THE EFFECTS OF PERIODONTAL DISTRACTION ON TOOTH VITALITY:

A SPLIT-MOUTH EXPERIMENTAL DESIGN

A Thesis

by

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ABSTRACT

Periodontal distraction is a minimally invasive procedure that has the potential to retract teeth rapidly and dramatically decrease the time required to close extraction sites. Reducing treatment time through accelerated space closure helps to mitigate the iatrogenic side effects associated with prolonged treatment and meet patient demand for faster treatment. The distraction process also shows promise in producing regenerate bone of sufficient quality and quantity for implant placement, but to date no μCT studies exist for confirmation. The biologic implications of periodontal distraction also remain unknown and require further elucidation before clinical acceptance. The purpose of this study is to evaluate whether rapid tooth movements with periodontal distraction cause loss of tooth vitality and whether the regenerate bone meets the restorative guidelines for dental implant placement. Seven dogs were fitted with intraoral distraction devices. On the experimental side, the maxillary 2nd premolars were extracted and the mesial inter-radicular bone was removed while maintaining the buccal and lingual cortices. A thin layer of bone distal to the 1st premolar was spared. No procedures were performed on the control side. After a 5 to 7-day latency, the 1st premolars were distalized at a rate of 1 mm/day for 6 days. A 3-week consolidation period was observed. Cast and intraoral measurements showed that the experimental teeth moved 4.7 and 4.8 mm, respectively. The rate of tooth movement achieved over the experimental period was 0.8 mm/day. Laser Doppler flowmetry showed pulsatile signals consistent with the heartbeat of each dog, suggesting pulpal vitality. μCT analyses showed slightly less dense and mature bone mesial to the 1st premolar, with complete to almost complete vertical and buccolingual bone fill. Minimal root resorption of the distracted teeth was noted. In conclusion, periodontal distraction accelerates tooth movement without detriment to tooth vitality or the health of the roots. It is capable of moving teeth at a daily rate of 0.8 mm/day and significantly reducing the treatment time in crowded, extraction cases. Moreover, it is a novel approach to produce bone for implant placement in patients with congenitally missing teeth or partially edentulous patients.

DEDICATION

I would like to dedicate this work to my parents, Yash and Neera Sangwan, for the sacrifices they made to provide me with best educational and life opportunities. To my brother, Rahul, thank you for always pushing me to be my best, while managing to set the bar infinitely higher! I am lucky to have all the love and support you all have shown me throughout my life.

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NOMENCLATURE

μCT	Microcomputed Tomography
DAD	Dentoalveolar Distraction
DO	Distraction Osteogenesis
EPT	Electric Pulp Testing
FFT	Fast Fourier Transform
H&E	Hematoxylin & Eosin
LDF	Laser Doppler Flowmetry
MOP	Micro-Osteoperforations
NiTi	Nickel Titanium
PD	Periodontal Distraction
PDL	Periodontal Ligament
RAP	Regional Acceleratory Phenomenon
VOI	Volume of Interest

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CHAPTER I

INTRODUCTION AND LITERATURE REVIEW

Orthodontic treatment duration varies based on the case complexity, treatment approach, and degree of patient compliance.[1, 2] Of these variables, the decision to extract teeth is a strong, predictive factor for the length of treatment. The need for extractions correlates with longer treatment time due to the time required to close extraction spaces. On average, extraction cases take 25-35 months to complete, while non-extraction cases finish in 21-27 months.[3] When extractions are required to achieve optimal results, this additional treatment time can create negative concern from patients and parents.

Orthodontists and patients will both benefit from treatment modalities that reduce treatment duration. Extended treatment leads to patient frustration and compliance burnout.[4] Prolonged treatment puts the patient at an increased risk of developing white spot lesions, caries, gingival inflammation, and root resorption.[5-8] By providing expedient care, orthodontists will maintain practice efficiency and meet the demand for faster treatment from all patients, but in particular adults. Adults are now seeking orthodontics in record numbers[9] and can experience slower tooth movement due to slower collagen fiber conversion and cell mobilization, and the propensity to develop hyalinized zones.[10]

Since it is difficult to alter pretreatment characteristics like age, case difficulty, required treatment mechanics, and the level of patient cooperation, increasing the rate of tooth movement is a promising way to expedite treatment. When continuous forces are applied, teeth move at a rate of 0.8- 1.2 mm per month, which is particularly troublesome in extraction cases where teeth have to move a longer distance.[11, 12] Accelerating tooth movement would allow orthodontists to treat to the same standard in less time, increase patient satisfaction, and mitigate the risks involved with longer treatment.

The following section will review the non-surgical and surgical interventions that exist to accelerate tooth movement and the rationale behind them. Subsequently, the literature pertinent to periodontal distraction will be presented to elucidate the potential for this procedure to enhance the rate of tooth movement in a minimally invasive manner.

Non-Surgical Adjuncts to Accelerate Tooth Movement

Bone metabolism and density can affect the rate of orthodontic tooth movement. In 2000, Verna et al found that increased bone turnover correlates with faster orthodontic tooth movement.[13] The authors induced hyper and hypothyroidism in Wistar rats to form 3 groups: rats with high, normal, and low bone turnover. They placed a 25 cN force on the maxillary first molars and noted that the high bone turnover group experienced greater rates of tooth movement and vice versa. In 1984, Goldie and King compared the rates of tooth movement in healthy and calcium-deficient rats. The authors noted faster rates of tooth movement in the calcium-deficient rat group and attributed the increased rate to the decreased bone density and increased bone turnover in the calcium-deficient rats.[14] Similarly, Ashcraft et al observed 3 to 4 times the amount of tooth movement in rabbits with corticosteroid-induced osteoporosis than a healthy, control group.[15]

Given the relationship between bone metabolism and the rate of orthodontic tooth movement, researchers have targeted pathways and cells involved in osseous remodeling to accelerate tooth movement. In 1988, Collins and Sinclair injected 1,25-dihydroxycholecalciferol (1,25D), the active form of vitamin D, into the periodontal ligament of cats to stimulate regional osteoclastic activity. Over a 21-day period, the teeth receiving weekly injections moved 60% further than the control group.[16] Yamaski et al administered local injections of prostaglandin E1, a bone resorption mediator, and found that it nearly doubled the rate of tooth movement.[17] Likewise, Kobayashi et al examined the effects of daily osteocalcin injections on the mesial movement of maxillary molars in rats. Osteocalcin is a bone matrix protein involved in bone remodeling and the authors found that the rats that received the injection had significant increases in tooth movement.[18]

While these pharmacological interventions share success in accelerating tooth movement, there are unintended consequences associated with them. First, giving routine injections may cause pain and discomfort to the patient and induce dental anxiety.[19] Second, administering frequent injections may prove inconvenient and time-consuming to the orthodontist and patient alike. In addition, the local and systemic effects of administering these agents warrants further studies to ensure it is safe for the patient. More research is also needed to find the optimal dosage and frequency of delivering such agents.

Other non-surgical adjunctive therapies used to expedite orthodontic treatment include pulsed electromagnetic waves, electrical currents, low-intensity laser irradiation, and intermittent resonance vibration. At this time, there is a lack of consistent high quality evidence to show that these techniques decrease treatment time enough to justify their use.[20-23] Although these approaches are relatively non-invasive, they may be inconvenient, cost prohibitive, and too reliant on patient compliance.

Surgically Facilitated Orthodontic Tooth Movement

The surgical assistance of tooth movement is a different, more invasive approach to expediting orthodontic treatment. The use of alveolar surgery to facilitate tooth movement dates back to 1892.[24] European pioneers believed that cortical bone was a physical impediment to tooth movement and tried to surgically reduce its thickness and disrupt its continuity to move teeth. In 1921, Cohn-stock removed palatal plate to reposition teeth;[25] in 1931, Bichlmayer excised wedges of bone to retract maxillary anterior teeth and reduce maxillary protrusion;[26] and soon after, Skogsborg and Ascher made vertical, interdental incisions in the buccal or lingual cortices to decrease treatment times by 20-25%.[27, 28]

In 1959, Köle introduced a surgical technique entailing corticotomies and osteotomies into English literature.[29, 30] He laid a full thickness flap to expose bone, made interdental decortications, and then connected these vertical cuts with a subapical horizontal osteotomy that traversed the alveolus. Köle outlined blocks of bone around the teeth to be moved because he believed the tooth and bone move together as a unit, without PDL-mediated bone remodeling. He reported treating cases in 6 to 12 weeks without root resorption, loss of vitality, or damage to the periodontium due to this "bony block movement."

Suya et al modified Köle's technique in 1991 by limiting the horizontal subapical cuts to the cortex only. Suya performed this corticotomy technique on 395 adult Japanese patients during fixed orthodontic treatment and reported less pain and relapse, and treatment completed in 6-12 months.[31]

Corticotomies and the Regional Acceleratory Phenomenon

In 2001, the Wilcko brothers finally brought corticotomies to the forefront of accelerated orthodontics by showcasing two cases treated in 6 months.[32] They raised buccal and lingual mucoperiosteal flaps, performed selective alveolar decortications, and unlike their predecessors, grafted bone at the site before reapproximating the flap. The Wilckos examined post-treatment computed tomography scans and found transient demineralization of alveolar bone near corticotomized teeth. They deduced that corticotomies induce osteopenia, which enhances PDL-mediated movement and leaves behind a soft tissue matrix that moves with the tooth and remineralizes in its final position. Corticotomies thus produced faster tooth movement through a demineralization-remineralization process rather than a mechanical movement of segments. The Wilckos debunked the "bony block" theory and became the first to attribute the success of corticotomies to a biological process, the Regional Acceleratory Phenomenon (RAP).

The Wilckos created a paradigm shift in the orthodontic community by linking corticotomies to the RAP, but the RAP itself was not a new concept. Harold Frost first described it in 1983.[33-35] The RAP refers to the physiologic healing response of osseous tissues to trauma. Injury to bone, such as a fracture, triggers a cascade of events to accelerate healing of the site. The noxious stimulus induces an inflammatory reaction that increases regional perfusion, the quantity of osteoblasts and osteoclasts, and the degree of osseous remodeling. As discussed previously, this transient osteopenia and accelerated bone turnover is favorable for faster tooth movement. The Wilckos proposed that corticotomies create controlled surgical insult to bone, invoke this metabolic state, and consequently move teeth faster than the rate of conventional orthodontics.

Experimental studies have verified the Wilckos' conjecture about corticotomies and the RAP.[36-40] Performing undisplaced, incomplete osteotomies in rabbit tibia induced the RAP and led to a five-fold increase in new bone.[38] Sebaoun et al found a three-fold increase in osteoclasts and the rate of bone apposition, a two-fold increase in PDL surface area, and increased osteopenia in rats that received decortications.[39] These metabolic changes occurred maximally at 3 weeks and immediately adjacent to the corticotomies. By week 11, the effects of the RAP had diminished. Another animal study concluded that corticotomies induce the RAP by finding an increase in cytokine expression, osteoclasts, and bone remodeling in rats that underwent corticotomies than just a soft tissue flap or orthodontic forces alone.[40]

Corticotomies: Clinical and Experimental Literature

The Wilckos' revelation prompted others to investigate whether corticotomy-facilitated orthodontics actually reduces treatment time. Most of the evidence are case reports, which demonstrate expedient results in treating a variety of cases including protrusive, crowded, and over-erupted molar cases, to name a few.[41-48] These results however, must be viewed with caution as anecdotal evidence lack controls and are subject to bias.

The few controlled, prospective human trials that exist back the claim that corticotomies accelerate tooth movement. In a randomized clinical trial, Fisher[49] showed that supplementing conventional surgical exposures of canines with corticotomies can shorten treatment by 28-33%, without harming the periodontal health of the canine. Lee et al[50] compared treatment times in 29 adults treated with conventional orthodontics with 20 adults receiving corticotomy-assisted orthodontics in the maxilla and segmental osteotomies in the mandible. The authors reported that the test group finished 8 months faster. The difference in sample size and pretreatment characteristics between the two groups however, casts doubt on the initial equivalence of the two groups.[3]

With limited, high quality clinical research to review, it becomes especially important to examine the outcomes of experimental studies. Prospective animal research has unequivocally shown that corticotomies enhance the rate of tooth movement, but with the caveat that this treatment effect is limited in duration. Cho et al[51] studied the amount of tooth movement in response to corticotomies in two beagle dogs. In this split-mouth study, the authors extracted second premolars in the maxilla and mandible, performed corticotomies on the right quadrants 4 weeks later, and then protracted the third premolar with a 150 g NiTi coil spring. Compared to the controls, the corticotomized teeth moved 2 times further in the mandible and 4 times further in the maxilla. In the mandible, the corticotomies proved advantageous for the first 6 weeks only, after which the rate of tooth movement became insignificant between the 2 sides.

Iino et al verified the brief treatment effect of corticotomies in a larger sample of 12 beagles.[52] The authors extracted mandibular second premolars, performed corticotomies on the left side 16 weeks post-extraction, and measured the amount of third premolar protraction with 0.5 N force applied. The experimental teeth moved twice as far and up to 5 times faster than the control teeth. The accelerated rate of tooth movement however, occurred in the first few weeks only. Mostafa et al performed same-day corticotomies following maxillary 2nd premolar extractions in 6 dogs and used mini-screw implants to distalize the first premolars.[53] Yet again, the test teeth moved up to 2 times faster but the difference in velocity between the corticotomy and control sides was not significant after 4 weeks.

In 2010 Sanjideh et al examined if performing corticotomies on the same day as extractions or repeating the procedure in 4 weeks increased the efficacy of corticotomies.[54] In this split-mouth experiment, the authors extracted mandibular third and maxillary second premolars in 5 foxhounds and performed same-day corticotomies on a randomly chosen side in each arch. They reported twice the amount of tooth movement on the experimental side, but there was no difference in the rates of movement after 42 days, suggesting again a treatment effect limited to six weeks in duration. A second corticotomy procedure after 4 weeks enabled faster rates for a longer period of time, but not enough to justify a second procedure.

To summarize, corticotomies can double the rate of tooth movement but for a narrow window of time. Once the RAP subsides, so does the impact of corticotomies on tooth acceleration and treatment time. Since the rate of bone turnover in dogs is approximately 1.5 times greater than that in humans, the estimated treatment effect in humans would last 2-3 months and allow 4 to 6 mm of tooth movement.[3] This may be beneficial in shortening the leveling and aligning stages of non-extraction cases or the retraction phase of extraction cases, but without randomized clinical trials, it is uncertain whether they will reduce overall treatment time enough to justify their use.

Flapless Corticotomies

Patient acceptance of corticotomies has been limited due to its invasive nature. Corticotomies pose inherent surgical risks and can result in post-operative complications including lingering pain, swelling, and subcutaneous hematomas of the head and neck region in extreme cases.[55] Traditional corticotomies also require full-thickness flaps, which can cause iatrogenic loss of alveolar bone height and bony dehiscences.[56] In laying a mucoperiosteal flap, the periosteal layer and vascular supply for the cortex are stripped. Since the periosteum supplies up to 90% of arterial blood to the cortex, the flap induces ischemic necrosis of osteoblasts in bone and PDL.[57, 58] Subsequent bone remodeling and osteoclastic activity results in bone loss.[59-61]

In light of these adverse effects, the orthodontic community has searched for less invasive surgical techniques to induce the RAP and accelerate tooth movement. It became popular to attempt flapless corticotomies with various devices to avoid the bone loss from raising a full-thickness flap. Each of these methods however, has failed in producing a RAP effect on par with conventional corticotomies to warrant their adoption in practice.

In a preliminary study in 2009, Kim et al performed transmucosal corticisions with a reinforced scalpel and surgical mallet. Within a 28-day period, the authors found greater bone remodeling with corticision than with conventional orthodontics.[62] In a follow-up study, Kim et al compared tooth movement from corticision to conventional orthodontic treatment.[63] The authors extracted the maxillary first premolars of 12 beagles and protracted their maxillary second premolars with a 150 g NiTi closed coil spring for 8 weeks. They found that the corticision group achieved peak velocity at 2 weeks and moved 3.75 times more than the control group. These results suggest that corticision does not enhance tooth movements more than traditional corticotomies and also have a limited treatment effect. The injuries from corticision however, extended further than traditional corticotomies and can result in dizziness in patients due to repeated malleting.[64] Hard and soft tissue grafting is also not possible with corticisions.

