Periodontal phenotype and supracrestal soft tissue dimensions – clinical correlations and their impact on post-extraction volumetric changes

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PERIODONTAL PHENOTYPE AND SUPRACRESTAL SOFT TISSUE DIMENSIONS – CLINICAL CORRELATIONS AND THEIR IMPACT ON POST-EXTRACTION VOLUMETRIC CHANGES

by

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Oral Science in the Graduate College of The University of Iowa

August 2017

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This is to certify that the Master’s thesis of

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ABSTRACT

Objectives:

Extraction of a tooth leads to a series of healing events that are intimately associated with dimensional changes in the alveolar ridge that typically result in a net volume loss. Previous studies have evaluated the extent and pattern of those resorptive changes, however it remains challenging to predict the degree of change that will occur, as numerous local and systemic factors may play a role in the biologic events that follow tooth extraction. The purpose of this study was to assess the role that phenotypic characteristics of the periodontium play in the alveolar ridge remodeling processes that take place following single tooth extraction.

Methods:

Healthy patients in need of a single tooth extraction in the maxillary arch from second premolar to second premolar (inclusive) and who met a predefined eligibility criteria were enrolled in this study. An impression of the maxillary arch was made and a cone beam computed tomography (CBCT) scan of the maxilla was obtained immediately prior to tooth extraction at the baseline visit. At the time of the extraction, clinical measurements were made including probing depth, bone sounding, buccal keratinized mucosa width, buccal and palatal alveolar bone thickness, and buccal and palatal soft tissue thickness. Fourteen weeks following the baseline intervention, patients returned to the clinic for a second impression of the maxillary arch and a second CBCT of the maxilla. Linear and volumetric bone measurements were made using the data obtained from the CBCT scans. The casts obtained from the impressions were digitally scanned and volumetric measurements were made from the digitized data to assess volume changes of the residual ridge. The primary outcome of interest was the volumetric percent reduction of the alveolar ridge following single tooth extraction. Spearman correlations were utilized to evaluate
relationships between variables and modeling was completed to predict the percentage of volumetric change in the hard and soft tissues using the clinical variables.

**Results:**

A total of 21 patients participated in the study, 19 patients are included in this analysis (one patient has yet to complete the study, one patient was later excluded due to lack of compliance). Of the 19 extraction sites included, 17 were maxillary premolar teeth. At baseline, the average buccal plate thickness was 1.09 mm. After 14 weeks, the average loss of alveolar bone width was 1.66 mm. The average loss of buccal bone height was 1.10 mm and mean loss of palatal bone height was 1.36 mm. The average percentage volumetric reduction of the bone as measured from a CBCT scan was 26.42% after 14 weeks of healing. Mean percentage volumetric reduction of the ridge, as measured from a digitized cast, was 18.89%. There was no statistically significant correlation noted between the bone and ridge volumetric measurements.

While there were no statistically significant correlations noted between the thickness of the buccal bone and the amount of volumetric bone remodeling, statistically significant negative correlations were found between the buccal bone thickness and the loss of alveolar bone width ($rs = -0.66418$, $p$-value = 0.0019). In addition, a statistically significant correlation was noted between the reduction in alveolar bone width and the loss of buccal ridge height ($rs = 0.55707$, $p$-value = 0.0132). Modeling methods found that increased thickness of the buccal soft tissue was predictive of increased percentage volumetric reduction of hard tissues ($coeff = 37.24$, $p$-value = 0.0301).

**Conclusions:**

Increased buccal soft tissue thickness was found to be predictive of increased percent volumetric reduction of alveolar bone. Thinner buccal bone was correlated with increased loss of
alveolar bone width. While statistically significant correlations were identified, further studies with larger sample size are needed to better understand these relationships.
PUBLIC ABSTRACT

Tooth extraction is one of the most common procedures in the practice of dentistry. Following the extraction of a tooth, the supporting bone undergoes changes that result in the loss of bone volume at the extraction site. These changes typically occur in a defined pattern; however the amount of the change is often unpredictable. The loss of the supporting bone can lead to difficulty in replacing the tooth in the future and may limit replacement options. The lack of predictability makes accurate treatment planning difficult in some cases.

The aim of this study was to assess the amount of dimensional changes that occur in both the hard and soft tissues and to determine if there are any clinical measurements that may help predict the amount of change that will occur following extraction. Clinical measurements of the hard and soft tissues were made at the time of the extraction. In addition, volumetric analysis of the reduction in hard and soft tissues was performed. It was found that the thickness of the bone facial to the tooth was inversely correlated to the amount of bone width lost after healing and increased soft tissue thickness facial to the tooth was predictive of increased loss of bone volume. While the results of the study are statistically significant, this was a small study and more patients are needed to better evaluate these relationships.
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CHAPTER 1. INTRODUCTION

1.1. The Periodontium

The periodontium is comprised of the hard and soft tissues which provide support to the teeth; its primary function is to attach the teeth to the bone. Also referred to as the attachment apparatus, the periodontium includes the gingival tissues, alveolar bone proper, cementum, and periodontal ligament (Hassell 1993).

The gingival tissues surrounding the teeth are unique in structure and function, and are typically separated into different anatomical sections. The most coronal portion of the gingival tissue is referred to as the free gingiva, which extends apically from the gingival margin. This portion surrounds each tooth, but is not directly attached to the tooth surface. The free gingiva is unique in that it is epithelialized on the external surface, the oral epithelium, as well as the surface adjacent to the tooth, the sulcular epithelium. The sulcular epithelium is adjacent to the tooth surface, but does not directly attach to the surface. (Hassell 1993, Lindhe and Lang 2015) The sulcular epithelium is typically non-keratinized, but studies have shown that with rigorous oral hygiene practice it can become keratinized (Kristoffersen, Caffesse et al. 1983). The virtual space between the sulcular epithelium and the tooth surface is referred to as the gingival sulcus or gingival crevice (Listgarten 1972, Hassell 1993).

Immediately apical to the free gingiva lies the junctional epithelium, which attaches to the tooth surface directly via hemidesmosomes (Kobayashi, Rose et al. 1976, Schroeder and Listgarten 1997). The junctional epithelium was originally referred to as the epithelial attachment, a term which was coined by Gottlieb in 1921 (Hallmon 1996). The junctional epithelium is a non-differentiated, stratified squamous epithelium that originates from the reduced enamel epithelium during tooth eruption (Nanci and Bosshardt 2006). As the tooth erupts, the reduced enamel
epithelium fuses with the oral epithelium to create the junctional epithelium (Engler, Ramfjord et al. 1965, Shimono, Ishikawa et al. 2003). Functionally, the junctional epithelium protects the underlying structures such as the periodontal ligament from invasion by external substances and microorganisms (Hassell 1993).

The connective tissue attachment is apical to the junctional epithelium and is interposed between the junctional epithelium and the crestal bone (Sanavi, Weisgold et al. 1998). The connective tissue, or lamina propria, is comprised of approximately 60% collagen fibers by volume, along with fibroblasts, blood vessels, and nerves in an amorphous ground substance. The collagen fibers are considered to be one of the most important aspects of the periodontium as they provide attachment of the gingiva to the tooth, as well as to the alveolar bone (Lindhe and Lang 2015). The principal fibers in the gingiva are classified as dentogingival, alveologingival, dentoperiosteal, circular, or transseptal. The dentogingival fibers originate from the cementum and attach into the lamina propria to provide gingival support. Alveologingival fibers originate in the periosteum and attach coronally, into the lamina propria, to attach the gingiva to the bone. The dentoperiosteal fibers provide protection to the periodontal ligament and anchor the tooth to the bone, attaching from the cementum, near the cemento-enamel junction (CEJ), to the alveolar crest. Circular fibers encircle the tooth within the free gingiva while transseptal fibers link the supracrestal cementum of adjacent teeth. (Hassell 1993, Lindhe and Lang 2015). The collagen within the lamina propria consists primarily of type I collagen; however six types of collagen have been identified in the gingival connective tissues. In addition to the collagen fibers, elastin fibers and oxytalan fibers are present within the lamina propria, along with many other components. Elastin is a flexible protein that allows the tissues to stretch and bend (Bartold 1995). Oxytalan fibers also contribute to the biomechanical properties of the lamina propria. While oxytalan has
been noted for some time, recent studies have further evaluated the possible adaptation this fiber type can have under the application of force (Everts, Niehof et al. 1998, Strydom, Maltha et al. 2012).

The biologic width is a histological concept that comprises the vertical dimension of both the junctional epithelium and the connective tissue attachment. This term was originally described in 1977 in an article by Ingber at al. who credited Dr. Walter Cohen for the term, which is based upon the findings of Gargiulo, Wentz, and Orban in 1961 (Ingber, Rose et al. 1977). This particular study on human cadaver heads found that the average dimension of the junctional epithelium was 0.97 mm and the average dimension of the connective tissue was 1.07 mm (Gargiulo, Wentz et al. 1961). While these averages are commonly referenced, there is also a wide range in the values of these dimensions between patients, as well as within the same patient. In fact, the biologic width has been noted to vary both by tooth type and site (Schmidt, Sahrmann et al. 2013). Overall, the connective tissue attachment has been noted to be the most consistent element with the most variation in dimension noted in the epithelial attachment, or junctional epithelium (Gargiulo, Wentz et al. 1961, Vacek, Gher et al. 1994). A study by Vacek and colleagues found the average dimension of the epithelial attachment to be 1.14 mm and the connective tissue to have an average dimension of 0.77 mm (Vacek, Gher et al. 1994). A systematic review by Schmidt et al. noted mean values of the biologic width to be 2.15-2.30 mm with large intra-individual and inter-individual variance.

The alveolar bone proper is also referred to as the cribiform plate. The areas of the alveolar bone proper where the principal collagen fibers from the periodontal ligament (aka Sharpey’s fibers) anchor is known as bundle bone, which plays an important role in the attachment of the tooth to the alveolar bone (Schroeder 1986, Nanci and Bosshardt 2006). This region of bone is
formed during the development of the teeth by cells from the dental follicle (Lindhe and Lang 2015).

