Tufts UNIVERSITY | School of Dental Medicine

A Comparison between Primary and Secondary Flap Coverage in Extraction Sites: A Pilot Study

A Thesis

Presented to the Faculty of Tufts University School of Dental Medicine

in Partial Fulfillment of the Requirements for the Degree of

Master of Science in Dental Research

By

Majdi Ahmed Aladmawy

August 2016

THESIS COMMITTEE

Thesis Advisor

Yong Hur, DMD, MSc

Clinical Assistant Professor

Department of Periodontology

Tufts University School of Dental Medicine

Committee Members

Bjorn Steffensen, DDS, MS, PhD

Professor and Chair

Department of Periodontology

Tufts University School of Dental Medicine

Paul Levi, DMD

Associate Professor

Department of Periodontology

Tufts University School of Dental Medicine

Wai Cheung, DDS, DMD, MS

Interim Assistant Program Director

Associate professor

Department of Periodontology

Tufts University School of Dental Medicine

Matthew Finkelman, PhD

Associate Professor and Director of Biostatistics & Experimental Design

Department of Public Health and Community Service

Tufts University School of Dental Medicine

Yumi Ogata, DMD, MSc
Assistant Professor
Department of Periodontology
Tufts University School of Dental Medicine

ABSTRACT

Aim and Hypothesis:

Once a tooth is extracted from its socket, bone loss with dimensional changes occurs within the first 6 months. Bone augmentation with the use of a barrier membrane can be used to preserve bone loss. This technique is called ridge preservation, and it is the focus of the current research.

The primary aim of this study was to evaluate the bone dimensional changes following extraction and ridge preservation with primary coverage (closed flap technique-CFT) compared to healing with secondary intention (open flap technique-OFT). We hypothesized that the CFT would have more potential than the OFT in maintaining vertical bone height due to less susceptibility from infection and inflammation.

The secondary aim was to evaluate patients' self-report of postoperative pain.

Materials and Methods:

This study had 10 patients (10 sites CFT and 10 sites OFT) with at least 2 sites planned: extraction and ridge preservation on one site and on the contra-lateral site tooth/teeth of the same arch, e.g. extractions of the maxillary right canine and the maxillary left canine. Following the extractions, both sites had ridge preservation and non-resorbable membranes. The CFT had the flap released buccally and coronally positioned covering the non-resorbable membrane, while OFT had no release of the buccal flap, leaving the membrane exposed. Standardized measurements utilizing a stent and a probe were used to evaluate the dimensional changes of the alveolar ridge at 4 sites: Center Height (CH), Buccal Height (BH), Coronal Width (CW) at 3 mm apical to the buccal crest, and Apical width (AW) at 5 mm apical to the buccal crest. In addition, the

difference in keratinized tissue width (KTW) between both sites was recorded at baseline and at six months. The data were analyzed with a Wilcoxon signed-rank test.

Results:

Statistical significance within a given group was found in both CFT and OFT when comparing baseline to 6 months for CH (mean difference of 8.1 mm, SD =1.9, median of 8mm, IQR of 3 $p = 0.005$ for CFT and 7.5 mm, SD= 1.8, median of 7 mm, IQR of 3, $p = 0.005$ for OFT). CFT yielded statistical significance in BH compared to baseline within group at 6 months; however, there was no statistically significant difference among groups in CH, BH, CW, or AW when comparing baseline to 6m differences. The KTW of the OFT group was significantly higher than that of the CFT (mean of 1.7 mm, SD= 0.6, median of 2, IQR of 1, $p = 0.004$). In contrast to CFT, OFT had significantly lower pain VAS scores at 24 hours following extraction (mean difference of 1.1 mm, SD= 0.5, median of 1 and IQR of 0 vs. mean of 3, SD= 0.8, median of 3, IQR= 2 respectively, $p = 0.006$). No statistical significance was found between groups at the 2 weeks follow up visit.

Conclusions:

There was a statistical significance gain in bone height in both groups from the apical portion of the socket to the CH stent point in the center of the socket when comparing baseline to 6 months. CFT had a statistical significance in BH unlike the baseline within group at 6 months. However, there was no statistical significance between the open and closed flap techniques following extraction and ridge preservation with a non-resorbable membrane at center, buccal, 3mm, and 5mm locations. Leaving the flap open led to a wider band of keratinized tissue and less pain compared to closing the extraction socket with a flap.

DEDICATION

It's an honor for me to dedicate this study to my father (may his soul rest in peace). He was a wonderful parent that made me who I am today. It's people like him that light up the path in a dark wilderness to help a person advance forward clear of distractions. He endured a lot of hardships from life to make sure that all the distractions are diverted from my educational path. For that I'm truly grateful.

ACKNOWLEDGMENTS

I would like to acknowledge all the periodontal staff and department for helping me in the recruitment process, and Center of continuous education committee and the research department personal for giving guidance.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

CFT= Closed Flap Technique

OFT= Open Flap Technique

CH= Center Height

BH= Buccal Height

CW= Coronal Width

AW= Apical Width

KTW= Keratinized Tissue Width

PD= Probing Depth

BI= Bleeding Index

MGJ= Mucogingival junction

FDBA= Freeze-Dried Bone Allograft

DFDBA= Demineralized Freeze-Dried Bone Allograft

GTR= Guided Tissue Regeneration

GBR= Guided Bone Regeneration

d-PTFE= high-density polytetrafluoroethylene

ePTFE= Expanded polytetrafluoroethylene

LIST OF SYMBOLS

¶ Osteogenics Biomedical Cytoplast™ TXT-200

§ BioHorizons MinerOss™

⌘ Ethicon Coated VICRYL® (polyglactin 910) Suture

♯ 3m Peridex™ Chlorhexidine Gluconate 0.12%

Δ Pfizer Advil®

A Comparison between Primary and Secondary Flap Coverage in Extraction Sites: A Pilot Study

Introduction

Alveolar bone dimensional changes following extraction:

When a clinician plans for a tooth extraction, bone remodeling follows as a consequence. The results might be unfavorable bone resorption with different volumetric patterns, due to different responses from osteoclastic / osteoblastic activity surrounding the extraction socket. This can cause aesthetic concerns with a fixed prosthesis or functional concerns in the site planned for implant therapy when planning to restore the extracted site. [1-6]

If extraction sockets are left undisturbed, they heal uneventfully within 1 month after extraction. Studies showed with their biopsies the different stages of wound healing in human extraction sockets. [7]

Amler et al. outlined the sequences from clot formation after extraction to a physiological hard and soft tissue contour after 50 days. Studies concluded from their histologic study of human extraction sockets that between the fourth and the 8th week after extraction, the cellular components and the connective tissue in the extraction socket proliferate and between the 8th and the 12th week the bone undergoes maturation and forms a trabecular pattern.[7] Bone resorption of varying amounts is a phenomenon that always occurs after extraction. The resorption may cause esthetic and functional disadvantages, which may even compromise future implant placement. [8] Functional forces such as bruxism, complete denture wear, and heavy bite forces have been implicated as contributing factors for accelerated bone loss together with different systemic conditions such as osteoporosis. [9, 10]

It has been described in the literature that more bone is resorbed on the buccal than on the lingual site. [11] The main reason for the increased amount of bone resorption on the buccal aspect is the thinner bony plate on the site's alveolar bone.

This thin bony plate also facilitates the occurrence of buccal dehiscence defects when teeth are still present. Dehiscence has been described to be the most commonly encountered problem in implant dentistry. [12] The occurrence of a dehiscence is equivalent to the

occurrence of a three-wall bone defect. The fewer bony walls present, the less space maintenance for a blot clot is provided by the extraction socket itself. Subsequently, the use of membranes has been found to increase regeneration in dehiscence defects. [13, 14]

The significance of ridge preservation today:

Araújo et al. reported, in an animal study, that the resorption occurred in two overlapping phases. The first phase involves resorption and replacement of the bundle bone with the woven bone. Substantial bone loss occurs due to the bone remodeling, resulting in vertical bone loss. The second phase had an additional resorption that occurred from the external surfaces of both bone walls. [15] Many studies suggest the use of bone graft material to prevent such bone resorption, especially when there is less than 2mm buccal bone. [16]

The majority of bone loss occurs in the first month after extraction. [6] The amount of bone loss in the first three years after tooth extraction varies around 40-60%. [17, 18] The technique to preserve the alveolar ridge volume by incorporating foreign materials into a human extraction socket was initially described in the mid 80s. These materials initially consisted of hydroxylapatite (HA) and were either root form dental implants or bone graft particles. [19, 20]

The clinician aims to preserve or gain a sufficient width and height of bone when teeth are removed. By evaluating the width of the ridge, Schropp et al. found a reduction of the width by approximately 50% from 12 to 5.9 mm. [6] Two-thirds of the bone loss occurred during the first three months of healing. The percentage of bone-width reduction has been found to be larger in the molar regions than in the premolar regions, and in the mandible than in the maxilla. Between the three and the six months evaluation, only minor bone changes were observed. Equally, only minor bone changes were observed between the six and the twelve months evaluation. The maximum bone loss evaluated, close to the adjacent teeth of the extraction socket after 12 months, was found to be 1.2 mm. A mean vertical loss of 1 mm could be determined in this study.

Tiefengraber et al. found in a prospective split-mouth study with a low number of evaluated patients, that much more horizontal bone width could be preserved after extraction, when only a Gore-tex membrane was placed over the extraction socket. After approximately 6 weeks, the GBR site lost 1.1 mm in the buccal-lingual dimension, while the control site had

lost 3.2 mm in the horizontal dimension. The radiologic examination of the vertical bone loss did not show any difference in this particular study. [21]

Ashman et al. found that ridge preservation after extraction prevents 40-60% of the bone loss. [22] Studies indicated from their prospective study that GBR procedures in extraction sockets heal without any complications. When an extraction socket is preserved, intra- and postoperative complications decrease. [21, 23]

This finding has been emphasized since the very beginning of ridge preservation procedures when HA was still the most commonly used graft material. [20]

Classifications and clinical considerations:

Bone regeneration requires space making for a blood clot that will need to be stabilized and then be reorganized and replaced with bone. [24]

Barrier membranes make space for a blood clot, preserve it, and exclude soft tissue ingrowth. Bone graft materials provide space and promote bone maturation by their osteoconductive activity. [25] Tinti et al. assumed that the envelope of bone determines the treatment and the predictability of regenerative procedures in bone defects like extraction sockets. [24]

They differentiated between two classes of extraction sockets:

Class 1 extraction sockets are those where the surrounding bone envelope is intact,

Class 2 extraction sockets are those where the envelope is not intact.

Guided bone regeneration is the common term that can be used to describe clinical approaches that preserve the alveolar ridge bone volume.

Christensen et al. proposed the following indications for ridge preservation procedures: [18]

1. Prevent collapse of the alveolar bone and soft tissue, which causes an unacceptable aesthetic situation in the anterior maxilla and mandible
2. Prevent collapse of the alveolar ridge, which might result in bone irregularities, and would cause an unacceptable fitting of the future prosthesis
3. After tooth extraction, to provide adequate bone volume for subsequent implant placement.

Hermann and Buser in 1996 presented basic guidelines that should be considered to achieve a predictable result with GBR procedures. [26]

1. Use of an appropriate membrane
2. Achievement of primary soft tissue healing
3. Creation and maintenance of a membrane-protected space
4. Close adaptation and stabilization of the membrane to surrounding bone
5. Sufficiently long healing period

Flap manipulation following extraction:

When teeth are extracted, either the tissue can be left untouched or the flap can be advanced to achieve partial or complete coverage of the extraction socket.

Rehrman A. in 1936 was the first person who elevated a buccal full-thickness flap and made two trapezoid vertical releasing incisions mesial and distal to the extraction socket. Releasing the periosteum eased tension and, subsequently, the buccal flap was used to achieve primary closure of the extraction site. He indicated the necessity of this technique when extraction sockets were connected to the maxillary sinus as a result of the occurrence of a perforation to the maxillary sinus after extraction.[27]

Flap elevation and osseous surgery with or without periosteal releasing incisions have been described as factors that may trigger postoperative bone resorption. [28, 29]

Marginal recession of adjacent teeth, defective papilla, and loss of keratinized mucosa have been described to be the result of flap manipulation to achieve partial or complete coverage of an extraction socket. [30-32] Block et al. made periosteal-releasing incisions, and achieved primary closure of the grafted extraction socket without using a membrane. [23]

Bartee described a technique using a non-resorbable PTFE membrane for ridge preservation without manipulating the soft tissue to prevent loss of the papilla, the vestibule, and the keratinized mucosa. He left the membrane exposed and did not manipulate the soft tissue. Consequently, he found that he was able to predictably preserve the before-mentioned structures and the bone volume. [31, 32]

Tissue thickness and GBR:

The tissue thickness after ridge preservation was also observed and compared to no-ridge preservation in a controlled clinical trial. [2] It was found that ridge preservation with the use of FDBA and a collagen membrane led to thinner tissue compared to no-ridge preservation. The technique used to measure soft tissue thickness has recently been published to evaluate tissue thickness with an ultrasonic device. [33, 34]

The significance of keratinized mucosa around implants:

The presence of thick keratinized mucosa is preferable when implants are placed in the aesthetic zone. Nevertheless, the absence of keratinized mucosa does not correlate with higher implant failure rates or increased recession in the presence of good oral hygiene. [35]

Esposito et al. stated in a review meta-analysis that patients do benefit from the presence of keratinized mucosa because it facilitates plaque removal and decreases trauma on the tissue, a risk factor for inflammation. [36]

Warrer et al. examined the significance of keratinized mucosa around implants in the presence of plaque-induced peri-implantitis in a monkey study. In this study, less bone loss was observed in the presence of keratinized mucosa. [37]

The use of soft tissue grafts to seal extraction sockets:

Soft tissue grafts have been used to seal extraction sockets. Literature shows the successful use of pedicle or connective tissue grafts to seal implants that were placed immediately after extraction into fresh extraction sockets. [38-40] On the other hand, connective tissue has been described as an unpredictable therapy for sealing extraction sockets, due to the unpredictable blood supply below the autogenous graft. [41] Tal found in a prospective study evaluating 42 maxillary anterior extraction sockets in 24 patients that more than 50% of the connective tissue grafts placed over extraction sockets are either partially vital or even non-vital. [41]

Materials used for ridge preservation

1. Resorbable and non-resorbable membranes:

A barrier membrane is often used in conjunction with bone grafting. Its purpose is to help isolate the alveolar bone defect from the ingrowth of epithelial and connective tissue cells. The socket will be filled with blood clot and the bone graft. This process will allow bone maturation on one side and epithelial growth on the other. The membranes used are divided into 2 types: resorbable and non-resorbable. Using a resorbable membrane does not require a surgical procedure for its removal, while a second surgical procedure is needed for a non-resorbable membrane. [42]

Prerequisites for an ideal barrier membrane include biocompatibility, cell barrier membrane, tissue integration, space making effect, and clinical manageability. [12] Membranes that have been used in GBR procedures are the following: PTFE, ePTFE, collagen, freeze-dried dura mater allografts, polyglactin 910, polylactic acid, polyglycolic acid, polyorthoester, polyurethane, polyhydroxybutyrate, calcium sulfate, micro titanium mesh, and titanium foils. [43] Studies in guided bone regeneration procedures have examined the use of resorbable membranes [4, 12, 44] or non-resorbable membranes [44, 45]. Lang et al. indicated that successful bone regeneration of 90-100% consistently occurred with an undisturbed healing period of at least 6 months. [46] The final soft tissue healing occurs months prior to bone maturation. [7]

In cases of early ePTFE membrane removal, Lang et al. found only 42-60% of regenerated bone. It was also found that an early exposure of a membrane to the oral environment does not per se preclude the possibility for regeneration to a certain degree, but rather represents a risk factor for infection. Large defects were found to regenerate less than small defects. ePTFE membranes seem to be of advantage when space maintenance is of particular importance. [46] This was confirmed in a study by Hurzeler et al. in which a resorbable membrane barrier made of poly (D,L-lactid – cotrimethylencarbonate) in a 70/30 ratio was compared to non-resorbable ePTFE barrier for vertical bone regeneration around implants in a monkey study. [45] The titanium reinforced membrane showed significantly superior results, which may be attributed to its superior ability of space maintenance and blood clot stabilization. A space making property is one of the fundamental requirements of a GBR

barrier [47]. Mellonig et al. compared the amount of regenerated bone in dehiscence type defects around implants treated either with a resorbable membrane barrier composed of a copolymer of lactide and glycolide or with a non-resorbable e-PTFE membrane. [48] According to this animal study, the superior result of the e-PTFE membrane is due to its superior space maintenance and blood clot stabilization. It can be concluded that these membranes are favorable in cases where large augmentations vertically or horizontally are necessary. Ridge preservation does not facilitate the same amount of space maintenance as vertical or large horizontal ridge augmentation does. The socket walls function as space maintainers without the need of additional space maintenance by the membrane itself. Resorbable membranes offer several different advantages. [43] Resorbable membranes improve tissue healing, incorporation of the membrane into the host tissue, and a quick resorption in less often occurring cases of exposure and, subsequently, decreased likelihood of infection. [43]

2. The significance of membrane exposure:

Studies in the past indicated that wound dehiscence, early membrane removal, or membrane exposure influenced guided bone regeneration procedures negatively. [12, 43, 49, 50] Membrane exposure seems to occur more often when non-resorbable membranes are used. In a meta-analysis, it was found that ePTFE membrane exposure following its surgical placement had a negative effect on GBR; however, it had minor effect on GTR procedures around natural teeth. [51] Nevertheless, there are studies that indicate a significantly worse treatment outcome when ePTFE membranes become exposed in GTR procedures around natural teeth. [52] Bartee in 2001 left non-resorbable PTFE membranes exposed and encountered a very low number of infections in his descriptive publication. He attributed this to the low porosity (<0.2 μm) of the dense membrane. The low porosity enables the clinician to leave the membrane exposed without extraordinary amounts of bacteria colonizing on the surface and subsequently a low risk of bone graft loss due to infection underneath. He also emphasized the necessity of the postoperative recall to clean the exposed membrane. [31] The patient should be advised to clean the membrane with a Q-tip.

