Volumetric Changes and Marginal Bone Loss Using Soft Tissue Allograft for Single Tooth Implant Therapy

BY

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Submitted as partial fulfillment of the requirements for the degrees of Master of Science in Oral Sciences in the Graduate College of the University of Illinois at Chicago, 2023

Chicago, IL

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This thesis is dedicated to my fiancé, David, who has been a constant source of support and encouragement during the challenges of residency and graduate school. This work is also dedicated to my loving family overseas.

ACKNOWLEDGEMENTS

I would like to thank Dr Sandra Al-Tarawneh for her insight and guidance as my thesis advisor. This work was supported by Dentsply Sirona Inc ®.

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LIST OF ABBREVIATIONS

MBL	Marginal Bone Loss
ROI	Region of Interest
STL	Standard Tessellation Language
IOS	Intra-oral Scanner
UIC	University of Illinois Chicago
WES	White Esthetic Score
PES	Pink Esthetic Score
CTG	Connective Tissue Grafts
FGG	Free Gingival Grafts
CBCT	Cone-Beam Computed Tomography
ADM	Acellular Dermal Matrix

SUMMARY

Background Literature: An increase in the volume of soft tissues around dental implants is advocated for the longevity of implant restorations and maintenance of health [1]. The use of soft tissue grafts has been implemented to help establish biologic and functional stability around dental implants. Autogenous grafts require a donor site with associated morbidities [2] and allogenic grafting materials were identified as a suitable alternative for implant site development [3,4]. Acellular dermal matrix allograft (e.g.: PerioDerm®) was shown as an effective treatment for soft tissue augmentation around teeth and dental implants [5]. However, the evidence around the use of allogenic materials for soft tissue augmentation is controversial [4,6,7] and most of the publications have incorporated collagen matrices rather than acellular dermal matrices [8–10]. Additionally, there is relatively little evidence on the volumetric changes associated with these grafts. Therefore, the aim of this study is to evaluate the volumetric soft tissue and marginal bone level changes with and without a submucosal connective tissue allograft (PerioDerm®).

Materials and Methods: Patients who need dental implant therapy were enrolled in a prospective randomized clinical trial. All implant sites did not require significant bone augmentation, received a single implant, and were randomly allocated to a control (-Graft) or test group (+Graft). A fully digital workflow for the surgery and restoration was implemented. Intraoral scans were taken before implant placement (T0), at time of final restoration delivery (T1) and at one-year post restoration delivery (T2). Periapical radiographs were taken at implant placement (T0), crown delivery (T1), and one-year post crown delivery (T2). Primary study outcome is the volumetric difference in buccal soft tissue levels as measured through 3-dimensional intra-oral scanning within a well-defined region of interest (ROI) (T2-T0), and secondary outcome is the change in

marginal bone levels (MBL) as measured by peri-apical radiographs (T2-T0).

Results: A total of 39 subjects were recruited but the resulting sample size is 35 subjects after 2 subjects were lost due to failure to follow-up and 2 subjects experienced biologic failure. 18 subjects received the allograft at the time of implant placement (test group) and 17 subjects did not receive any soft tissue augmentation (control group).

Both test and control groups showed an increase in buccal tissue volume without significant differences between the two groups for volumetric measurements ($P>0.05$) The secondary outcome of marginal bone loss showed slight loss in marginal bone levels in both groups with no significant difference on the mesial surface ($p=0.070$) nor the distal surface ($p=0.835$).

Conclusions: Within the limitations of this study, the results demonstrate healthy and stable peri-implant outcome in terms of volumetric changes and marginal bone levels when a submucosal connective tissue allograft (PerioDerm®) was used. The use of alternative grafting materials to autogenous grafts provides many advantages in terms of reducing surgical time, complications, and associated patients' morbidity. Overall, implementing a full digital workflow offers excellent reliability, efficiency, and accuracy.

1.0 INTRODUCTION

The esthetic and functional rehabilitation of a missing tooth with a dental implant requires careful surgical planning, execution, and management of the soft tissues. After tooth loss, bone and soft tissue resorption and remodeling occurs and often results in volumetric deficiencies [8,11–13]. To account for this, soft and hard tissue augmentation procedures are recommended to predictably create a proper site for prosthetically-driven implant placement [11].

Soft tissue augmentation is generally performed to improve the tissue quality (thickness and width of keratinized tissue) and/or quantity (tissue volume) [11]. Additionally, it is advocated to help preserve marginal bone levels due to the sufficient seal of the peri-implant soft tissue collar [14]. It was also shown that the thickness of peri-implant soft tissues can have an effect on marginal bone levels [15].

Soft tissue grafting has been implemented to improve the esthetic, biological, and functional harmony around dental implants and it is currently a part of dental implant therapy [8,13]. Adequate thickness and volume of soft tissue around dental implants is crucial for long-term maintenance of esthetics and function [15,16]. A lack of adequate keratinized tissue has been linked to increased plaque accumulation and inflammation around dental implants, which can lead to peri-mucositis and/or periodontitis [17]. Soft tissue augmentation is also advocated to help preserve marginal bone levels [14], as it was shown that the thickness of peri-implant soft tissues can have an effect on marginal bone levels [15].

Autogenous grafts harvested from the palate have been described as the gold standard in soft tissue grafts [7,9]. Disadvantages of these grafts include a secondary surgical site, increased post-surgical complications like pain, swelling, bleeding, palatal sensory dysfunction , infection, and

associated patient morbidity [11]. Therefore, alternative grafting materials have been the focus of recent research including xenografts and allogenic materials [3,4,11]. These materials were shown as effective for the augmentation of both the quantity and quality of soft tissues, while reducing procedure time and increasing patients' comfort [9,11,18].

Acellular dermal matrix (ADM) is a an allograft that is derived from human skin and has been used successfully as a substitute for palatal connective tissue in treating defects around teeth and dental implants [19,20]. One example is Perioderm® which has been used with promising results as a substitute for palatal connective tissue in treating defects around teeth and dental implants [19,20]. There is limited evidence on the effects of using acellular dermal allografts in the literature in regards to the volumetric changes and marginal bone levels. Most of the studies compared collagen matrices and autografts [3,4,8,9,18].

Implementing a digital workflow for obtaining data and subsequent measurements has proven to be a precise and reliable way for assessing volumetric changes [6,8,21]. Optical-based scanners have allowed the accurate analysis of volumetric differences which was not feasible with traditional methods, and presents a non-invasive and efficient workflow [22].

1.1 Objectives

The primary endpoint is the volumetric difference in soft tissue levels as measured through 3-dimensional intra-oral scanning. Secondary endpoint is the change in marginal bone levels (MBL) as measured by peri-apical radiographs.

1.2 Hypotheses

Based on our aims, we have formulated the following null hypotheses:

H_0: There is no association between the placement of a soft tissue allograft and the volume of soft tissues around dental implants

H_0: There is no association between the placement of a soft tissue allograft and marginal bone levels around dental implants

2.0 BACKGROUND

2.1 Peri-implant Mucosal Architecture

Controlling peri-implant gingival architecture starts with the proper diagnosis of the esthetic and functional demands as well as the prognosis of the outcome. In the diagnosis and treatment planning phase for a future implant site, several factors serve as crucial determinants of the treatment approach required [23,24]. Extra-oral considerations include the facial and lip support, upper lip length, buccal corridor, midline, jaw relationship, smile line, and symmetry [25]. Intraorally, inter-occlusal relationship, hard and soft tissue volume [26,27], and radiographic status are some of the factors that should be taken into account during the planning phase [23,28].

In order to achieve an optimal treatment result, a dental implant should be placed in the best three-dimensional position in the available bone with consideration to the final prosthesis and bone volume for proper soft tissue support [7,29,30]. Therefore, evaluation of the ridge morphology and architecture, status of the adjacent dentition, restorative space, and the white esthetic score (WES) [31] is important when assessing the hard tissues. In terms of the soft tissue outcome, the main objective is to maintain papillae, preserve a convex contour of the alveolar crest, and achieve a symmetric gingival margin with overall harmony in tissue levels [28,32]. Consequently, soft tissue color, texture, contour, morphotype, amount of keratinized tissue, and gingival zeniths' position should be evaluated. The pink esthetic score (PES) can serve as a helpful objective tool to assess peri-implant soft tissues as described by Fürhauser et al [33]. Overall, esthetic, biological, and functional success in implant therapy requires meticulous planning followed by careful surgical and prosthetic implementation.