Cementum is the outermost layer of the dental root surface. This mineralized tissue is different from any other mineralized tissue in the human body. It consists of approximately 65% hydroxyapatite by weight and contains collagen fibrils (Lindhe and Lang 2015). Cementum continues to be deposited on the root surface during life (Selvig 1965, Lindhe and Lang 2015). The fiber bundles of the periodontal ligament connect directly into the cementum. Four types of cementum have been described in the literature: acellular afibrillar cementum, acellular extrinsic fiber cementum, cellular mixed stratified cementum, and cellular intrinsic fiber cementum. The acellular extrinsic fiber cementum and cellular mixed stratified cementum each contain extrinsic fibers that make up the attachment of the tooth to the bundle bone (Bosshardt and Selvig 1997, Lindhe and Lang 2015).

The periodontal ligament (PDL) is a specialized type of connective tissue that interfaces between the cementum and the alveolar bone proper. This structure attaches the tooth to the alveolar bone proper and functions to distribute masticatory forces and act as a proprioceptive matrix during function (Beertsen, McCulloch et al. 1997). Various collagen bundle fibers are present in the PDL. Based upon the fiber arrangement, they can be divided into four main groups based upon their location or orientation: alveolar crest fibers, horizontal fibers, oblique fibers, and apical fibers (Lindhe and Lang 2015). The PDL also contains immune and mesenchymal pluripotent cells, blood and lymphatic vessels, nerves, among other elements.

In addition to the elements of the attachment apparatus discussed above, the periodontium also includes the keratinized and non-keratinized mucosa and the supporting alveolar bone. The oral mucosa is generally classified into the following types on a macroscopic level: masticatory
mucosa, lining mucosa, and specialized mucosa. The mucosa of the hard palate and the gingiva comprise the masticatory mucosa and the lining mucosa is found in areas such as the lips, vestibule, cheeks, floor of the mouth, ventral aspect of the tongue, and soft palate. The dorsal aspect of the tongue is comprised of specialized mucosa (Lindhe and Lang 2015). Histologically, the masticatory mucosa is typically keratinized, while the lining mucosa is non-keratinized (Karring and Loe 1970). The keratinized mucosa has been demonstrated to have higher tensile strength and stiffness when compared to non-keratinized mucosa (Goktas, Dmytryk et al. 2011). The dimension of the keratinized mucosa width is often evaluated during the clinical exam, as past studies have demonstrated the importance of adequate keratinized mucosa for periodontal health. A landmark study regarding the dimension of keratinized mucosa demonstrated that teeth with less than 2 mm had persistent inflammation and suggested that a minimum of 2 mm of keratinized mucosa was required for health (Lang and Loe 1972). While this concept is still commonly referenced, more recent studies have shown that with adequate oral hygiene and plaque control, health can be maintained with less than 2 mm of keratinized mucosa (Kennedy, Bird et al. 1985, Wennstrom 1987).

The alveolar bone process is the part of the mandible and the maxilla that envelops the major part of the roots of erupted teeth. The alveolar bone consists of cortical plates, trabecular bone, and the alveolar bone proper. The cortical plates of the alveolus consist of lamellae that are supported via Haversian systems (Nanci and Bosshardt 2006). The Haversian canals are small channels within the bone that contain blood vessels and nerves. The trabecular bone consists of cancellous bone and lies between the cortical plates and the alveolar bone proper. In the anterior region, the cortical bone may be directly fused to the alveolar bone proper, in absence of trabecular bone, depending upon anatomy and tooth position. The dimensions and structural properties of
alveolar bone vary depending on many factors and are often different between regions (Lindhe and Lang 2015). Alveolar bone is highly dynamic and has been shown to remodel in response to functional demands (Hassell 1993).

The assessment of the quality and quantity of the soft and hard tissues will be discussed in the following section.

1.2. *Periodontal Phenotype – Concepts and Evaluation*

The term periodontal phenotype refers to the phenotypic characteristics of the bone and soft tissues that make up the periodontium. Another term that is commonly used is periodontal biotype. While biotype is the traditional terminology, recent studies have elected to use the term phenotype, as the definition is considered to be more fitting (Stellini, Comuzzi et al. 2013).

Periodontal phenotype (biotype) is typically used to describe the bucco-lingual tissue thickness and gingival morphology. It has been noted that the gingival anatomy typically mimics the underlying bone (Ochsenbein and Ross 1969). Historically, periodontal phenotype has been classified into two basic forms: thick flat type and thin scalloped type (Sanavi, Weisgold et al. 1998). The thick flat type displays dense gingiva and is typically more resilient in the presence of inflammation. The thin scalloped type typically has less attached masticatory mucosa (keratinized) and is often supported by thin facial bone. Various studies have evaluated the relationship between tooth shape and periodontal phenotype (biotype). In general, long, narrow teeth are typically associated with a thin periodontium while wide crowns with large proximal contacts are associated with a thick phenotype (Weisgold 1977, Olsson and Lindhe 1991). More recent studies have called into question this concept as they have found no significant relationship between the crown height:width ratio and the perceived periodontal phenotype (Cook, Mealey et
al. 2011, Fischer, Grill et al. 2014) or crown shape and bone shape (Becker, Ochsenbein et al. 1997).

Often, periodontal phenotype is classified through a visual assessment of the tooth shape, tissue thickness, and overall appearance. Using this system is often quite subjective, hence multiple methods have been evaluated to propose a more reliable, objective method of evaluation. An early study utilized a transformer probe assembly to measure the thickness of both the attached and the free gingiva. This study found that the thickness at the depth of the sulcus to be directly proportional to the free gingival width. While the method was noted to be accurate to 0.01 mm, it did not attempt to correlate gingival thickness to an associated “biotype” (Goaslind, Robertson et al. 1977). A more recent study evaluated the use of an ultrasonic device for the determination of gingival thickness, determining the technique to be valid (Eger, Muller et al. 1996). However, this study failed to provide any valuable insight regarding the bone dimensions. In a later study completed by the same group of researchers, it was found that reliability was reduced because of the difficulty in measuring exactly on the same location, as well as variances in tissue, such as rugae (Muller, Schaller et al. 1999). While this method was shown to be valid and moderately reproducible, its clinical use is limited due to the difficulties with using the device, access to make the measurement, device availability and cost (De Rouck, Eghbali et al. 2009).

The use of a periodontal probe for the evaluation of the periodontal phenotype was described by Kan et al in 2003. The tissue was considered to be thin if a probe placed in the sulcus was clearly visible (Kan, Rungcharassaeng et al. 2003). In later studies, this method was found to be highly reproducible (De Rouck, Eghbali et al. 2009, Cook, Mealey et al. 2011). A recent study attempted to identify the thickness at which the periodontal probe is no longer visible through the gingival tissues and to evaluate the buccal bone thickness as it relates to probe visibility. While
probe visibility was associated with thinner measurements of gingival thickness, it failed to identify a threshold of gingival thickness above which the probe was no longer visible. When the probe was visible through the tissue, the mean buccal plate thickness tended to be smaller, but the difference was not statistically significant (Frost, Mealey et al. 2015). Furthermore, it is important to keep in mind that evaluation of the soft tissue alone does not completely describe the overall periodontal phenotype. Visibility of the periodontal probe may be an effective method for evaluating the soft tissue thickness of the free gingiva; however it does not take into account the phenotype of the bone.

In a 2013 study, gingival thickness and surrogate parameters were evaluated for possible correlations. Sixty Caucasian subjects were evaluated using clinical and radiographic measurements. Results of this study show that, though transparency of the tissue to the periodontal probe was negatively correlated with gingival thickness of the free gingiva, the prognostic value for attached gingiva or alveolar bone thickness was low. It was also found that crown width:length ratio had a positive relationship with all thickness parameters and it was a predictor for the thickness of the buccal alveolar bone at the crest. All other parameters were found to have no significant impact on the buccal alveolar bone thickness at the crest. This study highlights the difficulty in determining a clear distinction between “thin” and “thick” periodontal phenotypes (Stein, Lintel-Hoping et al. 2013).

Other studies have evaluated possible associations with the underlying alveolar bone. In 2009, Fu et al noted a moderate association between gingival biotype and the thickness of the buccal bone using both direct measurement and CBCT measurements in cadaver heads (Fu, Yeh et al. 2010). Cook and colleagues also noted this association using CBCT images, clinical examination, and dental casts (Cook, Mealey et al. 2011). A review completed in 2014 examined
the available literature regarding periodontal biotype and its dimensions and associations. It was noted that the dental, gingival, and osseous dimensions have a weak to moderate association and definitions of biotype are unclear. This review did note positive associations between gingival thickness, keratinized tissue, and bone morphotype (Zweers, Thomas et al. 2014). While the studies described above have shown phenotypic associations, La Rocca et al. did not find a direct correlation between gingival thickness and buccal bone thickness. Interestingly, this study did note evidence of a relationship between the crestal bone thickness and the width of the gingiva in the apico-coronal dimension (La Rocca, Alemany et al. 2012). These findings bring into question the possible relationship between the biologic width and the overall periodontal phenotype (bone and soft tissue).

1.3.Dental Extraction

Dental extraction is indicated when a tooth cannot be maintained due to function, health, or esthetics. The loss of function, health, and/or esthetics may occur due to a variety of reasons including caries, trauma, periodontal disease, endodontic failure, or manifestation of a systemic disease, among other possible causes. Dental caries and periodontal disease are commonly considered to be the two most common reasons for dental extraction. Data from the National Health and Nutrition Examination Survey (NHANES) in 2011-2012 reveals that 33% of adults age 20-39 in the United States are missing at least one tooth while 66% of adults age 40-64 are missing at least one tooth. In addition, 13% of adults age 65-74 are completely edentulous. The percentage of adults with complete edentulism increased to 25.8% in adults over 75 years of age (Dye, Thornton-Evans et al. 2015).
1.4 Wound Healing Following Extraction

The wound healing sequence is initiated immediately following tooth extraction and typically results in loss in alveolar ridge volume (Jahangiri, Devlin et al. 1998, Van der Weijden, Dell'Acqua et al. 2009). A histologic and histochemical evaluation of this process in humans was completed by Amler et al in 1960 (Amler, Johnson et al. 1960). The first step in alveolar healing is the formation of a blood clot during the first 24 hours. Starting on the second day, the blood clot is replaced with granulation tissue originating from the peripheral aspects of the socket. The replacement of the clot with granulation tissue was observed to be complete by day seven. The granulation tissue is then replaced with connective tissue beginning at the periphery of the socket on day four and completing by day twenty. Osteoid formation was noted on day seven and by day 38 the socket was at least two-thirds filled with bone. The epithelium migrates over the coronal aspect of the socket throughout healing and fusion of the soft tissue typically occurs in four to six weeks. By 100 days, the new bone filling the socket has radiopacity that matches the adjacent bone (Amler, Johnson et al. 1960). Evian et al. also evaluated the healing in human extraction sites and noted that cellular and connective tissue proliferation occurs four to six weeks following extraction. Active bone formation was present in the specimens gathered at four and six weeks, with reduction in osteoblastic activity noted at week eight. From week eight until week twelve, bone maturation was noted with a reduction in the amount of connective tissue present and an increase in trabeculation of the bone. At twelve to sixteen weeks post-extraction, mature trabeculation was noted in the healing site (Evian, Rosenberg et al. 1982).

