site, which received extraction alone over a period of 3 months. The results revealed that marked dimensional alterations had occurred in the extraction alone sites. More importantly, the placement of an immediate implant failed to prevent the remodeling that occurred in the socket walls. Therefore, after 3 months of healing, the heights of the buccal and lingual walls were similar for both groups. The authors cautioned that following tooth removal, the changes in ridge dimensions associated with immediate implant placement must be considered.

Human Extraction Socket Healing Sequence

Various authors studied the extraction socket healing sequence in humans. Amler (1960) examined histologically, a total of 75 human extraction sockets over a period of 50 days. In a study consisting of 12 clinical patients requiring extraction of all remaining maxillary teeth, Boyne (1966) examined the histological healing of one of the maxillary first premolar sockets over 23 days. Evian (1982) examined the histologic healing in 10 patients over a span of 16 weeks. Biopsies were taken at 4, 6, 8, 10, 12, and 16 weeks post-extraction. In general, the human healing sequence followed a similar pattern to the dog model (Table 4).

Table 4

Human Extraction Socket Healing over 100 Days

Time	Event
Day 1	Blood clot formation
Day 2-3	Granulation tissue appears
Day 4	Contraction of the blood clot begins
Day 20	Connective tissue replaces the granulation tissue
Day 7-10	New bone formation
Day 14	1/3 socket filled, Boyne (1966)
Day 38	2/3 socket filled, Amler (1960)
Day 100	Radiopacity of socket was identical to surrounding bone, Amler (1960)

One of the initial events in the healing sequence of both dog and human models is the formation of a blood clot at day 1 (Clafin 1936, Amler 1960). The first evidence of new bone formation in dogs was seen around day 5 and along the lateral aspect of the socket by day 11 (Clafin 1936). In humans, the first evidence of new bone was not detected until day 7-10. Complete socket fill was observed around day 30 in dogs. This is in contrast to Amler, who noted that only 2/3 of the socket was filled at day 38, and to Boyne, who reported only 1/3 of the socket filled at day 14. Mature, lamellar bone was seen in dogs at day 90 (Cardaropoli et al. 2003), and this was not evident until day 100 in humans (Amler 1960). Table 5 outlines a comparison of the socket healing sequence between the dog and human models.

Table 5

Events In Extraction Socket Healing

Event	Time	Species	Study
Blood Clot Formation	0 to 3 days	Dog	Claflin (1936)
	0 to 1 day	Human	Amler et al. (1960)
Fibroblast Proliferation	3 days	Dog	Claflin (1936)
	2 to 35 days	Human	Amler et al. (1960)
Osteoclast activity	3 to 31 days	Dog	Claflin (1936)
Osteoblast activity	5 to 31 days	Dog	Claflin (1936)
	7 days	Human	Amler et al. (1960)
	10 days	Human	Boyne (1966)
	28 days	Human	Evian et al. (1982)
First evidence of new bone	5 days 7-10 days	Dog Human	Clafin (1936) Amler (1960)
Complete socket fill	30 days	Dogs	Clafin (1936)
1/3 socket fill	14 days	Human	Boyne (1966)
2/3 socket fill	38 days	Human	Amler (1960)
Mature bone present	90 days 100 days	Dog Human	Cardaropoli et al. (2003) Amler (1960)

Alveolar Ridge Resorption Following Tooth Extraction

There have been many reports on the loss in height and width of bone following tooth extraction. Most of the bone that is lost occurs soon after the tooth is extracted. Loss of alveolar ridge width and height can be problematic if an endosseous dental implant is used as a tooth replacement option because there must be an adequate amount of bone surrounding the dental implant. The most critical question regarding the resulting ridge is the loss of horizontal dimension. The ridge position plays a critical role on dental implant placement and the subsequent occlusal relationship. Most studies

report that most of the ridge resorption occurs on the buccal, resulting in a shift of the center of the ridge towards the palatal/lingual. Pietrokovski and Massler (1967) studied 149 dental casts with one tooth missing. They found that the buccal surface of both the maxilla and the mandible resorb more than the lingual/palatal sides with a distinct shift of the center of the ridge to the palatal/lingual. The amount of facial resorption varies considerably between individual sites, however, there are several studies that have quantitated mean resorption. Schropp et al. (2003) evaluated 46 patients with a single premolar or molar extraction over a 12-month period and found that most (2/3) resorption happened within the first 3 months. Yilmaz et al. (1998) examined 5 patients (10 sites) with a single maxillary incisor extraction over a 12-month period and noted a 17% decrease in ridge width based on study cast measurements. The amount of buccal-lingual ridge resorption after tooth extraction has been reported from 17-60% with the ridge height decreasing by 1 mm, (Lekovic et al. 1997, Lekovic et al. 1998, Yilmaz et al. 1998, Camargo et al. 2000, Schropp et al. 2003, Iasella et al. 2003). Based on the data from these studies, it appears that mean change in ridge width following tooth extraction varies substantially, and this broad range should be considered whenever dental implants are considered as a future tooth replacement option. Table 6 consists of a list of studies that examined the mean change in the horizontal and vertical ridge dimensions following tooth extraction alone.

Table 6

Extraction Alone Studies

Extraction Alone Studies				
Study	**Reentry Time (months)**	**Mean Horizontal Change**	**Percent Horizontal Change**	**Mean Vertical Change**
Lekovic et al. 1997	6	-4.43 ± 0.52	-63.3%	-0.88 ± 0.26
Lekovic et al. 1998	6	-4.59 ± 0.23	-61.2%	-1.50 ± 0.21
Yilmaz et al. 1998*	12	-0.75 ± 0.59	-17.0%	-1.35 ± 1.05
Camargo et al. 2000	6	-3.06 ± 2.41	-40.8%	-1.00 ± 2.25
Iasella et al. 2002	4-6	-2.63 ± 2.29	-29.1%	-0.90 ± 1.60
Schropp et al. 2003*	12	-6.1 ± 3.00	-50.8%	-0.20 ± 1.60

* = measured from study casts

Ridge Preservation

With increasing demand for optimal esthetics, dental implants have gained enormous popularity as the ideal tooth replacement option. This translates into increased utilization of ridge preservation in the field of periodontal plastic and reconstructive surgery. The goal of ridge preservation is minimizing bone loss to preserve the maximum final, healed ridge dimensions. Despite the use of this grafting procedure, there will still be some horizontal and vertical loss of healed ridge dimension. Ridge preservation can be done using either a soft tissue or a hard tissue graft. Hard tissue grafts, which preserve the bony architecture of the ridge, are very important if an endosseous implant will be used to replace the missing teeth. Implants need support from the bone to maintain function; this means that there must be sufficient amount of bone (at

least 1 mm surrounding the implant in all directions). Ashman (2000) noted that when an extraction takes place and ridge preservation is not utilized the site of extraction could lose 40% to 60% of bone height and width within 2 to 3 years and subsequent loss of 0.25% to 0.5% annually. Similarly, Iasella (2002) reported as much as 4 mm loss of ridge width in extraction alone sites over 6 months. By performing an atraumatic tooth extraction, this dramatic change in ridge dimensions can be minimized. Garg (2001) noted that there are 5 careful steps in extracting a tooth atraumatically; 1) do not reflect the interdental papilla (especially in the esthetic zone), 2) focus on the actual process of tooth removal, 3) use elevators and forceps properly to reduce bony involvement and preserve bone contours, 4) section the tooth to help prevent bone loss, and 5) remove any soft tissue fragments or pathology. After extracting a tooth atraumatically, the type of bone defect present can be determined and this bone defect will influence the choice in the type of ridge preservation. According to Garg (2001), the bone defect can be categorized into one of the following categories: five-walled, four-walled, three-walled, two-walled, or one-walled defects.

Comparison studies have shown that intrasocket ridge preservation prevents most but not all ridge resorption. Lekovic et al. (1997) compared an extraction alone versus a non-resorbable barrier membrane (Gore-Tex) and Lekovic et al. (1998) compared an extraction alone versus a resorbable barrier membrane (Resolut®). In both studies, the teeth that were included were anterior teeth or premolars, which were atraumatically extracted and primary closure of the preservation sites obtained. Reentry in both studies occurred 6-months post-extraction. The results showed that either the non-resorbable (Gore-Tex) or the resorbable (Resolut®) barrier membranes both provided comparable

results with only an average of 0.35 mm of vertical resorption and an average of only 1.53 mm (20%) buccal-lingual resorption. Results from Lekovic et al. (1997, 1998) reveal that the horizontal loss of bone in the non-resorbable group (Gore-Tex) was 1.73 mm, while in the resorbable membrane (Resolut®) group was 1.32 mm and for the control group which did not receive any type of ridge preservation lost on average 4.5 mm. The non-resorbable membrane sites on average had 3.70 mm (2.5-times) less loss in horizontal width than sites treated with extraction alone while the resorbable membrane sites had 3.27 mm (3.5-times) less loss in horizontal width than sites treated with extraction alone. These two studies show that there is not much difference between the two experimental groups of resorbable vs. non-resorbable membrane for ridge preservation. The results did show that ridge preservation techniques utilizing either resorbable or non-resorbable barrier membranes greatly decrease the amount of horizontal and vertical bone resorption.

Yilmaz and coworkers, in a 16-patient, 27-socket study comparing the use of bioactive glass (PerioGlas®) cones in fresh maxillary incisor extraction sites vs. extraction alone, demonstrated that the use of bioactive glass (PerioGlas®) cones provided a slight gain (0.2 mm) in ridge width, and minimal (0.1 mm) loss of ridge height over a period of 12 months. This was in contrast to the extraction alone group, which demonstrated a much greater loss of ridge width (0.75 mm), and ridge height (1.35 mm). Measurements were made on study casts.

Camargo and coworkers, in a 6-month reentry, 32 nonmolar ridge preservation study examined the use of bioactive glass (BioGran®) and calcium sulfate (Capset®) vs. extraction alone. They reported that the mixture of bioactive glass (BioGran®) and

calcium sulfate (Capset®) resulted in a mean loss of ridge width and height of 3.48 mm and 0.4 mm, respectively. In contrast, the extraction alone group showed slightly less loss in ridge width (3.06 mm), and a greater loss in ridge height (1.0 mm) over 6 months. Iasella and coworkers, in a 4 to 6-month reentry study used 24 sockets and compared the use of freeze-dried bone allograft (FDBA) to extraction alone. After 4 months of healing, the sites grafted with FDBA gained 1.3 mm in ridge height and lost only 1.2 mm in ridge width, in comparison to the extraction alone group, which had twice the amount of loss in ridge width (2.6 mm), and 0.9 mm loss in ridge height.

In addition to the comparison studies, others have compared the effects of various different graft materials on the preservation of ridge dimensions. Nemcovsky and Serfaty (1996), in a 12-month, 23-patient, 23-socket study using non-resorbable hydroxyapatite (HA) crystals, showed a loss of ridge width of 0.6 mm and a loss of ridge height of 1.4 mm over 1 year. Simon et al. (2000) in a 4-month reentry study using particulate DFDBA as an intrasocket and a buccal overlay graft along with a barrier membrane (Resolut XT®), reported a mean net loss of approximately 1.0-1.5 mm of ridge height (15-76%) and a gain of about 1.0 mm in width (39-67%). The loss in ridge width was greatest at 3 mm apical to the alveolar crest, and decreased apically. Zubillaga and coworkers (2003), in a 4-month reentry, 10-patient, 11-socket study comparing the use of DFDBA (Regenafil®) and resorbable barrier membrane (Resolut®) with or without fixation, reported that the mean change in ridge dimensions over 4 months resulted in a loss of 1.8 mm width, and a gain of 1 mm height, respectively. Vance and coworkers (2004), in a 4-month reentry, nonmolar study using 24 extraction sockets comparing the use of anorganic bovine bone matrix (BioOss®) to a mixture of calcium sulfate and

carboxymethylcellulose (CalMatrix®), demonstrated that both groups resulted in a loss of ridge width of 0.5 mm. The BioOss® group showed a gain in ridge height of 0.7 mm, while the CalMatrix® group showed a loss of 0.3 mm. In a follow-up, 4-month reentry, nonmolar study by Adams and coworkers (2006) comparing the two different ridge preservation techniques: 1) intrasocket FDBA alone vs. 2) intrasocket plus a buccal overlay (extrasocket) FDBA, showed that the intrasocket alone group resulted in a loss of ridge width of 2 mm and no change in ridge height. In contrast, the overlay group showed a loss of 1.4 mm and a gain in ridge height of 2.2 mm.

As is evident from all the aforementioned studies, despite the use of ridge preservation techniques to minimize the amount of bone resorption after an extraction, a minimal loss (mean 2.16 mm) of ridge width and height may still occur. On the other hand, if ridge preservation was not performed, a substantial decrease in ridge width, ranging from 30-60% (2.7 to 6.1 mm) over 4-6 months can be anticipated (Lekovic et al. 1997, Lekovic et al. 1998, Iasella et al. 2003, Schropp et al. 2003).

