VOLUMETRIC AND LINEAR ANALYSIS OF SOFT TISSUE CHANGES AFTER TOOTH EXTRACTION AND SOCKET GRAFTING

Brenda Lizzet Lopez

A thesis submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Science in the Department of Periodontology, School of Dentistry

Chapel Hill
2018

Approved by:

Thiago Morelli

John Moriarty

Ryan Cook

ABSTRACT

Brenda Lizzet Lopez: Volumetric and Linear Analysis of Soft Tissue Changes After Tooth Extraction and Socket Grafting
(Under the direction of Thiago Morelli, John Moriarty & Ryan Cook)

Introduction: The success and survival of dental implants are dependent on proper three-dimensional positioning in the bone, the anatomical shape of the prosthetic restoration[1], the quantity and quality of the soft tissue,[2] and the presence of a balanced occlusion.[3] Adequate preservation of the alveolar bone dimension is of great importance to adequately place dental implants. Various methods have been utilized with the aim of preserving the alveolar ridge and soft tissue contours post tooth extraction due to the importance that it has on prosthetic and esthetic outcomes when replacing missing teeth. **Purpose:** To evaluate the linear and volumetric changes in soft tissue following site preservation/socket grafting with a xenograft bone mineral that was covered with either a collagen sponge or a 3D-collagen matrix at the 1 month, 3 month and 6-month post extraction time points. **Methods*:*** This clinical trial included twenty-four subjects who required tooth extraction, site preservation and implant placement. All patients received extraction and grafting with xenograft + 10% collagen (Geistlich Bio-Oss Collagen®) and were randomly assigned to a test or control group for closure of the extraction site. The control group received socket closure with a collagen dressing/sponge/plug (HeliPlug®) and test group with a 3D-collagen matrix (Geistlich Mucograft® Seal). Linear and volumetric soft tissue analysis were performed using Standard Tessellation Language (STL) files, obtained with an

intra-oral scanner and were analyzed via a non-contact reverse engineering system to compare the facial linear and volumetric soft tissue changes between the control and test group.

Results: The linear measurement analysis revealed less linear soft tissue loss with the collagen matrix. The difference between groups was not statistically significant. The volumetric analysis demonstrated a longitudinal decreased loss of soft tissue volume when a 3-D collagen matrix was used compared to a collagen sponge from month 1 to month 6. The longitudinal difference in volume was statistically significant between the two groups. **Conclusion:** This human investigation provides early evidence of the volumetric soft tissue changes after tooth extraction and socket grafting. The linear soft tissue analysis at the 1, 3 and 6-month time points did not show a statistical difference between the use of a collagen sponge and a 3-D collagen matrix. The results from the volumetric analysis demonstrated a reduced volume loss when a 3-D collagen matrix was used compared to a collagen dressing. The data provides early evidence in regards to decreased amount of volume loss using a 3-D collagen matrix. This finding may positively benefit clinicians when managing soft tissue contours around implants in the esthetic zone.

ACKNOWLEDGEMENTS

I would like to sincerely thank and acknowledge my mentor, Dr. Thiago Morelli for his wisdom, expertise, words of guidance, encouragement, and patience throughout the completion of my research project. I greatly appreciate your kindness and support during the entire process. Thank you to my mentor Dr. John Moriarty, for checking on every step of my project as it developed. Thank you for teaching me what I know as a clinician as this allowed me to use my skills during this clinical research project. Thank you to my mentor Dr. Ryan Cook for supporting me throughout this project. I am also thankful to the team from the UNC School of Dentistry Go Health Clinic. Thank you for your support and collaboration, this would not have been possible without you. A special thanks to my late mentor, Dr. Ricardo Teles, for being there as a professor and friend, your words of encouragement and wisdom will always remain with me. Thank you to my fellow co-residents, I am very fortunate for your friendship. Last but not least, thank you to the most important person in my life, my mother. Thank you for your unconditional love and support, you are my greatest motivation.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BMP	Bone morphogenic Protein
β-TCP	βeta-Tricalcium Phosphate
DBBM	Deproteinized Bovine Bone Mineral
DFDBA	Demineralized Freeze-Dried Bone Allograft
d-PTFE	High Density Polytetrafluoroethylene
e-PTFE	Expanded-Polytetrafluoroethylene
FDBA	Freeze-Dried Bone Allograft
FGG	Free Gingival Graft
GBR	Guided Bone Regeneration
GTR	Guided Tissue Regeneration
HA	Hydroxyapatite
PTFE	Polytetrafluoroethylene
SSS	Socket Seal Surgery
STL	Standard Tessellation Language

LIST OF SYMBOLS

©	Copyright Symbol
®	Registered Trademark
™	Trademark Symbol

A REVIEW OF THE LITERATURE

Alveolar Ridge Remodeling

The anatomical and physiological changes that occur after tooth extraction have been largely studied in the past.[4] It has been determined that bundle bone is the first to be absorbed after the loss of a tooth [5,6,7] compared to alveolar bone, which is slowly absorbed throughout life.[8,9] The remodeling of the alveolar process after extraction of a tooth results in height and width changes, which alter the orientation of the ridge towards the palatal/lingual position in relation to the original tooth position.[4]

A dog model evaluated the alveolar bone changes that occur after tooth extraction as a result of remodeling.[10] Histological analysis showed that at one week, bundle bone was present on all the walls of the extractions site. Bundle bone was the only component of the crestal region of the sites and formed the majority of the buccal plate. By week four, the bundle bone was completely absorbed from the crestal portion of the walls in the extraction site. By eight weeks, the height of the buccal wall was positioned about 2 mm apical to the lingual wall. This study also revealed that resorption after extraction occurs in two phases. In phase one, the bundle bone was resorbed and woven bone was formed. This results in a greater change in morphology of the buccal wall. In phase two, the resorption occurred from the outer surfaces of the walls of the extraction site.[10]

The bone contour and linear soft tissue changes after tooth extraction were clinically and radiographically studied by Schropp. The changes in soft tissue were analyzed using study casts

fabricated with irreversible hydrocolloid at baseline and at 12 monthsThe results showed a average width at baseline of 12.0 mm. The ridge width decreased by approximately 50%, average of 5.9 mm, 12-months post extraction. The majority of the loss in height occurred during the first 3 months post extraction.[11]

Major changes in alveolar ridge dimensions occur after tooth extraction without site preservation.[10,11,12] The remodeling process is also highly dependent on the buccal plate thickness. Particularly in the anterior maxilla, it has been reported that the buccal plate thickness in >70% of the anterior teeth is ≤1mm in thickness.[13,14] Site preservation is of great benefit for patients as it facilitates the placement of implants in the proper three-dimensional position by preserving the bone and tissue contours which yield positive functional and esthetic outcomes. A systematic review evaluating the efficacy of site preservation when compared to the lack site preservation reported that grafting at the time of extraction resulted in less bone contraction with a mean of 1.5 mm in height and 1.8 mm in width. The review did not specify any grafting material to be superior from another.[12]

History of Ridge Preservation

Various methods have been used in the attempts to reduce change in alveolar ridge dimension after tooth extraction. In the 1950s and 1960s, the clinical crowns of teeth with a poor periodontal prognosis were modified and retained with the purpose of maintaining the alveolar ridge to support full dentures.[15,16] Subsequently, Osburn proposed a technique that involved amputation of the clinical crown and retention of the tooth root to preserve the bone around teeth for the support of full dentures.[17] Implants are currently one of the most well established and accepted methods for tooth replacement. A critical necessity in allowing implant placement is the morphology of the alveolar ridge in the edentulus site. Various bone grafting and synthetic

materials have been used to preserve the alveolar ridge. Particularly, the preservation of the anterior ridge has led to the use of various materials aiming to increase the success rate of implant placement by maintenance of the alveolar ridge and soft tissue contours.