The canine model has been used to further study the healing cascade and events that occur following tooth extraction. Similar to the study by Amler et al., Cardaropoli and collaborators noted that blood clot formation occurs immediately after extraction and is then replaced with
granulation tissue. A connective tissue matrix then replaced the granulation tissue and an initial bone matrix was noted at 4 weeks. The canine study by Cardaropoli et al. was able to evaluate complete sections and noted that the healing started at the apical and lateral aspects of the socket and moved coronally. In addition, morphometric measurements were completed to evaluate the volumes of various tissue types in different locations throughout healing. At day 30, mineralized bone occupied 88% of the socket. This decreased through day 180, at which time the bone marrow occupied 85% of the volume (Cardaropoli, Araujo et al. 2003).

Although preclinical canine studies have led to obtaining fundamental information to understand the healing of extraction sites, it is important to note that there are variations in the overall metabolism and healing processes in canines and humans. Therefore, the rate at which the process and healing occurs cannot be directly translated to the human model. For example, a three-week old extraction socket in humans compares with a nine to ten day old socket in dogs and the healing noted at 8 weeks in dogs is comparable to 3.5 months in humans (Pagni, Pellegrini et al. 2012).

It is also noteworthy that normal biological processes may be significantly altered by different factors that may cause healing disruptions in extraction site. An early canine study by Claflin noted that healing is delayed in disturbed extraction wounds and the regeneration of the epithelium is slowed when packing of a dressing is required for a site (Claflin 1936). A human study was also completed to evaluate disturbed healing in extraction wounds and found that various types of disturbances can occur and each type corresponds to a stage of healing. Noted disturbances include alveolar osteitis (dry socket), suppurative osteitis, necrotizing osteitis, and fibrous healing. All of the noted disruptions can be significant and may delay healing (Amler 1999).
1.5. **Alveolar Ridge Remodeling**

Aside from understanding the sequence of biological and cellular events that follow tooth extraction, it is crucial to consider and comprehend the morphological changes that occur during the ridge remodeling. As the extraction socket heals, a process of alveolar ridge reshaping takes place and continues long after the initial healing phases of the extraction site. Early studies evaluating dry skull specimens and cadaver jaws noted that edentulous specimens were shaped differently and had lost vertical height (Rogers and Applebaum 1941). It was observed that in the maxilla, the buccal plate tended to resorb quicker and tends to be related to the direction and the angulation of the roots of the teeth. Another early study was designed to evaluate the morphologic changes that occur following tooth extraction. This study compared the edentulous ridge on one side to the corresponding dentate site on the contralateral side using measurements on dental casts. It was found that the buccal plate in the maxilla underwent more resorption than the palatal plate, leading to a palatal shift of the ridge. Similar findings were noted in the mandible (Pietrokovski and Massler 1967). While there were many limitations to this study, it was one of the first studies to quantitatively evaluate the remodeling that has been qualitatively described by many authors in previous investigations.

Since this study in 1967, numerous studies have been completed in order to better understand ridge remodeling processes. Changes in ridge height and width have been noted to occur rapidly after extraction and to progressively continue for several subsequent weeks (Johnson 1969). Using a mongrel dog model, Araujo and Lindhe assessed the changes via sequential buccolingual sections of the healing sockets at different time points after extraction of the distal root of third and fourth premolars. They noted a significant resorption of the buccal plate at 8 weeks, while
the lingual plate did not show this intense resorption. The resorption of the buccal plate resulted in loss of vertical height as well as ridge width (Araujo and Lindhe 2005). Again, it is important to note that 8 weeks of healing in the canine model correlates to 3.5 months of healing in human extraction sites (Claflin 1936, Pagni, Pellegrini et al. 2012). Similar patterns of remodeling have been noted in human studies, as well (Schropp, Wenzel et al. 2003).

In a recent systematic review, it was noted that clinicians should expect a reduction in alveolar ridge width ranging from 2.6 to 4.6 mm and loss in alveolar height ranging from 0.4 to 3.9 mm after tooth extraction (Ten Heggeler, Slot et al. 2011). Another systematic review published in 2009 found that the average reduction in alveolar ridge width after tooth extraction was 3.87 mm, while the mean loss in height at the mid-buccal aspect of the extraction site was 1.67 mm (Van der Weijden, Dell'Acqua et al. 2009). Similarly, a systematic review and meta-analysis published in 2012 noted an average horizontal ridge reduction of 3.79 mm and a mean vertical reduction of 1.24 mm at the mid-buccal for hard tissues. Soft tissues were found to increase 0.4-0.5 mm in thickness on both the buccal and the lingual at 6 months. This review and meta-analysis noted that, at 6 months post-extraction, horizontal bone loss of 29-63% and vertical bone loss of 11-22% is to be expected after tooth loss (Tan, Wong et al. 2012). It is generally acknowledged that rapid remodeling and reduction in ridge dimensions take place in the first 3 to 6 months following extraction. However, after the initial maturation of the site, gradual reductions in ridge dimensions typically continue (Schropp, Wenzel et al. 2003, Tan, Wong et al. 2012).

1.6. Impact of Periodontal Phenotype on Alveolar Bone Remodeling

It is well established that all sites will undergo alveolar bone remodeling following extraction. While remodeling occurs in all cases, the magnitude of remodeling and changes in ridge volume varies between sites and individuals. This variation has led researchers to evaluate...
clinical factors, in an effort to better predict the changes that may occur. It has been postulated that the previously described increase in resorption on the buccal aspect is exacerbated in sites presenting a thin buccal plate. This can be justified because, in this bony plate, the cortical bone is contiguous with the bundle bone leading to a reduction in trabecular bone, and subsequently blood supply, which may accelerate bone resorption following tooth extraction (Pagni, Pellegrini et al. 2012). Chappuis and colleagues utilized measurements on CBCT scans to evaluate changes following tooth extraction in the anterior maxilla. It was found that a thin buccal plate (≤1 mm) resulted in an average 7.5 mm of vertical bone loss at the buccal aspect, while sites with a thick buccal plate (>1 mm) only lost an average of 1.1 mm (Chappuis, Engel et al. 2013). Barone et al. found that in molar and premolar sites with a buccal plate of 1 mm there was significantly more horizontal bone resorption (4.3 ± 0.8 mm) than in sites with a buccal plate thickness of 3 mm or more (2.6 ± 0.5 mm) (Barone, Ricci et al. 2013). A study by Spinato and Galindo-Moreno et al. also noted that a thin buccal plate is related to increased dimensional changes after tooth extraction (Spinato, Galindo-Moreno et al. 2014). Similarly, studies evaluating ridge dimension alterations following extraction and immediate implant placement have noted that a thinner buccal plate is associated with increased dimensional changes of the hard tissues (Ferrus, Cecchinato et al. 2010, Tomasi, Sanz et al. 2010, Roe, Kan et al. 2012). The results of these and similar studies show a potential relationship between aspects of the periodontal phenotype and alveolar bone remodeling following tooth extraction.

Following this review of the literature regarding both periodontal phenotype and the remodeling that occurs after tooth extraction, it is apparent that more information regarding possible correlations between local phenotypic factors and dimensional outcomes is warranted by using 3D-assessment tools to separately evaluate the effect of the soft and bone tissue
compartments. Therefore, a case series study was designed to evaluate clinical and radiographic measures in effort to better understand possible relationships and correlations.
CHAPTER 2. HYPOTHESIS AND SPECIFIC AIMS

It was hypothesized that the clinical dimensions of alveolar bone and soft tissue would impact the amount of ridge remodeling that occurs following single tooth extractions.

The primary objective of this study was to assess the effect that phenotypic characteristics of the periodontium have on the remodeling of the alveolar ridge after single tooth extraction. The secondary objectives were to explore any correlations between the periodontal phenotype (bucco-lingual) and supracrestal (apico-coronal) soft tissue dimensions in the function of ridge remodeling patterns.

The primary outcome of interest in this study was the volumetric percent reduction of the bone following single tooth extraction. Additional outcomes of interest included correlations between the volume changes (as measured from the dental casts and cone beam CTs) and patient-reported outcome measures, such as wound healing, patient satisfaction, and patient discomfort.
CHAPTER 3. METHODS AND MATERIALS

3.1. Center and Ethical Approval

The clinical component of this study was conducted in the Graduate Periodontics clinic at The University of Iowa College of Dentistry and Dental Clinics from February 2016 to June 2017. Approval was obtained from The University of Iowa Institutional Review Board in February 2016, IRB identification number 201510790. This study has been registered at clinicaltrials.gov under identifier NCT02668289.

3.2. Population

Patients in need of a dental extraction of a maxillary premolar, canine, or incisor were eligible for the study. Patients who were interested in the study and who met the initial eligibility criteria were invited to participate in the clinical screening.

3.3. Clinical Screening

At the clinical screening visit, the consent form was reviewed in depth. The subjects were required to read and sign the consent form prior to beginning the screening process. The consent form included explanation of risks and benefits as well as the study timeline. Patients were given ample time to ask any questions that may arise. All patients must have read, understood, and signed the informed consent document prior to proceeding with screening.

