Master's Thesis

Observation of Changes in Alveolar Bone during the Course of Healing after Guided Bone Regeneration : A Prospective Study in Human

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Thesis submitted in partial fulfillment of the requirement for the degree of Mater of Science

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(Part I) Postoperative Complications Following Guided Bone Regeneration: The use of Double-flap technique

Conventional periosteal fenestration technique is the most commonly used technique for flap advancement in GBR (guided bone regeneration) procedures to achieve tension-free primary closure. However, its limitations include efficacy and morbidity. To overcome such drawbacks of the conventional technique, recently, the double flap-incision technique was reported and is now widely used by the investigators. The objective of the study is to compare the pain/discomfort level and the frequency of postoperative complications including membrane exposure rate (morbidity) as well as the amount of flap advancement (efficacy) between two different techniques.

Patients who needed vertical /horizontal ridge augmentation of partially edentulous upper and lower jaws were included in the study. Periosteal fenestration technique (PFT) was performed in 18 sites and double-flap technique (DFT) was performed in 11 sites by a single operator. The questionnaire regarded postoperative pain, swelling and bleeding one week after GBR procedures using a VAS scale from one to ten scores. Any other complications including membrane exposure, infection and paresthesia were recorded at follow-up visits up to 24 weeks after GBR.

A total of 23 patients with 29 surgical sites were enrolled for the study. The healing during six months period was uneventful in 22 surgical sites. Within the limitations of this study, there were no statistically significant differences in the pain/discomfort level for the patient in the following categories: pain (mean score 1.55 vs. 2.89; P=0.15), swelling (mean score 1.91 vs. 2.78; p=0.074), and bleeding (mean score 0.0 vs. 0.72; P=0.245). The frequency of post-operative complications (9.1% vs. 33.3%; P=0.149)

such as paresthesia, continuous discomfort (membrane dislocation) and the membrane exposure rate (9.1% vs. 11.1%; p= 0.874) were lower in DFT group and than PFT group. The mean flap advancement (mm) of Double-flap technique was significantly greater than the mean flap advancement of the conventional periosteal fenestration technique (9.64 mm vs. 7.13 mm; P=0.025).

Double-flap technique showed comparable clinical performance with conventional periosteal fenestration technique in GBR. Results also indicated that the DFT significantly enhances flap advancement compared to the conventional periosteal fenestration. This new technique can be utilized as an alternative option to the conventional technique.

(Part II) Observations in Alveolar Bone Volume Changes during the course of healing after Guided Bone Regeneration

Clinical observation demonstrates that the amount of initial bone volume created by guided bone regeneration (GBR) does not equal the amount of bone after healing. A review of literature has revealed a loss of alveolar bone width and height during the healing time. In the past literature, one study quantified the changes following GBR using collagen membrane and demineralized freeze-dried bone allograft (DFDBA) indicating significant non-uniform loss of augmented bone. However, none of the studies discussed the amount of bone changes after GBR using an expanded polytetrafluoroethylene (e-PTFE) membrane and freeze-dried bone allograft (FDBA). The objective of this study is to evaluate the changes of alveolar bone volume during the course of 6 months of healing after GBR using FDBA and an e-PTFE membrane.

18 surgical sites requiring vertical/horizontal ridge augmentation of partially edentulous upper and lower jaws prior to dental implant placement were included in the study. By using an acrylic stent as a reference point, the measurements of bone volume were evaluated three times: Original Bone (OB) just before bone grafting, Post GBR (PB) just after GBR, and Healing Bone (HB) six months after GBR. Vertical measurements were recorded at designated implant locations and horizontal measurements were recorded at 3mm, 5mm, and 7 mm from the bone crest at designated implant locations.

The results showed a significant change of alveolar bone volume during the course of 6 months healing following GBR using FDBA and e-PTFE membrane. The mean loss of augmented bone ranged from 4% to 21% during six months healing. There were unpredictable volume changes with vertical dimension and in areas with soft tissue invagination.

Vertical augmentation using FDBA and e-PTFE membrane is successful in maintaining the volume. A close adaptation, stabilization and firm fixation of the membrane are desired in the grafted sites with the non-resorbable membranes. Proper surgical planning is indispensable for clinicians who need to consider accurate over-augmention of alveolar bone to achieve a predictable outcome for GBR.

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PROTOCOL SUMMARY

Title:

I. Observation of changes in alveolar bone during the course of healing after guided bone regeneration

II. Post-Operative Complication Survey Following Guided Bone Regeneration (GBR) Procedures based on the different incision design

Objectives:

The primary objective of this study is to:

- Evaluate to quantitatively evaluate the amount of bone change following alveolar bone augmentation using freeze-dried bone allograft (FDBA) and expanded polytetrafluoroethylene (e-PTFE) membrane.

The secondary objectives of this study are to:

- Compare the post operative complications such as exposure rate, swelling and bleeding based on different incision techniques; the Double flap and periosteal fenestration.

Number of Subjects:

Twenty three human subjects.

Subject Type: Subjects with two to three missing teeth with ridge deformity scheduled to be treated with implant placement.

Study Design and Methodology: Clinical prospective study.

During the study, each subject is required to attend the following study visits: The numbers of visits are the same as standard care with exception of screening visit. If a subject misses day 1, day 7, or day 180, he/she will be automatically excluded for the research and will receive routine care from TUSDM.

- Screening visit
- Phase I visit
- Day 1
- Day 7
- Day 14
- Day 30
- Day 60
- Day 90
- Day 120
- Day 180

Treatment Protocol:	Each study subject is scheduled to receive GBR procedure for future implant sites. An acrylic stent will be utilized to measure Original Bone (OB), Post Guided Bone Regeneration (PB), and after Healing Bone (HB). The stent is a part of standard care. However, the stent will be modified to be used for the required measurements. Survey with post-operative questionnaire will be used for post-operative comparison of the two incision techniques. Dental implants will be placed into the augmented ridges after 6 months of healing.
Analysis:	To compare pre- and post- augmentation ridge height and width. To compare post-operative complications using a questionnaire form.

LIST OF ABBREVIATIONS

Abbreviation	Definition
OB	Original bone
PB	Post guided bone regeneration
HB	After healing bone
FDBA	Freeze-dried bone allograft
DFDBA	Demineralized freeze-dried bone allograft
GBR	Guided bone regeneration

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(Part I)

Table 1: Demographic Data

Total subjects (N)			23	
Split-mouth (N)			6	
Total sites (N)			29	
Double-flap (N)			11	
Periosteal Fenestration (N)		Conventional	18	12
		Modified		6
Maxilla (N)			2	
Mandible (N)			27	
Extraction sites			5	
Double-flap			2	
Conventional			3	
Age	Mean		57.96	
	Range		37-74	
Gender				
Male			11	
Female			12	
Smoking				
Non-smoker			23	
Current smoker			0	

Table 2: Pain / Discomfort Survey

	Pain scores (mean)	Swelling scores (mean)	Bleeding scores (mean)
Double-flap (N=11)	1.55	1.91	0
Conventional (N=18)	2.89	2.78	0.72

Table 3: Post-operative Complications

Flap design	Infection (N)	Continuous discomfort (N)	Paresthesia (N)	Membrane exposure (N)
Double-flap (N=11)	0	0	0	1
Conventional (N=18)	2	1	1	2

Table 4: Independent Sample t-Test

Group Statistics

	VAR00001	N	Mean	Std. Deviation	Std. Error Mean
VAR00002	1,00	11	,0909	,30151	,09091
	2,00	18	,3333	,48507	,11433

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
VAR00002	Equal variances assumed	13,642	,001	-1,486	27	,149	-,24242	,16319	-,57726	,09241
	Equal variances not assumed			-1,660	26,967	,109	-,24242	,14607	-,54215	,05730

Table 5: Generalized Estimating Equations

Exposure (generalized estimating equations):

Analysis Of GEE Parameter Estimates
Empirical Standard Error Estimates

Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		-2.1962	0.9478	-4.0539	-0.3386	-2.32	0.0205
Group	1	0.1694	1.0719	-1.9315	2.2704	0.16	0.8744
Group	2	0.0000	0.0000	0.0000	0.0000		

Table 6: Flap Advancement

	Flap advancement (mm; mean)
Double-flap (N=11)	9.64
Conventional (N=12)	7.13

(Part II)

Table 7: Resorption Rate at 6 months

		Mesial	Center	Distal
Vertical Resorption (Mean; %)		15	12	12
Horizontal Resorption (Mean; %)	a) 3mm apical to crest	11	7	8
	b) 5mm apical to crest	14	4	6
	c) 7mm apical to crest	21	10	10

Table 8: Vertical Resorption Rate at 6 month

	Mesial	Center	Distal
The initial augmentation (mm) ;OB-PB	3.09	3.35	3.19
Remained augmented bone (mm); OB-HB	2.60	2.99	2.86
Loss of augmented bone (mm)	0.49	0.36	0.33

Table 9: Horizontal Resorption Rate 3 mm apical to the crest

	Mesial	Center	Distal
The initial augmentation (mm) ;OB-PB	2.66	3.10	2.43
Remained augmented bone (mm); OB-HB	2.36	2.78	2.28
Loss of augmented bone (mm)	0.30	0.32	0.15