In a study that examined the amount of bacteria on exposed membranes in guided tissue regeneration, it was found that the amount of attachment level gain is significantly lower in cases when the amount of bacteria on their surface exceeds 106. [52] This stresses the idea that

GTR works almost equally effectively when membrane exposure is seen around natural teeth with low amounts of bacteria on the membrane, but there might be more cases in the GTR membrane exposure group, which show no, or lower attachment level gains. The concept aforementioned might be due to the cases where the level of bacteria on the membrane surface exceeds a certain pathologic number. This principle may also be applied to guided bone regeneration procedures, but the correlation remains unstudied so far. One prospective study with a low number of patients indicates that exposure of a resorbable membrane does not appear to have a deleterious effect in ridge preservation procedures. [53] Hammerle et al. stated in a review on bone regeneration by means of barrier membranes that bioresorbable membranes render similar success rates when compared to non-resorbable membranes for the treatment of horizontal defects. [43]

3. High-density polytetrafluoroethylene: ¶

Using a non-resorbable membrane provides better support for bone regeneration due to its rigidity. Expanded polytetrafluoroethylene (e-PTFE) membranes have been frequently used in the past, but are no longer available on the market. Currently, high-density polytetrafluoroethylene (d-PTFE) membrane is being used as an alternative to e-PTFE. Several studies indicated that d-PTFE membrane could predictably lead to the preservation of soft and hard tissues in extraction sites. [54-56] Successful uses of d-PTFE were demonstrated in animal and clinical investigations. [57-63]

(d-PTFE) is intended for GTR or GBR procedures when the goals of its use are tissue adaptation with the membrane and providing adequate space making. The membrane allows some tissue ingrowth while remaining non-porous to bacteria and epithelial cells. The space making property of the ePTFE membrane may decrease the chance of having a membrane exposure and loss of its function.

4. Freeze-dried bone allograft: [§]

There are various bone graft materials that could be utilized in extraction and ridge preservation procedures. Autogenous bone is considered the "gold standard" because of its biocompatibility, safety, and osteogenic potential. [64] However, there are some limitations when using autogenous bone. The limitations include the amount of donor tissue and higher resorption rate at the grafted site when compared to other bone graft materials. [47] Additional bone grafting materials include allografts, xenografts, and alloplasts. [22, 65-78] Demineralized freeze-dried bone allograft (DFDBA) and freeze-dried bone allograft (FDBA) are frequently used in site preservation procedures. [79]

FDBA is made of allograft mineralized cortical and cancellous chips. The hybrid mixture of cortical and cancellous bone particles provides an osteoconductive scaffold allowing for osteoblastic cell propagation to the spaces provided by the membrane, helping to form a future bone maturation site.

Some of the applications that allow us to use the allograft include: [80]

- Alveolar ridge and sinus augmentation.
- Tooth socket grafting
- Periodontal bony defects
- Bone preparation for implant placement

Methods described to investigate hard and soft tissue changes:

Most of the clinical parameters that were evaluated in the present study do not differ from a standardized clinical evaluation. These parameters, like the probing depth or the width of keratinized mucosa, will not be explained again, since they are the basis of periodontal evaluation worldwide. Clinical approaches described to measure bone remodeling following tooth extractions include taking impressions, [4] the radiographic subtraction method, [6] CT-Scans, and the use of acrylic stents. [2]

In summary:

There are two techniques that are commonly used for extraction and ridge/site preservation, either to close the wound of the extracted tooth by primary closure (i.e., closed flap technique) or to leave the extraction socket wound heal by secondary intention (i.e., open flap technique). Primary closure is the approximation of the flap edges into close intimate contact via sutures⌘ (covering the membrane), whereas healing by secondary intention leaves the flaps in their original location following extraction with the membrane exposed.

Iasella et al. presented clinical success of the procedure when they left the membrane exposed or without primary coverage. They found the sites treated with bone grafts and resorbable membrane had less alveolar bone resorption/remodeling following extraction when compared to sites without bone grafts and membrane. [2]

On the other hand, Lekovic and co-workers reported on extraction/ridge preservation with primary coverage. They found the closed flap technique reduced the alveolar bone dimensional changes following extraction when compared with the sites without site preservation. [3]

There are a few studies comparing the open and closed flap techniques in site preservation procedures. [58, 59, 81-83] However, the current literature is lacking in evidence to indicate which technique is superior. The limitations of those studies are: (A) having one continuous surgical flap on open and closed techniques, [58] (B) lack of split mouth design utilizing a non-resorbable membrane. [81, 82] Moreover, surgical techniques in ridge preservation procedures performed with d-PTFE membrane have not been thoroughly studied.

Therefore, the current pilot trial was conducted to compare the outcomes of the two surgical techniques, open and closed flap in ridge preservation, using clinical, and pain/discomfort analysis. This study is considered as a pilot study because the data are lacking in information regarding the standard deviation and the use of non-resorbable membrane that compare both open flap technique and closed flap technique following extractions.

Aim and Hypothesis:

The primary aim: of this study is to evaluate the bone dimensional changes (vertical height and width) following extraction and ridge preservation with primary coverage (closed flap technique) **CFT** in comparison to secondary intention (open flap technique) **OFT**.

The hypothesis: that the closed flap technique would have more potential to maintain vertical bone height when compared with the open flap technique, due to less susceptibility from infection and inflammation.

Primary outcome: mean difference between CFT and OFT in height and width gained, expressed in millimeters.

Secondary aims: to evaluate the keratinized tissue width KTW and the patients' self-report of postoperative discomfort (1-10 index)[84] for both CFT and OFT.

The hypothesis: OFT would have a higher KTW in comparison to CFT due to flap coronal advancement. OFT would have less post-operative pain/discomfort compared to CFT due to less flap dissection and elevation.

Secondary outcomes: mean differences between CFT and OFT in KTW at 6 months, and VAS pain scale differences between CFT and OFT at 24 hours and at 2 weeks post extraction.

Research Design

The study was conducted from January 2015 to January 2016, and the study protocol was approved by the Tufts Health Sciences Institutional Review Board, Boston, Massachusetts. Subjects were recruited from Tufts University School of Dental Medicine. A consultation visit was done to see if they satisfied the inclusion criteria of the current study. A written informed consent was obtained prior to enrollment. The study design was a single center pilot study, split mouth designed, planned to compare the bone dimensional changes following extraction and ridge preservation in surgical techniques that leave the flap open with the non-resorbable membrane exposed OFT and closed CFT. As such, each subject had one side assigned to CFT and the opposing side to OFT (10 sites CFT and 10 sites OFT).

Materials and Methods

1) **Inclusion Criteria**

- Be at least 18 years of age.
- Patient who is treatment planned at TUSDM for extraction and future implant placement and meets all medical and dental requirements of the TUSDM periodontology clinic for periodontal surgery (e.g., subjects with no diseases or medication allergies contraindicating periodontal surgery).
- Patient must have bilateral extraction (canine to molar) sites of teeth located on the same arch (e.g. upper right and upper left) treatment planned for future implant placement at TUSDM.
- The number of teeth planned for extraction (either one or two adjacent) and ridge preservation should match the same number of teeth (either one or two adjacent) from the contra-lateral side on the same arch.
- Presence of at least 3 intact bony walls and at least half of the fourth bony wall at each site as determined by bone sounding at Visit 1.

2) Exclusion Criteria

- Have any known disease that interferes with periodontal surgery and would not allow the patient to be treatment planned for the procedures in the TUSDM periodontology clinic (e.g., severe anemia, low white blood cell count, bleeding or coagulation disorder, uncontrolled hypertension (150/90), [85] recent myocardial infarction (within 6 months of enrollment), diabetes (HbA1C ≥7%), HIV/AIDS (self-reported), history of or currently undergoing head and neck radiation, history of or currently taking bisphosphonates).
- Have limited mental capacity and unable to give informed consent.
- Subject who has a disease or condition that may affect hard and soft tissue healing (e.g. previous or current head and neck radiation therapy, long term steroid use defined as more than two weeks in the past two years).
- Subject who has diseases that affect bone metabolism (e.g. osteoporosis, osteopenia).
- Pregnancy (self-reported). Bone density is affected temporarily by both pregnancy and lactation. [86]
- Current smokers. Smoking has some alterations on the tissue conditions, which might give masked or negative healing effects.
- Extraction socket with > 50% bone loss on the buccal or lingual/palatal bone as determined by bone sounding at Visit 1.
- Allergic to gentamycin, povidone-iodine, or surfacants as trace amounts may be contained in the FDBA.

Subject Screening

Informed consent was obtained. Subjects were instructed to read the informed consent form (ICF). If subjects decided to participate, he or she was instructed to sign the ICF and a copy of the ICF was given to the subject. Medical history and demographic information were recorded. Inclusion/exclusion criteria were evaluated.

An oral exam, including evaluation of oral cavity, soft and hard tissues, was completed following standard of care procedures at Tufts using a mouth mirror and dental explorer.

Clinical charting for each subject recorded the following:

- Keratinized tissue width (KTW). Measured from the Coronal Width (CW) stent hole to the mucogingival junction with periodontal probe, prior to the extraction procedure and another record was obtained prior to the implant surgery at 6 months using the same reference.
- Bleeding Index (BI) (six surfaces per tooth) for the oral cavity.
- Plaque index (PI) (O'Leary Index) [87] that was calculated by counting each tooth surface (buccal, lingual, mesial, and distal tooth surfaces) that has plaque stain via the use of disclosing tablets that follows the standard of care guidelines. The total number of plaque surfaces was divided by the total number or surfaces to give the mean percentage of the index.

Examination also noted the location of the planned extraction and ridge preservation sites (maxilla or mandible) and the number of teeth involved in each site (one or more teeth). Radiographs were reviewed to help determine if the subjects were included/excluded. Bone sounding was performed to help determine inclusion/exclusion criteria. Topical anesthesia was used on the buccal surfaces of the teeth that are planned for extractions/ridge preservation to reduce the possibility of pain of bone sounding. A UNC-15 probe was inserted through the sulcular epithelium to the buccal crestal height. Bone sounding helped in determining if there was sufficient bone height to provide containment of the socket defect. Maxillary and mandibular alginate impressions were taken for the diagnostic cast fabrication.

All subjects were enrolled in the study following completion phase I therapy (oral hygiene instructions, scaling and root planing, prophylaxis, removal of plaque- and calculus-retentive factors and occlusal adjustments if needed), or until a plaque score of < 15% and bleeding score of <10% was achieved.

Two impressions were taken from the patient's jaw that had the teeth extracted. The impressions were poured, and the undercut areas blocked out with wax to allow application of the stent suck down device. The stent covered the coronal and lingual aspect of the teeth that were adjacent to the extraction sites. The stent extended around the teeth planned for extraction to the marginal gingiva/mucosa on the buccal surface beyond the mucogingival junction. The stent was fabricated to measure the height and width of the alveolar ridge. The stent had 2 holes for bone height (vertical) measurement. One hole was located at the mid buccal area just above the buccal crestal bone height (BH), while the other hole was located in the center of the extraction socket lingual to the mid buccal hole (CH). The measurements of the bone height were measured with a UNC-15 perio probe that passed through the hole until it came into contact with the bone apically. Measurements of the probe were approximated to the nearest 0.5 mm. The mid buccal hole (BH) was the main outcome for the study to evaluate which technique would yield more vertical bone height.

In addition, the stent had additional holes to measure the alveolar bone width (horizontal component). The holes were located on the stent flanges (both in mid-buccal, 3mm and 5mm apical to the bone crest margin). The measurement of the bone width was done with a UNC-15 perio probe that passed through the hole until it came into contact with the buccal bone. These parameters were measured at baseline and 6 months post-op.

The clinical parameters were defined, measured and recorded on an Excel spread sheet as follows: (refer to Appendix A and Figure B)

- PI (Plaque Index), BI (Bleeding Index). [87] PI and BI of each subject at baseline and at 6 months visit.

- CH (Center Height) (measured vertically as the distance from the center extraction socket opening to the base of the extraction socket).
- BH (Buccal Height) (measured vertically as the distance from the corresponding stent opening to the mid-buccal crestal bone height).
- CW (Coronal Width): measured horizontally as the distance between the stent opening to the buccal bone located at 3 mm sub crestal to the mid-buccal crest.
- AW (Apical width): measured horizontally as the distance between the stent opening to the buccal bone located at 5 mm sub crestal to the mid-buccal crest.
- KTW (keratinized tissue width): the distance between BH stent mark and the muco-gingival junction.

All measurements were taken and recorded by one examiner (MA). Intra-examiner calibration was carried out by repeating the clinical parameters (CH, BH, CW, AW, KTW) at least 48 hours after the first set of measurements. The calibration was carried out on 10 fellow residents taking measurements at two different sites twice. The two sets of measurements were compared to determine intra-examiner reproducibility. There was a 100% agreement between the two passes.

Surgical visit

Medical history was reviewed and any changes were noted. Eligibility and subject withdrawal criteria were also reviewed to ensure the subject still qualified for the study.

The randomization was created using the statistical package R Version 2.11.1. Randomization was made to decide which side was in Group 1 and which side was in Group 2. The two sites (one set) chosen to be in the study each have a 50% chance of being in either group.

Clinical photographs of a fixed magnification were taken throughout the course of the study. In order to make the photographs as reproducible as much as possible, the same focal length and exposure time were used consistently. Photographs were taken with the same camera and lens at all times. Intraoral photographs were taken.

Topical anesthesia was applied followed by local anesthesia administration via infiltration with Lidocaine HCL 2% and Epinephrine 1:100,000 Injection into both buccal and lingual soft tissues. Atraumatic extraction with periotome instruments and extraction forceps was done. The extraction socket was debrided with surgical curettes and the socket was not compressed.

Care was given to maintain the buccal alveolar wall in order to reduce the amount of lateral forces applied to buccal bone. For multirooted teeth, the roots were sectioned first. The tooth sockets were carefully debrided to remove granulation tissue. Alveolar ridge height and width were measured with the stent. All the measurements were approximated to the nearest 0.5 mm.

Group 1 (CFT):

The lingual releasing incision was similar for both groups; however the buccal flap had two vertical releasing incisions placed at the closest line angles of the neighboring teeth mesially and distally. The vertical incisions followed a trapezoidal shape as it was extended apically beyond the Mucoginigval Junction (MGJ). The incision was made deep to the bone to allow for a full thickness elevation passed the MGJ. A split thickness dissection was made apical to the MGJ to allow for coronal repositioning of the flap margins. The flap was elevated from the alveolar bone by Glickman instrument and micro-elevator.

Group 2 (OFT):

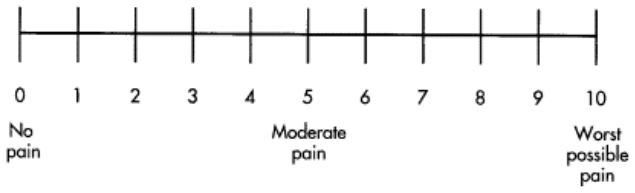
Intra-sulcular incisions were made on the buccal and lingual soft tissues. The buccal and lingual incisions were extended to involve at least one tooth towards the mesial and distal of the extraction site. The incision ended at the tooth line angle furthest away from the extraction site. The papilla was preserved and undermined to allow space for membrane adaptation. The buccal attached gingiva was also undermined to allow for the membrane adaptation; however, it did not exceed MGJ.

A UNC-15 periodontal probe in conjunction with the stent was used to measure bone height.

Once all the measurements were done, allograft bone FDBA[§] was hydrated following manufacturer's instructions and placed into the socket. The level of allograft bone fill was extended to the most coronal bone located in the alveolar housing.

A d-PTFE non-resorbable membrane was trimmed to the correct dimensional height of the alveolar ridge; the membrane was adapted to cover the bone graft particles and sound alveolar bone on both buccal and lingual surfaces. The membrane was placed at least 3 mm apical, underneath the flap margins. Following this Group 1 (CFT) had flaps repositioned to cover the membrane by the use of sutures. Sutures were placed to help support and stabilize the membrane. In Group 2 (OFT) the flaps were repositioned and the membrane left exposed by the use of sutures. Sutures were placed to help support and stabilize the membrane.

At the end of the surgery, the subjects were given a VAS pain questionnaire to fill out 24 hours following surgery. The subjects were asked to rate their pain at that time on a scale of 0-10 (0 being no pain at all and 10 being the worst possible pain). Each side was rated separately.



The subjects' postoperative instructions included not brushing or flossing in the area of the surgical procedures for 2 weeks. At the same time frame, the subjects were medicated with the antibiotic amoxicillin (500 mg three times a day for 7 days), chlorhexidine[#] (0,12%/1oz) twice daily for the same period of time and Ibuprofen [Δ] (600mg tid prn for three days) to manage postsurgical discomfort and inflammation.