Patients between 18 and 75 years of age who required extraction of a single tooth in the maxillary anterior and premolar area (maxillary second premolar to second premolar, inclusive) were eligible for the study. All patients must be able and willing to follow instructions for treatment. Following review of the study purpose, timeline, and consent, a complete medical and dental history was obtained. More details regarding the study timeline can be seen in figure 1 (Figure A1).
The exclusion criteria were as follows: more than 1 mm of recession present on the tooth planned for extraction and study inclusion; reported allergy or hypersensitivity to any materials to be used in the study; severe hematologic disorders such as hemophilia or leukemia; active severe infections diseases that may compromise normal healing; liver or kidney dysfunction/failure; current cancer treatment or within 18 months of completion of cancer treatment; history of IV bisphosphonate use; long-term history of oral bisphosphonate use (i.e. 10 years or more); severe metabolic bone diseases, such as Paget’s disease; pregnant or nursing mothers or those planning to become pregnant; heavy smoking (defined as more than 10 cigarettes/day) within 6 months of study onset; uncontrolled diabetes (defined as HbA1c >7.0%); concomitant use of medications for systemic conditions that may impact study outcomes; any other non-specified reason that from the point of view of the investigators makes the candidate a non-suitable subject for the study (e.g. limited mouth opening).

Following the initial screening, eligible patients underwent a site-specific clinical and radiographic exam. A new periapical radiograph was made if a recent radiograph was not available. Candidates exhibiting clinical or radiographic signs of active periodontal disease were excluded from the study. Subjects who were excluded from the study were invited to receive comprehensive care at The College of Dentistry and Dental Clinics. During the clinical screening, an in-depth discussion of treatment options was completed and any questions patients had about those treatment options were answered. If it was determined that there was a more appropriate treatment for the patient’s clinical situation and treatment desires, they were referred to the appropriate clinic within The College of Dentistry and Dental Clinics or back to their referring general dentist.

Eligible subjects who elected to participate in the study were scheduled for baseline surgery. At the time of the screening visit, an intraoral impression was made using Imprint 4 VPS
impression material (3M, St. Paul, MN). The impression was poured in microstone and within the timing guidelines given for the impression material according to manufacturer’s instructions.

3.4. Baseline Surgical Appointment

Prior to any study-related treatment at each visit, health history was reviewed and updated and eligibility for study participation was confirmed. Immediately prior to the surgical intervention, a cone beam computed tomography (CBCT) scan was obtained in the Department of Radiology (i-CAT, Imaging Sciences International). The scan was limited to the maxillary arch containing the tooth of interest in order to minimize radiation exposure to the patient. Protective lead apron was used for all patients. The field of view was 6 cm and the parameters were fixed at 120 kVp and 18.66 mAs with voxel size of 0.3 for all scans.

All surgical procedures were performed under local anesthesia. Prior to tooth extraction, clinical measurements of the supracrestal soft tissue were made as well as evaluation of plaque levels (Quigley and Hein 1962) (Turesky, Gilmore et al. 1970). Figure 4 displays the chart utilized to document plaque levels (Figure A4). The mucogingival junction was demarcated in the area using Schiller iodine solution (Maurer, Hayes et al. 2000). The width of keratinized gingiva was then measured at the mid-buccal point using a UNC-15 probe. The amount of recession was recorded when the CEJ could be identified. Probing depths were recorded at six sites on the tooth in question and bleeding on probing was reported. Bone sounding was then recorded at six sites on the tooth to be extracted.

The tooth extraction was completed in a minimally traumatic manner using microelevators and forceps. Trauma to adjacent soft tissues and alveolar bone was minimized. Following extraction, the socket was gently curetted and additional clinical measurements were completed. Blunt 2 Iwanson spring calipers (Hu-Friedy, Chicago, IL) were used 1 mm apical to the gingival
margin at the mid-buccal and mid-palatal to measure the thickness of the soft tissue. Pointed 1
Iwanson spring calipers (Hu-Friedy, Chicago, IL) were utilized 1 mm apical to the bone crest at
the mid-buccal and mid-palatal to measure the thickness of the bone. In order to accurately
determine the correct location for bone measurement, the distance from the free gingival margin
to the crest of the bone was directly measured using a UNC-15 probe. One millimeter was then
added to this measurement and the soft tissue was perforated using the UNC-15 probe at this depth
from the free gingival margin. Baseline intervention and clinical measurements are depicted in
figure 2 (Figure A2). More details regarding the location of bone and soft tissue thickness
measurements can be seen in figure 3 (Figure A3).

If a dehiscence of the bony socket was noted after tooth extraction, it was discussed with
the patient and they were given the option to have a ridge preservation procedure if desired. If the
patient elected for the ridge preservation procedure, they were then excluded from further study
procedures.

Detailed verbal and written post-operative instructions were given to the patients. Patients
were advised to take over-the-counter ibuprofen as needed for discomfort. No antibiotics were
prescribed unless patients reported signs of infection post-operatively.

3.5. Follow-up Appointments

3.5.1. Two-Week Post-Operative Visit

At the two-week post-operative visit, the wound healing was assessed using a modified
wound healing scale (Figure A5). Plaque levels on the teeth directly adjacent to the extraction site
were recorded, when applicable. Patients were asked to rate their discomfort following the surgical
procedure using a Visual Analog Scale (VAS) (Figure A6). Two-week post-operative photos can
be seen in figure 7 (Figure A7).
3.5.2. **Fourteen-Week Post-Operative Visit**

At the fourteen-week post-operative visit, clinical evaluation was again completed by the same calibrated periodontal resident (SR) that performed all clinical measurements throughout the study. Keratinized gingiva width was again measured and plaque levels were evaluated and recorded on the teeth adjacent to the extraction site (if applicable). Modified healing index was evaluated and recorded. Patients were asked to rate the overall discomfort that they experienced during this study, as well as their overall satisfaction with their study participation (Figure A6, Figure A8). Following clinical evaluation, another maxillary impression was made using Imprint 4 VPS impression material (3M, St. Paul, MN). The patient was then sent to the Department of Radiology for a second CBCT scan. Patients seeking tooth replacement options or who had the desire to seek additional treatment were scheduled in the appropriate clinic for further treatment outside of the study. An example of typical clinical appearance of the site at 14 weeks can be seen in figure 9 (Figure A9).

3.6. **Radiographic Evaluation**

A single examiner (SR) performed the three-dimensional radiographic evaluations. The CBCT volumetric datasets were exported as digital imaging and communication in medicine (DICOM) files which were opened with the program Simplant 16 Pro by Materialise (Dentsply Implants, Waltham, MA). With this program, a volume of interest (VOI) was selected (Figure A10). The soft tissue was separated from the hard tissues using a constant threshold across all scans. Volumetric analysis was performed on the alveolar bone to evaluate the volumetric changes. The baseline and 14-week follow-up scans were opened simultaneously in side-by-side windows to ensure the use of the same landmarks. The VOI was selected using the adjacent teeth and landmarks as reference points. Boundaries were a horizontal plane apical to the root tip, vertical...
boundaries from the midpoint of the interproximal space on either side to the horizontal plane apical to the root apex, and the facial and bony plates. The total volume in cubic mm (mm$^3$) of the VOI was then quantified. The absolute volume loss and percentage of volume lost could then be calculated by the examiner (SR).

The same examiner (SR) used the CBCT data to make bucco-lingual ridge width measurements and mid-buccal and mid-palatal height measurements. These linear measurements were made using the InVivo 5.4 software (Anatomage, San Jose, CA). The CBCT scans were again opened simultaneously in side-by-side windows and oriented on the same plane. A specific landmark was selected to identify the same section and plane in each scan. The change in linear measurement was calculated to determine the change in ridge width (Figure A12), as well as the mid-buccal and mid-palatal changes in vertical height (Figure A13).

3.7. Evaluation of Dental Casts

As previously mentioned, each impression was poured in microstone according to the manufacturer’s recommendations. The casts were then trimmed and any supragingival tooth structure of the extracted tooth was carefully removed from the baseline cast. All casts included the depth of the vestibule. The cast with the shallowest vestibule was used as the reference to ensure that the same apico-coronal height was evaluated in all subjects. It was noted that the shallowest vestibule was 6 mm from the gingival margin of the extracted tooth and the teeth adjacent to the extracted tooth. All casts were then marked 6 mm from the gingival margin of the extracted tooth. In order to identify the same distance on the 14-week follow-up casts, adjacent teeth and landmarks were utilized along with a straightedge. The markings were then removed with a bur to create a notch and to ensure they would appear on the digital scan of the casts. A digital scan of the sextant was then completed using the True Definition scanner (3M Unitek,
Monrovia, CA). The scans were exported as stereolithography (STL) files for further analysis. The digital scan information was then evaluated by a single examiner (SR) to determine the volumetric changes from baseline to 14-weeks. The STL file was opened using Meshmixer (Autodesk, San Rafael, CA) where the surface was made into a digital solid (Figure A14). The baseline and 14-week follow-up scans were open in the same environment and oriented to align using adjacent teeth as landmarks. The plane cut tool was then used to trim the digital cast to a selected VOI (Figure A15). The mesial and distal sections were created using the mid-interproximal as the landmark. The marks placed at 6 mm acted as the guide for the horizontal plane at the apical portion. The trimmed sections were then opened in Netfabb (Autodesk, San Rafael, CA) to calculate the volume of the selected area in mm³ (Figure A16).

3.8. Examiner Calibration

The examiner (SR) obtained probing depth measurements and bone sounding measurements on a volunteer in the same manner as completed for each study subject. Measurements were repeated at a separate time. For linear and volumetric CBCT data and volumetric cast data, measurements were repeated 7-14 days later and analyzed for reliability using a nonparametric measure of intra-class correlation as described by Rothery (Rothery 1979). The reliability analysis was completed using the statistics software R version 3.4.0 (Vienna, Austria).

3.9. Power Analysis

Sample size calculations were completed with the aim to provide adequate power for the primary outcome of interest – percentage change in ridge (hard and soft tissues) from baseline to 14 weeks following single tooth extraction. Based upon the findings of a previous study conducted within the Department of Periodontics at the University of Iowa College of Dentistry, a 10-20% reduction in the volume must be detectable (Gubler 2015).
Based upon calculations, 60 subjects would be required to detect relationships between two quantitative variables. This would allow for detection of correlations of 0.392 or greater with at least 90% power and correlations of 0.345 or greater with at least 80% power. In addition, a sample size of 60 would allow for reasonable comparison of up to six explanatory variables in multiple regression models.