In 2009, Dibart et al introduced piezocision for rapid tooth movement. In this technique, micro-incisions are performed on the buccal gingiva to allow access for a piezoelectric knife to make decortications that can induce the RAP.[64] Unlike corticisions, selective tunneling with piezocision enables hard and soft tissue grafting. In a histological study, Dibart et al evaluated the biologic response of alveolar bone to piezocision and conventional orthodontic forces in rats. The authors found that piezocision-assisted tooth movement doubles the rate of tooth movement and increases osteoclastic activity up to 1 week after the procedure, after which it declines and returns to control levels in 56 days. Mehr et al reported that piezocision enhances tooth movement 1.6 times in the first 4-5 weeks, but stated there was no difference in overall treatment duration.[65]

Ruso et al conducted a randomized, split-mouth study in 6 foxhound dogs and confirmed the acceleratory treatment effect of piezoincision on orthodontic tooth movement.[66] On the experimental side of the maxilla, piezosurgery was performed near the maxillary second premolars and the teeth were moved in a buccal direction for 9 weeks. The experimental teeth expanded 1.35 times more and tipped 2.05 times more than the control teeth. μCT analysis demonstrated decreased bone volume, density, and maturity near the experimental teeth. There are however, important safety considerations with this technique that makes its adoption in practice questionable. In a recent split-mouth μCT study for example, Patterson et al demonstrated that piezocision increased the risk of iatrogenic root resorption by 44% compared to conventional orthodontics.[67]

In 2012, Safavi et al tested the impact of flapless bur decortications on the rate of tooth movement in five dogs.[68] The authors implemented a split-mouth design and performed decortications on the experimental side only. They extracted maxillary first premolars and made 25 2 mm decortications near the second premolar and on the buccal cortex of the extracted tooth. They repeated the decortications at the end of the first and second month. They protracted the second premolars with absolute anchorage and a 150 g NiTi closed coil spring. The authors reported 0.82 mm more tooth movement in the first month but there was no statistical difference in tooth movement afterwards due to the healing and maturation of the bone. Over the course of the three-month study, there was no difference in the accumulated distance of tooth movement between the 2 sides.

In a randomized split-mouth study, Swapp et al demonstrated that inflicting cortical damage with surgical bone awls does not hasten tooth movements either.[69] The investigators extracted mandibular second premolars and protracted the third premolars with 200 g of force. The authors inflicted 60 flapless microfractures to the buccal and lingual cortices of the third premolar on the experimental side 4 weeks after extractions. μCT and histologic analysis revealed that there were significant decreases in bone volume fraction and density in the cortex, but not in the medullary bone mesial to the third premolar. Insignificant remodeling in the medullary bone resulted in no difference in tooth movements between the control and experimental sides.

Another flapless corticotomy technique involves making micro-osteoperforations (MOPs), which are thought to induce the RAP to accelerate tooth movement. MOPs are commonly made through the gingiva with the PROPEL device, a 1.4 mm mini-screw implant in an implant driver. In 2013, Alikhani et al reported that MOPs produce a 2.3-fold increase in the rate of tooth movement.[70] A follow-up study by Cramer et al in 2016 however, cast doubt on this conclusion.[71] In this split-mouth study in 7 beagles, 8 MOPs were placed with the PROPEL device 1 month after extraction of the third premolars on a randomly chosen side. The MOPS were 1.5 mm wide and 7 mm deep and 6 were placed 3 mm distal to the second premolar and 2 were placed in the premolar furcation. The maxillary second premolars were retracted bilaterally for 7 weeks with a 200 g NiTi closed coil spring. During the first 2 weeks, there was slightly greater tooth movement on the MOP side, but the difference was not significant. Over the entire 7 weeks, the teeth on the MOP side moved insignificantly more than the teeth on the control side. Furthermore, μCT evaluations indicated no differences in bone density or bone volume fraction of the medullary bone between the two sides, signifying that the procedure did not produce enough of a RAP effect to allow faster tooth movement.

In a split-mouth study, Van Gemert et al evaluated the spatial and temporal effects of MOPs on bone density in 13 beagle dogs.[72] Using the PROPEL device, the authors placed 34 MOPs in the mandibular furcal bone and allowed 2 or 4 weeks of healing prior to sacrifice. When comparing the control and experimental sides, they found a significant difference in the density of the cortical and trabecular bone, but this difference was less than 5% beyond 1.5 mm from the MOP margins. After 2 weeks of healing, the Vickers Hardness of the cortex bone was significantly less up to 0.75 mm from the MOP and so was the osteoclastic activity 2.5 mm from the margin. With 4 weeks of healing, the difference in bone density was noted only 0.5 mm from the MOPs and the Vickers Hardness of the cortex returned to control levels. The transient effect of MOPs on bone density and the quick remineralization of bone seen in this study helps explain why Cramer et al were not able to produce significant differences in tooth movement with MOPs.[71]

Periosteal Flaps and RAP

It has been shown that the RAP correlates with the amount of surgical damage inflicted.[73, 74] Flapless corticotomies influence tooth movement less than traditional corticotomies because they produce less surgical insult and thus less of a RAP effect. Conventional corticotomies produce intentional injury in two ways: through the elevation of a full-thickness flap and the decortications made. Flapless and conventional corticotomies both produce decortications but differ in whether a flap is raised. Up to this point, corticotomy studies failed to control for the impact flap elevation can have on the rate of tooth movement. It is worth isolating the effects of flaps on tooth movement because the periosteal layer is the predominant vascular source for long bones and Frost suggested that disruption in regional vascularization might influence the RAP.[33-35] Studies on flap elevation alone have shown however, that raising a full-thickness flap is sufficient to induce the RAP but does not accelerate tooth movement more than traditional corticotomies.

In 1994, Yaffe et al elevated mucoperiosteal flaps in rat mandibles and found that flap elevation alone is sufficient to produce the RAP effect.[75] The authors laid buccal and lingual full-thickness flaps, a buccal full-thickness flap, or no flap in 60 Wistar rats and evaluated subsequent bone remodeling. Alveolar bone resorption was noted as early as 10 days, and the rats that had buccal and lingual flaps elevated experienced the greatest amount of bone resorption. Maximum resorption occurred after three weeks and the experimental bone volume was similar to control bone after 120 days. These results suggested that flap elevation could produce the bone remodeling needed for faster tooth movement.

In 2015 Owen et al tested whether flap elevation can decrease bone density and accelerate mesial tooth movements in 7 beagles.[76] The authors extracted mandibular second premolars and elevated a buccal mucoperiosteal flap from the distal of the third premolar to the mesial of the first premolar on the randomly chosen experimental side. The contralateral control side received no flap surgery. The authors then protracted the third premolars bilaterally. At the end of eight weeks, micro-CT analysis indicated significantly less bone volume fraction and apparent density in the medullary bone mesial to the third premolar on the experimental side. These changes in bone density enabled the experimental teeth to move 25% faster than control teeth, but this rate is still slower than traditional corticotomies.

Corticotomies and Bone Healing

By quantifying the impact of flap elevation on the rate of tooth movement, Owen et al helped elucidate why traditional corticotomies have greater success in accelerating tooth movement than decortications or flaps alone. Flapless decortications and flap elevation alone are unable to inflict comparable surgical insult to produce the faster rates of tooth movement found with traditional corticotomies. As mentioned previously, corticotomies speed up tooth movement but the treatment effect is limited in duration. It becomes important to examine bone healing to understand why the RAP effect and rate of tooth movement subsides over time with conventional corticotomies.

Traditional corticotomies cannot facilitate long-term tooth acceleration because of fast bone healing. Bone healing occurs in three stages: the reactive, reparative, and remodeling phase.[3] During the reactive phase, the RAP occurs and surviving cells initiate an inflammatory response that increases local perfusion and recruits osteoblasts and osteoblasts near the site of injury. Granulation tissue also forms after approximately 2 weeks.[33, 77-79] The reactive phase produces conditions most favorable for rapid tooth movement.

During the reparative stage, a callus, or mass of hyaline cartilage and woven bone develops.[3, 80] Periosteal cells and fibroblasts within the granulation tissue differentiate into chondroblasts and osteoblasts that form these tissues.[78] The callus is replaced by immature lamellar bone but this mineralization process can take 1-4 months.[33] In the final phase, remodeling occurs over 1-4 years to form mature lamellar bone. Bone maturation becomes a physical impediment to tooth movement in these 2 phases.

The rate at which this healing process occurs depends on the extent of injury, blood supply, and stability of the bony segments. Healing will be slower if there is more injury, disrupted blood supply, and unapproximated bony segments. Corticotomies however, are stable, undisplaced fractures and stimulate a faster healing response.[3] Dentoalveolar bone has also been shown to heal faster, further limiting the initial advantageous biologic environment for tooth movement.[81] Consequently, alveolar bone matures rapidly and prevents corticotomies from achieving sustained high velocity tooth movement.

Distraction Osteogenesis

Since bone healing limits the acceleratory effect of corticotomies, it follows that greater surgical insult or bone removal is required to slow healing, and that orthopedic forces should be used to move teeth more rapidly. Both of these strategies involve keeping the rate of tooth movement ahead of the rate of bone maturation and healing. Dentoalveolar distraction (DAD) and periodontal distraction (PD) are two promising techniques that utilize osteotomies and orthopedic forces to achieve fast rates of tooth movement within the initial reactive phase of bone healing.

Distraction osteogenesis, also known as callus distraction, is a bone-lengthening procedure first used in the early twentieth century to elongate the long bones of malformed lower limbs.[82, 83] This technique did not gain popularity in the medical community until Ilizarov established a protocol that minimized post-operative complications.[84] Since then, the principles of DO have been applied to the craniofacial skeleton to address severe sagittal discrepancies and craniofacial deformities. In 1973, Snyder et al distracted a mandible 15 mm; [85] McCarthy et al used an extraoral distractor to lengthen the ramus;[86] and Polley and Figueroa elongated maxillas in patients with hypoplastic maxillas and craniofacial deformities.[87] Rapid palatal expansion is a popular application of DO used to address transverse skeletal discrepancies routinely in orthodontics. DAD and PD apply the principles of distraction osteogenesis at the dentoalveolar level to accelerate tooth movement.

Traditionally, DO is comprised of a 4 phases: surgery, latency, distraction, and consolidation.[84] In the surgical phase, an osteotomy is made in the bone to be lengthened. Prior to distraction, a latency period is observed to allow for callus formation. After latency, the distractor is placed and the callus is stretched in the osteotomy site incrementally at a rate of 1 mm/day to generate new bone. A consolidation period ensues to allow for bone maturation before appliance removal.

Dentoalveolar Distraction

In 2002, Kişnişci et al applied DO to the dentition and introduced DAD as a means to achieve rapid tooth movement.[88] The authors treated 11 patients with biscuspid extractions followed by canine distalization with DAD. In this protocol, the authors first laid a subperiosteal flap to expose the canine root and performed an osteotomy that outlined it. Next, the first premolar was extracted and the buccal cortex distal to the canine and mesial to the second premolar was removed. Bone interferences in the path of tooth movement and apical to the extraction socket were also removed. An osteotome was then used to mobilize the canine with surrounding spongy bone from the lingual cortical plate. The transport disc included the canine, the adjacent buccal cortex, and the trabecular bone surrounding it. Afterwards, an intra-oral distractor was fitted and turned 0.4 mm twice a day, starting the day of the surgery. The authors reported that the canine teeth made contact with the second premolars in 8-12 days without root resorption, dental ankylosis, tooth discoloration, or loss of vitality. This study however, lacked controls and did not state the amount of tooth movement achieved.

In 2005, Gürgan et al reported that rapid canine retraction with DAD has no long-term effect on periodontal health.[89] In this study, they extracted the first premolars of 18 patients, performed DAD, and began retraction of the canines at a rate of 0.8 mm/day within 3 days of the surgery. The authors reported it took 10.4 days on average to retract the cuspids until they made contact with the second premolar. They reported no difference in the plaque index, gingival index, pocket depth, and the width of keratinized and attached gingiva from the start of treatment to 1 year post-treatment. This investigation lacked controls however, and did not specify the overall treatment duration or the amount of tooth movement completed. Other clinical studies completed by the same authors have also suggested that DAD can retract canines at impressive rates, but these studies also lacked controls.[90, 91]

Sukurica et al performed DAD on 20 teeth in 8 patients with a 3-day latency period and assessed periodontal, pulpal, and root health.[92] The authors reported 5.35 mm of canine retraction in 14.7 days and significant canine tipping of approximately 9.1°. The authors found no difference in the plaque index before and after treatment and no gingival recession or loss of keratinized gingiva. Sukurica et al reported that only 7 teeth tested vital to electric pulp testing (EPT) 6 months after the DAD procedure. EPT however, is not reliable during active orthodontic treatment or after trauma like rapid distraction.[93, 94] Evaluation of periapical radiographs showed insignificant amounts of root resorption.

In a larger clinical study in 2017, Kurt et al found that canines can be retracted at a significantly higher rate with DAD than with conventional orthodontic mechanics.[95] The DAD group included 19 patients and 36 maxillary canines that were distracted 0.4 mm twice a day after a 3-day latency period. The elastics distalization group (DG) included 14 patients with 28 canines. In both groups, the first premolar was extracted and the canines were retracted fully before the incisors were retracted with closing loops. The authors reported that on average, the canines retracted 7.9 mm in 11.8 days with DAD and 5.3 mm in 200 days with intraoral elastics. The DAD canines showed about 11.5° of tipping, which was statistically significant. There was no significant amount of vertical or sagittal movement of the first molars, suggesting minimal anchorage loss and vertical control with DAD. The authors also reported no root resorption or loss of tooth vitality from DAD after checking with EPT and thermal stimulation at a six-month retention visit. As stated previously however, these testing methods are less valid after trauma.[93, 94] Finally, the study stated that DAD facilitated faster retraction of anterior teeth, but the amount of time required for incisor retraction and the overall treatment duration were not given to substantiate this claim. Initial pre-treatment characteristics, which could affect the rate of incisor retraction, were not clearly stated either.

Descriptions of the clinical studies on DAD are included in Table 1. The majority of these studies are case series publications that lacked controls. Limited conclusions can be drawn from this anecdotal evidence. There is also variability in terms of the DAD protocol used and little mention of the quality of the regenerate bone produced. As with the corticotomy literature, it becomes important to analyze prospective, randomized clinical control trials or experimental research to better understand the clinical and biologic effects of DAD. There are 2 experimental studies available that elucidate how the length of latency and the rate of distraction affect the bone regenerate.[96, 97]

In a split-mouth study in 6 foxhound dogs in 2011, Moore et al found that latency has little effect on the quality and quantity of regenerate bone.[96] The authors extracted mandibular first and third premolars and created a large periodontal defect in the area of the third premolar. They distalized the second premolar transport segment at a rate of 1 mm/day for 10 days. On one randomly selected side, the segment was distracted after a 5-day latency period and then consolidated for 6 weeks. On the other side, the segment was distracted immediately with 7 weeks of consolidation post-distraction. They reported that the transport segments distalized 7-8 mm in the 10-day period. μCT anaylsis of the bone regenerate showed that over 75% of the specimens had almost complete or complete vertical and buccolingual bone fill. The regenerate bone on the non-latency side had less trabecular separation than control bone, suggesting slight maturational differences between the two groups. All other parameters showed no significant differences. Moore et al concluded that latency had little effect on the amount or density of bone regenerate and that the regenerate bone for both groups was adequate for restorative prosthetics.

Spencer et al conducted a randomized, split-mouth study in 6 foxhound dogs and reported that distraction performed at 1 mm versus 2 mm per day did not affect the amount or density of regenerate bone.[97] The authors followed the same DAD protocol as the previous study except a 5-day latency and 6-week consolidation period was observed, and the teeth were moved for 5 days. They found no difference in the bone volume fraction, density, or trabecular morphology between the two rates of distraction.

Little is known about the long-term biologic effects of dentoalveolar distraction. Spencer et al noted that further research is needed to establish the long-term maintenance of regenerate bone, the vitality of teeth, and the health of nerve and blood supply.[97] In addition, few studies discuss patient perception and tolerance of the procedure. DAD is more invasive than corticotomies and patients may be hesitant to choose it as a treatment option.

Periodontal Distraction

Periodontal distraction is an alternative application of DO. It is a less invasive surgical procedure that may achieve greater patient acceptance and still achieve rapid rates of tooth movement. In 1998, Liou et al introduced periodontal distraction as a surgical procedure to expedite canine retraction.[98] The authors hypothesized that the periodontal ligament behaves like the midpalatal suture, and is a "suture" between the tooth and alveolar bone. They noted that with conventional orthodontic mechanics, the PDL is distracted slowly and the rate of osteogenesis is 1 mm/ month on the trailing side of tooth movement. Liou et al questioned whether the PDL could tolerate orthopedic forces like the midpalatal suture and be distracted at faster rates consistent with traditional distraction osteogenesis.

In their prospective clinical study, Liou et al treated 15 patients with periodontal distraction and distracted canines 6.5 mm in 3 weeks.[98] They extracted first premolars and performed vertical and oblique undermining groves through the extraction socket to weaken the interseptal bone distal to the canine. No flap was raised and the buccal and lingual cortices were left in tact. The depth of the undermining grooves was determined by the thickness of the interseptal bone on a periapical radiograph. They delivered the intraoral distraction device the day of extractions and started distracting the canines 0.5 mm to 1 mm/ day, until the canine was judged to be in its proper position.