Another VAS pain scale questionnaire was given at 14 days to evaluate pain on each side of the surgical procedure at that time. The subjects were asked to rate their pain since the surgery on a scale of 0-10. Each side was evaluated for the pain separately.

Statistical Analysis

Sample size

As this is a pilot study, no formal sample size calculation is required. Ten subjects were recruited and completed the study.

Statistical analysis

Descriptive statistics (e.g., means, medians, standard deviations, inter-quartile ranges) were computed for each group in this pilot study. The primary outcome was the mean difference in alveolar bone height change between groups; other outcomes were secondary. The data obtained were non-normally distributed, hence the Wilcoxon signed-rank test was used to assess statistical significance. P-values less than 0.05 were considered statistically significant. SPSS version 22 was used in the analysis.

Results

Demographics:

Of the 10 included subjects, 8 were males and 2 were females (80% males, 20% females of the total study population). The age range was 46 to 71 years old, mean age: 56.4 years old (SD = 9.1) Table 1. Healing was uneventful in all treatment groups. There were no complications.

Following the initial phase 1 therapy, which consisted of oral hygiene instructions, and prophylaxis / scaling and root planing on the full arch, measurements were made for both plaque index (PI) and bleeding index (BI). Baseline measurements were compared to 6 months follow-up and it was found that there were no statistically significant differences between baseline and 6 months for the subjects. (PI: $p = 0.643$; BI: $p = 0.809$) Table 2.

The study had 1 canine, 6 premolars, and 3 molars paired to each other on the contralateral side (a total of 20 sites received the extraction and ridge preservation procedure). Three patients had contiguous sites that needed extraction and ridge preservation on each side. One patient had a canine and 1st premolar planned for extraction on each side (total of 4 teeth), while the other 2 patients had 2 premolars on each side planned for the extraction.

Center height (CH): (Table 3) (Figures 12-14)

Both groups CFT and OFT had a statistically significant improvement of bone gain in height measured at the center of the extraction socket compared to the baseline (p = 0.005 for both groups). At 6 months, following extraction, the gain for the CFT had a mean difference of 8.1 mm, SD=1.9, median of 8 mm, and IQR= 3, when compared to the baseline. The OFT exhibited a mean gain of 7.5 mm, SD=1.8, median of 7 mm, and IQR= 3 compared to the baseline.

When comparing the bone gain difference in CFT against OFT, there was no statistically significant difference between the groups (p = 0.389). Measurements done at 6 months showed a statistically significant difference between CFT and OFT (mean bone height of 5.7 mm, SD=2 mm, median of 5.5 mm, and IQR=3 vs. a mean of 6.7 mm, SD=2.9, median of 6 mm, IQR= 4, respectively, p = 0.034).

Buccal height (BH): (Table 4) (Figures 15-17)

The buccal bone height at the baseline and at 6 months follow up had no statistical significance when comparing CFT to OFT. However, CFT had a statistically significant bone gain at 6 months when compared to the baseline (mean of 0.8 mm, SD=1, median of 1 mm, IQR=2, p = 0.046). The OFT had no statistically significant bone gain when compared to the baseline (mean of 0.3 mm SD=1.1mm, median of 0.5 mm, IQR=1 p = 0.429). When comparing the net gain of the buccal bone height in CFT to OFT, there was no statistical significance between the groups (p = 0.096).

Coronal bone width (CW): (Table 5) (Figures 18-20)

Both groups had no statistically significant difference between 6 months and baseline for the coronal bone width at 3 mm sub crestal to the mid-buccal surface. When comparing the two groups to each other at 6 months, there was a statistically significant difference in bone width

measurements, with OFT exhibiting higher values (mean of 4.6 mm, SD=1.5, median of 4.5 mm, IQR= 2) compared to CFT (mean of 3.5 mm, SD= 1.1, median of 3 mm, IQR= 1) (p = 0.031). However, there was no statistically significant difference when comparing the net loss of CFT with OFT in coronal bone width. (mean of -0.1, SD=1.1, median of 0, IQR= 1 and mean of -0.4, SD= 1.6 mm, median of -0.5 mm, IQR= 2 respectively) (p = 0.257).

Apical bone width (AW): (Table 6) (Figures 21-23)

Both the CFT and OFT groups had no statistically significant difference between the baseline and 6 months for the bone width at 5 mm sub crestal to the mid-buccal bone (mean of 0.1 mm, SD=0.3, median of 0 mm IQR=0, p= 0.317 and -0.1 mm, SD= 0.5, median of 0 mm, IQR=0, p=0.564 respectively). When comparing the two groups to each other at 6 months, there was no significant difference in bone width (p=0.132). For the net difference in bone width from baseline to 6 months comparing CFT to OFT, there was no statistically significant difference (p=0.317).

Keratinized Tissue Width (KTW): (Table 7) (Figure 24)

In CFT when comparing baseline to 6 months follow-up, there was a statistically significant loss in keratinized tissue width 1.7 mm, SD= 0.6 mm, median of 2 mm, IQR= 1 (p = 0.004). OFT had no statistically significant difference when comparing KTW baseline to 6 months (p= 0.946). OFT had a significantly higher KTW at 6 months (mean of 3.4 mm, SD= 1.2, median of 3.5 mm, IQR= 2) compared to CFT (mean of 2 mm, SD= 0.9, median of 2 IQR= 1) (p = 0.011). The net difference in KTW was also significantly greater in OFT than in CFT (p = 0.004).

VAS pain scale: (Table 8) (Figure 25)

At 24 hours, following extraction and ridge preservation, comparing CFT to OFT in the pain scale (mean of 3 SD= 0.8, median of 3 IQR= 2 and a mean of 1.1 mm, SD= 0.5, median of 1 IQR= 0 respectively), a statistically significant lower pain score was found for OFT (p = 0.006). At 2 weeks, following the extraction, there was no statistically significant difference

between CFT and OFT in the pain scale. (p = 0.132). Both CFT and OFT had a statistically significant reduction in pain when comparing 24 hours following surgery to 2 weeks following surgery (p = 0.006 and 0.008, respectively).

Discussion

The study had 10 subjects: 8 males and 2 females, 80% to 20% respectively. The population was not necessarily representative, because it depended on a convenience sample, for the subjects that met the inclusion criteria. The mean age of the population was 56.4±9.1, and age ranged from 46 to 71 years old, which was also a result of the convenience sample recruitment. The current study compared two surgical techniques following extraction and ridge preservation. Both areas had similar bone grafting material, freeze-dried bone allograft (FDBA) and a non-reinforced ePTFE membrane. The present findings confirm that complete preservation of the alveolar ridge dimension after tooth extraction is unlikely to be attainable. Several ridge preservation techniques have, in many cases, recorded some bone loss, even if extensive modifications were not reported. [2, 4]

Among the various regeneration techniques, the one proposed in this paper was the filling of the post-extraction alveolus with corticocancellous FDBA substitute. Two different techniques were consequently adopted: either a full flap procedure with complete coverage of the membrane (CFT) or a flapless procedure leaving the membrane exposed OFT. Undoubtedly, there are many factors affecting dimensional changes after tooth extraction, but some authors have focused their attention on the type surgical procedure performed: flap and flapless tooth extraction. In a report by Fickl et al.[90], it was observed that on a canine model OFT group had a lower extent of resorption than the flap group; conversely, Araujo and Lindhe [91] found that raising a flap during extraction may affect only the short-term dimensional alteration: the difference between flapless versus flapped procedure was negligible after 6 months.

In this study, when the two surgical procedures were compared to each other, there were no statistically significant findings related to bone dimensional changes. Both OFT and CFT had

statistically significantly difference in CH values at six months when compared to the baseline. This observation is in agreement with previous study findings that found a statistically significant finding when comparing grafted sites to none grafted sites when measuring at the center of the socket. There was an interesting observation in the current study in the mid-buccal socket wall height, where CFT yielded more bone height at 6 months than the baseline.

Both groups did manage to maintain the bone width at the coronal width (CW) and at the apical width (AW), located at 3 and 5 mm sub-crestal. CFT had a mean bone loss of 0.1 SD=1.1 mm and OFT had a loss of 0.4 mm SD=1.6. When the difference between the baseline and 6-month follow-up was calculated in both CFT and OFT groups, it was found that there were no statistically significant changes. This outcome might be attributed to the inert property of the non-resorbable membrane when compared to resorbable membrane. The resorbable membrane lacks the longevity and protection of the underlying tissue when it's left exposed as opposed to the non-resorbable membrane.

In the KTW variable, the OFT maintained a wider zone of KTW than the CFT. This finding was due to the maintenance of the apical keratinize mucosa, of which the MGJ was not displaced coronally in OFT, in contrast to CFT. In the current study, CFT relocated and shifted the MGJ coronally by a mean of 1.7 mm SD= 0.6.

Moreover, the analysis of VAS pain scale showed a statistically significant reduction in post-operative pain at 24 hours following extractions for the OFT group when compared to CFT (mean of 3, SD= 0.8, median of 3, IQR= 2 in the CFT and a mean of 1.1 SD= 0.5, median of 1, IQR= 0 in OFT). Therefore, results from this study support the hypothesis that in contrast to CFT, OFT has less pain and wider zone of KTW.

The CFT exhibited a statistically significant difference at 6 months when compared to the baseline in the amount of bone gained at the buccal bone crest (BH) (mean of 0.8 mm, SD=1, median of 1 mm, IQR=2). The OFT had no such statistically significant finding when

comparing values at 6 months to those at baseline (mean of 0.3 mm, SD= 1.1, median of 0.5 mm, IQR=1).

In general, the vertical component of bone augmentation is more difficult to gain than the horizontal grafting outcomes. Recent studies have reported that the use of several grafting materials placed in socket spaces significantly reduced the ridge height and width compared with unfilled control groups. However, it remains questionable whether this successful outcome is influenced by the presence or absence of a primary wound closure. [92, 93] Very similar results, also using a different graft substitute placed in the extraction sockets but with an OFT and membrane covering/secondary closure technique, were obtained by Aimetti et al., [94] who recorded a mean width loss of 1.6 mm for the test group. The results of height loss of 0.8 mm were worse than the alveolar ridge height remodeling recorded in this paper with a mean of 0.1 mm, SD= 1.1 for CFT and 0.4 mm, SD= 1.4 from OFT.

The difference between CFT and OFT in the net bone loss was not statistically significant in the horizontal dimension CW and AW. OFT had a slightly higher resorption when compared with the mean of CFT (CW loss of 0.4 mm SD= 1.6 mm and AW 0.1 mm SD= 0.5). This was probably due to the exposed non-resorbable ePTFE membrane. When the membrane is exposed, it may increase complications in maintaining the area free of inflammation at the margins of the membrane. As far as the OFT procedure was concerned, even if the compressive forces during the early healing process (due to sutures) seemed to be reduced by unattained primary closure, the tissue tensions were not avoidable; in fact, even if the reduction of the horizontal bone dimension was more than the CFT, it was observed at 0.4 mm SD= 1.6 mm. On the other hand, the primary closure attained for the CFT procedure seemed to maintain the vertical dimension better than that for the OFT procedure, at least on the buccal aspect, which is the site more subject to bone tissue alteration.

When considering the OFT procedure, the ePTFE membrane was left intentionally exposed to the oral cavity, and sutures were used primarily to stabilize the membrane. The promotion of secondary wound healing appeared to be slower than that of the primary healing of the flapped group, despite the presence of the two release incisions. Undoubtedly, the problems

were encountered by patients due to difficult cleaning of the extraction/ridge preservation area with an exposed membrane that probably played a role in the higher resorption.

Failure of the socket-preservation procedure is defined as excessive bone loss, resulting in inability to perform implant insertion without additional bone augmentation techniques.

Some of the limitations of the current study were the convenience sample included in the study and the number of teeth involved in the extraction sites. There were 3 patients with paired contiguous extraction sites. This observation might have a confounding effect on the outcomes. Literature reports that contiguous teeth extraction causes more alveolar ridge loss than a single tooth extraction. [95]

Moreover, the stent only allowed measuring a direct linear point located underneath it. These measurement points provide information at only those sites, as they lack in providing information on the three-dimensional ridge topography.

Further studies and analysis of other dependent variables such as primary or secondary wound closure and the investigation of a greater number of surgical procedures are necessary to confirm the current findings.

Conclusion

Within the study's limitations, it was found that there was no statistically significant difference between CFT and OFT in terms of alveolar ridge dimensions following tooth extraction. Both groups had a statistically significant gain in bone center height. Only the CFT had a statistically significant gain in buccal bone height compared to the baseline. However, OFT had a significantly wider zone of keratinized tissue and less post-operative pain at 24 hours than the CFT. There needs to be more clinical research with a similar design incorporating a larger sample size to arrive at a clearer conclusion.

References

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

2. Iasella JM, Greenwell H, Miller RL, et al. Ridge preservation with freeze-dried bone allograft and a collagen membrane compared to extraction alone for implant site development: a clinical and histologic study in humans. *J Periodontol* 2003;74:990-999.

3. Lekovic V, Camargo PM, Klokkevold PR, et al. Preservation of alveolar bone in extraction sockets using bioabsorbable membranes. *J Periodontol* 1998;69:1044-1049.

4. Lekovic V, Kenney EB, Weinlaender M, et al. A bone regenerative approach to alveolar ridge maintenance following tooth extraction. Report of 10 cases. *J Periodontol* 1997;68:563-570.

5. Nevins M, Camelo M, De Paoli S, et al. A study of the fate of the buccal wall of extraction sockets of teeth with prominent roots. *Int J Periodontics Restorative Dent* 2006;26:19-29.

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

7. Amler MH, Johnson PL, Salman I. Histological and histochemical investigation of human alveolar socket healing in undisturbed extraction wounds. *J Am Dent Assoc* 1960;61:32-44.

8. Evian CI, Rosenberg ES, Coslet JG, Corn H. The osteogenic activity of bone removed from healing extraction sockets in humans. *J Periodontol* 1982;53:81-85.

9. Devlin H, Ferguson MW. Alveolar ridge resorption and mandibular atrophy. A review of the role of local and systemic factors. *British dental journal* 1991;170:101-104.

10. Maeda Y, Wood WW. Finite element method simulation of bone resorption beneath a complete denture. *J Dent Res* 1989;68:1370-1373.

11. Pietrokovski J, Massler M. Alveolar ridge resorption following tooth extraction. *The Journal of prosthetic dentistry* 1967;17:21-27.

12. Oh TJ, Meraw SJ, Lee EJ, Giannobile WV, Wang HL. Comparative analysis of collagen membranes for the treatment of implant dehiscence defects. *Clin Oral Implants Res* 2003;14:80-90.

13. Douthitt JC, Gutmann JL, Witherspoon DE. Histologic assessment of healing after the use of a bioresorbable membrane in the management of buccal bone loss concomitant with periradicular surgery. *Journal of endodontics* 2001;27:404-410.

14. Jovanovic SA, Schenk RK, Orsini M, Kenney EB. Supracrestal bone formation around dental implants: an experimental dog study. *Int J Oral Maxillofac Implants* 1995;10:23-31.

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

16. Huynh-Ba G, Pjetursson BE, Sanz M, et al. Analysis of the socket bone wall dimensions in the upper maxilla in relation to immediate implant placement. *Clin Oral Implants Res* 2010;21:37-42.

17. Boyne PJ. Use of HTR in tooth extraction sockets to maintain alveolar ridge height and increase concentration of alveolar bone matrix. *Gen Dent* 1995;43:470-473.

18. Christensen GJ. Ridge preservation: why not? *J Am Dent Assoc* 1996;127:669-670.

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

20. Bell DH, Jr. Particles versus solid forms of hydroxyapatite as a treatment modality to preserve residual alveolar ridges. *The Journal of prosthetic dentistry* 1986;56:322-326.

21. Tiefengraber J, Diedrich P, Fritz U, Lantos P. Orthodontic space closure in combination with membrane supported healing of extraction sockets (MHE) a pilot study. *Journal of orofacial orthopedics = Fortschritte der Kieferorthopadie : Organ/official journal Deutsche Gesellschaft fur Kieferorthopadie* 2002;63:422-428.

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

23. Block MS, Finger I, Lytle R. Human mineralized bone in extraction sites before implant placement: preliminary results. *J Am Dent Assoc* 2002;133:1631-1638.

24. Tinti C, Parma-Benfenati S. Clinical classification of bone defects concerning the placement of dental implants. *Int J Periodontics Restorative Dent* 2003;23:147-155.

25. Brugnami F, Then PR, Moroi H, Kabani S, Leone CW. GBR in human extraction sockets and ridge defects prior to implant placement: clinical results and histologic evidence of osteoblastic and osteoclastic activities in DFDBA. *Int J Periodontics Restorative Dent* 1999;19:259-267.

26. Hermann JS, Buser D. Guided bone regeneration for dental implants. *Current opinion in periodontology* 1996;3:168-177.

27. VA R. Eine methode zur schliessung von kieferhohlen pcrforationen. . *Deutsche Zahnarztliche Wochenschrift* 1936;39:1136.

28. Wood DL, Hoag PM, Donnenfeld OW, Rosenfeld LD. Alveolar crest reduction following full and partial thickness flaps. *J Periodontol* 1972;43:141-144.

29. Moghaddas H, Stahl SS. Alveolar bone remodeling following osseous surgery. A clinical study. *J Periodontol* 1980;51:376-381.

30. Landsberg CJ. Socket seal surgery combined with immediate implant placement: a novel approach for single-tooth replacement. *Int J Periodontics Restorative Dent* 1997;17:140-149.