Table 7

Ridge Preservation Studies

Study	Reentry Time months	Treatment	Mean Horizontal Change mm	Percent Horizontal Change	Mean Vertical Change mm
Nemcovsky & Serfaty 1996	12	Nonresorbable HA crystals	-0.6 ± 0.66	N/A‡	-1.4 ± 0.50
Lekovic et al. 1997	6	ePTFE	-1.7 ± 0.56	-13.7%	-0.3 ± 0.26
Lekovic et al. 1998	6	Resolut	-1.3 ± 0.21	-17.8%	-0.4 ± 0.20
Yilmaz et al. 1998	6	PerioGlas cones	+0.2 ± 0.52	+3.6%	-0.1 ± 0.87
Camargo et al. 2000	6	BioGran Capset	-3.5 ± 2.68	-44.3%	-0.4 ± 3.18
Simon et al. 2000	4	DFDBA/ Resolut XT®	+1.1 ± NG*	-53.3%	-1.4 ± NG*
Zubillaga et al. 2003	4	Regenafil	-1.8 ± NG*	-16.8%	+1.0 ± NG*
Iasella et al. 2003	4	FDBA/ BioMend	-1.2 ± 0.93	-13.0%	+1.3 ± 2.00
Vance et al. 2004	4	BioOss/ BioGide	-0.5 ± 0.8	-5.2%	+0.7 ± 0.4
Vance et al. 2004	4	CalMatrix/ Capset	-0.5 ± 0.8	-5.6%	-0.3 ± 0.6
Adams et al. 2005	4	Intrasocket FDBA	-2.0 ± 0.9	-21.2%	0.0 ± 1.8
Adams et al. 2005	4	Intrasocket + Buccal overlay FDBA	-1.4 ± 1.0	-16.5%	+2.2 ± 2.65

‡ = no baseline measurements reported, unable to determine percentage
* NG = not given in article

Histologic Evaluation of Ridge Preservation

The goal of ridge preservation procedures is to prevent the collapse of the ridge by allowing the alveolar socket to fill in with as much bone volume as possible. The ideal bone grafting material will promote vital host bone to rapidly repopulate the socket and minimize the loss of ridge dimensions. It is very important to evaluate from a histologic point of view to determine how much bone is present relative to the amount of trabecular space. A bone quality index has been described by Lekholm and Zarb (1985) which includes Type I bone being homogenous compact bone, Type II being a thick layer of compact bone surrounding a core of dense trabecular bone, Type III being a thin layer of cortical bone surrounding dense trabecular bone of favorable strength and Type IV being a thin layer of cortical bone surrounding a low-density trabecular bone. Type I bone is preferred for implant placement since it has the highest density of cortical bone and Type IV is the least preferred due to its very low density.

Extraction alone studies

When extraction sockets are left alone and heal without any type of ridge preservation procedure the amount of vital bone present after 4-8 months of healing range from 33-54% with 34-67% of trabecular space (Iasella et al. 2003, Froum et al. 2002, Serino et al. 2003). In the canine model performing extraction alone in 9 sockets, Cardaropoli et al. (2003) reported only 15% vital bone and 85% trabecular space over 6 months. Histologic results from autogenous bone grafts have consisted of vital

(osteocytes within the lacunae) bone, non-vital bone, vascular channels, osteoblasts and secondary osteon formation. Cement lines usually surround the non-vital bone, which joins the immature new bone with the non-vital bone chips (Becker et al. 1994, 1996, 1998).

Allograft studies

Studies of demineralized freeze-dried bone allograft (DFDBA) used in ridge preservations procedures have reported conflicting results. Several studies have found that DFDBA particles are still present in biopsy cores resulting in non-vital DFDBA particles (Smukler et al. 1999, Froum et al. 2002, Vance et al. 2003). It has been reported that DFDBA has osteoinductive properties and should induce bone growth, but in several histologic samples the DFDBA particles are encapsulated in fibrous connective tissue with no evidence of either osteoblastic or osteoclastic activity (Becker et al. 1994, 1996, 1998). If DFDBA particles do not provide any osteoinductive properties, it is believed they might interfere with normal bone formation and may weaken the bone at the grafted site (Becker et al. 1994). The amount of non-vital bone graft particles remaining compared to the amount of vital bone may be an important factor. Several studies have reported that DFDBA particles do resorb and in some cases fully resorb leaving only vital bone (Froum et al. 2002, Smukler et al. 1999). Ridge preservation utilizing DFDBA has been seen histologically to have DFDBA particles surrounded by intimately apposed woven and lamellar bone with distinct cement lines and a lack of fibrous encapsulation. Osteoblasts were seen lining endosteal spaces and the new bone marrow exhibited a mild

degree of fibrosis without signs of inflammatory reaction (Brugnami et al. 1996, 1999, Smukler et al. 1999). Vance et al. (2004) examined 12 sockets grafted with a combination of DFDBA and an alloplastic putty consisting of calcium sulfate and carboxymethylcellulose (CalMatrix®) over 4 months. They reported 61% vital bone, 3% non-vital bone, and 36% trabecular space. The percentage of vital bone present after utilizing DFDBA in ridge preservation ranged from 35 to 60% with only 3-14% having non-vital bone (Smukler et al. 1999, Froum et al. 2002). Becker et al. (1996, 1998) reported more residual graft particles and fibrous encapsulation, which may be due to their failure to use an occlusive barrier membrane.

Freeze dried bone allograft (FDBA), has also been used in ridge preservation procedures and showed a histologic result of 28% vital bone, 37% non-vital bone and 35% trabecular space over 4-6 months (Iasella et al. 2003). The residual FDBA particles were often surrounded by vital woven or lamellar bone, or were encapsulated in fibrous connective tissue. The residual graft material was higher than the amount with DFDBA, which may be due to the shorter healing period of 4-6 months vs. up to 48 months for DFDBA.

Xenograft studies

Xenografts, mostly anorganic bovine bone, have also been utilized in ridge preservation procedures with similar results to allografts. Generally, bone encircled and adhered to the grafted particles in a concentric and/or lamellar arrangement. Newly formed bone was observed, mostly in direct connection with the grafted particles (Artzi et

al. 1998, 2001, Vance et al. 2004, Froum et al. 2004). Vance et al. (2004) showed that BioOss® had 26% vital bone with 16% non-vital bone and 58% trabecular space after 4 months of healing. This agrees with a 6-month study of 6 sockets grafted with BioOss® by Zitzmann et al. (2001) where they reported 27% vital bone, 30% non-vital bone, and 43% trabecular space. In contrast, Artzi et al. (2000) grafted 15 sockets in 15 patients using BioOss® reported much greater percentage of vital bone at 46%, along with 31% non-vital bone, and 23% trabecular space over 9 months. Froum et al. (2004) grafted 8 sockets with a nonresorbable anorganic bovine bone substitute (OsteoGraf R/N-300), 4 of which was combined with an ePTFE barrier, and the other 4 with Alloderm (ADM) as a barrier over 6-8 months. In the OsteoGraf/ePTFE group, they reported 18% vital bone, 21% non-vital bone, and 61% trabecular space. In the OsteoGraf/ADM® group, 42% vital bone, 13% non-vital bone, and 45% trabecular space. The difference in the amount of vital bone between the two groups could possibly be attributed to the choice of barrier used. The vascular channels in the Alloderm may have provided better revascularization compared to the ePTFE barrier.

Alloplast studies

Alloplastic materials such as bioactive glass, hydroxyapatite (HA) and calcium sulfate have shown percentage vital bone around 35-60% (MacNeill et al. 1999, Froum et al. 2002, 2004 and Guarnieri et al. 2004). Alloplasts are well tolerated by the host and have been shown to be osteoconductive in nature, but not osteoinductive. Guarnieri et al. (2004) in a 10 socket study utilizing medical grade calcium sulfate hemi-hydrate in

extraction sockets and found at 3 months that 100% of the graft had been resorbed and that there was 58% vital bone present throughout the preservation site. The site was also devoid of any inflammatory cells and connective tissue. The resorption time with calcium sulfate is much faster than the xenografts or the allografts mentioned above. MacNeill et al. (1999) compared the osseous healing of 4 different alloplasts: hydroxyapatite (HA, OsteoGraf/P), bioactive glass #1 (BioGran® 300-360 μm), bioactive glass #2 (PerioGlas® 90-710 μm), and calcium sulfate (Capset®) with autogenous bone, in osteotomy sites surgically created in rabbit tibia over 28 days. All graft sites showed evidence of new bone formation at 28 days with the Capset + autogenous bone showing the greatest mean percentage of vital bone (58.8%) and PerioGlas® showing the least (40.4%), while the BioGran and OsteoGraf/P group both showed 41.8% vital bone. Froum et al. (2002) treated 19 human sockets with BioGran® and reported similar results with 59% vital bone, 6% non-vital bone, and 35% trabecular space over 6-8 months. Froum et al. (2002) treated 8 sockets with absorbable HA (OsteoGraf R/LD), 4 of which were combined with an ePTFE barrier, and the remaining 4 with an Alloderm® (ADM) barrier. After 6-8 months of healing, the HA/ADM group showed 35% vital bone, 4% non-vital bone, and 62% trabecular space, while the HA/ePTFE group showed 28% vital bone, 12% non-vital bone, and 61% trabecular space. In contrast, Luczyszyn et al. (2005) grafted 15 sockets in 11 patients using absorbable HA (Algipore®) with an ADM barrier over 6 months. They reported only 1% vital bone, 42% non-vital bone, and 57% trabecular space. In contrast, Serino et al. (2003), in a non-graft study, treated 34 sockets in 32 patients over 6 months with a bioabsorbable polylactide/polyglycolic acid sponge (Fisiograft®) to encourage vascular ingrowth. They reported 67% vital bone and 33%

trabecular space. These results compare well to the results seen by Vance et al. (2004) with DFDBA and the calcium sulfate putty (CalMatrix®) and Guarnieri et al. (2004) with the medical grade calcium sulfate.

Summary of histologic results

When analyzing the histologic findings, the studies demonstrate that when ridge preservation procedures are performed with a variety of grafting materials, including allografts (DFDBA, FDBA), xenografts (anorganic bovine bone mineral), alloplasts (hydroxyapatite, calcium sulfate, and polylactide/polyglycolic acid sponge), the percentage of vital and nonvital bone as well as trabecular space varies considerably. The percentage of vital bone ranged 1-67%. The percentage of non-vital bone ranged from 0-42%. The amount of trabecular space present ranged from 33-85%.

Table 8

Comparison of Histologic Data on Extraction Alone studies

Author/Yr	Species	Healing months	% Vital Bone	% Trabecular Space
Cardaropoli et al. 2003	Dogs	6	15.0	85.0
Iasella et al. 2003	Human	4-6	54.0	46.0
Froum et al. 2002	Human	6-8	32.4	67.6
Serino et al. 2003	Human	6	44.0	56.0

Table 9

Comparison of Histologic Data on Ridge Preservation studies

Author/Yr	Graft Material	Particle Size	Healing months	% Vital Bone	% Non-Vital Bone	% Trabecular Space
Allografts						
Smukler et al. 1994	DFDBA	250 to 350 μm	8-23	38.6	5.6	55.8
Froum et al. 2002	DFDBA	250 to 500 μm	6-8	34.7	13.5	51.8
Vance et al. 2004	DFDBA/putty (CalMatrix®)	500-1000 μm	4	61.0	3.0	36.0
Iasella et al. 2003	FDBA	500-1000 μm	4-6	30.1	34.7	35.2
Xenografts						
Vance et al. 2004	BioOss®	250-500 μm	4	26.0	16.0	54.0
Artzi et al. 2000	BioOss®	250-1000 μm	9	46.3	30.8	42.6
Zitzmann et al. 2001	BioOss®	250-1000 μm	6	26.9	30.5	42.6
Froum et al. 2004	OsteoGraf R/N300 + ADM	250-420 μm	4	42.0	13.0	45.0
Froum et al. 2004	OsteoGraf R/N300 +ePTFE	250-420 μm	4	18.0	21.0	61.0
Alloplasts						
Froum et al. 2002	Bioactive Glass (BioGran®)	300-355 μm	6-8	59.5	5.5	35.0
MacNeill et al. 1999	Bioactive Glass (BioGran®)	300-360 μm	1	41.8	NG	NG
MacNeill et al. 1999	Bioactive Glass (PerioGlas®)	90 to 710 μm	1	40.4	NG	NG
MacNeill et al. 1999	HA (OsteoGraf/P)	NG	1	41.8	NG	NG
Froum et al. 2004	HA (OsteoGraf R/LD) + ADM	250-420 μm	4	35.0	4.0	62.0
Froum et al. 2004	HA (OsteoGraf R/LD) + ePTFE	250-420 μm	4	28.0	12.0	61.0
Luczyszyn et al. 2005	HA (Algipore®)	NG	6	1.0	42.0	57.0

	+ ADM					
Guarnieri et al. 2004	Calcium Sulfate	NG	3	58.0	0.0	NG
MacNeill et al. 1999	Calcium Sulfate (CapSet®) plus autogenous	1	NG	58.8	NG	NG
Non-graft study						
Serino et al. 2003	Polylactide/ Polyglycolic acid sponge (Fisiograft®)	NG	6	67.0	0.0	33.0

*NG= not given in article

Summary of Literature Review

Based on a review of the literature on extraction alone studies using the animal and human models, the healing sequence of an extraction socket begins with the formation of a blood clot around day 1, followed by neovascularization around day 3, and subsequent new bone formation starting at around 5-7 days (Clafin 1936, Cardaropoli et al. 2003, Amler 1960, Boyne 1966, Evian 1982). Complete socket fill was noted at day 30 in dogs (Clafin 1936), while only 2/3 of the socket was filled in humans at day 38 (Amler 1960). Mature, lamellar bone was seen as early as 90 days in dogs (Cardaropoli et al. 2003), and this was not present until day 100 in humans (Amler 1990).