Bone Grafting Materials

Hydroxyapatite crystals (HA) were placed in the extraction site as a method to preserve the alveolar ridge. This method proved effective in preserving the alveolar ridge in areas where prosthetic reconstructions were needed without the placement of implants.[18] The drawback with HA is the lack of resorption or replacement and thus not indicated when future implant placement is needed due to the lack of bone turn over. On the other hand, grafting materials such as xenografts, allografts or autografts possess osteogenic, osteoinductive and/or osteoconductive properties and promote bone formation or serve as scaffolds for bone formation.[19] Bone grafts used for site preservation are classified based on the source of origin. Autografts are obtained from the same individual and possess osteogenic, osteoconductive and some have osteoinductive properties.[19] Despite these qualities, it is not the preferred bone graft as it increases patient morbidity because it requires harvesting from an intra or extra-oral site.[20]

Allografts are bone grafts that are transferred from one subject to another genetically dissimilar subject of the same species.[19] The primary advantage of using an allograft is its unlimited availability and does not require a harvesting site. Allografts include demineralized freeze dried bone (DFDBA) or mineralized freeze-dried bone allografts (FDBA). Some DFDBA bone grafts have reported to have osteoinductive properties because they may possess bone morphogenic proteins (BMPs) expression.[21]

Xenografts are bone grafts obtained from species different from the recipient. Deproteinized bovine bone mineral (DBBM) commonly known as Bio-oss (Geistlich Pharma) is

the most used xenograft. They differ from allografts in that xenograft is osteoconductive and serves as a scaffold for the subjects own cells to laydown bone and lack osteoinductive properties.[19] The Bio-oss grafting material is also available as the Bio-oss Collagen.® The material is mixture of 90% cancellous bovine bone granules and 10% porcine collagen. The composition of the Bio-Oss Collagen® allows for it to be in a solid block form. The solid form permits easier handling during surgical procedures and shaping of the material into the morphology of the defect.[22,23] Xenografts have the advantage of slow resorption which aids in space maintenance while allowing new bone formation. [24,25] The low sintering process creates porosities within the bone particles which enable bone growth from the host cells. The ability for space maintenance and bone in-growth make xenografts most appropriate for site preservation compared to HA which lacks resorption and does not aid bone formation from native bone cells.[26]

Alloplasts are synthetic materials that are used for the purpose of site preservation. Several forms of synthetic materials including hydroxyapatite,[27] β-tricalcium phosphate (β-TCP),[27] calcium phosphate[28] and bioactive glass polymers[29] are commonly used as bone grafting materials for socket preservation.[30] The benefit of using alloplastic materials during site preservation is to preserve the alveolar ridge for non-implant supported prosthetics.[31] However, the lack of resorption and turnover such as with HA does not make it the material of choice when preparing implant placement.[27] Avila-Ortiz conducted a systematic review and meta-analysis to compare the effects of ridge preservation using xenografts, allografts and alloplasts. The results showed that xenografts and allografts, in conjunction with a barrier membrane, have a greater beneficial effect in bone height on the mid-buccal compared to alloplast materials.[32] Thus, the

use of xenografts and allografts for socket preservation are more beneficial for the conservation of the alveolar ridge when future implant placement is desired.

Soft Tissue Grafting

The placement of an autogenous gingival graft at the time of tooth extraction and site preservation to maintain the tissue contours was introduced by Landsberg and Bichacho.[33] The aim of this approach was to preserve ridge dimensions for a better esthetic outcome after implant and restoration placement. The "Socket Seal Surgery" (SSS) consisted of socket preservation using a bone graft and covering of the extraction site with a free gingival graft.[33] Additionally, a combination of an autogenous free-gingival and sub-epithelial connective tissue graft to preserve the soft tissue volume and esthetics during implant placement have also been described.[34,35] Yoshino et al. conducted a randomized clinical trial to compare immediate implant placement and provisionalization with and without connective tissue graft. The results showed the same implant success for both groups and highly favorable facial gingival levels in sites that received tissue grafting. These results indicate that esthetic outcomes can be enhanced with the use of soft tissue grafting at implant sites.[36] Other reports[37] in the literature indicate that sites that receive soft tissue grafting demonstrate more favorable tissue thickness and esthetics compared to sites that do not receive any form of tissue grafting. However, the major disadvantage to soft tissue grafts is the need for a second surgical site and co-morbidity to the patient.

Barrier Membranes

The use of barrier membranes for space maintenance and tissue/bone regeneration have been studied. Initial attempts to compartmentalize tissues for the attempt of bone regeneration can be traced to 1957 when Hurley and colleagues used cellulose acetate filters for guided bone

regeneration (GBR) in experimental spinal fusion. This work served as a foundation for the current GBR techniques used in implant dentistry.[38] Most recent, the development of resorbable and non-resorbable barrier membranes have been employed for the preservation of the alveolar bone dimensions at the time of tooth extraction.[39]

Scantlebury described five desired membrane characteristics that yield the best treatment outcomes. These qualities include biocompatibility, space-making, cell-occlusiveness, tissue integration, clinical manageability and tissue regeneration.[40] With this in mind, there are two types of commonly used membranes; resorbable and non-resorbable membranes. The use of non-resorbable barrier membranes during socket preservation have optimized the amount of ridge preservation compared to the conventional method that consisted of no barrier.[41] Additionally, both types possess advantageous and disadvantageous qualities in their clinical use. Non-resorbable, rigid and high density membranes, include polytetrafluoroethylene (PTFE) membranes and titanium mesh membranes.[42] PTFE membranes differ in their structure as expanded-PTFE (e-PTFE) or high density-PTFE (d-PTFE) membranes. These membranes require the fixation with titanium pins and offer considerable space maintenance and clot stabilization over extraction sites that consequently receive implant placement.[39] The outcomes of ridge preservation using e-PTFE barrier membrane may show adequate ridge preservation for future implant placement.[41]

Titanium mesh membranes possess the advantage of space compartmentalization and adequate stability, particularly when attempting vertical bone augmentation.[42] Jovanic and Nevis, introduced the titanium-reinforced membrane (Cytoplast®), consisting of PTFE with titanium integration, and reported superior outcomes compared to PTFE membranes alone as the membrane provides greater support, better adaptation and less collapse due to the titanium

support.[43] The major disadvantages of non-resorbable membranes are the risk for membrane exposure and infection during the course of healing as well as the need of a second surgery for membrane removal.[44] These disadvantages generated development of bioresorbable materials which may be derived from natural collagen polymers or synthetic materials.[39]

Disadvantages to resorbable membranes are the degree of unpredictable resorption which could affect the quantity of ridge preservation in addition to difficulty with clinical manipulation, and shortcomings with the ability to contain large particles.[39,45] Advantages of GBR using resorbable membranes at time of extraction include decrease in the loss of the alveolar bone dimensions, decreased risk of membrane exposure, decreased risk for infection and the lack for the need of a second surgical procedure.[46] In a systematic review by Jensen et al., it was found that the mean gain in ridge width for sites augmented with non-resorbable membrane was 2.9 mm. Sites augmented with resorbable membranes had a mean width gain of 4.2 mm and a lower complication rate.[41] Jung and colleagues evaluated the long-term survival of implants placed in sites that had previously been treated with GBR using DBBM with a resorbable membrane vs non-resorbable membrane (e-PTFE). The survival rates for the non-resorbable membrane group and resorbable membrane group were 92.6% and 91.9%, respectively, with no statistical significance. Thus, successful GBR yields high implant survival rates irrespective of membrane type.[47] The positive outcomes achieved in ridge width and lower complication rates with the use of bioresorbable materials has led to major preference for resorbable membranes in clinical application when performing GBR, GTR and socket preservation over non-resorbable membranes.[39]

Collagen Sponges

Collagen sponges/plugs are adjuncts in site preservation. They are used to cover the

extraction site after bone grafting. The sponges are composed of bovine deep flexor (achilles) tendon and recommended as wound dressing for clot stabilization.[48] The estimated resorption time is 10-14 days.[48] The principle of collagen plugs for site closure consists of atraumatic extraction, placement of a bone graft in the extraction site and closure of the socket with a collagen plug.[49] The use of the collagen plug is to seal the site and prevent loss of the bone grafting material. In addition, it aids clot formation and platelet aggregation.[49]A widely used method to preserve the hard and soft tissue dimensions at the time of extraction is the Bio-Col socket preservation technique. The technique consists of the addition of anorganic bovine bone mineral in the socket that is then covered by a collagen sponge. The Bio-Col technique also proposes the use of a barrier membrane, when desired, to prevent epithelial cell migration.[50] The major advantage of using an absorbable collagen sponge for site preservation compared to a membrane is the reduced cost to the practitioner and the patient.