2.1.1 Post-extraction Sequalae

After tooth extraction, significant dimensional changes of the alveolar ridge have been demonstrated [34,35] with systematic reviews showing an average of 29-63% horizontal alveolar ridge contraction after tooth extractions [36,37,38]. These defects are predominantly evident at the buccal contour, and can be a concern especially when planning implants in the esthetic zone [28,39]. Vertical tissue loss typically leads to recession and may expose the implant abutment or platform, whereas a horizontal deficiency can lead to unfavorable implant positioning and prosthetic complications [40]. Immediate implant placement was suggested to aid in reducing the alveolar ridge shrinkage after tooth extraction [41], but evidence shows that resorption will still occur despite this [42–44]. Healed extraction sockets are also volume deficient with 30-40% horizontal loss after extraction [42], so a delayed treatment approach may not be beneficial as well. To account for this, the application of hard and soft tissue grafts has been implemented in implant therapy, and is currently an essential part of clinical practice [6,13]. Augmentation procedures have been documented in the literature and can predictably create a proper site for prosthetically-driven implant placement [11].

2.1.2 Keratinized Tissue

Although controversial, an adequate thickness and width of keratinized tissue seems to be essential for long-term maintenance of natural dentition and dental implants [15,16]. Limited keratinized tissue around dental implants has been linked to a higher incidence of peri-implant mucositis and/or periodontitis [17]. The maintenance of adequate oral hygiene was shown to be more difficult in those implant sites, leading to more plaque accumulation, gingival inflammation,

recession, and ultimately attachment loss [45]. Research shows that the maintenance of adequate soft tissues around implants can lead to improvements in the plaque and gingival indices, and even marginal bone levels compared to sites lacking keratinized tissue [15,46]. However, contrasting evidence showed that the absence of keratinized tissue is not associated with peri-implant health, marginal bone loss, and plaque accumulation [1,47] and a minimum amount of tissue cannot be generalized [48]. On the other hand, it appears that certain clinical scenarios require adequate keratinized tissues, as depicted in this 10-year prospective study [49]. The findings from this study showed a significant increase in cases requiring antibiotic therapy for biologic complications when limited keratinized tissue was present [49]. It seems viable to ensure sufficient thickness of tissues when planning and providing implant therapy. After proper implant placement, the control of peri-implant tissues using properly contoured abutments and provisional crowns is essential to ensure uneventful healing and adequate tissue morphology.

2.1.3 Soft Tissue Augmentation

Augmentation procedures are advocated as an adjunct to implant placement regardless of the timing of implant placement [34,50] to preserve the alveolar ridge [39,51] and soft tissues [7,34,35]. It is proposed as a valuable tool to treat mucogingival defects and maintain optimal esthetics and function, and thus improving survival and success rates of implants and natural dentition [52]. The application of soft tissue grafts around dental implants emerged as an essential tool with two main goals: improving the tissue quality (thickness and width of keratinized tissue) and/or quantity (tissue volume) [11]. Another clinical indication include root coverage and treatment of recession,

which is associated with root caries, hypersensitivity, mechanical wear, and poor esthetics [53–55]. However, bone and soft tissue loss is still expected despite grafting procedures [35,56].

Many surgical techniques with different materials have been proposed in soft tissue augmentation. Grafts are generally divided into autogenous, xenogenic, allogenic, or synthetic materials.

2.1.4 Autogenous Grafts

Autogenous grafts are harvested from the same individual and are either free gingival grafts or connective tissue grafts. Free gingival grafts are typically harvested from a superficial area of the palate and consists mainly of lamina propria, with a greater amount of fibrous connective tissue and lower amount of adipose tissue [57]. Connective tissue grafts include a deeper portion of the palate and mainly contains submucosal tissue [57]. The maxillary tuberosity is a promising alternative donor site to the palate, which contains more lamina propria and less submucosa than a connective tissue graft harvested from the palate [58] and may provide less patient morbidity [59].

The main indication for autogenous grafts are increasing keratinized tissue width and treating mucogingival defects [53]. They were shown as an effective measure in reducing plaque levels, inflammation, and patient discomfort around dental implants with limited keratinized tissue [49,60]. Connective tissue grafts have been described as the gold standard in soft tissue augmentation [7,9]. However, It has been shown that grafts undergo significant shrinkage during the healing process (around 30%), so a graft larger than the recipient site is typically harvested, and this may contribute to the post-operative discomfort and surgical complications at the harvest site [61,62].

Autogenous grafts are associated with a higher patient morbidity, increased procedure time, surgical complications like hemorrhage, swelling, palatal sensory dysfunction, and infection [63–65].

Also poor color match with the surrounding tissue when free gingival grafts are utilized [65]. Furthermore, bleeding from the harvest site is common during the surgery and post-operatively regardless of the technique used [61]. The amount of available tissue might be deficient as well [66], and can be inadequate when treating multiple augmentation sites [63]. Another controlling factor for palatal harvesting is the thickness of the palatal mucosa, as limited residual thickness of the tissues over the bone has been related to greater analgesic consumption and carries a greater risk of flap over-thinning or tear [67].

2.1.5 Allogenic Grafts

Over the past few years, there has been an increase in the interest for alternative grafting materials that replace autogenous grafts to reduce patient morbidity and related complications [9,68]. Graft substitutes such as Acellular dermal matrix (ADM) [46,69] or collagen matrix [9,70] have gained popularity to address the shortcomings faced with autogenous grafts. Acellular dermal matrix (ADM) was originally introduced to the medical field to treat burn victims in 1992, and has been used in the medical and dental field as a substitute for connective tissue grafts [71,72]. One example is Perioderm® (Dentsply Sirona Inc, York, PA USA) which is a human skin allograft minimally processed to remove the epidermal and dermal cells. The purpose of this is to minimize the specific and non-specific inflammatory response [73]. After implantation, it serves as a scaffold which supports cell migration and capillary proliferation [74]. It has been used with promising results as a substitute for palatal connective tissue in treating defects around teeth and dental implants [19,20]. Recent randomized trials also demonstrated significantly more root coverage in the treatment of gingival recession when these grafts were utilized compared to non-grafted sites [75,76].

2.1.6 Marginal Bone Levels

Soft tissue augmentation is advocated to help preserve marginal bone levels due to the sufficient seal of the peri-implant soft tissue collar [14]. It has been advocated that a minimum of 3 mm of peri-implant mucosa is necessary for a stable epithelial connective tissue formation [77], and the thickness of peri-implant soft tissues was shown to have an effect on marginal bone levels [15]. Berglundh et al [78] reported that thin tissues can provoke crestal bone loss during formation of the peri-implant seal. A recent systematic review demonstrated that implants which received soft tissue augmentation showed less marginal bone loss when compared with non-augmented implants [79]. Another randomized controlled trial comparing thick and thin peri-implant soft tissue heights concluded that in implants surrounded by thin tissues, 1.5 mm of crestal bone loss occurred compared to 0.3 mm bone loss in those surrounded by thick tissues [77]. Adequate quantity and quality of tissues seems imperative for the maintenance of marginal bone levels around dental implants, however, the stability of crestal bone remains controversial [77].