3.10. Statistical Analysis

Statistical analyses were performed to summarize the data and to assess possible relationships between the extent of remodeling (percent volumetric reduction) and the measures of periodontal phenotype. Univariate statistics were calculated where appropriate to summarize the assessed variables. Descriptive statistics will utilize standard deviation. Bivariate statistics included Spearman correlations and Kruskal Wallis Test. The Spearman correlations were used to assess possible correlations between the extent of remodeling and measures of periodontal phenotype as well as correlations between the various measures of periodontal phenotype. Correlations between volumetric measurements and CBCT linear measurements were also assessed using Spearman correlations. The Kruskal Wallis Test was used to test for differences in extent of remodeling between male and female patients as well as differences between baseline and final measurements of keratinized gingiva width. Modeling was used to attempt to predict volume change from clinical variables. The model selection used to predict the volumetric change used variables that were shown to be significant correlated with the outcome variable. From that set, the best subsets model selection method was used with AIC as the criteria. The model with the lowest AIC was selected as the final model. Regression assumptions were verified. These calculations were carried out by a single statistician (A.W.) using the software SAS version 9.4 (Cary, NC). All calculations were carried out at the 5% significance level.
CHAPTER 4. RESULTS

4.1. Study Population

33 patients were appointed for clinical screening for study participation. One subject never completed the consent or screening process, as he was unable to read the consent due to visual impairment. Three patients did not qualify due to unstable periodontal status, two did not qualify due to lack of indication for extraction upon clinical evaluation, one was excluded due to smoking history, and one was excluded due to systemic health conditions. Four patients decided not to participate in the study after explanation of the study procedures and discussion of alternate treatment options. Twenty one (21) patients were accepted into the study for treatment. A total of nineteen patients (11 males and 8 females) completed the study and their data were included in the analysis. One patient did not complete the study and was lost to follow-up due to distance to the clinic, one patient has not yet completed the 14-week follow-up visit. This study did not meet the power analysis criteria due to unforeseen difficulty in patient recruitment.

4.2. Examiner Calibration

Reliability analysis was done using non-parametric measure of intraclass correlation (Rothery 1979) via the statistical software R version 3.4.0 (Vienna, Austria). This statistic can be interpreted in the same manner as an intra-class correlation coefficient (Rothery 1979, Cicchetti 1994). A total of 19 CBCT volumetric measurements were made and then repeated in a separate session. The reliability was found to be excellent at 0.961. Sixteen CBCT linear measurements were made and then repeated in separate sessions with a reliability statistic of 0.943 for buccal height change, 0.969 for palatal height change, and 0.968 for horizontal change. All linear reliability statistics can be interpreted as excellent. 18 volumetric measurements of the scanned dental casts were made and repeated in a separate session. The reliability statistic for this measure
was 0.948 which is also considered to be excellent. A total of 12 clinical measurements (6 probing depths and 6 bone sounding measurements) were made in two separate clinical sessions. All correlating measurements were within 1 mm of each other.

4.3. Baseline Parameters

The mean age of the study subjects was 55.42 ± 14.42 years (Table B1). The sites included in the study were maxillary central incisors (0), maxillary lateral incisors (2), and maxillary premolars (17 total: 10 first premolars, 7 second premolars). A breakdown of the treated sites is listed in Table 2 (Table B2). The average Plaque Index (PI) score was 0.92 (buccal: 0.84, palatal: 1.0) with a median score of 1 (range 0-3) at the baseline visit. The overall frequency of bleeding on probing for all sites was 37.72%. A breakdown of bleeding on probing by site is listed in Table 3. (Table B3).

Baseline probing depths were measured at six sites (i.e. mesiobuccal, midbuccal, distobuccal, mesiolingual, midpalatal, and mesiodistal). Average probing depth at all sites was 2.52 mm with a median of 2.5 mm. A complete breakdown of probing depth by site is listed in Table 4 (Table B4). Bone sounding was also completed at those six sites at baseline to assess the vertical dimension of the supracrestal soft tissue. Average dimension of the supracrestal soft tissue was 4.15 mm with a median of 4 mm. See Table 5 for a complete breakdown of bone sounding measurements by site (Table B5).

The average buccal soft tissue thickness was 0.49 mm (median: 0.50 mm, SD: 0.18) and the average palatal soft tissue thickness was 0.68 mm (median: 0.70, SD: 0.18). The average buccal plate thickness was 1.09 mm (median: 0.90, SD: 0.64) and the average palatal plate thickness was 1.27 mm (median: 1.40 mm, SD: 0.42). The average baseline width of keratinized mucosa was
4.47 mm (median: 4.50, SD: 1.60). A complete breakdown of these measurements can be seen in Table 6 (Table B6).

4.4. Wound Healing

Two minor post-operative complications were noted. One patient reported slightly altered sensation in the lip adjacent to the study extraction site. This resolved within two weeks of the patient reporting it. Another patient presented to the two week post op visit with increased inflammation and slight suppuration at the extraction site. Systemic antibiotic was prescribed and the patient reported resolution within 3 days. Though this complication was resolved, the patient was later lost to follow-up due to distance from the clinic. The average Modified Would Healing Scale (MWHS) score at the 2-week post-op was 1.42 ± 0.49 (median: 1). The average MWHS at the 14-week follow-up was 1.05 ± 0.22 (median: 1). Table 7 includes a summary of the data regarding MWHS (Table B7).

4.5. Patient Reported Outcomes

A Visual Analog Scale (VAS) was used to rate patient discomfort at follow-up visits and patient satisfaction at the 14-week follow-up visit. Patient discomfort level was reported at the 2-week follow-up appointment and at the 14-week follow-up appointment. At the 2-week post-op, the average discomfort was 14.57 ± 15.34 (median: 10.00, range: 0.00-46.92). At 14-weeks, the patients rated the overall discomfort throughout the study at 8.23 ± 13.11 (median: 3.64, range: 0.00-52.73). See Table 8 for a summary of patient discomfort (Table B8).

Patient satisfaction regarding the overall treatment and study participation was evaluated at the 14-week appointment. Patients reported very high satisfaction of 96.41 ± 4.51 overall (median: 98.18, range: 85.45-100.00).
4.6. **Linear Radiographic Evaluations**

Linear ridge width and height was measured on the CBCT scans at baseline and 14-week follow-up. The average loss of ridge width was $1.66 \pm 1.00$ mm (median: $1.44$ mm, range: 0.42-4.33 mm). Linear ridge height was measured on the CBCT at both the buccal and palatal aspects at baseline and at the 14-week follow-up. The average loss of ridge height was $1.10 \pm 0.67$ mm (median: $0.92$ mm, range: 0.23-2.38 mm) at the buccal and $1.36 \pm 0.66$ mm (median: $1.31$ mm, range: 0.49-3.16 mm) at the palatal. See Table 9 for complete details regarding linear radiographic changes (Table B9).

4.7. **Volumetric Evaluations**

The volume of the ridge on the CBCT was calculated at baseline and at the 14-week follow-up. The average volume of the selected area was 756.37 mm$^3$ at baseline and 554.09 mm$^3$ at the 14-week follow-up. The average reduction in raw measurement was 202.28 mm$^3$ (median: 186.47mm$^3$) and the average percent reduction in volume was 26.42% (median: 26.17%, SD: 13.63%).

The volume of the ridge on the scanned casts was calculated at baseline and at the 14-week follow-up. The average volume of the selected area was 565.38 mm$^3$ at baseline and 456.68 mm$^3$ at the 14-week follow-up. The average reduction in raw measurement was 109.02 mm$^3$ (median: 103.20 mm$^3$) and the average percent reduction in the volume was 18.89% (median: 20.16%, SD: 9.55%). Complete breakdown of volumetric measurements can be seen in Table 10 (Table B10).

4.8. **Correlations and Modeling**

When evaluating the possible correlations between baseline clinical measurements and ridge volume reduction, it was noted that statistically significant, positive correlations were noted between the volumetric change of the casts and probing depths (mesiobuccal, mesiopalatal, and
distopalatal) as well as between the volumetric change of the casts and bone sounding measurements (mesiobuccal, distobuccal, mesiopalatal, and distopalatal). Table 11 shows more information regarding these correlations (Table B11). In addition, the volumetric change of hard tissues on the CBCT had a significant positive correlation with mesiopalatal probing depth and buccal mucosa thickness. See Table 12 for more details regarding these correlations (Table B12).

When evaluating correlations between measurements relating to periodontal phenotype and the supracrestal soft tissue dimension, significant positive correlations were noted between palatal mucosa thickness and bone sounding measurements at multiple locations (mesiobuccal, mesiopalatal, and midpalatal). Many of the bone sounding measurements showed significant positive correlations between various sites. No significant differences were noted between the width of keratinized mucosa at baseline and at 14-weeks.

Statistically significant correlations were noted between the amount of linear horizontal change measured on the CBCT and the baseline thickness of the buccal plate. This was a negative correlation so as the buccal plate thickness increases, the reduction in horizontal linear ridge width decreases (rs = -0.66418, p-value = 0.0019). The linear buccal height change measured on the CBCT showed a statistically significant, positive correlation with the horizontal linear ridge width change (rs = 0.55707, p-value = 0.0132) and a statistically significant, negative correlation with the palatal plate thickness (rs = -0.4709, p-value = 0.0419). The linear palatal height change measured on the CBCT also showed statistically significant, positive correlation with the horizontal linear ridge width change (rs = 0.54234, p-value = 0.0164).

Using modeling techniques to attempt to predict volumetric changes, the following was found. A statistically significant model for the percentage of change in hard tissue volume via CBCT was found with buccal mucosa thickness as the predictor variable. For each millimeter of
increase in buccal mucosa thickness, an increase of 37.24% in volumetric reduction is expected based on this model (p-value = 0.0301). All model assumptions were found to be satisfied. A statistically significant model was also found for the percentage of change in soft and hard tissue volume via dental cast and mesiobuccal bone sounding. For every millimeter increase in mesiobuccal bone sounding, an increase of 5.43% in volumetric reduction is expected (p-value = 0.0061).
CHAPTER 5. DISCUSSION

The primary aim of this study was to evaluate the effects that phenotypic characteristics (width of keratinized tissue, soft tissue thickness, etc) of the periodontium have on the remodeling of the alveolar ridge after single tooth extraction. The secondary aims were to explore any correlations between the periodontal phenotype (bucco-lingual) and supracrestal (apico-coronal) soft tissue dimensions and to attempt to develop a classification system for overall periodontal phenotype.