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

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

33. Eger T, Muller HP, Heinecke A. Ultrasonic determination of gingival thickness. Subject variation and influence of tooth type and clinical features. *J Clin Periodontol* 1996;23:839-845.

34. Muller HP, Eger T. Masticatory mucosa and periodontal phenotype: a review. *Int J Periodontics Restorative Dent* 2002;22:172-183.

35. Wennstrom JL. Lack of association between width of attached gingiva and development of soft tissue recession. A 5-year longitudinal study. *J Clin Periodontol* 1987;14:181-184.

36. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. *European journal of oral sciences* 1998;106:721-764.

37. Warrer K, Buser D, Lang NP, Karring T. Plaque-induced peri-implantitis in the presence or absence of keratinized mucosa. An experimental study in monkeys. *Clin Oral Implants Res* 1995;6:131-138.

38. Edel A. The use of a connective tissue graft for closure over an immediate implant covered with occlusive membrane. *Clin Oral Implants Res* 1995;6:60-65.

39. Chen ST, Dahlin C. Connective tissue grafting for primary closure of extraction sockets treated with an osteopromotive membrane technique: surgical technique and clinical results. *Int J Periodontics Restorative Dent* 1996;16:348-355.

40. Bianchi AE, Sanfilippo F. Single-tooth replacement by immediate implant and connective tissue graft: a 1-9-year clinical evaluation. *Clin Oral Implants Res* 2004;15:269-277.

41. Tal H. Autogenous masticatory mucosal grafts in extraction socket seal procedures: a comparison between sockets grafted with demineralized freeze-dried bone and deproteinized bovine bone mineral. *Clin Oral Implants Res* 1999;10:289-296.

42. Hoidal MJ, Grimard BA, Mills MP, Schoolfield JD, Mellonig JT, Mealey BL. Clinical evaluation of demineralized freeze-dried bone allograft with and without enamel matrix derivative for the treatment of periodontal osseous defects in humans. *J Periodontol* 2008;79:2273-2280.

43. Hammerle CH, Jung RE. Bone augmentation by means of barrier membranes. *Periodontology 2000* 2003;33:36-53.

44. Ito K, Nanba K, Murai S. Effects of bioabsorbable and non-resorbable barrier membranes on bone augmentation in rabbit calvaria. *J Periodontol* 1998;69:1229-1237.

45. Hurzeler MB, Quinones CR, Caffesse RG, Schupbach P, Morrison EC. Guided periodontal tissue regeneration in Class II furcation defects following treatment with a synthetic bioabsorbable barrier. *J Periodontol* 1997;68:498-505.

46. Lang NP, Bragger U, Hammerle CH, Sutter F. Immediate transmucosal implants using the principle of guided tissue regeneration. I. Rationale, clinical procedures and 30-month results. *Clin Oral Implants Res* 1994;5:154-163.

47. Carranza FA, Newman MG, Takei HH, Klokkevold PR. *Carranza's clinical periodontology*. St. Louis, Mo.: Saunders Elsevier; 2006: xxxvi, 1286 p.

48. Mellonig JT, Nevins M, Sanchez R. Evaluation of a bioabsorbable physical barrier for guided bone regeneration. Part II. Material and a bone replacement graft. *Int J Periodontics Restorative Dent* 1998;18:129-137.

49. Kohal RJ, Mellas P, Hurzeler MB, Trejo PM, Morrison E, Caffesse RG. The effects of guided bone regeneration and grafting on implants placed into immediate extraction sockets. An experimental study in dogs. *J Periodontol* 1998;69:927-937.

50. Wang HL, Carroll MJ. Guided bone regeneration using bone grafts and collagen membranes. *Quintessence international (Berlin, Germany : 1985)* 2001;32:504-515.

51. Machtei EE. The effect of membrane exposure on the outcome of regenerative procedures in humans: a meta-analysis. *J Periodontol* 2001;72:512-516.

52. Ling LJ, Hung SL, Lee CF, Chen YT, Wu KM. The influence of membrane exposure on the outcomes of guided tissue regeneration: clinical and microbiological aspects. *Journal of periodontal research* 2003;38:57-63.

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

54. Fontana F, Maschera E, Rocchietta I, Simion M. Clinical classification of complications in guided bone regeneration procedures by means of a nonresorbable membrane. *Int J Periodontics Restorative Dent* 2011;31:265-273.

55. Hoffmann O, Bartee BK, Beaumont C, Kasaj A, Deli G, Zafiropoulos GG. Alveolar bone preservation in extraction sockets using non-resorbable dPTFE membranes: a retrospective non-randomized study. *J Periodontol* 2008;79:1355-1369.

56. Jovanovic SA, Nevins M. Bone formation utilizing titanium-reinforced barrier membranes. *Int J Periodontics Restorative Dent* 1995;15:56-69.

57. Bottino MC, Thomas V, Schmidt G, et al. Recent advances in the development of GTR/GBR membranes for periodontal regeneration--a materials perspective. *Dent Mater* 2012;28:703-721.

58. Kim DM, Nevins M, Camelo M, et al. The feasibility of demineralized bone matrix and cancellous bone chips in conjunction with an extracellular matrix membrane for alveolar ridge preservation: a case series. *Int J Periodontics Restorative Dent* 2011;31:39-47.

59. Kim DM, De Angelis N, Camelo M, Nevins ML, Schupbach P, Nevins M. Ridge Preservation With and Without Primary Wound Closure: A Case Series. *Int J Periodontics Restorative Dent* 2013;33:71-78.

60. Bartee BK, Carr JA. Evaluation of a high-density polytetrafluoroethylene (n-PTFE) membrane as a barrier material to facilitate guided bone regeneration in the rat mandible. *J Oral Implantol* 1995;21:88-95.

61. Bartee BK. The use of high-density polytetrafluoroethylene membrane to treat osseous defects: clinical reports. *Implant Dent* 1995;4:21-26.

62. Crump TB, Rivera-Hidalgo F, Harrison JW, Williams FE, Guo IY. Influence of three membrane types on healing of bone defects. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:365-374.

63. Walters SP, Greenwell H, Hill M, Drisko C, Pickman K, Scheetz JP. Comparison of porous and non-porous teflon membranes plus a xenograft in the treatment of vertical osseous defects: a clinical reentry study. *J Periodontol* 2003;74:1161-1168.

64. Sittitavornwong S, Gutta R. Bone graft harvesting from regional sites. *Oral Maxillofac Surg Clin North Am* 2010;22:317-330, v-vi.

65. Perelman-Karmon M, Kozlovsky A, Liloy R, Artzi Z. Socket site preservation using bovine bone mineral with and without a bioresorbable collagen membrane. *Int J Periodontics Restorative Dent* 2012;32:459-465.

66. Krauser JT, Rohrer MD, Wallace SS. Human histologic and histomorphometric analysis comparing OsteoGraf/N with PepGen P-15 in the maxillary sinus elevation procedure: a case report. *Implant Dent* 2000;9:298-302.

67. Minichetti JC, D'Amore JC, Hong AY. Three-year analysis of Tapered Screw-Vent implants placed into extraction sockets grafted with mineralized bone allograft. *J Oral Implantol* 2005;31:283-293.

68. Valentini P, Abensur DJ. Maxillary sinus grafting with anorganic bovine bone: a clinical report of long-term results. *Int J Oral Maxillofac Implants* 2003;18:556-560.

69. Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L, Cardaropoli G. Socket preservation using bovine bone mineral and collagen membrane: a randomized

controlled clinical trial with histologic analysis. *Int J Periodontics Restorative Dent* 2012;32:421-430.

70. Landi L, Pretel RW, Jr., Hakimi NM, Setayesh R. Maxillary sinus floor elevation using a combination of DFDBA and bovine-derived porous hydroxyapatite: a preliminary histologic and histomorphometric report. *Int J Periodontics Restorative Dent* 2000;20:574-583.

71. Valentini P, Abensur D. Maxillary sinus floor elevation for implant placement with demineralized freeze-dried bone and bovine bone (Bio-Oss): a clinical study of 20 patients. *Int J Periodontics Restorative Dent* 1997;17:232-241.

72. Ackermann KL. Extraction site management using a natural bone mineral containing collagen: rationale and retrospective case study. *Int J Periodontics Restorative Dent* 2009;29:489-497.

73. Aldredge WA, Nejat R. Delayed implant procedure using deproteinized bovine bone mineral: A report of 109 consecutive cases. *Compend Contin Educ Dent* 2011;32:66-71.

74. Heberer S, Al-Chawaf B, Jablonski C, Nelson JJ, Lage H, Nelson K. Healing of ungrafted and grafted extraction sockets after 12 weeks: a prospective clinical study. *Int J Oral Maxillofac Implants* 2011;26:385-392.

75. Kim YK, Yun PY, Lee HJ, Ahn JY, Kim SG. Ridge preservation of the molar extraction socket using collagen sponge and xenogeneic bone grafts. *Implant Dent* 2011;20:267-272.

76. Park JB. Healing of extraction socket grafted with deproteinized bovine bone and acellular dermal matrix: histomorphometric evaluation. *Implant Dent* 2010;19:307-313.

77. Rasperini G, Canullo L, Dellavia C, Pellegrini G, Simion M. Socket grafting in the posterior maxilla reduces the need for sinus augmentation. *Int J Periodontics Restorative Dent* 2010;30:265-273.

78. Lee DW, Pi SH, Lee SK, Kim EC. Comparative histomorphometric analysis of extraction sockets healing implanted with bovine xenografts, irradiated cancellous allografts, and solvent-dehydrated allografts in humans. *Int J Oral Maxillofac Implants* 2009;24:609-615.

79. Khan SN, Tomin E, Lane JM. Clinical applications of bone graft substitutes. *Orthop Clin North Am* 2000;31:389-398.

80. Avila G, Neiva R, Misch CE, et al. Clinical and histologic outcomes after the use of a novel allograft for maxillary sinus augmentation: a case series. *Implant Dent* 2010;19:330-341.

81. Barone A, Borgia V, Covani U, Ricci M, Piattelli A, Iezzi G. Flap versus flapless procedure for ridge preservation in alveolar extraction sockets: a histological evaluation in a randomized clinical trial. *Clin Oral Implants Res* 2015;26:806-813.

82. Barone A, Toti P, Piattelli A, Iezzi G, Derchi G, Covani U. Extraction socket healing in humans after ridge preservation techniques: comparison between flapless and flapped procedures in a randomized clinical trial. *J Periodontol* 2014;85:14-23.

83. Engler-Hamm D, Cheung WS, Yen A, Stark PC, Griffin T. Ridge preservation using a composite bone graft and a bioabsorbable membrane with and without primary wound closure: a comparative clinical trial. *J Periodontol* 2011;82:377-387.

84. Huskisson EC. Measurement of pain. *J Rheumatol* 1982;9:768-769.

85. Weber MA, Schiffrin EL, White WB, et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society

of Hypertension and the International Society of Hypertension. *J Clin Hypertens (Greenwich)* 2014;16:14-26.

86. Moller UK, Vieth Streym S, Mosekilde L, Rejnmark L. Changes in bone mineral density and body composition during pregnancy and postpartum. A controlled cohort study. *Osteoporos Int* 2012;23:1213-1223.

87. O'Leary TJ, Drake RB, Naylor JE. The plaque control record. *J Periodontol* 1972;43:38.

88. Toloue SM, Chesnoiu-Matei I, Blanchard SB. A clinical and histomorphometric study of calcium sulfate compared with freeze-dried bone allograft for alveolar ridge preservation. *J Periodontol* 2012;83:847-855.

89. Beck TM, Mealey BL. Histologic analysis of healing after tooth extraction with ridge preservation using mineralized human bone allograft. *J Periodontol* 2010;81:1765-1772.

90. Fickl S, Zuhr O, Wachtel H, Bolz W, Huerzeler M. Tissue alterations after tooth extraction with and without surgical trauma: a volumetric study in the beagle dog. *J Clin Periodontol* 2008;35:356-363.

91. Araujo MG, Lindhe J. Ridge alterations following tooth extraction with and without flap elevation: an experimental study in the dog. *Clin Oral Implants Res* 2009;20:545-549.

92. Darby I, Chen ST, Buser D. Ridge preservation techniques for implant therapy. *Int J Oral Maxillofac Implants* 2009;24 Suppl:260-271.

93. Horvath A, Mardas N, Mezzomo LA, Needleman IG, Donos N. Alveolar ridge preservation. A systematic review. *Clinical oral investigations* 2013;17:341-363.

94. Aimetti M, Romano F, Griga FB, Godio L. Clinical and histologic healing of human extraction sockets filled with calcium sulfate. *Int J Oral Maxillofac Implants* 2009;24:902-909.

95. Al-Askar M, O'Neill R, Stark PC, Griffin T, Javed F, Al-Hezaimi K. Effect of single and contiguous teeth extractions on alveolar bone remodeling: a study in dogs. *Clinical implant dentistry and related research* 2013;15:569-575.

APPENDICES

Appendix A: Tables

Appendix B: Figures

Appendix A: Tables

Table 1: Summary of demographic data.

Subjects (N=10)	Demographic Result
Age Mean (SD)	56.4 ± (9.1)
Age Range	46 to 71
Male	8
Female	2
Paired Canine	1
Paired Premolar	6
Paired Molar	3
Contiguous extraction pairs	3
Biopsy sites	12

Table 2: Means and standard deviations for plaque and bleeding scores at baseline following phase 1 therapy and at 6 months post extraction and ridge preservation.

Variables	Plaque at baseline	Plaque at 6 months	Bleeding at baseline	Bleeding at 6 months
Mean	16.2	16.0	14.9	15.0
Standard deviation	2.2	3.3	2.3	2.9
Median	16.5	15.5	14.5	14.0
IQR	3.3	4.8	2.8	4.0
P-Value	0.643		0.809	

Table 3: Stent measurement of bone height at center (CH)

Variables	CFT Mean	SD	CFT Median	IQR	OFT Mean	SD	OFT Median	IQR	*p* Value
Baseline	13.8	2.8	15	5	14.2	3.1	15	5	0.551
6 months following Sx	5.7	2	5.5	3	6.7	2.9	6	4	**0.034**
Difference	8.1	1.9	8	3	7.5	1.8	7	3	0.389
p Value			**0.005**				**0.005**		

Table 4: Stent measurement of bone height at mid-buccal (BH)

Variables	CFT Mean	SD	CFT Median	IQR	OFT Mean	SD	OFT Median	IQR	*p* Value
Baseline	6.2	2.3	6	3	6.1	1.7	6	2	0.763
6 months following Sx	5.4	2.3	5.5	3	5.8	1.7	6	2	0.157
Difference	0.8	1	1	2	0.3	1.1	0.5	1	0.096
p Value			**0.046**				0.429		

Table 5: Stent measurement of bone width at 3 mm sub-crestal (CW)

Variables	CFT Mean	SD	CFT Median	IQR	OFT Mean	SD	OFT Median	IQR	*p* Value
Baseline	3.4	1.4	3	1	4.2	2	4	4	0.071
6 months following Sx	3.5	1.1	3	1	4.6	1.5	4.5	2	**0.031**
Difference	-0.1	1.1	0	1	-0.4	1.6	-0.5	2	0.257
p Value			0.783				0.389		

Table 6: Stent measurement of bone width at 5 mm sub-crestal (AW)

Variables	CFT Mean	SD	CFT Median	IQR	OFT Mean	SD	OFT Median	IQR	*p* Value
Baseline	3.3	1.3	3	2	3.6	1.2	4	3	0.366
6 months following Sx	3.2	1.1	3	2	3.7	1	3.5	2	0.132
Difference	0.1	0.3	0	0	-0.1	0.5	0	0	0.317
p Value			0.317				0.564		

Table 7: Stent measurement of Keratinized tissue width (KTW)

Variables	CFT Mean	SD	CFT Median	IQR	OFT Mean	SD	OFT Median	IQR	*p* Value
Baseline	3.7	1.2	4	2	3.4	1.2	3.5	2	0.18
6 months following Sx	2	0.9	2	1	3.4	1.2	3.5	2	**0.011**
Difference	1.7	0.6	2	1	0	0	0	0	**0.004**
p Value			**0.004**				0.946		

Table 8: Pain (VAS scale 0-10)

Variables	CFT Mean	SD	CFT Median	IQR	OFT Mean	SD	OFT Median	IQR	*p* Value
24 hours following Sx	3	0.8	3	2	1.1	0.5	1	0	**0.006**
2 weeks following Sx	0.8	0.9	1	1	0.4	0.5	0	1	0.132
Difference	2.2	1.2	1	1	0.7	0.4	0	1	**0.023**
p Value			**0.006**				**0.008**		

Appendix B: Figures

Figure 1. Stent used to calculate crestal bone height and width.
Blue arrow: mid socket bone height measurement. (CH)
White arrow: buccal bone height measurement. (BH)
Green arrow: width at 3 mm from crestal bone height. (CW)
Yellow arrow: width at 5 mm from crestal bone height. (AW)
Red Line: Keratinized tissue width. (KTW).

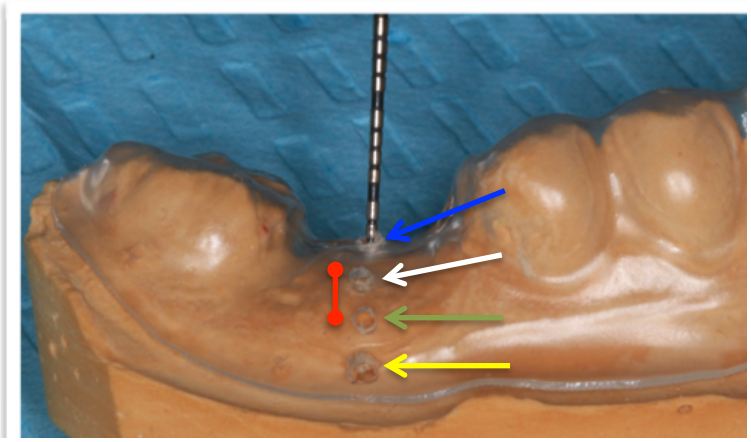


Figure 2: mean CH probing measurement at baseline and 6 months.