2.1.7 Digital Assessment of Volumetric Differences

Several techniques for evaluating volumetric changes after implant placement have been described in the literature. Historically, ultrasonic probing, transmucosal assessment (endodontic probing), calipers, and CBCT (Cone-Beam Computed Tomography) are some of the techniques used to evaluate changes in soft tissue thickness [62,80]. These methods generally measure the thickness of the soft tissues rather than the 3-dimensional volume [22]. With advances in digital technology, alternative non-invasive methods have been developed, including optical-based scanning. Optical scanners were introduced to the dental field for generating 3-dimensional

images and digital impressions as Standard Tessellation Language files (STL) [81] and were initially developed to obtain digital impressions of the teeth and soft tissues [22,82]. It is widely used in dentistry to improve patients' comfort while providing an efficient and accurate digital workflow [83,84]. Over the past few years, optical scanning emerged as a valuable tool for longitudinal quantitative evaluation of soft tissue volume at different time points [22], and consequently proven to be a precise and reliable way for measuring volumetric changes [6,8,21]. This is accomplished through the superimposition of 3-dimensional images and subsequent measurements at different stages. Implementing this allows the accurate analysis of volumetric differences in every anatomical plane which was not feasible with traditional methods, and presents a non-invasive, efficient workflow without unnecessary radiation exposure [22].

3.0 MATERIALS AND METHODS

3.1 Study Design

The study was designed as a prospective randomized controlled trial with a 1-year follow-up. The main study outcome is the volumetric change in the peri-implant buccal soft tissues as measured through 3-dimensional intra-oral scanning. The secondary outcome is the change in marginal bone levels (MBL). IRB approval was obtained for clinical trials #2019-0255. Figure 1 depicts the treatment and research steps that were taken. Informed consent was obtained from all subjects. Randomization was performed by the study coordinator at the time of surgery using a computer algorithm (Redcap).

3.2 Sample

A Sample size of 40 (20 subjects per group) was estimated by power analysis where the average difference between the graft and non-graft group would be 1 mm gain for 80% of the test group and 10% for the non-graft group ($n = 16$; α: 0.05, β: 0.9). This correlates with a recent prospective clinical trial with a similar intervention [7]. A significant difference was demonstrated at 20 subjects per group. Another study compared 8 subjects receiving the graft to 10 without soft tissue augmentation demonstrated significant 3-dimensional volumetric changes using a similar optical-based analytic methodology [85].

3.3 Eligibility

The subject population will be:

a. Patients at the University of Illinois Chicago Dental School who desire placement of a dental implant for an already missing tooth or
b. Patients at the University of Illinois Chicago Dental School who desire placement of a dental implant for a tooth that will soon be extracted or
c. Patients in the community who desire placement of a dental implant for an already missing tooth or for a tooth that will soon be extracted

3.4 Inclusion Criteria

- At least 18 years of age
- Willing and able to provide informed consent
- In need of one implant to replace a missing tooth
- At least 20 teeth in good condition and occlusion
- Sufficient bone volume for dental implant placement without required bone augmentation
- Site development (soft and/or bone tissue) performed at least 5 months before implant placement, when required

3.5 Exclusion Criteria

- Implant cannot be placed without bone graft
- Unable to pay for crown
- Current smoker
- Untreated rampant caries and uncontrolled periodontitis
- Current alcohol or drug abuse
- Uncontrolled diabetes
- Systemic or local disease or condition that would compromise post-operative healing and/or osseointegration
- Use of bisphosphonates
- History of radiation in the head and neck region
- Unable or unwilling to return for follow-up visits
- Unrealistic esthetic or functional demands
- Unlikely to be able to comply with study procedures
- Unwilling or unable to provide informed consent
- Vulnerable populations (minors, pregnant women, prisoners) will not be targeted in the study

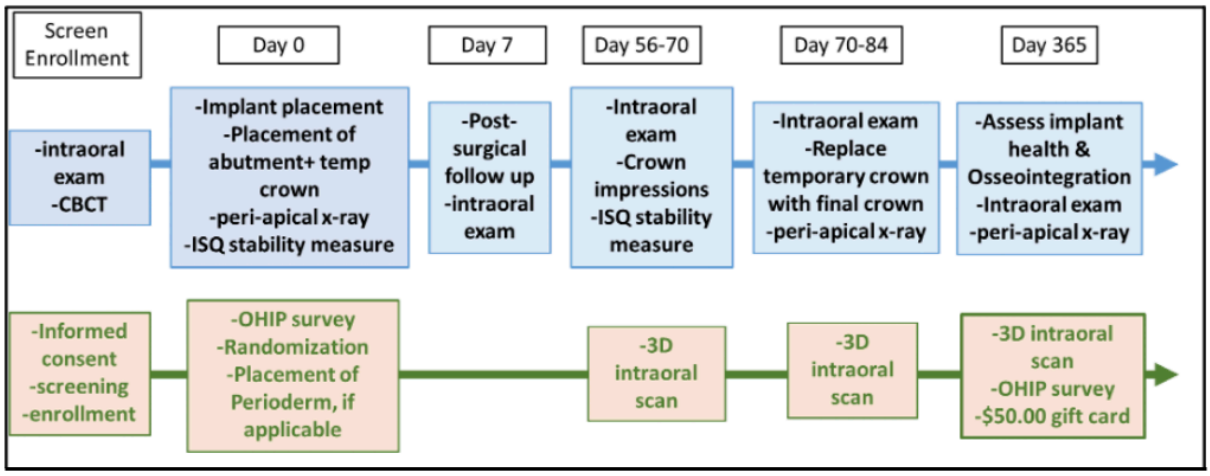
3.6 Enrollment

Subjects will be screened by the primary investigator, co-investigator, or an authorized UIC personnel in the UIC College of Dentistry Clinical Research Center. Patients attending the

UIC Dental Clinic who desire implant therapy will be examined and those found eligible for dental implant therapy will also get screened for possible study inclusion. Dental AxiUm records may be reviewed for the recruitment process.

3.7 Clinical Procedures

The study was done at the UIC Dental School Clinical Research Center and included multiple clinical visits which coincided with the research visits. The steps are depicted in Figure 1 where the clinical steps are in blue, and the research steps are in green. Both steps are described in detail below.



1. Blue timeline shows clinic visits for dental implant therapy. Green timeline shows activities being done for the purpose of this research

1. **First Visit: Screening/Study Enrollment**

   - Subject screening, enrollment, and informed consent

   - Medical and dental history

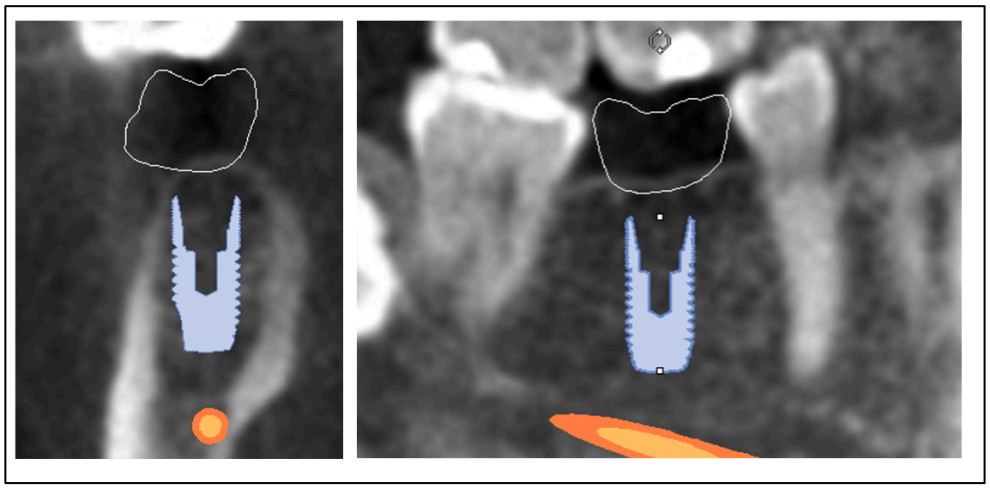
   - 3 dimensional intra oral scan using Trios® (3Shape®, Denmark)

   - CBCT imaging (iCAT)