Studies examining the histologic healing of the extraction socket have shown that when extraction sockets are left alone and heal without any type of ridge preservation procedure, the amount of vital bone present after 4-8 months of healing range from 33-54% with 34-67% of trabecular space (Iasella et al. 2003, Froum et al. 2002, Serino et al. 2003). In contrast, in the canine model, Cardaropoli and coworkers (2003) reported only

15% vital bone and 85% trabecular space over 6 months. More importantly, Araujo and coworkers (2005), in an 8-week study using the canine model, reported that the bundle bone began to disappear as early as 2-weeks post-extraction, and the buccal wall undergoes a greater amount of resorption than the lingual wall.

Reports of histologic results from autogenous bone grafts have yielded mostly of vital bone (osteocytes within the lacunae). Studies using allografts (DFDBA, FDBA) for ridge preservation (Smukler et al. 1994, Froum et al. 2002, Vance et al. 2004, Iasella et al. 2003) have yielded variable results. Percentage of vital bone ranged from 30-61%, % non-vital bone ranged from 3-35%, while % trabecular space ranged from 35-56%. This broad range of results could be attributed to the broad range in reentry time of 4-23 months. Ridge preservation studies using xenografts (BioOss®, OsteoGraf) showed similar results to allografts with a range of 18-46% of vital bone, 13-31% of non-vital bone, and 43-61% of trabecular space. A broader range of results was seen with studies using alloplasts (BioGran®, PerioGlas®, Algipore®, hydroxyapatite, calcium sulfate). From these studies, a range of 1-60% of vital bone, 4-42% of non-vital bone, and 35-57% of trabecular space over 1-8 months was reported. Lastly, Serino and coworkers examined the use of a polylactide/polyglycolic acid sponge (Fisiograft®) for ridge preservation and they reported 67% vital bone, an absence of non-vital bone, and 33% trabecular space.

Alveolar ridge resorption has been reported as a common sequelae following tooth extraction. Loss of alveolar ridge width and height can be problematic if a dental implant was selected as the tooth replacement option. While the dimensions of the healed alveolar ridge determine the feasibility for the placement of a dental implant, the

immediate, post-extraction ridge dimensions are equally important. Table 10 summarizes the root dimensions at the cervix as categorized by tooth types.

Table 10

Root Dimensions at the Cervix by Tooth Types (Ash-Wheeler 6th Edition 1984, Woefel 1990)

Tooth Types	Bucco-lingual/palatal dimensions mm		Mesio-distal dimensions mm	
	Ash-Wheeler	Woelfel	Ash-Wheeler	Woelfel
Mandibular incisors				
Central	5.3	5.4	3.5	3.5
Lateral	5.8	5.8	4.0	3.8
Maxillary incisors				
Central	6.0	6.4	7.0	6.4
Lateral	5.0	5.8	5.0	4.7
Mandibular & Maxillary canines	7.0	Mx: 7.6 Mn: 7.5	5.5	Mx: 5.6 Mn: 5.2
Mandibular 1st premolars	6.5	7.0	5.0	4.8
Mandibular 2nd premolars	7.0	7.3	5.0	5.0
Maxillary premolars (1st & 2nd)	8.0	1st: 8.2 2nd: 8.1	5.0	1st: 4.8 2nd: 4.7
Mandibular 1st molars	9.0	10.7	9.0	7.9
Mandibular 2nd molars	9.0	10.7	8.0	7.6
Mandibular 3rd molars	9.0	10.4	7.5	7.2
Maxillary 1st molars	10.0	9.0	8.0	9.2
Maxillary 2nd molars	10.0	8.8	7.0	9.1
Maxillary 3rd molars	9.5	8.9	6.5	9.2

As is evident from Table 10, different tooth types possess different bucco-lingual/palatal and mesio-distal dimensions. In general, incisors are the smallest, while molars are the

widest in dimension. As a result, ridge preservation becomes increasing critical for the smaller tooth types (especially, mandibular incisors) since even a small amount of horizontal ridge resorption can be detrimental.

Despite the use of a bone graft to preserve alveolar ridge dimensions, most studies have reported a net loss in horizontal and/or vertical ridge dimensions. Simon et al. (2000) in a 4-month reentry study using particulate DFDBA as an intrasocket and a buccal overlay graft along with a barrier membrane (Resolut XT®), reported a mean net loss of approximately 1.0-1.5 mm of ridge height (15-76%) and width (39-67%). The loss in ridge width was greatest at 3 mm apical to the alveolar crest, and decreased apically.

The goal of ridge preservation is to minimize the amount of ridge resorption after an extraction. As was evident from the extraction alone studies reviewed (Lekovic et al. 1997, Lekovic et al. 1998, Yilmaz et al. 1998, Camargo et al. 2000, Iasella et al. 2002, Schropp et al. 2003), the change in ridge width following tooth extraction varies substantially, and this broad range (30-60%) may have a profound influence on the future tooth replacement options available.

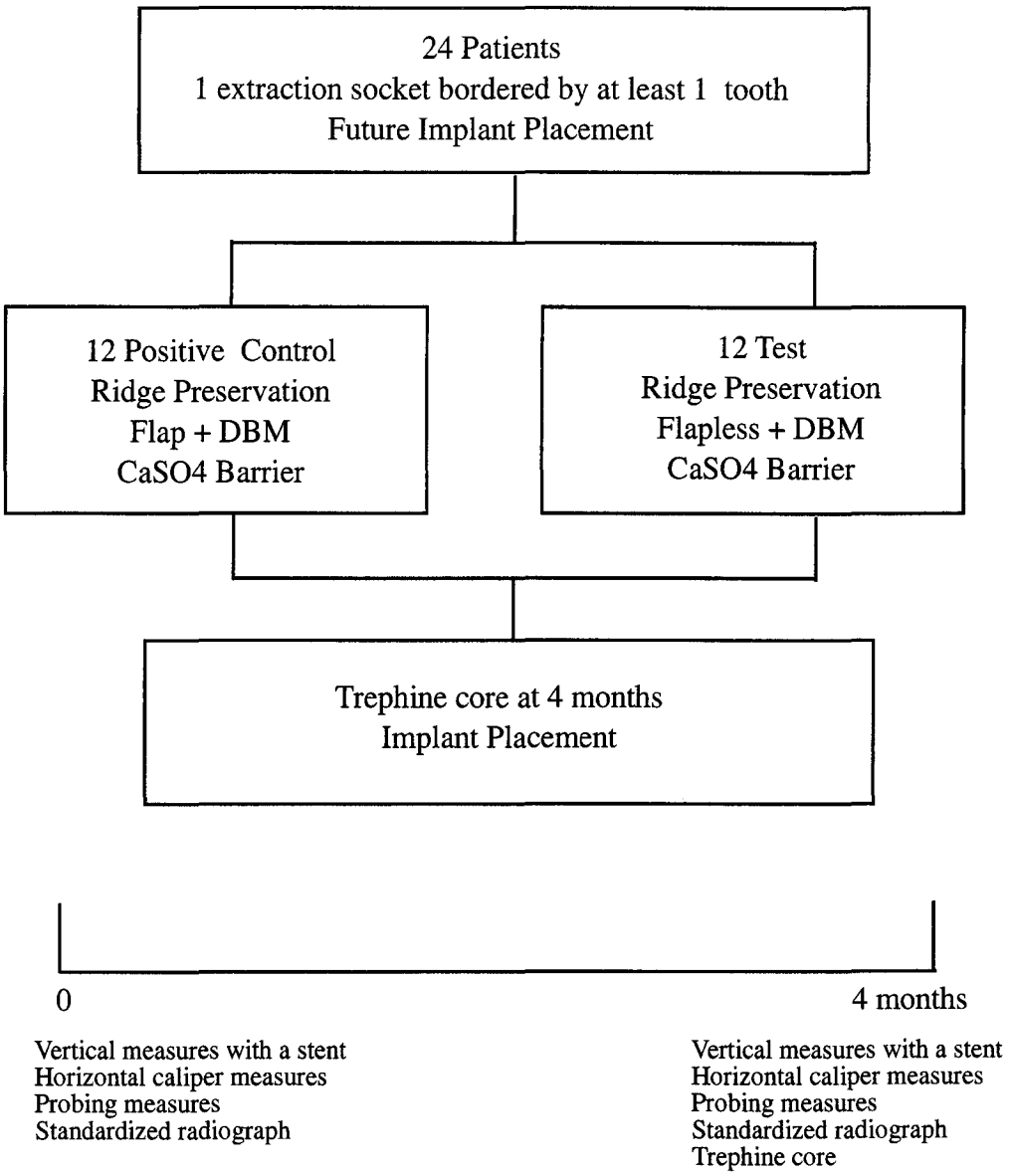
CHAPTER II

METHODS

Study design. Twenty-four patients were invited to participate in this randomized, controlled, blinded clinical trial. By random selection, using a coin toss, twelve positive control patients were selected to receive an intrasocket mineralized particulate allograft composed of cortical and cancellous chips 750 to 1400 μm (MinerOss, BioHorizons, Birmingham, AL) plus a demineralized bone matrix allograft (Grafton Matrix Plug, BioHorizons, Birmingham, AL), collectively referred to as DBM, and covered by a calcium sulfate barrier (CalForma®, Lifecore Biomedical, Inc, Chaske, MN) using a full-thickness flap technique. Twelve test patients received the same intrasocket DBM allograft covered by a calcium sulfate barrier using a flapless technique. Each patient received a post-surgical regimen of 50 mg of doxycycline hyclate (Warner Chilcott Inc. Morris Planes, New Jersey) 1 tab qd for 2 weeks; 375 mg of naproxen sodium (Geneva Pharmaceuticals, Inc. Broomfield, CO) 1 tab q12h for 1 week; chlorhexidine 0.12% (Colgate Oral Pharmaceutical Canton, Massachusetts), twice daily, and analgesics as needed.

At 4-months post-surgery, a trephine core was taken from the grafted site immediately prior to implant placement and submitted for histologic preparation using hematoxylin and eosin staining.

Figure 1



Patient Selection

Inclusion criteria

1 Have one non-molar tooth requiring extraction that will be replaced by a dental implant. The site must be bordered by at least one tooth.

2 Must be at least 18 years old.

3) Must sign an informed consent approved by the University of Louisville Human Studies Committee.

Exclusion Criteria

1) Debilitating systemic diseases, or diseases that affect the periodontium.
2) Molar teeth.
3) Allergy to any material or medication used in the study.
4) Require prophylactic antibiotics.
5) Previous head and neck radiation therapy.
6) Chemotherapy in the previous 12 months.
7) Long term NSAID or steroid therapy.

Post-Surgical Exclusion

Any site that is excluded after surgery will be reported and accounted for. Sites will be excluded if there is:

1) Loss of graft or barrier material.
2) Unanticipated healing complications that will adversely affect treatment results.

Presurgical Management

Each patient received a diagnostic work-up including standardized periapical radiographs (Appendix D), study casts, clinical photographs, and a clinical examination to record attachment level, probing depth, recession, and mobility of teeth adjacent to the

extracted sites. Customized acrylic occlusal stents were fabricated on the study casts to serve as fixed reference guides for the measurements (Appendix F).

Presurgical preparation included detailed oral hygiene instructions. Baseline data was collected just before the surgical phase of the treatment. Baseline data will include:

Clinical Measurements

- Plaque index: Silness and Loe 1964 (Appendix A).
- Gingival index: Loe 1967 – Gingival index (Appendix B).
- Gingival margin levels: Measured from CEJ to the gingival margin.
- Keratinized tissue: Measured from the gingival margin to the mucogingival junction
- Clinical attachment level: Measured from CEJ to the bottom of the clinical periodontal pocket.
- Clinical tooth mobility: Measured by using the modified Miller's Index.
- Horizontal Ridge width: A digital caliper was used to measure total ridge width to the nearest 10^{-2} mm at the mid point of the alveolar crest and 5 mm apical to the crest, measured post-extraction and prior to implant placement. For the test (flapless) group, only the crestal ridge width was measured at the post-extraction time point.
- Vertical Change in alveolar crest: Measurement from the stent to alveolar crest minus re-entry stent to alveolar crest values.
- Soft Tissue thickness: SDM gingival thickness meter, which uses ultrasonic waves to measure soft tissue thickness, was used to measure 3 mm apical to the soft tissue crest on buccal and palatal. At 4 months, the SDM gingival thickness meter was

again used to measure 3 mm apical to the soft tissue crest on buccal and palatal/lingual with the addition of one measurement at the center of the occlusal aspect of the ridge.