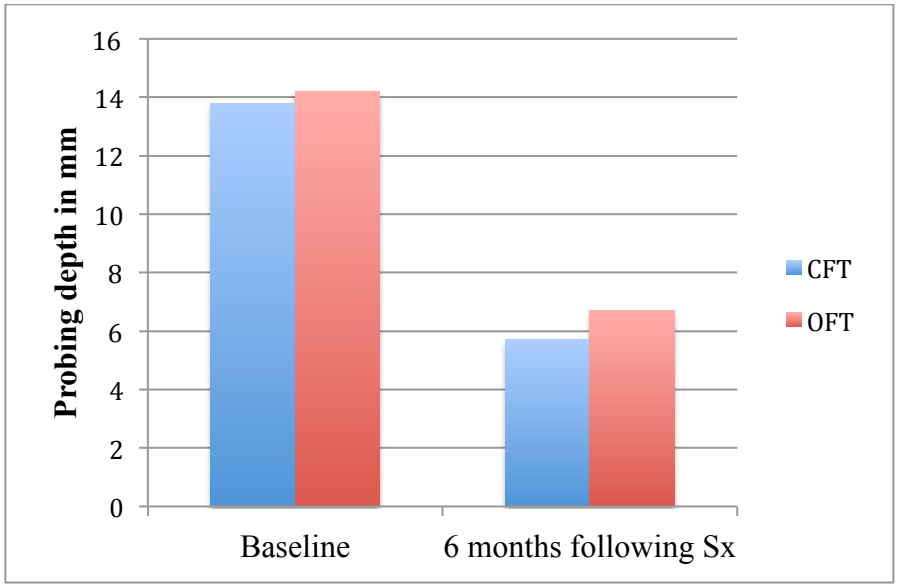


Figure 3: Net difference gain between baseline and 6 months at CH.

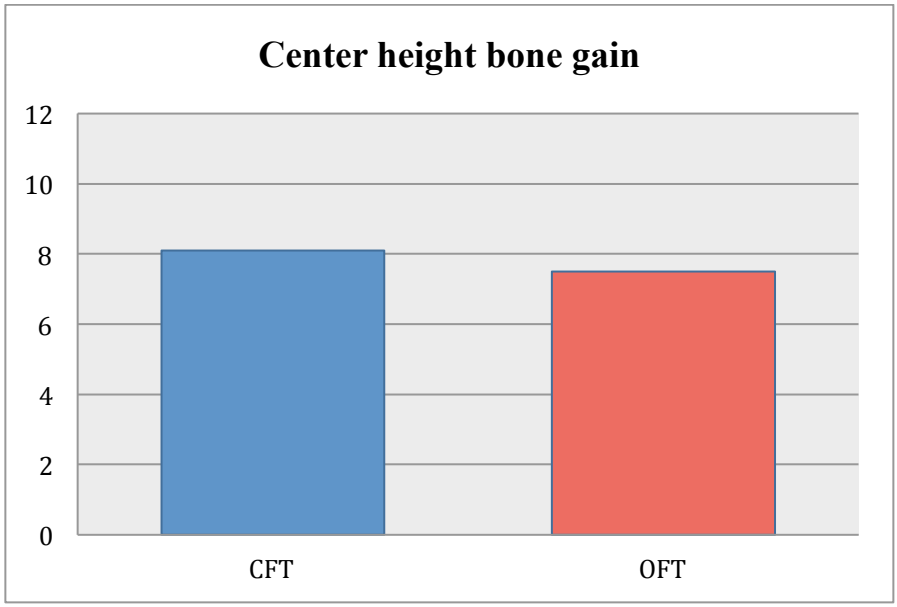


Figure 4: mean BH probing measurement at baseline and 6 months.

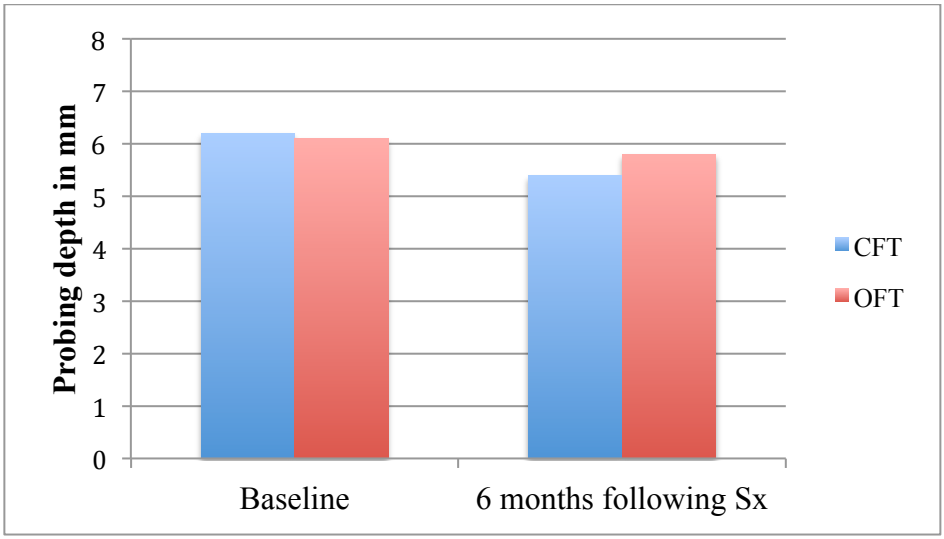


Figure 5: Net difference BH gain between baseline and 6 months comparing both groups.

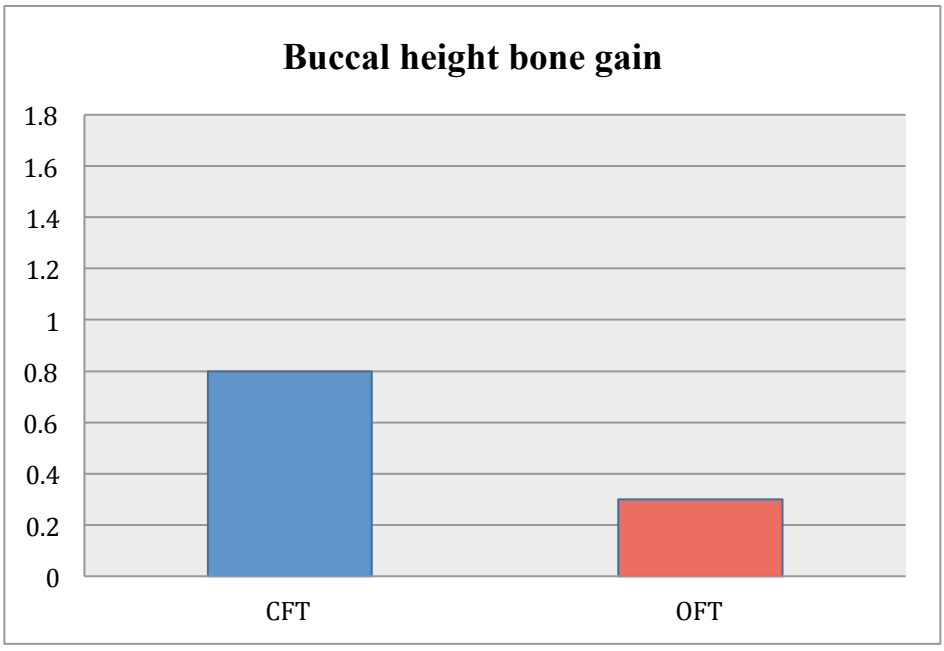


Figure 6: mean CW probing measurement at baseline and 6 months.

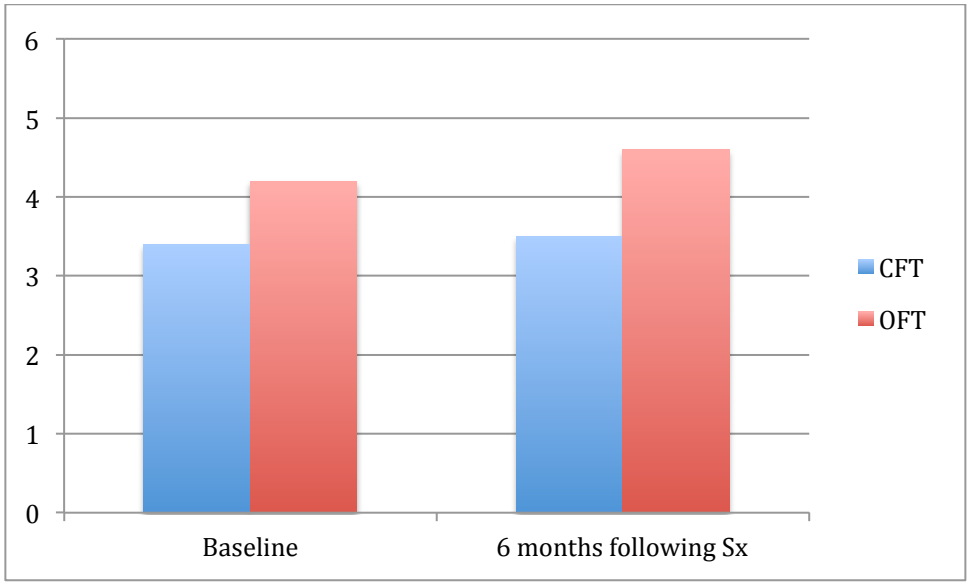


Figure 7: Net difference in CW gain/loss between baseline and 6 months comparing both groups.

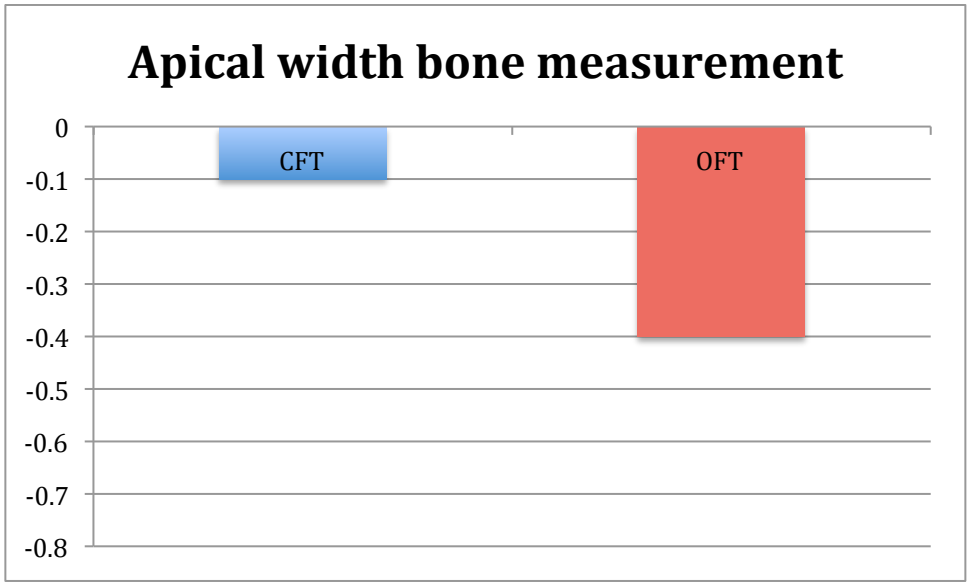


Figure 8: mean AW probing measurement at baseline and 6 months.

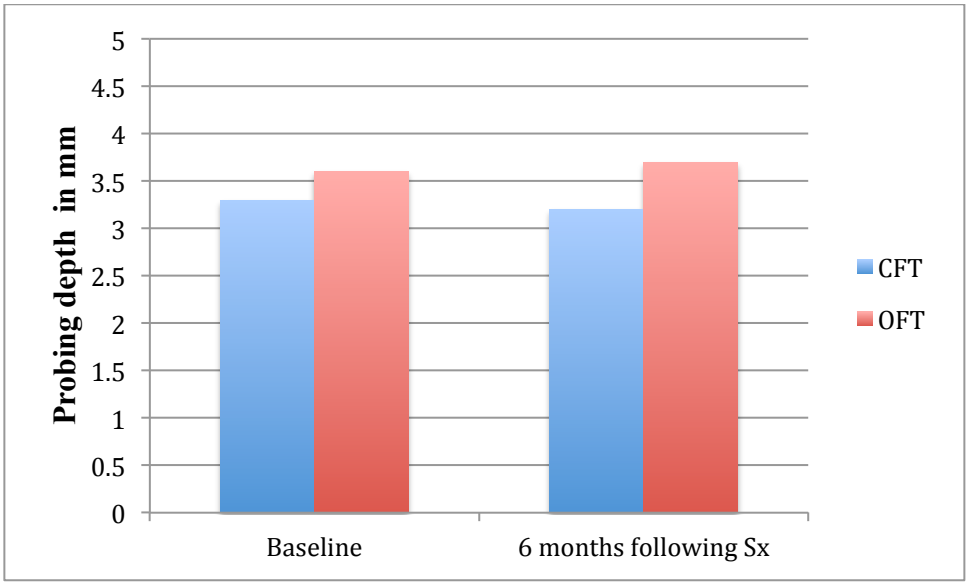


Figure 9: Net difference in AW gain/loss between baseline and 6 months comparing both groups.

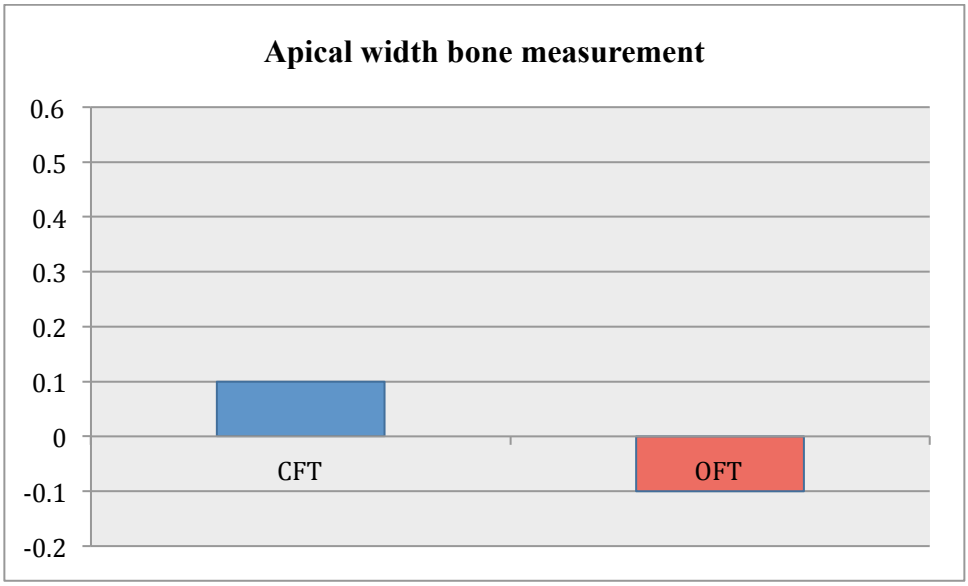


Figure 10: mean of KTW in CFT and OFT at baseline and 6 months.

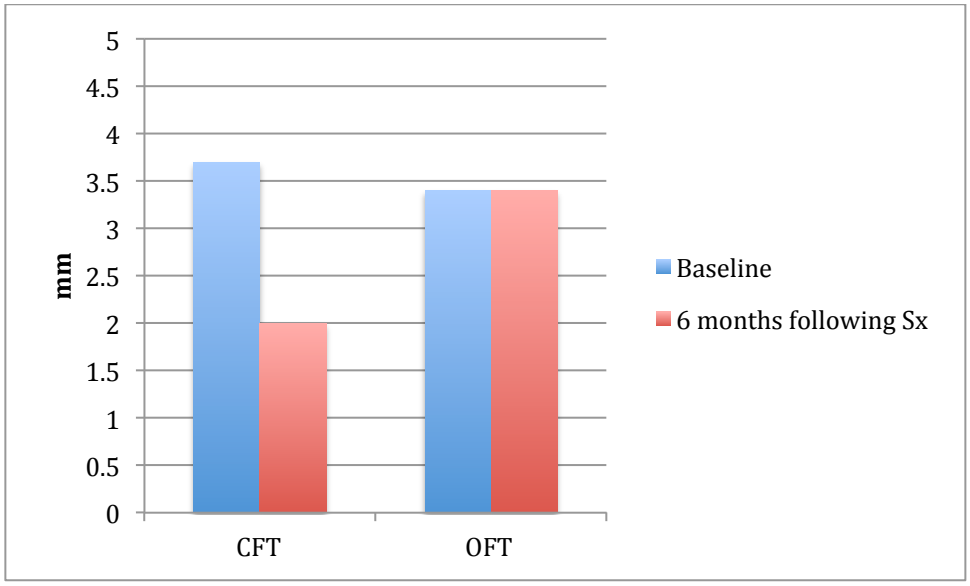


Figure 11: mean of the VAS pain scale at 24 hours and 2 weeks post extraction and ridge preservation.

