QUALITY AND INTENSITY OF PAIN ASSOCIATED WITH CONTINUOUSLY
APPLIED ORTHODONTIC STRESSES OF RELATIVELY HIGH AND LOW MAGNITUDES

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MASTER OF SCIENCE

by
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QUALITY AND INTENSITY OF PAIN ASSOCIATED WITH CONTINUOUSLY APPLIED ORTHODONTIC STRESSES OF RELATIVELY HIGH AND LOW MAGNITUDES

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ABSTRACT

The purpose was to assess longitudinally pain intensity and quality during tooth translation by 2 continuous stresses. Eight subjects (five males, 3 females) who required maxillary first premolar extractions had maxillary canines retracted segmentally using 4 kPa on one side and 78 kPa on the other. Subjects scored Modified McGill Pain Questionnaire-Short Forms (MMPQ-SF), Visual Analogue Scales (VAS), and Present Pain Intensities (PPI) for both sides at the beginning of 13 appointments during 4 phases: baseline, post-placement of separators, early and later tooth-loading.

Pain intensity (MMPQ-SF, VAS, PPI) and generalized/emotional subscale scores showed no significant differences between stresses. Localized subscale scores were higher for 78 kPa compared to 4 kPa sides. Females tended to report higher VAS and PPI compared to males. Significant differences were found between baseline and post-placement of separators and between baseline and early tooth-loading using MMPQ-SF and localized subscale scores.
The faculty listed below, appointed by the Dean of the School of Dentistry, have examined a thesis titled “Quality and Intensity of Pain Associated with Continuously Applied Orthodontic Stresses of Relatively High and Low Magnitudes,” presented by Jodi K. Hentscher-Johnson, candidate for the Master of Science in Oral Biology degree, and hereby certify that in their opinion it is worthy of acceptance.

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CHAPTER 1

INTRODUCTION

Pain is a common experience among patients undergoing orthodontic treatment. This experience is often referred to as the most negative effect of orthodontic treatment (Oliver and Knapman 1985). The perception of what is painful is different among individuals. However, the vast majority of patients experience some sort of discomfort during treatment. Prevalence of pain was reported during orthodontic treatment in approximately 90% to 95% of subjects (Scheurer et al. 1996; Bergius et al. 2002) with similar findings by other authors (Ngan et al. 1989; Jones and Chan 1992; Ngan et al. 1994). Pain has been shown to be a subjective response and dependent upon several factors. Such factors include gender, age, pain threshold, magnitude of force applied, previous pain experiences, and present emotional state and stress (Ngan et al. 1989; Brown and Moerenhout 1991; Bergius et al. 2000).

Patients’ attitudes toward orthodontic treatment can also be affected by the perception of pain. It was concluded from a survey of subjects that pain was the most discouraging factor during treatment and the most likely reason to discontinue care (Oliver and Knapman 1985). Pain has also been implicated as a major factor in patients avoiding treatment. Many orthodontists may be unaware of the magnitude of pain experienced by patients since much of the pain is felt hours after an office visit. Several studies have shown that once a force is applied to a tooth, pain intensity increases between 4 and 24 hours but falls to normal levels at day seven (Ngan et al. 1989; Jones and Chan 1992; Scheurer et al. 1996). Practitioners usually inform their patients that they will experience some discomfort during treatment, but rarely discuss its intensity and duration. Having knowledge of this complex process will
allow the practitioners to be empathetic toward patients, to educate and inform patients of this common side-effect and to aid in pain management appropriately.

Historically, tooth movement with light forces was thought to serve in controlling the amount of pain experienced (Burstone 1962; Profitt, et al. 2007). This theory was promoted by the premise that light forces were more biologic and therefore more efficient and less painful. However, existing research has not been able to confirm a relationship between the force applied and the subsequent pain, mainly because the force applied in previous studies has not been a well-controlled and quantified variable. Recent studies have focused on the pain levels associated with conventional and self-ligating brackets (Scott et al. 2008; Fleming et al. 2009; Pringle et al. 2009; Tecco et al. 2009). However, no studies thus far have measured and compared force levels from the different methods of ligating archwires. Two studies to date (Ogura et al. 2009; Luppanapornlarp et al. 2010) have attempted to compare pain intensities associated with different applied force magnitudes. These will be described in more detail below (see “Effects of Different Orthodontic Appliances”). In general the results of these studies suggest higher pain intensities associated with higher applied forces. Nevertheless, while previous literature has provided insight to pain as a complex process, no studies have evaluated pain associated with controlled tooth movement by known stresses.

**Tooth Movement and Magnitude of Force/Stress**

One of the main objectives in orthodontic therapy is to apply forces to the teeth in order to move them to their appropriate positions. Once force is placed on the tooth, certain biological reactions occur in the periodontium which lead to cell death, inflammatory changes, and circulatory disturbances. Therefore, tissue damage in orthodontic therapy is an
inevitable prerequisite to the stimulation of bone resorption and tooth movement. The periodontal ligament (PDL) and the surrounding bone are capable of remodeling and reorganizing to permit tooth movement when optimal forces are applied to teeth. The tooth movement cycle consists of three phases: (1) an early, immediate small movement due to the compression of the tissues surrounding the tooth; (2) a delay period of uncertain length during which no tooth movement occurs and the tissues show histological signs of necrotic (hyalinization) damage; and (3) a period of late, rapid tooth movement when extensive remodeling takes place after the damage is resolved (Storey 1973). The delay period in the tooth movement is thought to be due to the remodeling of the damaged tissue (Storey 1973) and the length is affected by the extent of damage (King and Fischlschweiger 1982). Studies have indicated that heavier forces (greater than 200 cN) increase the amount of tissue damage (King and Fischlschweiger 1982; Chutimanutskul et al. 2006; Gonzales et al. 2008) and consequently, the length of the delay period. Traditional beliefs suggest the use of light continuous forces (less than 40 cN) during orthodontic tooth movement to reduce adverse tissue reactions (Burstone 1962; King and Fischlschweiger 1982; Chutimanutskul et al. 2006). While light forces are thought to evoke direct bone resorption in the direction of tooth movement, heavy forces create blood vessel strangulation with subsequent necrosis (hyalinization) in the areas of PDL compression and lead to undermining resorption. Therefore, the magnitude of orthodontic force is believed to be an important factor not only in the magnitude of tooth movement but also in adverse effects related to tooth movement.

To have the most efficient orthodontic treatment, tooth movement using optimal forces is desired. The optimal force for tooth movement is one that produces a maximum
rate of tooth movement without tissue damage or discomfort (Burstone 1962). The thought previously was that avoiding a ‘lag phase’ would produce faster movement of teeth, while at the same time lessen the pain experienced. Unfortunately, much of the previous thought was based on early work (Reitan 1967; Rygh and Reitan 1972; Dickenson 2002; Edwards et al. 2005) from animal models using tipping mechanics with forces of unknown magnitude.

While there still remains a paucity of research using controlled tooth movement with a quantified magnitude of force, future research utilizing tissue-, cellular-, and molecular-level analyses of orthodontically treated teeth in human subjects with this type of tooth movement would be beneficial. Fortunately, recent data are available from quantified magnitudes of stresses using continuous controlled tooth movements.

Current research contradicts the previous thought that lighter forces produce more efficient movement. It was found that forces of approximately 300 cN when compared to 50 cN increased the rate and amount of tooth movement, but had adverse effects on rotation and loss of anchorage (Yee et al. 2009). Iwasaki et al. (2000, 2005, 2006, 2009) applied controlled stresses ranging from 4 kPa to 78 kPa for maxillary canine translation, which required average forces between 18 cN and 360 cN. Combined data from the first 3 studies suggested 26 kPa to be the optimal stress associated with the maximum mean speed of tooth movement of 0.063 mm/day but maintained that stresses as small as 4 kPa still produced effective tooth movement of approximately 1mm per month. In the most current report on the translation of 66 maxillary canines (Iwasaki et al. 2009), these authors observed that a stress of 78 kPa produced a larger average tooth movement than lower stresses. They also found that 95% of the teeth showed steady distal movement, while only 3 teeth demonstrated
a ‘lag phase’ and were moved with stresses of 4, 52, and 78 kPa. This does not support the theory that the presence of a lag phase is related to higher stresses (or forces). Therefore, since the association of the delay period or ‘lag phase’ with the amount of tissue damage resulting from heavier forces has been challenged, questions regarding pain due to higher forces may also be proposed.

Studies utilizing the same applied stress to the same type of tooth in different individuals have observed variability in the rate of tooth movements between individuals, with 2 times higher average movement in growing subjects when compared to non-growing subjects and more than 5 times faster movement in some subjects compared to others (Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009). This indicates there are characteristics that are specific for each individual that might influence their biologic response to mechanical force.

**Biological Aspects of Pain associated with Tooth Movement**

The mechanisms by which orthodontic pain results from force are not yet understood. It has been suggested that pain perceptions are due to blood flow changes in the periodontal ligament (Kvam et al. 1987). Other studies have indicated the presence of prostaglandins, substance P, and other substances to be associated with discomfort.

Two types of pain have been described in the past literature including the immediate and delayed pain responses to orthodontic therapy (Burstone 1962). The immediate response can be explained by the initial compression of the PDL felt during orthodontic therapy. The delayed response has been attributed to partial compression of the PDL that still allows blood flow and over time results in hyperalgesia of the PDL. This type of pain arises a few hours
after appliance placement (Burstone 1962) and is caused by an increased sensitivity of the
nerve fibers to noxious stimuli such as prostaglandins, histamines, and substance P (Ferreira
et al. 1978). Prostaglandin E\textsubscript{2} and sympathomimetic amines have been shown to evoke a
delayed hyperalgesic reaction with a slow onset leading to a plateau and declining thereafter
(Ferreira et al. 1978; Sachs et al. 2002). Therefore, orthodontic treatment induces a
hyperalgesic response that in turn can lower a patient’s pain tolerance.

A combination of pressure, ischemia, and inflammation results from tooth movement.
It has been suggested that the pain experienced during tooth movement is associated with the
development of ischemic areas in the PDL that will undergo necrosis (Storey 1973).
According to Burstone (1962), clinical studies have suggested that the magnitude of the force
applied to a tooth has a definite relationship to the pain experienced, but does not imply that a
linear relationship exists. The belief is that the greater the force, the larger the areas of
ischemia in the PDL that will necrose, and thus the greater the pain encountered. The use of
lighter forces has therefore been suggested to reduce pain. However, recent studies that did
not control for tooth movement have found no relationship between the applied force and the
associated pain (Jones and Richmond 1985) and the controversy on whether or not light
forces will decrease the degree of pain during tooth movement remains unanswered.

Inflammatory Factors associated with Tooth Movement and Pain

In order for teeth to move, the tissues must undergo an inflammatory process. As a
tooth displaces after the application of a mechanical force, the PDL compresses and induces
an inflammatory reaction. This requires reorganization of the PDL and the activation of
osteoclastic and osteoblastic activities for bone remodeling to occur. The inflammatory
process results from biologically active substances known as cytokines that are expressed by cells in the periodontium in response to mechanical stress (Uematsu et al. 1996). Several cytokines have been linked to orthodontic tooth movement. These cytokines that are released in response to an acute inflammatory reaction include interleukin-1beta (IL-1β), interleukin-1 receptor antagonist (IL-1RA), tumor necrosis factor (TNF), and interleukin-8 (IL-8). These cytokines promote the inflammatory process by stimulating the release of mediators such as Prostaglandin-E₂ (PGE₂) and the neuropeptide substance P (SP). Furthermore, the mixture of these bioactive molecules initiates nociceptor changes in the nervous system (Diatchenko et al. 2005). After the application of orthodontic force, increased levels of IL-1β in the gingival crevicular fluid have been reported in previous studies (Saito et al. 1991; Grieve et al. 1994; Alhashimi et al. 2001; Giannopoulou et al. 2006). IL-1 has been implicated as a potent stimulator of bone resorption (Uematsu et al. 1996). IL-1β has also been linked to the production of cyclo-oxygenase products (Saito et al. 1991) and IL-8 (Sachs et al. 2002). PGE₂ is a regulator of the inflammatory process and a potent stimulator of bone resorption that is synthesized in response to mechanical stress (Grieve et al. 1994) and IL-1β (Saito et al. 1991). This is in agreement with a study that found the production of PGE₂ peaked after IL-1β, suggesting that IL-1β has a stimulatory effect on PGE₂ (Giannopoulou et al. 2006). Another study using tipping mechanics found a significant increase in the intensity of staining for PGE and IL-1β when the PDLs of cat maxillary canines were under tension compared to when no tension was applied (Saito et al. 1991). This indicates that there is an increase of PGE and IL-1β in response to mechanical stress.
Inflammation often leads to the sensitization of pain receptors. One study utilizing rats investigated if the administration of TNF, IL-1β and IL-8 induced mechanical nociceptor hypersensitivity and if eicosanoids and sympathomimetic mediators were involved in the nociceptor hypersensitivity that the cytokines induced (Sachs et al. 2002). The authors’ findings indicate that TNF, IL-1β and IL-8 were all able to induce a mechanical nociceptor hypersensitivity response. Their results showed that hypersensitivity induced by IL-1β and IL-8 was due to the endogenous release of eicosanoids and sympathomimetic amines, respectively. TNF induced hypersensitivity was found to be due to both mediators. This also implied that pain resulting from mechanical stimulation is a peripheral mechanism.

Substance P (SP) is a multifunctional neuropeptide that has also been associated with the mechanism of bone remodeling during orthodontic tooth movement. SP is present in the nerve fibers that supply the tooth pulp and periodontium in humans and has been associated with periodontal inflammation (Dinarello 2000; Diatchenko et al. 2005) and tooth pain (Linden et al. 1997). One study investigated the pain perception associated with separator placement, the effect of this procedure on IL-1β, SP, and PGE2 levels in the Gingival Crevicular Fluid (GCF), and the association between the levels of these substances and pain perception (Giannopoulou et al. 2006). The visual analogue scale (VAS) was used to record the pain intensity and GCF samples were collected from experimental and control teeth to evaluate changes in the levels of the substances being tested. They reported that the mean VAS values increased significantly at 1 hour and 24 hours after separator placement and decreased to lower values at 7 days after placement. Significant differences were noted between the control and experimental groups after separator placement for the levels of IL-
1β, SP, and PGE₂. All substances increased 24 hours after separator placement and partially decreased at day 7 while still remaining at elevated levels relative to baseline. The level of PGE₂ was associated with the intensity of pain at 1 hour after placement of the separator. At day 1, IL-1β was found to have a strong association with pain intensity. No markers had an association with the pain intensity at day 7. SP and PGE₂ both peaked at 24 hours which might indicate a relationship among the two and also indicates that these substances serve as potential stimuli in the delayed type of pain. These findings agree with those from another study (Yamaguchi et al. 2009) which showed significantly elevated levels of SP in GCF from experimental sites compared to control sites 24 hours after placement of orthodontic brackets. These results suggest that IL-1β, SP, and PGE₂ are involved in the PDL inflammation and pain development during orthodontic therapy.

Some of the characteristics that are suggested to be specific for tooth movement have also been associated with pain perception. Recent investigations have studied IL-1 gene cluster polymorphisms to test if there was an association with IL-1β and Interleukin-1 Receptor antagonist (IL-1RA) secretion, and examined the levels of IL-1β and IL-1RA in GCF and its association with tooth movement (Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009). IL-1β is more potent for bone resorption and inhibition of bone formation, while IL-1RA is a naturally occurring receptor antagonist cytokine that controls the IL-1 effects (Dinarello 2000). Studies have demonstrated a positive correlation between controlled tooth movement and concentrations of IL-1β and IL-1RA (Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009). These studies further implicated a genetic role in the inflammatory process and tooth
movement by correlating specific genotypes of the IL-1 gene cluster with higher ratios of IL-1β relative to IL-1RA and faster tooth movement. This suggested that there would be faster tooth movement if IL-1β was greater relative to IL-1RA at experimental sites compared to control sites. Since IL-1β has been shown to be involved in the PDL inflammation and pain development during orthodontic therapy, it would be interesting to explore possible associations with the genotypes of the IL-1 cluster and pain perceptions.