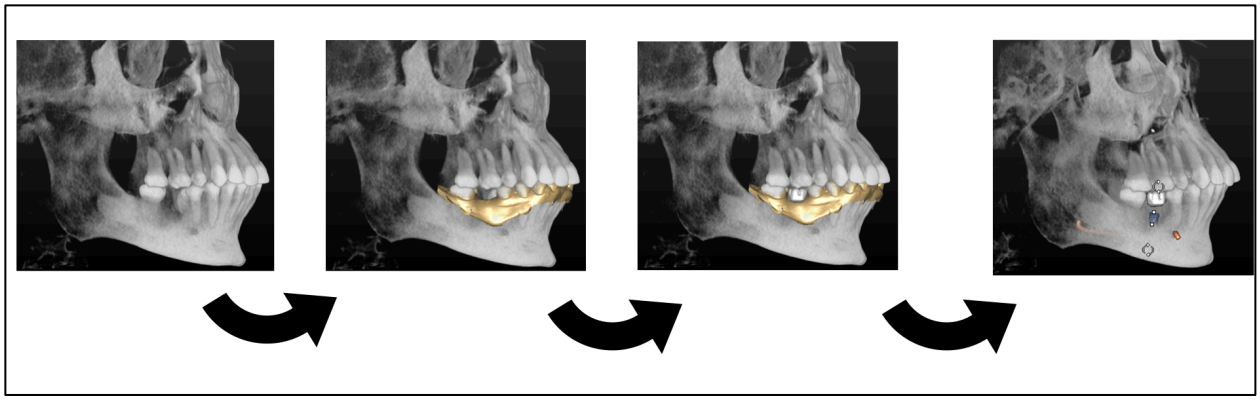
   - Each subject will be assigned a unique study ID. Data will be coded to that ID.

   - The Enrollment Log, needed to link a subject's study code to identifiers, will be stored separately

2. Digital images from intra-oral scanner



3. CBCT section showing dental implant planning for site #30



4. STL and CBCT merged as part of the implant planning

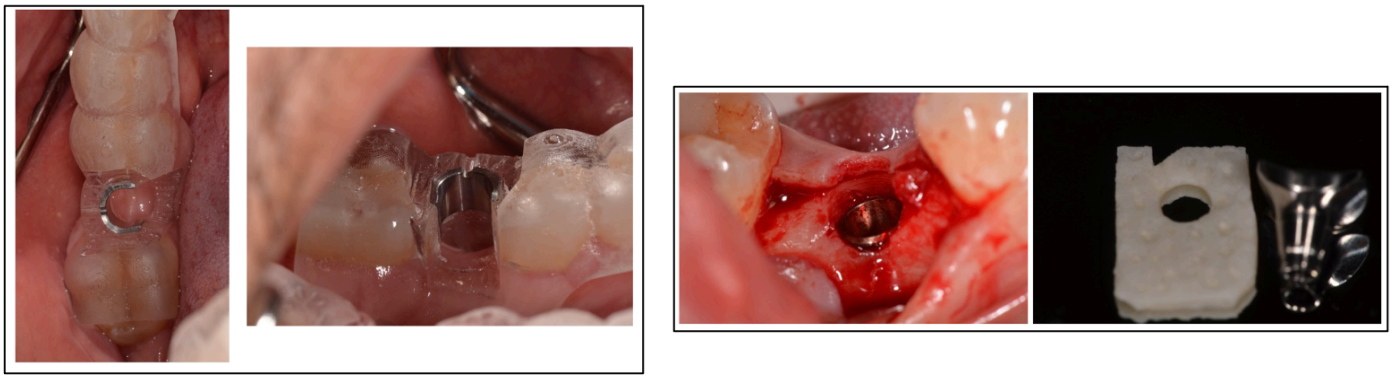
2. Second Visit: Implant Surgery

- Subjects were randomized into (+Graft or -Graft) by an authorized study personnel

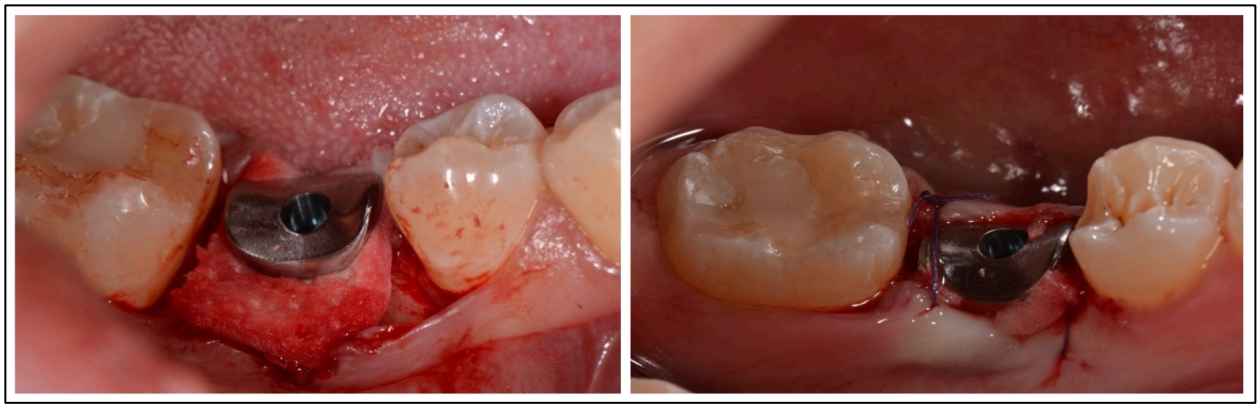
- Implant placement (Dentsply, Astra Tech®) was done (+ or – Graft). Primary stability was assessed with Ostell (W&H Impex Inc. MI, USA). Implants with stability greater than 65 ISQ were immediately provisionalized with abutment and temporary crown

- If the implant is not stable, then a customized healing abutment was placed, and a removable temporary was provided within 24 hours

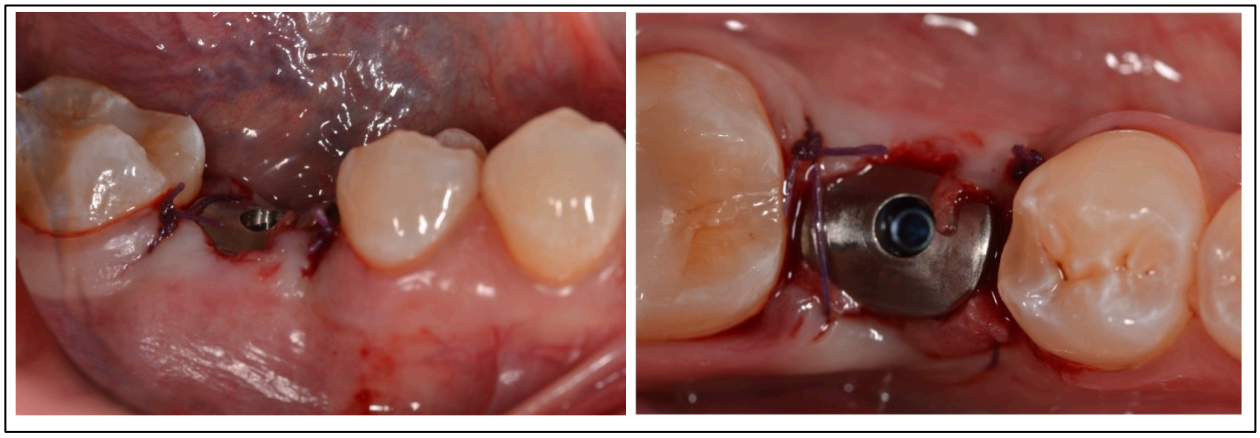
- A periapical radiograph was taken after the implant placement



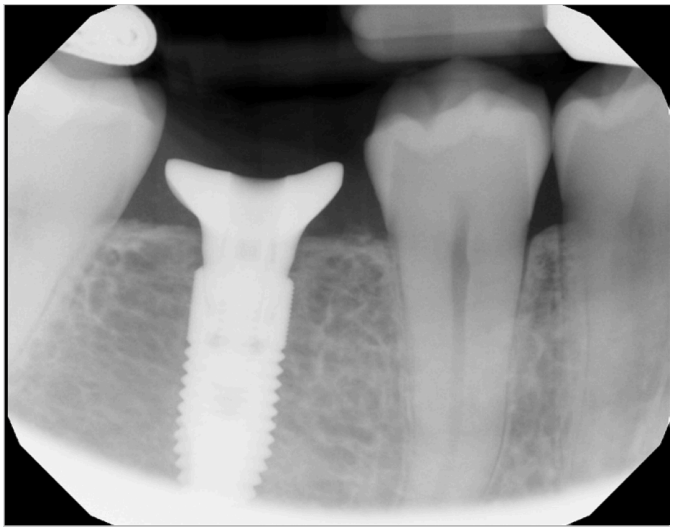
5. Surgical Guide (Left), and allograft (Perioderm®) for the +Graft group (Right)



