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Clinical evaluation of socket preservation using Platelet Rich Fibrin in comparison with Freeze Dried Allograft: A Randomized Clinical Trial

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Publication Date
2016

Peer reviewed|Thesis/dissertation

Clinical Evaluation of Socket Preservation using Platelet Rich Fibrin in Comparison with Freeze Dried Allograft: A Randomized Controlled Clinical Trial

by

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THESIS

Submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in

Oral and Craniofacial Sciences

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

[redacted]

DEDICATION

I would like to dedicate this Master's Thesis to all my Periodontology faculty and friends at the University of California San Francisco for making this journey a wonderful and great experience.

ACKNOWLEDGEMENTS

I would like to thank Dr Mark Ryder, Dr Georgios Kiurtsidis, Dr Pinelopi Xenoudi and Dr John Dollard for their support and assistance for my master thesis.

I would like to acknowledge Dentis, USA for their generous support in funding our research.

Finally, I would like to thank my fellow co-residents for their continuous support to complete this study.

Clinical evaluation of socket preservation using Platelet Rich Fibrin in comparison with Freeze Dried Allograft: A Randomized Clinical Trial

Yogalakshmi Rajendran, BDS

ABSTRACT

Background: The primary objective of this study was to evaluate the clinical efficiency of Platelet Rich Fibrin (PRF) alone or PRF combined with freeze-dried bone allograft (FDBA) as compared to FDBA alone or no graft (blood clot) in improving alveolar dimensional stability during ridge preservation.

Methods: 33 patients with a non-molar tooth that required extraction and implant placement were randomly assigned to one of four groups. For group A, the extraction socket was allowed to heal with a blood clot. For group B, the sockets were treated with PRF plug. For Group C, the extraction socket was treated with a mixture of PRF with 0.5cc of Freeze Dried Bone Allograft. Finally, group D sockets received 0.5cc of Freeze Dried Bone Allograft. Clinical measurements of alveolar ridge height and horizontal ridge width were taken after extraction (baseline) as well as at the time of implant placement (3 months).

Results: A statistically significant reduction in the vertical height loss was seen in Group C (PRF+FDBA) 1.5±2.3mm when compared to Group A (blood clot) 4±2.0mm. Similarly, a statistically significant reduction was noted for alveolar vertical height loss for Group B (PRF) 1.6±2.1mm when compared to Group A (blood clot) 4±2.0mm. There was no statistically significant difference in horizontal ridge width between groups.

Conclusion: The results of the study showed that the vertical height loss was significantly less in PRF group (1.6±2.1mm) and PRF with FDBA group (1.5±2.3mm) when compared to blood clot group (4±2.0mm). There was a clear trend for greater ridge width preservation with PRF and FDBA combined.

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BACKGROUND

The healing process of the extraction socket is widely researched and studied. Animal study[1] conducted by Araujo and Linde, showed that there is substantial change in the ridge dimension after a tooth extraction. The dimensional change after extraction is more pronounced on the buccal bone than on the palatal bone. Extraction of teeth not only causes hard tissue changes but also soft tissue alterations. Extraction of more than one tooth can cause further significant alterations in the height and width of the alveolar ridge[2]. A systematic review[3] concluded that after a tooth extraction the horizontal bone loss is more significant than the vertical bone loss. The review[3] showed that after the tooth extraction the horizontal bone loss at 6 months was approximately 2.46 - 4.56mm and the vertical bone loss was around 0.8 - 1.5mm. The resorption pattern is rapid during the first 3– 6 months after extraction, followed by a slow gradual reduction throughout life. Prosthodontic options for replacing the missing teeth after extraction are tooth-supported fixed, removable prostheses or implant-supported prostheses. The alveolar width dimension changes post extraction will eventually compromise the final esthetic results and prosthodontic rehabilitation for replacing the missing teeth.

Ridge preservation is a technique to preserve alveolar ridge dimensions during the healing of an extraction site. To minimize the resorption of the alveolar ridge various types of bone graft materials such as autografts, allografts, xenografts and growth factors are used in the ridge preservation technique[4]. A systematic review[5] by Avila–Ortiz et.al has revealed that the clinical gain after socket preservation using either allograft or xenograft is up to 1.89 mm in bucco-lingual

width and up to 2.07 mm for mid-buccal height. Several growth factors[6], such as platelet-derived growth factors (PDGF), insulin like growth factor (IGF)[7], and bone morphogenetic proteins (BMPs), are used to promote bone regeneration for post extraction healing.