Another genetic component that codes for the enzyme catechol-O-methyltransferase (COMT) has been studied in subjects with temporomandibular disorder. COMT has been suggested to effect analgesia and pain perception and has also been linked to the pain regulatory mechanism (Slade et al. 2008). Recent studies have indicated the COMT genotype to be correlated with human pain perception and with a history of orthodontic treatment (Slade et al. 2005). In a study (Diatchenko et al. 2005) that examined 202 females, enzymatic activity of COMT was determined by three halotypes: LPS (low pain sensitivity), APS (higher pain sensitivity), and HPS (highest pain sensitivity). These three halotypes accounted for approximately 11% of the variation in pain perception. Diatchenko et al. (2005) specified that low COMT enzymatic activity was associated with heightened sensitivity, while high COMT enzymatic activity was related to lower sensitivity. Another study (Nackley et al. 2007) confirmed these findings by reporting that COMT inhibition resulted in increased pain sensitivity. The genetic basis of this process might help explain the inter-individual variability among patients in regards to tooth movement and pain perception.
Pain Experienced during Orthodontic Treatment

Prevalence and Nature of Orthodontic Pain Experiences

Physical pain has been described as an unpleasant or aversive feeling that results from actual or potential injury to the body. Pain has been further described to include psychological, environmental, and cognitive components. Thus, pain is a complex experience that is often associated with orthodontic treatment. One study reported the mean pain at 24 hours after initial archwire placement was 42 mm on a 100 mm visual analog scale (VAS) (Scheurer et al. 1996). This indicates that pain is a significant factor associated with orthodontic therapy. In the existing literature, pain has been described as the most negative aspect of treatment, a major reason for discontinuing therapy, and as a factor in avoiding orthodontic treatment (Oliver and Knapman 1985; Brown and Moerenhout 1991). Among the 51 subjects in a previous study, 28% wished to discontinue wearing the appliance because of pain intensity and 39% reported pain to be the worst aspect of treatment (Oliver and Knapman 1985).

Almost all patients undergoing orthodontic treatment experience pain. Existing literature has indicated that patients may feel tension, pressure, soreness of teeth, and pain as a result of orthodontic treatment (Ngan et al. 1989). The prevalence of experiencing at least some degree of pain among subjects has ranged from 70% to 95% (Oliver and Knapman 1985; Ngan et al. 1989). Most studies found pain to increase 4 hours after insertion or activation of appliances. The majority of the past research confirmed the pain intensity peaks at approximately 24 hours after administration of orthodontic forces. The intensity thereafter decreases to rather normal levels on day 7 (Jones 1984; Ngan et al. 1989; Brown and
Moerenhout 1991; Jones and Chan 1992; Scheurer et al. 1996; Erdinc and Dincer 2004; Giannopoulou et al. 2006). However, a variety of findings also exist concerning the duration of pain. As many as 25% to 42% of subjects still experienced pain after 7 days in past studies (Scheurer et al. 1996; Bergius et al. 2002). The intensities of pain perceived by these subjects were quite low with a mean pain intensity score of less than 20 on a 0-100 scale, but were still considered problematic. Subjects have also reported higher levels of pain for longer periods of time during “biting” and “chewing activities” (Scheurer et al. 1996). Fortunately, previous studies indicate that subjects can adapt as treatment progresses and sensations cease or disappear from their focus of attention (Jones and Chan 1992; Sergl et al. 1998). A study that followed individuals for 14 days, noted a gradual decrease in pain intensity over time (Brown and Moerenhout 1991). Another study supported this finding with results showing adaptation to a new appliance taking place within the first 7 days and indicated that this adaptation may be explained by the changes in subjects’ perceptions of adverse stimulation (Sergl et al. 1998). The major cause of this pain in orthodontics is the application of forces to induce tooth movement (Jones 1984; Oliver and Knapman 1985; Brown and Moerenhout 1991; Scheurer et al. 1996). Past research has described and measured the prevalence and intensity of pain associated with orthodontic therapy. However, the factors that influence a patient’s perception of pain still remain unclear.

Pain is a subjective response and it is common to note the inter-individual variation in painful experiences. While some patients report agonizing pain associated with tooth movement, others report little or no pain with the same application of force (Burstone 1962). Pain responses over 7 days following insertion of initial archwires recorded by VAS in 50
subjects (28 females, 22 males, mean age 13.6 years) showed mean and average maximum values for the test period of 27.5 and 49.1 with high inter-individual variation as demonstrated by standard deviations of 19.2 and 27.2, respectively (Firestone et al. 1999). Thus, reactions to pain sensations vary among individuals and can depend on a number of factors. This has lead several investigators to look for factors that could be useful in predicting which patients will experience the most pain. Unfortunately, there is still a paucity of publications in this important area of research. It is clear that pain plays a part in orthodontic treatment and a thorough understanding of this complex process will aid the patients and practitioners.

Effects of Different Orthodontic Appliances

Orthodontic treatment often requires tooth movement. This is accomplished through the use of fixed or removable appliances. An existing study reported no significant difference in the pain intensities of subjects wearing fixed appliances and subjects wearing removable appliances (Oliver and Knapman 1985). Conversely, in another investigation, it was observed that subjects treated with fixed and functional appliances reported significantly more tension, pressure, sensitive teeth, or pain than the subjects wearing removable appliances (Sergl et al. 1998). It was also shown that subjects with fixed appliances reported higher values of the intensities of pressure, tension, pain, and sensitivity of teeth when compared to functional appliances (Sergl et al. 1998). This finding is credited to the different qualities of these appliances. While the actions of fixed appliances would create a sensation that was focused more on the periodontal ligament (PDL) and surrounding structures, functional appliances are more likely to create adverse effects from pressure and tension in
the jaw muscles and oral mucosa. Additionally, any dental pressures resulting from functional appliances would most likely be distributed over a number of teeth. In any case, results from fixed appliances seem to offer the most information when studying the effects of tooth movement and the pain associated with it.

In an attempt to describe if the amount of crowding was associated with the pain experienced after archwire placement, one study found no correlation (Jones and Richmond 1985). Unfortunately the amount of crowding was not specified in the study and the number of subjects examined was small (n=24). Although it can be reasoned that the amount of tooth displacement from the arch form reflects the amount of force applied to the tooth, this study still failed to control for the magnitude of force applied. Crowding is also usually a 3-dimensional problem, while this study only addressed crowding in 1 plane using the irregularity index. The magnitude of force is also affected by the interbracket width and the length of the wire. The previous study failed to take either of these factors into account. Other studies examining the pain perception after placement of two different sized archwires, found no statistically significant difference in the initial pain perceived between the two archwires (Jones and Chan 1992; Erdinc and Dincer 2004). These studies assumed that the stiffer archwire would create a higher magnitude of force on the teeth. However, the magnitude of force on each tooth is a result of the 3-dimensional position of the tooth in the arch and the amount of wire deflection to achieve ligation. Unfortunately, these studies failed to control for the magnitude and particular type of force applied and therefore, no conclusions can be reached regarding the differences in the magnitudes of force among the archwires.
Only recently have studies examined the relationship of pain to the magnitude of the force applied to the teeth. One study attempted to evaluate the pain intensity during the first 7 days after application of relatively lighter and heavier continuous orthodontic forces to maxillary premolars (Ogura et al. 2009). In this experiment, 20 cN and 200 cN were applied to maxillary premolars with specially manufactured NiTi closed-coil springs. The pain intensity was measured daily, for the first 7 days using the visual analogue scale (VAS) to record spontaneous and biting pain. Results indicated that pain intensity while biting may be greater after the application of the heavier continuous force for approximately 8 hours to 5 days when compared to the lighter force. No other significant differences were observed in spontaneous pain for either group and in biting pain for the light-force group. While this study accounted for the magnitude of force applied to the teeth, it failed to control carefully or measure tooth movement. Another study examined pain intensity using the VAS at 1 hour, 24 hours, 1 week, 1 month, and 2 months after initiating canine retraction with continuous forces of 50 cN and 150 cN in a split mouth design (Luppanapornlarp et al. 2010). This study found that the mean VAS for teeth receiving 150 cN force was 35.2 (±16.9) out of a possible score of 100 and significantly higher than the mean VAS for teeth receiving 50 cN force which was 20.2 (±24.1) at 24 hours. No significant differences in mean VAS between teeth receiving different forces were found at any other time point. Unfortunately, this study also failed to use determinate mechanics. However, results were that average tooth movements after 2 months were 1.28 (±0.70) mm and 1.13 (±0.63) mm for the 150 cN and the 50 cN sides respectively, and not significantly different (Luppanapornlarp et al. 2010).
Host Factors

Psychological factors have been shown to be the greatest contributors to a patient’s perception of pain (Bartlett et al. 2005). These factors may influence a patient’s adaptation to pain and discomfort during orthodontic treatment (Brown and Moerenhout 1991; Jones and Chan 1992). This suggestion was supported in a prospective study investigating the relationships between pain sensations, attitudes toward orthodontic treatment, and effects on compliance during treatment (Sergl et al. 1998). A distinct correlation was shown between subjects’ attitudes toward orthodontic treatment and the intensity of discomfort. Subjects who perceived their malocclusion to be severe and felt they would benefit esthetically from orthodontic treatment reported less pressure, sensitive teeth, and pain over time when compared to subjects who had poor attitudes toward orthodontic therapy. The study also indicated that individual stress-related factors and anxiety could significantly influence the intensity of discomfort caused by an appliance. Anxiety is a psychological factor that can influence the perception of pain. One study examined subjects’ expectations of pain before treatment and the reported pain after treatment and found a positive correlation (Firestone et al. 1999). The authors interpreted their results as reflecting a subject’s general measure of anxiety. This concurs with a prospective study that found a significant positive correlation between pain and the state of anxiety (Bartlett et al. 2005). In this study, they found that a telephone call to the subject after appliance placement/activation served to reduce the subject’s level of anxiety. This in turn significantly reduced the intensity of the reported pain. Another investigation concluded that prolonged pain assessments were predicted by high ratings of pain associated with low motivation for orthodontic treatment and elevated
dental anxiety (Bergius et al. 2008). Depression is another psychological factor that affects pain perception. Depression and chronic pain syndromes often coexist (Sherman et al. 2004; Bar et al. 2005; Giannakopoulos et al. 2010). However, controversy exists on the relationship between depression and experimental pain perception. Some studies have shown that depressed individuals report greater pain intensities and reduced tolerances to ischemic pain when compared to non-depressed controls. On the other hand, studies have found that depressed subjects have increased thresholds and tolerances to ischemic pain (Sherman et al. 2004). These discrepancies might be explained by study design differences. Unfortunately, no literature is available on the relationship of orthodontic pain to depression and future studies are warranted.

Other factors, such as age and gender, have been suggested to have an influence on the perception of pain. One study (Blankenburg et al. 2010) of 176 subjects evaluated pain using several modalities among three age groups: young children (6-8 years), older children (9-12 years) and adolescents (13-16 years). Results showed age effects between the group of children and the group of older children and adolescents, with thermal and mechanical detection increasing and heat, blunt pressure, and mechanical pain sensitivity decreasing as the subject ages. This indicates that the age distribution of pain differs for specific pain conditions and therefore, specific pain cannot be inferred from other pain conditions. While it is difficult to compare different age groups with pain since many of the orthodontic treatment plans differ among age groups, correlations have still been made. Some reports have shown age to be a factor in pain perception with adolescent groups reporting a higher level of pain than preadolescent and adult subjects (Brown and Moerenhout 1991; Scheurer
et al. 1996). These studies have found the most sensitive age to be between 13 and 16 years. This could be related to the lower levels of psychological well-being exhibited by adolescents. Other findings indicate that adults showed statistically significantly higher discomfort levels (Jones 1984; Jones and Chan 1992). However, these studies did not take emotions, attitudes, or personality factors into account, all of which have been shown to modify the perception of pain. Several other studies have failed to find a relationship between orthodontic pain and age (Ngan et al. 1989; Bergius et al. 2008).

A correlation has been suggested between gender and pain perception. Most epidemiological studies have shown women have a higher prevalence than men for most pain conditions (Scheurer et al. 1996; Riley et al. 1998; Bergius et al. 2002; Edwards et al. 2005; Komiyama et al. 2007; LeResche et al. 2007). A study that was investigating sex differences in pain responses in healthy subjects who were less than 60 years of age performed a meta-analysis and found that women reported higher pain severity at lower thresholds and had less tolerance to noxious stimulation than males (Riley et al. 1998; Edwards et al. 2005). Another study (Komiyama et al. 2007) evaluating tactile and pain thresholds in the orofacial region of 22 men and 22 women with an age range of 20-31 years, found that women were more sensitive compared to men. LeResche et al. (2007) recognized the literature suggested that pain elsewhere in the body, female gender and possibly pre-existing depressive symptoms were associated with onset of temporomandibular pain in adults and wanted to test further that theory on adolescents. After analyzing 1310 boys and girls that were initially 11 years old for 3 consecutive years, this study found that female gender, negative somatic and psychological symptoms, number of existing pain conditions, and report of being neutral or
dissatisfied with life at age 11 years were all predictors of onset of facial pain meeting Research Diagnostic Criteria for Temporomandibular Disorders (LeResche et al. 2007). Therefore, biological, psychological, and social factors can likely contribute to differences in pain responses among genders. Differences in pain perception between sexes have been affected by physiological variables including the reproductive status, hormone levels and menstrual cycle of female subjects. One study demonstrated pain thresholds to be lower in females during their menses (Giamberardino et al. 1997). However, inconsistent observations have been reported on menstrual cycle effects on pain response with little or relatively minor interaction effect evident (Sherman and LeResche 2006). Studies have also indicated that females are more likely to visit a physician and to report pain as a symptom than males which can lead to an over-estimation of the differences (Isacson and Bingefors 2002; Bingefors and Isacson 2004). While numerous studies have used several modalities to study general and specific pains, many of these modalities most likely are separable at higher levels of the nervous system and thus have different responses. Correlations between gender and orthodontic pain perception in regards to tooth movement have rarely been reported in the literature. Some studies have found no correlation (Jones 1984; Ngan et al. 1989; Jones and Chan 1992; Sergl et al. 1998; Erdine and Dincer 2004) while another study found that girls reported more discomfort than boys (Scheurer et al. 1996; Bergius et al. 2002). Two recent studies (Freytag 2008; Schumacher 2009) that measured the intensity and quality of pain indicated that females reported higher magnitudes of pain intensity on the visual analogue scale (VAS), but reported nearly identical levels on a modified McGill Pain questionnaire which measured the quality of pain. However, these studies did not take
psychological, biological, and social factors into account, did not measure the applied orthodontic forces, and had relatively small sample sizes, indicating a need for larger well-controlled studies.

There is a lack of data relating ethnic and socioeconomic status to orthodontic pain. Ethnic and socioeconomic status may influence pain perception. One study (Plesh et al. 2002) found that pain increased significantly with a higher socioeconomic status. When these investigators controlled for this variable, they further found that facial/jaw pain was reported twice as much in Caucasians than in African-Americans and that Caucasians exhibited earlier onset than African-Americans. However, other studies have shown quite different results when using experimental pain. Differences in responses to multiple experimental pain modalities (heat pain, cold pressor pain, and ischemic pain) have been reported among African Americans, Hispanics, and non-Hispanic white subjects, with the African Americans and Hispanics exhibiting lower pain tolerances and rating pain intensity higher when compared to whites (Campbell et al. 2005; Rahim-Williams et al. 2007). A study (Campbell et al. 2008) using nociceptive flexion reflex as a measure of spinal reflex found that African Americans expressed reflexes at lower stimulus relative to non-Hispanic whites. Ethnic differences were also found among Japanese and Belgian Caucasian subjects when evaluating tactile and pain thresholds of the orofacial region (Komiyama et al. 2007) with Japanese subjects being more sensitive after using various modalities to stimulate intra-orally and extra-orally. Since there is a lack of research regarding pain related to orthodontic treatment and ethnicity, no conclusions can be inferred and future studies are encouraged.
Due to the pain experienced during orthodontic treatment, analgesics are often indicated. There is a paucity of research regarding pain associated with tooth movement and no standards of care for controlling discomfort associated with orthodontic treatment (Bernhardt et al. 2001). Analgesic use has often paralleled the level of the pain perceived (Jones 1984; Scheurer et al. 1996; Erdinc and Dincer 2004). Most of the analgesics were consumed during the first 2 days after the application of force and decreased significantly by day 3. These studies have also suggested that analgesic use might be associated with anxiety level. Whatever the reason, pain control in orthodontic treatment is a necessity. Current studies have focused on the use of preemptive analgesics to control pain associated with orthodontics (Bernhardt et al. 2001; Polat and Karaman 2005; Polat et al. 2005; Bird et al. 2007; Bradley et al. 2007; Minor et al. 2009). These studies indicate that the use of analgesics one hour before archwire adjustment or separator placement can significantly reduce the pain intensity for several hours after the adjustment. Additional postoperative doses were recommended to control orthodontic pain thereafter.