6. Customized healing abutment with the allograft

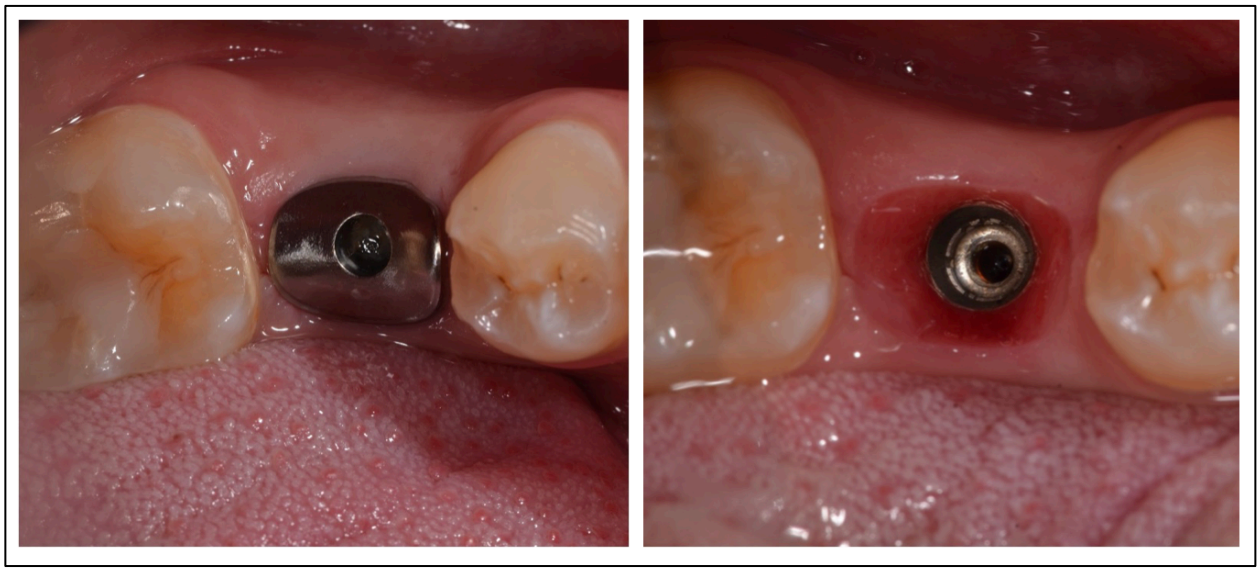


7. Lateral (Left) and occlusal (Right) views of the implant placement

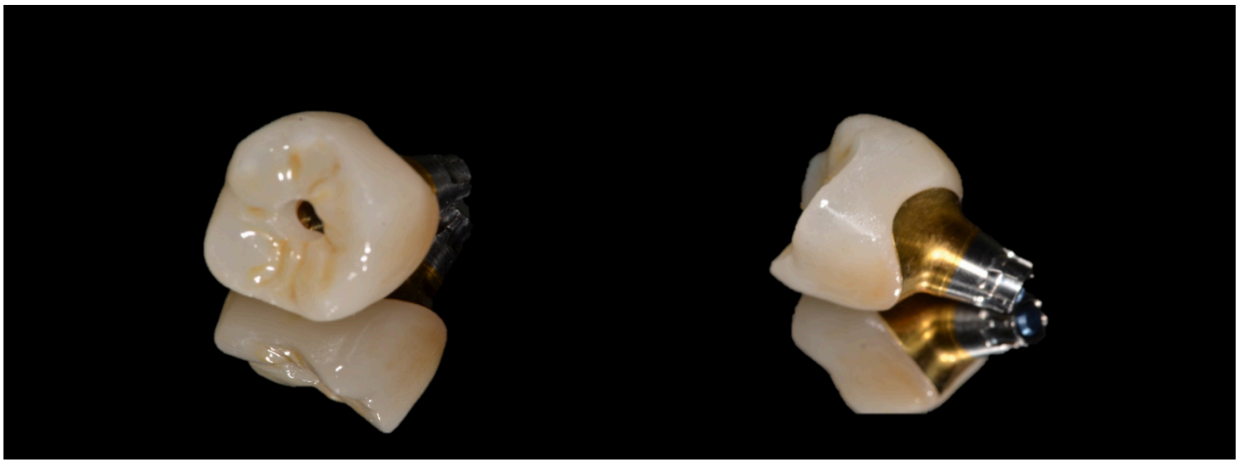


8. Periapical radiograph of #30 implant placement with customized healing abutment

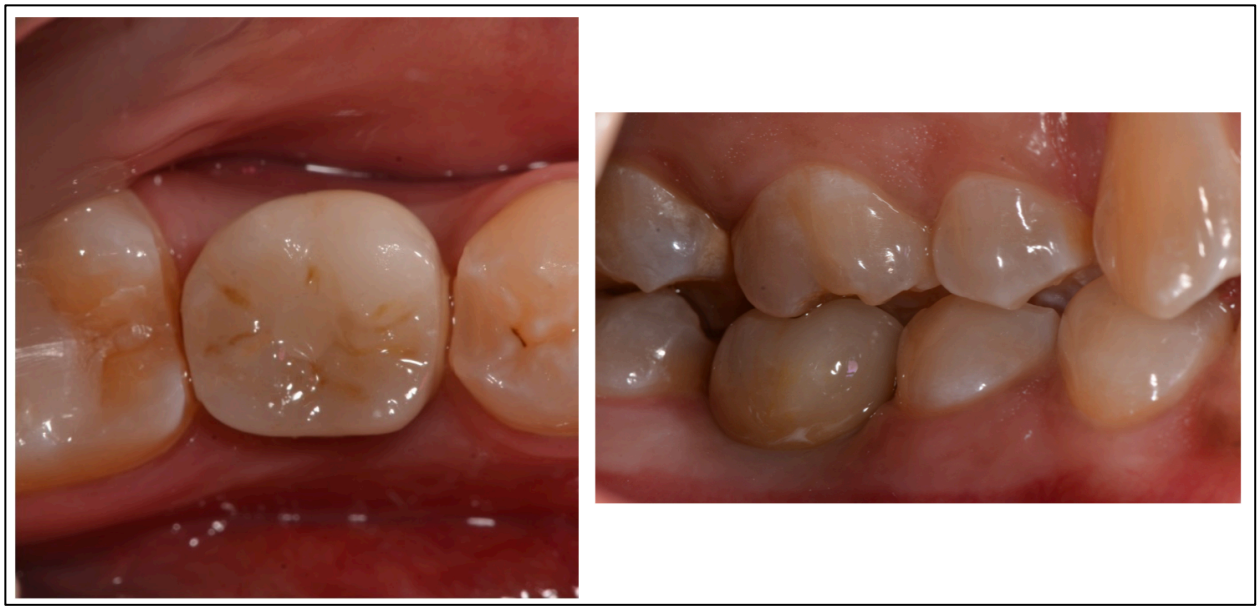
3. **Third Visit: 7 Day Follow-up**
    - One-week post-surgical follow-up which is the standard of care
4. **Fourth Visit: 8 Week Crown Impression**
    - Implant health and osseointegration assessed by tactile evaluation
    - Three-dimensional intra-oral scan taken for the final crown
    - If the implant failed to integrate, then appropriate measures were taken for the implant removal and the subject was discontinued from the study
5. **Fifth Visit: 10-12 Week Crown Delivery**
    - Implant crown definite crown was delivered
    - If the implant failed to integrate, then appropriate measures were taken for the implant removal and the subject was discontinued from the study