Platelet-rich fibrin (PRF) was first introduced by Choukroun[8] in 2001 and it is prepared without using any anticoagulants like bovine thrombin. The PRF[9-11] protocol involves: venous blood drawn in a 10ml glass tube and centrifuged at 3000rpm for 8min. The three layers formed in the tube after centrifugation are: a base of red blood cells at the bottom, supernatant layer of acellular plasma on the top (supernatant), and a clot of PRF between them. The membrane consists of a fibrin matrix enriched with platelets, cytokines, leukocytes, and growth factors[12]. This property of the PRF membrane helps accelerate the wound healing. The regeneration potential of the PRF membrane has led to its application in various treatments such as sinus floor elevation, ridge augmentation, socket preservation, root coverage, intra-bony defects, and furcation defects[13-15]. An in-vitro study[16] has revealed that the PRF membrane maintains a very slow release of potential growth factors (Transforming Growth Factor b-1 (TGFb-1), platelet derived growth factor AB, PDGF-AB; vascular endothelial growth factor, VEGF) for a period of one week. The gel like consistency of the PRF membrane allows ease in manipulation and suturing.

The purpose of this randomized controlled clinical trial was to evaluate the clinical efficiency of PRF alone or PRF combined with freeze-dried bone allograft (FDBA) as compared to FDBA alone or no graft (blood clot) in improving alveolar dimensional stability during ridge preservation.

MATERIALS AND METHODS:

Patient enrollment:

The Institutional Review Board of the University of California San Francisco reviewed and approved the research protocol. The clinical trial was conducted according to the principles outlined in the Declaration of Helsinki on clinical research, as revised in 2000. This study was conducted in University of California San Francisco between December 2014 – May 2016. The patients included in the study were 17 males and 16 females (aged 24 to 74 years: mean age: 58.7 ± 13.4). All the surgical procedures were performed by three operators – DC, SP and YR. The patients were randomly assigned into 1 of 4 ridge preservation treatment modalities. All treatment and measurements were performed by one of three periodontal residents at a single clinical site. The three residents were blinded to treatment modality and were also previously calibrated with the same measurement methodology.

The inclusion criteria for the study patients were:

a. 18 years or older
b. With non-molar tooth requiring extraction
c. With intact buccal and lingual plate within approximately 3-4 mm from gingival crest
d. Had no clinical or radiographic signs of periapical pathology
e. Had good oral hygiene

Patients were excluded if they:

a. Were unable to comply with necessary scheduled visits
b. Had poor oral hygiene
c. Had failing/failed endodontic treatment with history/presence of sinus tracts
d. Were pregnant or intended to become pregnant
e. Were current or past smokers
f. Were immunosuppressed
g. Had type I or type II diabetes
h. Were diagnosed with any blood disorders.

Thirty-three patients whose treatment plan was extraction of non-molar tooth were included in the study. Written informed consent was obtained from each patient. The patients were randomly assigned (10 in each group) to one of the four groups listed in Table 1. After patient assignment, alginate impressions were taken in order to fabricate a stent for use during the clinical measurements.

Surgical Protocol:

Minimally traumatic tooth extraction was completed under local anesthesia. After debriding the extraction sockets, the horizontal and vertical ridge dimensions of the socket were recorded. The measurements of the socket were taken using a pre-fabricated stent, caliper* and a periodontal probe$^{\propto}$.

Figure 1 shows a picture of the guide on a patient's cast. The pre-fabricated stent was made on the patients' study models to establish a standard index and reference for the clinical measurements. The vertical height was measured from the mid buccal crest to the bottom of the stent using the stent and a periodontal probe $^{\propto}$. The bucco-lingual horizontal width was measured from the coronal, middle and the apical third of the socket with a caliper and the stent. All the extractions were flapless and the caliper* perforated through the soft tissue until the bone was sounded.

After completion of the clinical measurements, the sockets were treated based on the assigned treatment group. For group A, the extraction socket was allowed to fill with a blood clot. For group B and C - the PRF was prepared according to the protocol outlined by Chourkron[8]. Prior to the extraction, venous blood was collected in three 10ml sterile glass tube via venipuncture of the antecubital vein. The blood sample was immediately centrifuged at 3000 rpm for 8 minutes.