A comparable technique was introduced by Wang, the "Allograft-Plug/Allo-Plug" technique, consisting of the use of an allograft bone mineral for site preservation. The purpose was to eliminate unintegrated bone grafting particles that occurred when using xenograft bone grafting in the "Bio-Col" technique. The "Allo-Plug" technique uses an allograft bone mineral and a collagen plug to seal the site. The authors found an average of 68.5% bone formation and 4.8% residual grafting material with the use of this technique.[51] A similar technique proposed by Gupta et al., uses a xenograft bone grafting material during site preservation, followed by the placement of a collagen plug and a resorbable membrane for site closure.[52] Kotsakis et al. evaluated the efficacy in preservation of the ridge dimension with the use of a collagen plug. They found a reduction in loss of dimension of approximately 12%.[49] This is comparable to other studies in which a xenograft and a collagen plug demonstrated a width resorption of 14.26%.[53]

Mucograft® Seal

The Geistlich Mucograft® Seal provides an alternative to soft tissue harvesting, collagen plug and barrier membranes for the purpose of socket preservation.[54] The Mucograft® Seal is a three-dimensional matrix bilayer of type I and type III collagen that provides adequate clot stabilization. The porous layer allows for rapid infiltration by the hosts mesenchymal cells and the material provides attachment to the host tissues and blocks cell migration.[55] The membrane is specifically designed for socket preservation. Clinically significant augmentation in keratinized tissue, texture and color blending have been obtained with the use of the Mucograft® in the treatment of keratinized tissue augmentation around teeth and implants.[54,56]

The Geistlich Mucograft® Seal can be used over bone graft material during socket preservation in preparation for future implant placement.[47] A study conducted by Jung et al. compared the use of Geistlich Mucograft® Seal with Bio-Oss® Collagen to other socket preservation methods; 1. Bio-Oss® Collagen along with FGG, 2. BioOss® Collagen with Mucograft® Seal, 3. β-tricalcium-phosphate-particles with polylactid coating (β-TCP), and 4. Spontaneous healing (control). The results indicated that the use of Bio-Oss® Collagen with either Geistlich Mucograft® Seal or a FGG, yielded less vertical and horizontal alveolar ridge alterations compared to the control group 6 months after extraction.[47]

Conclusion

Various clinical approaches and materials have been developed to minimize loss of alveolar ridge dimensions and soft tissue loss subsequently of tooth extraction. New materials and innovative treatment approaches have emerged due to the unavoidable loss of hard and soft tissue that occurs as part of the natural remodeling process after tooth extraction. A greater

emphasis on the importance of the preservation of the ridge and soft tissue contours has also been influenced by the increase in implant placement as a method for tooth replacement. Further research regarding current materials for soft tissue management is needed to gain a better understanding of the advantages of implementing new materials into clinical practice. The aim of this project is to expand the current available information on soft tissue changes after tooth extraction and socket preservation comparing a 3-D collagen matrix and a collagen sponge.

REFERENCES

1. Lima de Andrade C, Carvalho M, Del Bel Cury A, Sotto-Maior B. Biomechanical Effect of Prosthetic Connection and Implant Body Shape in Low-Quality Bone of Maxillary Posterior Single Implant-Supported Restorations. Int J Oral Maxillofac Implants 2016;31(4).

2. Barbisan A, Dias CS, Bavia PF, Sapata VM, César-Neto JB, Silva CO. Soft Tissues Changes After Immediate and Delayed Single Implant Placement in Esthetic Area: A Systematic Review. J Oral Implantol. 2015;41(5).

3. Sheridan RA, Decker AM, Plonka AB, Wang HL. The Role of Occlusion in Implant Therapy: A Comprehensive Updated Review. Vol. 25, Implant Dentistry. 2016. p. 829–38.

4. Pietrokovski J, Massler M. Alveolar ridge resorption following tooth extraction. J Prosthet Dent. 1967;17(1):21–7.

5. Boyne PJ. Osseous repair of the postextraction alveolus in man. Oral Surgery, Oral Med Oral Pathol. 1966;21(6):805–13.

6. Hsieh YD, Devlin H, Roberts C. Early alveolar ridge osteogenesis following tooth extraction in the rat. Arch Oral Biol. 1994;39(5):425–8.

7. Devlin H, Sloan P. Early bone healing events in the human extraction socket. Int J Oral Maxillofac Surg. 2002;31(6):641–5.

8. Carlsson GE, Bergman B, Hedegård B. Changes in contour of the maxillary alveolar process under immediate dentures a longitudinal clinical and x-ray cephalo-metric study covering 5 years. Acta Odontol Scand. 1967;25(1):45–75.

9. Ashman A. Postextraction ridge preservation using a synthetic alloplast. Implant Dent [Internet]. 2000;9(2):168–76. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11307396

10. Araújo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. J Clin Periodontol. 2005;32(2):212–8.

11. Schropp L, Wenzel A. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12-month prospective study. J Prosthet Dent [Internet]. 2004;91(1):92. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022391303007455

12. Vignoletti F, Matesanz P, Rodrigo D, Figuero E, Martin C, Sanz M. Surgical protocols for ridge preservation after tooth extraction. A systematic review. Clin Oral Implants Res. 2012;23(SUPPL. 5):22–38.

13. Huynh-Ba G, Pjetursson BE, Sanz M, Cecchinato D, Ferrus J, Lindhe J, 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(1):37–42.

14. Januário AL, Duarte WR, Barriviera M, Mesti JC, Araújo MG, Lindhe J. Dimension of the facial bone wall in the anterior maxilla: A cone-beam computed tomography study. Clin Oral Implants Res. 2011;22(10):1168–71.

15. Miller P. Complete dentures supported by natural teeth. Tex Dent J. 1965 Sep;83:4–8.

16. Morrow RM, Dc U, Powell JM, Jameson WS. of a Simplified. :414–24.

17. Osburn RC. Preservation of the alveolar ridge: a simplified technique for retaining teeth beneath removable appliances. J Indiana State Dent Assoc. 53(1):8–11.

18. Nemcovsky CE, Serfaty V. Alveolar ridge preservation following extraction of maxillary anterior teeth. Report on 23 consecutive cases. J Periodontol [Internet]. 1996;67(4):390–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8708965

19. Shahgoli S, Levine MH. Introduction and overview of bone grafting. N Y State Dent J [Internet]. 2011;77(2):30–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21678868

20. Rose L. Periodontics: medicine, surgery, and implants. St. Louis, Miss: Elsevier Mosby; 2004.

21. Brand RA. Marshall R. Urist, 1914–2001. Clin Orthop Relat Res [Internet]. 2009;467(12):3049–50. Available from: http://link.springer.com/10.1007/s11999-009-1067-4

22. Trevisiol L, Nocini PF, Albanese M, Sbarbati A, D'Agostino A. Grafting of large mandibular advancement with a collagen-coated bovine bone (bio-oss collagen) in orthognathic surgery. J Craniofac Surg. 2012;23(5):1343–8.

23. Rohner D, Hallermariam S HB. Le Fort I osteotomies using Bio-Oss Collagen to promote bony union: aprospective clinical split -mouth study. Int J Oral Maxillofac Surg. 2013;42:585–92.

24. Araújo MG, Liljenberg B, Lindhe J. Dynamics of Bio-Oss®Collagen incorporation in fresh extraction wounds: An experimental study in the dog. Clin Oral Implants Res. 2010;21(1):55–64.

25. Artzi Z, Tal H, Dayan D. Porous Bovine Bone Mineral in Healing of Human Extraction Sockets. Part 1: Histomorphometric Evaluations at 9 Months. J Periodontol [Internet]. 2000;71(6):1015–23. Available from: http://www.joponline.org/doi/10.1902/jop.2000.71.6.1015

26. Draenert M, Draenert A, Draenert K. Osseointegration of hydroxyapatite and remodeling-resorption of tricalciumphosphate ceramics. Microsc Res Tech. 2013;76(4):370–80.

27. Mayer Y, Zigdon-Giladi H, Machtei EE. Ridge Preservation Using Composite Alloplastic Materials: A Randomized Control Clinical and Histological Study in Humans. Clin Implant Dent Relat Res. 2016;18(6):1163–70.

28. Mendoza-Azpur G, Olaechea A, Pinazo M, Gomez C, Salinas E, De La Rosa M, et al. Histomorphometric evaluation of ridge preservation with and without connective tissue graft over buccal plate using different types of bone substitute: An animal study. Implant Dent. 2015;24(6):686–92.

29. Ioannou AL, Kotsakis GA, Kumar T, Hinrichs JE, Romanos G. Evaluation of the bone regeneration potential of bioactive glass in implant site development surgeries: a systematic review of the literature. Clin Oral Investig. 2015;19(2):181–91.

30. Froum S, Orlowski W. Ridge preservation utilizing an alloplast prior to implant placement--clinical and histological case reports. Pr Periodontics Aesthet Dent. 2000;12(4):393–402; quiz 404.