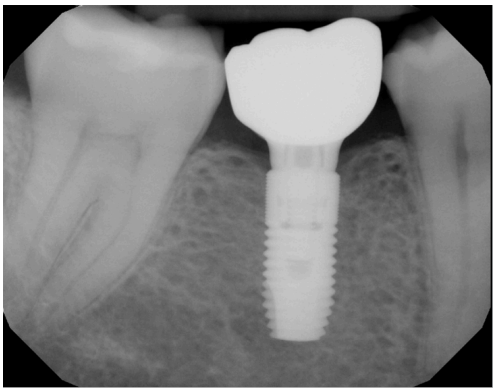
9. Complete soft tissue healing after 8 weeks



10. Definitive screw-mentable implant crown



11. Occlusal (Left) and lateral (Right) views of the final crown



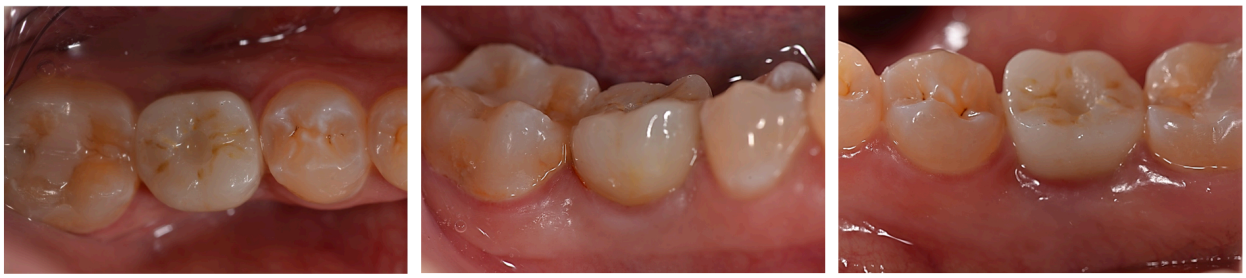
12. Periapical radiograph with the final crown on implant #30

6. **Sixth Visit: 1 Year follow-up**

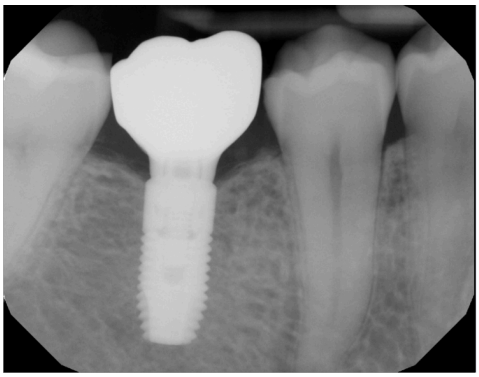
- One-year post-surgical follow-up which is the standard of care

- 3 dimensional intra oral scan using Trios® (3Shape®, Denmark)

- Periapical radiograph



13. 1 year follow-up of #30 implant restoration

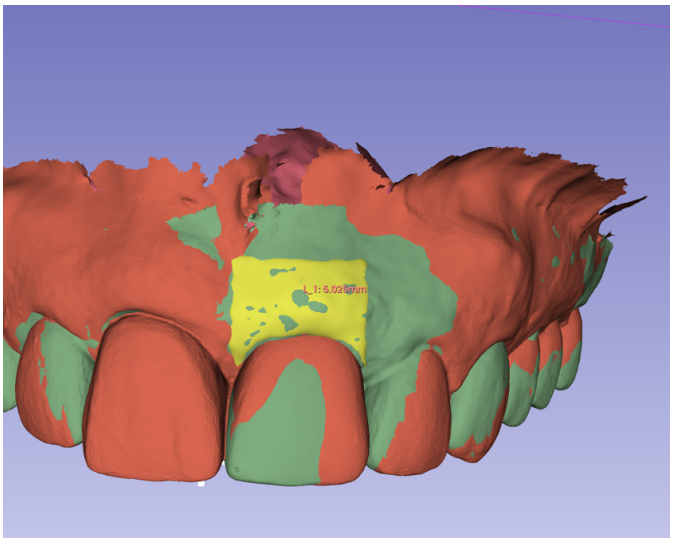


14. Periapical radiograph of #30 one year after the implant placement

3.8 Volumetric Measurements

For the volumetric assessments, an intra-oral scanner (Trios®, 3Shape®, Denmark) was used to obtain stereolithographic images at baseline (T0), crown delivery day (T1), and one year after crown delivery (T2) following the manufacturer's protocol. An image analysis software, Geomagic Control X (3D Systems, Morrisville, EUA) was used to digitally superimpose the

baseline (T0) and one year follow-up (T2) digital scans into one coordinate system. Fixed reference points on the teeth adjacent to the implant sites were used for the alignment and the result was checked through the best-fit algorithm. This software allows the precise transfer of the fixed coordinates on the digital scans to ensure that the subsequent measurements are done in an accurate and reproducible manner. The aligned scans were then imported into 3D Slicer (Harvard University, National Institutes of Health, Cambridge, Massachusetts) for the subsequent measurements by a single blinded examiner. A ROI (Region of Interest) was chosen on the buccal aspect of the implant site according to a previously described protocol [6,13,85]. The following zones were delineated for the measurement of volumetric soft tissue changes: Apico-coronally, the coronal border was chosen at a point just apical to the gingival zenith, and the apical border is at a point 5 mm apical to a perpendicular line drawn from the coronal border (Figure 16). Mesio-distally, two lines drawn perpendicular to the cemento-enamel junction of the adjacent teeth and occlusal plane that passes through the mid-point of the mesial and distal papillae [22] (Figure 16). This area was kept consistent for each patient throughout the measurements and over time but were different between subjects due to anatomic and treatment size differences. The software calculated the volumetric difference between the two ROIs (T2-T0). In order to account for the difference in size of the selected area, the percentage volume change was subsequently reported (% v, mm^3).



15. Sterelithographic images from T0 (Green), and T2 (Red) merged and the region of interest was selected (Yellow)

3.9 Marginal Bone Loss Measurements

Digital periapical radiographs were obtained using the paralleling technique while ensuring that the implant-abutment interface and the threads were clearly visible. Subsequently, ImageJ Software (National Institutes of Health, Bethesda, Maryland, USA) was used for the calibration of the images and measurements. This is an open-tool software used for the analysis of scientific images [86,87]. After calibration of the images, the implant-abutment interface was chosen as the start point and measurements were done to the alveolar crestal level. The first calculation was done at implant placement on the mesial and distal sides (T0), and the same measurement was repeated after a follow-up period of one year (T2). Bone above the implant platform was demarcated as no bone loss. The difference between these values depicts the amount of bone loss (T2-T0).

3.10 Statistical Analysis

Data was recorded in Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) and statistical analysis was done with SPSS Statistics 25 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were applied including the mean, standard deviation, and standard error around the mean. The independent samples t-test was conducted to assess mean differences between the control and test groups. The level of significance was set at 5% (0.05) with a confidence interval of 95%. The independent samples effect size was also reported.

4.0 RESULTS

4.1 Patient Groups

A total of 39 patients were included in the study. 19 patients received the graft at the time of implant placement and 20 patients did not receive the graft. Two patients did not return for the 1-year follow-up and were excluded from the study. Two implants had a biologic failure (loss of osseointegration) and were handled accordingly, then also excluded from the study. The resulting sample size is 35 subjects with 18 subjects receiving the graft (test group) and 17 subjects not receiving it (control group).

4.2 Volumetric Differences

4.2.1 Descriptive Statistics

Mean percentage difference in volume was 15.45% ± 19.03% for the grafted group (+Graft) and 16.82% ± 61.96% for the non-grafted group (-Graft) (Table 1). The standard error around the mean reported was 4.49% and 15.02% for the grafted and non-grafted groups respectively (Table 1).

I. Descriptive Statistics for Volumetric Difference (%)

Group Statistics

	Grafted	N	Mean	Std. Deviation	Std. Error Mean
PercentDiff	Grafted	18	15.4522%	19.03689%	4.48704%
	Non Grafted	17	16.8240%	61.96171%	15.02792%

4.2.2 Independent Samples Test

The independent samples T-Test was conducted to check the relationship between the difference in volumetric change (%) between grafted (+Graft) and non-grafted (-Graft) groups. With equal variances not assumed, there was no significant difference present between the test and control groups (p=0.931) as shown in Table 2. Since the standard deviation between the groups is different, the independent samples effect size was reported using Glass's delta with a value of -0.022 (Table 3), so a small effect size is noted.