From cephalometric superimpositions, the authors reported minimal anchorage loss of the first molar. 73% of the first molars did not move mesially while 27% moved less than 0.5 mm. The authors explained this phenomenon by citing the effects of heavy forces on tooth movements. The canines moved rapidly with weakened osteal resistance, while the molar entered a 2-3 week lag phase from the heavy, orthopedic forces. The canine completed retraction before the molar could clear the hyalinized PDL tissues.

Liou et al found minimal apical and lateral canine root resorption, but could not determine whether the distracted teeth remained vital. The authors used EPT prior to the start of treatment and at least 1 month after canine distraction. All teeth responded positively to EPT at the start of treatment. After distraction however, only 5 out of 15 maxillary canines and 4 out of 11 mandibular canines demonstrated vitality. EPT however, is not reliable during active orthodontic treatment, which explains why the neighboring second premolars also responded negatively to vitality testing.[93, 94,117] The authors suggested that future studies use Laser Doppler flowmetry to assess pulpal blood flow rather than nerve function, which can be affected by trauma.

Periodontal Distraction: Clinical Literature

Several clinical studies have tested the efficacy of periodontal distraction, but most are case reports or series and limited conclusions can be drawn from them.[98 -109] The findings of clinical studies on PD with at least 2 subjects are summarized in Tables 2-4. Of note, is a randomized, split-mouth clinical trial conducted by Mowafy et al in 2011. The authors compared PD with intermittent, orthopedic forces to PD with continuous orthodontic forces.[103] The authors extracted maxillary first premolars and performed the PD surgical procedure outlined by Liou et al.[98] They determined the amount of force applied by the screw-based distractor with a torque wrench and set the force of the NiTi closed coil spring to be half that value. The patients were instructed to turn the screw-based distractor once daily to achieve 0.25 mm of distraction. Every 7th day, the patients were seen to recalibrate the force values. The canines were distracted until they made contact with the second premolar.

At the end of the experiment, the canines with the screw-based distractor distalized 5.9 mm in 5.3 weeks and tipped 10.47°**,** while the canines on the coil side moved 4.7 mm in 27.8 weeks and tipped 0.27°**.** The rate of canine movement on the coil side was comparable to conventional tooth movement. The between-side differences highlight that orthopedic forces are integral to achieving rapid tooth movement with PD. In addition, the rate of distraction in this study was slower than that used by Liou and coworkers.[98] More time was required to retract the canines, suggesting that faster distraction rates should be implemented, as long as there are no side effects. In this report, the authors found a mean anchorage loss of 2.5 mm on the screw side and 2.81

mm on the coil side, which was not statistically different. Anchorage loss occurred on the orthopedic side because canine retraction took longer than the 2-3 week lag period of the molar.

In 2014, Leethanakul et al conducted a randomized clinical trial that showed that PD performed with conventional orthodontic forces has a limited treatment effect.[104] In this split-mouth study, 18 subjects had bilateral maxillary first premolar extractions. On the randomly selected experimental side, interseptal bone reduction was performed at the time of extraction, excluding the buccal and lingual undermining groves made by Liou et al. Buccal mini-screw implants were placed between the second premolar and first molar and the canines were retracted off of it and lingual buttons with elastomeric threads with a net force of 150 g. Over the 3-month experimental period, the control group moved a mean 3.4 mm while the test group moved 5.4 mm. The authors reported that canine movement was significantly greater from T0-T1, T1-T2, and from T1-T3 for the experimental group. From T2-T3 however, there was no significant difference in the rate of tooth movement, suggesting that the clinical treatment effect for PD with conventional forces wanes over time. The authors also postulated that more buccal and lingual bone reduction is needed to accommodate the width of the canine during retraction. There was no significant difference in the amount of tipping between the two sides.

Periodontal Distraction: Experimental Literature

Ren et al implemented a similar design in 10 beagle dogs and showed that periodontal distraction combined with 150 g of retraction force can double the amount of tooth movement over a 4-week period.[110] The rates of tooth movement however, declined remarkably after 1 week. In this split mouth study, the mandibular second premolars were extracted and on the experimental side, the interseptal bone was undermined. The first premolars were distalized immediately with buccal and lingual closed coil springs with a net force of 150 g. The experimental teeth moved significantly further each week and in total over the 4 weeks. In the experimental group however, approximately 67% of the total tooth movement occurred in the first week and the rate of tooth movement dropped by 86% after the first week. This showed that orthodontic forces used concomitantly with PD are unable to sustain the rapid rates of tooth movement that can differentiate this procedure from traditional corticotomies.

In order to extend the treatment effect of PD, orthopedic forces must be used in conjunction with the procedure. In 2008, Ai et al performed a split-mouth trial in eight beagle dogs and extracted mandibular second premolars bilaterally.[111] On the experimental side, buccal and lingual mucoperiosteal flaps were raised and interseptal surgery was performed. Immediately following surgery, an intra-oral distractor was activated at a rate of 0.25 mm twice a day for 2 weeks. On the contralateral control side, power chains providing an elastic force of 100 g were used to retract the first premolar. The dogs were sacrificed after 2, 3, 4, and 10-week consolidation periods.

During the first week, the experimental first premolars were distracted a mean 1.75 mm compared to 0.79 mm on the control side. After 2 weeks, the test teeth distracted 3.66 mm opposed to 1.15 mm on the contralateral side. Both of these differences were statistically different and it is important to note that with the use of orthopedic forces, the rate of tooth movement was sustained over the 2nd week of tooth movement unlike in the previous study. On the experimental side, 47% of tooth movement occurred during the first week, while only 21% of tooth movement occurred on the control side.

Ai et al also noted minimal anchorage loss and approximately 7.5° of tipping after 1 week and 16.5° after 2 weeks, which was significant compared to the control teeth, which tipped 4° and then 11.5° the following week. From periapical radiographs, the authors concluded that there was minimal resorption of the apical and lateral portion of roots on both sides. They stated that 4 experimental teeth exhibited slight blunting of the apex and that only 1 out of 16 premolar roots displayed resorption and surface irregularity.

The dogs in this study were sacrificed sequentially after 2, 3, 6, and 10 weeks of consolidation to allow for chronologic histologic analysis. Hematoxylin & Eosin (H&E) staining revealed that after 2 weeks of consolidation, the experimental PDL fibers were elongated on the tension side and more compressed on the control side. In the distraction gap, PDL fibroblasts and mesenchymal cells were observed and new, irregular trabecular bone was sparsely present. Hyalinized tissues were present in reduced amounts on the test side. By week 3, two-thirds of the distraction site was filled with new and irregular bone and there was little trabecular separation. 6 weeks post-distraction, the distracted PDL width returned to control levels and trabecular maturation and bone remodeling was evident. At 10 weeks, the authors stated that the periodontium returned to its initial status.

In 2009, Lv et al reached a similar conclusion and found that periodontal distraction achieves rapid tooth movement.[112] In a split-mouth trial in eight beagles, the mandibular second premolars were extracted and periodontal distraction was performed without raising flaps. Following surgery, the first premolars were distalized immediately at a rate of 0.5 mm/day. On the control side, the mandibular second premolars were extracted and the first premolars were distalized with buccal and lingual coil springs with a combined force of 100 g. The 8 dogs were split into the following 4 groups based on the length of distraction and consolidation: T1) distraction/ distalization for 1 week, T2) distraction/ distalization for 2 weeks, T4) distraction for 2 weeks and 2 weeks of retention/ distalization for 4 weeks, T8) distraction for 2 weeks and retention for 6 weeks/ distalization for 4 weeks and retention for 4 weeks. In addition to assessing tooth movement, this group completed histologic analysis.

At T1, T2, and T4, all experimental teeth moved further than the contralateral teeth at a significant level. The authors reported that the first premolars moved a mean 5.0 mm compared to 1.2 mm on the control side at T4. For at least the first 2 weeks, the experimental tooth-displacement curve differed from the classic tooth-displacement curve. At T4, the control side experienced significantly greater third premolar anchorage loss. The control teeth mesialized a mean 0.5 mm compared to 0.3 mm on the test side.

The results of the histologic analysis were consistent with the previous study from Ai et al[111]. During the first two weeks, PDL cells widened and were vital. An increased number of osteoblasts and osteoids were observed on the PD tension side, with osteoblasts covering the bone surface. At week 4, the new trabecular bone was longer and bulkier than the control side. Masson staining showed more regenerate bone deposition in the test group. By week 8, trabecular bone was striated, superficial osteoids were partially calcified, and new lamina was formed.

On the compression side, the PDL narrowed and blood vessels were compressed in the first week. In week two, hyalinization could be seen and evidence of direct and indirect osteoclastic resorption was present. The control side however, experienced greater hyalinization and undermining resorption, with some pyknotic nuclei even seen. At week 4, due to interseptal bone resorption, the periodontium distal to the premolar joined with the extraction socket. TRAP staining indicated more osteoclastic activity on the mesial and distal side of the experimental teeth. By week 8, the experimental and control sides normalized.

Unlike previous studies, Lv et al evaluated the histologic status of the pulp. In the second week, pulpal hyperemia was noted in experimental teeth. By week 8 however, these teeth exhibited normal pulpal status. There was no pulpal necrosis observed. The authors also evaluated root resorption and found small areas of root resorption at week 4. In the 8th week however, the resorptive lacunae partially repaired with cementum.

The studies described above implemented different rates of distraction and consequently achieved different rates of tooth movement. Shimojima et al questioned how different rates of distraction would affect the amount of tooth movement achieved and the initial response of the tension-side PDL.[113] They performed a split-mouth study with 5 beagle dogs and assigned each mandibular first premolar to 1 of 3 rates of distraction: 0.25 mm/day (group 1), 0.25 twice a day (group 2), and 0.5 mm twice a day (group 3). The protocol consisted of bilateral 2nd premolar extractions with PD surgery followed by immediate distraction for a total of 4 days. The authors reported that the mean tooth movement over the experimental period was 0.91 mm, 1.75 mm, and 3.41 mm, for groups 1 to 3 respectively. The average tipping of the first premolar was 5.28°, 8.71°, and 21.92°, for groups 1 to 3 respectively. All inter-group comparisons for the amount of tooth movement and tipping were significant. With this degree of tipping, the authors noted that the amount of tooth movement is over stated. They attributed the significant amount of tipping to the lack appliance stiffness and being unable to place it in a position that retracts the tooth through its center of resistance.

Histologic analysis revealed that the width of the PDL was dependent on the rate of distraction and was significantly different between the 3 groups. The average PDL width was 375.1 μm, 595.6 μm, and 1144.9 μm for groups 1, 2, and 3. In group 1, there was minor bleeding observed and derangement of the PDL fibers. In groups 2 and 3 however, the PDL ruptured at 1/3 of its original width but the Sharpey's fibers remained attached to the tooth and alveolar bone. Blood clots filled in the PDL space and even more bleeding was evident in group 3. This finding is different from the findings of Ai et al[111] and Lv et al[112], who did not report the PDL tearing at a distraction rate of 0.5 mm/day. Shimojima et al sacrificed their dogs immediately after the 4-day treatment period however, and so their study does not give insight into the long-term PDL response to these rates of distraction.

In a follow-up study, Nagano et al reported that the initial pulpal response to PD-assisted tooth movement at rate of 0.5 mm/day and conventional orthodontic mechanics is similar.[114] The authors used a split-mouth design in six beagle dogs to compare retraction of the maxillary first premolars, following second premolar extractions, with periodontal distraction versus a closed coil spring (CCS). They initiated distraction immediately at a rate of 0.25 mm twice a day for a total of 4 days and sacrificed the animals after either 5 or 12 days.

Over the 4-day period, the teeth in the PD group moved significantly further. The PD teeth distracted 2.0 mm and the teeth in the CCS group moved 1.1 mm, which is high for conventional orthodontic mechanics. The authors assessed pulpal vitality with Laser Doppler flowmetry (LDF) and reported that after 5 days, the blood flow was 70% of the baseline readings on the PD side and 80% of the baseline readings on the CCS side. On the experimental side, the authors noted partial blood flow recovery every 12 hours post-distraction, while the CCS group showed a steady decline in blood flow over time. H&E histologic evaluation revealed that compared to untreated teeth, the PD and CCS group had fewer odontoblast cells present. The group sacrificed on day 12 showed even less odontoblastic cells. Slight vacuolar degeneration was seen in the odontoblast layer at 5 and 12 days but no pulpal necrosis, severe vacuolar degeneration, or reticular atrophy was noted.

TUNEL staining was used to quantify odontoblastic apoptosis. There were no TUNEL-positive cells in the untreated group, but the positive cell rate was 1.94 ± 1 .95 in the PD group and 1.95 ± 1.94 in the CCS group, which was not statistically different. At day 12, the rate decreased to 0.23 ± 0.65 in the PD group and 0.17 ± 0.55 in the CCS group, which was also not statistically different. The standard deviations in these 2 groups are high in both instances however, casting doubt on the reliability of these measurements.

Nagano et al evaluated odontoblastic differentiation by examining the proliferation of cell nuclear antigen (PCNA) with immunohistochemical staining. In the untreated group, the positive cell rate was 10.3 ±. 5.1. On day 5, this value was 16.8 ± 4.4 in the PD group and 17.1 ± 5.5 in the CCS group. Both of these positive cell rates were significantly higher than the untreated group, indicating more odontoblastic differentiation. In the beagles sacrificed after 12 days, the positive cell rate increased to 25.4 ±. 6.7 in the PD group and 23.7 ± 5.3 in the CCS group. These values were not statistically different from each other but both were significantly different from the untreated group, and most positive cells were found in the odontoblastic layer.

Periodontal Distraction and Tooth Vitality

The orthodontic literature currently does not have conclusive evidence on the effects of periodontal distraction on tooth vitality. Nagano et al demonstrated that the initial response of pulpal tissues to periodontal distraction at a rate of 0.5 mm/day is similar to conventional orthodontics. However, they only moved teeth for 4 days and did not have a long enough consolidation period to discuss long-term tooth vitality. Liou et al reported that 35% of the teeth were non-responsive to EPT 1 month post-distraction, but EPT is not reliable during orthodontic treatment.[93, 94, 117] On the contrary, Kumar et al found no vitality loss pre and post-distraction with EPT.[105] Kharkar et al distracted at a rate of 0.5 mm/day and assessed tooth vitality at a 12-month follow up visit and found that all teeth were vital.[109] Their study however, was based on a sample size of 6 patients and did not evaluate blood flow, which may be more reliable to evaluate pulpal vitality after trauma than sensibility testing.

No studies on periodontal distraction adequately assess pulpal vitality when distracting at faster rates of 1 mm/day. In addition, no study to date has examined the quality and quantity of the regenerate bone via µCT analysis. The primary purpose of this study is to evaluate the pulpal health of teeth distracted at a rate of 1 mm/day with LDF. Secondarily, this studies aims to evaluate if the quality and quantity of the regenerate bone is sufficient for implant placement. A well-controlled, animal study is needed to answer these questions.

CHAPTER II

MATERIALS AND METHODS

Sample

Seven skeletally mature females hound dogs, approximately 15- 26 months of age and weighing 68-86 pounds, were purchased from a breeding facility. The canine model was chosen for this study to ensure that the clinical and biologic implications of PD could be extrapolated to humans. Dogs are an appropriate model for studying bone remodeling and tooth movement because their dentition and periodontium are comparable to humans.[115, 116] The hound dogs in this study were healthy with fully erupted dentitions. The Institutional Animal Care and Use Committee at Texas A&M University College of Dentistry approved the housing, care, and experimental protocol (IACUC 2018-0257-CD0). One dog served as a pilot dog and the remaining six were experimental dogs.

Pre-surgical Preparation

Upon arrival, the dogs were weighed, underwent a check of health and an intraoral exam to ensure full eruption of their dentitions, and were quarantined for 10 days to help with acclimation. Identifying tattoo markers were placed on each dog. After the quarantine period, initial records were taken on each animal. To obtain these records, the dogs underwent 12 hours of fasting and were then sedated with an intramuscular injection of ketamine (2.2 mg/kg IM) mixed with xylazine (0.22 mg/kg IM). Dental prophylaxis was completed with a Cavitron Select ultrasonic scaler (Dentsply, York, PA) irrigated with 0.12% chlorhexidine gluconate. Maxillary alginate impressions were taken using a custom Triad tray (Dentsply, York, PA) and poured in orthodontic die stone for study models. Occlusal and periapical radiographs were taken of the maxillary right and left quadrants using a Planmeca Intraoral X-Ray unit (Planmeca USA, Roselle, IL) and size 3 film.

At the next appointment, the dogs followed the same fasting schedule and were again sedated IM with the ketamine and xylazine mixture. Intraoral photos were taken of both maxillary quadrants. Calibrated periapical radiographs of the maxillary left and right quadrants were taken to assess the root angulation of the first premolars. The quadrant with the less distally angulated premolar was chosen as the experimental side to avoid root damage from the vertical osteotomy cuts. The contralateral side served as the control side.

Crown lengthening of the experimental first premolar was performed to aid in retention of the distraction device. 2% lidocaine with 1:100,000 epinephrine was administered via buccal infiltration to the site to ensure animal comfort during the procedure. Next, the gingiva was removed with a scalpel and a #4 round bur was used to remove 1-2 mm of bone. A calibrated periapical radiograph was taken to verify adequate bone removal, and post-operative photos were taken.