**Pain Measurements**

In order to devise a method to control pain, it is necessary to obtain a measurement of the intensity and the quality of the discomfort experienced. The majority of patients undergoing orthodontics are adolescents; therefore, it is imperative to provide them tools that are easily understood so that they may provide meaningful feedback. The Visual Analog Scale (VAS) has been used in the majority of the orthodontic research assessing discomfort to measure the intensity of pain and has been found to be valid and reliable (Dalton and McNaul 1998). The VAS is a horizontal line that is 100 mm long where one end
corresponds to “no pain” and the other end indicates “worst pain possible.” Subjects mark along the line at the level where they perceive their pain. The mark is then measured from the left margin of the line to the nearest millimeter to quantify the pain level (Melzack 1975).

While the VAS is a quick and easy validated measure of pain, it only provides information on the intensity of pain and neglects the quality of pain perceived. The McGill Pain Questionnaire (MPQ) was developed to specify the qualities of pain experienced in clinical settings. Originally, 78 descriptor words were included in the questionnaire to describe the pain experienced. This questionnaire was shown to be an effective means for pain measurement in adults (Melzack 1975). Unfortunately, this many words caused the questionnaire to be too time consuming and not clinically practical. Years later, Melzack developed a shorter version, the McGill Pain Questionnaire – Short Form (MPQ-SF) that consisted of only 15 descriptor words. It included a VAS, a Present Pain Intensity (PPI) measure which corresponded to the current pain level on a 1-5 intensity scale (Melzack 1975), and an intensity scale for each word where 0 = none, 1 = mild, 2 = moderate, and 3 = severe. Although the form was markedly shortened, Melzack was able to show a high correlation between the long and short forms for assessing pain (Melzack 1987).

While the MPQ-SF assessed multidimensional aspects of pain, its applicability to orthodontics was questioned. A clinical study consisting of 200 female subjects with a median age of 36 years indicated that the MPQ-SF was appropriate for assessing dental pain and that certain adjectives were unique to specific pain conditions (Turp et al. 1997). Unfortunately, its applicability to adolescence was not examined. This indicated a need for a questionnaire that was specific to adolescent orthodontic patients in order to assess their
discomfort accurately. Another clinical study (Bird et al. 2007) that used the MPQ-SF to analyze the pain responses to separator placement in adolescents concluded that future studies need to address the MPQ-SF suitability for orthodontic patients. A modified MPQ-SF (MMPQ-SF) that was specific for only orthodontic patients was developed in 2008 by Freytag. This questionnaire used 15 descriptor words that were applicable throughout orthodontic treatment and were easily understood by adolescents. This questionnaire was tested on 13 subjects in a pilot study (Freytag 2008) and an additional 60 subjects in a follow up study (Schumacher 2009). These studies found high correlations among MMPQ-SF and VAS, MMPQ-SF and PPI, and the VAS and PPI. Additionally, combined data from these studies showed that eleven of the 15 descriptors (pressure, sore, aching, throbbing, tight, pulling, uncomfortable, strange, frustrating, annoying, miserable) were discriminating for pain (Iwasaki et al. 2010). A two-factor solution of these 11 descriptors accounted for 64% of the variance in responses. This analysis distinguished two groups of descriptors that fit into categories of general/emotional and localized subscales. The generalized subscale includes the following descriptors: uncomfortable, strange, frustrating, and annoying. The localized subscale includes: pressure, sore, aching, throbbing, tight, pulling, and miserable. Therefore, the previous studies indicate that the MMPQ-SF is a valid tool for orthodontic pain evaluation in adolescents when compared to the VAS.

Pain experienced during orthodontic tooth movement is an important area in clinical practice and in research. Unfortunately, there is a lack of research regarding pain in orthodontics (Krishnan 2007). Most orthodontic appliances deliver a relatively complicated set of forces and moments that are indeterminate and not quantitatively predictable. These
appliances can result in different types of tooth movements (i.e. tipping, rotation, bodily movement, root movement) which may have a differential effect on pain perception. Therefore, a limitation of most of the previous studies investigating pain in orthodontics is that the orthodontic treatment procedure was not controlled for. Instead, studies utilized different orthodontic appliances or studied subjects at different stages of treatment. Several of the previous studies on pain also used different experimental designs, such as the number and schedule of the questionnaires and the method of self-report. The majority of these studies lacked the use of controlled force systems to move teeth and followed subjects for only short durations. Furthermore, applied forces/stresses in the majority of the previous studies were not quantified and the nature and speed of tooth movement were not measured.

There is a paucity of research of well-controlled experimentally based human studies using controlled tooth movement and quantified magnitude of stresses. While current studies have implemented protocols to control for tooth movement and stress applied, there are still no studies of the relationship of pain profiled over time during controlled tooth movement by known magnitudes of stress. As a result, orthodontics still lacks a definitive pain management protocol for patients.

**Problem Statement**

Therefore, the purpose of this study is to gather longitudinal data to quantify and describe the pain experience (intensity and quality) during controlled human tooth movement at two levels of stress (4 kPa and 78 kPa) using a validated self-report: a modified version of the McGill Pain Questionnaire Short Form designed for orthodontic patients (MMPQ-SF), the Visual Analogue Scale (VAS), and the Present Pain Intensity (PPI).
Hypotheses

1. There will be a differential effect on pain intensities for each controlled stress applied over time.

2. There will be a differential effect on pain qualities for each controlled stress applied over time.

3. There will be a differential effect on pain intensities and qualities regardless of stress over 4 phases of treatment: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Day 14-84.
CHAPTER 2
MATERIALS AND METHODS

The protocol for the current study was approved by the University of Missouri – Kansas City Adult Health Sciences Institutional Review Board with consultant review and approval from Children’s Mercy Hospital Institutional Review Board (Appendix A). Similar protocols for maxillary canine translation have been employed in previous studies (Iwasaki et al. 2000; Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009). The current study was conducted on a convenience sample of patients treated at the Graduate Orthodontic Clinic at the University of Missouri – Kansas City between December 2009 and January 2011.

Subjects

Subjects meeting the following inclusion criteria (Chandler 2006) were enrolled in the current study:

1. Must have been a healthy patient who demonstrated good oral hygiene and minimal gingival inflammation,
2. Had only permanent teeth present in the maxillary dental arch and at least six erupted permanent teeth in each quadrant,
3. Had an approved treatment plan that required bilateral extraction of maxillary first premolars and bilateral retraction of maxillary canine teeth for orthodontic correction of the malocclusion,
4. Had anatomy that could accommodate the planned orthodontic hardware,
5. Did not use tobacco products or products containing alcohol (including mouthwash products) during the study, and
6. Had no history of chronic pain.

The study was open to all ages. Furthermore, subjects were encouraged to avoid use of analgesics and/or non-steroidal anti-inflammatory drugs during the study. Subjects were
asked at each visit to report use of analgesics and if use was recorded, those subjects were expected to be excused from the study.

During the subjects’ first appointments, recruitment, informed consent, and baseline assessments took place. That is, subjects presented to the graduate orthodontic clinic for a records appointment to gather appropriate information for treatment planning. Analysis of clinical records and development of an orthodontic treatment plan were conducted prior to determining subject eligibility for this study and signing of the consent form. The subjects who fit the inclusion criteria specifications were given the appropriate information to participate in this study. The study was fully explained and questions were answered to make sure that potential subjects and their guardians completely understood the information presented while voluntary participation was emphasized. Informed consent (Appendix B) was presented in a private room that was conducive to discussion and questions about the study. Potential subjects were offered a delayed consent. Adolescents were asked to assent to participation. Those who fail to assent were not enrolled in the study.

**Experimental Protocol**

Subjects presented to the clinic for three appointments prior to premolar extractions in preparation for application of orthodontic forces, defined as Days -35, -28 and -21. During the first appointment, Day -35, separators were placed adjacent to the maxillary molars to provide space for orthodontic bands\(^1\) to be seated. The second appointment, Day -28, consisted of the fitting of orthodontic bands and making an impression for the construction of a fixed anchorage appliance known as a Nance appliance (Fig. 1). If second molars were

\(^1\) 0.018 bands, 3M Unitek, 2724 South Peck Rd., Monrovia, CA 91016
erupted, they were banded at this appointment. At the third appointment, Day -21, the Nance appliance was cemented, brackets\textsuperscript{2} were bonded to the second premolar and canine, maxillary molars and second premolars were linked on each side by a custom stainless steel arch wire segment (0.017x0.025-inch) that passively engaged the slots and tubes of the edgewise appliance and figure-8 ligation using stainless steel wire (0.010-inch), and a maxillary dental alginate impression was made. This impression was used to construct a maxillary dental model. This model facilitated fabrication of the vertical loop auxiliary wires (0.016x0.022-inch stainless steel) that were used for canine retraction and construction of custom impression trays\textsuperscript{3}. Subjects also started on an alcohol-free chlorhexidine mouth rinse\textsuperscript{4} at this appointment. They were instructed to use the antibacterial mouth rinse twice daily and continue use throughout the study. An appointment for maxillary first premolar extractions was then arranged.

After first premolars were extracted, subjects were appointed at least two weeks post-extraction for a visit called Day 0 to allow a standardized minimum healing time. Canine retraction forces were initiated at Day 0. Each subject was scheduled for 10 appointments for observation while retraction forces were being applied, starting at Day 0, 1, 3, 7 and 14, and then scheduled at 14 day intervals until the end of the study at Day 84. No appliances were placed and no extractions were performed on the mandibular arch.

At the beginning of all 13 appointments (Days -35, -28, -21, 0, 1, 3, 7, 14, 28, 42, 56, 70, and 84) in the study protocol, subjects were asked to fill out separate pain questionnaires.

\textsuperscript{2} 0.018 twin brackets, 3M Unitek, 2724 South Peck Rd., Monrovia, CA 91016
\textsuperscript{3} Triad TruTray, Dentsply Inc. 221 W. Philadelphia St., P.O. Box 872, York, PA 17405
\textsuperscript{4} G.U.M., Sunstar Americas Inc. 4635 W. Foster Ave., Chicago, IL 60630
that were each made up of 3 sections for the right and left sides. The questionnaires included
a modified McGill Pain Questionnaire-Short Form (MMPQ-SF_{Ortho}) (Freytag 2008,
Schumacher 2009) for orthodontic pain qualities as well as intensity (as indicated by
averages of summed severity scores) and the VAS and PPI that were specific for pain
intensity (Appendix C).
Fig. 1. Occlusal view of appliances. Maxillary teeth with passive and active experimental appliances for Subject 5F2. The passive components consist of: Nance Appliance with acrylic button adapted to the palate and connected by a trans-palatal wire soldered to the upper first molar bands. The active components consist of: a vertical loop auxiliary wire, linking maxillary canine bracket to auxiliary tube on maxillary first molar band, activated by a calibrated closed coil spring.
The first section consisted of the MMPQ-SF<sub>Ortho</sub> that included 15 descriptor words derived from the following domains: 1) Sensory – discriminative, 2) Affective – emotional, 3) Evaluative – cognitive and intensity (Freytag 2008). Subjects were asked to rate each descriptor word on a 4-point Likert severity scale with 0 = no pain, 1 = mild, 2 = moderate, and 3 = severe. Eleven of the 15 descriptors were shown previously to be particularly discriminating for orthodontic pain and these fit into two subscales: general/emotional and localized. The generalized subscale included the following descriptors: uncomfortable, strange, frustrating, and annoying. The localized subscale included: pressure, sore, aching, throbbing, tight, pulling, and miserable (Iwasaki et al. 2010). The second section included the Visual Analogue Scale (VAS) which consisted of a horizontal line that was 100 mm long where the left-hand end corresponded to “no pain” and the right-hand end indicated “worst pain possible.” Subjects were asked to mark along the line at the level where they perceive their pain. The mark was then measured from the left margin of the line to the nearest 0.5 millimeter to quantify the pain level. The third section, known as the Present Pain Intensity (PPI), asked subjects to rate their current pain level on a 0-5 intensity scale where 0 = no pain, 1 = little pain, 2 = moderate pain, and 3 = bad pain, 4 = horrible pain, 5 = extreme pain (Melzack 1975). Questionnaires were completed based on the specific time point in the study. The order in which subjects filled out the questionnaire was altered at each appointment. That is, subjects who filled out the questionnaire for the right side first at one appointment filled out the questionnaire for the left side first at the next visit. After completing the questionnaires, subjects had their oral hygiene evaluated using the Modified Gingival Index (Lobene et al. 1986) and received oral hygiene instruction. During each of
the 10 appointments after premolar extraction, a supra-gingival oral prophylaxis was performed to help minimize gingival inflammation. Furthermore, to verify tooth movement, a light body polyvinylsiloxane\(^5\) impression was made at each appointment starting at Day 0 using a custom impression tray coated with tray adhesive\(^6\). Impressions were poured up with Type III dental stone\(^7\) to document changes in the position of the maxillary canines relative to the anchor segments with models from 10 time-points per subject.

The orthodontic appliances for anchorage and canine retraction were designed as per previous studies (Iwasaki et al. 2000; Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009). Orthodontic anchorage for all subjects was achieved by: 1) customized fabrication of a Nance appliance with a button of acrylic adapted to the palate and connected by a trans-palatal wire (0.036-inch stainless steel) soldered to the upper first molar bands (Fig. 1), 2) a passive rectangular stainless steel archwire segment and figure-8 ligation linking maxillary posterior teeth on each side (Fig. 2). The retraction mechanism was made up of a 0.016 x 0.022-inch diameter stainless steel auxiliary wire customized to be passive. It engaged and was ligated to the maxillary canine bracket and extended back through the tube on the molar band on the same side. This auxiliary wire also had a vertical loop that was activated by a calibrated nickel titanium closed coil spring\(^8\). The vertical loop was located just distal to the maxillary canine, and its vertical height matched the estimated center of resistance (\(C_R\)) position for the specific canine (Fig. 2). The estimated center of resistance was obtained from the following equation (Tanne et al. 1988):

---

\(^5\) Extrude, Kerr Corp. 28200 Wick Rd., Romulus, MI 48174
\(^6\) VPS Tray Adhesive, Kerr Corp. 28200 Wick Rd., Romulus, MI 48174
\(^7\) Golden Stone, Pemaco Inc., St. Louis, MO
\(^8\) G & H wire, 2165 Earlywood Dr., Franklin, IN 46131
\[ C_R = 0.24 \left[ L_r \right] \]

where \( L_r \) is the root length that was measured from a corrected periapical radiograph of the canine. When the loop was activated, the vertical legs of the loop separated and the horizontal components displaced gingivally creating a desired apicodistal countermoment at the canine bracket for bodily canine translation (Yang and Baldwin 1974). Therefore, with posterior anchorage well controlled, net bodily movement of the canine was expected.
Fig. 2. Left buccal view of appliances. Passive and active experimental appliances for Subject 5F2. The passive components shown are: a custom, passive stainless steel arch wire segment with figure-8 ligation linking the second premolar, first molar and second molar; while the active components (retraction mechanism) consist of a vertical loop auxiliary wire, linking maxillary canine bracket to auxiliary tube on maxillary first molar band, activated by a calibrated closed coil spring.
Two retraction forces that delivered continuous stresses of approximately 4 kPa and 78 kPa were randomly assigned to the right and left maxillary canines of each subject. The force that was selected to produce the desired stress levels ranged between 7 cN and 420 cN. Subjects were blinded to the magnitudes of stress that were assigned to the right and left sides. The force and stress levels were determined for each maxillary canine from previously described methods (Iwasaki et al. 2000), by estimating the area of PDL compression which corresponded to the distal root surface area. A periapical radiograph with a known reference of a 5 mm length wire that was taped to the crown of the tooth was made of each maxillary canine. The reference was used to correct the magnification for each radiograph made, so that the corrected canine root length from the alveolar crest to the apex was obtained.