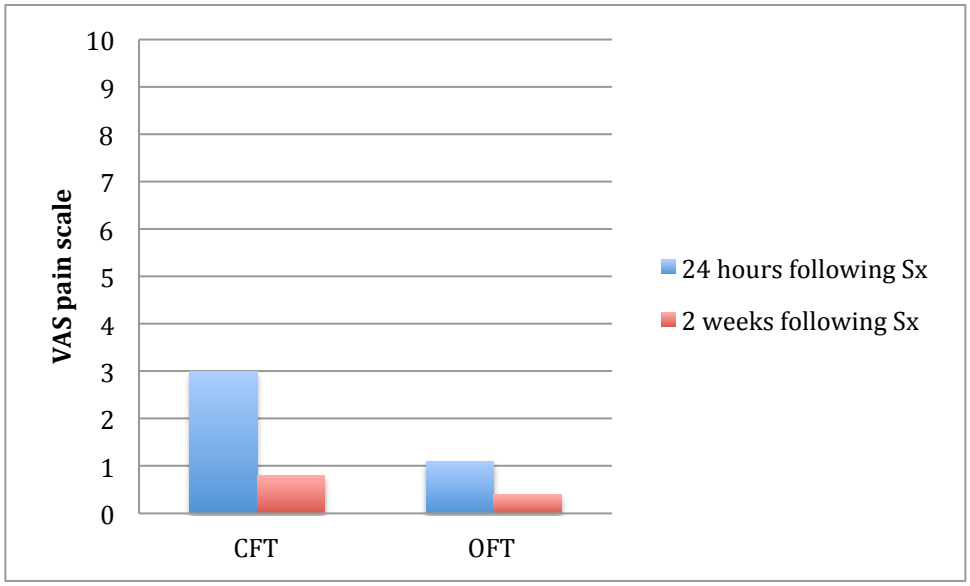


Figure 12: Side-by-side boxplots for both groups showing the baseline measurements done on CH position.

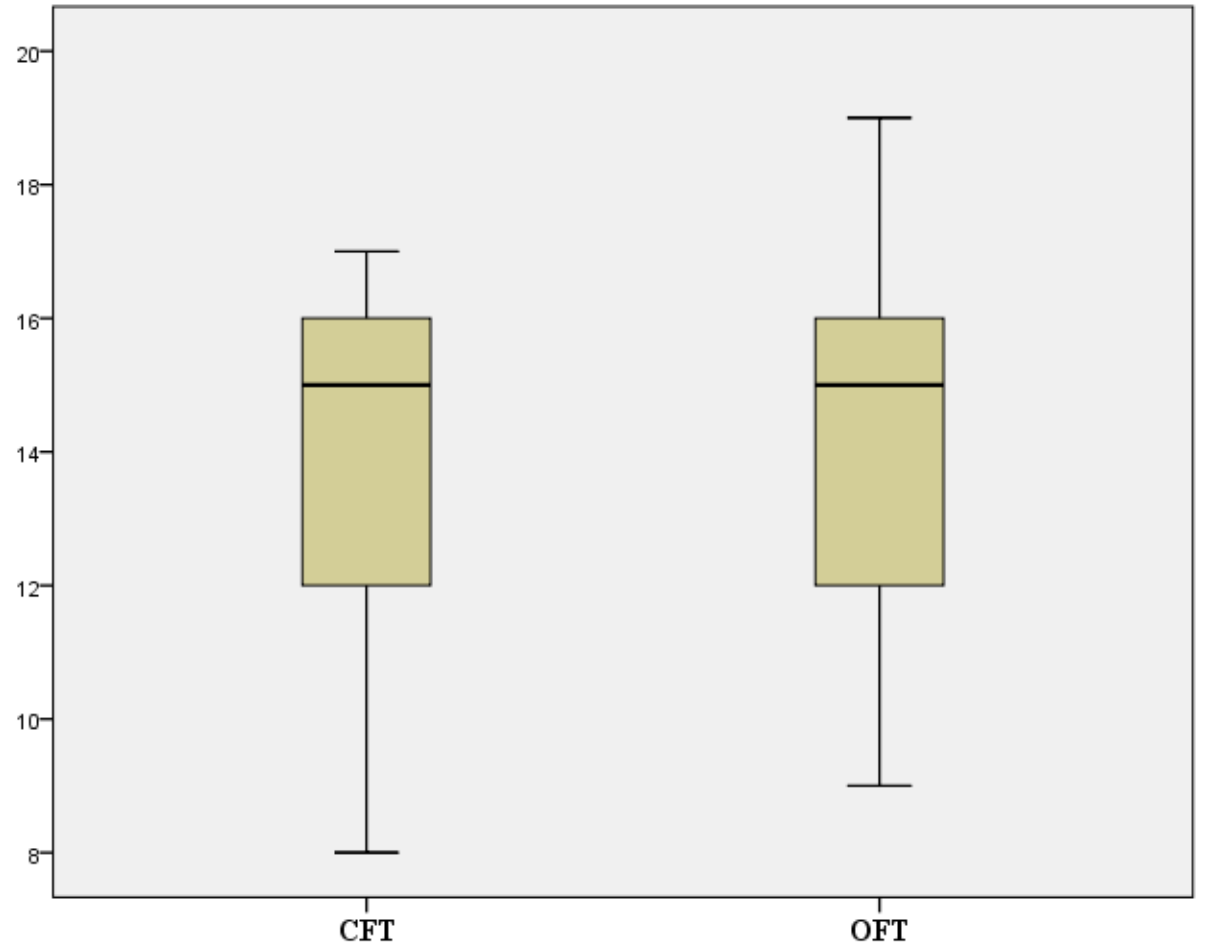


Figure 13: Side-by-side boxplots for both groups showing the 6 months follow up measurements done on CH position.

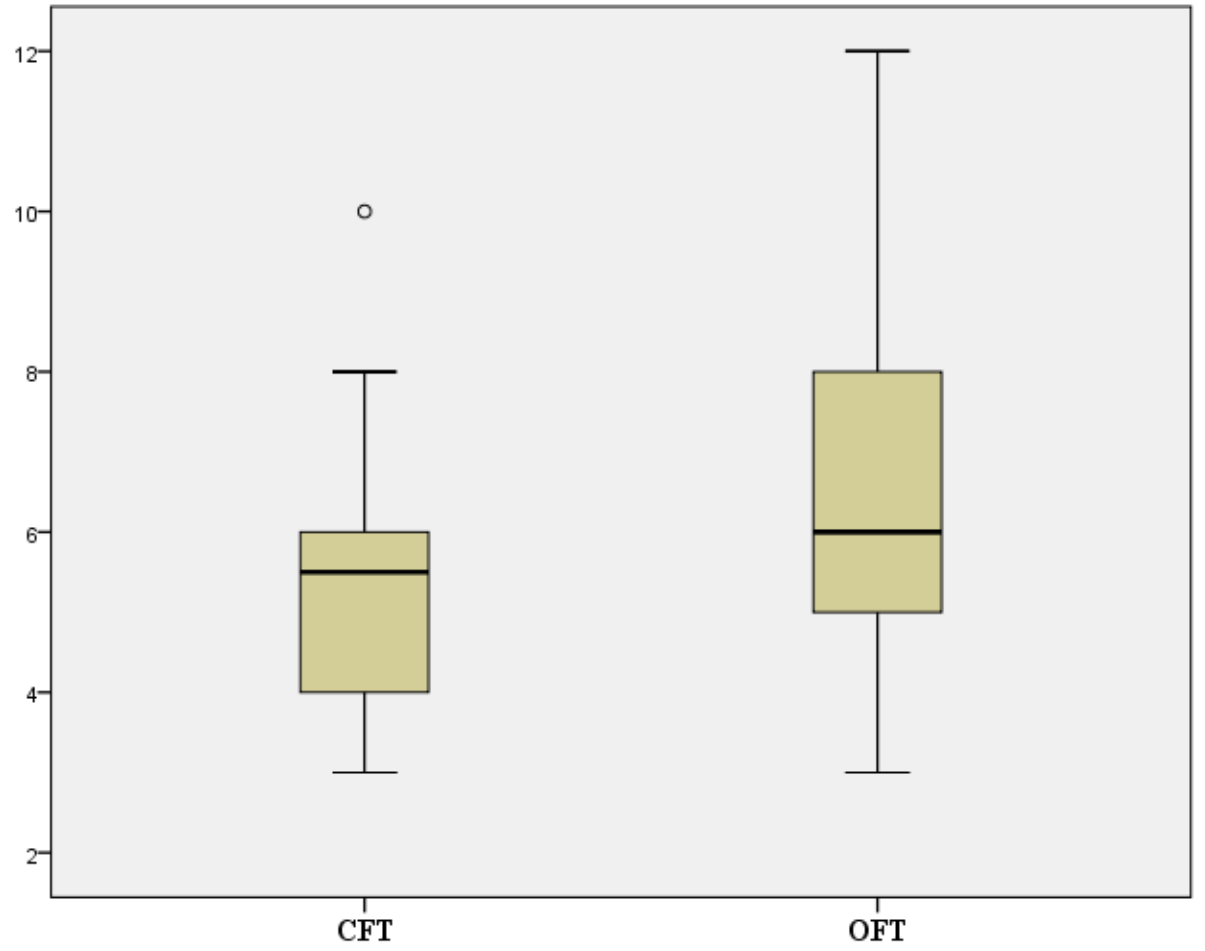


Figure 14: Side-by-side boxplots for both groups showing the difference in millimeters from baseline to 6 months follow up at CH location.

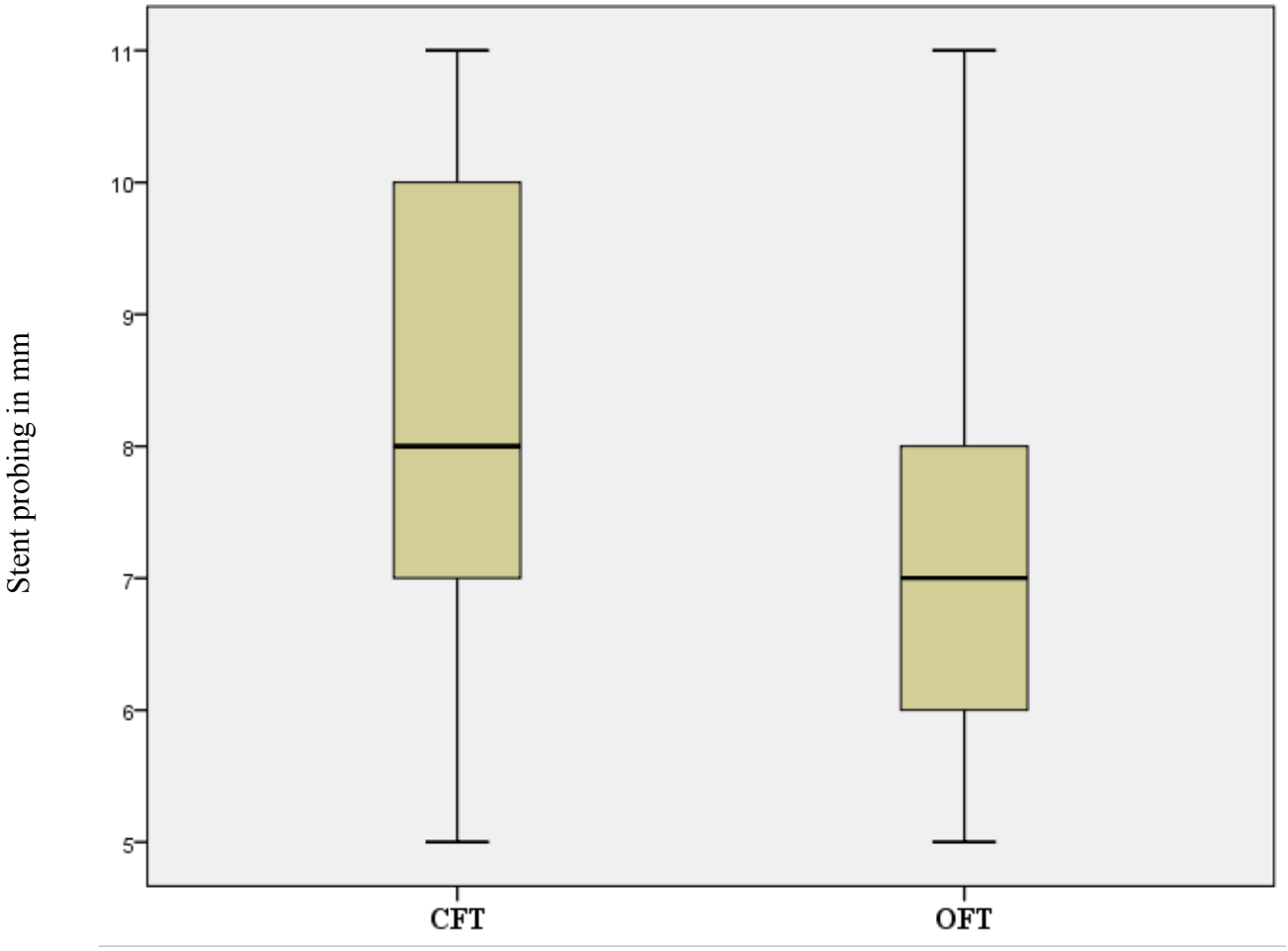


Figure 15: Side-by-side boxplots for both groups showing the baseline measurements done on BH position

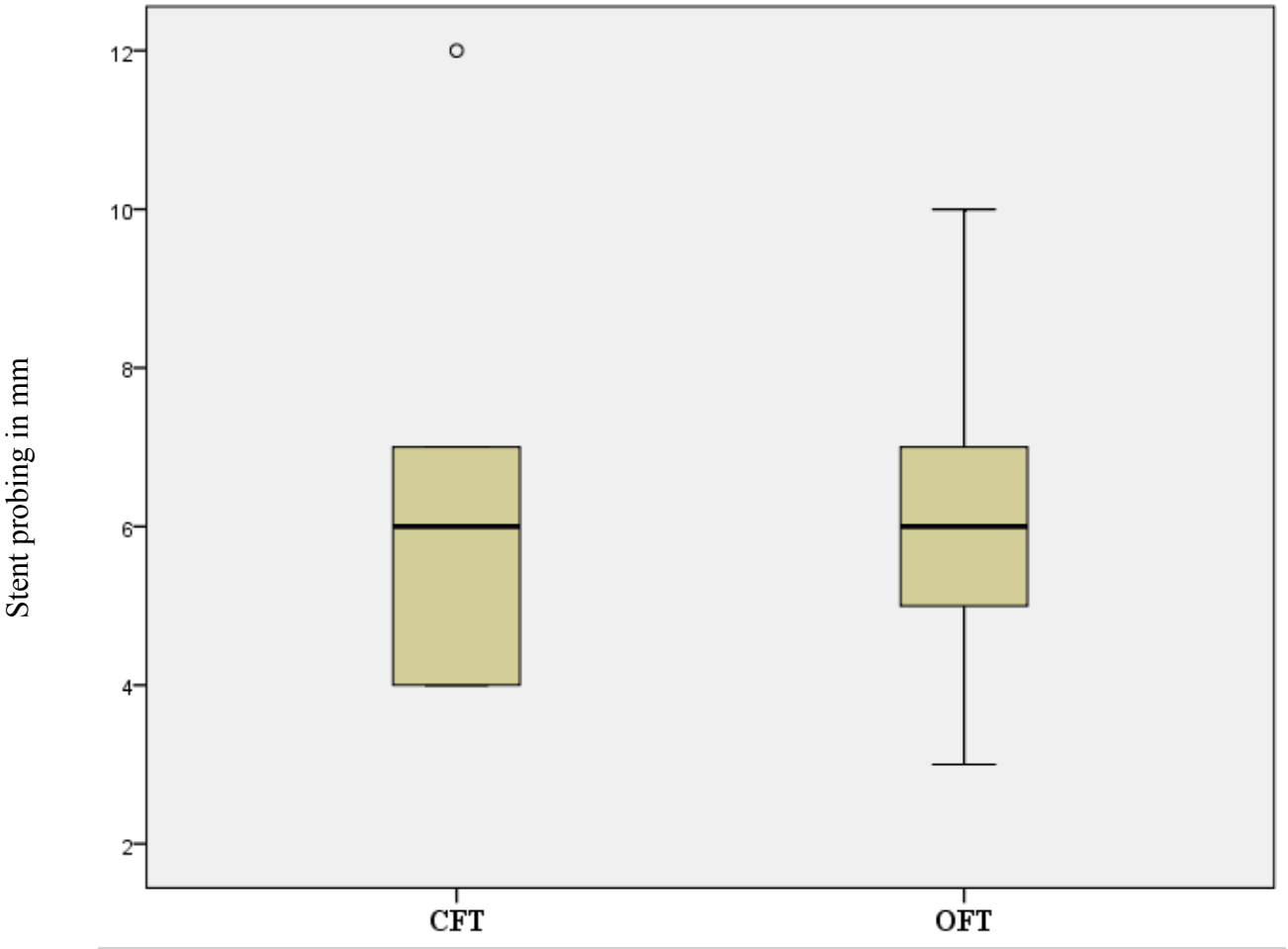


Figure 16: Side-by-side boxplots showing the 6 months follow up measurements done on BH position.