Table 10: Horizontal Resorption Rate 5 mm apical to the crest

	Mesial	Center	Distal
The initial augmentation (mm) ;OB-PB	2.45	2.81	2.43
Remained augmented bone (mm); OB-HB	2.09	2.67	2.32
Loss of augmented bone (mm)	0.36	0.14	0.11

Table 11: Horizontal Resorption Rate 7 mm apical to the crest

	Mesial	Center	Distal
The initial augmentation (mm) ;OB-PB	1.97	2.16	2.08
Remained augmented bone (mm); OB-HB	1.73	2.04	1.94
Loss of augmented bone (mm)	0.24	0.12	0.14

Table 12: Resorption Rate at 6 months with membrane exposure

		Mesial	Center	Distal
Vertical Resorption (Mean; %)		55	80	65
Horizontal Resorption (Mean; %)	a) 3mm apical to crest	61	45	60
	b) 5mm apical to crest	43	41	38
	c) 7mm apical to crest	46	44	32

Table 13: Repeated-measures ANOVA

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Vertical	3	36	1.70	0.1845
Horizontal	2	24	4.17	0.0278

See where significant differences lie:

Middle vs. Mesial	1	12	6.85	0.0225
Distal vs. Mesial	1	12	5.60	0.0356
Middle vs. Distal	1	12	0.06	0.8069

Table 14: Paired Sample t-Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		Mean	Std. Deviation	Std. Error Mean
					Lower	Upper			
Pair 1	VAR00001 – VAR00002	.25774	.44379	.03424	.19014	.32533	7.528	167	.000

Table 15: Paired Sample t-Test

	Paired Differences	t	df	Sig. (2-

										tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		Mean	Std. Deviation		Std. Error Mean
		Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper	
Pair 1	VAR00001 - VAR00002	.30000	.63124	.16871	-.06447	.66447	1.778	13		.099
Pair 2	VAR00003 - VAR00004	.36429	.50931	.13612	.07022	.65835	2.676	13		.019
Pair 3	VAR00005 - VAR00006	.24286	.33447	.08939	.04974	.43597	2.717	13		.018
Pair 4	VAR00007 - VAR00008	.49286	.53989	.14429	.18113	.80458	3.416	13		.005
Pair 5	VAR00009 - VAR00010	.32857	.64621	.17271	-.04454	.70168	1.902	13		.079
Pair 6	VAR00011 - VAR00012	.14286	.23440	.06265	.00752	.27820	2.280	13		.040
Pair 7	VAR00013 - VAR00014	.12143	.35340	.09445	-.08262	.32547	1.286	13		.221
Pair 8	VAR00015 - VAR00016	.36429	.38751	.10357	.14054	.58803	3.517	13		.004
Pair 9	VAR00017 - VAR00018	.15000	.43633	.11661	-.10193	.40193	1.286	13		.221
Pair 10	VAR00019 - VAR00020	.10714	.37306	.09971	-.10826	.32254	1.075	13		.302
Pair 11	VAR00021 - VAR00022	.14286	.17415	.04654	.04230	.24341	3.069	13		.009
Pair 12	VAR00023 - VAR00024	.33571	.42173	.11271	.09221	.57921	2.979	13		.011

LIST OF FIGURES

Figure 1: Periosteal fenestration technique (PFT)

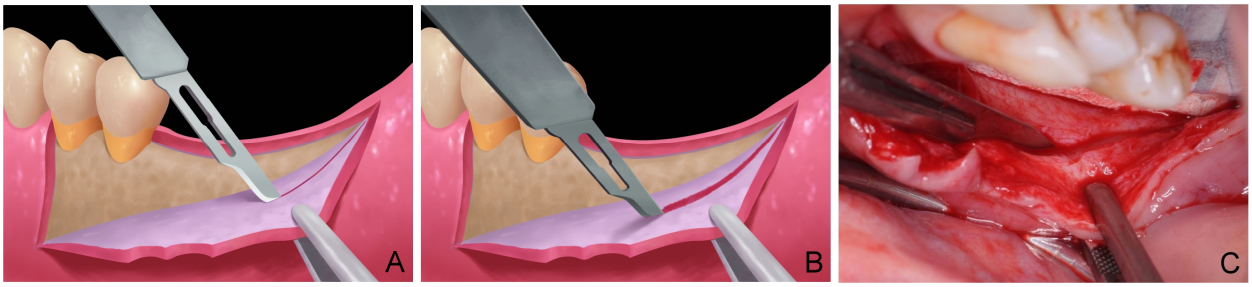
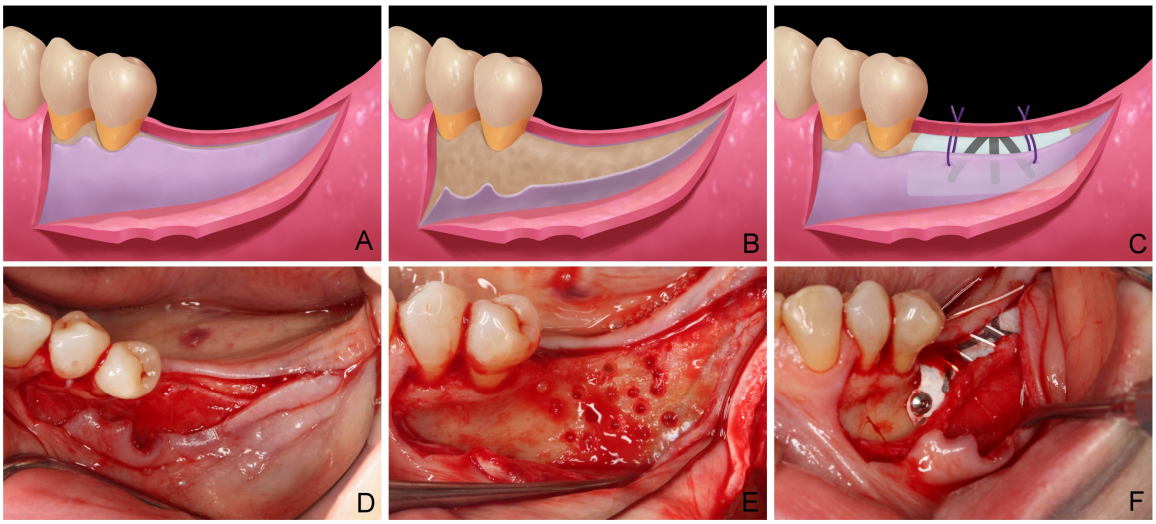


Figure 2: Double-flap technique (DFT)



A) and D) The mucosal layer is elevated leaving the periosteal layer on the alveolar bone

B) and E) The periosteal layer of the double flap is reflected from the alveolar bone

C) and F) The periosteal layer was used to stabilize the membrane using periosteal sutures.

Figure 3: Comparison of two incision techniques

DFT (Test) vs. PFT (Control)

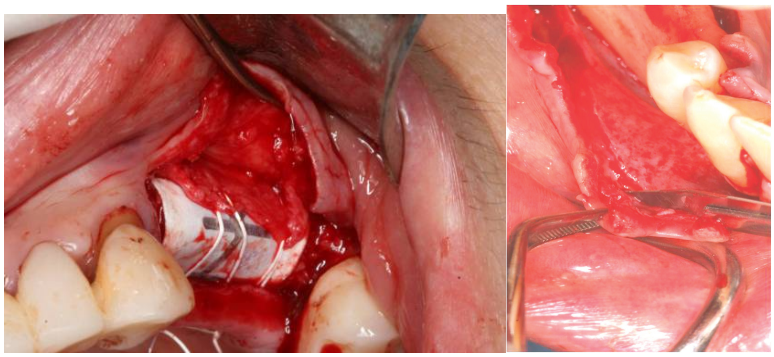


Figure 4:

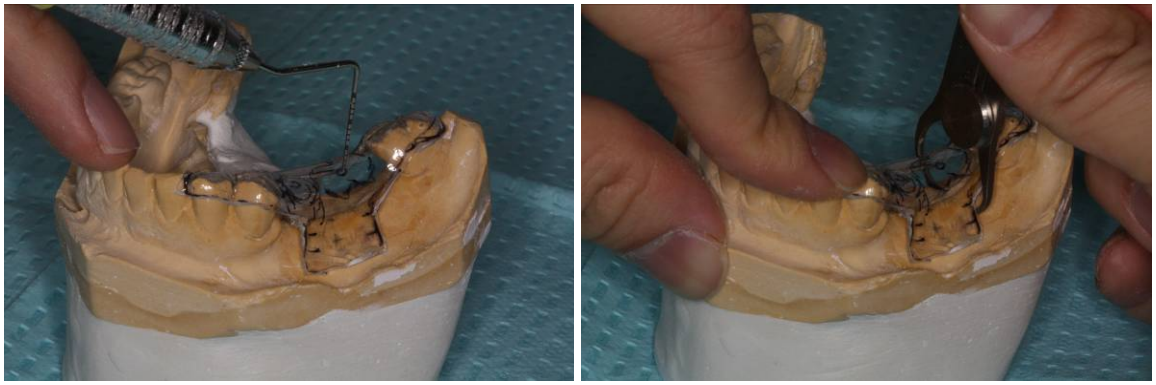


Figure 5: Original Bone (OB) and Post GBR (PB) Measurements

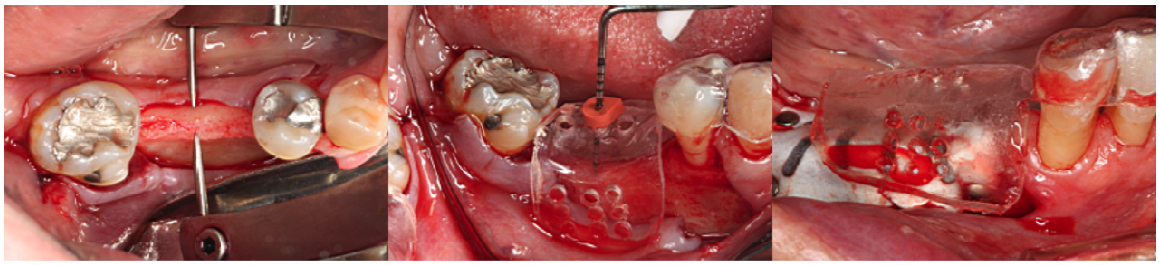


Figure 6: Before and After GBR

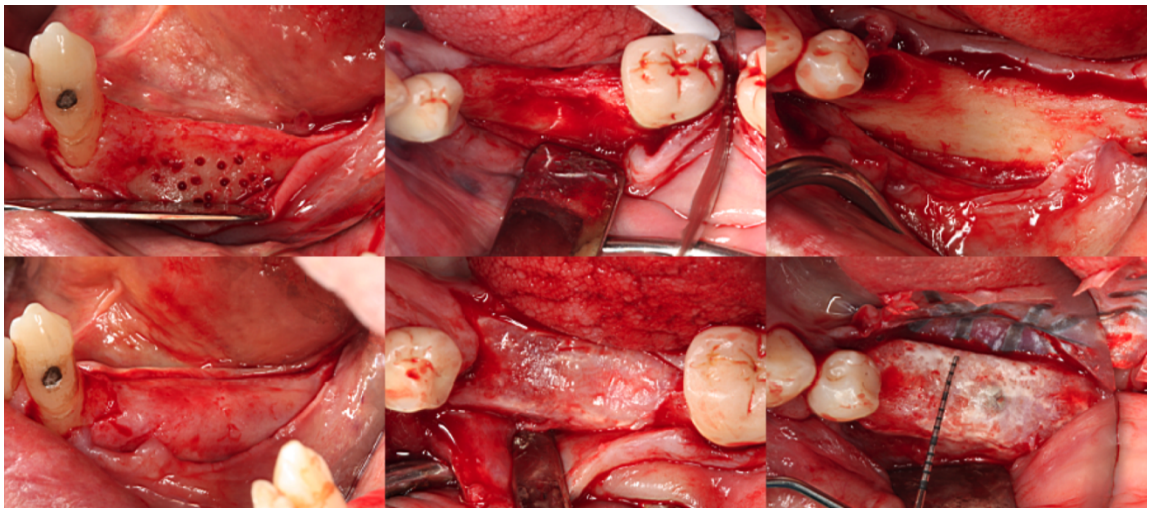


Figure 7: Flap Advancement DFT (Test) vs. PFT (Control)

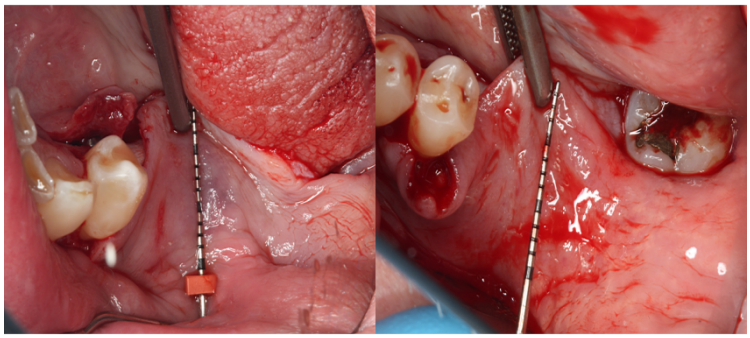
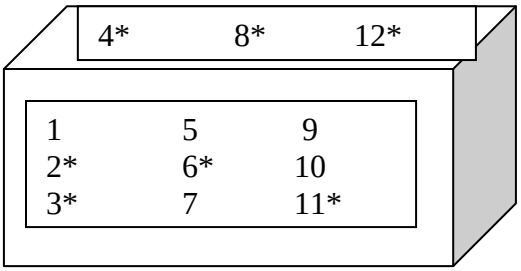


Figure 8:



*Statistically significant

Figure 9: The periosteal suture on the periosteal layer is able to anchor the graft site toward the flap base

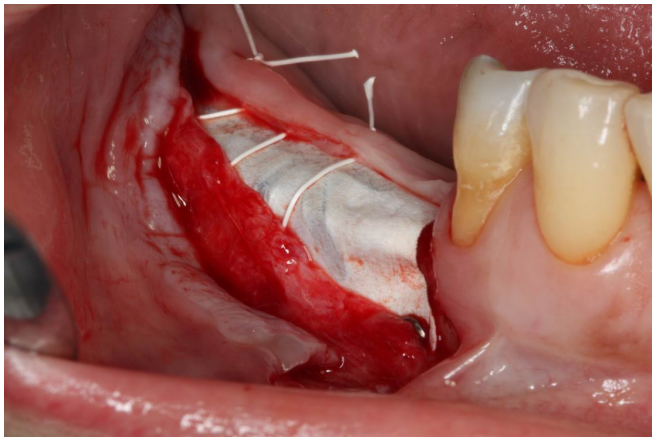


Figure 10: Schematic drawing of extra stabilization by periosteal layer

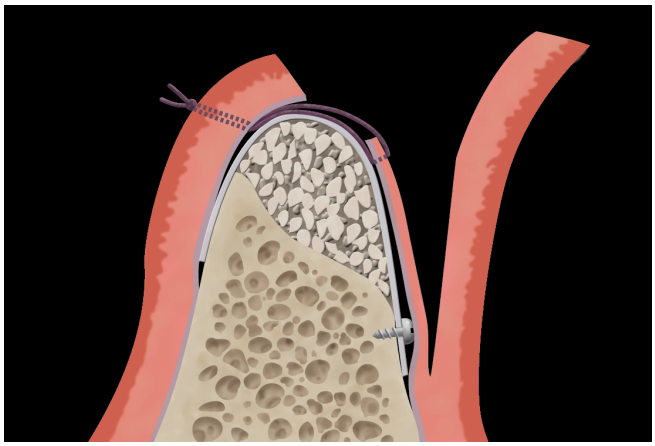
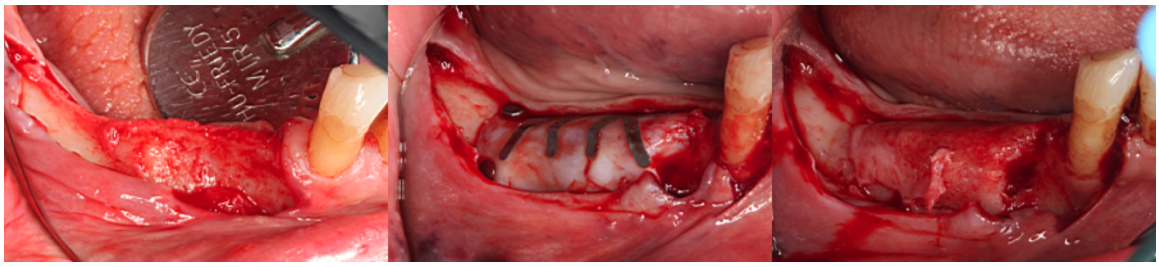


Figure 11: Soft Tissue Invagination



Observation of Changes in Alveolar Bone during the Course of Healing after Guided Bone Regeneration : A Prospective Study in Human

I. Background and Rationale

Vertical alveolar bone augmentation procedures are considered a major challenge in dentistry. A few modalities exist: guided bone regeneration (GBR), distraction osteogenesis (DO), and onlay autogenous block bone grafting. Among these, the data from clinical and scientific investigations in the past two decades have been shown the use of guided bone regeneration (GBR) to be a proven method of regaining a diminished alveolar ridge.[1-5] The success of GBR has increased the use of dental implants and has pushed the boundaries of science with many clinicians experimenting with a variety of membranes, such as bio-absorbable and non-absorbable.[6-8] Recently, the systematic review by Fiorellini et al. concluded that the survival rate of dental implants placed in augmented sites is similar to dental implants placed in native bone.[9] The continuous advancement of GBR has raised clinician and patient expectations of outcomes that recreate normal occlusal function, healthy soft and hard tissue anatomy, and ideal esthetics.