Mesiodistal and labiolingual widths were measured intraorally with a Boley gauge at the cementoenamel junction (CEJ). The total distal root surface area, accounting for root surface curvature, was then calculated from the following formula (Iwasaki et al. 2000):

\[
A_a = L_r a (1 - b^2/a^2)^{1/2}
\]

where \( A_a \) is the total distal root surface area adjusted for curvature, \( L_r \) is the corrected root length, \( a \) is half the labiolingual width of the canine at the CEJ, and \( b \) is half the mesiodistal width of the canine at the CEJ. The force magnitude to be applied to each canine was then determined from the following equation:

\[
F_{\text{retraction}} = \sigma A_a
\]

where \( F_{\text{retraction}} \) is the force magnitude applied to the canine and \( \sigma \) is the average stress (4 or 78 kPa) over the adjusted root surface area.
The force that was used to activate the vertical loop auxiliary wire was produced by a calibrated nickel-titanium alloy closed coil spring. These closed coil springs were designed and calibrated to deliver a known stress during activation. Bench-top measurements were obtained from the springs while loaded and unloaded at approximately 37°C and calibrated for the unloading phase. A spring that delivered the specific desired force for the range of activation that matched the clinical extension of the spring was selected for each canine. The closed coil spring was ligated on one end to the posterior anchorage segment by a hook on the buccal of the first molar band and on the other end by a hook crimped just distal to the vertical loop auxiliary wire. It was essential to verify the activation of each spring for the desired force delivery at each appointment starting with Day 0 and adjust the amount of the extension or change the spring needed to maintain the desired applied stress since canines typically moved during the study. Appliances were also checked for breakage and lost components and were accounted for at each appointment.

Subjects were paid $30.00 for each appointment from Day 0 to Day 84 as reimbursement of their time and efforts to participate in the study. Payments were prorated and delivered to each subject after each appointment attended. Failed appointments did not result in compensation.

**Data and Statistical Analyses**

The intensity of pain was assessed using the VAS and the PPI, plus the averages of severity scores from the 11 descriptors of the MMPQ-SF$_{Ortho}$ (MMPQ-SF$_{Ortho11}$). Eleven descriptors were used in the analyses since previous studies (Iwasaki et al. 2010) found that 11 of the 15 descriptors were discriminating for pain, while the other 4 descriptors were not.
The qualities of pain were assessed using averages of the sums of the severity scores for: the 4 descriptor words in the generalized subscale and the 7 descriptor words in the localized subscale of the MMPQ-SF_{Ortho}. The interaction effects on pain intensity and qualities as functions of stress were assessed for all pain measures. Distributions of data were assessed by plotting person-level trajectories of outcomes over time for the two sides per subject according to the stress applied to the maxillary canine (4 versus 78 kPa) and using descriptive statistics.

The statistical design for Hypotheses 1 and 2 was a two-factor, repeated measures design with stresses and time as the two within-subjects variables. Additionally, the variable gender was included in the model to control for the potential differential effect of gender on pain report. The outcome data for pain intensity (VAS, PPI, and the MMPQ-SF_{Ortho11}) and pain qualities (averages of the severity scores for generalized and localized subscales of the MMPQ-SF_{Ortho}) were tested with both linear and quadratic terms to determine best model fit. A mixed effects model was used to examine the interaction and main effects with subjects as a random effect and stress, time, and gender as fixed effects. The random intercept mixed model was used to fit models as data were clustered within subjects. The significance level was set at $\alpha = 0.05$.

For Hypothesis 3, the effects on pain intensity and qualities regardless of stress magnitude over the 4 phases of treatment: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Days 14-84, were assessed using measures from VAS, MMPQ-SF_{Ortho11}, and the subscale scores for MMPQ-SF_{Ortho}. Mean measurements were obtained for each phase of treatment and then
analyzed using a single factor, repeated measures ANOVA. Where the omnibus test showed significant results ($p < 0.05$), the Fisher-Hayter post hoc test was used to compare pair-wise effects.

In addition, intercorrelations among measures: VAS, PPI, MMPQ-SF$_{Ortho1}$, and the subscale scores for MMPQ-SF$_{Ortho}$, were assessed using Spearman rank correlation coefficients.
CHAPTER 3

RESULTS

Nine subjects met the inclusion criteria and were recruited for the study. Once subjects were identified as potential candidates for the study, they and/or their guardians were given the appropriate information to participate in the study. Informed consent forms and assent forms were presented and signed by all participants. One subject was unable to participate in the study due to the time requirement and withdrew from the study. Of the nine subjects consented, eight subjects began and completed the study.

The sample consisted of five males and three females (detailed demographics are reported in Table 1). Two of the subjects were less than 12 years of age, five of the subjects were between the ages of 12 and 18 years, and one subject was over the age of 18 years. Subjects’ ethnicities were: one African American, four Hispanics, two Caucasians, and one Middle Eastern.
<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Ethnicity</th>
<th>Age (Year.Month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5M1</td>
<td>Male</td>
<td>African American</td>
<td>12.6</td>
</tr>
<tr>
<td>5F1</td>
<td>Female</td>
<td>Hispanic</td>
<td>14.2</td>
</tr>
<tr>
<td>5M2</td>
<td>Male</td>
<td>Caucasian</td>
<td>11.8</td>
</tr>
<tr>
<td>5M3</td>
<td>Male</td>
<td>Middle Eastern</td>
<td>13.7</td>
</tr>
<tr>
<td>5M4</td>
<td>Male</td>
<td>Hispanic</td>
<td>22.5</td>
</tr>
<tr>
<td>5F2</td>
<td>Female</td>
<td>Caucasian</td>
<td>17.6</td>
</tr>
<tr>
<td>5F3</td>
<td>Female</td>
<td>Hispanic</td>
<td>10.1</td>
</tr>
<tr>
<td>5M5</td>
<td>Male</td>
<td>Hispanic</td>
<td>17.0</td>
</tr>
</tbody>
</table>
All subjects presented to the clinic for Day 0 at least 2 weeks after premolar extractions. If a subject was not able to attend on days that followed the protocol, she/he was then scheduled on a day closest to the desired protocol day. If a subject failed to attend a scheduled appointment and was unable to present to the clinic until the next protocol day, data for that missed appointment were not collected. The study protocol was followed with a few noted exceptions. Two subjects did not miss any protocol days (5M2, 5M4), five subjects missed 1 protocol day (5M1, 5F1, 5M3, 5F2, 5M5) on Day 28 or later, and one subject missed 2 protocol days (5F3) on Day 42 and Day 70. No questionnaire was given to subject 5M1 on Day -35. The total number of days that subjects’ visits differed from the protocol ranged from 1 day to 8 days.

Four of eight subjects experienced broken or loose appliances (Table 2). When broken/loose appliances were reported, subjects were asked to refer to only tooth pain when filling out pain questionnaires. Subjects were also asked to report when breakage occurred. All broken and loose appliances were replaced or fixed.

Subject 5F3 reported use of analgesics (Children’s Ibuprofen) on Day 0, 4 hours after application of force. The subject was seen on Day 1 nineteen hours after use of analgesics. Due to the small sample size and the timing of the medication with respect to completion of the forms, the subject was not dismissed from the study and data were included in analyses.

Subjects had their oral hygiene evaluated using the Modified Gingival Index at each visit. All subjects showed good gingival status at all time points with a mean score (± standard deviation) of 0.13 (±0.33).
<table>
<thead>
<tr>
<th>Subject</th>
<th>Stress (kPa)</th>
<th>Day</th>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>5F2</td>
<td>4</td>
<td>14</td>
<td>Loose Spring</td>
</tr>
<tr>
<td></td>
<td>78</td>
<td>67</td>
<td>Loose Spring</td>
</tr>
<tr>
<td>5M2</td>
<td>4</td>
<td>43</td>
<td>Loose Spring</td>
</tr>
<tr>
<td>5M4</td>
<td>4</td>
<td>1</td>
<td>Broken Spring</td>
</tr>
<tr>
<td></td>
<td>78</td>
<td>8</td>
<td>Broken Spring</td>
</tr>
<tr>
<td></td>
<td>78</td>
<td>43</td>
<td>Broken Wire</td>
</tr>
<tr>
<td></td>
<td>78</td>
<td>84</td>
<td>Broken Wire</td>
</tr>
<tr>
<td>5M5</td>
<td>4</td>
<td>3</td>
<td>Loose Spring</td>
</tr>
</tbody>
</table>
Impressions were made at each protocol visit for each subject from Day 0 to Day 84 to verify tooth movement via the resulting dental models (Fig. 3a and 3b). A qualitative assessment of tooth movement indicated that maxillary canines in all subjects distalized from before initiation of treatment to Day 84 of the research protocol. Subjects 5M4 and 5M5 showed the least movement of approximately 1 mm distalization on the 4 kPa side. Subjects 5M2 and 5F3 expressed the most movement with approximately 8 mm distalization on the 78 kPa side. However, on the 78 kPa side, loss of control was evident in these subjects with distolingual rotation and slight distal crown tipping.

Since eleven of the 15 descriptors were found previously to be discriminating for pain (Iwasaki et al. 2010), our study used averages of these descriptors for all statistical analyses. The four descriptors excluded from the analyses were used infrequently in the current study and when selected were rated at “1” (mild) pain. More specifically, four subjects selected “cutting” (4 kPa side: subjects 5F1 (Day 7), 5M2 (Day 1), 5M3 (Day -21), and 5F2 (Day -14 and Day 3; 78 kPa side: subjects 5F1 (Day 1 and Day 7), 5M2 (Day 1), and 5F2 (Day -14)), and one of these subjects also selected “burning” (subject 5M3: Day 1, 4 kPa side and Day 32, 78 kPa side).
Fig. 3a. Tooth movement verification. Occlusal views of dental models from subject 5M2: left - before initiation of treatment, right - at Day 84 of the research protocol. The subject’s right canine was loaded with a stress of 4 kPa, while the left canine was loaded with a stress of 78 kPa. Distal movement of the both canines is evident at Day 84. The 4 kPa and 78 kPa sides show approximately 2 mm and 8 mm distal movement, respectively.
Fig. 3b. Tooth movement verification. Occlusal views of dental models from subject 5M4: left - before initiation of treatment; right - at Day 84 of the research protocol. The subject’s left canine was loaded with a stress of 4 kPa, while the right canine was loaded with a stress of 78 kPa. Distal movement of the both canines is evident at Day 84. The 4 kPa and 78 kPa sides had approximately 1 mm and 4 mm distal movement, respectively.
Results from all subjects for 4 kPa and 78 kPa sides were plotted by scores for each measure versus time (Day -35 to Day 84) (Fig. 4-8). Subjects tended to score higher on Day -28 (appointment following separators) and Days 1-14 during the study period. Peak VAS for 4 kPa and 78 kPa of 64/100 and 74/100, respectively, for subject 5M3 occurred on Day 1 (Fig. 4a and 4b). Scores decreased to rather low levels at Day 14 and remained quite low thereafter. After Day 14, VAS scores for 78 kPa stress were slightly elevated compared to 4 kPa. Peak PPI scores of 2/5 for both stresses also occurred on Day 1 (Fig. 5a and 5b). Scores leveled off to zero at Day 14 and after for the 4 kPa side, while scores remained slightly elevated for 4 subjects (5M1, 5M3, 5M4, and 5F2) beyond Day 14 for the 78 kPa side. Peak MMPQ-SF \textsubscript{Ortho11} scores occurred on Day 1, with a maximum of 7/33 for subject 5M3 for both sides (Fig. 6a and 6b). These scores tended to level off to low levels on the 4 kPa side, but remained slightly elevated on the 78 kPa side throughout the remainder of the study period. Peak generalized (Fig. 7a and 7b) and localized (Fig. 8a and 6b) subscale scores were 4/12 and 5/21, respectively, and showed similar trends for stress over time, as for other pain scales. One exception was subject 5F1 who had this peak score of 4/12 for the generalized subscale for Days -28, -21, 0, 1, and 7.
Fig. 4a. 4 kPa VAS scores. Scores for each subject during the study on the side receiving a stress of 4 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 100.
Fig. 4b. 78 kPa VAS scores. Scores for each subject during the study on the side receiving a stress of 78 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 100.
Fig. 5a. 4 kPa PPI scores. Scores for each subject during the study on the side receiving a stress of 4 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 5.
Fig. 5b. 78 kPa PPI scores. Scores for each subject during the study on the side receiving a stress of 78 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 5.
Fig. 6a. 4 kPa MMPQ-SF$_{Ortho11}$ scores. Scores for each subject during the study on the side receiving a stress of 4 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 33.
Fig. 6b. 78 kPa MMPQ-SF_{Ortho11} scores. Scores for each subject during the study on the side receiving a stress of 78 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 45.
Fig. 7a. 4 kPa MMPQ-SFOrtho Generalized/Emotional scores. Scores for each subject during the study on the side receiving a stress of 4 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 12.
Fig. 7b. 78 kPa MMPQ-SF$^{\text{Ortho Generalized/Emotional}}$ scores. Scores for each subject during the study on the side receiving a stress of 78 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 12.
Fig. 8a. 4 kPa MMPQ-SF<sub>Ortho Localized</sub> scores. Scores for each subject during the study on the side receiving a stress of 4 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 21.
Fig. 8b. 78 kPa MMPQ-SF\textsubscript{Ortho Localized} scores. Scores for each subject during the study on the side receiving a stress of 78 kPa after completing the questionnaires on Day -35 to 84. Day -35 was a baseline where no orthodontic appliances were worn, Day -28 was approximately 1 week after separator placement, and Day -21 was when delivery of Nance appliance and passive segments occurred. Data were collected on protocol days or the day closest to the desired protocol day if a subject was unable to attend. Maximum possible score on vertical scale = 21.
Correlations between Pain Measurements

To verify validity of the MMPQ-SF\textsubscript{Ortho11} and the two pain subscales compared with the VAS and PPI, Spearman rank order correlations were calculated. The coefficients (r) of the MMPQ-SF\textsubscript{Ortho11}, generalized subscale and localized subscale with VAS were: $r = 0.661$, 0.422, and 0.672, respectively; and with PPI were: $r = 0.833$, 0.711 and 0.683, respectively; which indicate relatively strong relationships among these measurements of pain.

Mixed Effects Models

Mixed effects regression models were used to assess the effect of stress over time for Days -35 and 1 – 84, baseline through the loading period studied, on pain intensity and quality. Initially, a linear model was fitted using maximum likelihood estimates. Since descriptive statistics indicated that the trajectory of pain over time was not strictly linear, a nested model was subsequently fitted with a quadratic term for observation, and change in model fit assessed using the likelihood ratio test. Models fitted with the quadratic term were determined to not improve fit and were eliminated from the final model. Additionally, including an interaction term for time X stress did not contribute to the model fit above that which was obtained with main effects, and thus, the interaction term was eliminated from the final models. Preliminary analyses suggested that outcomes were different for males and females; therefore gender was added to the models to determine if gender mediated the effect of stress on pain. Models that explored the interaction of gender with stress, gender with time or the three way interactions were determined to be inferior to models with main effects of stress, time and gender. Therefore, models with main effects are the only models that will be reported.
Pain Intensity Measures

Models with the main effects of stress, time and gender on the VAS (Fig. 4a and 4b, Table 3) determined that gender (p=0.024) and time (p=0.0001) were significantly related to outcomes for Days -35 and 1 - 84. Females reported pain as measured by VAS, on average, 5.2 mm higher compared to males. There was no significant difference in pain reported with respect to stress: 4 kPa compared to 78 kPa (p=0.591). Pain intensity (Fig. 4a and 4b), reported for 4 kPa and 78 kPa using VAS, on average peaked at Day 1 and then decreased, leveling off to rather low levels throughout the remainder of the study period.