31. Quinn JH, Kent JN, Hunter RG, Schaffer CM. Preservation of the alveolar ridge with hydroxylapatite tooth root substitutes. J Am Dent Assoc. 1985;110(2):189–93.

32. Avila-Ortiz G, Elangovan S, Kramer KWO, Blanchette D, Dawson DV. Effect of Alveolar Ridge Preservation after Tooth Extraction. J Dent Res [Internet]. 2014;93(10):950–8. Available from: http://journals.sagepub.com/doi/10.1177/0022034514541127

33. Landsberg CJ, Bichacho N. A modified surgical/prosthetic approach for optimal single implant supported crown. Part I--The socket seal surgery. Pract Periodontics Aesthet Dent [Internet]. 1994 Mar;6(2):11–7; quiz 19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7670061

34. Stimmelmayr M, Allen EP, Reichert TE, Iglhaut G. Use of a combination epithelized-subepithelial connective tissue graft for closure and soft tissue augmentation of an extraction site following ridge preservation or implant placement: description of a technique. Int J Periodontics Restorative Dent. 2010;30(4):375–81.

35. Thalmair T, Hinze M, Bolz W, Wachtel H. The Healing of Free Gingival Autografts for Socket-seal Surgery: a Case Report. Eur J Esthet Dent [Internet]. 2010;5(4):358–68.

36. Yoshino S, Kan JYK, Rungcharassaeng K, Roe P, Lozada JL. Effects of Connective Tissue Grafting on the Facial Gingival Level Following Single Immediate Implant Placement and Provisionalization in the Esthetic Zone: A 1-Year Randomized Controlled Prospective Study. Int J Oral Maxillofac Implants [Internet]. 2014;29(2):432–40.

37. Ma A, Nhm A, Agt P, Duncan W, Cm F, Esposito M. Interventions for replacing missing teeth : alveolar ridge preservation techniques for dental implant site development (Review). 2015;(5).

38. Fonseca R. Oral and Maxillofacial Surgery. Vol 3. Saunders; 2017.

39. Rakhmatia YD, Ayukawa Y, Furuhashi A, Koyano K. Current barrier membranes: Titanium mesh and other membranes for guided bone regeneration in dental applications. J Prosthodont Res. 2013;57(1):3–14.

40. Scantlebury T V. 1982-1992: A Decade of Technology Development for Guided Tissue Regeneration. J Periodontol [Internet]. 1993;64(11s):1129–37. Available from: http://www.joponline.org/doi/10.1902/jop.1993.64.11s.1129

41. Jensen SS, Terheyden H. Bone augmentation procedures in localized defects in the alveolar ridge: clinical results with different bone grafts and bone-substitute materials. Int J Oral Maxillofac Implants [Internet]. 2009;24 Suppl:218–36. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19885447

42. Rasia dal Polo M, Poli PP, Rancitelli D, Beretta M, Maiorana C. Alveolar ridge reconstruction with titanium meshes: A systematic review of the literature. Med Oral Patol Oral Cir Bucal. 2014;19(6):e639–46.

43. Jovanovic SA, Nevins M. Bone formation utilizing titanium-reinforced barrier membranes. Int J Periodontics Restorative Dent. 1995 Feb;15(1):56–69.

44. von Arx T, Hardt N, Wallkamm B. The TIME technique: a new method for localized alveolar ridge augmentation prior to placement of dental implants. Int J Oral Maxillofac Implants. 11(3):387–94.

45. McGinnis M, Larsen P, Miloro M, Beck FM. Comparison of resorbable and nonresorbable guided bone regeneration materials: a preliminary study. Int J Oral Maxillofac Implants. 2000;13(1):30–5.

46. Lekovic V, Camargo PM, Klokkevold PR, Weinlaender M, Kenney EB, Dimitrijevic B, et al. Preservation of Alveolar Bone in Extraction Sockets Using Bioabsorbable Membranes. J Periodontol [Internet]. 1998;69(9):1044–9. Available from: http://www.joponline.org/doi/10.1902/jop.1998.69.9.1044

47. Jung RE, Philipp A, Annen BM, Signorelli L, Thoma DS, Hämmerle CHF, et al. Radiographic evaluation of different techniques for ridge preservation after tooth extraction: A randomized controlled clinical trial. J Clin Periodontol. 2013;40(1):90–8.

48. Patterson Dental. HeliPLUG Collagen Wound Dressing [Internet]. Available from: https://www.pattersondental.com/Supplies/ItemDetail/074986675

49. Kotsakis G, Chrepa V, Marcou N, Prasad H, Hinrichs J. Flapless Alveolar Ridge Preservation Utilizing the “Socket-Plug” Technique: Clinical Technique and Review of the Literature. J Oral Implantol [Internet]. 2014;40(6):690–8. Available from: http://www.joionline.org/doi/abs/10.1563/AAID-JOI-D-12-00028

50. Sclar a G. Preserving alveolar ridge anatomy following tooth removal in conjunction with immediate implant placement. The Bio-Col technique. [Internet]. Vol. 7, Atlas of the oral and maxillofacial surgery clinics of North America. 1999. p. 39–59. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11905323

51. Wang HL, Tsao YP. Mineralized bone allograft-plug socket augmentation: Rationale and technique. Implant Dent. 2007;16(1):33–41.

52. Gupta D, Gundannavar G, Chinni DD, Alampalli RV. Ridge Preservation done Immediately following Extraction using Bovine Bone Graft Collagen Plug and Collagen Membrane. Int J Oral Implantol Clin Res. 2012;3:8–16.

53. 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(4):267–72.

54. Nevins M, Nevins ML, Kim S-W, Schupbach P, Kim DM. The use of mucograft collagen matrix to augment the zone of keratinized tissue around teeth: a pilot study. Int J Periodontics Restorative Dent. 2011;31(4):367–73.

55. Ghanaati S, Schlee M, Webber MJ, Willershausen I, Barbeck M, Balic E, et al. Evaluation of the tissue reaction to a new bilayered collagen matrix in vivo and its translation to the clinic. Biomed Mater. 2011;6(1).

56. Lorenzo R, García V, Orsini M, Martin C, Sanz M. Clinical efficacy of a xenogeneic collagen matrix in augmenting keratinized mucosa around implants: A randomized controlled prospective clinical trial. Clin Oral Implants Res. 2012;23(3):316–24.

VOLUMETRIC AND LINEAR ANALYSIS OF SOFT TISSUE CHANGES AFTER TOOTH EXTRACTION AND SOCKET GRAFTING

Introduction

According to the definition of the American Academy of Periodontology, alveolar ridge preservation is a surgical treatment performed to prevent ridge collapse and to conserve ridge dimensions following removal of a tooth with the end goal of implant placement. This procedure is carried out by implementing biomaterials and/or membranes.[1] A greater focus on preservation of the alveolar ridge after extraction has emerged as dental implants become a predominant therapy to replace missing teeth. The success and survival of dental implants are dependent on proper three-dimensional positioning in the bone, the anatomical shape of the prosthetic restoration, the quantity and quality of the soft tissue, and the presence of a balanced occlusion. Adequate preservation of the alveolar bone dimension is of great importance to adequately place dental implants. Various methods have been utilized with the intent of preserving the alveolar ridge post-tooth extraction due to the importance that it has on prosthetic and esthetic outcomes when replacing missing teeth. The objective of this study was to evaluate the linear and volumetric soft tissue changes following socket grafting with a xenograft bone substitute and a 3-D collagen matrix (Bio-Oss Collagen® + Mucograft Seal®) compared to socket grafting with a xenograft bone substitute with the use of a collagen plug (Bio-Oss Collagen® + HeliPlug®).

Materials and Methods

Study Population

This study consisted of 24 subjects (Table 1), ten men and fourteen women, with a mean age of 50.83 ± 11.53 years (range 31 to 69 years). All patients were treated at the University of North Carolina School of Dentistry Go Health Clinic. Both the test and the control group consisted of 12 subjects with one maxillary premolar to premolar tooth that was determined non-restorable by a general dentist.

Inclusion criteria:

1. Adult males or females age 18 to 80 years (inclusive).
2. Subjects were able and willing to follow study procedures and instructions in English.
3. Subjects must have read, understood and signed an informed consent.
4. Subjects must have a maxillary premolar, canine, lateral incisor, or central incisor with a non-restorable prognosis or a hopeless periodontal prognosis (Kwok and Caton[2]) in which an implant was indicated without sinus displacement required.
5. Subjects undergoing implant placement were in adequate periodontal health prior to implant placement. This includes having probing depth ≤ 4 mm for all remaining teeth in the same quadrant of the proposed implant placement. Patients with periodontal probing depths up to 5 mm were included if bleeding on probing was absent. Subjects were considered periodontally stable prior to implant surgery.