The expanded polytetraflouroethylene (e-PTFE) membrane has been studied extensively in animals and humans and is considered a standard for bone augmentation. [10] Multiple clinical and histologic studies reported its ability to regenerate new bone and decrease patient morbidity. The volume of regenerated bone generally is more encouraging with

non-resorbable e-PTFE membranes than with bioabsorbable membranes. [11, 12] From Zitzmann et al. (2001), it can be suggested that the combined use of e-PTFE membrane and deproteinized bovine bone mineral (DBBM) results in higher marginal bone level (MBL) values compared to a collagen membrane and DBBM. [13] However, the procedure remains technique sensitive, therefore, the ideal techniques for a predictable outcome has yet to be defined. The maintenance of primary wound closure throughout the healing period is critical to the successful outcome of GBR using an e-PTFE membrane. Despite the success demonstrated with e-PTFE membranes in GBR application, complications of soft tissue dehiscence with membrane exposure and infection impaired the outcome of therapy with a decreased gain in bone fill reported (Machtei EE. 2001, Simion M, 1994).[14, 15] In 40-60% of cases reported with exposure, there is up to 50-80% less bone regenerated compared to non-exposed.[14] The sites treated with e-PTFE membrane were 2.04 times more likely to develop mucosal problems than with collagen membrane[13]. Decreased bone fill associated with e-PTFE membranes, compared to collagen membrane, was related to a higher exposure rate. [16]

The addition of bone graft material to the GBR technique increases the amount of achievable vertical regeneration. [17] Particulate autograft bone is considered as the gold standard for osseous tissue regeneration. [18] The use of autogenous bone has advantages because of its intrinsic osteogenic properties and a more rapid course of bone regeneration. However, the application is limited due to donor site morbidity, increased cost, the characteristic of resorption, and inadequate volume.[19] We encounter situations in which autogenous bone grafts are not feasible, or patients refuse to have bone harvested from extraoral sources.

Allografts are grafts transferred between members of the same species, which are genetically dissimilar. They have the advantage of being available in higher quantities and eliminating the morbidity associated with a second surgical site. The allograft has been used as a substitute for autografts or as an autograft expander.[20] The use of particulate allograft bone replacement substitute has been reported for numerous applications, including sinus augmentation, ridge augmentation, and extraction socket applications. [21-23] In a comparative study using FDBA or DFDBA for localized ridge and sinus augmentation, histologic observations showed regeneration of 42% new bone area with no statistical difference between the two materials.[24]

Currently, there are studies in progress to investigate the efficacy of growth factors for guided bone regeneration, such as recombinant human bone morphogenic proteins (rhBMP-2) and rhPDGF-BB (Recombinant Human Platelet Derived Growth Factor) as alternatives to autogenous bone graft.[25, 26]

At present, rhBMP-2 is approved by the FDA (Food and Drug Administration) for sinus augmentations and localized alveolar ridge augmentations for defects associated with extraction sockets. However, the use of BMP-2 for defects not associated with extraction socket is not indicated.

PDGF-BB is involved in wound healing that stimulates the regenerative potential of periodontal tissues such as bone, cementum, and periodontal ligament.[27] Simion et al. reported cases using rhPRGF-BB in combination with a deproteinized bovine bone graft in humans, suggesting the potential usage for bone augmentation.[28] The same author reported a case of GBR to treat severe ridge deficiency using a 1:1 ratio of autogenous bone graft and deproteinized bovine bone particles in combination with rhPDGF-BB and

showed a successful result.[29] Byun et al. reported a case of GBR augmenting a buccal fenestration defect associated with simultaneous implant placement using autogenous bone and rhPDGF-BB combined with β-TCP. They applied autogenous bone as the inner grafting material and rhPDGF-BB + β-TCP as the outer grafting material and reported a successful result.[30]

However, all of the human studies mentioned above are case reports and there were no controlled studies with large sample sizes to validate the efficacy of PDGF-BB for GBR. At present, the use of rhPDGF-BB for GBR is not approved by the FDA. The use of rhPDGF-BB is limited to the treatment of intrabony defects, furcations, and gingival recession associated with periodontal defects.

Flap advancement is required as part of guided bone regeneration procedures to attain tension-free primary closure along the incision line. Flap advancement may also be an integral part of other surgical procedures, such as root coverage. Primary closure results in decreased discomfort and faster healing and is critically important in attaining desired objectives. Obtaining and maintaining primary wound closure is necessary for the successful outcome of guided bone regeneration. Failure to attain tensionless closure may result in a soft tissue dehiscence along the incision line that can cause a poor outcome and/or postoperative complications. Greenstein described the minor flap advancement as a flap advancement of several millimeters, the moderate advancement as a flap advancement of 3 to 6 mm, the major flap advancement as a flap advancement equal to or greater than 7 mm. The author concluded that the technique for the flap advancement is dependent on the extent of bone augmentation.[31] For the critical size of GBR procedures, the major flap advancement is often needed.

Numerous investigators have made contributions with regard to procedures and the understanding of biologic benefits derived from coronally advanced flaps [32-36]. Langer and Langer proposed the usage of an overlapped flap to achieve primary closure over implant placement.[32] A beveled incision provides increased surface area, which allows some overlapping of the soft tissue to ensure coverage of the implant fixture. Buser and co-workers employed a reverse beveled incision for guided bone regeneration with a similar effect.[33] Tinti and Parma-Benfenati suggested a palatal sliding flap advancement, which offers preservation of the masticatory mucosa.[34] Fugazzotto rotated palatal connective tissue and periosteum to cover the regenerative site to achieve passive soft tissue coverage.[35, 36] While the approaches mentioned above may be advantageous for practitioners to achieve primary closure, none of these studies have been studied through a clinical trial, i.e., there is no objective comparison with a control group.

Among the flap advancement techniques, periosteal fenestration technique is the most commonly used for GBR procedures to release flap tension. It involves severing the periosteum along with the underlying submucosa. (Figure1) However, to achieve tension free primary closure using this technique, deep and/or multiple periosteal fenestrations are often required. Particularly, deep incisions are needed to achieve major flap advancement greater than 7 mm.[31] The disadvantage of deep periosteal fenestration is that if the muscle layer is incised, the patient experiences increased morbidity such as swelling, hemorrhage, and discomfort. These postoperative discomfort/complications after guided bone augmentation procedures have often been documented and associated with poor surgical outcomes.[13]

To overcome such drawbacks of the conventional technique, and to decrease the

incidence of complications, the authors pursued an ideal incision design; a novel incision design, the double-flap technique was recently introduced to the Department of Periodontology at Tufts University.[37]

The double-flap technique was described by Hur et al. as a technique used for facilitating flap advancement to achieve tension-free primary closure for guided bone regeneration.[37](Figure 2) The major flap advancement can be easily attained with this technique by utilizing the mucosal flap as an outer layer for wound closure because of the tension-free nature of the alveolar mucosa.

This new technique is now frequently used for GBR procedures in the Department of Periodontology at Tufts University. With the Double-flap technique, the residents and faculty members have observed more flap advancement, less patient pain/discomfort and fewer postoperative complications such as dehiscence, edema, necrosis, and membrane exposure compared with the periosteal fenestration technique.

As mentioned above, in the past literature, no systematic effort has been made to quantify their clinical performance associated with different incision-flap designs that could help reduce the patient pain/discomfort level and the frequency and/or severity of complications. [32-36] Therefore, an evaluative comparison is necessary to determine the efficacy and validity of the double-flap technique. (Figure 3)

The previous studies reported 3 to 5mm vertical ridge augmentation. They measured the differences between the amount of preoperative bone and the amount of bone after healing.[17, 38, 39] Clinical observation has suggested that the amount of initial bone volume created by guided bone regeneration does not equal the amount of bone after healing.

A review of the literature has revealed a loss of alveolar bone volume during the healing time after GBR. The studies of Lekovic et al. [40, 41] reported a loss of alveolar bone height and width during healing time after bone grafting procedures. In their studies, bone grafting procedures were performed in conjunction with tooth extractions covered with an expanded polytetrafluoroethylene (e-PTFE) membrane and a bioabsorbable membrane made of glycolide and lactide polymers in experimental sites.[40, 41] These sites were compared with the control sites that did not receive any membrane. The results have shown significantly better ridge volume retention in experimental sites than in control sites. They also reported a 25% loss of ridge width with e-PTFE barrier membrane and a 17% loss of ridge width with the bioabsorbable membrane. However, it is noted that they did not increase ridge width and height outside of the extraction sockets. Their procedures were intended to preserve alveolar ridge after extractions.

To the knowledge of the authors, there is only one study by Simon that reported the quantitative loss of augmented bone during healing time. They quantify the changes following ridge augmentation using a collagen membrane and DFDBA [42]. Clinical measurements with standardized stent were taken 3mm, 5mm and 7mm from the alveolar crest for ridge width measurements. Height measurements were taken in the midpoint of the edentulous ridge and 3mm mesial and distal to the midpoint. Their results revealed significant non-uniform loss of augmented bone during healing. The reported loss of width of augmented bone ranged from 52% to 58% at 3mm from the crest, 48% to 67% at 5mm from the crest, and 39% to 47% at 10mm from the crest. They also reported the loss of height of augmented bone, and the results showed that it ranged approximately from 60% to 76%.