Many previous studies have evaluated the dimensional and morphologic changes that take place following tooth extraction. A canine model in a study published by Araujo and Lindhe noted that more significant resorption occurs at the buccal plate while the lingual, or palatal, plate is not typically impacted in the same manner (Araujo and Lindhe 2005). Similar patterns have been noted in human studies as well (Schropp, Wenzel et al. 2003) with recent systematic reviews focusing on the linear quantity of height and width loss after healing. Systematic reviews have noted an average horizontal ridge reduction of approximately 3.8 mm and an average loss of buccal height of 1.25-1.67 mm (Van der Weijden, Dell'Acqua et al. 2009, Tan, Wong et al. 2012). Our study found a lower magnitude of ridge width loss (1.66 ± 1.00 mm) than noted in these reviews; however, the loss of buccal ridge height (1.10 ± 0.67 mm) is comparable to the values found in these reviews. It is important to point out that in the review by Van der Weijden et al, the radiographic horizontal ridge reduction was much lower than the clinical reduction of width at only 1.21 mm. In both systematic reviews discussed here, only two studies were included that utilized cone beam scans to evaluate the changes in hard tissues. These two studies (Fiorellini, Howell et al. 2005, Kerr, Mealey et al. 2008) are difficult to compare to our present study due to variations in measurement techniques and the included types of teeth. The lower degree of ridge
width loss is likely impacted by the fact that nearly all of the teeth included in our study were maxillary premolars (17/19). In general, the buccal bone at maxillary premolar sites tends to be thicker than in the canine to canine region (Huynh-Ba, Pjetursson et al. 2010, Braut, Bornstein et al. 2011, Wang, Shen et al. 2014). A study by Huynh-Ba et al noted the average width of buccal bone at maxillary premolars to be 1.1 mm while the thickness from maxillary canine to canine is 0.8 mm on average (Huynh-Ba, Pjetursson et al. 2010). This difference in bone thickness likely contributes to the differences observed. The inherent variation in CBCT measurements is another possible explanation for the lower than expected change in horizontal width. While efforts were made to standardize the measurements as much as possible, the reference point could vary slightly between scans and difficulty was experienced in identifying the bone in some cases. A past study evaluating bone dimensions using CBCT scans of the anterior region noted that in some cases the buccal plate was “missing” or unable to be identified in 10% of teeth (Braut, Bornstein et al. 2011). Though measurements were difficult, high reliability was noted upon analysis of repeated measurements (0.968).

While the previously noted studies have evaluated the dimensional changes that occur in a linear fashion, fewer studies have evaluated these changes volumetrically. A study by Thalmair et al. evaluated the volumetric changes of the entire ridge (hard and soft tissues) following multiple treatment modalities. In a control group with only simple extraction, the reduction in ridge volume was found to be $41.41 \pm 15.96 \text{ mm}^3$ (Thalmair, Fickl et al. 2013). It is difficult to extrapolate this measurement to the raw volumetric changes seen on the casts in our study ($109.02 \pm 57.20 \text{ mm}^3$) as the methodologies and size of the regions selected varied between studies.

Similar to our study, Chappuis et al. evaluated the changes in the hard tissues utilizing two CBCT scans; however the data was not expressed in terms of volume (Chappuis, Engel et al. 2013).
Therefore, it is again difficult to compare the findings in that study to the findings in our study. It is important to note that while the study by Chappuis et al. did not assess volume changes, they did note a relationship between the amount of vertical bone loss and the thickness of the buccal plate at the time of the extraction. Similarly, Barone and colleagues found that the extent of ridge remodeling appeared to have a relationship with the thickness of the buccal plate (Barone, Ricci et al. 2013). This finding was reiterated in a more recent study by Spinato and Galindo-Moreno et al (Spinato, Galindo-Moreno et al. 2014). Aside from these studies, there are few studies that attempt to relate the degree of dimensional change to the overall periodontal phenotype and measurements of the soft and hard tissues in the area. The present study was designed in attempt to fill this void in the literature.

While buccal bone thickness did not directly correlate with the amount of volumetric change, our study did note significant correlations with various linear changes. The degree of linear horizontal width loss noted on the CBCT had a statistically significant negative correlation with the buccal plate thickness at the time of extraction (rs = -0.66, p-value = 0.0019). This indicates that a thinner buccal plate is correlated with increased loss of horizontal bone width. This finding is in agreement with the previously mention studies. Similarly, correlations were noted between the linear buccal height change and the horizontal width change (rs = 0.56, p-value = 0.0132) and the thickness of the palatal plate (rs = -0.47, p-value = 0.0419). Additionally, the linear palatal height change is correlated to the horizontal width change (rs = 0.54, p-value = 0.0164). It is interesting to note the correlation seen between the buccal height change and the palatal plate thickness. Due to the small sample size this may be an erroneous relationship, or it may indicate a potential impact of the overall periodontal phenotype.
The fact that a relationship between buccal bone thickness and the volumetric changes is not seen can likely be explained by the methodology utilized for calculating the change in volume of the hard tissues. The initial CBCT scan of hard tissues included the root of the tooth that was to be extracted for the study. Though the VOI was selected in a manner which would allow for any supracrestal tooth structure to be removed, the root of the tooth is comprised of tissues that are of higher mineral content than that of bone. Once the tooth was removed and the ridge had healed for 14 weeks, there were typically areas of less mineralized bone that would not appear as hard tissue in the VOI. A previous study has noted that on CBCT scans, the mineral density of cementum has a range of 1240-1340 mg/cc and dentin has a mineral density of 1480-1590 mg/cc while bone has a much larger range at 570-1415 mg/cc (Djomehri, Candell et al. 2015). In general, this led to an overestimation of the amount of volumetric change that occurred in the hard tissues as depicted on the CBCT. Attempts to lower the scan threshold to capture an increased amount of the less mineralized tissue led to increased scatter and artifact in the scans and therefore, less reliability. The lack of a relationship between buccal bone thickness and volumetric change in this study also may be due the previously mentioned high proportion of premolar sites as well as the fact that the average buccal bone thickness was greater than 1 mm.

When comparing the volumetric changes seen in the CBCT analysis to the volumetric changes seen in the analysis of the digitized casts, no correlation was noted. This finding is not surprising as changes in the soft tissue can mask the degree of remodeling that occurs in the alveolar bone. Chappuis and colleagues found that soft tissue thickness increased 7-fold in site with a thin bone phenotype and results in masking of the underlying bone deficiency (Chappuis, Engel et al. 2015). This change occurred despite similar baseline soft tissue thickness and highlights the importance of adequate diagnostic imaging when planning for implant therapy.
It is interesting to note that in this study, the buccal tissue width was the most significant variable in regard to predicting the percentage of volumetric change of the hard tissue volume on the CBCT scan. While this could be attributed to the small sample size, the methods used for selecting the model aid in adjusting for small sample size. Additionally, the model was found to be statistically significant (p-value = 0.0301) and the degree of the relationship was large (coeff = 37.24). It is possible that this relationship could be related to patient soft tissue and collagen metabolism or potential increased likelihood of rapid soft tissue migration into the extraction site. This brings to light the importance of focusing on the entire periodontal phenotype rather than only buccal bone thickness but also this also emphasizes the many, potentially confounding, variables related to the degree of alveolar ridge remodeling.

When using the same modeling techniques to attempt to predict volumetric changes in both the hard and soft tissues as measured on the digitized dental casts, a statistically significant model (p-value = 0.0061) was found for mesiobuccal bone sounding (coeff = 5.43). This relationship may be explained by the fact that with an increased height of supracrestal soft tissue, there is more potential for reduction of soft tissue and therefore more potential for loss of volume. Bone sounding has been found to match direct measurement of the supracrestal soft tissue height 83.2% of the time and is within 1 mm 87.9% of the time (Kan, Kim et al. 2017). While there can be a large range of difference between the two measurements, overall bone sounding is considered to be an accurate, minimally invasive method for measuring the supracrestal soft tissue height. It is important to note that correlations were seen between all interproximal measurements of bone sounding and the overall volume change as assessed by the digitized cast and Spearman correlations. This correlation was not seen with the bone sounding measurements at the mid-buccal or the mid-palatal sites. As expected, when evaluating correlations between parameters of
periodontal phenotype, various sites of bone sounding were often noted to be correlated. No statistically significant correlations were noted between the parameters typically considered in the evaluation of periodontal phenotype (buccal soft tissue thickness and buccal bone thickness) and the supracrestal soft tissue dimensions.

Patient reported outcomes revealed that overall, patients were very satisfied with their participation in the study and overall perception of discomfort was low. There was a large range of discomfort levels at both the 2-week post-op and the 14-week follow-up visit; however, in general, patients had low levels of discomfort.

The follow-up for this study design was 14 weeks following the baseline intervention of tooth extraction. This time point is based upon past studies and the available literature regarding the healing of the alveolar ridge following tooth extraction. Past histology studies completed on human samples have found that at 14 weeks, a calcified lamellar matrix of bone is expected to be present. The radiographic appearance of the bone in the extraction site has been found to match the adjacent bone at approximately 100 days follow extraction (Amler, Johnson et al. 1960, Evian, Rosenberg et al. 1982). Additionally, it has been noted that the most rapid remodeling of the alveolar ridge occurs in the initial 3 months following extraction (Schropp, Wenzel et al. 2003, Tan, Wong et al. 2012). Fourteen weeks was selected in order to best evaluate the dimensional changes that occur in a reasonable amount of time for patient follow-up and to avoid any disruptions in the sequence of patient care.