Results for pain measured using PPI (Fig. 5a and 5b) were modeled (Table 4) in a similar fashion to those on the VAS. The effects of gender (p=0.001) and time for Days -35 and 1 – 84 (p=0.0001) were found to be statistically significant, while the effect of stress (p=0.123) was not.

The results of the mixed model (Table 5) for the total MMPQ-SF<sub>Ortho11</sub> (Fig. 6a and 6b) indicated that stress (p=0.119) and gender (p=0.241) were not significant predictors for MMPQ-SF<sub>Ortho11</sub>. Over Days -35 and 1 – 84, the MMPQ-SF<sub>Ortho11</sub> decreased and this effect was significant (p=0.0001) regardless of stress or gender.

Pain Quality Measures

The two groups of descriptors in the MMPQ-SF, generalized/emotional (Fig. 7a and 7b) and localized (Fig. 8a and 8b) pain subscales, were analyzed using a mixed-effects linear regression model; again, nested models using a quadratic term were fitted initially to determine if linear or quadratic best fit the data (Tables 6 and 7, respectively). Gender was not a significant predictor for either of the two subscales (generalized: p=0.126, localized:
p=0.836), while time, for Days -35 and 1 – 84, was a significant predictor for both
(generalized: p=0.0001, localized: p=0.004). Stress was not a significant predictor of the
generalized subscale (generalized: p=0.783); however, it was a significant predictor for the
localized subscale (localized: p=0.011).
### TABLE 3

**VAS MIXED-EFFECTS MULTIPLE LINEAR REGRESSION MODEL**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>p</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>1.05</td>
<td>1.95</td>
<td>0.591</td>
<td>-2.78 - 4.87</td>
</tr>
<tr>
<td>Gender</td>
<td>5.21</td>
<td>2.31</td>
<td>0.024</td>
<td>0.69 - 9.73</td>
</tr>
<tr>
<td>Time</td>
<td>-1.33</td>
<td>0.34</td>
<td>0.0001</td>
<td>-2.00 - 0.66</td>
</tr>
<tr>
<td>Constant</td>
<td>13.6</td>
<td>4.31</td>
<td>0.002</td>
<td>5.15 - 22.06</td>
</tr>
</tbody>
</table>

### TABLE 4

**PPI MIXED-EFFECTS MULTIPLE LINEAR REGRESSION MODEL**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>p</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>0.12</td>
<td>0.08</td>
<td>0.123</td>
<td>-0.03 - 0.28</td>
</tr>
<tr>
<td>Gender</td>
<td>0.29</td>
<td>0.08</td>
<td>0.001</td>
<td>0.12 - 0.45</td>
</tr>
<tr>
<td>Time</td>
<td>-0.06</td>
<td>0.01</td>
<td>0.0001</td>
<td>-0.09 - 0.04</td>
</tr>
<tr>
<td>Constant</td>
<td>0.51</td>
<td>0.17</td>
<td>0.004</td>
<td>0.16 - 0.85</td>
</tr>
</tbody>
</table>
### TABLE 5
**MMPQ-SF Ortho11 Mixed-effects Multiple Linear Regression Model**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>p</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>0.38</td>
<td>0.25</td>
<td>0.119</td>
<td>-0.10</td>
</tr>
<tr>
<td>Gender</td>
<td>0.46</td>
<td>0.39</td>
<td>0.241</td>
<td>-0.31</td>
</tr>
<tr>
<td>Time</td>
<td>-0.18</td>
<td>0.04</td>
<td>0.001</td>
<td>-0.26</td>
</tr>
<tr>
<td>Constant</td>
<td>1.57</td>
<td>0.57</td>
<td>0.006</td>
<td>0.46</td>
</tr>
</tbody>
</table>

### TABLE 6
**Generalized Subscale MMPQ Mixed-effects Multiple Linear Regression Model**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>p</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>0.04</td>
<td>0.15</td>
<td>0.783</td>
<td>-0.26</td>
</tr>
<tr>
<td>Gender</td>
<td>0.79</td>
<td>0.51</td>
<td>0.126</td>
<td>-0.22</td>
</tr>
<tr>
<td>Time</td>
<td>-0.10</td>
<td>0.02</td>
<td>0.001</td>
<td>-0.14</td>
</tr>
<tr>
<td>Constant</td>
<td>0.91</td>
<td>0.36</td>
<td>0.012</td>
<td>0.20</td>
</tr>
<tr>
<td>Variable</td>
<td>Coefficient</td>
<td>Standard Error</td>
<td>p</td>
<td>95% Confidence Interval</td>
</tr>
<tr>
<td>----------</td>
<td>-------------</td>
<td>----------------</td>
<td>--------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Stress</td>
<td>0.41</td>
<td>0.16</td>
<td>0.011</td>
<td>0.09</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.04</td>
<td>0.20</td>
<td>0.836</td>
<td>-0.44</td>
</tr>
<tr>
<td>Time</td>
<td>-0.08</td>
<td>0.03</td>
<td>0.004</td>
<td>-0.14</td>
</tr>
<tr>
<td>Constant</td>
<td>0.56</td>
<td>0.36</td>
<td>0.118</td>
<td>-0.14</td>
</tr>
</tbody>
</table>
Pain Experience in Phases

Since the pain measures were not significantly affected by stress, measures from VAS, MMPQ-SFOrtho11, and the subscale scores for MMPQ-SFOrtho from the two sides were subsequently averaged for each subject and then the data were collapsed into 4 phases: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Day 14-84. Among the 4 phases, mean scores (± standard deviation) for: VAS were 0.88 (±1.41), 9.72 (±9.96), 13.48 (±11.82), and 2.04 (±2.54) (Fig. 9a); MMPQ-SFOrtho11 were 0.00 (±0.00), 2.19 (±2.03), 1.81 (±1.40), and 0.31 (±0.25) (Fig. 9b); generalized subscale scores were 0.00 (±0.00), 1.13 (±1.41), 0.73 (±1.08), and 0.08 (±0.10) (Fig. 9c); and localized subscale scores were 0.00 (±0.00), 1.06 (±1.15), 1.06 (±0.63), and 0.23 (±0.25) (Fig. 9d).

A single factor, repeated measures ANOVA on VAS, MMPQ-SFOrtho11, and the subscale scores for MMPQ-SFOrtho assessed the effect of pain intensity and quality over the 4 phases of treatment. The omnibus test showed significant results (p < 0.05) across the phases for all outcome measures: VAS (p=0.013), MMPQ-SFOrtho11 (p=0.001), generalized subscale (p=0.023), and localized subscale (p=0.001). Fisher-Hayter post hoc tests were then used to conduct pair-wise comparisons. Pairwise comparisons were not significant for the VAS or the generalized subscale. Scores for Baseline to Post-placement of separators and Baseline to Early tooth-loading were found to be significantly different in the MMPQ-SFOrtho11, and the localized subscale.
Fig. 9a. VAS mean measurements. Measurements obtained for each of the following 4 phases of treatment: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Days 14-84.

Fig. 9b: MMPQ-SF Ortho11 mean measurements. Measurements obtained from each of the following 4 phases of treatment: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Days 14-84.
Fig. 9c: Generalized subscale MMPQ-SF\textsubscript{Ortho} mean measurements. Measurements obtained from the for each of the following 4 phases of treatment: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Days 14-84.
Fig. 9d: Localized subscale MMPQ-SF_{Ortho} mean measurements. Measurements obtained from the for each of the following 4 phases of treatment: (1) Baseline – Day -35; (2) Post-placement of separators – Day -28; (3) Early tooth-loading – Days 1-7; and (4) Later tooth-loading – Days 14-84.
CHAPTER 4

DISCUSSION

The main purpose of this study was to gather longitudinal data to quantify and describe the pain experienced (intensity and quality) during controlled tooth movement at 2 levels of continuous stress. Eight subjects (5 males, 3 females) participated in this split-mouth design over a time period of approximately 113 days. Extractions of the maxillary first premolars and retraction of the maxillary canines with two different stresses (4 kPa and 78 kPa) on either side of the mouth were performed on each subject using segmental mechanics in order to control tooth movement and minimize confounding variables. Previous studies using similar protocols (Iwasaki et al. 2000; Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009) demonstrated that using these mechanics, differential bodily movement of the maxillary canines could be achieved. That is, orthodontic appliances in this study were set-up to provide anchorage (resistive forces) to counteract active forces applied to translate the maxillary canines distally; hence, net stresses affected only the maxillary canines. Pain questionnaires that included the MMPQ-SF_{Ortho}, VAS, and PPI were given and filled out for both sides of the mouth by each subject before each appointment throughout the study protocol.

**Mechanical Stimuli as Controlled versus Uncontrolled Variables**

To date, no previous study has quantified stress distribution and compared it with pain intensity and quality. The current protocol not only measured the magnitude of force applied to each canine, but calibrated this to the size and shape of the canine root to achieve a specific target stress (4 or 78 kPa) for each tooth to be moved. In addition, the active
component was designed to deliver this distally-directed force plus a counter-moment to achieve approximately even stress distribution along the length of the PDL. That is, the mechanical stimuli applied in this study were controlled and quantified to be equivalent for a given target stress. This is in contrast to the majority of past studies where applied forces were not measured or resulted in uncontrolled tipping or both. For example, several past studies have utilized separators (Brown and Moerenhout 1991; Bergius et al. 2002; Giannopoulou et al. 2006) and archwires (Brown and Moerenhout 1991; Jones and Chan 1992; Scheurer et al. 1996; Erdinc and Dincer 2004) to measure pain intensity associated with tooth movement. Unfortunately, these studies failed to control for the magnitude and particular type of force applied. In addition, applied forces/stresses were not quantified and the nature and speed of tooth movement were not measured. Therefore, the mechanical stimuli in these studies were uncontrolled variables.

Only two recent studies (Ogura et al. 2009; Luppanapornlarp et al. 2010) have attempted to compare pain intensities associated with different known force magnitudes. One study examined the pain intensity during the first 7 days after application of relatively lighter (20 cN) and heavier (200 cN) continuous orthodontic forces in the apical direction to maxillary second premolars (Ogura et al. 2009). The mechanical set up in this study consisted of a Ni-Ti coil spring that attached from the second premolar bracket to an archwire that engaged the first premolar and the first molar and was stepped up apical to the second premolar bracket to provide a point of attachment. Although this study accounted for the magnitudes of forces and attempted to apply these continuously, the type of tooth movement was not controlled carefully and was considered tipping with intrusion.
Therefore, stress along the PDL was not uniform with higher stress levels at the crestal PDL on the buccal side and at the apical PDL on the lingual side. In addition, while the force levels for the lighter group (20 cN) are comparable to the current study, the force levels for the heavier group (200 cN) are relatively smaller. Another study examined pain intensity after initiating canine retraction with continuous forces of 50 cN and 150 cN in a split mouth design (Luppanapornlarp et al. 2010). This study used a transpalatal arch as anchorage and sliding mechanics on archwire segments that engaged posterior teeth and the canine.

Maxillary canines were retracted with Ni-Ti coil springs attached from the posterior segment to the hook of the canine bracket. While this study also failed to control carefully tooth movement and tended to result in tooth tipping, other limitations to this design include force-delivery changes due to binding of the canine bracket and possible changes in spring characteristics during retraction.

**Maximum Pain Experiences during Orthodontics**

The current study recorded a VAS maximum value on Day -28 (post-separator placement) of 33/100. While this is relatively low, subjects in this study were generally seen approximately 4-7 days after separator placement which allowed time for the pain to level off. This is in agreement with one study (Bergius et al. 2002) that reported maximum peak values of 100 on the VAS 24 hours after separator placement and an average score of less than 20 on day 7.

Using the mechanics and armamentarium that the current study required for canine retraction, the VAS showed maximum peak scores at Day 1 of 64/100 and 74/100 for 4 and 78 kPa stresses, respectively. Previous studies have reported maximum scores of 100 on the
VAS 21-24 hours after initial archwire placement (Jones and Chan 1992; Scheurer et al. 1996; Erdinc and Dincer 2004) with a mean score of 42/100 at 24 hours (Scheurer et al. 1996). Another study utilizing the same questionnaire as the current study found a peak score of 93 on the VAS after rectangular archwires were placed for the first time (Freytag 2008). Ogura et al. (2009) evaluated pain intensity during 7 days after initiating tipping and intrusive continuous forces of 20 cN and 200 cN and found peaks at 32 hours with a score of 38/100 and at 12 hours with a score of 63/100, respectively. The peak score for this light-force group was notably lower than that of the light-stress group (4 kPa) in the current study, while the heavy-force/stress peak scores in both studies were more similar. Additionally, the current study recorded VAS peak values on Day 7 of 13/100 and 34/100 for 4 kPa and 78 kPa, respectively. The 20 cN group in the Ogura et al. (Ogura et al. 2009) study showed a maximum score of 10/100 from Days 4-7, which were similar to results for the 4 kPa group in the current study. Meanwhile, the 200 cN group showed a maximum score of 20/100 from Days 4-6 and of 10/100 on Day 7, which were somewhat lower than the 78 kPa group in the current study. Although smaller magnitudes of force were applied in the Ogura et al. (2009) study, these were in a different direction and the loading areas were not measured so stresses could not be compared. Another study utilized sliding mechanics for retracting canines with continuous forces of 50 cN and 150 cN to assess pain intensity using the VAS at 1 hour, 24 hours, 1 week, 1 month, and 2 months (Luvpanapornlarp et al. 2010). This study found that the mean VAS for teeth receiving 150 cN force was 35.2/100 (±16.9) and significantly higher than the mean VAS for teeth receiving 50 cN force which was 20.2/100 (±24.1) at 24 hours.
This study did not report maximum peak values at any time point so no direct comparisons can be made. Pain intensity during different types of tooth movements seems to be different.

The current study showed the same maximum scores for low and high stresses on Day 1 for PPI (2/5) and MMPQ-SF_{Ortho11} (7/33). One study (Freytag 2008) also found maximum values of 4/5 for the PPI after initial round archwire placement and of 33/45 for the total MMPQ-SF score including all 15 words when rectangular archwires had been in place for four or more months. These scores are relatively higher when compared to the current study. Unfortunately, this previous study did not take the type of tooth movements into account and the mechanical stimuli were indeterminate. The results from the current study using controlled tooth movement showed fairly low peak scores relative to scores in other studies that utilized different types of mechanics for tooth movement.