∝- UNC15 Periodontal Probe, Hu-Friedy, Chicago, IL

* - Ridge mapping caliper, G.Hartzel & Son, Concord, CA

∂- HeliPlug, Osteohealth, Shirley, NY

##- 5-0 Vicryl, ACE Surgical Supply, Brockton, MA

Ψ - FDBA -0.5 c.c, Corticocancellous, ACE Surgical Supply, Brockton, MA

The PRF plug of appropriate dimension was placed into the extraction sockets until it filled crest of the group B patients. For group C, the PRF was cut into small pieces and placed in a sterile metal bowl. 0.5cc of Freeze Dried Bone Allograft[Ψ] (FDBA) was mixed with the PRF in the sterile metal bowl. The mixture of PRF with FDBA[Ψ] was placed in the extraction socket until it filled the crest. For group D, socket was filled with 0.5cc FDBA[Ψ] until the crest. For all the groups, the treated sockets were covered with Heliplug[∂], sutured with horizontal mattress 5-0 vicryl[##] and coated with PeriAcryl® (cyanoacrylate adhesive).

All the patients were instructed to rinse with 0.12% chlorhexidine gluconate twice a day for ten days. All the patients were seen for post- operative follow up at 2 weeks to remove the sutures, and again at 1 month to assess healing. After 90 days of healing the patients were scheduled for dental implant placement. Each patient's individualized thermoplastic stent was then used to repeat the same clinical measurements. After recording the clinical measurements, crestal incision was made and a full-thickness flap was reflected to prepare the osteotomy for the dental implant placement. Implant site osteotomy were completed according to the manufacture's protocol and the dental implants were placed.

Statistical Methods:

A four-way analysis of variance was used to evaluate the statistical significance between the

groups from baseline to final clinical measurement. The clinical measurements were considered significant when $P<0.05$. Unpaired t-test was used to evaluate the difference between the groups over time.

RESULTS:

Socket preservation was completed for all 33 patients, 17 males and 16 females (aged 24 to 74 years: mean age: 58.7 ± 13.4). The extracted teeth consisted of: 7 Maxillary Incisors, 2 Maxillary Canines, 18 Maxillary Premolars and 6 Mandibular Premolars. Baseline characteristics of the patients are listed in Table 2. The mean values of the clinical measurement for all the groups for baseline and 3 months healing are listed in Table 3 and 4.

There was significant difference in the alveolar crest height change between group A (Collaplug) and group C (PRF+FDBA). Clinically, group C (PRF+FDBA) showed decreased height loss and coronal width loss when compared to other groups (Figure 3). There was no statistically significant difference in horizontal ridge width between the groups (Table 5).

DISCUSSION:

The purpose of this randomized controlled blinded study was to determine the clinical efficiency of PRF alone or PRF combined with freeze-dried bone allograft (FDBA) in improving alveolar dimensional stability following ridge preservation. The vertical height preservation is important for ideal esthetic results and for placement of ideal length implant. In our study, there was

statistically significant difference in the alveolar height change from baseline to 3 months between group C (PRF+FDBA) and group A (Blood Clot) and between group B (PRF) and group A (Blood Clot). There was no statistically significant difference between the groups in horizontal ridge dimensions when compared from baseline to 3 months. The horizontal ridge preservation is essential for a favorable implant position. PRF offers a space maintenance property which is enhanced with the addition of bone graft material. In our study there was a trend in horizontal ridge width preservation in PRF with FDBA group compared to the blood clot group.

Several studies have investigated the alveolar ridge changes following ridge preservation using various bone graft materials. The challenge is to choose the ideal graft that acts as a scaffold and a good space maintainer to preserve the ridge. There is difference in the amount of new bone formation and amount of the residual graft material after ridge preservation procedure between studies. This is due to the different technique and materials used for such procedures[17]. The flap elevation, usage of a membrane, and the application of a bone graft material has been shown to enhance the outcomes of the buccal and lingual vertical height preservation[5]. Vertical height preservation will have an impact on dental implants because it allows the implant to be placed in an ideal restorative position. Alveolar ridge preservation can result in sufficient bone to place an implant and reduces the need for additional grafting procedures.