However, none of the studies discussed the amount of bone changes after ridge augmentation using a non-resorbable membrane and allograft material. Moreover, the measurement by Simon was associated with extraction sockets[42]. We hypothesized that, following guided bone regeneration using FDBA and e-PTFE membrane: a significant amount of bone width and height changes will occur and that the changes will not be uniform over the regenerated sites.

Purpose:

The purpose of this paper is to quantitatively evaluate, from non-space-making defects, the amount of bone change following alveolar bone augmentation using FDBA and e-PTFE membrane in a clinical controlled trial. The two different flap designs that were compared were: double-flap incision versus conventional periosteal fenestration for flap advancement for primary closure, associated with titanium reinforced e-PTFE membrane and FDBA for alveolar ridge augmentation. Hard tissue changes were evaluated over a period of 6 months after ridge augmentation. It was compared in the three horizontal and one vertical dimension for designated implant sites.

II. Aim and Hypothesis

Hypothesis:

The primary hypothesis is that the extent of initial augmentation created by guided bone regeneration techniques does not, from a quantitative standpoint, equal the actual amount of bone remaining after healing is completed. Secondarily, different incision designs, the double-flap and periosteal fenestration, will affect exposure rate and post-operative complications such as pain, swelling and bleeding. Thirdly, the amount of flap advancement is greater with the double-flap technique than with the conventional periosteal fenestration technique.

Specific Aims:

The following assessments were made on the surgical sites:

1. Changes in alveolar bone width in different locations. (All population)
2. Changes in alveolar bone height. (All population)
3. Comparative exposure rate during the healing of six months. (double-flap population vs. all periosteal fenestration population)
4. Comparative pain/swelling/bleeding analysis using a survey form. (double-flap population vs. all periosteal fenestration population)
5. Comparative the amount of flap advancement measured during the surgery. (double-flap population vs. conventional periosteal fenestration population excluding modified periosteal fenestration population.)

III. Material and Methods

A. Experimental Design

Twenty-three patients referred to the Postdoctoral Clinic in the Department of Periodontology Tufts University School of Dental Medicine presenting partial edentulism for one or more sites will be selected for this study. The age of the patients ranged from 37 years to 74 years with good general health. All patients required guided augmentation to allow for implant placement and to improve the crown-implant ratio. They received written information about the surgery and signed an informed consent as is standard of care. The numbers of surgical sites were twenty-nine sites.

Standardization of Measurements

The measurements for the patients were evaluated three times: 1) Original bone (OB): before bone grafting, 2) Post guided bone regeneration (PB): just after rigde augmentation, and 3) after healing bone (HB): six months after healing. Mucogingival flaps were reflected for GBR procedures (1 and 2) and placement of endosseous implant (3). A stent was made for a reference point. The stent was made by a suck down shell of the diagnostic cast from the impression. It has three holes at designated implant location and adjacent areas for vertical measurements and three indications at 3mm, 5mm and 7mm at a lateral position on the vertical holes.

Alveolar height:

A UNC-15 periodontal probe (Hu-Friedy, Chicago, IL, USA) was utilized for height measurements. The distance between occlusal reference point of the stent to the crest of

the alveolar ridge was measured at the three different locations (at the midpoint of the edentulous ridge and at 3mm mesial and distal to the midpoint) for each surgical site. (Figure 4)

Alveolar width:

A UNC-15 periodontal probe (Hu-Friedy, Chicago, IL, USA) was utilized for width measurements. The distance between the buccal reference point of the stent to the buccal surface of the alveolar ridge were measured at three different points, 3mm apical to the alveolar crest (point a), 5mm apical to the crest (point b) and 7mm apical to the crest (point c). The measurements were made at the midpoint of the edentulous ridge and at 3mm mesial and distal to the midpoint) for each surgical site. Facial-lingual/palatal width measurements were taken at 3mm apical to the alveolar crest, using Boley gauge caliper (Hu-Friedy, Chicago, IL, USA) at the midpoint of the edentulous ridge. (Figure 4)

The selection of the designated incision technique for the guided bone augmentation procedure and a decision for tooth extractions were not a part of the research. The extraction was determined by a pre-existing treatment plan. However, the selection of incision design was made by randomly (e.g., coin flipping) since there are no criteria to choose one technique over the other.

Surgical procedure

Local anesthesia was attained using three carpules of lidocaine with 1:100,000 epinephrine. A crestal incision was made over the edentulous ridge. Vertical releasing incisions were placed on the buccal and lingual as needed. Either the double-flap

technique (DFT) or the periosteal fenestration technique (PFT) was utilized for each bone augmentation procedure. In the DFT group, a partial-thickness flap is raised first separating the mucosal flap from the overlying periosteum. Subsequently, the periosteum was elevated exposing the underlying alveolar process. (Figure 2) In the PFT group, a buccal and a lingual/palatal mucoperiosteal full-thickness flap was raised. The periosteal fenestration technique was utilized to advance the mucoperiosteal flap. (Figure 1)

Alveolar bone augmentation procedures were performed using mineralized freeze-dried bone allograft (FDBA; Mineross, Osteotech, Eatontown, NJ) and titanium reinforced expanded polytetrafluoroethylene (e-PTFE) membrane (Gore-Tex Regenerative Membrane, W.L. Gore & Associates, Flagstaff, AZ) by a single operator.

The titanium reinforced e-PTFE membrane was shaped to the desired contours and trimmed at least 1 mm away from the adjacent teeth surfaces to minimize the potential risk of infection. FDBA was hydrated with sterile saline solution and placed into the defect. The membrane was placed over the graft material and fixed buccally and lingually/palatally using bone tacks (ACE Surgical, Brockton, MA). In the DFT group, the periosteal flap was sutured first, using periosteal sutures to secure the regenerative site. Next the mucosal flap was closed using horizontal mattress and simple interrupted sutures. For the PFT group, the mucoperiosteal flap was closed utilizing horizontal mattress and simple interrupted sutures using 4-0 e-PTFE (Gore-Tex CV-5, W.L. Gore & Associates, Inc.) and 5-0 polyglactin 910(Vicryl, Ethicon Inc.) sutures.

The patient was instructed to take the prescribed Augmentin (amoxicillin/clavulanic acid) and methylprednisolone (Medrol Dosepak) one day prior to the surgery for ten days. Clindamycin was prescribed in patients with penicillin allergy. An anti-inflammatory

agent (Ibuprofen) was prescribed to the patient for three days after surgery. The patient was instructed not to brush or floss in the area of the surgical procedures for three weeks. The patient was advised to rinse with a 0.12% chlorhexidine gluconate solution three times a day until suture removal. Simple interrupted sutures were removed 7–14 days after surgery and horizontal mattress sutures were removed 21 days after surgery.

Study Measurements

Flap advancement was measured by a blinded investigator. The center of the flap was grasped at 3mm from the margin and pulled by a pair of periodontal forceps. The advancement was stopped if there was noticeable blanching or tension from the flap. The differences between before and after the releasing incision, DFT or PFT, were recorded in millimeters. Intra-examiner calibration exercises were performed prior to the study to minimize measurement discrepancies. The measurements were repeated two times and the average was used.

The pain/discomfort level questionnaires were obtained from the patients one week after GBR regarding postoperative pain, swelling and bleeding. Visual Analogue Scale (VAS scale) was used for the questionnaire (range: 0-10 for each pain, swelling and bleeding).

Post-operative complications including membrane exposure, infection, paresthesia, and continuous discomfort were recorded at 1, 2, 4, 8, 12, 16 and 24 weeks follow-up visits following the GBR procedure. Premature membrane exposure is defined as any type of loss of primary closure during the six-month healing period. Post surgical infection is defined as any redness, swelling, pain, heat, or drainage that requires an additional course of antibiotics. Infection associated with membrane exposure was considered as a

membrane exposure. Paresthesia is altered sensation the patient might experience which ranges from a tickling sensation to numbness. Continuous discomfort is defined as chronic pain that the patient experiences after suture removal ranging from a dull aching to sporadic sharp pain.

Implant surgery

Implant therapy is not part of the research. Surgical procedures for the implant placements were followed as described below:

1. The surgical protocol for implant therapy was followed as standard of care of the procedures.
2. Implant installation surgery was performed after the healing period six months.

Study Visits

Screening (Visit 1)

- Signed written consent was obtained.
- Eligibility was determined using inclusion/exclusion criteria.
- Clinical / Radiographic evaluation with existing patient record
- A surgical stent was fabricated. The stent is a part of standard care. However, the stent has been modified to be used for the measurements. The surgical stent has three indications at 3mm, 5mm and the 7mm lateral position. (Figure 2, 5)

Phase 1 therapy (Visit 2)

- Try-in of the stent

Day 1: Base Line/Augmentation Visit (Visit 3)

- Ridge height and thickness were recorded with a caliper gauge and a UNC-15 periodontal probe (Hu-Friedy, Chicago,. IL, USA) prior and post ridge augmentation.
- Each measurements of the thickness of the ridge were taken 3 mm, 5 mm, and 10 mm from the most coronal part of the edentulous ridge according with the stent.