While statistically significant correlations were noted in the present study, further clinical studies are needed to better understand the relationships between the periodontal phenotype and alveolar ridge remodeling after tooth extraction.
CHAPTER 6. CONCLUSIONS

The purpose of this study was to evaluate the volumetric changes that occur following single tooth extraction and possible relationships between these changes, measurements of periodontal phenotype, and supracrestal soft tissue dimensions. According to the results of this study, the thickness of the buccal plate at the time of the extraction is related to the amount of reduction in alveolar bone width that occurs after 14 weeks of healing. A thicker buccal plate was correlated with less reduction in alveolar bone width. Additionally, it was noted that increased buccal mucosa thickness may be predictive of an increased volumetric loss of alveolar bone. The relatively small sample size was a significant limiting factor in the data analysis, therefore additional studies with larger sample sizes are needed.
APPENDIX A – FIGURES

**Figure A1.** – Study Timeline

**Figure A2.** – Baseline Measurements and Surgery
Figure A3. – Diagram of Clinical Measurements

- A - Buccal mucosa thickness
- B - Lingual mucosa thickness
- C - Buccal bone thickness
- D - Lingual bone thickness
- E - Keratinized mucosa width

Figure A4. – Plaque Index

| PLAQUE INDEX (Quigley Hein – Modified By Turesky et al. 1970) |
|---------------------------------|---------------|------------------|------------------|------------------|------------------|
| 0  | No plaque                      | 1  | Cervical plaque flecks | 2  | Thin layer, <1 mm    | 3  | >1mm, but <1/3   | 4  | >1/3, but <2/3   | 5  | >2/3 covered     |
| B  | L                             | B  | L                        | B  | L                         | B  | L                         | B  | L                         |

Figure A5. – Modified Wound Healing Index

| Modified Wound Healing Scale (Mod-CWHS) |
|-----------------------------------------|-------------------------------------|
| 1 | Uneventful wound healing with no gingival edema, erythema, suppuration, discomfort or graft exposure |
| 2 | Uneventful wound healing with slight gingival edema, erythema, or discomfort but no suppuration |
| 3 | Poor wound healing with significant gingival edema, erythema, discomfort, loss of graft or any suppuration |

Figure A6. – Visual Analog Scale used for patient reported discomfort

<table>
<thead>
<tr>
<th>DISCOMFORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less ------</td>
</tr>
</tbody>
</table>
Figure A7. – 2-week Follow-up

Figure A8. – Visual Analog Scale used for patient satisfaction

<table>
<thead>
<tr>
<th>How satisfied are you after participating in the study?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less:.......................................................................... More</td>
</tr>
</tbody>
</table>

Figure A9. – 14-Week Follow-up
Figure A10. – Selection of VOI on CBCT

Figure A11. – Example of Baseline and 14-Week VOI selection
**Figure A12.** – Linear Ridge Width on CBCT

Baseline | 14-Week

**Figure A13.** – Linear Buccal and Palatal Height on CBCT

Baseline | 14-Week
Figure A14. – Digitized Cast Section

Figure A15. – Selected Area of Interest from Digitized Cast

Figure A16. – Example of Volumetric Change from Digitized Cast
Figure A17. – Scatterplot with LOWESS for Buccal Plate Thickness vs. Horizontal Change

![Buccal Plate Thickness vs Horizontal Change](image)

Figure A18. – Scatterplot with LOWESS for Palatal Height Change vs. Horizontal Change

![Palatal Height Change vs Horizontal Change](image)
Figure A19. – Scatterplot with LOWESS for Palatal Plate Thickness vs. Buccal Height Change

Figure A20. – Scatterplot with LOWESS for Horizontal Change vs Buccal Height Change
APPENDIX B – TABLES

Table B1. – Baseline Patient Based Parameters

<table>
<thead>
<tr>
<th>Baseline Parameter</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age (years)</td>
<td>55.42 ± 14.42*</td>
</tr>
<tr>
<td>Gender</td>
<td>F-8; M-11</td>
</tr>
<tr>
<td>BMI</td>
<td>29.4 ± 3.7*</td>
</tr>
</tbody>
</table>

*Standard deviation

Table B2. – Extraction Numbers by Site

<table>
<thead>
<tr>
<th>Tooth Type</th>
<th>Number Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxillary Central Incisors</td>
<td>0</td>
</tr>
<tr>
<td>Maxillary Lateral Incisors</td>
<td>2</td>
</tr>
<tr>
<td>Maxillary Canines</td>
<td>0</td>
</tr>
<tr>
<td>Maxillary First Pre-Molars</td>
<td>10</td>
</tr>
<tr>
<td>Maxillary Second Pre-Molars</td>
<td>7</td>
</tr>
</tbody>
</table>

Table B3. – Bleeding on Probing by Site

<table>
<thead>
<tr>
<th>Area</th>
<th>Frequency with BOP (N = 19)</th>
<th>Percent with BOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesio buccal</td>
<td>6</td>
<td>31.58</td>
</tr>
<tr>
<td>Mid buccal</td>
<td>2</td>
<td>10.53</td>
</tr>
<tr>
<td>Disto buccal</td>
<td>9</td>
<td>47.37</td>
</tr>
<tr>
<td>Disto palatal</td>
<td>10</td>
<td>52.63</td>
</tr>
<tr>
<td>Mid palatal</td>
<td>8</td>
<td>42.11</td>
</tr>
<tr>
<td>Meso palatal</td>
<td>8</td>
<td>42.11</td>
</tr>
</tbody>
</table>

Table B4. – Baseline Probing Depths (mm)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesio buccal Probing Depth</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>2.84</td>
<td>0.76</td>
</tr>
<tr>
<td>Meso palatal Probing Depth</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>2.89</td>
<td>0.74</td>
</tr>
<tr>
<td>Mid buccal Probing Depth</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1.63</td>
<td>0.50</td>
</tr>
<tr>
<td>Mid palatal Probing Depth</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>2.16</td>
<td>0.69</td>
</tr>
<tr>
<td>Disto buccal Probing Depth</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>2.74</td>
<td>0.65</td>
</tr>
<tr>
<td>Disto palatal Probing Depth</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>2.89</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Table B5. – Baseline Bone Sounding (mm)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesial Buccal Bone Sounding</td>
<td>3</td>
<td>6.5</td>
<td>4</td>
<td>4.39</td>
<td>1.06</td>
</tr>
<tr>
<td>Mesial palatal Bone Sounding</td>
<td>3</td>
<td>6</td>
<td>4</td>
<td>4.47</td>
<td>1.07</td>
</tr>
<tr>
<td>Mid Buccal Bone Sounding</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>2.97</td>
<td>0.68</td>
</tr>
<tr>
<td>Mid palatal Bone Sounding</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td>4.32</td>
<td>1.00</td>
</tr>
<tr>
<td>Distal buccal Bone Sounding</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td>4.21</td>
<td>1.03</td>
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<tr>
<td>Distal palatal Bone Sounding</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td>4.53</td>
<td>1.22</td>
</tr>
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</table>
### Table B6. – Baseline Clinical Measurements (mm)

<table>
<thead>
<tr>
<th>Variable</th>
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<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
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</thead>
<tbody>
<tr>
<td>Buccal Mucosa thickness</td>
<td>0.20</td>
<td>0.90</td>
<td>0.50</td>
<td>0.49</td>
<td>0.18</td>
</tr>
<tr>
<td>Palatal Mucosa thickness</td>
<td>0.30</td>
<td>1.10</td>
<td>0.70</td>
<td>0.68</td>
<td>0.18</td>
</tr>
<tr>
<td>Buccal bone thickness</td>
<td>0.20</td>
<td>2.40</td>
<td>0.90</td>
<td>1.09</td>
<td>0.64</td>
</tr>
<tr>
<td>Palatal bone thickness</td>
<td>0.40</td>
<td>2.00</td>
<td>1.40</td>
<td>1.27</td>
<td>0.42</td>
</tr>
<tr>
<td>Keratinized gingiva width</td>
<td>0</td>
<td>6.50</td>
<td>4.50</td>
<td>4.47</td>
<td>1.60</td>
</tr>
</tbody>
</table>

### Table B7. – Wound Healing Index at Follow-up Appointments

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1.42</td>
<td>0.49</td>
</tr>
<tr>
<td>14 weeks</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1.05</td>
<td>0.22</td>
</tr>
</tbody>
</table>

### Table B8. – Patient Reported Discomfort

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td>0</td>
<td>46.92</td>
<td>10</td>
<td>14.57</td>
<td>15.34</td>
</tr>
<tr>
<td>14 weeks</td>
<td>0</td>
<td>52.73</td>
<td>3.64</td>
<td>8.23</td>
<td>13.11</td>
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</tbody>
</table>

### Table B9. – Linear Radiographic Dimension Changes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBCT buccal height change</td>
<td>0.23</td>
<td>2.38</td>
<td>0.92</td>
<td>1.10</td>
<td>0.67</td>
</tr>
<tr>
<td>CBCT palatal height change</td>
<td>0.49</td>
<td>3.16</td>
<td>1.31</td>
<td>1.36</td>
<td>0.66</td>
</tr>
<tr>
<td>CBCT horizontal change</td>
<td>0.42</td>
<td>4.33</td>
<td>1.44</td>
<td>1.66</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Table B10. – Volumetric Ridge Changes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Volume CBCT (mm³)</td>
<td>478.98</td>
<td>940.72</td>
<td>773.83</td>
<td>756.37</td>
<td>127.91</td>
</tr>
<tr>
<td>Final Volume CBCT (mm³)</td>
<td>325.82</td>
<td>771.35</td>
<td>568.50</td>
<td>554.09</td>
<td>128.48</td>
</tr>
<tr>
<td>Raw Change CBCT (mm³)</td>
<td>12.56</td>
<td>431.23</td>
<td>186.47</td>
<td>202.28</td>
<td>116.53</td>
</tr>
<tr>
<td>Percent Change CBCT (%)</td>
<td>1.62</td>
<td>49.49</td>
<td>26.17</td>
<td>26.42</td>
<td>13.63</td>
</tr>
<tr>
<td>Initial Volume Cast (mm³)</td>
<td>303.04</td>
<td>796.79</td>
<td>595.89</td>
<td>565.68</td>
<td>122.12</td>
</tr>
<tr>
<td>Final Volume Cast (mm³)</td>
<td>289.71</td>
<td>717.46</td>
<td>457.24</td>
<td>456.68</td>
<td>108.26</td>
</tr>
<tr>
<td>Raw Change Cast (mm³)</td>
<td>13.33</td>
<td>212.19</td>
<td>103.20</td>
<td>109.02</td>
<td>57.20</td>
</tr>
<tr>
<td>Percent Change Cast (%)</td>
<td>4.40</td>
<td>39.30</td>
<td>20.16</td>
<td>18.89</td>
<td>9.55</td>
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</table>
### Table B11. – Statistically Significant Correlations with Volume Change via Cast