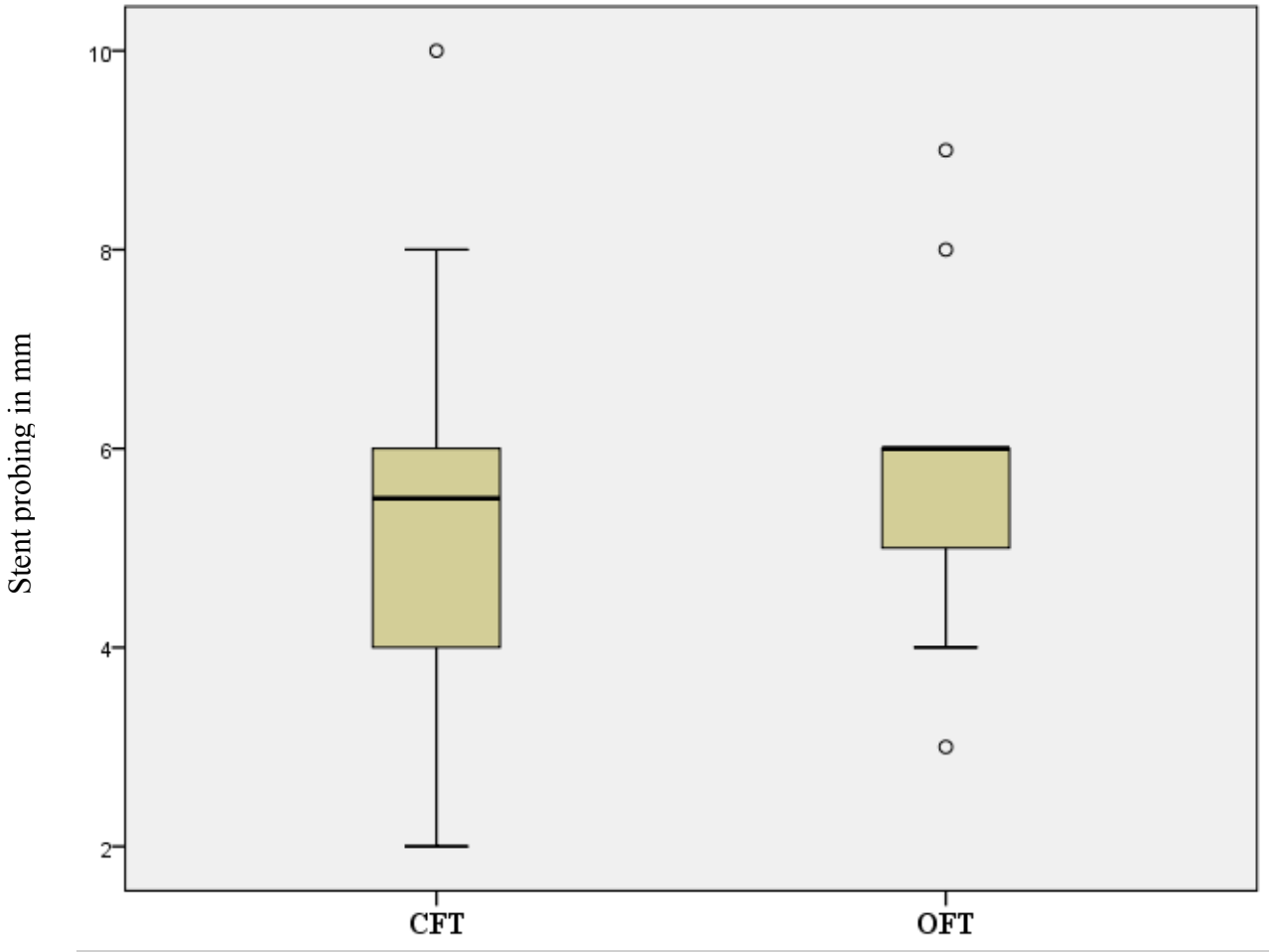


Figure 17: Side-by-side boxplots for both groups showing the difference in millimeters from baseline to 6 months follow up at BH location.

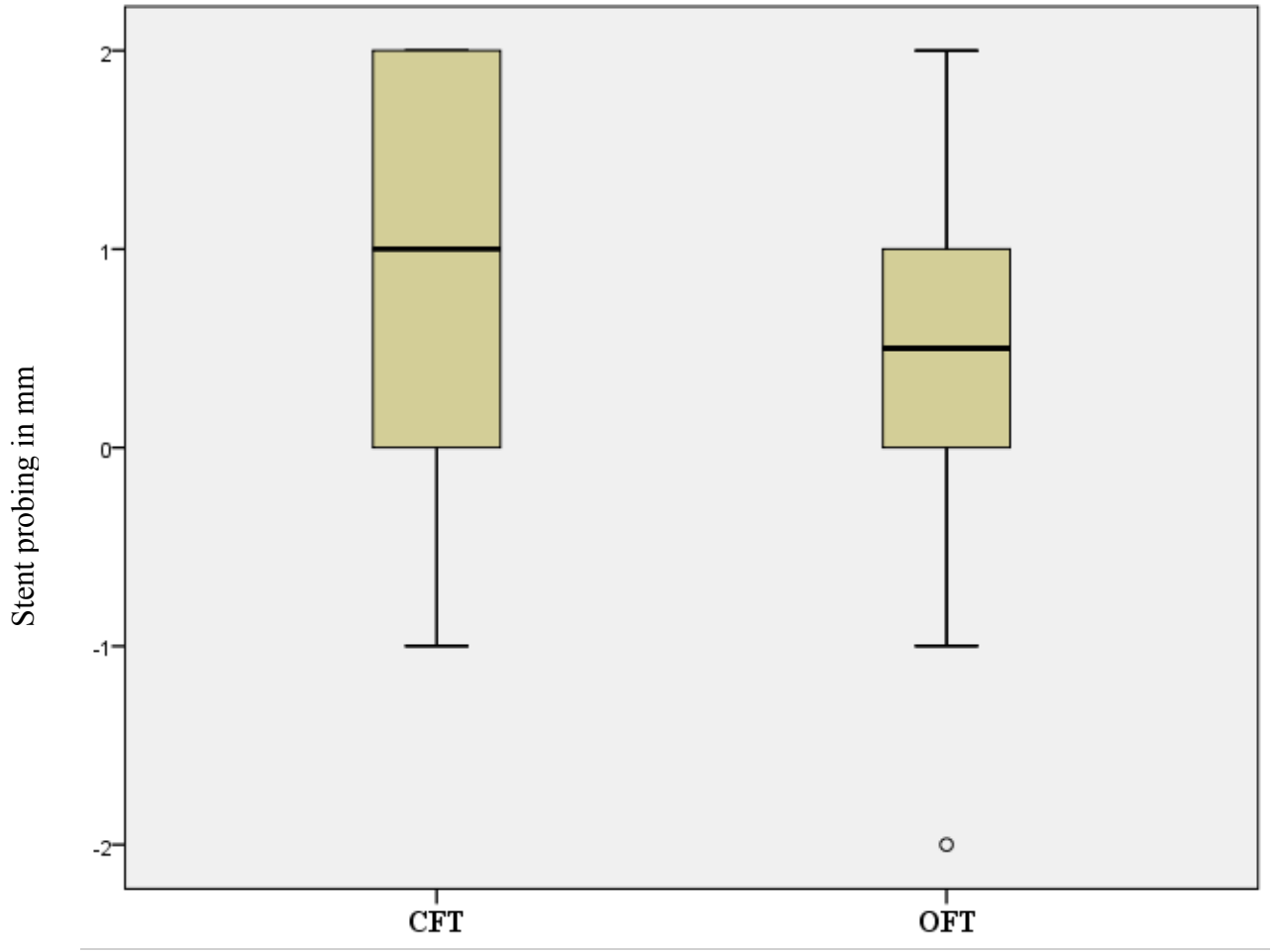


Figure 18: Side-by-side boxplots for both groups showing the baseline measurements done on CW position

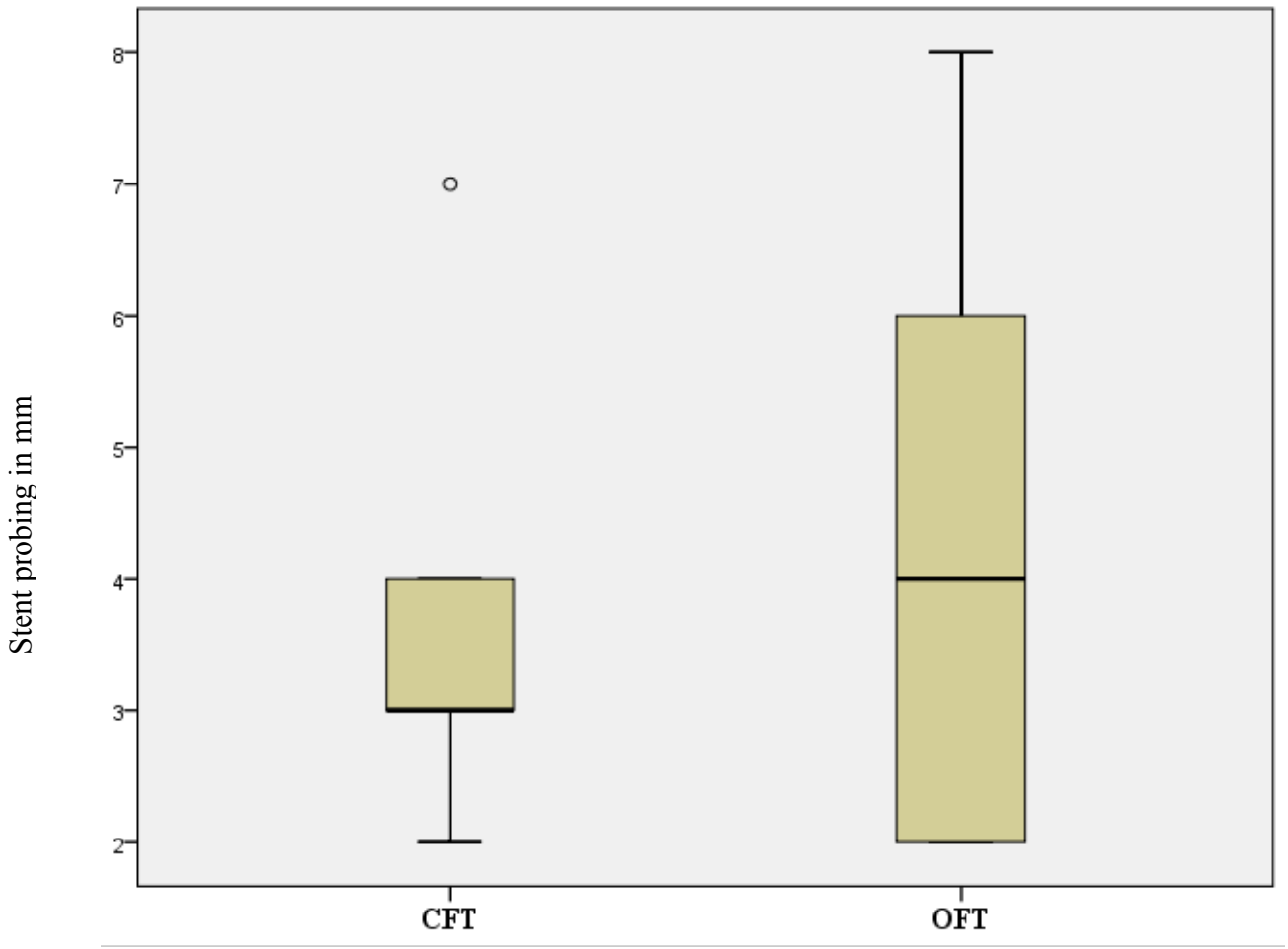


Figure 19: Side-by-side boxplots showing the 6 months follow up measurements done on CW position.

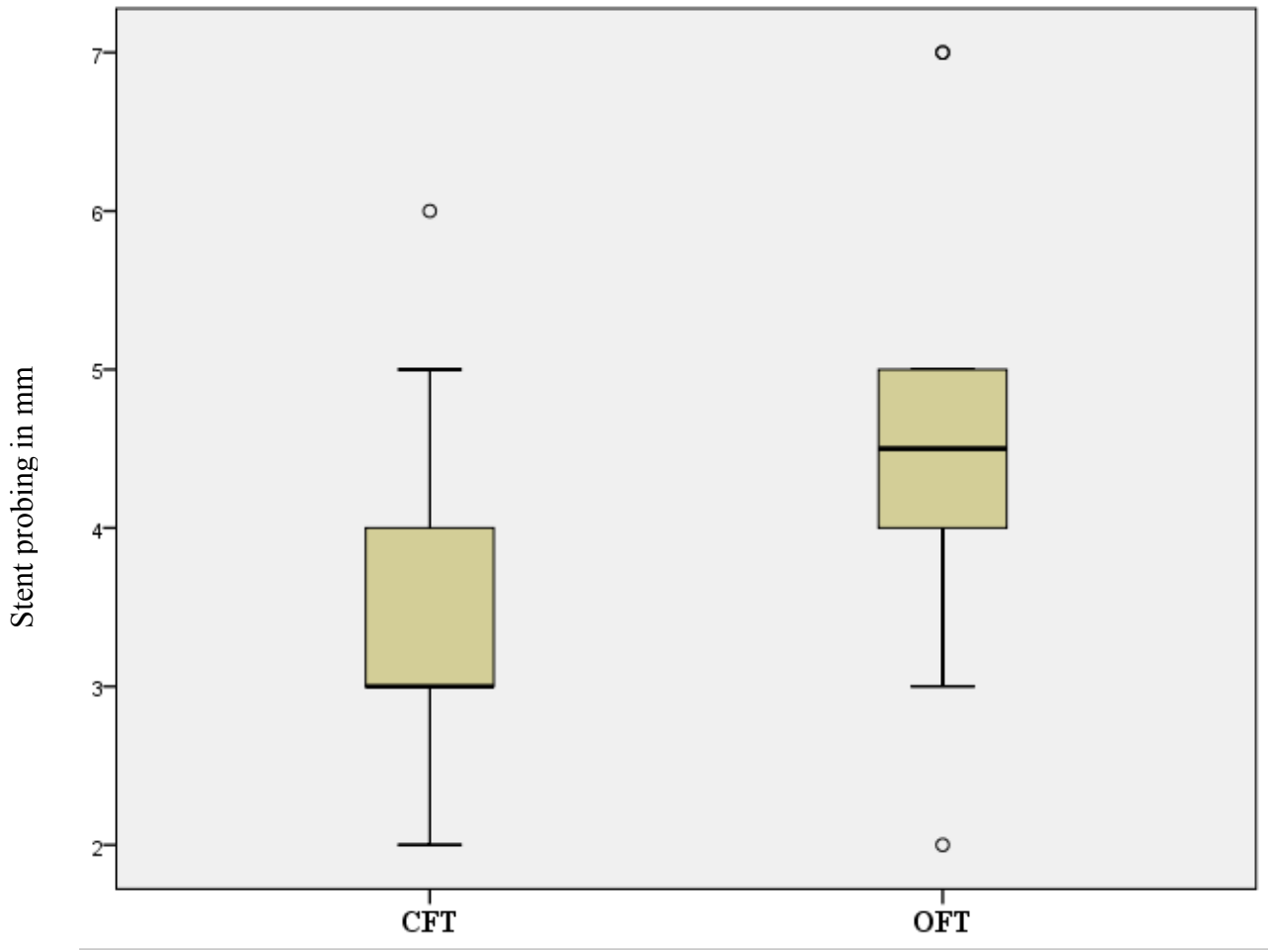


Figure 20: Side-by-side boxplots for both groups showing the difference in millimeters from baseline to 6 months follow up at CW location.

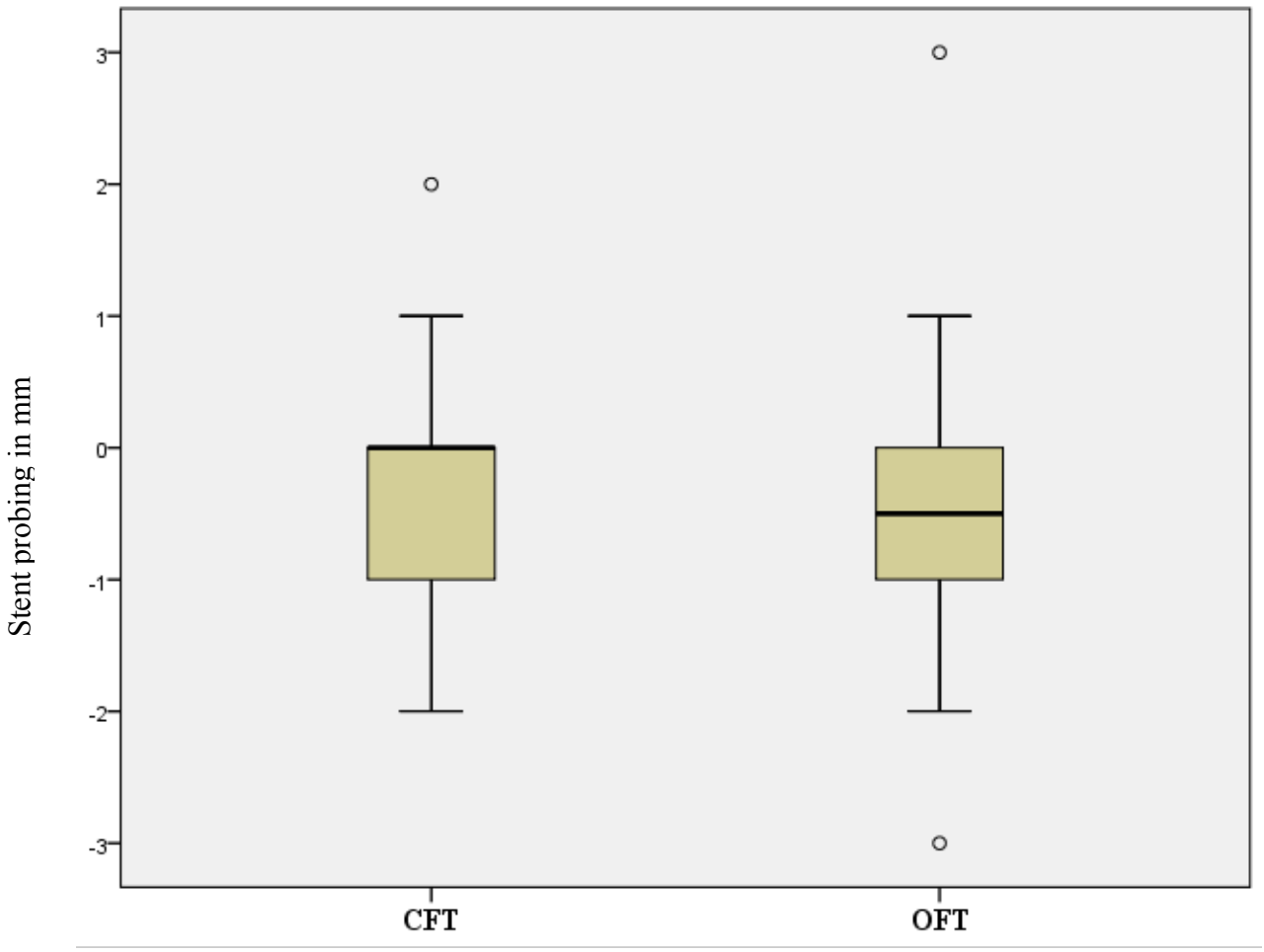


Figure 21: Side-by-side boxplots for both groups showing the baseline measurements done on AW position.