- Radiographic examination: A customized stent was constructed using Triad® light cured resin (Appendix F) and a Rinn-XCP on the patient model (Appendix D) to ensure standardization of the projection.
- Clinical photographs.

Surgical treatment

At the surgical appointment, the SDM gingival thickness meter was used prior to anesthesia to determine soft tissue thickness. Patients were then anesthetized with 2% lidocaine containing epinephrine in both 1:100,000 and 1:50,000 concentrations.

The main difference between the flapless and flap groups resides in the surgical treatment. For the flap group, a full-thickness, papilla-sparing, mucoperiosteal flap was elevated on the buccal and palatal/lingual to expose the alveolar ridge. Teeth were elevated and atraumatically extracted with periotomes, elevators, and forceps. Multi-rooted teeth were sectioned to facilitate the atraumatic extraction process. In contrast, for the flapless group, the same surgical treatment was performed using a flapless approach. The extraction socket was then curetted to remove all soft tissue. After flap reflection, the acrylic stent was used to obtain vertical bone height relative to the stent.

A digital caliper was applied to the ridge to measure the total alveolar ridge width at the mid-socket crest and 5 mm apical to the crest (only at the crest for the flapless group at baseline). For the flapless group, a 2 mm core of soft tissue at the level of the

buccal and palatal/lingual crest was removed using a trephine to facilitate the baseline clinical measurements of the ridge width. In both the flap and flapless groups, 0.5 cc of mineralized particulate allograft composed of cortical and cancellous chips was thoroughly mixed with one package of demineralized bone matrix plug, after each was hydrated separately. The mixture was placed into the socket to the level of the socket crest. In the flap group, the flaps were replaced and sutured with 5-0 Maxon sutures. A set of criss-cross sutures was placed over the bone graft in both groups to serve as a retentive feature for the calcium sulfate barrier. The calcium sulfate barrier was mixed according to the manufacturer's instructions, and applied over the bone graft. The calcium sulfate was contained by the buccal and palatal/lingual flaps. A second set of criss-cross sutures was placed over the barrier after it had completely set. Patients were given naproxen 375 mg (Geneva Pharmaceuticals, Inc. Broomfield, CO), one tab q 12 h, doxycycline hyclate 50 mg (Warner Chilcott Inc. Morris Planes, New Jersey), 1 tab qd, chlorhexidine 0.12% (Colgate Oral Pharmaceutical Canton, Massachusetts), twice daily, and analgesics as needed.

At 4 months, another standardized radiograph was taken. All baseline measurements were repeated along with all soft tissue measurements using the SDM gingival thickness meter at the buccal, occlusal, and palatal/lingual aspects of the edentulous ridge. Patients were again anesthetized with 2% lidocaine containing both 1:100,000 and 1:50,000 concentrations of epinephrine, and full-thickness, mucoperiosteal flaps were elevated on the buccal and palatal/lingual. Papilla were again preserved and not included in the flap design. The acrylic stent was placed and measurements were obtained of vertical ridge height relative to the stent. The digital caliper was used to

measure alveolar ridge width at the mid-buccal crestal sites and 5 mm apical to the crest. A blinded examiners performed all clinical measurements for both the initial and final data collection points.

A 2.0 X 6 mm trephine (H & H Company Ontario, California) was used with copious chilled irrigation to remove a trephine core from the experimental or control site. The osseous core was removed from the trephine using a periodontal probe that was placed into a window and elevated. The core was subsequently placed directly into a bottle of 10% buffered formalin for histologic preservation. An osteotomy site was then prepared with a surgical handpiece, using copious irrigation, and each patient received an endosseous root form dental implant. Flaps were replaced, and sutured with 4-0 silk sutures. Patients were again given naproxen 375 mg, doxycycline hyclate 50 mg and analgesics as needed.

Histologic analysis. Trephine cores (2.0 X 6 mm) were decalcified, sectioned and prepared for histologic analysis using hematoxylin and eosin staining. 12 to 15 step serial sections were taken from the center of each longitudinally sectioned trephine core. 6 randomly selected fields, 1 per slide if possible, were used to obtain percent cellular bone, acellular bone, and trabecular space using an American Optics® light microscope at 150X, with a 10X objective and Nikon® 15X reticle eyepieces (Appendix G).

Statistical analysis. For the statistical analysis, a two-way ANOVA test was used to evaluate the statistical significance of the following:

- the differences between the two treatment groups

- the differences between the initial and 4-month osseous tissue measurements, as well as, the clinical indices.

Independent groups t-test was performed for the histomorphometric analysis.

CHAPTER III

RESULTS

A total of 16 females and 8 males with a mean age of 55.0 ± 14.4, ranging from 26 to 78, were enrolled. The flap group consisted of 1 maxillary central incisor, 7 maxillary premolars, 1 mandibular central incisor, 1 mandibular canine, and 2 mandibular premolars. The flapless group consisted of 5 maxillary incisors, and 7 maxillary premolars. There were 2 smokers in the flap group and 6 in the flapless group. Smokers were excluded if they smoked more than 1 pack per day.

Clinical Indices. Plaque index, gingival index and bleeding on probing for both the flap and flapless group had low initial values that changed only slightly by the 4 month reentry ($p > 0.05$, Table 13). There were no statistically significant differences between the flap and flapless groups for these indices ($p > 0.05$).

Horizontal Alveolar Ridge Width Changes. Flap cases had a mean initial width at the crest of 8.5 ± 1.5 mm, which decreased to 7.5 ± 1.5 mm at the 4 month reentry for a significant mean loss of 1.0 ± 1.1 mm ($p < 0.05$, Table 12). Flapless cases presented with a mean initial width at the crest of 8.3 ± 1.3 mm, which decreased to 7.0 ± 1.9 mm at the 4 month reentry for a significant mean loss of 1.3 ± 1.0 ($p < 0.05$). Flap cases presented with a mean width 5 mm apical to the crest of 9.2 ± 1.6 mm, which decreased to 8.6 ± 1.4 mm for a mean loss of 0.6 ± 1.0 ($p > 0.05$). There were no ridge width measurements 5

mm apical to the crest for the flapless group at baseline. At the 4-month reentry, flapless cases had a mean width 5 mm apical to the crest of 8.0 ± 1.6 mm. There were no statistically significance differences between flap and flapless groups at the crest or at 5 mm apical to the crest ($p > 0.05$).

Change in mid-Facial Vertical Height. Over a period of 4 months, the flap group showed a statistically significant decrease in the mean facial height of 0.9 ± 1.3 mm ($p < 0.05$). In the flapless group, there was a statistically significant mean loss of facial height of 0.5 ± 0.9 mm ($p < 0.05$). There were no statistically significant differences in mean facial height between the flap and flapless groups ($p > 0.05$). Refer to Table 13.

Change in mid-Lingual Vertical Height. Lingual height in the flap group showed a statistically significant mean loss of 0.9 ± 1.3 mm (($p < 0.05$, Table 13). The flapless group had a mean loss of 0.7 ± 1.1 mm ($p < 0.05$). There were no statistically significant differences in lingual height between the flap and flapless groups ($p > 0.05$).

Change in Mesial and Distal Vertical Height. Mesial height in the flap group decreased 0.8 ± 0.8 mm while the distal crest lost 0.9 ± 0.7 mm ($p < 0.05$, Table 13). In the flapless group, the mean mesial height decreased 0.2 ± 0.5 mm while the distal height lost 0.3 ± 0.7 mm ($p < 0.05$). There were no statistically significant differences between the flap and flapless groups for either mesial or distal height ($p > 0.05$).

Histologic evaluation. A high percentage of vital bone was found in both groups (Table 14). Histologic analysis revealed that flap sites healed with 35 ± 15% vital bone, 19 ± 12% non-vital bone, 46 ± 17% trabecular space. The flapless FDBA sites healed

with 44 ± 10% vital bone, 17 ± 13% non-vital bone, 39 ± 9% trabecular space. Between the two groups there was no statistical significance ($p > 0.05$).

Implant placement. Implants were successfully placed at all treated sites for the flapless group. Implant placement was delayed at two sites in the flap group: One site needed sinus augmentation prior to implant placement while the other required restorative work on adjacent teeth prior to implant placement.

Bone quality. Bone quality was assessed subjectively as Type I through IV for all sites (Lekholm and Zarb, 1981). The flap group was comprised of one Type I, two Type II, eight Type III, and one Type IV sites. The flapless group consisted of one Type I, seven Type II, three Type III, and one Type IV sites (Table 16).

Soft Tissue Thickness. Soft tissue thickness increased from 0.1 to 0.4 mm on the facial and lingual for both the flap and flapless groups (Table 15). This increase was statistically significant only on the lingual for both groups ($p < 0.05$). In the flapless group the occlusal soft tissue was significantly thicker than the flap group at the 4 month reentry ($p < 0.05$).

Table 11

Clinical Indices for Flap and Flapless Sites

Mean ± sd in index units

		Initial	Final	Change
Plaque	Flap	0.1 ± 0.2	0.2 ± 0.2	-0.1 ± 0.2
Index	Flapless	0.1 ± 0.2	0.0 ± 0.1	0.1 ± 0.2
Gingival	Flap	0.1 ± 0.1	0.0 ± 0.0	0.1 ± 0.1
Index	Flapless	0.1 ± 0.2	0.0 ± 0.1	0.1 ± 0.2
Bleeding on Probing	Flap	0.2 ± 0.2	0.1 ± 0.2	0.1 ± 0.3
	Flapless	0.2 ± 0.3	0.1 ± 0.2	0.1 ± 0.2

Table 12

Horizontal Ridge Width for Flap and Flapless Sites

Mean ± sd in mm

	Initial	Final	Change	Range
Flap at Crest	8.5 ± 1.5	7.5 ± 1.5	-1.0 ± 1.1*	-2.5 to -0.9
Flapless at Crest	8.3 ± 1.3	7.0 ± 1.9	-1.3 ± 1.0*	-2.7 to +0.5
Flap at 5 mm	9.2 ± 1.6	8.6 ± 1.4	-0.6 ± 1.0	-2.5 to 1.5
Flapless at 5 mm		8.0 ± 1.6		

* = $p < 0.05$ between initial and 4-month values

Table 13

Vertical Ridge Height Change for Flap and Flapless Sites

Mean ± sd in mm

Location	Flap	Flapless	Flap	Flapless
	Mean Change ± sd in mm		Range in mm	
Mid-Buccal	-0.9 ± 1.3*	-0.5 ± 0.9*	-2.5 to 2.5	-2.0 to 1.0
Mid-Lingual	-0.9 ± 1.3*	-0.7 ± 1.1*	-2.5 to 1.0	-2.5 to 1.5
Mesial	-0.8 ± 0.8*	-0.2 ± 0.5*	-2.2 to 0.5	-1.0 to 0.7
Distal	-0.9 ± 0.7*	-0.3 ± 0.7*	-1.8 to 0.2	-1.8 to 1.0

* = $p < 0.05$ between initial and 4-month values

Table 14

Histologic Data at Implant Placement for Flap and Flapless Sites

Mean ± sd

Group	Time	n	% Vital	% Non-vital	% Trabecular
Flap	4 month	12	35 ± 15	19 ± 12	46 ± 17
Flapless	4 month	12	44 ± 10	17 ± 13	39 ± 9

Table 15

Soft Tissue Thickness Change for Flap and Flapless Sites

Mean ± sd in mm

	Initial	Final	Change	Range
Flap				
Buccal	1.1 ± 0.5	1.3 ± 0.6	0.2 ± 0.7	-1.2 ± 1.4
Lingual	2.0 ± 1.0	2.3 ± 1.3	0.3 ± 0.7*	-1.4 ± 1.6
Occlusal		1.7 ± 0.5		1.2 ± 2.9
Flapless				
Buccal	0.9 ± 0.4	1.0 ± 0.4	0.1 ± 0.3	-0.4 ± 0.6
Lingual	2.3 ± 0.5	2.7 ± 0.5	0.4 ± 0.5*	-.0.6 ± 1.3
Occlusal		2.3 ± 0.8+		0.8 ± 3.1