Day 7, 14, 30, 60, 90, 120 (Visit 4-8)

- Survey Questionnaire
- Membrane exposure was recorded on the survey form.

Day 180 (Implant surgery- Visit 9)

- Ridge height / thickness was measured with a caliper gauge with the stent.

B. Sample size and Statistical Analysis

Original Bone (OB) refers to data derived from at the time of flap reflection before bone graft procedure. Post Guided Bone Regeneration (PB) stands for the data obtained immediately after ridge augmentation procedure. After Healing Bone (HB) refers to the data derived from following 6 months healing interval and represents residual bone (original and remaining allograft) related to alveolar width and height.
Resorption rate was calculated as follows. The amount of remaining allograft bone at the time of 6 months following ridge augmentation procedure (HB - OB) is divided by the amount of augmented allograft bone immediately after ridge augmentation procedure (PB-OB).

Alveolar width measurements:

Alveolar facial lingual/palatal width is measured at 3 points (a,b,c points). (a: 3mm apical to the alveolar crest b: 5mm apical to the alveolar crest c: 7mm apical to the alveolar crest) (Figure 5 and 6)

Alveolar height measurements:

Alveolar height is determined by measuring the distance from a fixed reference point on the stent to the alveolar crest. (Figure 5 and 6)

Sample Size Calculation

(1) The statistical software package nQuery Advisor (Version 7.0) was used to calculate the sample size needed for reliable results. Assuming that the resorption rate has a standard deviation of 3.0, a sample size of 30 is adequate to obtain a confidence interval with a half-width of 1.176.

Statistical Analysis

(2) The comparison of resorption rate at 3 points (a, b, c points) and vertical point were tested by repeated measures ANOVA. The significance level is set at alpha＝0.05.

(3) The comparison of resorption rate at 3 points (mesial, center, distal points) was tested by repeated measures ANOVA. The significance level is set at alpha＝0.05.

(4) Paired-t test was performed to explore if there is the bone volume change between the amount of initial augmentation created by guided bone regeneration techniques and the actual amount of bone remaining after six months of healing.

(5) Independent Sample t-Test was performed to explore the difference of post-operative complication rate between the conventional flap and the double-flap technique.

(6) Generalized Estimating Equations was used to detect the difference of exposure rate between the conventional flap and the double-flap technique.

(7) Generalized Estimating Equations were performed to explore the difference of complication (pain, swelling) obtained by questionnaires (0-10 scores each) between the periosteal fenestration technique and the double-flap technique. A cut point of 2.5 was used for pain and swelling.

(8) Fisher's exact test on the patient with unilateral site was performed to explore the differences of bleeding obtained by questionnaires (0-10 scores each) between the periosteal fenestration technique and the double-flap technique.

(9) Mixed-effects model was performed on the people to see the differences of flap advancement between the conventional periosteal fenestration technique and the double-flap technique.

C. Subject Characteristics

Inclusion Criteria

Each study subject must meet all of the following inclusion criteria to be enrolled in the study:

1. Subjects can be male or female at least 18 years of age.
2. Subjects must be healthy without systemic disease or condition (e.g. uncontrolled diabetes, HIV, smoking etc).
3. Maxillary or mandibular edentulism of two or three teeth (or planned extractions).
4. Subjects treatment planned for future implants in areas with less than 6 mm in width of the alveolar process.
5. Subjects must have voluntarily signed the informed consent.

Exclusion Criteria

Any study subjects meeting any of the following exclusion criteria were not enrolled in the study:

1. A female subject who is pregnant or lactating.
2. A subject currently smokes more than ten cigarettes a day.
3. A subject who has uncontrolled diabetes mellitus as defined by HbA1C, $\geq$ 7%.
4. A subject who has any known disease that interferes with periodontal surgery.
5. A subject who had a myocardial infarction within 6 months of enrollment.
6. A subject who has HIV or hepatitis.
7. A subject who has a history of serious drug-related reaction to antibiotics and analgesics.
8. A subject has a history of psychological problems or limited mental capacity.

IV. Results

(Part I)

A total of 23 patients with 29 surgical sites (26 mandibular posterior with six split mouth patients) were enrolled in the study. Double-flap Technique (DFT) was performed on 11 sites and Periosteal Fenestration Technique (PFT) was performed on 18 sites (Table 1). Conventional periosteal fenestration technique was used for 12 sites and modified periosteal fenestration technique (MPF) was utilized for 6 out of 18 sites. Six months after GBR surgeries, clinical and radiographic evaluation revealed a noticeable increase in the vertical/horizontal thickness of most of the surgical sites. However, the sites with post-operative complications such as exposure, infection, and membrane dislocation showed lesser amount of bone regeneration in the PFT group. (Six in PFT group vs. one in DFT group)

A Pain/ Discomfort survey showed that, overall, there was less pain/discomfort for the patients in the DFT group than those in the PFT group in terms of pain (mean1.55 vs. 2.89; P=0.15), swelling (mean 1.91 vs. 2.78; p=0.074), and bleeding (mean 0.0 vs. 0.72; P=0.245). However, there were not statistically significant differences in pain, swelling, and bleeding between DFT and PFT groups. (Table 2)

Over the healing time of six months after GBR surgeries, there were fewer numbers of post-operative complications for the patients in the DFT group than those in the PFT group (6/18 in PFT group vs.1/11 in DFT group). (Table 3) Overall, the post-operative complication rate was 24.1%. The mean complication rate was lower in the DFT group

(9.1%) than in the PFT group 33.3%. However, there was no statistically significant difference regarding the complication rate between the PFT group and the DFT group (p=0.149). (Table 4)

Primary closure was achieved predictably in both groups. During six months of healing, three sites in three patients showed membrane exposure with one site in the DFT group, and two sites in the PFT group. Overall, the membrane exposure rate was 10.3 %. The mean membrane exposure rate was lower in the DFT group (9.1%) than in the PFT group (11.1%). However, there was no statistical difference between the DFT group and the PFT group regarding membrane exposure rate (p=0.874). (Table 5)

Description of Surgical Complications

Pt.1: A small membrane exposure in the DFT group occurred on top of a lingual tack two months after the GBR procedure. The size of the exposure was 1mm diameter initially. The area was maintained by the use of 0.2% chlorhexidine gluconate mouth wash three times a day and followed up weekly for one month. The membrane was removed three months after the GBR procedure. The size of exposure was 5mm at the time of the membrane removal. The site was minimally affected by the exposure.

Pt. 2: One exposure in a patient in the PFT group complained of the continuous discomfort of the surgical site three weeks after the GBR procedure without membrane exposure. The patient was followed up biweekly and membrane exposure was noticed two months after GBR procedure. The size of the exposure was 15×5 mm. A membrane

removal surgery was performed. During the procedure, the dislocation of the tack and the membrane was confirmed.

Pt. 3: Another patient in the PFT group presented with a small membrane exposure five months after the GBR procedure without any discomfort. The size of the membrane exposure was 0.5 mm. The area was maintained by the use of 0.2% chlorhexidine gluconate mouth wash three times a day and implant surgery was performed one month after exposure. After flap reflection during implant surgery, dislocation of the tack and the membrane was noticed. The membrane was torn in two parts.

Pt. 4: One patient complained of a slight numbness (paresthesia) two weeks after the GBR procedure in the PFT group. The patient was followed up on a weekly basis. The tactile sensation was improved in the first two months, but there was no improvement after two months. The patient had a slight decreased tactile sensation confirmed by two-point discrimination tested by caliper. However, the paresthesia did not disrupt the patient's daily functions. Implant placement surgery was performed six months after the GBR procedure.

Pt. 5: One patient experienced continuous discomfort after the GBR procedure without any membrane exposure or infection. Membrane removal procedure was performed three months after GBR surgery.

Pt.6, Pt.7: Two patients experienced infection during the healing period. Pt. 6 started to

have infection with suppuration on the area two weeks after the GBR procedure. The patient was followed up weekly. Systemic antibiotics (Ciprofloxacin 500mg orally every 12 hours) were prescribed for four weeks. Augmentin (amoxicillin 500mg/clavulanic acid 125mg) was prescribed five weeks after the GBR. The infection subsided and the healing was uneventful until implant surgery. The site had a history of a failed GBR procedure. Pt. 7 started to have infection three months after the GBR surgery. Systemic antibiotics (Ciprofloxacin 500mg orally every 12 hours) were prescribed for three weeks and the infection subsided.

The mean flap advancement (mm) in the DFT group was significantly greater than the mean of the flap advancement of the conventional periosteal fenestration (9.64 mm vs. 7.13 mm). (Figure 7) There was a statistically significant difference between these two groups (P=0.025). (Table 6)

(Part II)

18 sites underwent post healing bone measurements at 6 months following the GBR procedure. Four surgical sites with post-operative complication such as continuous discomfort, infection, and membrane exposure (patient 1, 2, 5, and 6) were excluded for the statistical analysis but compared with the 14 sites with uneventful healing.