Appliance Design

The maxillary impressions were poured in die stone for fabrication of the orthodontic appliances (Figure 1A). Orthodontic band material (Dentauram, Ispringen, Germany) was adapted and welded to fit the maxillary canine, first premolar, and third premolar. A Herbst tube (Ormco, Orange, CA) of 0.072” diameter was soldered to buccal of the third premolar bands. The arm of a 12 mm mini rapid palatal expander (Forestadent, Pforzheim, Germany) was soldered to the canine bands and inserted through the herbst tubes on the bands of the third premolars. Orthodontic wire of diameter 0.045” was soldered to the first premolar and the RPE arm. Throughout the experiment, the dogs were maintained on a soft food diet to prevent damage of the orthodontic appliances.

Surgery

The dogs fasted for 12 hours prior to the start of the surgical procedure and were administered the aforementioned ketamine and xylazine mixture IM. Each dog received dental prophylaxis with an ultrasonic scaler and irrigation with 0.12% chlorhexidine gluconate. Prior to surgery, the dogs received atropine (0.05 mg/kg) to prevent isoflurane-induced bradycardia. They were intubated and administered general anesthesia with 1.5% isoflurane in oxygen at a rate of 1 L/minute.

Local anesthesia (2% lidocaine 1:100,000 epinephrine) of the surgical sites was achieved via infiltration. Vital signs were monitored throughout the procedure. Before the start of the procedure, baseline tooth vitality readings of both maxillary first premolars were recorded for 1 minute with a LDF probe (MoorVMS-LDF, Devon, UK). The probe was oriented down the long axis of the tooth and care was taken to isolate the probe with nitrile material from the surrounding periodontium, to avoid noise and contamination signals (Figure 2).

The first premolars were susceptible to iatrogenic root damage because of their distal inclination. Surgical exposure of the root apex helped guide bur angulation while performing the osteotomies. In order to visualize the root apex, the length of each root was measured on a calibrated periapical radiograph and a gingival incision followed by a surgical cut was made at this depth (Figure 3). After visualizing the root apex, the maxillary 2nd premolar on the experimental side was hemisected, elevated, and delivered via forceps. The PD osteotomies outlined by Liou et al were performed through the extraction site.[98] All surgical osteotomies were performed under a constant spray of sterile saline solution to prevent bone necrosis. The interseptal bone distal to the 1st premolar was reduced in thickness to 1 mm with a surgical 44C bur. The bone 1 mm distal of the first premolar was left intact to preserve the periodontal ligament and to aid in future periodontal regeneration. The bone distal to this thin, interproximal bone was removed up to and including the inter-radicular bone of the 2nd premolar to allow for 6mm of distraction. In order to ensure no osseous interferences were present, the depth of the osteotomies was extended 1-2 mm beyond the measured root length (Figure 4A). The buccal and lingual walls of the cortex were left intact but the lingual cortex was thinned to minimize any bony resistance to tooth movement. A surgical guide, approximately 5 mm in diameter, was moved back and forth in the osteotomy site to determine whether any bony interference needed to be removed (Figure 4B).

In order to weaken the interseptal bone and aid in rapid distraction, oblique distobuccal and distolingual undermining grooves were made to the depth of the osteotomies. These oblique osteotomies connected with the vertical osteotomies and extended approximately a quarter of the way around the first premolar (Figure 5). Following surgery, a calibrated periapical radiograph was taken to ensure adequate bone removal.

Appliance Delivery

The surgical site was irrigated with a NaCl solution, and 3.0 Vicryl sutures were used to close the site. The appliance bands were perforated with a small round bur to aid in retention. The experimental premolar was pumiced and rinsed and then etched with 37% phosphoric acid for 15 seconds and rinsed. The distraction device was cemented in place with 3M Glass Ionomer cement according to manufacturer instructions. Cotton roll isolation with manual retraction of the cheeks was sufficient to obtain an adequate dry field. The distractor was turned forward three ¼ revolutions to verify tooth movement and then was turned back. A small notch was drilled into the canine and first premolar for consistent intraoral caliper placement for tooth movement measurements. Antibiotics and analgesics were given to the dogs post-surgery for prevention of infection and pain reduction. Specifically, ketaprofen (1 mg/kg) was administered intramuscularly post-surgically. Clindamycin (11 mg/ kg) and nalbuphine (2 mg/kg) were administered intramuscularly to the dogs 2x/day post-surgically for one week and as needed until sacrifice. The dogs also received chlorhexidine gluconate rinse daily for 7 days to aid in the healing of the gingiva.

Latency and Appliance Reactivation

For each dog, a 5 or 7-day latency period was observed before distraction was started. At the end of latency, calcein green was injected as a bone marker for future histologic analysis and the first premolar was distracted distally at a rate of 1 mm/day for 6 days. The distraction screw was turned 4 ¼ revolutions to achieve 1 mm of activation. Afterwards, an intraoral caliper was used to measure the distance between the notches made in the canine and first premolar. Three measurements were averaged to determine the amount of daily tooth movement.

At the end of the distraction period, each dog received an injection of alizarin red as a bone marker for histologic analysis. A 3-week consolidation period followed to allow for bone remodeling. Prior to sacrifice, the dogs received another injection of calcein green for histologic purposes.

Euthanasia

The dogs were nil per os for 12 hours and sedated IM with ketamine with xylazine. The orthodontic bands were sectioned off of the teeth with a bur and then peeled off. The remaining glass ionomer was removed from the tooth with a high speed and diamond bur. Final records consisting of periapical radiographs, intraoral photographs, and alginate impressions were taken. The periapical radiographs were taken to evaluate apical root resorption and the degree of first premolar tipping. The impressions were poured up in die stone to make casts, for measuring tooth movements. In addition, vitality readings were recorded with the same LDF machine and protocol to check for tooth vitality (MoorVMS-LDF, Devon, UK).

Surgical plane anesthesia was confirmed by checking reflexes. Both common carotid arteries were exposed and cannulated and both external jugular veins were severed. 2 cc of Beuthanasia-D was injected intracardially and cessation of heart function was confirmed with a stethoscope. The cranium was perfused with 1 L of normal saline followed by 0.5 to 1 L of the fixative, 4% paraformaldehyde solution. The maxilla was then harvested and stored in 4% paraformaldehyde until the samples were sectioned. The specimens were then placed into 0.5% paraformaldehyde until μCT analysis was performed.

Tooth Movement

The amount of tooth movement was measured with intra-oral calipers and by comparing the initial and final casts. The intra-oral caliper measurements were made initially and at each day over the 6-day distraction period. From this data, the rate of tooth movement was calculated. On the casts, the distance from the mesial of the canine to the middle of first premolar was measured on the control and experimental sides. The middle of the first premolar was used because the mesial surface of the tooth was exposed with crown lengthening, but by the end of consolidation, gingiva had regrown in this area.

The amount of first premolar tipping was assessed from periapical radiographs in Viewbox 4.0 (DHAL Software, Kifissia, Greece). A reference line was drawn through the alveolar crest of the canine to the mesial of the third premolar (Figure 6). Lines were drawn down the long axis of the first premolar and third premolar mesial root and the angles made between these lines and the horizontal reference line were recorded. Since the third premolar angulation should have changed minimally, if at all, the change in third premolar angulation was used to adjust for radiographic distortion.

Vitality

Vitality was assessed with LDF. In order to minimize noise, the LDF probe was isolated with nitrile material and stabilized on the tooth by hand. If required, notches to stabilize the probe were drilled in the enamel of the tooth. Throughout the procedure, the heart rate of the dog was monitored. The LDF probe was placed onto the tooth and readings were taken for 1 minute. Fast Fourier Transform (FFT) analysis was performed on 2 separate 10-second intervals that showed the most stable readings. FFT analysis was performed to provide the power of the signal at different frequencies. Since the pulsatile signal of the pulpal tissue should be consistent with the heartbeat of the dog, the experimental teeth were considered vital if a peak in the signal was present within the heart rate range of each dog, and if the power of the signal was not statistically different from the control side (Figure 7).

Microcomputed Tomography Assessment of Bone Density

After sacrifice, the maxilla was sectioned from the canine root to 1-2 mm distal of the first premolar (Figure 8). The samples were then placed in 30 mm wide µCT tubes with the occlusal surfaces perpendicular to the long axis of the tubes. The tubes were filled with 0.5% paraformaldehyde and sealed with parafilm (Pechiney Plastic Packaging Company, Chicago, IL). The segments were scanned using the Scanco µCT 35 scanner (ScanCo Medical, Basserdorf, Switzerland) at 30 µm resolution, using 55 kVp, 145 µA and 800 ms integration time. The software Analyze V12.0 was used to conduct µCT analyses (AnalyzeDirect, Overland Park, KS).

µCT imaging was used to perform qualitative analyses of root resorption, to compare the width and height of the regenerate bone, and to assess the quality and quantity of the regenerate bone mesial to the first premolar. For the latter, the volume of interest (VOI) included the lamina dura and the least mature trabecular bone in the regenerate area. The lamina dura and trabecular VOI was taken from bone adjacent to the middle 80% of the root length and along an imaginary line that connected the root canals of the canine and first premolar. The middle 80% of the root length was determined by finding the total number of slices between the alveolar crestal bone and the root apex and then removing the top and bottom 10% of those slices.

For the lamina dura VOI, the distal limit was set at the root surface. The lamina dura contour was a 1 mm square that included the PDL space and lamina dura (Figure 9A). The trabecular bone contour was a circle with a 1 mm diameter. The distal limit of the circle was set at the mesial portion of lamina dura bone (Figure 9B). Both VOIs were then analyzed for bone density, bone volume fraction, and trabecular number, thickness, and separation.

Microcomputed Tomography Assessment of Regenerate Bone Width and Height

The regenerate bone was 3D reconstructed with the μCT imaging software. The 3D reconstructions were viewed from the occlusal and the palatal sides in order to make width and height measurements respectively. The differences in the buccolingual and vertical dimensions of the regenerate and control bone were classified as minimal (0-2 mm), moderate (2-4 mm), or severe (>4 mm) discrepancies.

Root Resorption

The amount of root resorption was assessed qualitatively with μCT imaging. Each side of the root was analyzed for the presence of resorptive lacunae. In addition, the lengths of the roots on the initial and final calibrated periapical radiographs were compared to estimate the amount of apical root resorption. Since the radiographs were not standardized, a horizontal reference line was drawn from the alveolar crestal bone distal to the canine to the furcal bone of the 3rd premolar. Then, lines were drawn down the long axis of the first premolar root and the mesial root of the third premolar. Since the third premolar should have moved minimally, the change in the length of the root of the third premolar was used as an adjustment factor for radiographic distortion.

Statistical Analysis

The statistical analyses for this study were conducted in IBM SPSS® version 26 (IBM Corp., Armonk, NY). All data was normally distributed and paired t-tests were used to compare initial to final measurements and between-side differences.

CHAPTER III

RESULTS

Following the PD surgeries, the dogs healed normally with no signs of infection or swelling. After the surgical procedure for Dog B, the appliance fabricated for Dog B did not fit properly. A new appliance was placed within 24 hours.

Tooth Movements and Tipping

According to the intra-oral caliper measurements, the experimental teeth moved 4.8 ± 0.5 mm in total (Table 7; Figure 10), which was statistically significant ($p<.001$). There were no statistically significant differences in the rates of tooth movement over the 6-day experimental period. The mean rate of tooth movement was 0.8 ±. 0.01 mm/day (Figure 11). The cast measurements showed that the experimental teeth moved 4.7 ± 0.4 mm and that the control teeth moved 0.2 ±. 0.24 mm (Figure 12). A paired t-test demonstrated that the experimental teeth moved significantly further than the control teeth ($p< .05$). The mean amount of tipping for the first premolar was 12.8 ±. 2.0°, which was statistically significant compared to the control side ($p<.001$).

Vitality

Fast Fourier Transform (FFT) analysis showed that the pulsatile signals from the pulpal tissue were consistent with the heart rate of the dogs recorded during the procedure. The mean power of the pre-treatment FFT signals was 0.06 ± 0.05 PU and

0.06 ± 0.03 PU, for the control and experimental sides respectively. The difference in the power of the pre-treatment signals was not statistically significant (Figure 13, p=.987). The mean power of the post-treatment FFT signals was 0.03 ± 0.04 PU and 0.04 ± 0.04, for the control and experimental sides respectively. The difference in the power of the post-treatment signals was also not statistically significant (Figure 13, p=.757).

Root Resorption

The difference in first premolar root length, after adjusting for radiographic distortion, was 0.22 ± 0.41 mm, which was not statistically significant (Figure 14, p=.360). Qualitative µCT analysis showed that every tooth had resorptive lacunae present (Table 8). Root resorption was present on the lingual surface of every experimental tooth and on almost all of the buccal surfaces (Figure 15B). Half of the teeth had root resorption on the mesial while the other half had resorption on the distal surface of the root. Dog D and F had root resorption on all surfaces while Dog G and C had root resorption on all surfaces except the distal and mesial side, respectively. Dog B had resorption on the buccal and lingual surfaces while Dog E had resorptive lacunae on the distal and lingual surfaces.

Regenerate Bone

Bone volume fraction and bone densities were less on the PD side (Table 9 and 10, Figures 16- 21), but only the difference in material density was statistically different for the lamina dura (p=.005) and trabecular bone samples (p=.029). There was no difference in the trabecular morphology between the regenerate and control trabecular bone. For the lamina dura samples, the trabecular thickness was statistically different (p=.015).

Between-side differences in the width and height of bone were not statistically significant (p=0.104 and p=0.175 respectively). In 5 dogs, differences in the buccolingual dimension of the regenerate and control bone were minimal and less than 1.5 mm (Figure 22). Dog F exhibited 2.75mm of width reduction. Differences in the height of regenerate and control bone were minimal and less than 1 mm for all dogs (Figure 23).

CHAPTER IV

DISCUSSION

Rapid tooth movement with periodontal distraction at a rate of 1 mm/ day does not cause loss of tooth vitality. In the present study, FFT analysis of LDF readings showed pulsatile signals in the pulpal tissues consistent with the heart rate of each dog, and there were no statistical between-side differences in the power of the signals. In addition, pulpal blushing was seen in one of the dogs, demonstrating blood flow (Figure 24). One clinical study that moved teeth at a rate of 0.5 mm/day also reported vitality of all teeth based on EPT post-distraction.[105] However, two studies that moved teeth at similar rates to those in the present study reported loss of vitality for 35% of teeth[98] in one, and 31% of teeth in the other.[107] Both were based on post-distraction EPT.

Importantly, EPT is limited in its ability to assess tooth vitality because it tests nerve function rather than blood flow to the pulp. EPT utilizes low-grade current to elicit a response from peripheral Aδ fibers. Pulpal C fibers have a higher firing threshold and do not respond to EPT. Aδ fibers however, are particularly susceptible to oxygen deprivation and can lose function during traumatic tooth movement even though the pulp still has blood flow and is vital.[94] Moreover, orthodontic forces elevate the threshold response and this effect can last for up to 9 months.[117] The aforementioned studies that showed loss of vitality both evaluated their subjects soon after distraction. One study checked canine vitality immediately following distraction and the other waited at least 1 month. In the latter, neighboring lateral and second premolars also tested non-vital from orthodontic therapy, which highlights the limitations of sensibility testing. EPT readings also cannot distinguish between reversible and irreversible pulpitis.[94] Kharkar et al, who mitigated the risk of false EPT readings by testing for tooth vitality 12 months post-distraction, found that PD at a rate of 0.5 mm/day does not cause loss of vitality.[109]

Experiments using dogs indicate that PD is compatible with maintaining pulpal health. Histologically, it has been shown that the pulp exhibits hyperemia after 2 weeks of daily distractions, and normal pulpal status after 6 weeks of consolidation.[112] Another study that assessed pulpal blood flow with LDF found that blood flow was 70% of baseline readings after 4 days of distraction at 0.5 mm/day, and 80% of initial levels with conventional orthodontic mechanics.[114] Due to the intermittent forces produced by PD, blood flow decreased with each distractor activation and partially rebounded after 12 hours. The closed coil springs on the control side provided continuous forces and thus a steady decline in blood flow was seen over time. TUNEL and PCNA staining showed no significant differences in odontoblastic apoptosis and differentiation between PD and conventional orthodontics.

PD can distract teeth rapidly at a rate of 0.8 mm/day. In the current study, intra-oral caliper measurements showed that the experimental teeth moved a mean 4.8 mm, which was significant ($p<.001$). The average daily rate of tooth movement was 0.8 mm/day, which was also significant ($<.001$). The cast measurements were consistent with the intraoral findings and showed 4.7 mm of tooth movement over the experimental period. One study that activated the distractor at the same rate, reported 3.41 mm of tooth movement over 4 days.[113] The daily rate of tooth movement was 0.85 mm/day, which aligns with the findings of this study. Another report stated that they moved teeth at a rate of 0.5 mm to 1 mm, but did not specify how many teeth had distractors activated at a rate of 1 mm/day to make direct comparisons.[98] At a rate of 0.8 mm/day, PD can close 7 mm extraction sites in 9 days rather than 6 months. This significant reduction in treatment time can increase patient satisfaction and prevent the adverse effects associated with prolonged orthodontic therapy.