* = $p < 0.05$ between initial and 4-month values

+ = $p < 0.05$ between flap and flapless groups

Table 16

Bone Quality at Implant Placement

	n	Type 1	Type 2	Type 3	Type 4
Flap	12	1	2	8	1
Flapless	12	1	7	3	1

Table 17

CEJ to Osseous Crest Change at Adjacent Teeth

Mean ± sd in mm

	n	Initial	Final	Change
Flap				
Mesial	11	3.8 ± 1.8	4.1 ± 1.4	-0.3 to 1.1
Distal	9	4.3 ± 1.0	4.2 ± 1.5	0.1 to 1.0
Flapless				
Mesial	12	3.6 ± 0.9	3.8 ± 0.8	-0.2 to 0.7
Distal	10	4.2 ± 1.5	4.3 ± 1.5	-0.1 to 0.9

Table 18

Tooth Type Analysis of Crestal Width Change from 4 U of L Ridge Preservation Studies*

Mean ± sd in mm

Tooth Type	n	Initial	Final	Change
Maxillary Incisor	19	7.8 ± 1.0	6.3 ± 1.3	-1.5 ± 1.0
Mandibular Incisor	1	6.1	5.1	-1.0
Maxillary Canine	4	8.8 ± 0.9	7.3 ± 1.9	-1.5 ± 1.0
Mandibular Canine	2	7.9 ± 2.6	8.1 ± 2.3	0.2 ± 0.2
Maxillary Premolar	51	9.5 ± 1.1	8.4 ± 1.3	-1.1 ± 1.1
Mandibular Premolar	9	8.4 ± 1.4	7.9 ± 1.0	-0.5 ± 0.9

*Iasella, Vance, Adams, Siu

Table 19

Comparison of Histologic Data from Three Studies

Mean ± sd

Study	Treatment	Time	n	% Vital	% Non-vital	% Trabecular	% Amorphous
	FDBA/BioMend	4 - 6 mo	12	28 ± 14	37 ± 18	26 ± 11	9 ± 6
Iasella et al.							
2003	Extraction Alone	4 - 6 mo	10	54 ± 12	*	34 ± 12	12 ± 9
	Calmatrix	4 mo	12	61 ± 9	3 ± 3	32 ± 10	4 ± 4
Vance et al							
2004	BioOss	4 mo	12	26 ± 20	16 ± 7	54 ± 15	4 ± 6
	Block	4 mo	8	33 ± 25	24 ± 18	38 ± 15	4 ± 4
Cordini et al.							
2005	DBM	4 mo	2	56 ± 9	5 ± 5	37 ± 5	1 ± 2

* = No non-vtal bone present since there was no graft placed

CHAPTER IV

DISCUSSION

In this 4 month randomized, controlled, blinded clinical study of ridge preservation a flapless technique was compared to a flap reflection technique. For both groups the socket was grafted using a mineralized particulate allograft mixed with a demineralized bone matrix plug allograft and a calcium sulfate barrier. There were no statistically significant differences in ridge dimension changes between groups although there was a trend toward slightly less loss of ridge height for the flapless group.

In this study there were no statistically significant differences in the change in horizontal ridge width between groups. The flapless group showed a loss in ridge width of 1.3 mm, which was slightly greater than the flap group of 1.0 mm.

Ridge preservation studies show substantially improved final ridge dimensions when compared to treatment by extraction alone (Lekovic et al. 1997, Lekovic et al. 1998, Iasella et al 2003). Extraction alone most often leads to extensive ridge resorption. In general, the longer the time period studied, the greater the ridge resorption reported (Lekovic et al. 1997, Lekovic et al. 1998, Schropp et al. 2003, Iasella et al. 2003). The ridge width dimension is compromised to a greater degree than ridge height that, in general, is minimally affected. Ridge preservation does not totally eliminate loss of ridge width and most studies show that some minimal loss still occurs.

This study showed more loss of ridge dimension with a preservation procedure than 2 of the earlier studies at this institution (Iasella et al. 2003, Vance et al. 2004), but less than one previous study (Adams et al. 2006, Table 20). This intermediary result may be due to the number of maxillary incisor and canine sites treated. Iasella et al. (2003) included 4 maxillary anteriors, Vance et al. (2004) included 3, and Adams et al. (2006) included 10. This study included a total of six, 1 in the flap group and 5 in the flapless group. In general, maxillary incisor or canine sites tend to have less initial and final ridge width than the maxillary and mandibular premolars we have previously tested. All of the sites in this study that ended with compromised crestal ridge width were of the maxillary incisor or canine tooth type. They also had resorption near the maximum end of the range. Additional studies of incisor and canine tooth types are needed to determine the best treatment for these sites.

Both groups lost ridge height at all locations (mid-buccal, mid-lingual, mesial and distal). Although these changes were not statistically significant between groups, the flapless group showed less loss of ridge height than the flap group. The flap group showed a loss of ridge height of about 0.8-0.9 mm at all locations. The flapless group showed the greatest loss at the mid-lingual site (0.7 mm), and the least at the mesial site (0.2 mm, Table 13).

Trephine cores were taken from the center of the grafted socket at 4 months for histomorphometric analysis. There was about 40% vital bone and 18% non-vital bone (residual graft particles) in each group with no statistically significant difference between groups (Table 14). This is consistent with previous reports of the 4 to 6 month histologic

composition of the ridge following placement of FDBA into grafted sockets (Iasella et al 2003, Adams et al. 2006, Table 19).

The soft tissue increased in thickness by a mean of 0.2 mm in both groups (Table 15). An increase in soft tissue thickness may provide better protection for the graft and, ultimately, better implant esthetics by providing a thicker soft tissue cover to hide any show through of metallic color.

The degree of undercut was a significant factor in determining whether the implant was placed totally within bone. The greater the degree of undercut, the more likely that the implant placement would be compromised by bone dehiscence or fenestration. Approximately 50% of the flapless group had a fenestration while none of the flap group was affected. This was due, in part, to the option to graft the undercut area. Four undercut areas in the flap group received an overlay graft. That option was not available for the flapless group leading to the greater incidence of fenestration. This problem occurred at 4 sites in the maxillary anterior area and 2 sites in the premolar area. The undercut may lead to fenestration of the implant, even if there is adequate crestal ridge width to allow for implant placement. When the undercut is severe a substantial portion of the implant may not be within bone.

Implant placement was delayed at two sites (a maxillary premolar and a mandibular premolar) in this study. One site needed sinus augmentation prior to implant placement while the other required restorative work on adjacent teeth prior to implant placement.

This study evaluated loss of crestal width in extraction sites with at least one adjacent tooth. Eighteen of 24 sites had 2 adjacent teeth. Loss of crestal width may be

greater when there are no adjacent teeth, especially when all teeth in an arch are being removed. Thus the means and ranges reported in this study may not be generalizable and should be limited in application to sites with adjacent teeth. Further study is warranted to document the resorptive response when an arch is edentulated.

Based on the results of this study, the changes in ridge dimensions did not show any statistically significant differences between the flap or flapless ridge preservation techniques. Frequency data, however, indicated that the flapless ridge preservation technique is most appropriate in sites not affected by an undercut. Thus, as with most procedures, there are indications and contraindications, for use of the flapless technique. The flapless approach is best suited to sites without an undercut, while a flap reflection approach permits grafting of the undercut. If the goal is to place an implant totally within bone, the degree of undercut should be considered when choosing a ridge preservation technique.

CHAPTER V

CONCLUSIONS

Within the limits of this study design it may be concluded that:

1) Crestal ridge width was preserved to the extent that an implant could be placed for both the flap and flapless groups. There were no statistically significant differences ($p < 0.05$) between the two groups.

2) Loss of ridge height was clinically insignificant and less than 1 mm for both groups. There were no statistically significant differences between the two groups.

3) The percentage of vital and nonvital bone was similar for both groups and there were no statistically significant differences ($p > 0.05$) between groups.

4) Soft tissue thickness was increased for all surfaces (facial, lingual and occlusal). The increase was statistically significant only for the lingual. There was a statistically significant difference between groups ($p < 0.05$) only for the occlusal surface.

5) There was a greater incidence of implant fenestration (6 of 12) for the flapless group while there was no fenestration in the flap group.

Table 20

Horizontal Ridge Width Loss from previous U of L studies

Mean ± sd in mm

	Initial	Final	Change
Iasella FDBA	9.2 ± 1.2	8.0 ± 1.4	-1.2 ± 0.9
Vance Calmatrix	8.9 ± 1.8	8.4 ± 1.5	-0.5 ± 0.7
Vance BioGide/BioOss	9.7 ± 1.1	9.2 ± 1.1	-0.5 ± 0.8
Adams Intra FDBA	9.4 ± 1.2	7.4 ± 1.5	-2.0 ± 0.9*
Adams Overlay FDBA	8.5 ± 1.0	7.1 ± 1.2	-1.4 ± 1.0*
Siu Flap DBM	8.5 ± 1.5	7.5 ± 1.5	-1.0 ± 1.1*
Siu Flapless DBM	8.3 ± 1.3	7.0 ± 1.9	-1.3 ± 1.0*

* = $p < 0.05$ between initial and 4-month values

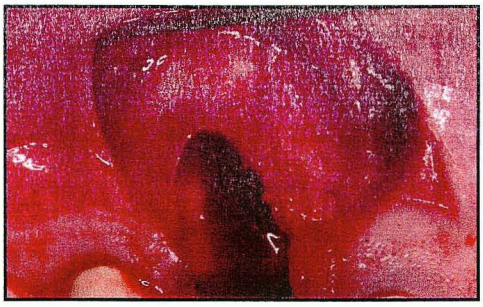
Table 21

Soft Tissue Thickness changes in Ridge Preservation/Augmentation Sites

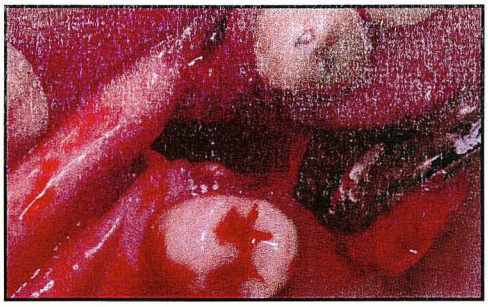
Mean ± sd in mm

Study/Yr	Treatment	B	O	L
Iasella 03	Extr	0.4		0.5
Vance 04	Calmatrix	0.1		-0.1
Kirkland 00	Guidor	-1.1	-1.5	-0.8
Iasella 03	Biomend Ext	-0.1		-0.6
Vance 04	BioGide	-0.2		0.0
Cordini	ADMg-Block	0.3	0.5	0.3
Cordini	ADMg-Flex	0.6	0.0	0.1
Lahey	ADM-Block	0.3	0.8	0.4
Lahey	ADM-Partic	0.6	0.3	0.3
Adams	ADM-Intra	0.9		0.8
Adams	ADM-In-Ov	0.7		0.8
Siu	Flap FDBA	0.2		0.3
Siu	Flapless FDBA	0.1		0.4