While all pain measures showed a peak at Day 1 in the current study, the maximum scores among the sample for these measures were relatively low compared to the maximum possible scores. Additionally, it was also noted that scores tended to increase in response to initial loading when compared to post-separator placement, however, peak scores among the subjects were variable from Day -28 (post-separator placement) to Day 1 after initiation of stress. Some subjects reported notably higher scores on Day 1 when compared to Day -28 for both stresses, while others showed comparable scores from Day -28 to Day 1 for both stresses. Only one subject showed a considerable decrease from Day -28 to Day 1 on the 78 kPa side.
Correlation Results

To evaluate pain intensity, measures from a VAS, PPI, and MMPQ$_{Ortho11}$ were used. The VAS has been found to be a reliable and valid method to measure pain intensity in previous studies (Dalton and McNaull 1998). A validity study found high correlations among MMPQ-SF$_{Ortho15}$ (total scores from all 15 descriptors) and VAS, MMPQ-SF$_{Ortho15}$ and PPI, and the VAS and PPI, where $r^2$ values were: 0.67, 0.74, 0.50, respectively, when used in an orthodontic population (Iwasaki et al. 2010). Furthermore, high correlations were noted between the VAS and PPI and total scores from 11 descriptors comprising the generalized and localized subscales and the subscales individually. The current study also found the same positive correlation between VAS and PPI ($r^2 = 0.50$) but lower correlations among other measures and the same rank order, where $r^2$ values were: 0.44 and 0.69 for MMPQ-SF$_{Ortho11}$ and VAS, and MMPQ-SF$_{Ortho11}$ and PPI, respectively. It was also noted that VAS and PPI had similar correlations with the localized subscale ($r^2 = 0.45, 0.47$) while their correlations with the generalized subscale were notably different ($r^2 = 0.18, 0.50$). This suggests that VAS may be more appropriate for describing the feeling of pain (localized - sensory) rather than conveying the perception of the experience (generalized - affective). PPI, on the other hand, gives an overall pain score and appears to take into account the affective and sensory aspects of pain. The current study and previous studies indicate that the MMPQ-SF$_{Ortho11}$, and the generalized and localized subscales are valid tools for orthodontic pain evaluation in adolescents and young adults, comparable to the VAS and PPI.
Effects of Continuous Stresses over Time

The current study collected longitudinal data over a period that included three preparatory days (Day -35, -28, -21) and 10 time points over approximately 84 days during canine retraction. This allowed comparison of pain during baseline, post-separator placement, and continuous stress application of known magnitudes. Many of the other studies assessing pain during orthodontic therapy followed patients for relatively short periods of time, ranging from 24 hours to 16 days. One study described previously examined pain intensity at only 5 time points using the VAS at 1 hour, 24 hours, 1 week, 1 month, and 2 months after initiating canine retraction (Luppanapornlarp et al. 2010). While this allowed assessment of pain after an attempted continuous magnitude of force was applied, no baseline was recorded for comparison.

The current study was designed to detect differences in pain response over a relatively long period of time. Because the number of observations in the current study was large, the effect of stress, gender and time on pain intensity and quality was assessed using a mixed effects model. This model fit a trajectory for each subject at baseline and from Day 1-84 and then compared groups. A linear model was found to be the best fit for the current study’s data since the person-level trajectories peaked on Day 1 and then subsequently decreased. Previous studies have not been able to use this type of analysis as they did not have longitudinal data with controlled variables.

The pain trend observed was similar to previous studies in which pain increased and peaked between 4 and 24 hours after the application of a force and then decreased to lower or normal levels at day 7 (Jones 1984; Ngan et al. 1989; Brown and Moerenhout 1991; Jones
and Chan 1992; Scheurer et al. 1996; Erdinc and Dincer 2004; Giannopoulou et al. 2006). In the current study, a significant difference in pain intensity (VAS, PPI, MMPQ-SF_{Ortho11}) and quality (generalized and localized subscales) was reported over time. Pain scores (intensity and quality) peaked at Day 1 and then leveled off to lower levels throughout the remainder of the study period. This may be due to the inflammatory reaction from compression of the PDL after initial force application. Several cytokines and inflammatory mediators have been linked to the pain perception associated with tooth movement. One study found an association between IL-1β, SP, and PGE_2 levels in the GCF and pain perception after separator placement (Giannopoulou et al. 2006). It would be interesting to analyze the amount of inflammatory mediator levels in the GCF during controlled tooth movement and investigate if it has an effect on the pain intensity perceived.

Due to the fact that pain decreased from Day 1 to the end of the study period, it must be speculated that some sort of adaptation to pain occurs with time. This may be due to the biological factors mentioned above and measurement of these in combination with pain scores during orthodontic tooth movement could help support or refute this. However, psychological and social factors may also be associated with orthodontic treatment and pain. Orthodontic appliances are generally uncomfortable initially and they often require a time period of physical and psychological adjustment. When a subject is unaware of the type of pressure and pain that they will experience with orthodontics, they might be more apprehensive and experience or report more pain initially. Over time, subjects may become more acclimated to their appliance, be more prepared for treatment, and consequently report less pain. Psychological factors including stress, anxiety, and depression have been shown to
contribute to a patient’s perception of pain (Brown and Moerenhout 1991; Bartlett et al. 2005). One study found that a structured telephone call made within the first 24 hours after orthodontic appliance placement significantly reduced pain intensity and the state of anxiety the following week when compared to a control group that did not receive a phone call (Bartlett et al. 2005). However, the control group still showed a reduction in pain intensity and anxiety after peak values at 24 hours. Furthermore, subjects’ attitudes and expectations have been shown to contribute to anxiety and the anticipation of pain (Sergl et al. 1998).

**Higher versus Lower Stress Effects**

In the past, lighter forces were thought to promote increased tooth movement while at the same time minimizing pain (Burstone 1962; Profitt et al. 2007). Unfortunately, as discussed above, no studies have evaluated pain in relation to the force applied with controlled tooth movement. In contrast to the notion that lighter forces result in increased tooth movement, previous studies have found that higher forces/stresses have produced more efficient tooth movement (Iwasaki et al. 2000; Iwasaki et al. 2001; Iwasaki et al. 2005; Iwasaki et al. 2006; Iwasaki et al. 2009). One study discovered that 78 kPa produced a larger average tooth movement than lower stresses with stresses as small as 4 kPa still producing effective tooth movement (Iwasaki et al. 2009). Therefore, the current study chose a high stress of 78 kPa versus a low stress of 4 kPa to evaluate pain intensities and qualities. The different magnitudes of stress used in this study were expected to result in different pain intensities and qualities reported.

No statistically significant differences were detected in pain intensity, using measures of VAS, PPI, MMPQ-SF_{Ortho11}, between 4 kPa and 78 kPa. Conversely, two previous studies
that attempted to compare pain intensities associated with different applied force magnitudes using a split-mouth design, found that higher applied forces were associated with higher pain intensities (Ogura et al. 2009; Luppanapornlarp et al. 2010). However, these studies used different forces/stresses from the current study and had several limitations. Although pain intensity associated with a stress of 4 kPa was not found to be significantly different when compared to a stress of 78 kPa in the current study, there were slightly elevated scores among all pain intensity measures with the 78 kPa stress after Day 14. Previous research has indicated that higher stresses produce increased amounts of tissue damage (King and Fischlschweiger 1982; Chutimanutskul et al. 2006; Gonzales et al. 2008) that can lead to hyalinization and undermining resorption. While controlled tooth movement with lighter stress is expected to reduce the blood flow and stimulate bone resorption, higher stresses are anticipated to lead to blood constriction and necrosis. Therefore, higher stresses may strain the adaptive capabilities of the periodontium over time more than the lower stresses. Failure to detect a significant difference in pain scores for high versus low stress might be due to the split-mouth design and/or small sample size in the current study.

There were no significant differences found between the two stresses (4 kPa and 78 kPa) using the generalized subscale. The descriptors that make up the generalized subscale (‘uncomfortable’, ‘strange’, ‘frustrating’, and ‘annoying’) convey perceptions of an experience. Therefore, subjects tended to score words similarly in the generalized subscale and describe their experience similarly regardless of the amount of stress applied. Conversely, a significant difference was found with the localized subscale with respect to stress. Since localized words were scored higher to describe the pain on the 78 kPa side
compared to the 4 kPa side, this suggests that subjects had more localized (sensory) pain associated with the heavier stress side when compared to the lighter stress. Descriptors in the localized subscale (‘pressure’, ‘sore’, ‘aching’, ‘throbbing’, ‘tight’, ‘pulling’, and ‘miserable’) describes the feeling and types of pain. This makes sense in the current study as net stress is intended to only affect the canine since the resistive forces are distributed over the larger area of the anchorage component and this is counteracted by the active force applied to translate the maxillary canine distally. Subjects in the current study also had brackets placed at least two weeks before initiation of stress to allow adequate adaptation to the appliance. Therefore, most of the pain perceived relative to stress reflects the type of mechanics being applied. A previous study (Schumacher 2009) found that one generalized descriptor (‘strange’) and 3 localized descriptors (‘pressure’, ‘sore’, and ‘aching’) were used most frequently after initial archwire placement. However, some of the pain reported in this previous study may be due to placement of brackets the same day during initial archwire placement and the pain related to the brackets.

**Gender Effects**

In the current study, a significant difference was found in pain intensity (using VAS and PPI) relative to gender with female subjects reporting 5.2 mm higher on the VAS compared to males. While some studies (Jones 1984; Ngan et al. 1989; Jones and Chan 1992; Sergl et al. 1998; Erdinc and Dincer 2004; Bird et al. 2007) have found no gender differences related to pain, the current study is in agreement with previous studies that also found that females reported higher pain intensities than males when separators (Bergius et al. 2002) or archwires were placed (Scheurer et al. 1996; Freytag 2008; Schumacher 2009).
However, the current study found no significant gender differences in the MMPQ-SF\textsubscript{Ortho11},
and the generalized and localized subscales. This indicates that males and females tended to
report the same types/feelings of pain during controlled tooth movement. The two studies
(Freytag 2008; Schumacher 2009) that utilized the same questionnaire as in the current study
also noted that there were no gender differences in levels of pain measured by the MMPQ-
SF. This provides further support that gender-based differences may be eliminated when
utilizing the MMPQ-SF developed by Freytag (2008). However, sample sizes were limited.

**Comparison of Pain Experience in Phases**

The current study assessed phases of treatment that included baseline, post-placement
of separators, early tooth-loading, and later tooth-loading regardless of stress. While the
analysis suggests an overall quadratic trend, no pairwise effects were found among the
phases using the VAS or the generalized subscale. Nevertheless, mean scores for each phase
showed relatively low levels at baseline and later tooth-loading and higher levels at the
appointment after placing separators and the week after initiating force utilizing controlled
tooth movement. In the current study, application of forces/stresses to the teeth appears to be
slightly more painful on average than 4-7 days post-placement of separators. One study
described previously measured pain intensities at 1 hour, 1 day, and 7 days after separator
placement and found mean VAS values of 11, 13, and approximately 4, respectively
(Giannopoulou et al. 2006). This relates to the current study as pain intensity decreased but
did not reach baseline values after 7 days. The current study, however, had slightly higher
average mean VAS scores (9.72 ±9.96) approximately 4-7 days after separator placement.
Another study recorded a mean VAS of 20.2/100 and 35.2/100 at 24 hours, 8.05/100 and
8.09/100 at 1 week, 9.44/100 and 10.45/100 at 1 month, and 10.97/100 and 15.03/100 at 2 months for continuous forces of 50 cN and 150 cN, respectively (Luppanapornlarp et al. 2010). Unfortunately, this study did not record scores at baseline or after separator placement. While the results cannot be directly compared since the current study used mean values collapsed over several time periods, the trend previously described can be observed among both studies.

The results of this study found that pain intensity (MMPQ-SFOrtho11) and quality (localized subscale) levels from baseline to post-placement of separators were significantly different. Subjects generally had no pain at baseline and significantly higher pain scores 4-7 days after separators were placed. Other studies have found similar results with an increase in pain intensity after placing separators (Bernhardt et al. 2001; Bergius et al. 2002; Giannopoulou et al. 2006; Bird et al. 2007). However, one of these previous studies (Bird et al. 2007) only recorded the pain perception until awakening the next morning after placement. This study assessed the quality of pain through the use of a McGill Pain Questionnaire where the subjects selected one word per group out of five groups of words that described their pain instead of rating each word. They found the most commonly selected words to describe pain were ‘annoying’, ‘sore’, and ‘tight’. While ‘annoying’ was the most commonly selected word immediately after separator placement, ‘sore’ was chosen most commonly at bedtime and the next morning. Descriptors ‘sore’ and ‘tight’ fit in the localized subscale which further supports the current findings that placement of separators have a localized (sensory) pain effect. Another previous study (Bergius et al. 2002) followed subjects for 7 days following separator placement. This study found that while the majority
of subjects reported pain the evening following placement, 42% still reported pain at day 7 which corresponds to the approximate day subjects in the current study were seen.

The current study also found a significant difference in pain intensity (MMPQ-SF<sub>Ortho11</sub>) and quality (localized subscale) levels from baseline to early tooth-loading during controlled tooth movement. Subjects had no pain at baseline and significantly more pain during the early tooth-loading phase. This agrees with the majority of studies that imply that the application of forces to induce tooth movement is the major cause of pain in orthodontics (Jones 1984; Oliver and Knapman 1985; Brown and Moerenhout 1991; Scheurer et al. 1996). However, this does not concur with a previous study (Iwasaki et al. 2010) that found no significant differences in the use of localized descriptors across treatment stages compared to the generalized subscale. In this study, generalized words were scored significantly higher after initial archwire placement compared to middle and end of treatment archwires. However, this study had limitations as it was a cross-sectional study that examined stages of treatment that were base on different archwires used during comprehensive care. This study also did not take into account the types of mechanics and magnitudes of forces being experienced. The current study provided the same type of controlled mechanics for each subject and followed them over a relatively long period of time. Furthermore, the current study found no significant difference between baseline and later tooth-loading. This may be due to an adaptive process that develops in response to continuous stimuli with the progression of treatment.
Clinical Implications

The current study was a human-based study that offered further insight on pain intensities and qualities experienced during controlled tooth movement that can be extrapolated to the orthodontic community in the clinical setting. Based on current and previous studies, pain is a common factor and is most prevalent the day following the application of force/stress. Furthermore, the magnitude of force/stress may not be associated with high versus low pain intensities and generalized pain qualities. This suggests that any magnitude of force/stress will produce pain and needs to be managed appropriately.

With this additional knowledge, practitioners are more prepared to educate and inform their patients of the pain they will perceive after inducing tooth movement. They may also aid in pain management by suggesting or prescribing analgesics in the hours before and after the application of force/stress. While inter-individual variation has been noted, pain management may last for some patients beyond 7 days. However, for the majority of patients, pain management should be focused on the day following force/stress application.

Limitations

The limitations in this preliminary study need to be addressed in future research. This study was low-powered because the sample size was only 16 teeth/sides from 8 subjects; 5 being male and only 3 being female. Furthermore, this study involved adolescents and adults with 7 of the subjects being below the age 18 years, and one subject being 22 years old during the study. There was an insufficient number of subjects to detect a relationship between age and pain, however, it was noted that the older subject reported higher levels of pain with MMPQ-SF_{Ortho11}, localized subscale, VAS, and PPI from Day 56-84 on the 78 kPa
side. The current study also included a variety of ethnicities, but had insufficient subjects/groups to extrapolate any relationships.

Because the current study was a split-mouth design, subjects were susceptible to cross over effects in which pain on one side of the mouth may affect pain on the other side. Subjects were also followed over a relatively long period of time; however, not all subjects were able to attend all protocol days. By plotting person-level trajectories of outcomes over time, the mixed effects model was able to predict missing data.

Broke and loose appliances were also experienced during the current studies protocol. Due to the power of this study, data were not discarded if an appliance was loose or broken. The current study generally did not observe an increase or decrease in pain responses when a subject presented with a broken or loose appliance with the exception of one subject (5M4) who reported decreased scores after presenting with a broken spring (Day 8) and increased scores after presenting with a broken wire (Day 84). Therefore, broken and loose appliances may have had an effect on the pain intensity and quality reported. One subject reported use of analgesics 19 hours before data collection at Day 1. It was assumed that 19 hours was sufficient time for the analgesic effect to diminish and the data set was not thrown out.

**Future Studies**

While the current study was conducted on a convenience sample and was able to gather preliminary data, follow up studies with larger sample sizes need to be conducted to increase the power of this data. Future studies should utilize the questionnaire in the current study with different mechanics and types of tooth movement to provide us with a more thorough understanding of the different types of descriptors associated with these particular
types of movements. This would allow clinicians to prepare patients on the types of feelings that they might experience during treatment. It would also be interesting to see if there are differences in pain perception in studies that utilized different stresses at different times during canine retraction rather than using a split mouth design. That is, canine retraction could be initiated with one stress for a period of time, and then the same canine could be retracted with a different stress after an adequate rest period.

While the current study had its limitations, future studies with larger sample sizes to detect potential gender-related, age-related, and ethnicity-related differences are warranted. These future studies should also exclude data associated with broken/loose appliances and/or use of analgesics. Furthermore, studies should also attempt to investigate if a relationship exists for pain perception between separators and initial tooth loading. This may provide a predictive model that can be used clinically in assessing which subjects will likely experience more pain during treatment.