Platelets contain essential mitogenic and chemotactic growth factors which are important in wound healing. Wound healing studies have shown that the fibrin, PDGF, and transforming growth factors

(TGF-b) are essential to increase the integrin and fibroblast proliferation[21]. Platelet concentrates are useful in wound healing because they function as a sealant with a sustained delivery of mitogenic and chemotactic growth factors. PRF is an autologous blood product which is prepared without any addition of thrombin. PRF contains platelets, B and T lymphocytes, stem cells and growth factors that are entrapped in its fibrin network. It has been suggested that the fibrin network can prevent the growth factors from proteolysis and increase the function of the growth factors for a longer period of time[22]. An in-vitro study has shown that the PRF has a controlled and sustained release of growth factors like TGF-1 and PDGF-AB and the highest release was seen at 2 weeks[23]. PRF has been shown to increase proliferation and differentiation of osteoblast, pre-keratinocyte, and gingival fibroblast[23].

PRF is easy to prepare, does not require any anticoagulant and it is a cost effective material. It has a rich fibrin matrix with a steady and sustained release of growth factors[9]. PRF has been shown to permit rapid angiogenesis and remodeling of fibrin with a resistant connective tissue[12]. Due to its significant properties and handling characteristics, hard tissue regenerative procedures can benefit from the application of PRF.

In this study, all the 33 patients received dental implant placement after 3-month post extraction. All the dental implants were placed with good primary stability. The dental implants ranged in diameter from 3.3 to 4.5mm and in length from 10 to 12mm. The overall success rate of the dental implants was 97% with the loss of one implant during early loading. After four months of follow-up, the patients were sent to the restorative dentist for receiving implant crowns. There were no surgical complications and all the surgeries healed uneventfully. 13% of the sites required

additional grafting at the time of implant placement.

Our alveolar ridge preservation study showed a trend in preserving horizontal alveolar ridge dimensions and significant reduction in vertical height loss with the use of PRF. The mitogenic and chemotactic properties of PRF along with the space maintenance characteristics of the allograft can help in preserving alveolar ridge dimensions after tooth extraction. This characteristic of PRF can also be used in hard and soft tissue regeneration procedures to accelerate wound healing.

In several studies, the clinical evaluation was done after six months of healing following the ridge preservation procedure[20]. In this study, a shorter re-entry period of 3 months was used to evaluate if PRF could accelerate the bone regeneration. In this study, the shorter re-entry of 3 months led to successful implant placement in all four groups. The results of this study demonstrate that the use of PRF can considerably reduce the loss of vertical ridge dimension when compared to socket healing with a blood clot. Ridge preservation with PRF can minimize the need for additional grafting for dental implant placement. However, the limitations of the study include small sample size and shorter follow up period. Further studies are required to evaluate the efficacy of PRF for soft tissue and hard tissue regeneration.

Conclusion:

We conclude that ridge preservation with PRF combined with FDBA significantly limits the loss of hard tissue ridge height when compared to blood clot. Horizontal ridge maintenance in PRF with FDBA group (group C) was better when compared to the other groups. Further studies need

to be carried out with a larger sample size and longer follow up to identify the role of PRF as a biologic in hard tissue regenerative procedures.

Table 1. Study Groups:

Group A	Group B	Group C	Group D
No bone graft used Collagen plug only	PRF and collagen plug only	PRF and FDBA bone graft with collagen plug	FDBA bone graft collagen plug