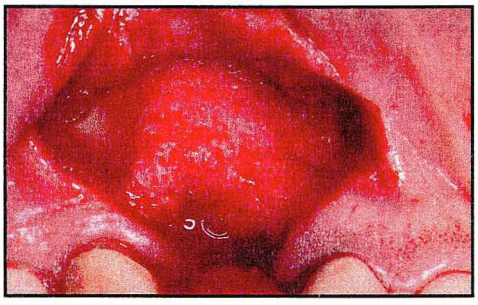
Figure 2. Flap Case #1



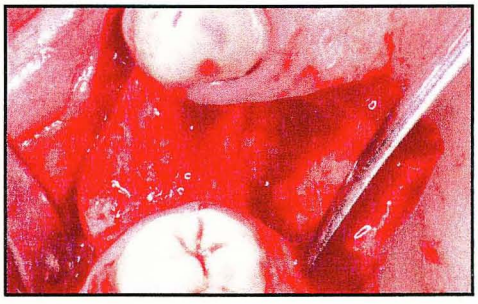
a) Post-Extraction Facial



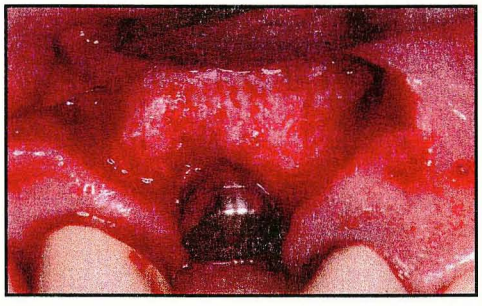
b) Post-Extraction Occlusal



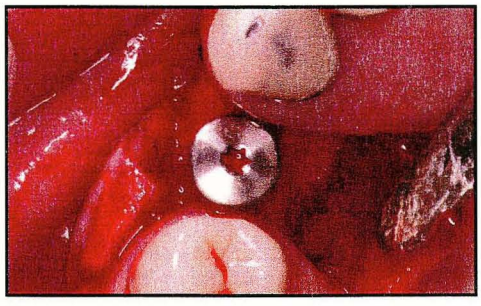
c) Ridge at Reentry Buccal



d) Ridge at Reentry Occlusal

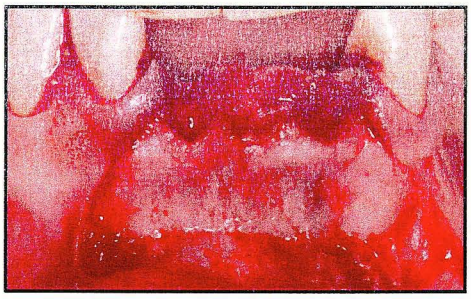


e) Implant Placement Facial

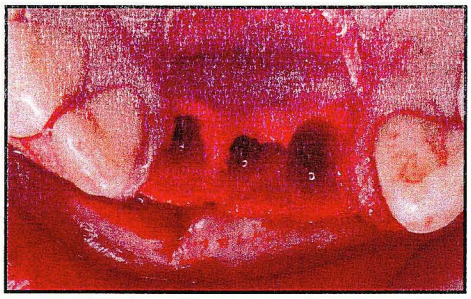


f) Implant Placement Occlusal

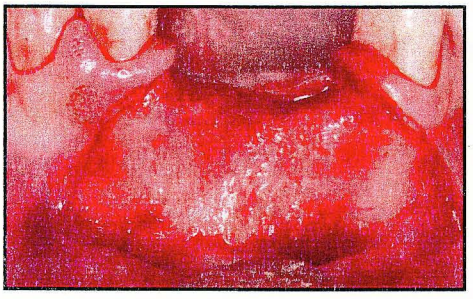
Figure 3. Flap Case #2



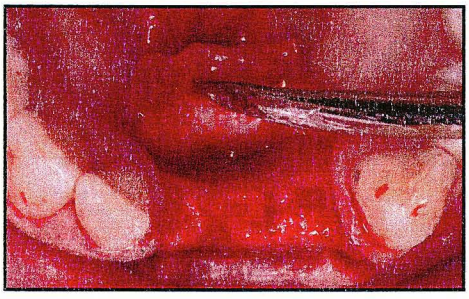
a) Post-Extraction Facial



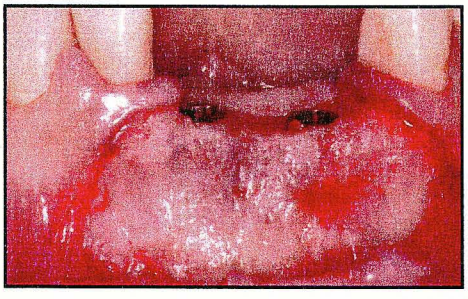
b) Post-Extraction Occlusal



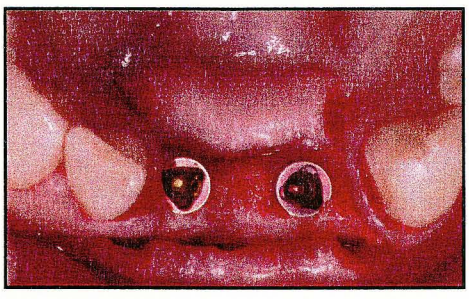
c) Ridge at Reentry Buccal



d) Ridge at Reentry Occlusal

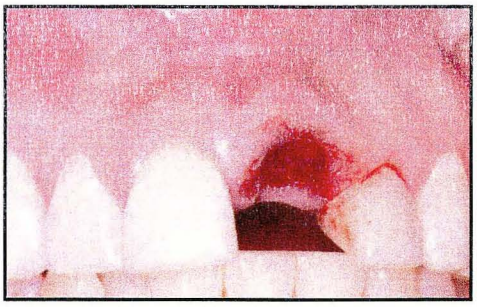


e) Implant Placement Facial

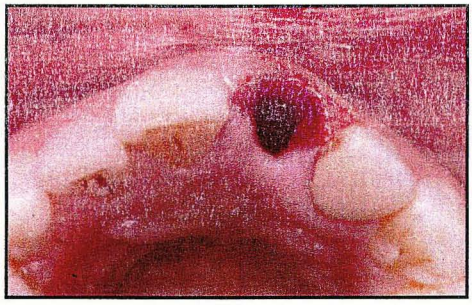


f) Implant Placement Occlusal

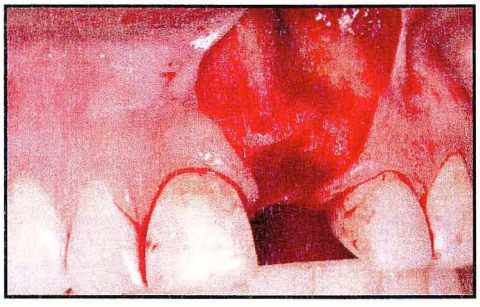
Figure 3. Flapless Case #1



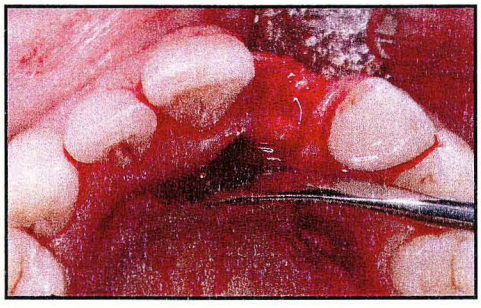
a) Post-Extraction Facial



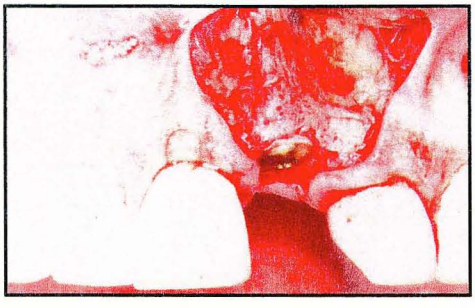
b) Post-Extraction Occlusal



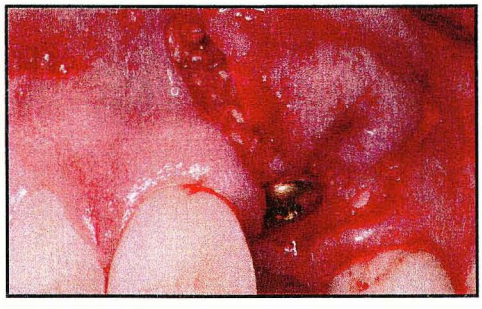
c) Ridge at Reentry Buccal



d) Ridge at Reentry Occlusal

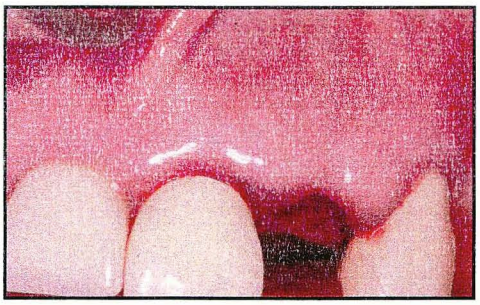


e) Implant Placement Facial



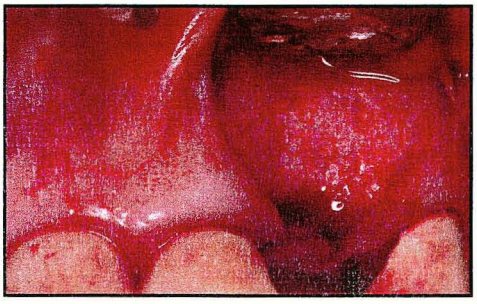
f) Implant Placement Occlusal

Figure 4. Flapless Case #2

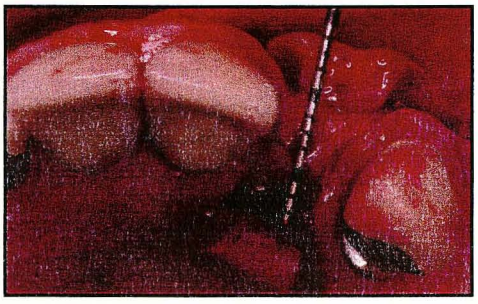


a) Post-Extraction Facial

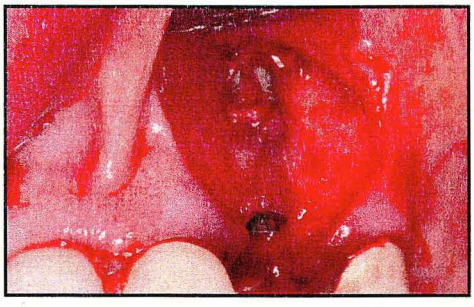
b) Post-Extraction Occlusal



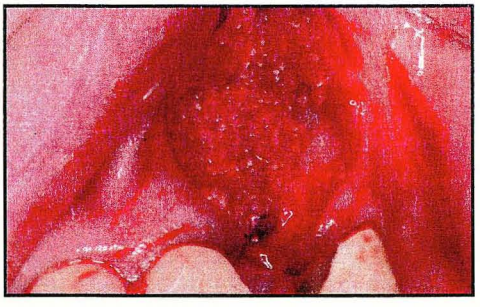
c) Ridge at Reentry Buccal



d) Ridge at Reentry Occlusal



e) Implant Facial & Fenestration



f) Graft & Collagen Membrane

REFERENCES

Amler MH, Johnson PL, Salaman I. Histologic and histochemical investigation of human alveolar socket healing in undisturbed extraction wounds. J Am Dent Assoc 1960;6:132-144.

Araujo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. J Clin Periodontol 2005;32(2):212-218

Araujo MG, Sonohara M, Hayacibara R, Cardaropoli G, Lindhe J. Lateral ridge augmentation by the use of grafts comprised of autologous bone or a biomaterial. An experiment in the dog. J Clin Periodontol 2002;29(12):1122-1131

Araujo MG, Sukekava F, Wennstrom JL, Lindhe J. Ridge alterations following implant placement in fresh extraction sockets: an experimental study in the dog. J Clin Periodontol 2005;32(6):645-652

Artzi Z, Nemcovsky CE. The application of deproteinized bovine bone mineral for ridge preservation prior to implantation. Clinical and histological observations in a case report. J Periodontol 1998;69(9):1062-1067.

Artzi Z, Tal H, Dayan D. Porous bovine bone mineral in healing of human extraction sockets: Part 1: histomorphometric evaluations at 9 months. J Periodontol 2000;71(6):1015-1023

Artzi Z, Tal H, Dayan D. Pourous bovine bone mineral in healing of human extraction sockets: 2. Histochemical observations at 9 months. J Periodontol 2001:72(2):152-159.

Ashman A. Postextraction ridge preservation using a synthetic alloplast. Implant Dent 2000;9(2):168-176.

Ashman A, Lopinto J. Placement of implants into ridges grafted with bioplant HTR synthetic bone: histological long-term case history reports. J Oral Implantol 2000;26(4):276-290

Bahat O, Deeb C, Golden T, Komarnyckij O. Preservation of ridges utilizing hydroxyapatite. Int J Periodontics Restorative Dent 1987;7(6):34-41

Bartee BK. Extraction site reconstruction for alveolar ridge preservation. Part 2: membrane-assisted surgical technique. J Oral Implantol 2001;27(4):194-197

Bartee BK. Extraction site reconstruction for alveolar ridge preservation. Part 1: rationale and materials selection. J Oral Implantol 2001;27(4):187-193

Becker W, Becker BE, Caffesse R. A comparison of demineralized freeze-dried bone and autologous bone to induce bone formation in human extraction sockets. J Periodontol 1994;65(12):1128-1133.

Becker W, Clokie C, Sennerby L, Urist MR, Becker BE. Histologic findings after implantation and evaluation of different grafting materials and titanium micro screws into extraction sockets. Case Reports. J Periodontol 1998;69(4):414-421.

Becker W, Schenk R, Higuchi K, Lekholm U, Becker B. Variations in bone regeneration adjacent to implants augmented with barrier membranes alone or with demineralized freeze-dried bone or autologous grafts: A study in dogs. Int J Oral Maxillofac Implants 1995;10(2):143-154.

Becker W, Urist M, Becker BE, Jackson W, Parry DA, Bartold M, Vincenzzi G, De Georges D, Niederwanger M. Clinical and histologic observations of sites implanted with intraoral autologous bone grafts or allografts. 15 human case reports. J Periodontol 1996;67(10):1025-1033.

Becker W, Urist MR, Tucker LM, Becker BE, Ochsenbein C. Human demineralized freeze-dried bone: inadequate induced bone formation in athymic mice. A preliminary report. J Periodontol 1995;66(9):822-828.

Berglundh T, Lindhe J, Jonsson K, Ericsson I. The topography of the vascular systems in the periodontal and peri-implant tissues in the dog. J Clin Periodontol 1994;21(3):189-193

Bernard G. Healing and repair of osseous defects. Dent Clin North Am 1991;35(3):469-478.