<table>
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<tr>
<th>Variable</th>
<th>Raw Change</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rs</td>
<td>p-value</td>
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<tr>
<td>Mesiobuccal probing depth</td>
<td>0.59</td>
<td>0.0085</td>
</tr>
<tr>
<td>Mesiopalatal probing depth</td>
<td>0.57</td>
<td>0.0102</td>
</tr>
<tr>
<td>Distopalatal probing depth</td>
<td>0.46</td>
<td>0.0484</td>
</tr>
<tr>
<td>Mesiobuccal bone sounding</td>
<td>0.68</td>
<td>0.0014</td>
</tr>
<tr>
<td>Mesiopalatal bone sounding</td>
<td>0.53</td>
<td>0.0186</td>
</tr>
<tr>
<td>Distobuccal bone sounding</td>
<td>0.55</td>
<td>0.0155</td>
</tr>
<tr>
<td>Distopalatal bone sounding</td>
<td>0.61</td>
<td>0.0053</td>
</tr>
</tbody>
</table>

### Table B12. – Statistically Significant Correlations with Volume Change via CBCT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Raw Change</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rs</td>
<td>p-value</td>
</tr>
<tr>
<td>Mesiopalatal probing depth</td>
<td>0.50</td>
<td>0.0283</td>
</tr>
<tr>
<td>Buccal mucosa thickness</td>
<td>0.52</td>
<td>0.0235</td>
</tr>
</tbody>
</table>
APPENDIX C – ADDITIONAL FORMS

C. 1. Informed Consent Document

INFORMED CONSENT DOCUMENT

Project Title: Periodontal Phenotype and Supracrestal Soft Tissue Dimensions - Clinical Correlations and Their Impact on Post-Extraction Volumetric Changes

Principal Investigator: Dr. Sarah Rinehart, DDS

Research Team Contact: Dr. Gustavo Avila-Ortiz, DDS (319) 335-7232
Dr. Sarah Rinehart, DDS (xxx) xxx-xxxx
Karen Kluesner (319) 335-7377

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits entailed, and about your rights as a research subject.

• If you have any questions about or do not understand something in this form, you should ask a member of the research team for more information.
• You should discuss your participation with anyone you choose, such as family or friends.
• Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you are a candidate for tooth removal (extraction).

The purpose of this research study is to determine the changes that occur to the gums and bone after tooth extraction. We will compare the anatomy of the area of extraction before and after the tooth is extracted. This procedure is considered to be standard practice.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 65 people are expected to take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?
If you agree to take part in this study, your involvement will last for 4-6 months. This participation consists of a minimum of 4 visits (including this visit) averaging about 2 hours per visit, but some visits may range from 1-4 hours.

**WHAT WILL HAPPEN DURING THIS STUDY?**

**Screening visit**
After reading and signing this informed consent form, you will complete a detailed medical and dental history form. We will review this form with you to ensure you can safely participate in the study. You will also have an oral exam to determine if you qualify for the study. If you are a woman of childbearing age, you will be tested for pregnancy. If you are pregnant or trying to become pregnant, you cannot participate in the study. You will also have digital dental x-rays of the area for tooth extraction, which is standard of care. You will also have dental impressions (molds of your teeth), which are made in order to collect data for some of the research measurements. This visit will last about 2-3 hours.

**Baseline visit**
In less than 8 weeks after the screening visit, you will have the tooth extraction, which will be just like an extraction performed for patients who are not enrolled in the study.

After numbing the area, clinical measurements will be gathered. These measurements are non-invasive and will not harm the gums or surrounding teeth. The extraction (removal of the tooth) will be performed and the tooth socket (the area surrounding the tooth that was removed) will be cleaned, which is what would happen to patients who are not enrolled in the study. At this time, measurements of the area will be taken. These measurements will not cause you any extra discomfort.

Subjects will be given prescriptions for an antibiotic, a pain reliever and a mouth rinse. You will also receive home care instructions before you leave. After the surgical procedure, a dental scan (CBCT) will be taken for research measurements. This visit will last about 2 ½-3 hours.

**Post-operative follow up visits**
Subjects will return to the clinic at 2 weeks, which is standard of care. You will have an oral exam, check-up, and the researchers will monitor how well you are healing. This visit will last ½ to 1 hour.

At 14 weeks after tooth extraction the final visit of this study will be scheduled. In this visit you will have an oral exam, in which measurements of the healed extraction area will be made under local anesthesia. Also, a second scan (CBCT) will be obtained to determine how much bone is available after the healing period. The second CBCT will evaluate the amount of bone volume and if implant treatment if desired, is standard of care when planning for dental implant placement and limited ridge volume is suspected. A second dental impression will be made to collect information
about the soft tissue in the area of the extraction. Recommendations on further therapy, including the potential for implant therapy, will be provided based on the findings from this last visit.

**WHAT ARE THE RISKS OF THIS STUDY?**

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

**Risks associated with tooth extraction**
The standard risks of tooth extraction might be experienced whether or not you participate in this study. These might include postoperative swelling, bruising, or sustained bleeding, local infection, alveolar osteitis (dry socket) and nerve damage (temporary or permanent sensorial alterations), and while rare, you may also develop an oroantral (mouth and sinus) or oronasal (mouth and nose) communication (opening) while having a maxillary (upper) tooth extracted.

**Radiation Risk**
The maximum amount of radiation from the research-related radiation procedures in this study is about equal to the average environmental radiation everyone experiences in 16 days. Although there are no proven harmful effects from this amount of radiation, long term effects on your health such as cancer cannot be ruled out with certainty. This dose estimate takes into account only the exposure to research procedures in this project. If you have participated in other research studies involving radiation exposure, you should be aware that the risk of effects of radiation exposure is thought to add up across all your exposures (including studies performed as part of your medical care).

**Radiation Exposure in Women Capable of Becoming Pregnant**
You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposure to research-related radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

**WHAT ARE THE BENEFITS OF THIS STUDY?**

There may not be any benefits for study participation aside from receiving recommended dental treatment (tooth extraction). We also hope that, in the future, other people will benefit from this study because we may be able to better predict healing following tooth extraction and create more ideal treatment plans.
WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could choose to be a regular, non-research patient in the College of Dentistry or any other dental clinic of your choice. Other treatment options, besides tooth extraction, include not having the extraction done, having the extraction with bone grafting at the same time (ridge preservation), or having the extraction with simultaneous implant placement in the socket. The latter treatment option is not always possible and its indication will depend on the position of the tooth and how much bone is supporting it.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

The study will cover the costs for your x-rays, CBCT scans, and extraction. You will not be charged for any of these services if you participate in the study. If tooth replacement is desired, a provisional, removable tooth replacement can be prepared for you, but you will be charged the standard fee.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will receive two payments of $25.00 at the 2 week visit and $50.00 at the 14 week visit. You may need to provide your address if a check will be mailed to you.

WHO IS FUNDING THIS STUDY?

The Department of Periodontics and College of Dentistry and Dental Clinics is funding this research study. This means that the University of Iowa is providing the funds to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any complication, illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?
We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

☐ Federal government regulatory agencies
☐ People who use the registry
☐ Auditing departments of the University of Iowa
☐ The University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will protect your privacy throughout the research study by doing the following; ID codes will be assigned to each subject, and no personal identifiers will be used for the ID code. The protected health information (PHI) gathered for the study will be limited to PHI that affects your inclusion/exclusion criteria and ongoing participation in the study. No other PHI will be collected. Only members of the research team will have access to your information. Records will be kept in locked cabinets within locked offices and password protected computers. Only 3 individuals will have access to these records: Karen Kluesner, Dr. Gustavo Avila, and Dr. Sarah Rinehart.

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

**WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?**

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires University of Iowa College of Dentistry to obtain your permission for the research team to access or create “protected health information” about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once University of Iowa College of Dentistry has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under “Confidentiality.”

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff.
You cannot participate in this study unless you permit us to use your protected health information. If you choose not to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes University of Iowa College of Dentistry to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to:

Gustavo Avila-Ortiz, DDS, MS, PhD
Mailing Address: University of Iowa College of Dentistry, 801 Newton Rd. Iowa City, IA 52240

However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

**IS BEING IN THIS STUDY VOLUNTARY?**

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won’t be penalized or lose any benefits for which you otherwise qualify.

**What if I Decide to Drop Out of the Study?**

If you choose, you may leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

If you decide to leave the study early, we will ask you to contact one of the contact persons listed. It may be recommended that you return for post-operative appointments that are not within the study.

**Will I Receive New Information about the Study while Participating?**

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we will promptly provide you with that information.
Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue, because your condition has become worse, because you are or became pregnant, because funding for the research study has ended, etc.

WILL YOU KEEP MY NAME ON FILE TO GIVE TO OTHERS?

We will keep information about you in a special kind of computer listing called a registry. A registry keeps information about you on file so that other researchers, not involved in this particular study, may contact you in the future about whether you are interested in being in different research studies. The registry will contain information such as your name, address, age, and selected medical information such as diagnosis and treatment. We will keep the information in this registry secure in locked cabinets behind a locked door. You may request that your personal information be removed from this file at any time by contacting:

Gustavo Avila-Ortiz, DDS, MS, PhD
Mailing Address: University of Iowa College of Dentistry, 801 Newton Rd. Iowa City, IA 52240
Phone: (319) 335-7232
E-mail: gustavo-avila@uiowa.edu

[ ] Yes       [ ] No I give you permission to put my name and personal information in a registry so that other researchers can contact me in the future about different research studies.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself or if you experience a research-related injury, please contact: Dr. Gustavo Avila-Ortiz – (319) 335-7232, Dr. Sarah Rinehart – (xxx) xxx-xxxx, or Karen Kluesner (319) 335-7377.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking “Info for Public” on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.
This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed):
__________________________________________________________

Do not sign this form if today’s date is on or after $STAMP_EXP_DT.

_________________________________________ _______________________________
(Signature of Subject)      (Date)

Statement of Person who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject’s legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_________________________________________ _______________________________
(Signature of Person who Obtained Consent)   (Date)
BIBLIOGRAPHY