II. Independent Samples T-Test for Volumetric Difference (%)

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means							
						Significance				95% Confidence Interval of the Difference	
		F	Sig.	t	df	One-Sided p	Two-Sided p	Mean Difference	Std. Error Difference	Lower	Upper
PercentDiff	Equal variances assumed	4.275	.047	-.090	33	.465	.929	-1.37182%	15.30573%	-32.51156%	29.76792%
	Equal variances not assumed			-.087	18.839	.466	.931	-1.37182%	15.68349%	-34.21674%	31.47310%

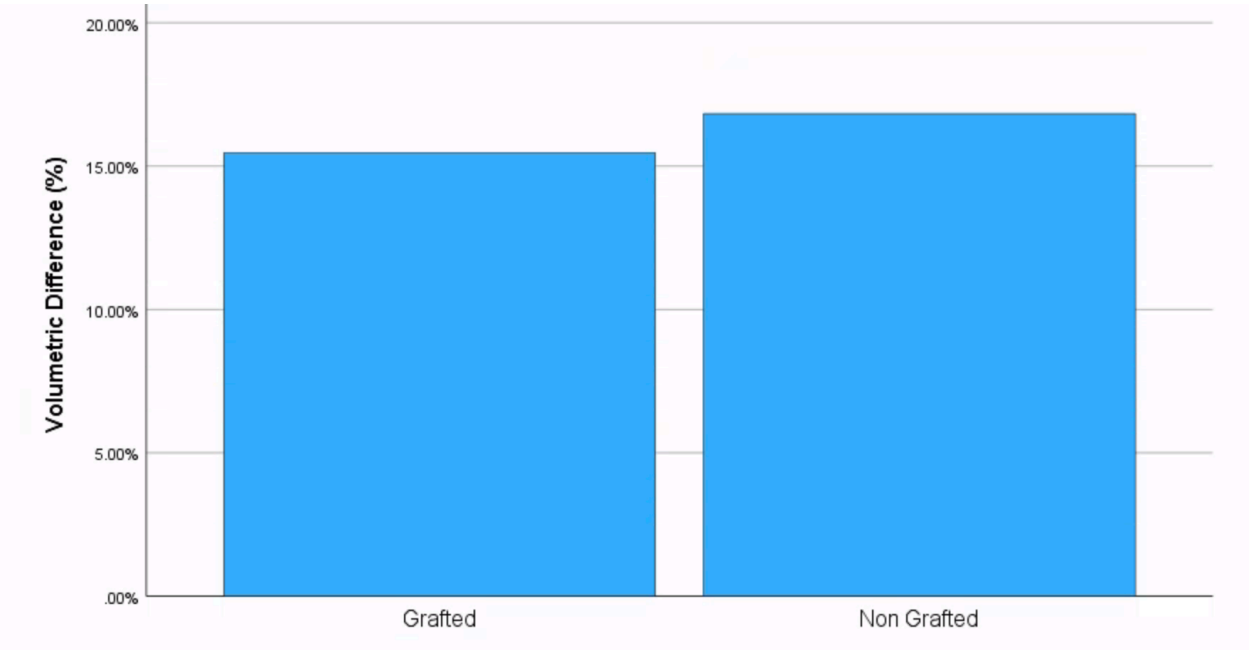
III :Independent Samples Effect Sizes for Volumetric Difference (%)

Independent Samples Effect Sizes

		Standardizer[a]	Point Estimate	95% Confidence Interval Lower	Upper
PercentDiff	Cohen's d	45.25648%	-.030	-.693	.633
	Hedges' correction	46.31857%	-.030	-.677	.618
	Glass's delta	61.96171%	-.022	-.685	.641

a. The denominator used in estimating the effect sizes.
Cohen's d uses the pooled standard deviation.
Hedges' correction uses the pooled standard deviation, plus a correction factor.
Glass's delta uses the sample standard deviation of the control group.

The bar graph in Figure 16 shows the volumetric percentage difference in grafted (+Graft) and non-grafted (-Graft) groups, with the non-grafted (control) group showing more percentage gain in volume compared to the grafted (test) group. However, this is not statistically significant (p=0.931). Our results indicate that there is a general increase in volume for both control (16.8%) and test groups (15.5%), with the group not receiving the graft showing a slightly higher increase, although this was not found statistically significant.



16. Bar Graph showing the Volumetric Difference between Grafted and Non Grafted sites

4.3 Marginal Bone Loss

4.3.1 Descriptive Statistics

For the mesial (M) surface, the mean bone loss for the grafted group (+Graft) is -0.166±0.33, whereas it was 0.01±0.11 for the non-grafted (-Graft) group. The standard error around the mean reported was 0.078 and 0.027 for the grafted and non-grafted groups respectively (Table 4). For the distal surface, the mean bone loss for the grafted group is -0.124±-0.11. The standard error around the mean reported was 0.063 and 0.063 for the grafted and non-grafted groups respectively (Table 4). An average loss was observed compared to baseline levels on both mesial and distal surfaces.

IV. Descriptive Statistics for Marginal Bone Loss (MBL; mm)

Group Statistics

	Grafted	N	Mean	Std. Deviation	Std. Error Mean
1Y-Placement (M)	Grafted	18	-.1656	.32950	.07766
	Non Grafted	17	-.0088	.11067	.02684
1Y-Placement (D)	Grafted	18	-.1239	.26571	.06263
	Non Grafted	17	-.1053	.25831	.06265

4.3.2 Independent Samples Test

The independent samples T-Test was conducted to check the relationship between the marginal bone loss on the mesial and distal surfaces between grafted and non-grafted groups. On the mesial surface, with equal variances not assumed, there was no significant difference present between the test and control groups (p=0.070) as shown in Table 5. On the distal surface, with equal variances not assumed, there was no significant difference present between the test and control groups (p=0.835) as shown in Table 5. Since the standard deviation between the groups is different, the independent samples effect size was reported using Glass's delta with a value of -1.41 and -0.072 for the mesial and distal surfaces respectively (Table 6), so a small effect size is noted.

V. Independent Samples T-Test for Marginal Bone Loss on the Mesial (M) and Distal (D) Surfaces

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means							
						Significance				95% Confidence Interval of the Difference	
		F	Sig.	t	df	One-Sided p	Two-Sided p	Mean Difference	Std. Error Difference	Lower	Upper
1Y-Placement (M)	Equal variances assumed	23.038	.000	-1.863	33	.036	.071	-.15673	.08412	-.32788	.01441
	Equal variances not assumed			-1.907	20.986	.035	.070	-.15673	.08217	-.32762	.01416
1Y-Placement (D)	Equal variances assumed	.264	.611	-.210	33	.418	.835	-.01859	.08866	-.19897	.16178
	Equal variances not assumed			-.210	32.969	.418	.835	-.01859	.08859	-.19883	.16164