Patients were recruited and randomly assigned to two groups (Figure 1):

Group 1. The control group received extraction and site preservation with xenograft bone substitute (Bio-Oss Collagen®) and collagen dressing (HeliPlug®).

Group 2. The test group received extraction and site preservation with xenograft bone substitute (Bio-Oss Collagen®) and 3D-collagen matrix (Mucograft Seal®).

All recruited subjects were previously approved and treatment planned for extraction, site preservation and implant placement by non-study personnel to avoid any potential conflict of interest. Subjects had radiographic images that demonstrated and confirmed the parameters of the tooth planned for extraction. Subjects qualified for only one tooth extraction, site preservation and dental implant.

Surgical Procedure

Extraction and socket preservation procedures were completed by the same clinician (Figure 2). All surgeries were performed under local anesthesia using lidocaine with epinephrine (Xylocaine 2%®-Epinephrine 1:100,000 and 1:50,000, Dentsply Pharmaceutical, York, PA, USA). Subjects were randomly allocated the control or test group. All subjects had atraumatic tooth extraction that was completed with minimal sectioning of teeth or bone. Thorough curettage of the extraction socket was completed and was rinsed with sterile saline. Upon completion of extraction, control subjects received site preservation therapy with the use of a xenograft bone substitute (Bio-Oss® Collagen, 250 mg). The extraction site was covered with collagen dressing (HeliPlug®). Suturing was completed with resorbable suture material (5-0 Vicryl-Ethicon, Inc., Somerville, NJ) to stabilize the collagen sponge. The test group received site preservation therapy with xenograft bone substitute (Bio-Oss® Collagen, 250mg) and the grafting material was covered with a 3D-collagen matrix (Mucograft Seal®). Suturing was completed using non-resorbable suture material (6-0 Prolene – Ethicon, Inc., Somerville, NJ) and resorbable suturing material (5-0 Vicryl – Ethicon, Inc., Somerville, NJ) to stabilize the collagen

matrix as recommend by the Mucograft® Seal manufacturing guideless (Figure 3). Subjects in both groups were instructed to rinse twice daily with 0.12% chlorhexidine gluconate for 30 seconds and to avoid brushing or touching the area for two weeks. Subjects were given prescriptions for postoperative medications. No temporary appliance was offered as part of the study. At two weeks, subjects were advised to resume gentle brushing of the surgical site with a soft toothbrush. Sutures were removed at the two-week post-operative appointment.

Data Collection and Processing

Subjects were seen at various follow up periods. Intra-oral scanning (Trios, 3Shape scanner) obtained at the 1 month, 3 month and 6-month post-operative periods were used for analysis (Fig 2). The purpose of the intra-oral scanning was to conduct soft tissue analysis to compare the linear and volume changes between the study groups. Soft tissue changes were evaluated by obtaining STL files originated from the intra-oral scanned images that were analyzed by non-contact reverse engineering software (Geomagic Software). The linear measurements were obtained at the levels 1 mm, 3 mm and 5 mm apical to the facial gingival margin (Figure 4). The volumetric analysis was obtained by measuring the volume of the facial soft tissue from the highest point of the interproximal papilla (mesial and distal to the tooth examined) and extended apically to the length of the tooth root (Figure 5).

Results

Population Sample

A total of 24 patients were admitted and completed the soft tissue analysis study. Ten males between ages 38 and 69 years (mean age 50.6 ± 12.29) and fourteen females between ages 31 and 68 years (mean age 51.0 ± 11.42). The sample consisted of 4 central incisors, 7 lateral incisors, 1 canine, 7 first premolars and 5 second premolars (Table 2).

Soft Tissue Linear Analysis

Repeated measures were used to analyze the collected data. Results derived from the linear soft tissue remodeling analysis demonstrated that site preservation with the use of a xenograft bone substitute (BioOss Collagen®) + collagen dressing (HeliPlug®) showed a greater linear bucco-lingual loss of soft tissue at the 1 mm, 3 mm and 5 mm below the gingival margin at the 1, 3 and 6 month follow up (Figure 5 A, B, C). At the one month follow up the control group (BioOss Collagen® + HeliPlug®) showed an average linear loss of soft tissue of 1.53 mm, 0.96 mm and 0.58 mm at the 1mm, 3mm, and 5mm, respectively, below the buccal gingival margin. The test group (BioOss Collagen® + Mucograft Seal®) showed a lesser amount of linear soft tissue loss with an average of 1.48 mm, 0.71 mm and 0.11 mm at the 1mm, 3mm, and 5mm, respectively. There was an average increase in the loss of linear soft tissue in both groups at the 3 and 6 month follow up. At 3 months, the control sites showed an average loss of 2.20 mm, 1.92 mm and 1.17 mm at 1mm, 3mm, and 5mm respectively below the buccal gingival margin. The average linear soft tissue loss at the test site was 1.92 mm, 1.47mm and 0.84 mm at the 1mm, 3 mm and 5mm respectively. At the 6-month time point, the control sites, showed an average loss of 2.07 mm, 1.8 mm and 1.36 mm at 1mm, 3mm, and 5mm respectively below the buccal gingival margin. The average linear soft tissue loss at the test site was 1.97 mm, 1.58 mm and 1.04 mm at the 1mm, 3 mm and 5mm respectively (Table 3, Figure 6). The soft tissue changes demonstrated loss on both study groups. The linear analysis between the test and control were not statistically significant at any of the evaluated time points.

Soft Tissue Volumetric Analysis

The results of the volumetric analysis demonstrated less facial soft tissue loss with the use of a 3-D collagen dressing at the time of extraction and site preservation (Table 4). At the one month follow up, the control group (BioOss Collagen® + HeliPlug®) demonstrated an average soft tissue loss of 50.8 mm^3 compared to the test group (BioOss Collagen® + Mucograft Seal®) which showed an average of 32.0 mm^3 in volumetric soft tissue loss. Both groups showed volumetric loss from the 1 month to the 3 month follow up. At the 3-month assessment, the facial soft tissue volumetric analysis demonstrated that the test sites lost an average in soft tissue dimension of 64.8 mm^3 compared to 86.6 mm^3 in the control group. At the 6-month time point, there was less loss of volume in the test sites, average of 68.8 mm^3 compared to 87.6 mm^3 in the control sites (Figure 7). The linear mixed model of repeated measures showed a statistically significant difference in loss of soft tissue volume with longitudinal change from month 1 to month 6 ($p=0.009$). The average volumetric difference was of about 25% less loss in the 3-D collagen matrix group.

Discussion

The importance of site preservation at time of tooth extraction to decrease the loss in ridge dimension has been established.[3,4] A greater loss in ridge height and width occurs when site preservation is not completed. Socket grafting is the preferred and most effective method of treatment to preserve the hard and soft tissue after tooth extraction. The esthetic zone is considered an area of high risk for ridge alteration consequently of tooth extraction.[5] A buccal wall thickness of 1-2 mm has been suggested to avoid significant ridge resorption at time of tooth extraction.[6] However, clinical[7] and radiographic[8] evaluations of the thickness of the buccal

wall of maxillary anterior teeth and premolars have found that in the majority of cases, the average buccal bone thickness for anterior teeth is <1mm. Only <10% of buccal walls have a width 2 mm.[7] Soft tissue biotype is also of interest when considering extraction and site preservation for future implant placement. A recent study analyzed the interplay between biotype (thick vs thin) and the underlying facial bone thickens after tooth extraction in which a collagen sponge was used to stabilize the clot. Digital impressions of the soft tissue were taken and analyzed using a digital software. The facial bone thickness was analyzed using CBCT images. The authors concluded that soft tissue type did not have an influence in soft tissue contour at 8 weeks of healing between thick and thin tissue biotypes.[5] It is also accepted that dimensional bone and tissue changes is an unavoidable outcome of extraction. Accordingly, site preservation is highly encouraged as it can reduce loss of ridge loss by -1.47 mm vertically and -1.83 mm horizontally.[9]