The PD literature is consistent in showing that amount of distractor activation is not completely expressed in the rate of tooth movement. In the present study, the teeth were moved 4.8 mm and the distractor was opened 6 mm, producing a distraction activation ratio (RDR) of 0.8. In the clinical literature, the RDR ranges from 0.22 to 0.54 (Table 6). One animal study had a RDR of 0.51, while the others had higher RDRs, ranging from 0.71 to 0.99. Dog studies have higher RDR values because tooth movement was recorded for a shorter, fixed period of time and a greater fraction of the total movement can be attributed to tipping, as this is likely the first type of movement to occur in the distraction process. In addition, distraction completed over a longer period of time might be expected to produce less tooth movement because bone healing could impede tooth movements. Finally, faster bone turnover in dogs could also partially account for the discrepancy in RDR values between the clinical and animal studies.

Tipping should be expected when rapidly moving teeth with PD. In this study, the distracted teeth tipped a mean 12.8° distally. Three studies that moved teeth at 0.75 mm/day or higher[102, 107, 113] reported tipping between 7.2° and 21.9°. For teeth distracted at 0.25 mm to 0.5 mm/day, studies report 5.3° to 16.5° of tipping.[111, 113] The amount of tipping in the present study falls within these ranges. Tipping of distracted teeth occurs because the distractor applies force occlusal to the tooth's center of resistance, but this is necessary because there are anatomical limitations to placing the appliance more gingivally. Differences in appliance designs and rigidity help explain some of the variation, with less rigid appliances causing more tooth tipping. Liou et al suggested that tipping can be advantageous while moving teeth with heavy forces because it results in less apical displacement and consequently less trauma to the pulpal blood supply.[98]

After 3 weeks of consolidation, PD at a rate of 1 mm/day produces regenerate bone that is slightly less dense than mature control bone. In the present study, the apparent densities of the regenerated trabecular and lamina dura bone were less but not significantly different from the control bone. However, there was a significant difference in the material density. The difference in material density signifies that the regenerate bone is less mineralized and woven bone is still present. One study that evaluated the timeline for alveolar bone healing found a mix of woven and lamellar bone after 6 weeks.[81] In fact, after remodeling is initiated, it can take 1-4 years to achieve mature bone structure.[33, 118, 119] Equivalent material density would not be expected with 3 weeks of consolidation.

Compared to control bone, the trabecular regenerate bone had thinner and more numerous trabeculae, that were less sparse, but the between-side differences were not statistically significant. The lamina dura adjacent to the first premolar was less mature than the trabecular bone. It had more trabeculae present and the trabeculae were significantly thinner than control bone (p=.015). Trabecular spacing was equivalent between the 2 sides, however. It is expected that the trabecular morphology exhibits less maturity at this stage of consolidation. Full alveolar bone maturation can take 8-12 weeks.[81]

Currently, there are no other μCT studies that have examined the quality and quantity of the regenerate bone formed from PD. However, μCT analysis of bone allowed to consolidate for 6-weeks after DAD showed that the regenerate bone was less dense and mature than the control side.[96, 97] The reparative and remodeling bone healing phases, from callus formation to remineralization, can take 1-4 months.[33] After a 3-week consolidation period, it is expected that the bone will be less dense and continue to mineralize over time.

Mature alveolar bone should have fewer, thinner, and sparser trabeculae.[118] Based on the trabecular maturity indicators, the regenerate trabecular and lamina dura bone was less mature than control bone. None of the maturity markers were significantly different for the trabecular bone, suggesting that it was more mature than the lamina dura bone, which had significantly thinner trabeculae. This finding is logical since the lamina dura bone is closest to the premolar and should be the last bone to remodel. The lamina dura bone did show equivalent trabecular spacing on both sides, but the p value was low. If the sample size was bigger, it is likely that this difference would be statistically significant as well.

The effects of distraction on bone volume fraction depend on the type of distraction. The regenerate trabecular and lamina dura bone volume fraction in the present study was not statistically different from untreated bone. In contrast, two dog studies on DAD[96, 97] found a significant difference in bone volume fraction after DAD. The significantly smaller bone volume fraction can be attributed to the more invasive DAD surgical protocol. The distracted transport disc included the buccal and lingual cortices, and only the lingual periosteum and mucosa were left in tact. It is reasonable to expect a smaller bone volume fraction with this surgical damage than with PD.

After distraction, the vertical and buccolingual dimensions of regenerate bone are comparable to untreated bone. In the present study, between-side differences in height were minimal (<1mm) for all dogs; differences in width between the control and experimental bone were also minimal (<2mm) in all cases, except 1 dog that showed a moderate (2.75 mm) difference. Moore and coworkers reported that over 75% of the samples exhibited complete or almost complete bone regeneration in the vertical and buccolingual dimensions after DAD.[96] In another DAD study, 92% of specimens demonstrated less than 1 mm of vertical bone loss.[97] The bone fill in the present study meets the restorative guidelines for implant placement,[120, 121] suggesting an alternative application of PD is to retract single-rooted teeth to provide adequate bone for restorative prosthetics.

The PD protocol in this study resulted in minimal apical root resorption. Based on periapical radiographs taken pre and post-distraction, there was no significant difference in root length after PD. Multiple clinical studies have used periapical radiographs to assess root resorption and the consensus is that PD causes none to minimal root resorption and no ankylosis.[98, 102,105,109] External root resorption is an unavoidable consequence of orthodontic tooth movement. Generally, the amount of root resorption is clinically insignificant and repairable, but certain precipitating factors increase the likelihood and severity of this phenomenon. Treatment duration has been linked to the incidence of root resorption in orthodontic patients.[7, 122, 123] Rapidly distracting teeth with PD can decrease the duration of tooth movement and could mitigate the risk of root resorption. Root resorption is also thought to develop 1-3 weeks after orthodontic forces are applied.[7] Since retraction with PD is completed so quickly, the start of root resorption might be prevented. The surgical procedure also undermines interseptal bone and removes osseous interferences that could otherwise produce pressure-induced root resorption.

μCT analysis showed resorptive lacunae present on all lingual root surfaces and on almost all buccal surfaces. One dog study distracted teeth for 2 weeks at 0.5 mm/day and reported the presence of small regions of root resorption on all premolars histologically after 2 weeks of consolidation. By week 8 however, partial repair of these resorptive cavities with cementum was observed.[112] This study suggests that the repair of resorptive lacunae occurs after the discontinuation of forces, but other studies have shown that this process starts earlier while forces are applied.[124-127] One dog study demonstrated ongoing cellular cementum repair of 24% of lesions while intrusive forces were applied.[127]

The presence of resorptive lacunae on the lingual surfaces of all teeth can be explained by the biomechanics of distraction, the appliance design and rigidity, and the dentoalveolar anatomy in dogs. From the canine to third premolar in dogs, the alveolar ridge is slightly curved (Figure 1), but distraction appliances are rigid and distract teeth in a linear fashion due to appliance stiffness. In order to reduce the likelihood that the teeth would retract against the cortical plates, the distractor guide bars were placed on the lingual side of the appliance, so that tooth movement could follow the alveolar ridge as closely as possible. An extension arm was soldered from the guide rods to the premolar band in effort to provide some flexibility in tooth movement. Although steps were taken to modify the appliance design and ensure adequate bone removal, it is likely that the teeth still experienced pressure-induced root resorption, especially on the lingual surface, since the force vector of the appliance was applied from the lingual.

Clinical Significance

Periodontal distraction is a minimally invasive surgical procedure that can be completed at the time of extractions to reduce overall treatment time and mitigate the iatrogenic side effects associated with longer treatment durations. At a rate of 0.8 mm/day, PD can close extraction spaces in 9 days without loss of tooth vitality and with minimal root resorption. This procedure is indicated for crowded, extraction cases, without buccolingually displaced canines, where quick anterior alignment can be achieved with the RAP after canine retraction. It may reduce the need for skeletal anchorage in such cases because it produces minimal anchorage loss. PD can also be utilized to distract single-rooted teeth and create sufficient bone for implant placement in patients with congenitally missing teeth or in partially edentulous patients. Further studies into curvilinear distraction could make this procedure a viable option for creating bone for implant placement in congenitally missing lateral incisor cases.

CHAPTER V

CONCLUSIONS

1. Periodontal distraction at a rate of 1 mm/day does not cause loss of tooth vitality.
2. Periodontal distraction can rapidly distract single-rooted teeth at a rate of 0.8 mm/day.
3. Periodontal distraction at a rate of 1 mm/day has little effect on the vertical and buccolingual dimensions of the regenerate bone.
4. After 3 weeks of consolidation, the regenerate bone from periodontal distraction is slightly less mature and dense but of sufficient quality and quantity for implant placement.
5. Periodontal distraction at a rate of 1 mm/day causes minimal root resorption.

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APPENDIX A

FIGURES

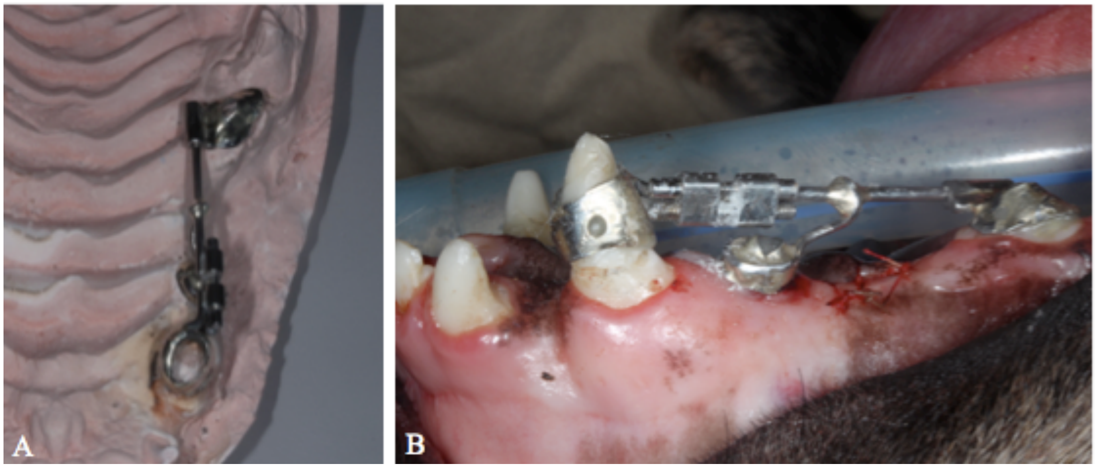


Figure 1: Appliance design and placement. A) Occlusal view of appliance on cast. B) Buccal view of cemented appliance.

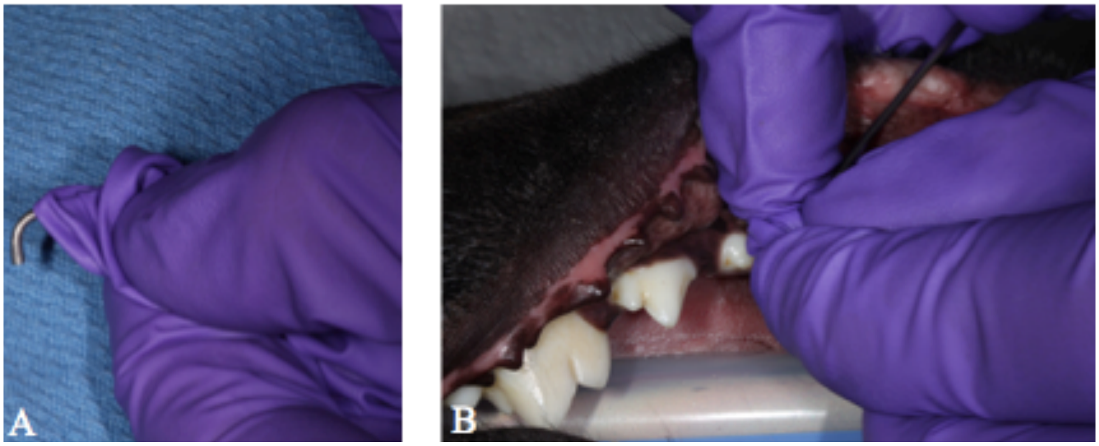


Figure 2: LDF probe isolation and stabilization. A) The LDF probe wrapped in nitrile glove to block noise from the surrounding periodontium. B) The probe was stabilized by hand.

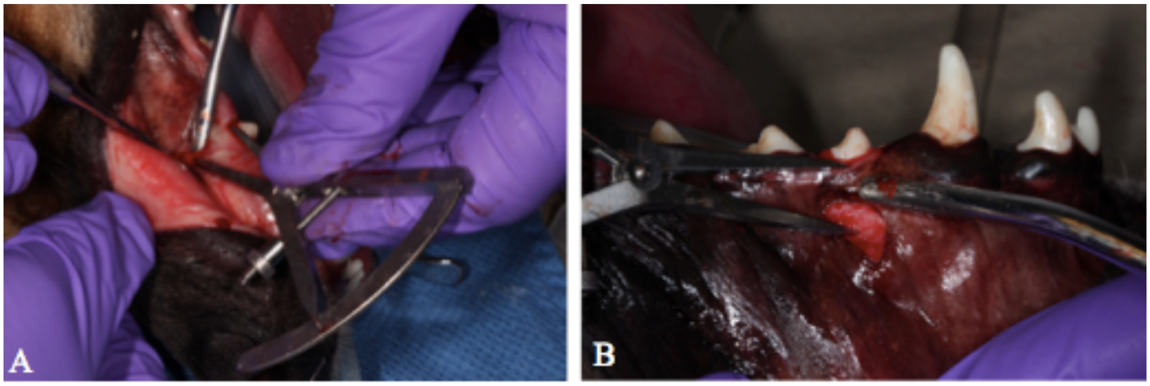


Figure 3: Surgical root exposure. While performing vertical osteotomies, the first premolars were susceptible to iatrogenic root damage because of their distal inclination. Surgical exposure of the root apex helped guide bur angulation while making osteotomies. A) Measurement of the root length. B) Surgical exposure of the root apex.

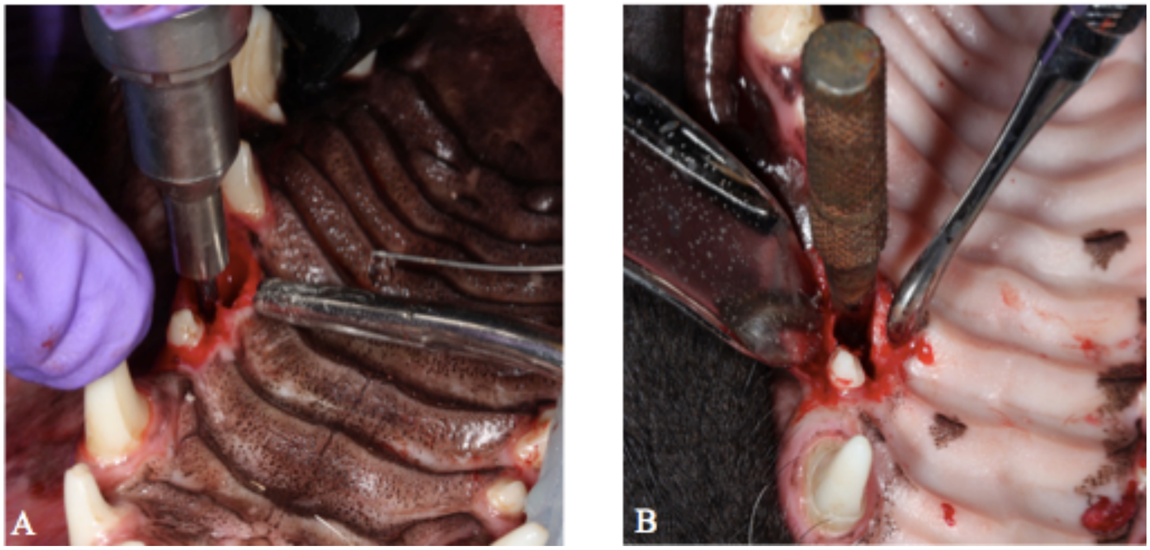


Figure 4: Surgical osteotomies and elimination of osseous interferences. A) Vertical osteotomies made with the 44C bur to the depth of 1-2 mm beyond the root apex. B) Surgical guide used to check for bony interferences.