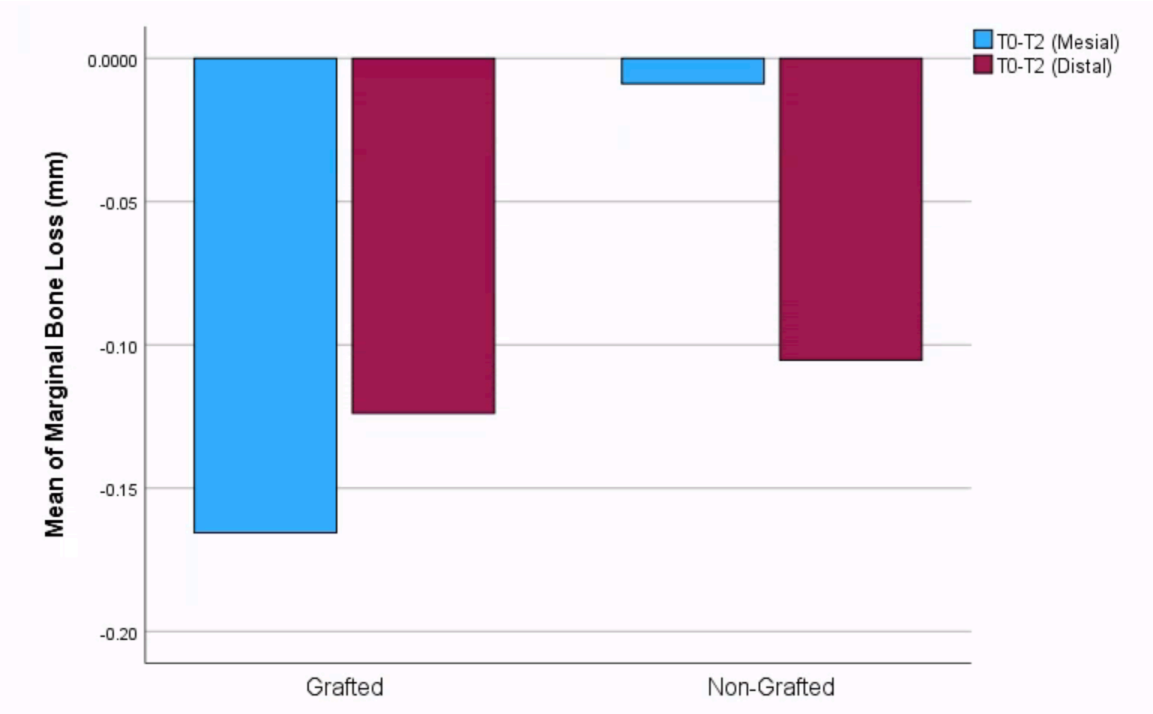
VI. Independent Samples Effect Sizes for Marginal Bone Loss on the Mesial (M) and Distal (D) Surfaces

Independent Samples Effect Sizes

				95% Confidence Interval	
		Standardizer[a]	Point Estimate	Lower	Upper
1Y-Placement (M)	Cohen's d	.24873	-.630	-1.306	.054
	Hedges' correction	.25457	-.616	-1.276	.053
	Glass's delta	.11067	-1.416	-2.224	-.580
1Y-Placement (D)	Cohen's d	.26215	-.071	-.733	.593
	Hedges' correction	.26830	-.069	-.717	.579
	Glass's delta	.25831	-.072	-.734	.592

a. The denominator used in estimating the effect sizes.
Cohen's d uses the pooled standard deviation.
Hedges' correction uses the pooled standard deviation, plus a correction factor.
Glass's delta uses the sample standard deviation of the control group.

The bar graph in Figure 17 shows the mean of marginal bone loss in grafted and non-grafted groups for the mesial and distal surfaces. For the mesial surface, the grafted (test) group resulted in more marginal bone loss average compared to the non-grafted (control) group. However, this is not statistically significant (p=0.070). For the distal surface, the grafted group showed slightly more marginal bone loss compared to the non-grafted group, but this was not statistically significant (p=0.835).



17. Bar Graph showing the Mean of Marginal Bone Loss between Grafted and Non-Grafted sites. Blue: Mesial Surface; Red: Distal Surface

5.0 DISCUSSION

In this study, a submucosal connective tissue allograft (PerioDerm®) was evaluated as an alternative grafting material to autografts. The main aim was to assess the volumetric changes in buccal soft tissue contours associated with this graft with a 1-year follow-up after crown delivery. The secondary outcome observed was the marginal bone loss associated with the use of these grafts.

In the group receiving the graft, sufficient clinical integration of the graft with no signs of inflammation was observed. In general, soft tissue augmentation at implants sites demonstrated neither a benefit nor a drawback in terms of changes in volume and marginal bone levels. Based upon the available evidence, we failed to find sufficient evidence to reject the null hypothesis that there is no association between the placement of a soft tissue allograft and the volume of soft tissues around dental implants, this also applies to our secondary null hypothesis that there is no association between the placement of a soft tissue allograft and marginal bone levels around dental implants. However, our findings indicate a positive improvement in buccal architecture when Perioderm® was used.

To this date, no other studies assessed the effects of using Perioderm® in soft tissue augmentation for implant therapy. Most studies investigated the use of xenogenic collagen matrices or autogenous materials [3,4,9,46]. Our results indicate that there is a general increase in volume for both control and test groups although this was not found statistically significant. These findings are consistent with the results of other studies [6,9,13]. Preclinical studies reported similar increases in soft tissue thickness in dental implant sites treated with collage-based matrices [8]. Schneider et al [6] found a positive correlation when a soft connective tissue graft was used and

reported an average volume increase of 0.55 ± 0.53 after one month. Other studies that analyzed the volumetric changes after insertion of the final restoration reported similar findings, with only minimal changes in soft tissue volume up to -0.15 mm 1 year after delivery [6,34,62]. Another study compared the use of acellular dermal matrix (Alloderm®) to connective tissue grafts and found minimal gain in soft tissue thickness [88].

Interestingly, measurements of the marginal bone levels on the mesial surface showed different trends than the distal surface. For the mesial surface, the grafted group depicted a marked increase in marginal bone loss average compared to the non-grafted group although the difference was not found to be significant. For the distal surface, the grafted group showed slightly more marginal bone loss compared to the non-grafted group, but this was not statistically significant.

Results from the current study demonstrate stable outcomes in terms of marginal bone levels and show a trend with additional comparable studies. The findings that soft tissue augmentation with adequate keratinized tissue is not associated with improvements in marginal bone loss when compared to non-augmented sites is in accordance with a recent systematic review [22]. This review failed to find sufficient evidence regarding graft placement in conjunction with apically positioned flaps on marginal bone levels. In contrast to previous literature, a systematic review [89] showed that soft tissue augmentation with sufficient keratinized tissue is associated with improvements in marginal bone levels and bleeding indices, while another study by Wiesner et al [90] showed a higher loss of marginal bone level in the test group. It has been suggested that the thickness of peri-implant bone can support the overlying soft tissues [29] and also a minimum amount of soft tissue is crucial to preserve the peri-implant bone [89], so a bi-directional relationship between per-implant hard and soft tissues is likely.

The assessment of volumetric differences using a digital protocol has proven to be reliable and accurate in vitro and in clinical studies [6,8,21] and presents a non-invasive and precise method for assessing volumetric changes in soft tissue levels. Traditionally, transmucosal assessment and endodontic probing were utilized which measure the soft tissue thickness rather than the 3-dimensional volume [22]. In this study, volumetric differences were expressed as percentage changes within a region of interest (ROI) that was kept consistent for each patient throughout the measurements and over time but were different between subjects due to anatomic and treatment size differences. This could potentially limit the comparison between the groups. However, the mean of the region of interest (ROI) did not differ significantly between the groups and the incorporation of percentage change can account for that. Therefore, valid volumetric changes and comparisons were conducted in this study.

5.1 Limitations

- Sample size
- Some implants were placed immediately, others were placed in a delayed approach
- Existing mucogingival defects on adjacent teeth not accounted for
- Variation in the surgical technique i.e.: some implants were placed with a flap and some with a flap-less approach
- Implant placement in anterior and posterior regions where residual bone thickness varies
- Some implants were restored immediately with a temporary crown, while other received a healing abutment

5.2 Future Directions

Future research should focus on the histologic analysis of the use of acellular dermal matrices and the impact of the surgical approach when placing these grafts.

6.0 CONCLUSIONS

Within the limitations of this research, results from the current study demonstrate healthy and stable peri-implant outcome in terms of volumetric changes and marginal bone levels when a submucosal connective tissue allograft (PerioDerm®) was used. The use of alternative grafting materials to autogenous grafts provides many advantages in terms of reducing surgical time, complications, and associated patients' morbidity.

More studies with longer term evaluations and larger cohorts are needed to confirm the stability of the results from this evidence. Overall, implementing a digital workflow offers excellent reliability, efficiency, and accuracy. Digital protocols will likely progress in the future with the advancements in technology in clinical practice.

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