For this reason, site preservation is highly recommended to preserve the soft and hard tissue dimensions when considering implants for tooth replacement. Soft tissue, resorbable and non-resorbable membranes, collagen sponges and various bone grafting materials have been used to help maintain ridge morphology and soft tissue at time of tooth extraction. The porcine 3-D collagen matrix (Geistlich Mucograft®) has been used for soft tissue regeneration as an alternative to using an autogenous donor graft from the patient.[10,11] As a modification, the Geistlich Mucograft® Seal, was specifically designed for soft tissue regeneration over an extraction site. The collagen matrix has been shown to promote faster healing[12], integration,[12,13] and adaptation when used in combination with the Geistlich Bio-Oss Collagen.®

A recent study by Natto and investigators compared the clinical, radiographic soft and hard tissue dimensional changes after socket preservation using FDBA with a collagen sponge (control) and the Geistlich Mucograft® Seal (test). Clinical soft tissue measurements were performed using radiographic stents. The linear measurements showed both treatment modalities were effective in preserving the alveolar ridge. The mean width reduction with the collagen sponge was 1.47 mm (20.40%) compared to 1.21 mm (14.91%) with the collagen membrane. The results did not show significant difference between the groups.[14] In another 6-month study, soft tissue analysis of socket preservation was performed in four groups that received 1. β-TCP particles with no soft tissue treatment, 2. DBBM + 10% collagen covered with a collagen matrix (Geistlich Mucograft®), 3. DBBM + 10% collagen covered with soft tissue graft and 4. No site preservation (control). The linear soft tissue analysis was performed using scanned models that were analyzed with digital software. Although the results did not show statistical significance, at 6 months, the groups treated with a Mucograft® and soft tissue graft had a reduced amount of soft tissue loss, -1.2 ± 0.5 mm and -1.2 ± 0.7 mm respectively, compared to the β-TCP and the no treatment groups, -1.7 ± 0.7 mm and -1.8 ± 0.8mm, respectively.[15]

In our investigation, 12 test and 12 control subjects received socket preservation with xenograft grafting material (Bio-Oss Collagen®). In the control group, the site was covered with a collagen sponge (HeliPlug®) and the test group with a 3D-collagen matrix (Geistlich Mucograft® Seal). Clinical evaluation was obtained with the use of an intraoral scanner (Trios, 3Shape) and soft tissue analysis was performed using an advanced non-contact reverse engineering software (Geomagic Software). Our study conducted linear measurements at 1mm, 3mm and 5mm below the gingival margin. Volumetric soft tissue analysis consisted of tissue that extended from the interproximal papilla (mesial and distal) to the length of the root. Comparable

to the results found by Natto et al., and Schneider et al., our linear results demonstrated less soft tissue loss using the 3D-collagen matrix (Geistlich Mucograft® Seal) compared to a collagen sponge (HeliPlug®). Similarly, the results were not statically significant. Statistical significance in longitudinal change was found in the volumetric tissue changes between the test and control groups. At 6 months, an average volume loss of 68.61 mm^3 was seen in the Geistlich Mucograft® Seal group compared to 87.65 mm^3 in the HeliPlug® group. Based on this data, the findings indicate that the use of a 3D-collagen matrix pose a more beneficial soft tissue response which potentially impacts implant esthetic outcome when considering placement of implants in the esthetic zone. Limitations to our study include a small sample size and a wide spread of teeth as it included premolars, canines, lateral and central incisors. Further studies are needed with a larger sample that can analyze the benefits of this technique in a more uniform sample.

Conclusion

Based on the results of the volumetric analysis, the treatment of site preservation with Bios Collagen® + Mucograft Seal® can benefit clinicians when managing soft tissue contours around implants in the esthetic zone.

Acknowledgments

This study was funded by Geistlich, Inc and supported by NIH/NIDCR K23-DE025093. The authors thank the UNC School of Dentistry Go Health Clinical Research Center for their support and collaboration.

Tables

Table 1: Demographics of study population

	N	Average Age (yrs)	Male	Female
Test	12	45.25	5	7
Control	12	56.42	5	7

Table 2: Distribution of teeth

	Central	Lateral	Canine	1st Premolar	2nd Premolar
Test	1	4	0	4	3
Control	3	3	1	3	2

Table 3: Average linear soft tissue loss (mm).

		1 mm		3mm		5mm	
		Test	Control	Test	Control	Test	Control
Month 1	Mean	-1.48	-1.53	-0.71	-0.96	-0.11	-0.58
	Standard dev.	0.77	0.70	0.50	0.75	0.38	0.83
Month 3	Mean	-1.92	-2.20	-1.47	-1.92	-0.84	-1.17
	Standard dev.	0.58	0.90	0.70	0.82	0.77	0.49
Month 6	Mean	-1.97	-2.07	-1.58	-1.80	-1.05	-1.36
	Standard dev.	0.64	0.75	0.62	0.62	0.53	0.58

Table 4: Average volumetric soft tissue loss (mm^3)

		Test	Control
Month 1	Mean	-32.02	-50.86
	Standard dev.	26.64	32.36
Month 3	Mean	-64.87	-86.65
	Standard dev.	27.26	33.65
Month 6	Mean	-68.61	-87.65
	Standard dev.	25.41	39.19

Figures

Figure 1: Subjects who met the inclusion criteria where randomly assigned to the test or the control group.