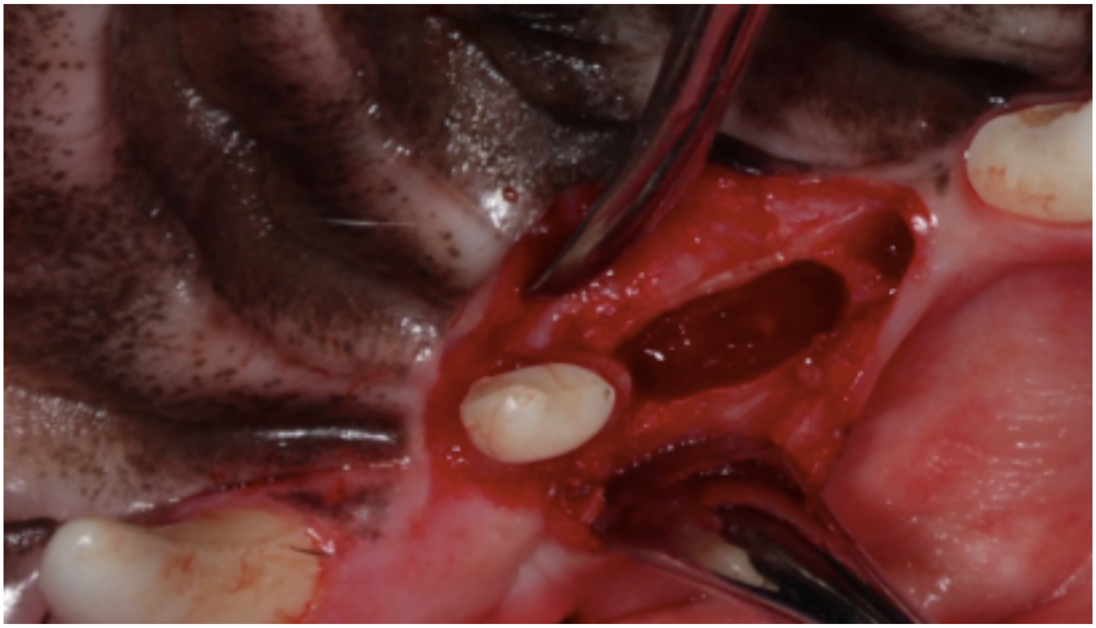


Figure 5: Completed periodontal distraction surgery. Note the buccal and lingual walls are in tact. The tooth has adequate buccal and lingual clearance to distract distally. The vertical undermining grooves around the 1st premolar can be seen.

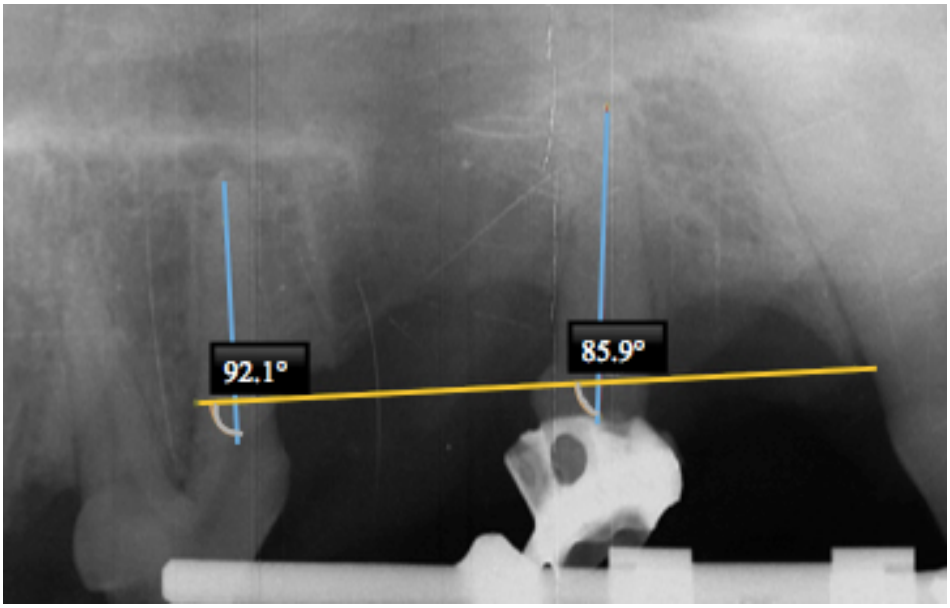


Figure 6: Calculation of premolar tipping. Root angulation was calculated in relation to a reference line drawn from the bone distal to the canine to that mesial of the 3rd premolar. The change in 3rd premolar angulation was used to adjust for radiographic distortion.

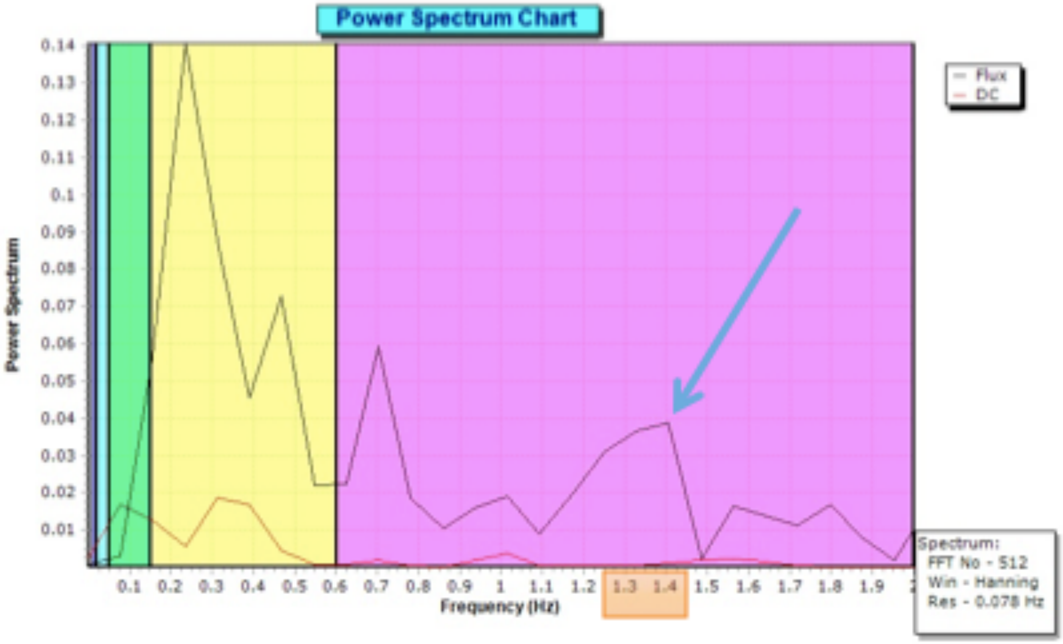


Figure 7: FFT analysis of vitality data. FFT sample analysis showing a peak pulsatile signal (arrow) consistent with the documented heart rate range of the dog during the procedure (shown in orange).

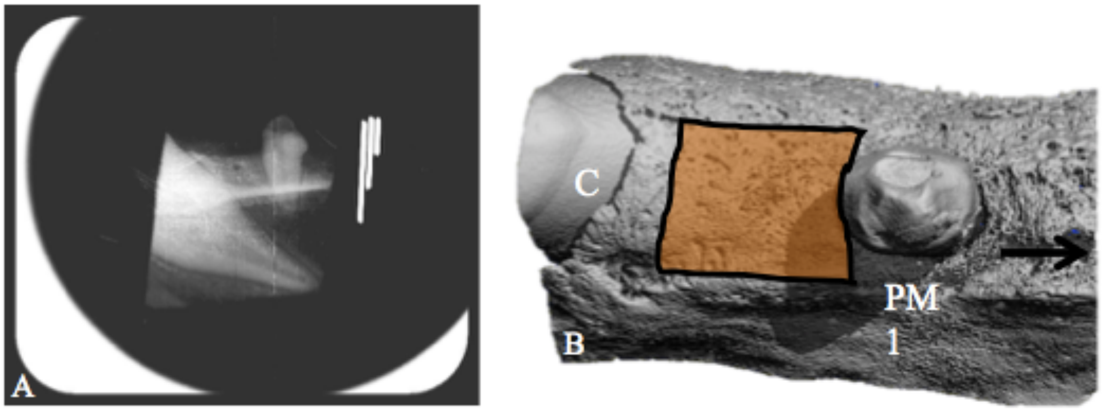
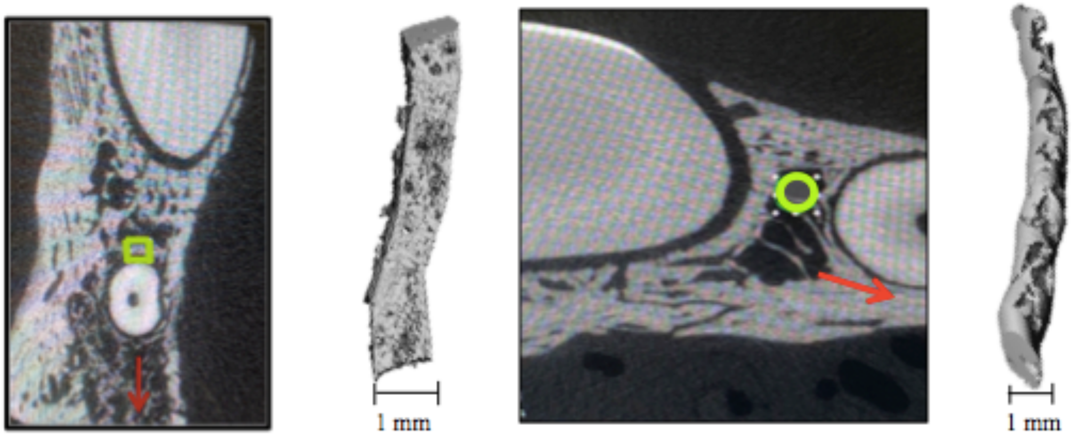


Figure 8: Region of interest for microcomputed tomography analysis. A) The specimen included the first premolar and regenerate bone as shown in this radiograph. B) Three-dimensional reconstruction of the specimen used. The regenerate bone is shown in orange.



A) Lamina Dura

B) Trabecular Bone

Figure 9: Volume of interest for microcomputed tomography bone analysis. A) Sample lamina dura contour for 1 slice with three-dimensional reconstruction. B) Sample trabecular contour for 1 slice with three-dimensional reconstruction.

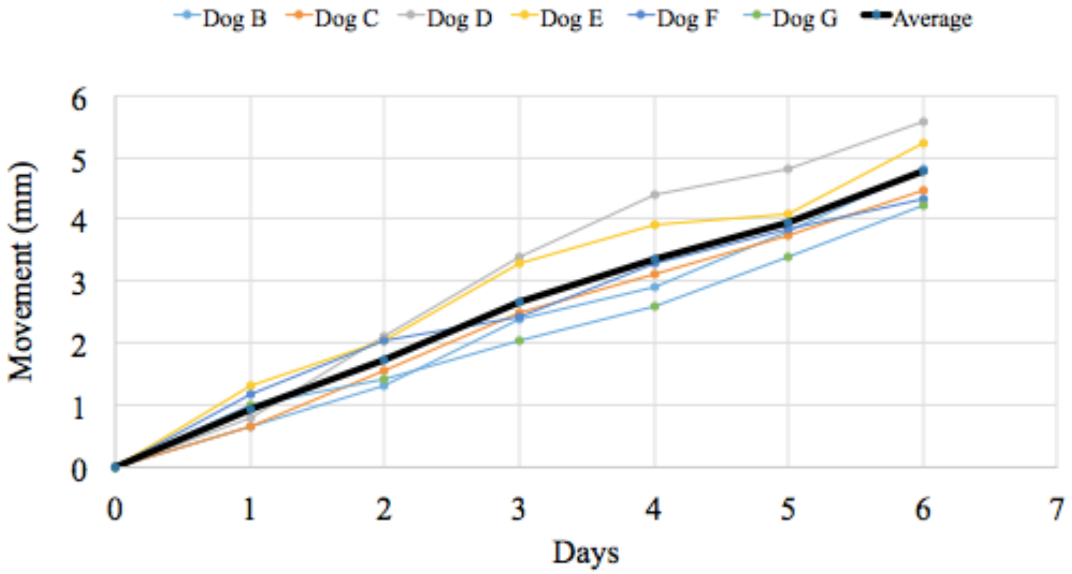


Figure 10: Intra-oral measurements of tooth movement. Over the 6-day period, the experimental teeth moved 4.8 mm on average.

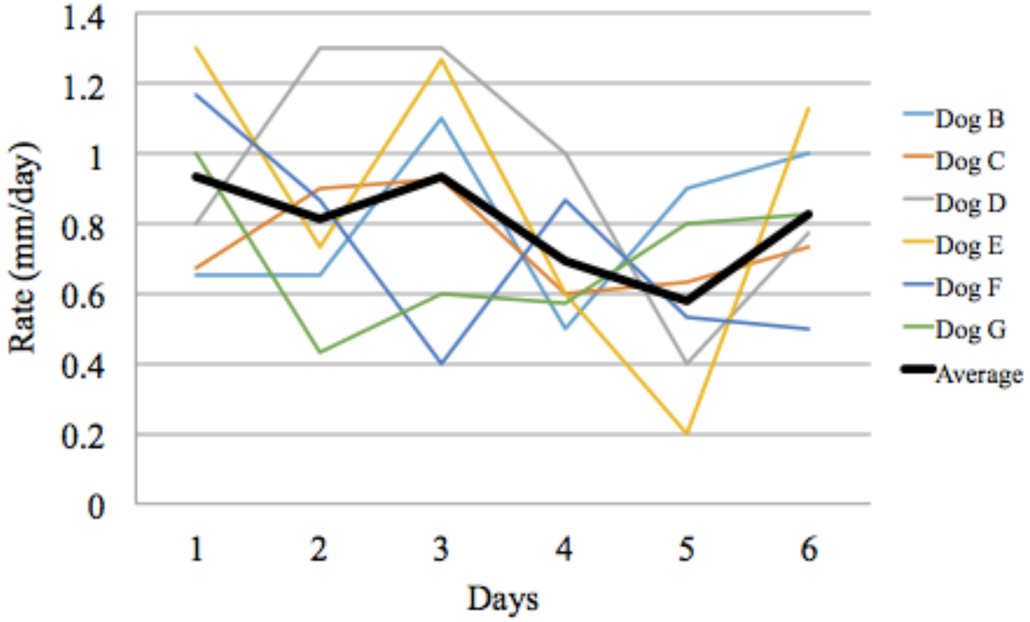


Figure 11: Mean daily rates from intra-oral measurements. The average rate of tooth movement was 0.8 mm/day.

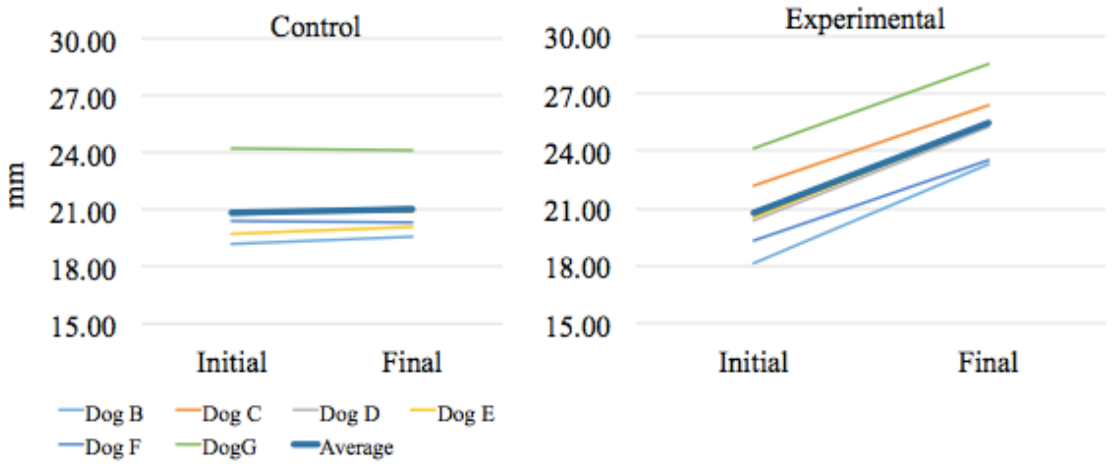


Figure 12: Tooth movement from cast measurements. The experimental teeth moved 4.7 mm and significantly further than control teeth (p=0.027).