Great inter-individual variance in pain has been reported in the literature (Jones and Chan 1992). It has been shown that pain is subjective and dependent on several factors including but not limited to previous pain experiences, present emotional state, stress, and expectations of treatment (Ngan et al. 1989; Brown and Moerenhout 1991; Bergius et al. 2000). Utilizing questionnaires that assess personality, stress, depression and anxiety along with pain measurements during orthodontic tooth movement would be helpful in possibly establishing a relationship that would be clinically useful for the practitioner that may then be able to predict pain responses during the different phases of treatment. Furthermore, a genetic component, catechol-O-methyltransferase (COMT), has been linked to pain
perception and orthodontic treatment (Slade et al. 2008). This study suggested that patients with this genetic variant have heightened pain sensitivities. The current study showed intra- and inter-subject variability in pain intensity and qualities over time with two different stresses. However, psychological, biological, and social factors were not taken into account when assessing pain. In addition, the current study only verified tooth movement with qualitative assessments. Generally, most subjects experienced more tooth movement and pain on the 78 kPa side; however, due to the low power of this study, no conclusions could be made. Future research on pain intensity and quality relative to a more thorough quantitative assessment of tooth movement is warranted to assess if a relationship exists between pain experienced and the amount of tooth movement. Furthermore, studies need to assess all these factors among individuals while assessing pain intensity and qualities during controlled tooth movement. Controlling for these variables will enhance our knowledge of the intensity and qualities of pain experienced during orthodontic treatment and allow the clinician to prepare patients adequately.
CHAPTER 5

CONCLUSIONS

1. There were no significant differences in pain intensities (MMPQ-SF_{Ortho11}, VAS, and PPI) for each controlled stress applied over time.

2. There were no significant differences in generalized pain qualities but significant differences in localized pain qualities for each controlled stress applied over time, where higher stress was associated with higher localized pain scores.

3. There were significantly increased pain intensity (MMPQ-SF_{Ortho11}) and pain quality (localized subscale) levels from baseline to post-placement of separators and from baseline to early tooth-loading.
LITERATURE CITED


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Freytag L. Personal communication. Kansas City (MO); 5 August 2008.


Schumacher C. Personal communications. Kansas City (MO); 4 August 2009.


APPENDIX A

IRB APPROVAL
Appendix A: IRB Approval

February 23, 2010
Laura Iwasaki, DDS, MSc, Ph.D.
UMKC- School of Dentistry
Dentofacial Orthopedics
Kansas City, MO 64108

Dear Dr. Iwasaki:


The IRB reapproves research protocol #07-29 as submitted. The requested continuation involves no changes to the protocol or consent form. The data set associated with this study is considered identifiable. The consent form as previously approved remains in effect. You must obtain signed written consent from all subjects. In reviewing your consent procedure for this study, your inclusion of the following special classes of subjects was taken into account: children and minors. You are granted permission to continue your study as described effective immediately. The study is next subject to continuing review on or before 2/22/2011, unless closed before that date. As with the initial approval, changes to the study must be promptly reported and approved. Please contact Debbie Miller at 816-235-6150 or Millerdd@umkc.edu if you have any questions or require further information.

Sincerely,

Deborah Miller
IRB Administrator
Research Office
UMKC Adult Health Sciences
Institutional Review Board

*This e-mail is an official notification intended only for the use of the recipient(s). This letter indicates the status of the UMKC Adult Health Sciences IRB review of the referenced research project. When...*
appropriate, a member of the UMKC Adult Health Sciences IRB staff will be contacting the recipient(s) informing them of other IRB documents related to this project that are available to either 1) be picked up at the IRB office – 5319 Rockhill Road or 2) be mailed via campus mail or postal service - i.e.; revisions to consent form, advertisements, etc. If a signed copy of this letter is needed, please contact a member of the IRB staff. If you have received this communication in error, please return it to the sender immediately and delete any copy of it from your computer system.
APPENDIX B

INFORMED CONSENT
CONSENT FORM FOR PARTICIPATION IN A RESEARCH STUDY
Collection and storage of human biomaterials for research

Biomechanical, Developmental, and Genetic Determinants for Rate of Orthodontic Tooth Movement in Humans

Introduction
You are being asked to volunteer for a research study.

This study is being conducted at the University of Missouri - Kansas City (UMKC), School of Dentistry. The investigators in charge of this study are Dr. Laura Iwasaki and Dr. Jeff Nickel. The Sponsor of the study is: The American Association of Orthodontists Foundation.

You are eligible to participate in this study because you have been accepted for orthodontic treatment at the UMKC School of Dentistry Graduate Orthodontic Clinic and you have permanent teeth.

Background
The information in this form is meant to help you decide whether or not to take part. If you have any questions, please ask.

You may take home an unsigned copy of this consent form to think about or to discuss your participation with family or friends before making your decision. You must read and sign the consent form before you have any procedures done for the study. If you decide to participate, a copy of this form will be given to you for your records.

Genetic factors involve genes. Genes are the factors people are born with, which determine traits such as what color your hair and eyes are. Genes can influence susceptibility to certain diseases. Genes are made up of DNA. Your DNA is like a huge database of chemical bases that carry the "blue prints" or instructions to tell each and every cell in your body what they should do.

Purpose of This Research Study
Some people's teeth move faster than other people's teeth during braces (orthodontic) treatment. The purposes of this research study are to find out:
- what factors affect how fast teeth move during orthodontic treatment, and
- how you feel during the treatment.

There will be approximately 40 subjects in the study at UMKC School of Dentistry.

Study Procedures and Treatments
The orthodontic treatment used in this study is a regular type of treatment. You will be fitted with brackets and bands which are typical of all "braces". The type of orthodontic therapy will be similar or the same as if you were not in the study. For the study, we will measure the amount of pressure (force) used to move your teeth, the movement of your teeth, and the chemicals in the fluids around your teeth. We will also test certain genes that you inherited from your parents to see whether or not they make your teeth move quicker or slower than usual. You will be asked to fill-in 2 forms with questions about whether or not you feel any pain in your mouth at each study visit.
Cheek-wipe or saliva sample: A sample of your genetic material will be collected by gently wiping the inside of your cheeks with a small sterile brush or by having you spit into a small container. Sample collection will take about 1 minute. This sample will be tested before or while you are wearing braces. The tests will determine what types of genes you have at specific location on your DNA, called the "Interleukin-1 gene cluster." Because this information is not expected to be of benefit to you, results of your gene tests will not be provided. Your cheek-wipe or saliva samples will not be saved after the tests.

Dental x-rays: The x-rays that you have made as a part of regular orthodontic treatment planning and monitoring can be used for this study. Some of these x-rays will be made with a marker beside your tooth so that the size and shape of your tooth roots can be measured. This will not interfere with the diagnostic quality of your x-rays.

Planned tooth removal: The teeth to be removed are part of your approved orthodontic treatment plan, so no teeth will be removed just for the study.

Additional visits: You will be seen 6 times in addition to your regular orthodontic visits. These additional visits will take about one hour and will allow your tooth movement to be followed more closely than usual. To do this, samples of fluid will be taken from your mouth, your teeth will be professionally cleaned, and additional molds of your teeth will be made. The 6 additional visits will take place over a span of 84 days. Once the pressures to move your teeth are begun (Day 0) you will be scheduled to return 1 day, 3 days, and 7 days later. These are the first 3 extra visits. The other 3 extra visits will be scheduled 14, 42, and 70 days after tooth movement has begun. At all visits for the study you will be asked to complete 2 forms.

Fluid samples: Samples will be taken from your mouth using a type of sterilized filter paper that soaks up the fluid from between the gum and the tooth. This will take about 2 minutes. The chemicals in this fluid can be measured in a laboratory. During the study, fluid samples will be taken 11 times in total, at each of the 6 additional visits and at 5 other regular visits for your braces. Your fluid samples will not be saved after the measurements.

Dental molds: In routine orthodontic treatment, molds of your teeth are normally made before and after the "braces" work is done, and at some times during the treatment. For this study, 10 molds of your top teeth will be made over a span of 12 weeks. One of these molds will be made at each of the 6 additional visits and the other 4 molds will be made during regular orthodontic appointments. It will take about 20 minutes to clean your teeth and then make a mold.

Mouth rinses and dental cleaning: You will be given a mouth rinse called “chlorhexidine” to help eliminate bacteria from around the teeth and gums. This mouth rinse is to be used twice daily. You will be shown good ways of keeping your teeth clean. You will be asked to use these ways and apply extra effort to keep your teeth very clean. At each visit during the study, you will also be provided with professional dental cleanings.

Forms: At the beginning of each visit you will be asked to complete a 1-page form about whether or not you feel any pain in your mouth on your left side. You will also be asked to complete a 1-page form about whether or not you feel any pain in your mouth on your right side.
Final Visit: will occur on Day 84 after pressures to move your teeth are begun.

Follow-up: your orthodontic treatment will continue as planned in the Graduate Orthodontic Clinic at UMKC School of Dentistry.
When your participation in the study ends, you will continue to have access to regular orthodontic care just as you would if you did not participate in the study.

Possible Risks or Side Effects of Taking Part in this Study
Possible risks and discomforts you could experience during this study include:

Cheek-wipe or saliva sample: Taking a sample from the insides of the cheeks or by having you spit into a container is not associated with any known risks. The wiping of the cheeks to collect a sample will be similar to the rubbing of the cheeks that occurs during normal tooth brushing. In people who get mouth ulcers easily, this and other kinds of pressures on the soft tissues of the mouth can cause an ulcer.

Fluid samples: Taking fluid samples from around your teeth is not associated with any known risks.

Dental x-rays: The x-rays that you have made as a part of regular orthodontic treatment planning and monitoring can be used for this study. The amount of x-ray exposure will be limited as much as possible by the materials and equipment used and by using special protective shields.

Dental molds: The making of molds of your teeth may be slightly uncomfortable because some people's teeth are sore after they start to move. The molds will be made in a way that minimizes the amount of pushing on the teeth.

Braces: During the first couple of weeks after the braces are placed, your teeth may be sensitive, especially while chewing tough foods. This is normal and common to orthodontic treatment. Due to the nature of the study, you must not take regular pain reducing agents (medicine) such as Aspirin, Tylenol, Advil, Motrin, or other "pain killers". These drugs may slow the movement of your teeth. You may take medicine for pain if you need it during the study, but if you do you must inform one of the study doctors and you will be withdrawn from the study at that time.

In some people, wearing braces can cause shortening of the roots of the teeth.

Mouth rinses and dental cleaning: If your teeth are not cleaned thoroughly and regularly, the chlorhexidine (mouth) rinse will have a tendency to stain the teeth and the "glue" used for the braces. With good oral hygiene (regular flossing and brushing) at home this should not be a problem. Any stain that develops will be removed during the professional dental cleanings done as part of the study.

Genetic testing: The main risk in having your genes tested is that the results of the tests may be accidentally found out by other people. Safeguards will be in place to keep this from happening. Only the investigators in charge of the study and the Institutional Review Board will have access to the results of the genetic testing. This information will be stored in a secure (locked) place and
coded so that your name or other identifiers will not be used with the results. Currently, the genes
that you will be tested for in this study are not known to be linked to any major disorder, so you will
not be told about the results. If new information is discovered about these genes, we will try to
contact you to share this information with you.

It is possible that other rare side effects could occur that are not described in this consent form. It is
also possible that you could have a side effect that has not occurred before.

Important Information for Women
Women who are breast-feeding and women who are pregnant can have braces and may participate
in this study. However, if you are pregnant you may want to avoid having any x-rays made, unless it
is an emergency situation. If you become pregnant during this study, please call or tell one of the
investigators. She/he can discuss with you the timing of any x-rays planned. If a planned x-ray is
needed for the study while you are pregnant, you can stop being in the study.

Possible Benefits of Taking Part in this Study
If you participate in the study, you will be using a special mouth rinse, your oral hygiene will be closely
monitored, your teeth will be cleaned more frequently, and your braces will be examined with closer
scrutiny. The extra procedures can improve the health of the gums and may improve the results of
the orthodontic tooth movement during the study. The measurement of the speed of your tooth
movement in this study may help to more accurately predict the expected time to complete your
treatment. You may not get any benefit from being in this research study.

Costs for Taking Part in this Study
There are no additional costs to you to be in this research study. You will be responsible for doctor
and or dental clinic charges as usual except for those directly related to the research study.
You or your insurance company will have to pay for orthodontic treatment and the dental extractions
(removal of teeth) that are part of your planned orthodontic treatment.

Payment for Taking Part in this Study
To compensate you for your time and transportation expenses you will be paid $30.00 after
completion of each of the following 10 study visits: Days 0 (start of tooth movement), 1, 3, 7, 14, 28,
42, 56, 70, and 84. If you complete the study the total amount of credit will be $300.00. You will be
paid only for the visits you complete.

Alternatives to Study Participation
The alternative is to not participate.

Confidentiality and Access to your Records
Results of this research may be published for scientific purposes or presented to scientific groups;
however, you will not be identified. The study sponsor, the Institutional Review Board, or other
regulatory agencies may be given access to research study records and any pertinent medical and
dental records which contain your identity. Medical and dental records that identify you and the
consent form signed by you will be reviewed to verify the study procedures that were performed and
the data (information) reported about you. Medical and dental records from treatment you received

Page 4 of 6
Version Date: Dec. 16, 2009
UMKC Adult Health Sciences
Institutional Review Board
Init: 000 Approved From 2/24/11 to 2/22/11 Subject Initials _____

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prior to giving your consent to participate in this clinical study will also be reviewed, if available, to verify your medical and dental histories and your eligibility for this study. Your medical and dental records will be kept as confidential as possible under local, state and federal law, but absolute confidentiality cannot be guaranteed.

If you should withdraw or be withdrawn from the study, the study data collected prior to withdrawal may still be processed along with other data collected as part of the study. For purposes of follow-up studies and if any unforeseen circumstances arise, subject identification will be filed at UMKC School of Dentistry under adequate security and with accessibility restricted to research personnel only.

By signing this consent form you are authorizing such access to your medical and dental records.

In Case of Injury
The University of Missouri-Kansas City appreciates the participation of people who help it carry out its function of developing knowledge through research. Although it is not the University’s policy to compensate or provide medical treatment for persons who participate in studies, if you think you have been injured as a result of participating in this study, please call the investigator, Dr. Laura Iwasaki, at 816-235-2134 or the IRB Administrator of UMKC’s Adult Health Sciences Institutional Review Board at 816-235-6150.

Contacts for Questions about the Study
If you have any questions or concerns regarding this study, or if any problems arise, you may call the study investigator Dr. Laura Iwasaki, at (816-235-2134). To express concerns of pressure about your participation in the study or ask questions you may also contact the IRB Administrator of UMKC’s Adult Health Sciences Institutional Review Board at 816-235-6150.

Emergency Contact
In the event of an emergency, where you feel that it is necessary that you contact an investigator immediately, rather than waiting until regular office hours, you should call Dr. Jeff Nickel at 816-527-0106.

Voluntary Participation:
Your participation in this research is voluntary; you are free to discontinue participation in this study at any time and for any reason; refusal to participate will involve no penalty or loss of care to which you are normally entitled; you may also discontinue participation at any time without penalty or loss of benefits to which you are entitled. You will be removed from the study, if at any time, it is necessary because of medical reasons. Additionally, you will be informed of any significant findings developed during the course of this research. You volunteer and consent to participate in this research study.

You have read this Consent for Research or it has been read to you. Further, the purpose of the study, risks involved, and procedures which will be performed have been explained to you. You have had the chance to ask questions, and you may ask questions at any time during the course of the study by calling Dr. Laura Iwasaki or Dr. Jeff Nickel at 816-235-2134.
UMKC AHS IRB #: 07-29

Signature (Volunteer Subject) ___________________________ Date ____________

Signature (Authorized Consenting Party) ___________________________ Date ____________

Signature of person obtaining consent ___________________________ Date ____________

Date consent form written: Dec. 16, 2009
PARENTAL PERMISSION AND CHILD ASSENT FOR PARTICIPATION IN A RESEARCH STUDY
Collection and storage of human biomaterials for research

Biomechanical, Developmental, and Genetic Determinants for Rate of Orthodontic Tooth Movement in Humans

Introduction
We are asking your child to be in this research study. Please read the information below and ask questions about anything that you do not understand before you make a decision.