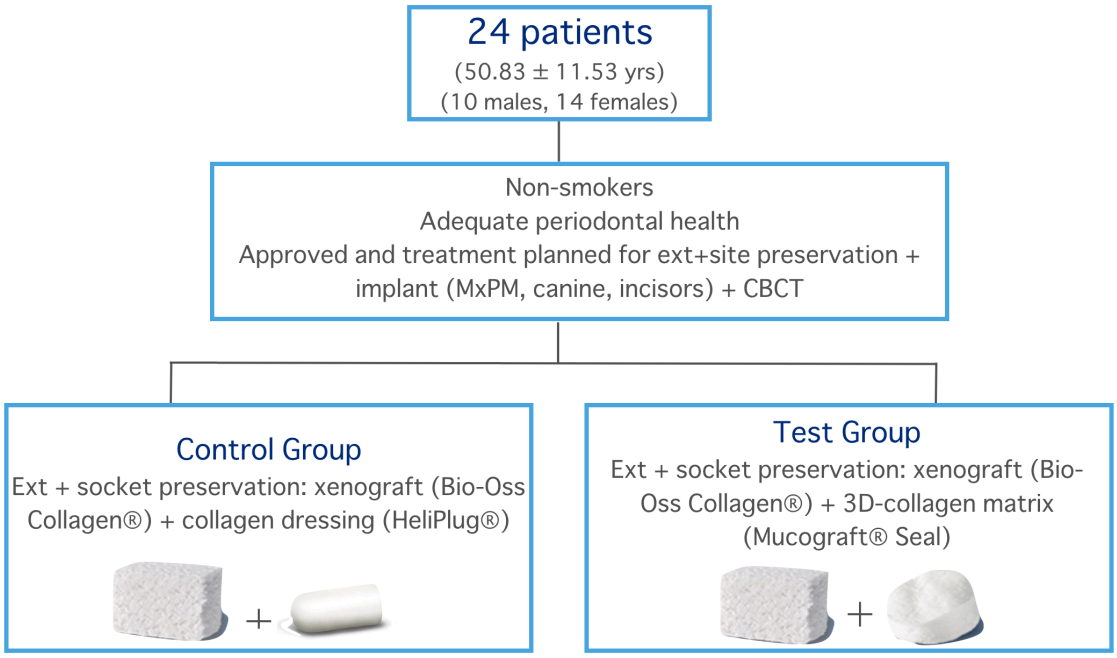


Figure 2: Timeline of Treatment Procedures

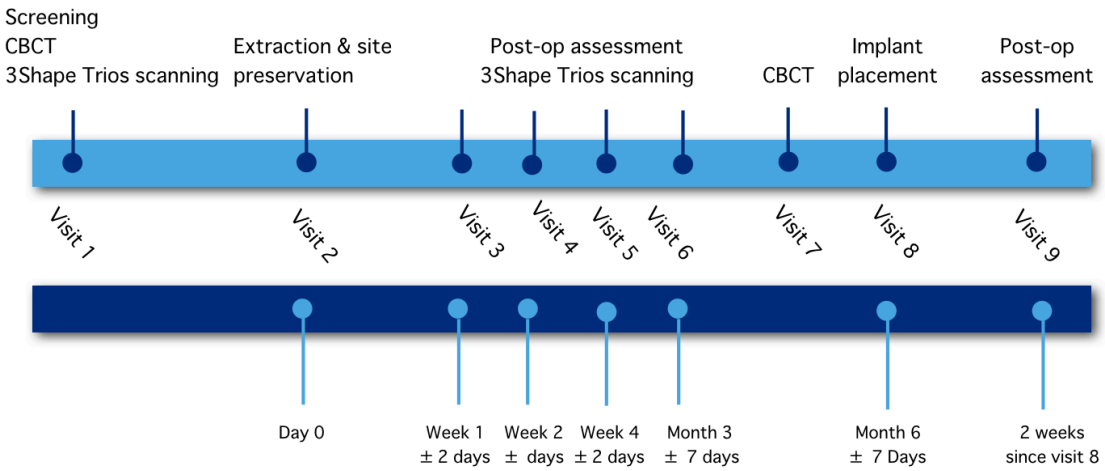
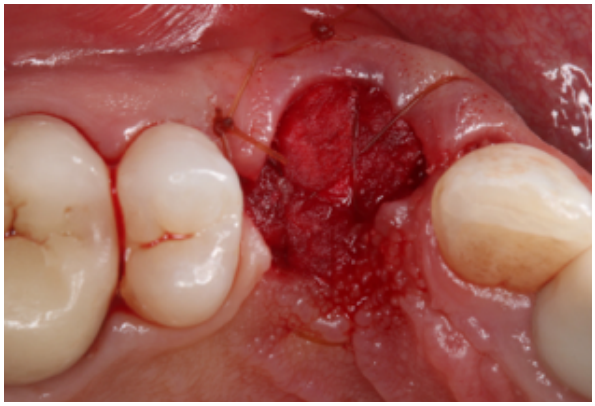


Figure 3: Fig 3A; site preservation with collagen sponge (control), Fig. 3B; site preservation with 3-D collagen matrix.

3A



3B

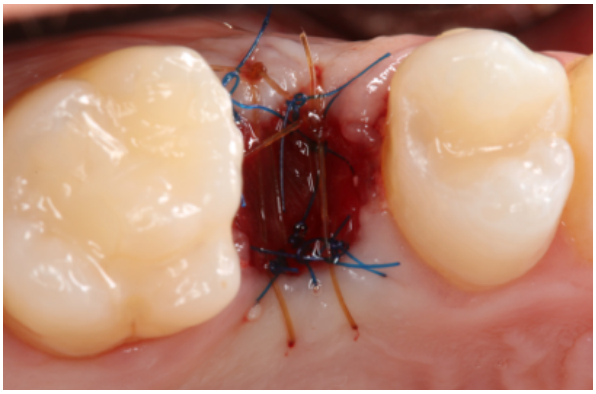


Figure 4: Visual representation of the linear analysis; digital images where obtained with an intra-oral scanner. The images were converted into STL files and linear soft tissue changes were analyzed by segmentation at 1 mm, 3mm and 5 mm below the gingival margin (3 mm and 5 mm shown). Negative numbers indicate soft tissue loss, positive numbers indicate soft tissue gain. Image shows tissue loss displayed in shades of blue.

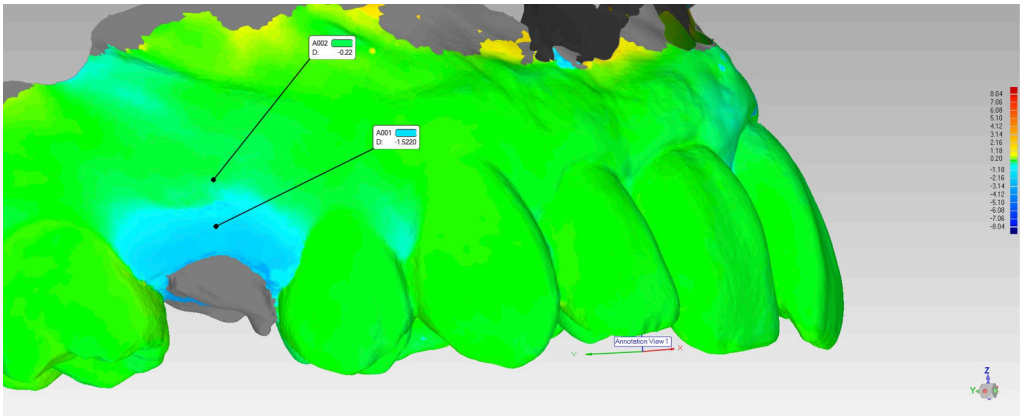
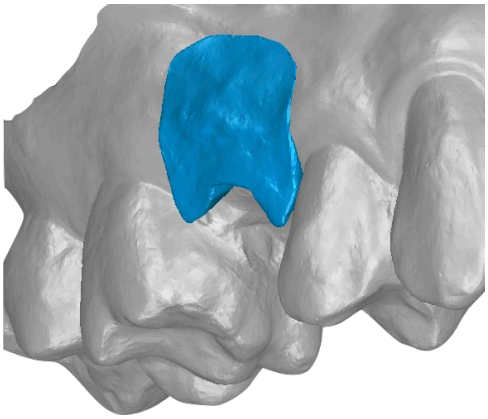


Figure 5: Visual Representation of the volumetric analysis; the facial volume measured was obtained from the highest point of the mesial and distal papilla and extended apically to the length of the tooth root.



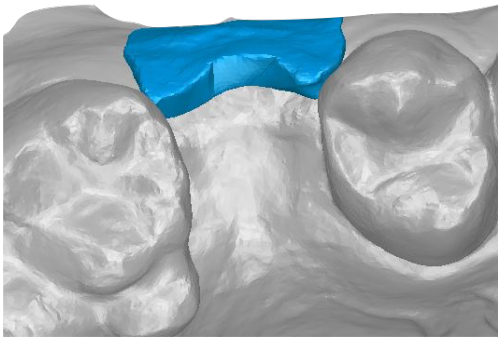


Figure 6: Linear Measurement Analysis

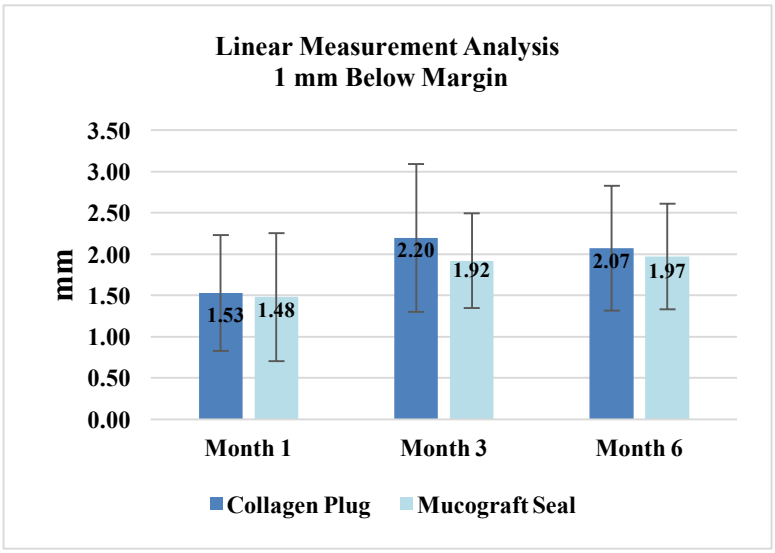


Fig. 6A. Average linear soft tissue loss at 1 mm from gingival margin with standard error.

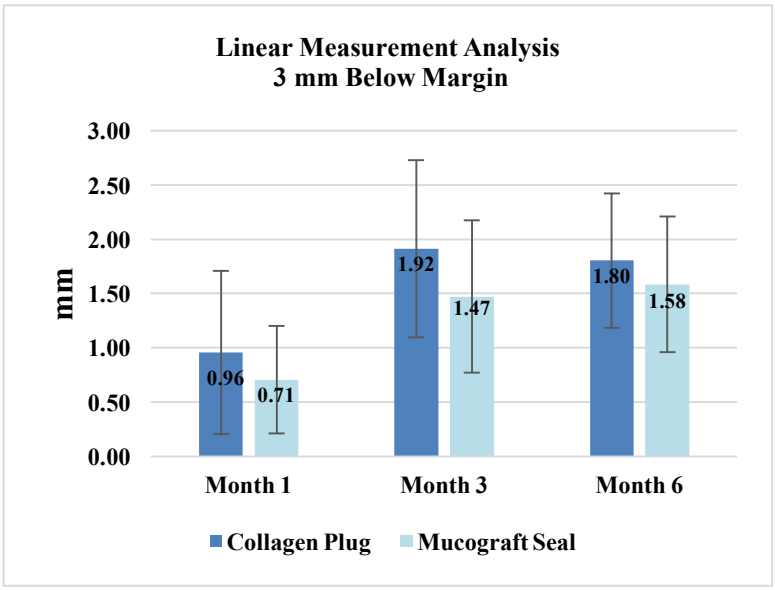


Fig. 6B. Average linear soft tissue loss at 3 mm from gingival margin with standard error.