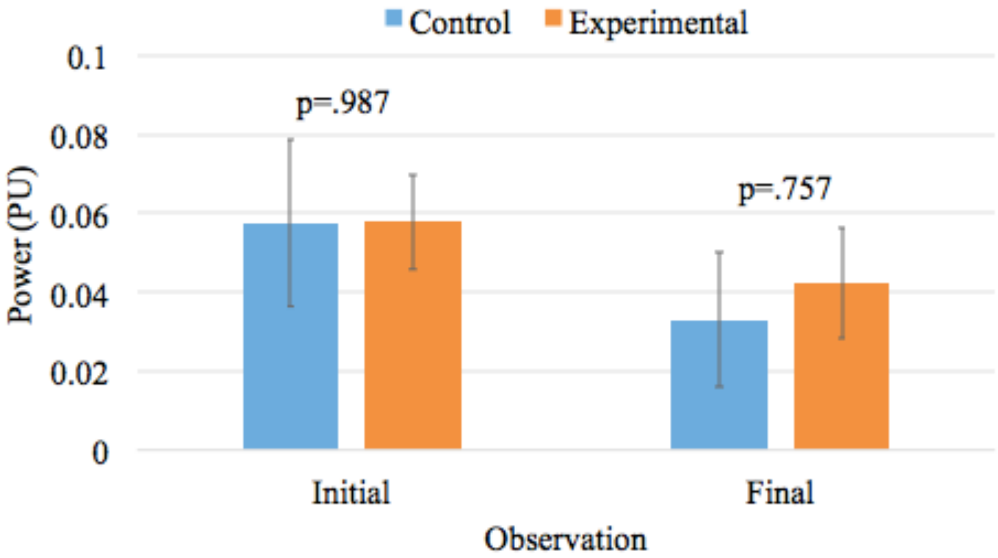


Figure 13: Power of peak frequency signals. The power of the peak frequency signals was not significantly different between the 2 sides at the initial or final time point.

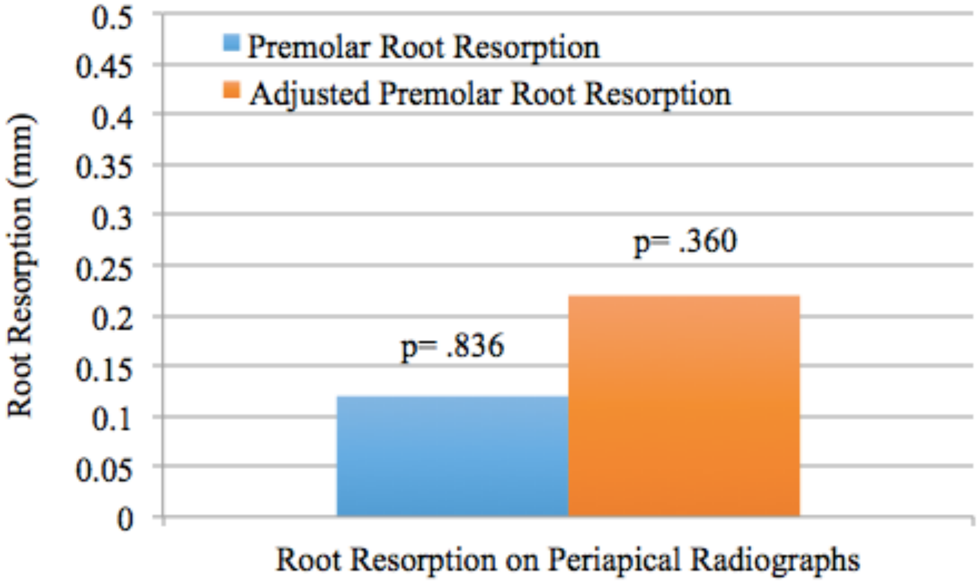


Figure 14: Root resorption from periapical radiographs. Insignificant amounts of root resorption resulted from the procedure. Changes in root length were measured on periapical radiographs and adjustments were made for radiographic distortion.

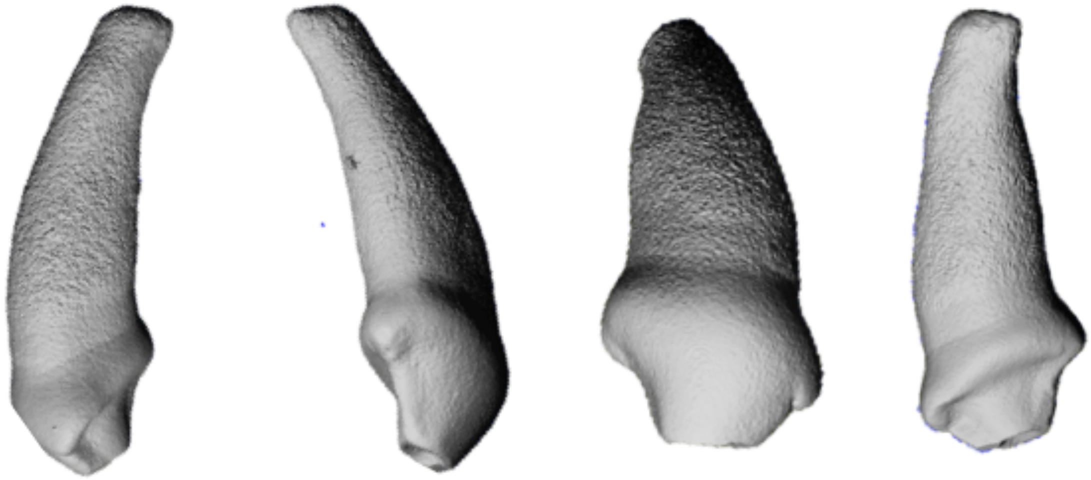


Figure 15A: Control teeth roots. The roots of control teeth looked smooth and regular.

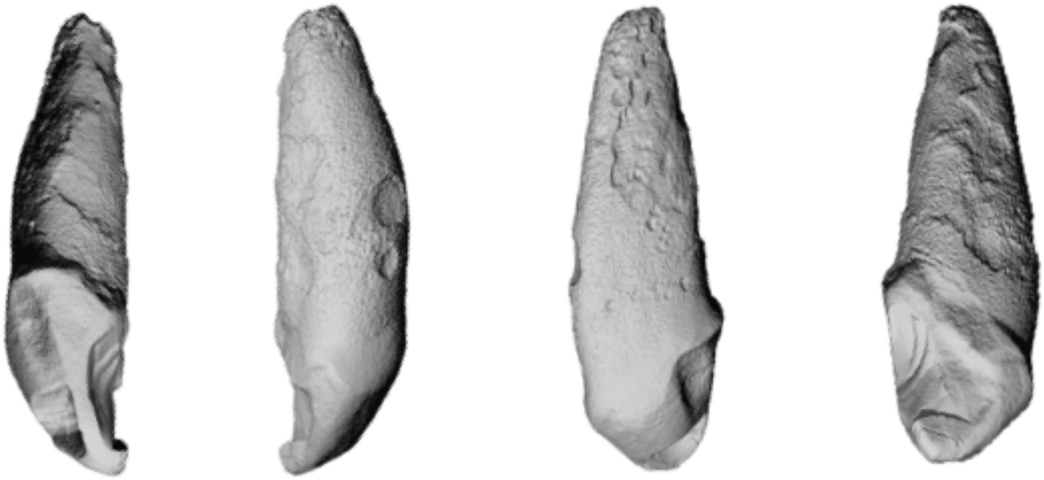


Figure 15B: Periodontal distraction root resorption. The root resorption seen on these experimental teeth were among the worst in the 6 dogs and were not representative of the entire sample.

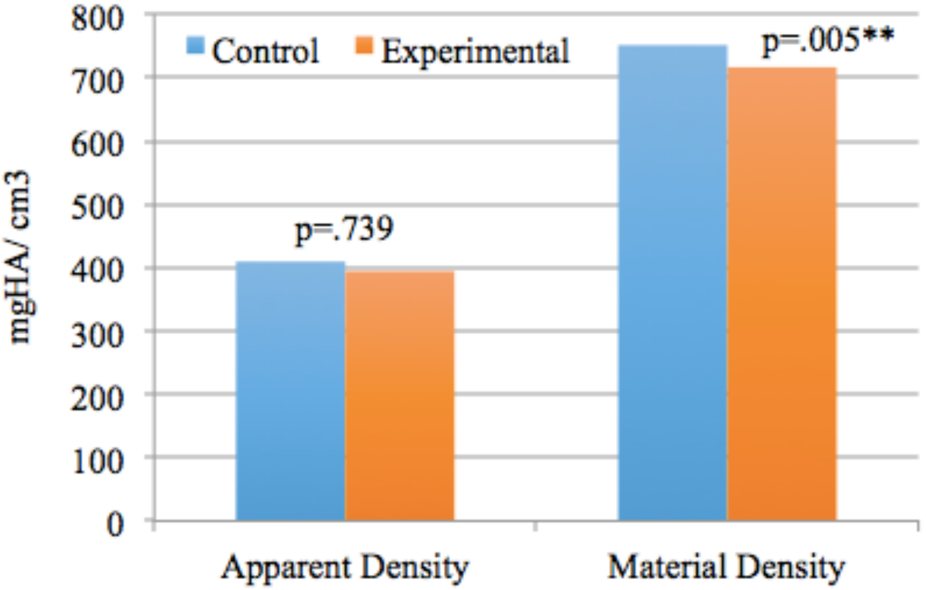


Figure 16: Comparison of apparent and material density for the trabecular bone samples. Only the material density was statistically different between the experimental and control trabecular bone samples.

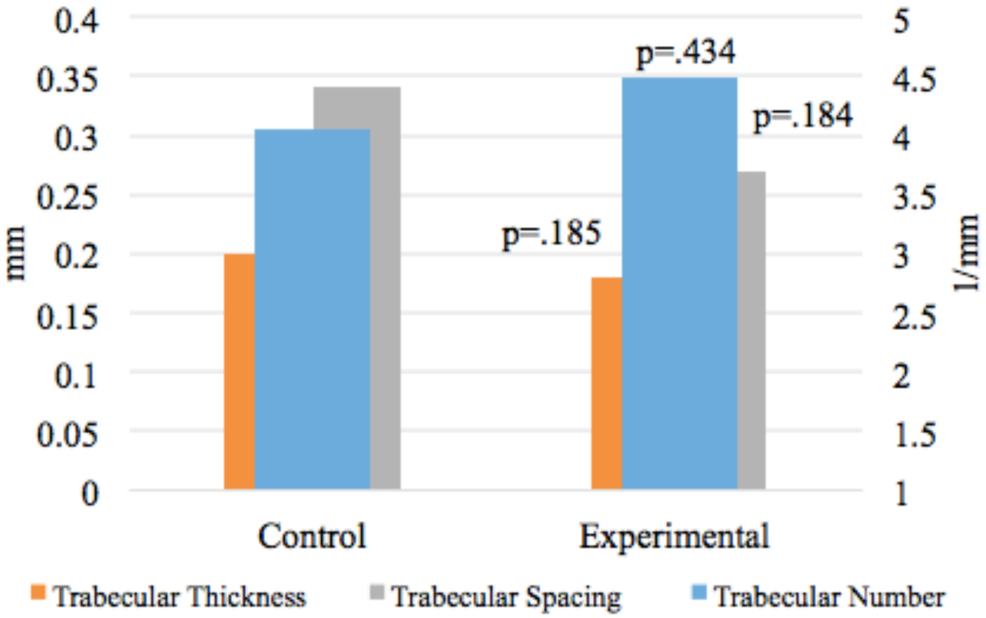


Figure 17: Comparison of trabecular morphology for the trabecular bone samples. There were no statistical between-side differences in the trabecular number or morphology for the trabecular bone samples.

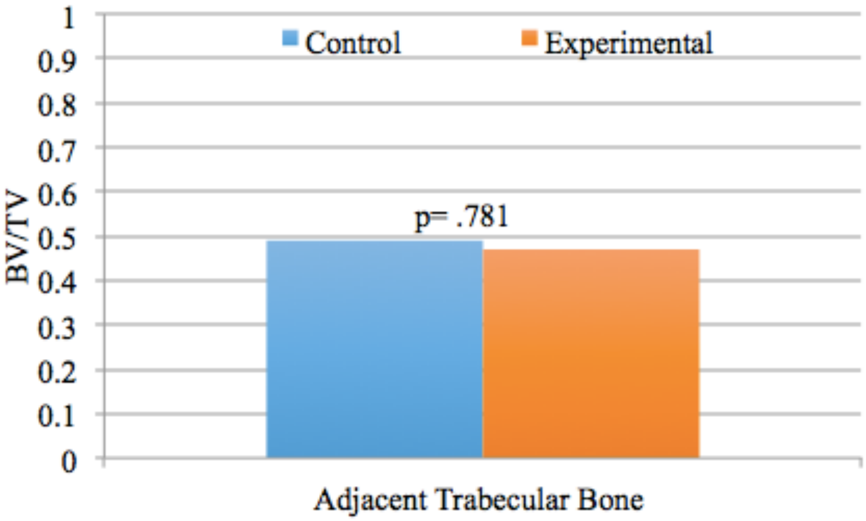


Figure 18: Comparison of bone volume fraction for the trabecular bone samples. There was no statistical difference in the bone volume fraction for the control and experimental trabecular bone samples.

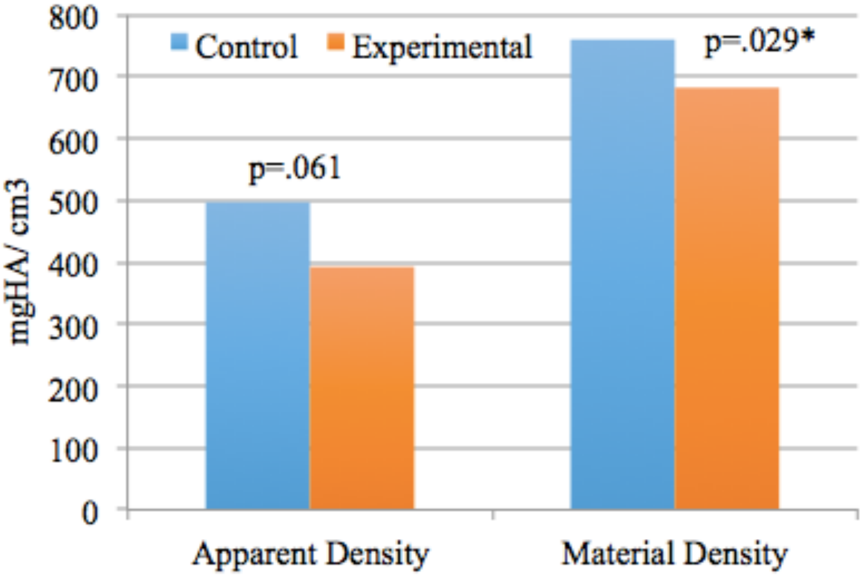


Figure 19: Comparison of apparent and material density for the lamina dura samples. Only the material density was statistically different between the experimental and control lamina dura bone samples.

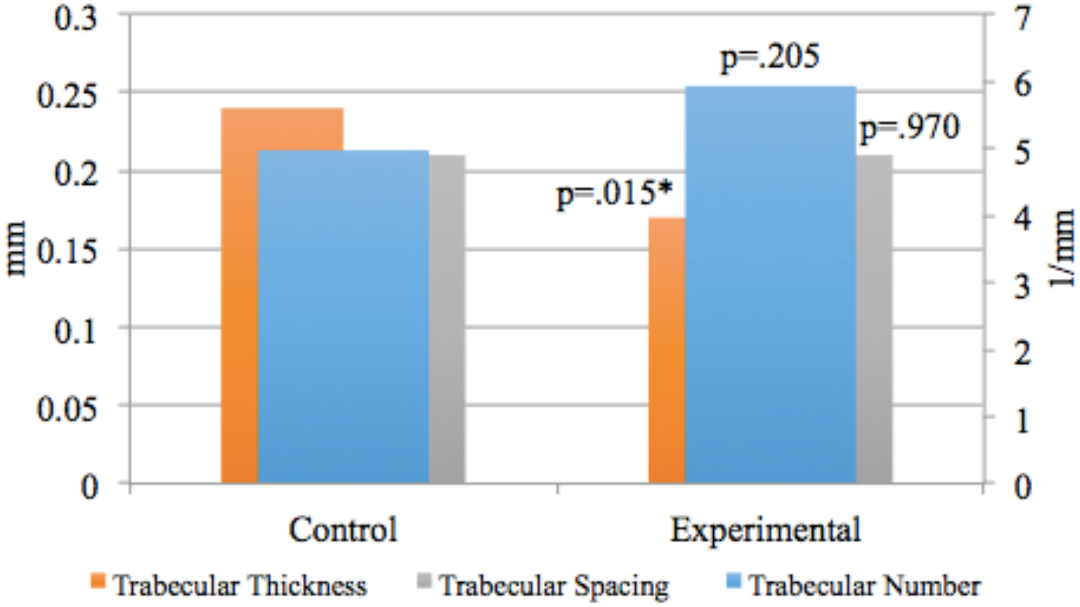


Figure 20: Comparison of trabecular morphology for lamina dura samples. Only the difference in trabecular thickness was statistically significant for the lamina dura samples.