Figure 1. Prefabricated stent prepared using triad material and patient's model

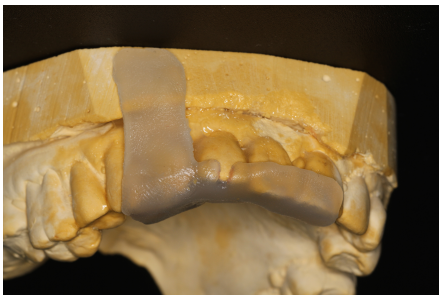
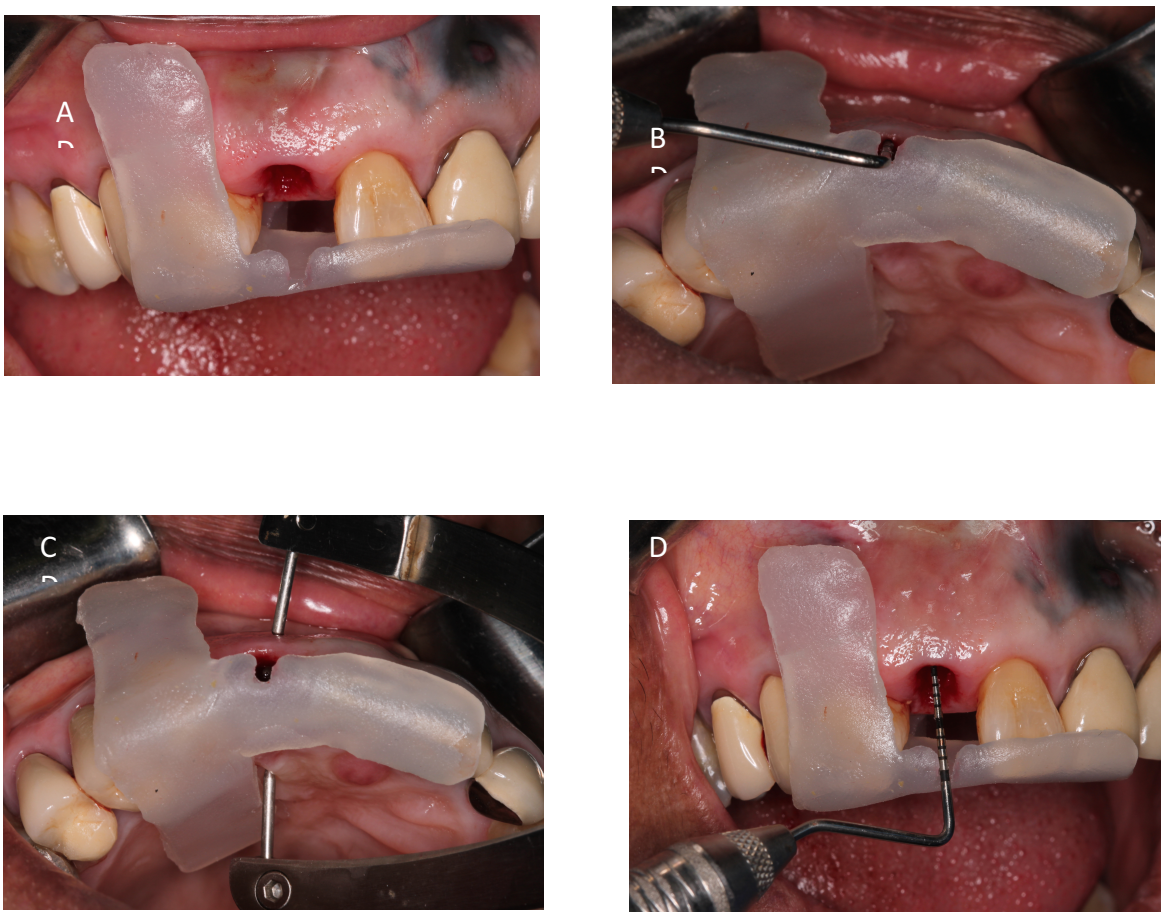


Table 2.

Baseline Characteristics of the Study Patients

Characteristics	Group A N = 9	Group B N = 8	Group C N = 8	Group D N = 8
Age - yr	56.8±13.1	62.3±14.2	58.1±12.7	57.4±15.7
Gender				
Male	5	5	4	3
Female	4	3	4	5
Tooth position				
Incisor	1	1	2	3
Canine	-	2	0	0
Premolar	8	5	6	5

Figure 2: Stent in place to record clinical measurements.



A) Facial view of the stent. **B)** Occlusal view of the stent. **C)** Caliper used to sound bone for horizontal ridge width. **D)** Periodontal probe used to measure the vertical height from the bottom the stent to the crest of the buccal bone

Table 3

Initial Clinical Measurement (mm,mean±SD)