Resorption rate 6 months after GBR

There was a mean resorption rate of 9.7% in the 14 grafted sites for the bone volume.

A mean range of between 4% and 21% of bone change was observed during six months of healing after GBR using FDBA and e-PTFE membrane. There was less predictable volume maintenance in the mesial horizontal dimension (11%-21% change vs. 9.7% change overall) and vertical height dimension (12%-15% change vs. 9.7% change overall). On the mesial corner of the membrane, soft tissue invagination was frequently observed. The area with soft tissue invagination showed unpredictable bone volume retention.

The four sites with post-operative complications such as membrane exposure and infection showed 50.8% resorption. These sites showed a wide range of resorption rates (32% - 80%). Notably, the patient with membrane exposure showed more significant volume change in the localized area. On the contrary, the patient with infection or mobilization of the membrane showed more significant resorption in the generalized areas.

Resorption rate based on the locations (14 sites)

The vertical bone measurement made at HB indicated a 13% mean resorption rate of the grafted bone ranging from 12% to 15% at the designated implant locations. The horizontal measurement made at HB indicated an 8.7% mean resorption rate of the grafted bone ranging between 8% and 11% at 3 mm below the crestal level, 8% ranging between 4% and 14% at 5 mm below the crestal level, and 10.3% ranging between 10% and 21% at 7 mm below the crestal level. (Table 7-12)

Through repeated measures ANOVA, the findings of this study failed to show a statistical significance of the vertical resorption rate among three points (a,b,c points) and vertical points at the alpha=0.05 level (p=0.185). A statistical significant difference was detected in the horizontal resorption rate among mesial, center and distal measurements through repeated measures ANOVA (p=0.028). The significant difference was found between the mesial resorption rate and the center resorption rate (p=0.022) and between the mesial resorption rate and the distal resorption rate (p=0.036) at the alpha=0.05 level. However, neither are statistically significant after applying the Bonferroni correction (p=0.0167). (Table 13)

The paired-t test showed that there is a statistically significant bone volume change between the amount of initial augmentation created by the guided bone regeneration techniques, using FDBA with the non-resorbable membrane, and the actual amount of bone remaining after six months of healing (p=0.001). (Table 14)

The location-specific analysis demonstrated that the differences are significantly more prominent on the heights and the mesial aspects of the regenerated sites (P=0.05). (Table 15, Figure 8)

V. Discussion

(Part I)

Flap advancement is required as part of guided bone regeneration (GBR) procedures to attain tension-free primary closure. Primary closure decreases discomfort, promotes faster healing, and is critically important in attaining the desired bone augmentation. Failure to attain tensionless closure may result in a soft tissue dehiscence along the incision line that can cause a poor outcome and/or postoperative complications. Postoperative complications after GBR procedures, such as pain, swelling, bleeding, and infection have often been documented and associated with poor surgical outcomes.

The conventional periosteal fenestration technique (PFT) is the most commonly used surgical method for flap advancement. However, to achieve tension free primary closure using this technique, deep and/or multiple periosteal fenestrations are often required. Particularly, deep incisions are needed to achieve major flap advancement greater than 7 mm. The disadvantage of deep periosteal fenestration is that if the muscle layer is incised, the patient experiences increased morbidity such as swelling, hemorrhage, and discomfort. To overcome such drawbacks of the conventional technique, and to decrease the incidence of complications, the double-flap incision technique (DFT) was recently introduced.[37]

Developed two years ago in the Department of Periodontology at Tufts University School of Dental Medicine, the double-flap technique (DFT) for Guided Bone Regeneration described in this study has been proven to be a practical method with fewer

side effects. Hur *et al.* described in the case report that the significance of the double-flap technique (DFT) is its facilitation of flap advancement by the tension-free nature of the mucosal flap (outer layer) and enhancement of soft tissue maintenance during the course of healing after guided bone regeneration procedure.[37] Another advantage of this technique is the stabilization of the graft material by using periosteum layer (inner layer) for suturing. With this new technique, the residents and faculty have observed a reduction in the amount of soft tissue complications such as dehiscence, edema, necrosis, and membrane exposure in comparison to the periosteal fenestration technique.

The present study compared the two different incision designs, double-flap and periosteal fenestration technique, regarding pain/discomfort level (pain, swelling, and bleeding) and post-operative complications such as infection, continuous discomfort (membrane dislocation), paresthesia, and premature membrane exposure. Moreover, the amount of flap advancement was compared in the prospective controlled clinical trial for the first time.

The results from the pain/discomfort questionnaire showed that there was less discomfort for the patients in the DFT group compared with those in the PFT group in terms of pain (mean1.55 vs. 2.89; P=0.15), swelling (mean 2.00 vs. 2.78; p=0.074), and bleeding (mean 0.0 vs. 0.72; P=0.245). (Table 2) Within the limitations of this study, there is no statistical difference between DFT group and PFT group for each of these (pain, swelling and bleeding). However, the lack of statistically significant results may be due to the low sample size. Another potential limitation is the subjective nature of the pain/discomfort

level scoring system. In this study, the pain/discomfort level questionnaire was obtained from the patient using the Visual Analogue Scale (VAS) as a scoring system. A numeral scale ranging from 0 to 10, along with the descriptions of the values, was provided to the patient in order to reduce the cognitive differences between the techniques. However, the perception of pain/discomfort level is different among subjects. Each individual has different thresholds of pain/discomfort. This may have yielded a bias and influenced the statistical analysis of this study.

A total of eight post-operative complications were observed during six months of healing time (7/18 in PFT group vs.1/11 in DFT group) in the study. Overall, the post-operative complication rate was 27.6%. The mean complication rate was lower in DFT group (9.1%) than in PFT group (38.9%). Although there was no statistically significant difference between PFT group and DFT group (P=0.087) (Table 4) regarding the complication rate, this may be due to the limited sample size. These results suggest that future research projects need to investigate whether the double-flap technique potentially reduces the incidence of complications.

In PFT group, a total of seven complications were observed. These consisted of two sites with infection, two sites with continuous discomfort/membrane dislocations, one site with paresthesia, and two sites with membrane exposure. In DFT group, only one complication with membrane exposure was observed.

In PFT group, two patients experienced continuous discomfort after GBR. During

membrane removal procedures in these cases, membrane/tack dislocations were found. The same finding was observed in all two patients who had membrane exposure in PFT group. The stabilization of the membrane by firm fixation with tacks/screws is a key to minimizing those complications. However, it is recognized that the stabilization of membrane with tacks and screws is challenging for clinicians while dealing with type I hard bone for GBR procedure. The double-flap technique has a significant advantage for the stabilization of membrane and graft material. The double-flap consists of two flaps, the periosteum flap (inner layer) and the mucosal flap (outer layer). The periosteal flap can be utilized for the stabilization of membrane and graft material with horizontal mattress suture technique. (Figure 9,10) Four of the seven total complications in PFT group were associated with membrane/tack dislocation. The double-flap can be used as an alternative to conventional periosteal fenestration technique to minimize those complications.

One patient in PFT group experienced slight paresthesia in lower lip after GBR procedure. Greenstein proposed a dome-shaped incision in the area of the mental foramen for the GBR procedure in the posterior mandibular region. In the paper, the authors advised that making deep incisions coronal and mesial to the mental foramen need to be avoided due to unknown location of branches of the mental nerve. In this study, 27 sites out of 29 sites were in the posterior mandible. The shallow incision can be helpful to avoid the incidence of nerve damage.[31] However, clinicians often encounter situations in which deep and/or multiple periosteal incisions are required to achieve tension-free primary closure. Therefore, it is a challenge for clinicians to achieve successful results in

this area of critical size defect with conventional periosteal fenestration technique. The authors feel that the double-flap technique offers significant advantages over the conventional periosteal fenestration technique because there is little risk of damage to the branches of the mental nerve due to the nature of the flap design without the deep incision.

In this study, a total of three sites in three patients showed membrane exposure with one site in the DFT group, two sites in the PFT group in the healing time. Overall, the membrane exposure rate was 10.3 %. The mean membrane exposure rate is lower in the DFT group (9.1%) than in the PFT group (11.1%). There is no statistical difference between the DFT group and the PFT group regarding the membrane exposure rate ($p= 0.874$). However, there are only three total membrane exposure sites and it is difficult to draw the conclusion from the result.

During implant surgery, we observed that one of the patients in the PFT group with membrane exposure had the membrane torn in two parts and the membrane and tacks dislocated. It suggests that the strong chewing force by mastication is contributed to the occurrence of membrane exposure. After GBR surgery, patients received thorough post-operative instruction about the importance of avoiding force and pressure on the surgical sites, but after the initial healing, they tended to forget that the same care is still required until the membrane is removed at the time of implant surgery. Therefore, repetitive reinforcement of the post-operative instruction at each follow-up visit is critical. Also, the patient's compliance is essential for the successful GBR.