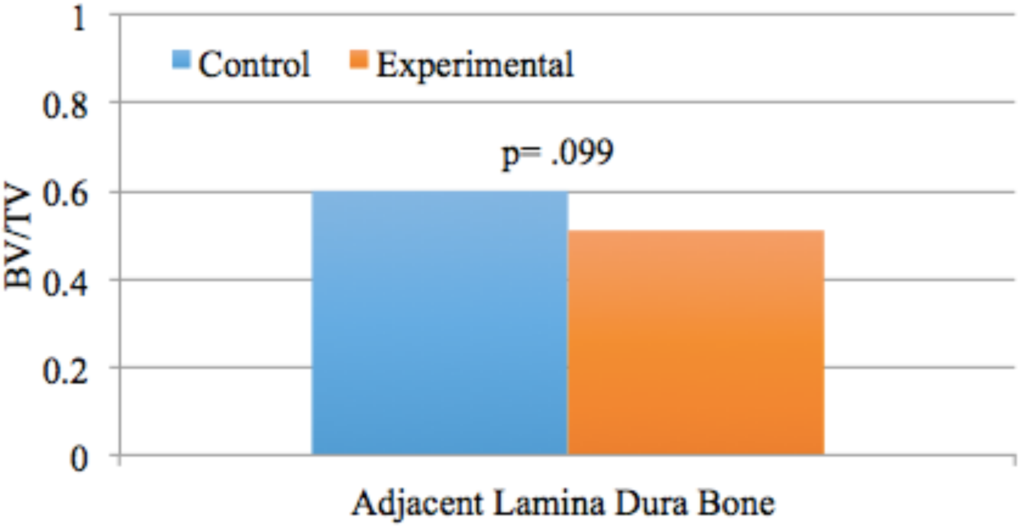


Figure 21: Comparison of bone volume fraction for the lamina dura samples. There was no statistical difference in the bone volume fraction for the control and experimental lamina dura bone samples.

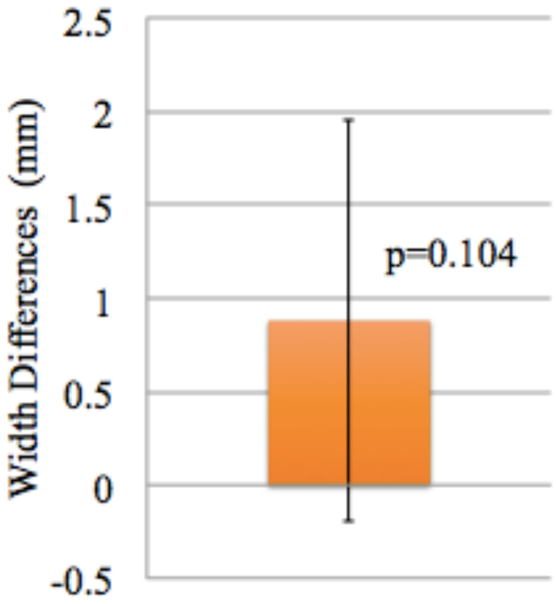


Figure 22: Differences in the buccolingual dimension between control and regenerate bone. The differences in the buccolingual dimension of the regenerate and control bone were minimal for all but one dog, which had moderate changes (<3mm) in bone width.

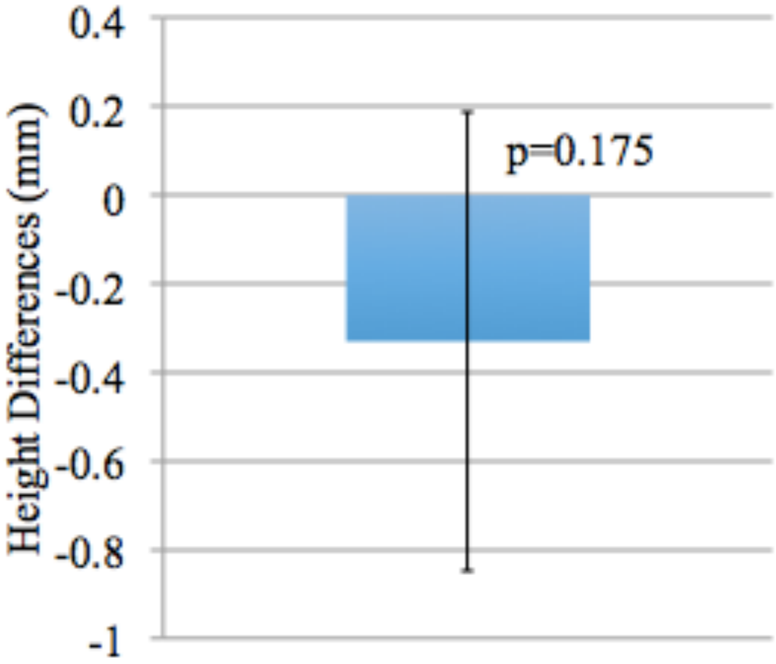


Figure 23: Differences in the vertical dimension of control and regenerate bone. The differences in the height of the regenerate and control bone were minimal (<1mm) for all specimens.

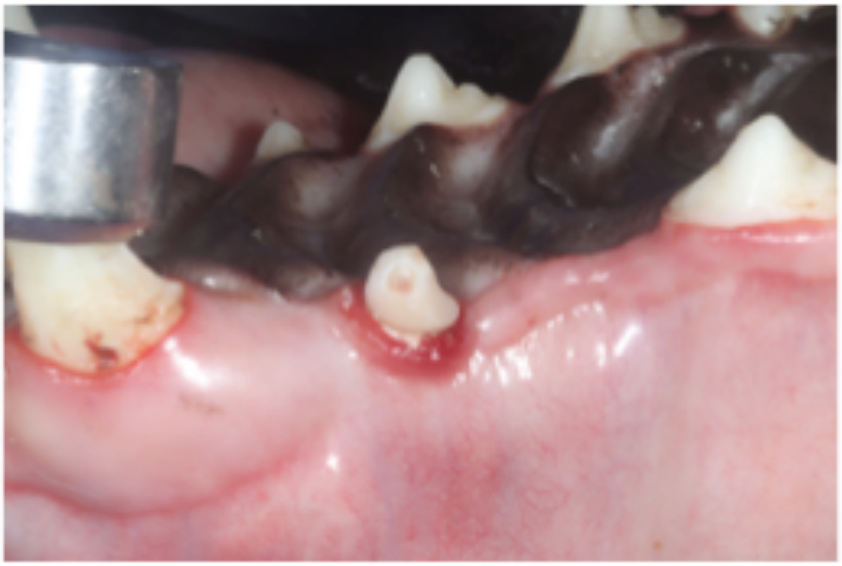


Figure 24: Pulpal blushing. Pulpal blushing was seen on one dog at the end of the experimental period, indicating that the tooth was most likely vital.

APPENDIX B

TABLES

Reference	**Study Design**	**N**	**Control Group**	**Latency**	**Rate Per Day**	**Canine Retraction time**
Kişnişci et al 2002[88]	Case series	11	No	0 days	0.8 mm	8-14 days
Iseri et al 2005[91]	Case series	10	No	1-3 days	0.8 mm	10 days
Gürgan et al 2005[89]	Case series	18	No	1-3 days	0.8 mm	10.36 days
Kişnişci et al 2011[90]	Retrospective Case series	73	No	1-2 days	0.8 mm	10 days
Sukurica et al 2007[92]	Case series	8	No	3 days	1.0 mm	14.7 days
Kurt et al 2017[95]	Case series	33 total (19 DAD, 14 control)	Yes (intraoral elastics)	3 days	0.8 mm	11.8 days

Table 1: Comparison of clinical studies on dentoalveolar distraction. N= # of subjects**.**

Reference	Study Design	N	Control	Intervention
Liou et al 1998[98]	Case Series	5	No	Bilateral extractions PD with orthopedic forces
Sayin et al 2004[102]	Case Series	18	No	Bilateral extractions PD with orthopedic forces
Kumar et al 2009[105]	Case Series	8	No	Bilateral extractions PD with orthopedic forces
Kharkar et al 2010[109]	Clinical trial	12	No	Bilateral extractions PD or DAD with orthopedic forces
Mowafy et al 2011[103]	Split-mouth, RCT	30	Yes (CCS)	Bilateral extractions E: PD with orthopedic forces C: PD with orthodontic forces
Kumar et al 2012[106]	Case series	5	No	Bilateral extractions PD with orthopedic forces and lingual powerchain
Khanna et al 2014[108]	Split-mouth, Clinical trial	25	Yes (CCS)	Bilateral extractions E: PD with orthodontic forces (CCS from MSI) C: Orthodontic forces (CCS from MSI)
Leethanakul et al 2014[104]	RCT	18	Yes (B/L elastomeric threads)	Bilateral extractions Retraction from MSI E: PD (w/o B/L grooves) with orthodontic forces C: Orthodontic forces
Kateel et al 2015[107]	Clinical trial	8	No	Bilateral extractions E: PD (w/flaps) with orthopedic forces C: PD with orthodontic forces

Table 2: Description of periodontal distraction clinical studies. Available periodontal distraction clinical studies with a sample size of 2 or greater. E=experimental, c= control, n= # of subjects, ccs= closed coil spring.

Reference	Forces Used	Latency	Rate Per Day	Tooth Movement	Tipping (°)	Anchorage Loss
Liou et al 1998[98]	Orthopedic	0 d	0.5-1 mm	6.5 mm in 3 weeks	N/A	Superimpositions 73%: 0 mm 27%: <. 0.5 mm
Sayin et al 2004[102]	Orthopedic	0 d	0.75 mm	In 3 weeks: Mx: 5.76 mm Md: 3.5 mm	Mx: 11.47 Md: 7.16	Mx: 0.56 mm Md: None
Kumar et al 2009[105]	Orthopedic	0 d	0.5 mm	5.25 mm in 20.33 d	15.33	Minimal
Kharkar et al 2010[109]	Orthopedic	PD: 0 d DAD: 2 d	PD: 0.5 mm DAD: 0.5 mm	PD: 19.5 d DAD: 12.5 d Distance not given	PD: 15.33 DAD: 10.61	PD: 0.25 mm DAD: 0.32 mm
Mowafy et al 2011[103]	E: Orthopedic C: CCS with ½ force	0 d	0.25 mm	E: 5.9 mm in 5.3 weeks C: 4.7 mm in 27.9 weeks	E: 10.47 C: 0.27	E: 2.5 mm C: 2.81 mm NS
Kumar et al 2012[106]	Orthopedic	0 d	0.4 mm	6.42 mm in 3.5 weeks	15.1	Minimal
Leethanakul et al 2014[104]	E: 150 g C: 150 g	N/A	N/A	In 3 months: E: 5.4 mm C: 3.4 mm	E: 7.50 C: 4.5 NS	N/A
Khanna et al[108]	E: 150 g C: 150 g	N/A	N/A	In 3 months: E: 6.9 mm C: 5.31 mm	N/A	NS
Kateel et al 2015[107]	Orthopedic	PD: 0 d DAD: 3 d	0.8 mm	PD: 6.63 mm in 15.38 d DAD: 6.91 mm in 14.5 d	PD: 14.94 DAD: 14.88	PD: 0.91 mm DAD: 0.84 mm

Table 3: Periodontal distraction clinical studies and tooth movement. Summarized tooth movement, tooth tipping, and anchorage loss data for available periodontal distraction clinical studies with a sample size of 2 or greater. E=experimental, c= control.

Reference	Distraction Rate Per Day	Tooth Movement	Root Resorption	Pulp Vitality
Liou et al 1998[98]	0.5-1 mm	6.5 mm in 3 weeks	Periapicals None to light blunting/irregular No ankylosis	EPT 35% vital
Sayin et al 2004[102]	0.75 mm	In 3 weeks: Mx: 5.76 mm Md: 3.5 mm	Periapicals No significant root resorption of canines	N/A
Kumar et al 2009[105]	0.5 mm	5.25 mm in 20.33 days	Radiographic analysis Minimal	EPT pre and 1 month post-distraction No vitality loss
Kharkar et al 2010[109]	PD: .5 mm DAD: .5 mm	PD: 19.5 d DAD: 12.5 d Distance not given	Periapicals PD: 1 case minimal root resorption DAD: no root resorption	EPT: removal of device, 6 and 12 mo post-op No vitality loss
Mowafy et al 2011[103]	0.25 mm	5.9 mm in 5.3 weeks	N/A	N/A
Kumar et al 2012[106]	0.4 mm	6.42 mm in 3.5 weeks	N/A	N/A
Khanna et al 2014[108]	N/A	In 3 months: E: 6.9 mm C: 5.31 mm	N/A	N/A
Leethanakul et al 2014[104]	N/A	5.4 mm in 3 months	N/A	N/A
Kateel et al 2015[107]	0.8 mm	PD: 6.63 mm in 15.38 d DAD: 6.91 mm in 14.5 d	N/A	EPT post- distraction 31% teeth vital

Table 4: Periodontal distraction clinical studies and pulpal vitality. Summarized results from clinical studies on how periodontal distraction impacts root and pulpal health. E=experimental, c= control.

Reference	Rate Per Day	Total Tooth Movement	Time	Pulpal Vitality
Ai et al 2008[111]	0.5 mm	3.6 mm	2 weeks	N/A
Lv et al 2009[112]	0.5 mm	5.01 mm	2 weeks	Histology Teeth Vital
Shimojima et al 2012[113]	0.25 mm 0.5 mm 1 mm	0.91 mm 1.75 mm 3.41 mm	4 days	N/A
Nagano et al 2018[114]	0.5 mm	1.98 mm	4 days	LDF Teeth Vital

Table 5: Periodontal distraction experimental literature and pulpal vitality. Only 2 animal studies have tested pulpal vitality after PD. E=experimental, c= control.

Reference	Latency	Distraction Rate Per Day	Mean Total Distraction	Total Tooth Movement	RDR (Rate of Movement to Distractor Activation Ratio)	Tipping (°)
Sayin et al 2004[102]	0 d	0.75 mm	15.75 mm	In 3 weeks: Mx: 5.76mm Md: 3.5 mm	Mx: 0.36 Md: 0.22	Mx: 11.47 Md: 7.16
Kumar et al 2009[105]	0 d	0.5 mm	10.17 mm	5.25 mm in 20.33 d	0.52	15.33
Kumar et al 2012[106]	0 d	0.4 mm	9.8 mm	6.42mm in 3.5 weeks	0.66	15.1
Kateel et al 2015[107]	PD: 0 d	0.8 mm	12.30 mm	6.63 mm in 15.38d	0.54	PD: 14.94
Ai et al 2008[111]	0 d	0.5 mm	Week 1: 3.5 mm Week 2: 7.0 mm	Week 1: 1.75 Week 2: 3.6	Week 1: 0.50 Week 2: 0.51	Week 1: 7.5 Week 2: 16.5
Lv et al 2009[112]	0 d	0.5 mm	7 mm	5.01 mm in 2 weeks	0.71	N/A
Shimojima et al 2012[113]	0 d	0.25 mm 0.5 mm 1 mm	1 mm 2 mm 4 mm	In 4 days: 0.91 mm 1.75 mm 3.41 mm	0.91 0.88 0.85	5.28 8.71 21.92
Nagano et al 2018[114]	0 d	0.5 mm	2 mm	1.98 mm	0.99	N/A

Table 6: Distractor activation expression for periodontal distraction. Comparison of distractor activation to actual tooth movement achieved in clinical and animal periodontal distraction studies. E=experimental, c= control.

Measurement	Units	Experimental	SD	Control	SD	Prob
Cast C-P1	mm	4.66	0.43	.019	0.24	0.027
Intraoral C-P1	mm	4.77	0.53	0	0	<.001
Intraoral Mean Rate	mm/ day	0.80	0.14	0	0	<.001
Radiographic Tipping	deg (°)	12.75	1.98	0	0	<.001

Table 6: Tooth movement and tipping data. Accumulated tooth movement and tipping data from the 6-day experimental period**.**

Dog	Mesial	Distal	Buccal	Lingual
Dog B			X	X
Dog C		X	X	X
Dog D	X	X	X	X
Dog E		X		X
Dog F	X	X	X	X
Dog G	X		X	X

Table 7: Microcomputed tomography qualitative assessment of root resorption.

Trabecular Bone	Experimental		Control		Difference
	Mean	SD	Mean	SD	Prob
Bone Volume Fraction (bone volume/total volume)	0.47	0.11	0.49	0.14	0.781
Apparent Density (mg HA/cm^3)	394.26	73.48	409.50	102.04	0.739
Material Density (mg HA/cm^3)	716.33	25.13	751.21	24.35	**0.005**
Trabecular Number (1/mm)	4.49	0.98	4.05	1.44	0.434
Trabecular Thickness (mm)	0.18	0.02	0.20	0.04	0.185
Trabecular Spacing (mm)	0.27	0.07	0.34	0.13	0.184

Table 8: Microcomputed tomography analysis of the adjacent trabecular bone.

Trabecular Bone	Experimental		Control		Difference
	Mean	SD	Mean	SD	Prob
Bone Volume Fraction (bone volume/total volume)	0.47	0.11	0.49	0.14	0.781
Apparent Density (mg HA/cm^3)	394.26	73.48	409.50	102.04	0.739
Material Density (mg HA/cm^3)	716.33	25.13	751.21	24.35	**0.005**
Trabecular Number (1/mm)	4.49	0.98	4.05	1.44	0.434
Trabecular Thickness (mm)	0.18	0.02	0.20	0.04	0.185
Trabecular Spacing (mm)	0.27	0.07	0.34	0.13	0.184

Table 9: Microcomputed tomography analysis of the adjacent lamina dura bone.