Botticelli D, Berglundh T, Lindhe J. Resolution of bone defects of varying dimension and configuration in the marginal portion of the peri-implant bone. An experimental study in the dog. J Clin Periodontol 2004;31(4):309-317

Botticelli D, Berglundh T, Persson LG, Lindhe J. Bone regeneration at implants with turned or rough surfaces in self-contained defects. An experimental study in the dog. J Clin Periodontol 2005;32(5):448-455

Boyne PJ. Osseous repair of the postextraction alveolus in man. Oral Surg Oral Med Oral Pathol 1966;21(6):805-813.

Brugnami F, Then PR, Moroi H, Kabani S, Leone CW. GBR in human extraction sockets and ridge defects prior to implant placement: Clinical results and histologic evidence of osteoblastic and osteoclastic activities in DFDBA. Int J Periodontics Restorative Dent 1999;19(3):259-268.

Brugnami F, Then PR, Moroi H, Leone CW. Histologic evaluation of human extraction sockets treated with demineralized freeze-dried bone allograft (DFDBA) and cell occlusive membrane. J Periodontol 1996;67(7):821-825.

Bunyaratavej P, Wang HL. Collagen membranes: A review. J Periodontol 2001;72(2):215-229.

Buser D, Dula K, Hess D, Hirt HP, Belser UC. Localized ridge augmentation with autografts and barrier membranes. Periodontol 2000 1999;19(2):151-163.

Camargo PM, Lekovic V, Weinlaender M, Klokkevold PR, Kenney EB, Dimitrijevic B, Nedic M, Jancovic S, Orsini M. Influence of bioactive glass on changes in alveolar process dimensions after exodontia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90(5):581-586

Cardaropoli G, Araujo M, Lindhe J. Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs. J Clin Periodontol 2003;30(9):809-818.

Cardaropoli G, Araujo MG, Hayacibara R, Sukekava F, Lindhe J. Healing of extraction sockets and surgically produced - augmented and non-sugmented - defects in the alveolar ridge. An experimental study in the dog. J Clin Periodontol 2005;32(5):435-440

Carmagnola D, Berglundh T, Araujo M, Albrektsson T, Lindhe J. Bone healing around implants placed in a jaw defect augmented with Bio-Oss. An experimental study in dogs. J Clin Peridontol 2000;27(11):799-805.

Carmagnola D, Berglundh T, Lindhe J. The effect of a fibrin glue on the integration of BioOss® with bone tissue. J Clin Periodontol 2002;29(5):377-383

Clafin R. Healing of disturbed and undisturbed extraction sites. J Am Dent Assoc 1936;23(6):945-959.

Cohen H. Localized ridge augmentation with hydroxylapatite. Report of a case. J Am Dent Assoc 1984;108(1):54-56.

Cordini F. Ridge augmentation comparing cancellous block allograft to demineralized bone matrix and utilizing an acellular dermal matrix as a barrier membrane. [Thesis]. 2004. Louisville, Kentucky. University of Louisville.

De Leonardis D, Pecora GE. Prospective study on the augmentation of the maxillary sinus with calcium sulfate: Histological results. J Periodontol 2000; 71(6):940-947.

de Wijs F, de Putter C, de Lange G, de Groot K. Localized residual ridge augmentation with solid hydroxyapatite blocks: Part I - an animal experiment. J Prosthet Dent 1993;69(5):510-513.

Devlin H, Ferguson MJ. Alveolar ridge resorption and mandibular atrophy. A review of the role of local and systemin factors. Br Dent J 1991;170;101-104.

Doblin JM, Salkin LM, Mellado JR, Freedman AL, Stein MD. A histologic evaluation of localized ridge augmentation utilizing DFDBA in combination with e-PTFE membranes and stainless steel bone pins in humans. Int J Periodontics Restorative Dent 1996;16(2):121-130.

Dragoo MR, Sullivan HC. A clinical and histological evaluation of autogenous iliac bone grafts in humans. Part I. Wound healing 2 to 8 months. J Periodontol 1973; 44(10):599-613.

Evian C, Rosenberg E, Coslet J, Corn H. The osteogenic activity of bone removed from healing extraction sockets in humans. J Periodontol 1982;53(2):81-85.

Fiorellini JP, Nevins ML Localized ridge augmentation/preservation. A systematic review Ann Periodontol 2003;8(1):321-327

Fowler EB, Breault LG, Rebitski G. Ridge preservation utilizing an acellular dermal allograft and demineralized freeze-dried bone allograft: Part I. A report of 2 cases. J Periodontol 2000;71(8):1353-1359.

Fowler EB, Breault LG, Rebitski G. Ridge preservation utilizing an acellular dermal allograft and demineralized freeze-dried bone allograft: Part II. Immediate Endosseous Implant Placement. J Periodontol 2000;71(8):1360-1364.

Froum S, Cho S, Rosenberg E, Rohrer M, Tarnow D. Histologic Comparison of Healing Extraction Sockets Implanted With Bioactive Glass or Demineralized Freeze-Dried Bone Allograft: A Pilot Study. J Periodontol 2002;73(1):94-102.

Froum S, Cho SC, Elian N, Rosenberg E, Rohrer M, Tarnow D. Extraction sockets and Implantation of Hydroxyapatites with membrane barriers a histologic study. Implant Dent 2004;13(2):153-161.

Froum S, Orlowski W. Ridge preservation utilizing an alloplast prior to implant placement-clinical and histological case reports. Pract Periodontics Aesthet Dent 2000;12(4):393-402.

Ganz SD, Valen M. Predictable synthetic bone grafting procedures for implant reconstruction: part two J Oral Implantol 2002;28(4):178-183

Garg AK. Alveolar ridge preservation during and after surgical tooth removal. Dent Implantol Update 2001;11(8):57-62.

Greenwell H, Vance G, Munninger B, Johnston H. Superficial-layer split-thickness flap for maximal flap release and coronal positioning: A surgical technique. Int J Periodontics Restorative Dent 2004;24(6):521-527.

Grobler V. The history of dentistry in South Africa 1652-1900. Thesis, University of Pretoria, May 1974.

Gross J Ridge preservation using HTR synthetic bone following tooth extraction. Gen Dent 1995;43(4):364-367

Guarnieri R, Pecora G, Fini M, Nicoli Aldini N, Giardino R, Orsini G, Piattelli A. Medical grade calcium sulfate hemihydrate in healing of human extraction sockets: Clinical and histological observations at 3 months. J Periodontol 2004;75(5):902-908.

Hoexter DL. Osseous regeneration in compromised extraction sites: A ten year case study. J Oral Implantol 2002;28(1):19-24

Hollinger J, Wong ME. The integrated processes of hard tissue regeneration with special emphasis on fracture healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;82(6):594-606

Horowitz RA. Extraction environment enhancement: critical evaluation of early socket healing in long-term barrier-protected extraction sockets. Compend Contin Educ Dent 2005;26(10):703-713

Howell TH, Fiorellini J, Jones A, Alder M, Nummikoski P, Lazaro M, Lilly L, Cochran D. A feasibility study evaluating rhBMP-2/absorbable collagen sponge device for local alveolar ridge preservation or augmentation. Int J Periodontics Restorative Dent 1997;17(2):125-140.

Iasella JM, Greenwell H, Miller RL, Hill M, Drisko C, Bohra AA, Scheetz JP. Ridge preservation with freeze dried bone allograft and a collagen membrane compared to extraction alone for implant site development: A clinical and histologic study in humans. J Periodontol 2003;74(7):988-997.

Iasella JM, Greenwell H, Miller RL, Hill M, Drisko C, Bohra AA, Scheetz JP. Ridge Preservation with freeze-dried bone allograft and a collagen membrane compared to extraction alone for implant site development: A clinical and histologic study in humans. J Periodontol 2003;74(7):990-999.

Keller EE, Tolman DE, Eckert S. Surgical-prosthodontic reconstruction of advanced maxillary bone compromise with autogenous onlay block bone grafts and osseointegrated endosseous implants: A 12-year study of 32 consecutive patients. Int J Oral Maxillofac Implants 1999;14(2):197-209.

Kent JN Reconstruction of the alveolar ridge with hydroxyapatite. Dent Clin North Am 1986;30(2):231-257

Kirkland G, Greenwell H, Drisko C, Wittwer JW, Yancey J, Rebitski G. Hard tissue ridge augmentation using a resorbable membrane and a particulate graft without complete flap closure. Int J Periodontics Restorative Dent 2000;20(4):383-389.

Kleinman H, Klebe R, Martin G. Role of collagenous matrices in the adhesion and growth of cells. J Cell Biol 1981;88:473-485.

Kuboki Y, Hashimoto F, Ishibashi K. Time-dependent changes of collagen crosslinks in the socket after tooth extraction in rabbits. J Dent Res 1988;67(6):944-958

Kwon HJ, el Deeb M, Morstad T, Waite D. Alveolar ridge maintenance with hydroxyapatite ceramic cones in humans. J Oral Maxillofac Surg 1986;44(7):503-508

Lahey B. Ridge augmentation comparing cancellous block allograft to particulate freeze dried bone allograft utilizing an acellular dermal matrix barrier membrane. [Thesis]. 2005. Louisville, Kentucky. University of Louisville.

Landsberg CJ Socket seal surgery combined with immediate implant placement: a novel approach. Int J Periodontics Restorative Dent 1997;17(2):140-149

Lekholm U, Zarb GA. Patient selection and preparation. In Branemark P-I, Zarb GA, Albrektsson T, editors: Tissue integrated prostheses: osseointegration in clinical dentistry. Quintessence Int 1985;199-209.

Lekic PC, Rajshankar D, Chen H, Tenenbaum H, McCulloch CA. Transplantation of labeled periodontal ligament cells promotes regeneration of alveolar bone Anat Rec 2001;262(2):193-202

Lekovic V, Camargo PM, Klokkevold PR, Weinlaender M, Kenney EB, Dimitrijevic B, Nedic M. Preservation of alveolar bone in extraction sockets using bioabsorbable membranes. J Periodontol. 1998;69(9):1044-1049.

Lekovic V, Kenney EB, Weinlaender M, Han T, Klokkevold P, Nedic M, Orsini M. A bone regenerative approach to alveolar ridge maintenance following tooth extraction. Report of 10 cases. J Periodontol 1997;68(6):563-570.

Lin WL, McCulloch CA, Cho MI. Differentiation of periodontal ligament fibroblasts into osteoblasts during socket healing after toth extraction in the rat. Anat Rec 1994; 240(4):492-506

Loe H. The gingival index, the plaque index and the retention index systems. J Periodontol 1967;38(Suppl):610-617.

Luczyszyn SM, Papalexiou V, Novaes AB Jr, Grisi MF, Souza SL, Taba M Jr. Acellular dermal matrix and hydroxyapatite in prevention of ridge deformities after tooth extraction. Implant Dent 2005;14(2):176-184

MacNeill SR, Cobb CM, Rapley JW, Glaros AG, Spencer P. In vivo comparison of synthetic osseous graft materials. A preliminary study. J Clin Periodontol 1999;26(4):239-245.

Marcus SE, Brown LJ, Zion GR. Tooth retention and tooth loss in the permanent dentition of adults: United States, 1988-1991. J Dent Res 1996;75(SI):684-695.

Mellonig J. Decalcified freeze-dried bone allograft as an implant material in human periodontal defects. Int J Periodontics Restorative Dent 1984;6(1):41-55.

Mellonig J. Freeze-Dried bone allografts in periodontal reconstructive surgery. Dent Clin North Am 1991;35(3):505-520.

Mellonig J, Bowers G, Cotton W. Comparison of bone graft materials. Part II. New bone formation with autografts and allografts: A histological evaluation. J Periodontol 1981;52(6):297-302.

Minichetti JC, D'Amore JC, Hong AY, Cleveland DB. Human histologic analysis of mineralized bone allograft (Puros) placement before implant surgery. J Oral Implantol 2004;30(2):74-82.

Minsk L. Extraction-site ridge preservation. Compend Contin Educ Dent 2005;26(4):272, 274-276

Misch C, Misch C, Resnik R, Ismail Y. Reconstruction of maxillary alveolar defects with mandibular symphysis grafts for dental implants: A preliminary procedural report. Int J Oral Maxillofac Implants 1992;7(3):360-366.

Murray VK Anterior ridge preservation and augmentation using a synthetic osseous replacement graft. Compend Contin Educ Dent 1998;19(1):69-74

Nemcovsky CE, Artzi Z. Split palatal flap. I. A surgical approach for primary soft tissue healing in ridge augmentation procedures: Technique and clinical results. Int J Periodontics Restorative Dent 1999;19(2):175-182.

Nemcovsky CE Serfaty V. Alveolar ridge preservation following extraction of maxillary anterior teeth. Report on 23 consecutive cases. J Periodontol 1996;67(4):390-395.

Novaes AB, Souza SL. Acellular dermal matrix graft as a membrane for guided bone regeneration: A case report. Implant Dent 2001;10(3):192-196.

O'Brien TP, Hinrichs JE, Schaffer EM. The prevention of localized ridge deformities using guided tissue regeneration. J Periodontol 1994;65(1):17-24.