The mean flap advancement (mm) of the double-flap technique was significantly greater than the mean flap advancement of the conventional periosteal fenestration technique (9.64 mm vs. 7.14 mm). (Figure 7) There is a statistically significant difference between these two groups (P=0.025). (Table 6)

Overall, the double-flap technique reduces the pain/discomfort level for patients such as pain, swelling, and bleeding; post-operative complications such as paresthesia, continuous discomfort (membrane dislocation); and the membrane exposure rate as compared to the conventional periosteal fenestration technique.

This study showed that the double-flap technique (DFT) yields a predictable outcome for guided bone regeneration. It is a practical technique to enhance flap advancement for the tension-free primary closure, and to stabilize the wound in the course of healing. Within the limitations of this study, there were not statistically significant differences in the pain/discomfort level, the complication rate or the membrane exposure rate between the double-flap technique and the periosteal fenestration technique. However, overall, the double-flap technique showed preferable results in the previously stated aspects compared to the periosteal fenestration technique. A small sample size and other factors may have impacted the statistical results of this study. Further studies are required with a larger sample size and modifications to the study methods to investigate the efficacy of the double-flap technique.

(Part II)

The study showed a significant change of alveolar bone volume during the course of a six months healing phase subsequent to GBR procedures using FDBA and e-PTFE membrane.

The following is a summary of the results of this study.

1. The bone loss pattern was not uniform for both vertical bone loss and/or horizontal bone loss.

2. The vertical bone loss is greater than the horizontal bone loss.

3. The horizontal bone loss in the mesial and distal locations is greater than the horizontal bone loss in the center location.

4. The horizontal bone change in the mesial sites was more prominent compared to the distal sites.

5. The horizontal bone loss 7mm apical to the alveolar crest is greater than the horizontal bone loss 3mm and 5mm apical to the alveolar crest.

6. The most significant bone resorption was observed in the areas with soft tissue invagination. It was noticed that the location was frequently related to difficult membrane adaptation due to the presence of a mental nerve.

Current investigation showed the significant change of alveolar bone volume during the course of a six months healing phase following GBR using FDBA and e-PTFE membrane. The mean loss of augmented bone ranged from 4% to 21% during the six months of healing. The results can be compared with 39-76% volume changes reported by Simon et al.[42] The authors used a resorbable membrane and DFDBA for GBR procedures. Our study results indicate a higher rate of success in maintaining the volume than in Simon's study. This finding is consistent with previous investigations comparing a resorbable and a non-resorbable membrane.[11, 13]

The complications such as membrane exposure and infection resulted in the loss of bone graft. From the current investigation, we noticed that bone resorption rates related with post-surgical complications are more significant as compared to the resorption rate on surgical sites with uneventful healing. For a successful GBR, thorough surgical planning, the appropriate surgical technique, and patient compliance are required to achieve the ideal treatment goal for the procedure.

Bone augmentation for the critical size defect using non-resorbable membrane is one of the most technique sensitive procedures in dentistry. The lack of tension-free primary closure is a typical cause of complications such as membrane exposure and infection. The failure of tension-free primary closure is possibly the cause of some of the complications. The findings of diminished bone volume for the site with post-operative complications correspond with other studies by Zitzmann et al. and Simion et al. that the membrane exposure site showed less bone regeneration.[43]

The study showed that the vertical bone resorption rate is greater than the horizontal bone resorption rate. Compared to a resorbable membrane, the titanium-reinforced e-PTFE membrane could resist compression, because this membrane has a framework which can support itself. However, compression on the surgical site, food contact during mastication, and mechanical forces by patient's daily function, such as swallowing or speaking, can cause the collapse of the membrane and influence the amount of bone regeneration. The collapse of the membrane reduces the space for bone regeneration. Similar observations were reported in previous studies by Simion et al. and Jovanovic et al.[43, 44]

Micro-movement of the membrane results in a loss of the bone graft. Space creation and space maintenance under the membrane for bone ingrowth are essential for achieving successful GBR. Immobilization of the membrane by proper fixation is one of the keys for success. This study showed greater bone resorption rate in the mesial locations than in the center and the distal locations. Fibrous tissue invagination under the membrane was often observed on the mesial margin of the membrane during reentry for placement implant surgery. (Figure 11) It may be that the presence of a mental foramen location on the mesial aspect of posterior mandible prevents ideal fixation.

Macro-movement or dislocation of the membrane can cause infection resulting in failure of adequate bone regeneration. The patient with membrane dislocation resulting from a fractured fixation tack showed a greater amount of bone resorption. We observed granulation tissue under the membrane along with massive bone resorption. Authors suggest fixation screws rather than fixation tacks for hard bone on the posterior mandible.

VI. Conclusion

The double-flap technique presented in the study showed comparable clinical performance with conventional periosteal fenestration technique in guided bone regeneration. Within the limitations of this study, between the double-flap technique and the periostal fenestration technique, there were no statistically significant differences in the pain/discomfort level for the patient, such as pain, swelling, and bleeding; frequency of post-operative complications such as paresthesia, continuous discomfort (membrane dislocation); and membrane exposure rate. However, overall, the double-flap technique showed lower pain/discomfort level for patients as well as lower numbers of post-operative complications when compared to the conventional periosteal fenestration technique. Results further indicated that the double-flap technique significantly enhances flap advancement compared to the conventional periosteal fenestration that facilitates primary closure after guided bone regeneration. Used appropriately, this new technique may reduce the probability and severity of post-operative complications and achieve predictable outcomes for guided bone regeneration. The double-flap technique can be utilized as an alternative option to the conventional technique.

The study showed a significant change of alveolar bone volume during the course of a six months healing phase subsequent to GBR when using FDBA and an e-PTFE membrane. One should expect more predictable bone growth under a non-resorbable membrane compared to a resorbable membrane. A close adaptation, stabilization and firm fixation of the membrane is desired for the grafted site with the e-PTFE membrane and FDBA. Proper surgical planning is critical for clinicians who need to consider accurate overaugmention of alveolar bone to achieve predictable outcomes for GBR.

VII. References

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VIII. Appendix

COMPLICATION SURVEY

Name:

Day of survey:_____ (__ th days after surgery)

Day of surgery:

LOCATION (please check the appropriate box):

▢ Maxillary Left ▢ Maxillary Anterior ▢ Maxillary Right

▢ Mandibular Left ▢ Mandibular Anterior ▢ Mandibular Right

Number of Teeth Involved: Two ( ) Three ( )

Extraction of Teeth Yes ( ) No ( )

Question A-C: Your experience during the first 4 days after the surgery (please circle the number on the scale where appropriate)

A: Pain – Severity (1-10):

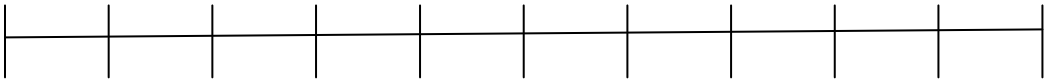
Slight (0-3): No or little discomfort

Moderate (4-6): pain which bothered you, or mildly affected your daily functions

Severe (7-10): pain could not be tolerated, or pain which disrupted your daily functions (ex: difficulty to eat, difficulty to speak)

No pain — Worst possible pain

0 1 2 3 4 5 6 7 8 9 10



B: Swelling – Severity (1-10):

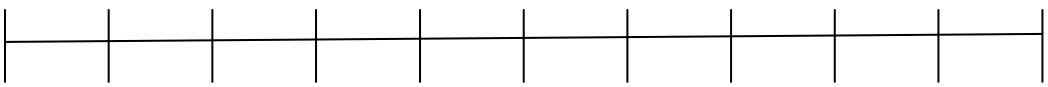
Slight (0-3): No abnormal feeling or slighty visible change in appearance to a feeling of fat which you could not be recognize at a glance

Moderate (4-6): moderate visible change which you could recognize apparently or easily in size and shape in addition to a feeling fat

Severe (7-10): very noticeable change in the size and shape

No Swelling — Very Noticiable

0 1 2 3 4 5 6 7 8 9 10



C: Bleeding – Severity (1-10): Slight (0-3) Mod. (4-6) Severe (7-10)

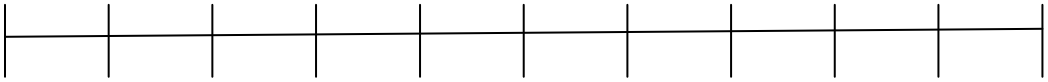
Slight (0-3): No to minimal bleeding ranged from no detectable bleeding to a trace of blood clot without any care

Moderate (4-6): oozing or mild bleeding which would stop by home care

Severe (7-10): bleeding could not be stopped with home care or telephone instructions

No Bleeding — Bleeding could not be stopped

0 1 2 3 4 5 6 7 8 9 10



D: Other clinical findings during healing period (to be checked and filled by a research assistant):

▢ membrane exposure:

if yes,

▢ (Early) Before Suture removal (< 2 weeks after surgery)

▢ (Moderate-1) 2-4 weeks after surgery

▢ (Moderate-2) 4-6 weeks after surgery

▢ (Slight) > 6 weeks after surgery

▢ premature loss of grafting material,

▢ infection, if yes, what treatment was done _____

▢ foul smell

▢ pus discharge

▢ temperature

▢ bruise, if yes, size ___ ×___ mm

▢ paralysis, if yes, describe symptom _____