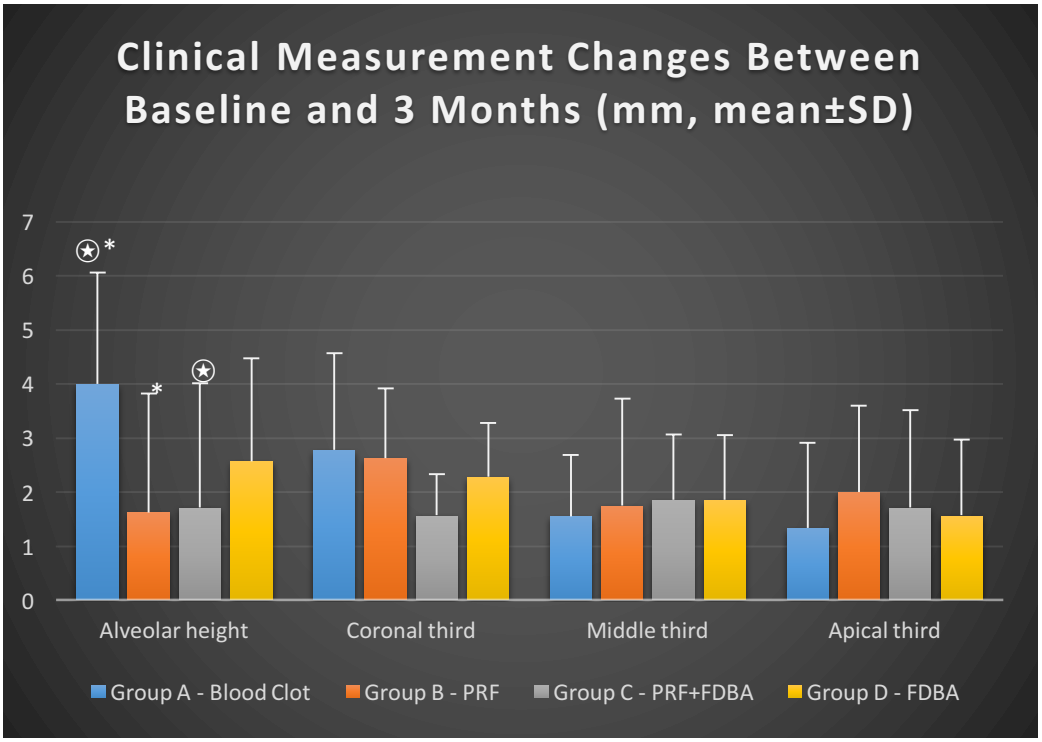
Groups	Alveolar Crest Height	Coronal Third	Middle Third	Apical Third
Group A	9.4±2.9	8.4±1.8	9.2±2.0	9.1±3.1
Group B	12.1±3.4	9.1±1.2	10.1±1.7	11.3±1.7
Group C	9.8±2.1	7.4±1.8	9.8±2.4	10.5±2.5
Group D	12.5±3.0	7.8±2.1	9.1±2.4	10.7±1.7

Table 4.

3 - Months Clinical Measurement (mm, mean±SD)

Groups	Alveolar Crest Height	Coronal Third	Middle Third	Apical Third
Group A	13.4±2.9	5.6±1.4	7.6±2	7.7±1.9
Group B	13.7±3.4	6.5±1.5	8.3±2.0	9.3±2.1
Group C	12.4±2.4	6.4±2.4	8±2.8	8.8±3.4
Group D	15.1±1.8	6.1±1.6	7.2±1.4	9.1±1.3

Figure 3: Ridge changes from baseline to 3 months.



$p<0.05$ between Group A and C and Group A and B in Alveolar Crest Height Changes. The mean values were calculated from individual patient data.

* - group B statistically significant than group A

⍟ - group C stastically significant than group A

Table 5

Clinical Measurement Changes Between Baseline and 3 Months (mm, mean±SD)

Mean ± SD (mm)	Group A Blood Clot	Group B PRF	Group C PRF+FDBA	Group D FDBA
Loss of Ridge Height	4.0±2.06*¶	1.63±2.2*	1.50±2.33¶	2.38±1.92
Loss of Ridge Width (Coronal)	2.78±1.79	2.63±1.3	1.50±0.76	2.38±1.06
Loss of Ridge Width (Middle)	1.56±1.13	1.75±1.98	1.86±1.21	1.86±1.21
Loss of Ridge Width (Apical)	1.33±1.58	2.0±1.6	1.71±1.8	1.57±1.4

$p<0.05$ between Group A and C and Group A and B in Alveolar Crest Height Changes. The mean values were calculated from individual patient data.

*Statistically significant difference noted between group B and A

¶ Statistically significant difference noted between group C and A

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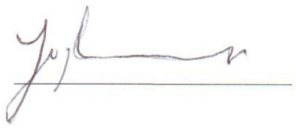

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