Payne J, Cobb C, Rapley J, Killoy W, Spencer P. Migration of human gingival fibroblasts over guided tissue regeneration barrier materials. J Periodontol 1996;67(3):236-244.

Penarrocha M, Garcia-Mira B, Martinez O. Localized vertical maxillary ridge preservation using bone cores and a rotated palatal flap. Int J Oral Maxillofac Implants 2005;20(1):131-134

Piattelli M, Scarano A, Piattelli A.Vertical ridge augmentation using a resorbable membrane: A case report. J Periodontol 1996;67(2):158-161.

Pietrokovski J, Massler M. Alveolar ridge resorption following tooth extraction. J Prosth Dent 1967;17(1):21-27

Pietrokovski J, Sorin S, Hirschfeld Z. The residual ridge in partially edentulous patients. J Prosthet Dent 1976;36(2):150-158.

Pitaru S, Tal H, Soldinger M, Azar-Avidan O, Noff M. Collagen membranes prevent the apical migration of epithelium during periodontal wound healing. J Periodont Res 1987;22(4):331-333.

Quinn JH, Kent JN. Alveolar ridge maintenance with solid nonporous hydroxyapatite root implants. Oral Surg Oral Med Oral Pathol 1984;58(5):511-521

Quinn JH, Kent JN, Hunter RG, Schaffer CM. Preservation of the alveolar ridge with hydroxyapatite tooth root substitutes. J Am Dent Assoc 1985;110(2):189-193

Reynolds MA, Bowers GM. Fate of demineralized freeze-dried bone allografts in human intrabony defects. J Periodontol 1996; 67(2):150-157.

Sandor GK, Kainulainen VT, Queiroz JO, Carmichael RP, Oikarinen KS. Preservation of ridge dimensions following grafting with coral granules of 48 post-traumatic and post-extraction dento-alveolar defects. Dent Traumatol 2003;19(4):221-227

Schallhorn RG, Hiatt WH, Boyce W. Iliac transplants in periodontal therapy. J Periodontol 1970;41(10):566-580.

Schropp L, Wenzel A, Kostopoulos L, Karring T. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12 month prospective study. Int J Periodontics Restorative Dent 2003;23(4):313-323.

Schwartz Z, Mellonig JT, Carnes DL Jr, De La Fontaine J, Cochran DL, Dean DD, Boyan BD. Ability of commercial demineralized freeze-dried bone allograft to induce new bone formation. J Periodontol 1996;67(9):918-926.

Schwartz Z, Somers A, Mellonig JT, Carnes DL, Dean DD, Cochran DL, Boyan BD. Ability of commercial demineralized freeze-dried bone allograft to induce new bone formation is dependent on donor age but not gender. J Periodontol 1998;69(4):470-478.

Schwartz Z, Weesner T, van Dijk S, Cochran DL, Mellonig JT, Lohmann CH, Carnes DL, Goldstein M, Dean DD, Boyan BD. Ability of deproteinized cancellous bovine bone to induce new bone formation. J Periodontol 2000;71(8):1258-1269.

Serino G, Biancu S, Iezzi G, Piatelli A. Ridge preservation following tooth extraction using a polylactide and polyglycolic sponge as space filler: a clinical and histological study in humans. Clin Oral Implants Res 2003;14(5):651-658

Shapoff CA, Bowers GM, Levy B, Mellonig JT, Yukna RA. The effect of particle size on the osteogenic activity of composite grafts of allogeneic freeze-dried bone and autogenous marrow. J Periodontol 1980;51(11):625-630.

Silness J, Löe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal conditions. Acta Odontol Scand 1964;22(1):121-135.

Simion M, Jovanovic SA, Trisi P, Scarano A, Piattelli A. Vertical ridge augmentation around dental implants using a membrane technique and autogenous bone or allografts in humans. Int J Periodontics Restorative Dent 1998;18(1):9-24.

Simon BI, Von Hagen S, Deasy MJ, Faldu M, Resnansky D. Changes in alveolar bone height and width following ridge augmentation using bone graft and membranes. J Periodontol 2000;71(11):1774-1791.

Smukler H, Landi L, Setayesh R. Histomorphometric evaluation of extraction sockets and deficient alveolar ridges treated with allograft and barrier membrane: A pilot study. Int J Oral Maxillofac Implants 1999;14(3):407-416.

Sobolik CF. Alveolar bone resorption. J Prosthet Dent 1960;10:612-619.

Soehren SE, Van Swol RL. The healing extraction site: A donor area for periodontal grafting material. J Periodontol 1979;50(3):128-133.

Sottosanti J. Calcium sulfate: A biodegradable and biocompatible barrier for guided tissue regeneration. Compend Cont Educ Dent 1992;13(3):226-234.

Stentz WC, Mealey BL, Nummikoski PV, Gunsolley JC, Waldrop TC. Effects of guided bone regeneration around commercially pure titanium and hydroxyapatite-coated dental implants. I. Radiographic analysis. J Periodontol 1997;68(3):199-208.

Sy IP Alveolar ridge preservation using a bioactive glass particulate graft in extraction site defects. Gen Dent 2002;50(1):66-68

Tatum OH Jr. Osseous grafts in intra-oral sites. J Oral Implantol 1996;22(1):51-52.

Tawil G, El-Ghoule G, Mawla M. Clinical evaluation of a bilayered collagen membrane (Bio-Gide) supported by autografts in the treatment of bone defects around implants. Int J Oral Max Implants 2001;16:857-863.

Urist MR, Strates BS. Bone morphogenetic protein. J Dent Res 1971;50(9):1392-1406.

Valen M, Ganz SD. A synthetic bioactive resorbable graft for predictable implant reconstruction: part one J Oral Implantol 2002;28(4):167-177

Vance GS, Greenwell H, Miller RL, Hill M, Johnston H, Scheetz JP. Comparison of an allograft in an experimental putty carrier and a bovine-derived xenograft used in ridge preservation: A clinical and histologic study in humans. Int J Oral Maxillofac Implants 2004;19(4):491-497.

Woefel JB Dental Anatomy: Its Relevance to Dentistry. Fourth Edition Book 1990;

Woodyard JG, Greenwell H, Hill M, Drisko C, Iasella JM, Scheetz J. The clinical effect of acellular dermal matrix on gingival thickness and root coverage compared to coronally positioned flap alone. J Periodontol 2004;75(1):44-56.

Yang J, Lee HM, Vernino A. Ridge preservation of dentition with severe periodontitis. Compend Contin Educ Dent 2000;21(7):579-583

Yilmaz S, Efeoglu E, Kilic AR. Alveolar ridge reconstruction and/or preservation using root form bioglass cones J Clin Periodontol 1998;25(10):832-839

Zitzmann NU, Naef R, Scharer P. Resorbable versus nonresorbable membranes in combination with Bio-Oss for guided bone regeneration. Int J Oral Maxillofac Implants 1997;12(3):844-852.

Zitzmann NU, Scharer P, Marinello CP, Schupbach P, Berglundh T. Alveolar rdige augmentation with Bio-Oss: A histologic study in humans. Int J Periodontics Restorative Dent 2001;21(3):289-296.

Zubillaga G, Von Hagen S, Simon BI, Deasy MJ. Changes in alveolar bone height and width following post-extraction ridge augmentation using a fixed bioabsorbable membrane and demineralized freeze-drired bone osteoinducive graft. J Periodontol 2003;74(7):965-975

Appendix A

The Plaque Index

The plaque index of Silness and Loe (1964) will be measured. Scores will be as follow:

0 - No plaque

1 - A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface.

2 - Moderate accumulation of soft deposits within the gingival pocket, or on the tooth and gingival margin, which can be seen with the naked eye.

3 - Abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

Each gingival unit (buccal, lingual, mesiobuccal, distobuccal, mesiolingual, and distolingual) of the individual tooth was given a score from 0-3, called the plaque index for the area. The scores from the 6 areas of the tooth were added and divided by 6 to give the plaque index for the tooth.

Appendix B

Gingival Index

The gingival index of Loe (1967) will be measured for the test and control sites. Scores will be recorded as follows:

0 = Normal gingiva.

1 = Mild inflammation - slight change in color slight edema, no bleeding on probing.

2 = Moderate inflammation - redness, edema, and glazing, bleeding on probing.

3 = Severe inflammation - marked redness and edema, ulceration and tendency to spontaneous bleeding.

Each gingival unit (mesiobuccal, buccal, distobuccal, distolingual, lingual, mesiolingual) of the tooth will be given a score 0-3. The scores for each unit will be added together and divided by 6 to give the gingival index for that tooth. The score of the test tooth and the two adjacent teeth will be added and divided by 3 to give the gingival index for the test of control sites.

Appendix C

Bleeding on Probing Index

Tagge et al. (1975) reported on the use of an index of bleeding upon probing to show the amount of hemorrhage within the periodontal sulcus. The following is the index used to record bleeding on probing:

0 = No bleeding

1 = Mild – a bleeding point appearing 10 to 30 seconds after withdrawing the probe.

2 = Moderate – bleeding when probing produces an almost immediate, but non-continuous bleeding.

3 = Severe – bleeding when gentle probing elicits immediate and continuous bleeding.

Appendix D

Standardized Radiographic technique

An occlusal stent was used to provide a stable foundation for the radiograph holder. A light cured resin material was placed on a Rinn radiograph holder and positioned to allow as near as possible paralleling technique. This material was light cured so that standardized radiographs can be compared. Radiographs were taken at baseline and 4 months.

Appendix E

Arithmetic determinations:

Ridge width (Post-extraction) = A digital caliper was used to measure total ridge width to the nearest 10^{-2} mm at one point, mid socket, at the alveolar crest and 5 mm from the alveolar crest.

Ridge width (4 month re-entry) = Again, a digital caliper measured total ridge width to the nearest 10^{-2} mm at one point, mid socket, at the alveolar crest and 5 mm from the alveolar crest.

Change in alveolar crest - direct = Initial: stent to alveolar crest minus re-entry stent to alveolar crest.

Alveolar Crest Width = Crestal width was measured with digital calipers during the initial surgical appointment and evaluated to determine if a relationship exists between ridge width and height and the thickness of the crestal bone.

Tissue thickness = [Initial: SDM gingival thickness meter 3 mm apical to the soft tissue crest on buccal and palato/lingual] - [4 month SDM gingival thickness meter 3 mm apical to the soft tissue crest on buccal and palato/lingual with the addition of one measurement at the center of the occlusal aspect of the ridge].

Appendix F

Stent fabrication

Rigid stents were made of 3 mm thick light cured resin material in order to provide reproducible measurements. The tooth to be extracted was ground off the model and the light cured resin material was pressed over a cast. Three channels were prepared on the labial and three on the palato/lingual aspect of the stent in which a North Carolina periodontal probe was placed so that mesial, mid and distal measurements could be made on the labial and palato/lingual aspects of the crestal bone. Additionally, two channels were also prepared on the occlusal portion of the stent to provide measures of mesial and distal occlusal ridge height. Holes were prepared with a high-speed hand-piece. In this way, reproducible probing spots and directions of probe insertions were possible.

Appendix G

Histologic Analysis

Ten serial sections from each study subject were stained and made available for histologic analysis. Three slides and two fields per slide (6 fields in total) will be randomly selected from to evaluate the percent vital bone, percent non-vital bone, percent trabecular space, and number of osteoblasts using a reticle (with a 10 X 10 boxed field) at a power of 150X. A box is to be counted as containing a specific histologic tissue if it was filled 90% or more by the respective tissue. The mean percentages of the various histologic components will be tabulated and reported as mean percentages.

CURRICULUM VITAE

Trever Leonard Siu, DMD, MS

EDUCATION

2004-2007 University of Louisville Graduate Periodontics
Certificate in Periodontics

2004-2007 University of Louisville
Master of Science in Oral Biology

2000-2004 Boston University Goldman School of Dental Medicine
Doctor of Dental Medicine (D.M.D.)

1995-1999 University of British Columbia
Bachelor of Science (B.S.) BioChemistry

LICENSURE

August 2005-Present State of Arizona Dental License

June 2004-Present Commonwealth of Kentucky Dental License

Category II Laser certification 2004

DEA licensure granted 2004

CPR certification (valid until June 2008)

ACLS certification (valid until March 2009)

PROFESSIONAL ASSOCIATIONS

Kentucky Dental Association member

Arizona Dental Association member

American Academy of Periodontology member

Academy of Osseointegration member

RESEARCH ACTIVITIES

Siu T, Greenwell H, Hill M, Dib Z, Sheetz J. Ridge Preservation Comparing a Flap versus a Flapless Technique Using Demineralized Bone Matrix Allograft and a Calcium Sulfate Barrier. Submitted for publication.

Dib Z, Greenwell H, Hill M, Siu T, C, Scheetz J. Ridge Augmentation Comparing. Submitted for publication.

EXTERNSHIPS

Anesthesiology Rotation, University of Louisville Hospital May 2005

Internal Medicine Rotation, University of Louisville Hospital June 2005