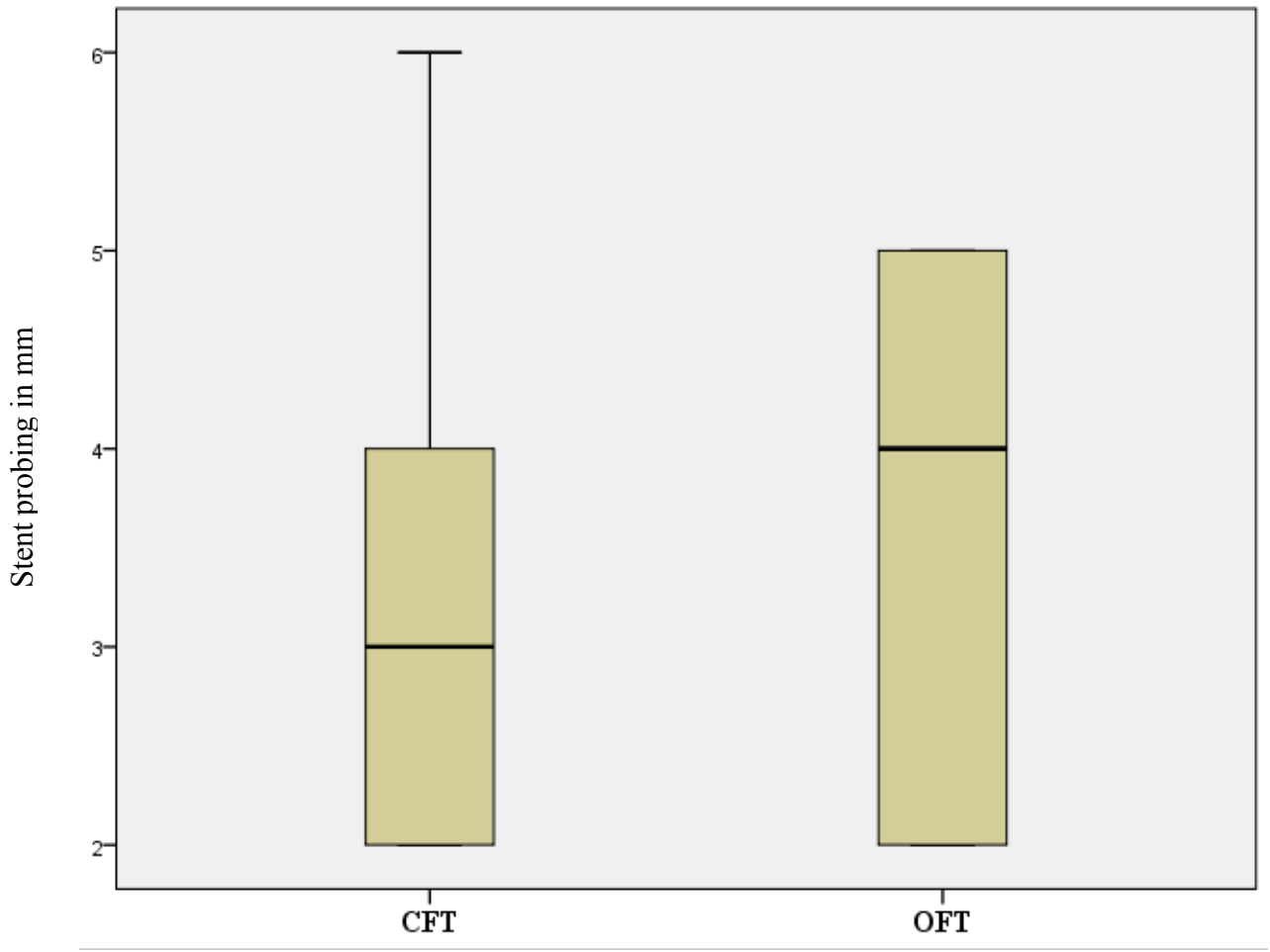


Figure 22: Side-by-side boxplots showing the 6 months follow up measurements done on AW position.

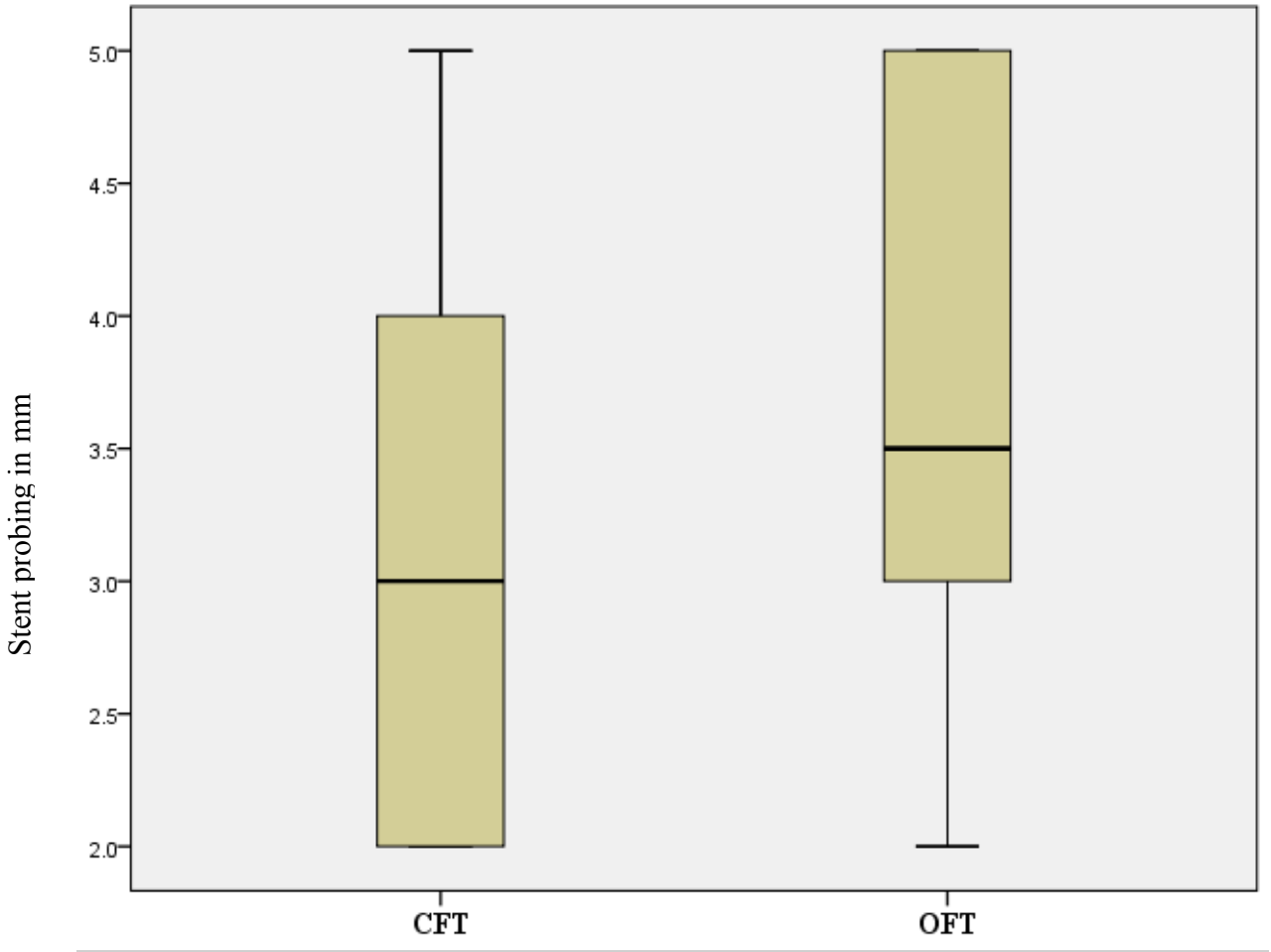


Figure 23: Side-by-side boxplots for both groups showing the difference in millimeters from baseline to 6 months follow up at AW location.

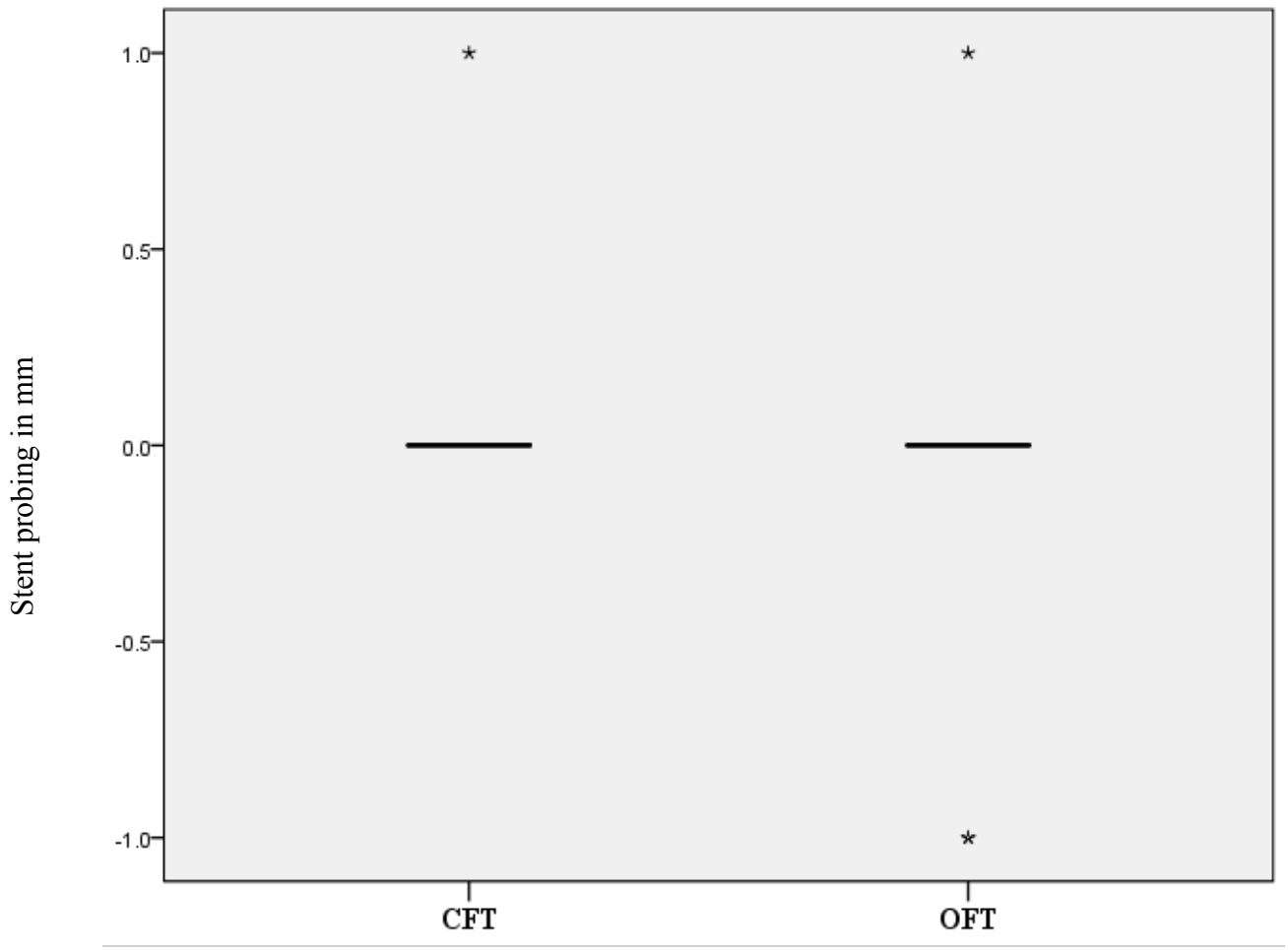


Figure 24: Side-by-side boxplots for both groups showing the difference in millimeters from baseline to 6 months follow up for KTW measurements.

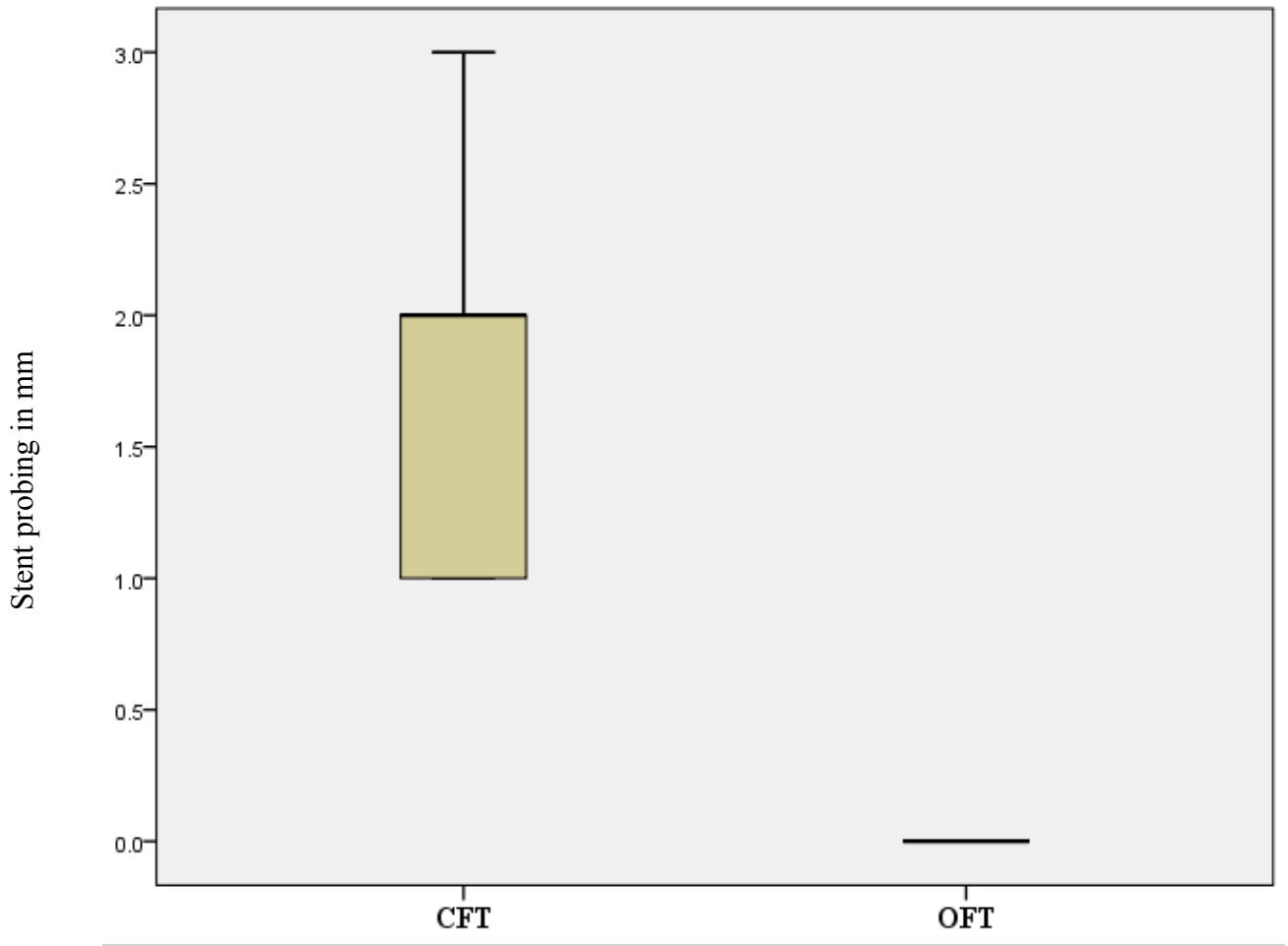


Figure 25: Side-by-side boxplots for both groups showing the post-operative pain at 24 hours following surgery using the VAS scale (0-10).