You may take home an unsigned copy of this consent form to think about or to discuss your child's participation with family or friends before making your decision. You must read and sign the consent form before your child has any procedures done for the study. If you decide to allow your child to participate, a copy of this form will be given to you for your records.

This study is being conducted at the University of Missouri - Kansas City (UMKC), School of Dentistry. The investigators in charge of this study are Dr. Laura Iwasaki and Dr. Jeff Nickel. Other health care professionals may help them. The sponsor of the study is: The American Association of Orthodontists Foundation.

Your child is eligible to participate in this study because she/he has been accepted for orthodontic treatment at the UMKC School of Dentistry Graduate Orthodontic Clinic and she/he has permanent teeth.

Background
People are born with genes that they inherit from their parents. Genes determine features about people like the colors of their eyes and hair. A gene is a segment of DNA, which is found in each cell of the body. DNA is like an instruction book to tell each cell what it should do.

Purpose of This Research Study
Some people's teeth move faster than other people's teeth during braces (orthodontic) treatment. The purposes of this research study are to find out:
- what factors affect how fast teeth move during orthodontic treatment, and
- how your child feels during the treatment.

There will be approximately 40 subjects in the study at UMKC School of Dentistry.

Study Procedures and Treatments
The orthodontic treatment used in this study is a regular type of treatment. Your child will be fitted with brackets and bands which are typical of all "braces". The type of orthodontic therapy will be similar or the same as if your child was not in the study. For the study, we will measure the amount of pressure (force) used to move your child's teeth, the movement of her/his teeth, and the chemicals in the fluids around her/his teeth. We will also test certain genes that your child inherited to see whether or not they make her/his teeth move quicker or slower than usual. Your child will be asked to fill-in 2 forms with questions about whether or not she/he feels any mouth pain at each study visit.
Cheek-wipe or saliva sample: A sample of your child's genetic material will be collected by gently wiping the inside of your child's cheeks with a small sterile brush or by having your child spit into a small container. Sample collection will take about 1 minute. This sample will be tested before or while your child is wearing braces. The tests will determine what types of genes your child has at specific location on her/his DNA, called the "Interleukin-1 gene cluster." Because this information is not expected to be of benefit to your child, results of the gene tests will not be provided. Your child's cheek-wipe or saliva samples will not be saved after the tests.

Dental x-rays: The x-rays that your child has made as a part of regular orthodontic treatment planning and monitoring can be used for this study. Some of these x-rays will be made with a marker beside your child's tooth so that the size and shape of her/his tooth roots can be measured. This will not interfere with the diagnostic quality of your child's x-rays.

Planned tooth removal: The teeth to be removed are part of your child's approved orthodontic treatment plan, so no teeth will be removed just for the study.

Additional visits: Your child will be seen 6 times in addition to her/his regular orthodontic visits. These additional visits will take about one hour and will allow your child's tooth movement to be followed more closely than usual. To do this, samples of fluid will be taken from your child's mouth, her/his teeth will be professionally cleaned, and additional molds of her/his teeth will be made. The 6 additional visits will take place over a span of 84 days. Once the pressures to move your child's teeth are begun (Day 0) she/he will be scheduled to return 1 day, 3 days, and 7 days later. These are the first 3 extra visits. The other 3 extra visits will be scheduled 14, 42, and 70 days after tooth movement has begun. At all visits for the study your child will be asked to complete 2 forms.

Fluid samples: Samples will be taken from your child's mouth using a type of sterilized filter paper that soaks up the fluid from between the gum and the tooth. This will take about 2 minutes. The chemicals in this fluid can be measured in a laboratory. During the study, fluid samples will be taken 11 times in total, at each of the 6 additional visits and at 5 other regular visits for your child's braces. Your child's fluid samples will be used up for the measurements, so none will be stored after the measurements.

Dental molds: In routine orthodontic treatment, molds of your child's teeth are normally made before and after the "braces" work is done, and at some times during the treatment. For this study, 10 molds of your child's top teeth will be made over a span of 12 weeks. One of these molds will be made at each of the 6 additional visits and the other 4 molds will be made during regular orthodontic appointments. It will take about 20 minutes to clean your child's teeth and then make a mold.

Mouth rinses and dental cleaning: Your child will be given a mouth rinse called "chlorhexidine" to help to eliminate bacteria from around the teeth and gums. This mouth rinse is to be used twice daily. Your child will be shown good ways of keeping her/his teeth clean. Your child will be asked to use these ways and apply extra effort to keep her/his teeth very clean. At each visit during the study, your child will also be provided with professional dental cleanings.
Forms: At the beginning of each visit your child will be asked to complete a 1-page form about whether or not she/he feels any mouth pain on the left side. Your child will also be asked to complete a 1-page form about whether or not she/he feels any mouth pain on the right side.

Final Visit: will occur on Day 84 after pressures to move your child's teeth are begun.

Follow-up: your child’s orthodontic treatment will continue as planned in the Graduate Orthodontic Clinic at UMKC School of Dentistry.

When your child’s participation in the study ends, she/he will continue to have access to regular orthodontic care just as she/he would if she/he did not participate in the study.

Possible Risks or Side Effects of Taking Part in this Study

Possible risks and discomforts your child could experience during this study include:

Cheek-wipe or saliva sample: Taking a sample from the insides of the cheeks or by having your child spit into a small container is not associated with any known risks. The wiping of the cheeks to collect a sample will be similar to the rubbing of the cheeks that occurs during normal tooth brushing. In people who get mouth ulcers easily, this and other kinds of pressures on the soft tissues of the mouth can cause an ulcer.

Fluid samples: Taking fluid samples from around your child’s teeth is not associated with any known risks.

Dental x-rays: The x-rays that your child has made as a part of regular orthodontic treatment planning and monitoring can be used for this study. The amount of x-ray exposure will be limited as much as possible by the materials and equipment used and by using special protective shields.

Dental molds: The making of molds of your child’s teeth may be slightly uncomfortable because some people’s teeth are sore after they start to move. The molds will be made in a way that minimizes the amount of pushing on the teeth.

Braces: During the first couple of weeks after the braces are placed, your child’s teeth may be sensitive, especially while chewing tough foods. This is normal and common to orthodontic treatment. Due to the nature of the study, your child must not take regular pain reducing agents (medicine) such as Aspirin, Tylenol, Advil, Motrin, or other “pain killers”. These drugs may slow the movement of your child’s teeth. Your child may take medicine for pain if she/he needs it during the study, but if she/he does you must inform one of the study doctors and she/he will be withdrawn from the study at that time.

In some people, wearing braces can cause shortening of the roots of the teeth.

Mouth rinses and dental cleaning: If your child’s teeth are not cleaned thoroughly and regularly, the chlorhexidine (mouth) rinse will have a tendency to stain the teeth and the “glue” used for the braces. With good oral hygiene (regular flossing and brushing) at home this should not be a
problem. Any stain that develops will be removed during the professional dental cleanings done as part of the study.

Genetic testing: The main risk in having your child's genes tested is that the results of the tests may be accidentally found out by other people. Safeguards will be in place to keep this from happening. Only the investigators in charge of the study and the Institutional Review Board will have access to the results of the genetic testing. This information will be stored in a secure (locked) place and coded so that your child’s name or other identifiers will not be used with the results. Currently, the genes that will be tested for in this study are not known to be linked to any major disorder, so you will not be told about the results.

It is possible that other rare side effects could occur that are not described in this consent form. It is also possible that your child could have a side effect that has not occurred before. In the event that this happens, there are personnel on-site at the School of Dentistry who are trained to handle emergency situations and there are emergency facilities close by at the Children's Mercy Hospital and Truman Medical Center.

Important Information for Females/Daughters
Females who are breast-feeding and who are pregnant can have braces and may participate in this study. However, females who are pregnant may want to avoid having any x-rays made, unless it is an emergency situation. If your child becomes pregnant during this study, please call or tell one of the investigators. She/he can discuss with you the timing of any x-rays planned. If a planned x-ray is needed for the study while your child is pregnant, your child can stop being in the study.

Possible Benefits of Taking Part in this Study
If your child participates in the study, she/he will be using a special mouth rinse, her/his oral hygiene will be closely monitored, her/his teeth will be cleaned more frequently, and her/his braces will be examined with closer scrutiny. The extra procedures can improve the health of the gums and may improve the results of the orthodontic tooth movement during the study. The measurement of the speed of your child's tooth movement in this study may help to more accurately predict the expected time to complete your child’s treatment. Your child may not get any benefit from being in this research study.

Costs for Taking Part in this Study
There are no additional costs to you for your child to be in this research study. You will be responsible for doctor and or dental clinic charges as usual except for those directly related to the research study. You or your insurance company will have to pay for orthodontic treatment and the dental extractions (removal of teeth) that are part of your child’s planned orthodontic treatment.

Payment for Taking Part in this Study
To compensate you for your child's time and transportation expenses you will be paid $30.00 after completion of each of the following 10 study visits: Days 0 (start of tooth movement), 1, 3, 7, 14, 28, 42, 56, 70, and 84. If you complete the study the total amount of credit will be $300.00. You will be paid only for the visits your child completes.

Alternatives to Study Participation
The alternative is to not participate.

Confidentiality and Access to Your Child's Records
Results of this research may be published for scientific purposes or presented to scientific groups; however, your child will not be identified. The study sponsor, the Institutional Review Board, or other regulatory agencies may be given access to research study records and any pertinent medical and dental records which contain your child's identity. Medical and dental records that identify your child and the consent form signed by you will be reviewed to verify the study procedures that were performed and the data (information) reported about your child. Medical and dental records from treatment your child received prior to giving your consent to participate in this clinical study will also be reviewed, if available, to verify your child's medical and dental histories and your child's eligibility for this study. Your child's medical and dental records will be kept as confidential as possible under local, state and federal law, but absolute confidentiality cannot be guaranteed.

If your child should withdraw or be withdrawn from the study, the study data collected prior to withdrawal may still be processed along with other data collected as part of the study. For purposes of follow-up studies and if any unforeseen circumstances arise, subject identification will be filed at UMKC School of Dentistry under adequate security and with accessibility restricted to research personnel only.

By signing this consent form you are authorizing such access to your child's medical and dental records.

In Case of Injury
The University of Missouri-Kansas City appreciates the participation of people who help it carry out its function of developing knowledge through research. Although it is not the University's policy to compensate or provide medical treatment for persons who participate in studies, if you think your child has been injured as a result of participating in this study, please call the investigator, Dr. Laura Iwasaki, at 816-235-2134 or the IRB Administrator of UMKC's Adult Health Sciences Institutional Review Board at 816-235-6150.

Contacts for Questions about the Study
If you have any questions or concerns regarding this study, or if any problems arise, you may call the study investigator Dr. Laura Iwasaki, at (816-235-2134). To express concerns of pressure about your child's participation in the study or ask questions you may also contact the IRB Administrator of UMKC's Adult Health Sciences Institutional Review Board at 816-235-6150.

Emergency Contact
In the event of an emergency, where you feel that it is necessary that you contact an investigator immediately, rather than waiting until regular office hours, you should call Dr. Jeff Nickel at 816-527-0106.

Voluntary Participation
Your child's participation in this research is voluntary; your child is free to discontinue participation in this study at any time and for any reason; refusal to participate will involve no penalty or loss of
care to which your child is normally entitled; your child may also discontinue participation at any time without penalty or loss of benefits to which she/he is entitled. Your child will be removed from the study, if at any time, it is necessary because of medical reasons. Additionally, you will be informed of any significant findings developed during the course of this research. Your child volunteers and assents (agrees) to participate in this research study.

Permission of Parent or Legally Authorized Representative
You have read this Consent for Research or it has been read to you. Further, the purpose of the study, risks involved, and procedures which will be performed have been explained to you. You have had the chance to ask questions, and you may ask questions at any time during the course of the study by calling Dr. Laura Iwasaki or Dr. Jeff Nickel at 816-235-2134.

You give permission for ________________________________ to participate in this research study. A copy of this signed form will be given to you.

Signature of Parent/Legally Authorized Representative

Date

Relationship to Participant

Signature of Parent/Legally Authorized Representative

Date

Relationship to Participant

Assent of Minor
I have been told what I will be asked to do if I am in this study. I have been told that I don’t have to be in this study. I may quit the study at any time, and no one will be mad at me. I have had a chance to discuss the study and ask questions. My questions have been answered. I agree to be in the study and do what I am asked to do so long as I continue in the study.

Signature of Minor

Date
UMKC AHS IRB #: 07-29

Study Personnel
I have explained the purposes, procedures, and risks involved in this research study in detail to:

_________________________ and ___________________________
Print name(s) of Parents/Legally Authorized Representative Print child’s name

who, in my opinion is capable of assenting to participate in this study.

_________________________ ___________________________
Signature of person obtaining consent Date

Date consent form written: Dec. 16, 2009
APPENDIX C

QUESTIONNAIRE
Appendix C: Modified MPQ-SF

Subject ID #

The words below are sometimes used to explain how your mouth feels while you have braces. Place an "X" in the column to indicate the level of pain you feel for each word.

<table>
<thead>
<tr>
<th>No.</th>
<th>Word</th>
<th>0 no pain</th>
<th>1 mild</th>
<th>2 moderate</th>
<th>3 severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>sore</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>aching</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>throbbing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>tight</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>cutting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>burning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>tingling</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>pulling</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>dull</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>uncomfortable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>strange</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>frustrating</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>annoying</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>miserable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Place an "X" along this line to indicate how bad your pain is -- the left of the line means no pain at all and the right end means worst pain possible.

<table>
<thead>
<tr>
<th>No Pain</th>
<th>Worst: Pain Possible</th>
</tr>
</thead>
</table>

Place an "X" in the space that best indicates your level of pain right now -- only mark one.

<table>
<thead>
<tr>
<th>0</th>
<th>No pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Little pain</td>
</tr>
<tr>
<td></td>
<td>Moderate pain</td>
</tr>
<tr>
<td>2</td>
<td>Bad pain</td>
</tr>
<tr>
<td>3</td>
<td>Horrible pain</td>
</tr>
<tr>
<td>4</td>
<td>Extreme pain</td>
</tr>
<tr>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
NAME
Jodi Kay Hentscher-Johnson

DATE AND PLACE OF BIRTH
July 28, 1982, Saint Louis, Missouri

MARITAL STATUS
Married to Scott Johnson

EDUCATION

<table>
<thead>
<tr>
<th>Year</th>
<th>Degree</th>
<th>Institution</th>
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<tr>
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<td>BS/Biology</td>
<td>Fontbonne University Saint Louis, Missouri</td>
</tr>
<tr>
<td>8/2011</td>
<td>MS Oral Biology</td>
<td>University of Missouri – Kansas City School of Dentistry Kansas City, Missouri</td>
</tr>
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</table>

INTERNSHIP AND/OR RESIDENCIES

<table>
<thead>
<tr>
<th>Year</th>
<th>Type</th>
<th>Institution</th>
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<td>7/2009-8/2011</td>
<td>Orthodontic Residency</td>
<td>University of Missouri – Kansas City School of Dentistry Kansas City, Missouri</td>
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PROFESSIONAL ORGANIZATIONS

Omicron Kappa Upsilon
American Association of Orthodontists
American Association of Orthodontists Foundation
American Dental Association
American Student Dental Association
Illinois Dental Association
HONORS

Magna Cum Laude, Doctor of Medical Dentistry Class of 2009, SIUE-SDM
SIUE-SDM Research Fellowship, 2008-2009
Omicron Kappa Upsilon Academic Excellence Award, 2006
Dr. and Mrs. Sim’s Academic Scholarship, 2006, 2007, 2008
Cum Laude, Bachelor of Science in Biology Class of 2004, Fontbonne University
Outstanding Science Student Award - Fontbonne University, 2004
Dean’s List, Fontbonne University, SIU-SDM