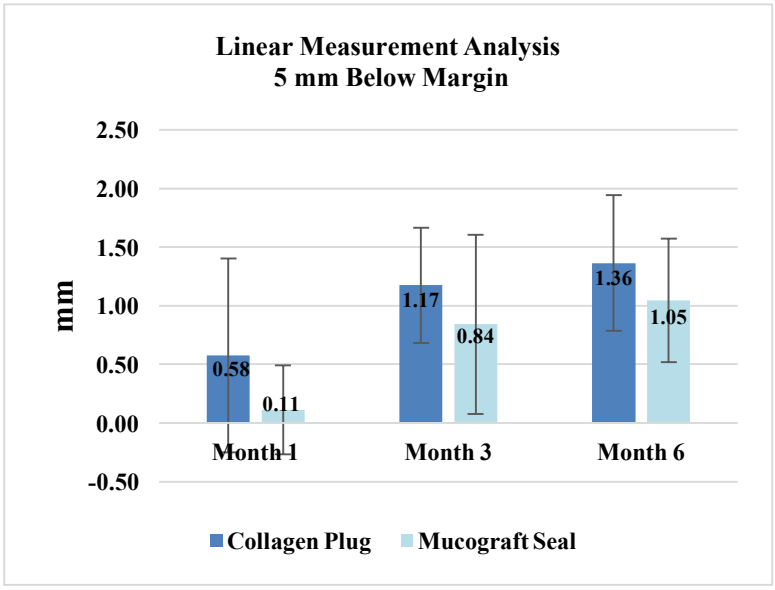
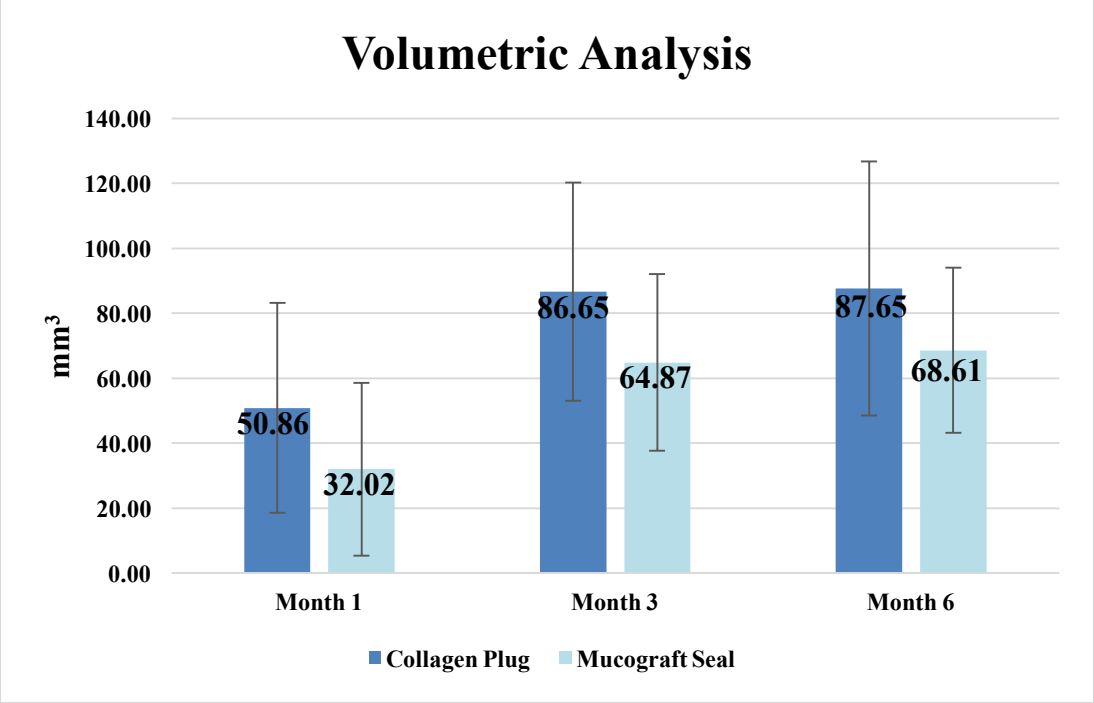


Fig. 6C. Average linear soft tissue loss at 5 mm from gingival margin with standard error.

Figure 7: Volumetric measurement analysis of soft tissue loss at the 1 month, 3 month and 6 month follow up with standard error.



REFERENCES

1. American Academy of Periodontology [Internet]. [cited 2018 Mar 21]. Available from: https://members.perio.org/libraries/glossary/entry?GlossaryKey=da428173-f0c0-43b0-982c-dc0f4f3b74b1&tab=groupdetails

2. Kwok V, Caton JG. Commentary: Prognosis Revisited: A System for Assigning Periodontal Prognosis. J Periodontol [Internet]. 2007;78(11):2063–71. Available from: http://www.joponline.org/doi/10.1902/jop.2007.070210

3. Schropp L, Wenzel A. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12-month prospective study. J Prosthet Dent [Internet]. 2004;91(1):92. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022391303007455

4. Araújo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. J Clin Periodontol. 2005;32(2):212–8.

5. Chappuis V, Engel O, Shahim K, Reyes M, Katsaros C, Buser D. Soft Tissue Alterations in Esthetic Postextraction Sites: A 3-Dimensional Analysis. J Dent Res. 2015;94:187S–193S.

6. Spray JR, Black CG, Morris HF, Ochi S. The influence of bone thickness on facial marginal bone response: stage 1 placement through stage 2 uncovering. Ann Periodontol [Internet]. 2000 Dec;5(1):119–28. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11885170

7. Huynh-Ba G, Pjetursson BE, Sanz M, Cecchinato D, Ferrus J, Lindhe J, 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(1):37–42.

8. Vera C, De Kok IJ, Reinhold D, Limpiphipatanakorn P, Yap AKW, Tyndall D, et al. Evaluation of buccal alveolar bone dimension of maxillary anterior and premolar teeth: a cone beam computed tomography investigation. Int J Oral Maxillofac Implants [Internet]. 2012;27(6):1514–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23189304

9. Vignoletti F, Matesanz P, Rodrigo D, Figuero E, Martin C, Sanz M. Surgical protocols for ridge preservation after tooth extraction. A systematic review. Clin Oral Implants Res. 2012;23(SUPPL. 5):22–38.

10. Sanz M, Lorenzo R, Aranda JJ, Martin C, Orsini M. Clinical evaluation of a new collagen matrix (Mucograft® prototype) to enhance the width of keratinized tissue in patients with fixed prosthetic restorations: A randomized prospective clinical trial. J Clin Periodontol. 2009;36(10):868–76.

11. McGuire MK, Scheyer ET. Xenogeneic Collagen Matrix With Coronally Advanced Flap Compared to Connective Tissue With Coronally Advanced Flap for the Treatment of Dehiscence-Type Recession Defects. J Periodontol [Internet]. 2010;81(8):1108–17. Available from: http://www.joponline.org/doi/10.1902/jop.2010.090698

12. Jung RE, Philipp A, Annen BM, Signorelli L, Thoma DS, Hämmerle CHF, et al. Radiographic evaluation of different techniques for ridge preservation after tooth extraction: A randomized controlled clinical trial. J Clin Periodontol. 2013;40(1):90–8.

13. Thoma DS, Sancho-Puchades M, Ettlin DA, Hämmerle CHF, Jung RE. Impact of a collagen matrix on early healing, aesthetics and patient morbidity in oral mucosal wounds - A randomized study in humans. J Clin Periodontol. 2012;39(2):157–65.

14. Natto ZS, Parashis A, Steffensen B, Ganguly R, Finkelman MD, Jeong YN. Efficacy of collagen matrix seal and collagen sponge on ridge preservation in combination with bone allograft: A randomized controlled clinical trial. J Clin Periodontol. 2017;44(6):649–59.

15. Schneider D, Schmidlin PR, Philipp A, Annen BM, Ronay V, Hämmerle CHF, et al. Labial soft tissue volume evaluation of different techniques for ridge preservation after tooth extraction: A randomized controlled clinical trial. J Clin Periodontol. 2014;41(6):612–7.