The Effect of AcceleDent on Arch Alignment and Pain Level During Orthodontic Treatment with SureSmile

BY

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THESIS

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This thesis is dedicated to my family – my incredibly supportive husband Nemanja, son Luka, parents Ilija and Danica, and brother Zoran. I will forever be grateful for their limitless, selfless sacrifices and support that helped me fulfill my dream.
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<td>Full Form</td>
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<tr>
<td>ABO</td>
<td>American Board Of Orthodontics</td>
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<tr>
<td>CBCT</td>
<td>Cone Beam Computed Tomography</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>CRE</td>
<td>Cast/Radiographic Evaluation</td>
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<tr>
<td>CuNiTi</td>
<td>Copper Nickel Titanium</td>
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<td>DIFF</td>
<td>Differences</td>
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<td>FACES</td>
<td>Family and Child Experience Survey</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>ICC</td>
<td>Intra-class Correlation Coefficient</td>
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<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
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<tr>
<td>LLLT</td>
<td>Low-level Light Therapy</td>
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<td>MBT</td>
<td>McLaughlin Benett Trevisi</td>
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<tr>
<td>MD</td>
<td>Mean Deviation</td>
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<td>MOP</td>
<td>Micro-osteoperforation</td>
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<td>NiTi</td>
<td>Nickel Titanium</td>
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<tr>
<td>NSAID</td>
<td>Non-steroidal Anti-inflammatory Drug</td>
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<td>OGS</td>
<td>Objective Grading System</td>
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<tr>
<td>PAOO</td>
<td>Periodontally Accelerated Osteogenic Orthodontics</td>
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<td>PDL</td>
<td>Periodontal Ligament</td>
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<tr>
<td>RANKL</td>
<td>Receptor Activator of Nuclear Factor Kappa-B Ligand</td>
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<td>RAP</td>
<td>Rapid Acceleratory Phenomenon</td>
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<td>Standard Deviation</td>
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<td>SIG</td>
<td>Significant</td>
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<td>SS</td>
<td>Stainless Steel</td>
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<td>STD</td>
<td>Standard</td>
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<tr>
<td>TAD</td>
<td>Temporary Anchorage Device</td>
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<tr>
<td>UIC</td>
<td>University of Illinois at Chicago</td>
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<tr>
<td>USB</td>
<td>Universal Serial Bus</td>
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<tr>
<td>VAS</td>
<td>Visual Analog Scale</td>
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<td>WIRB</td>
<td>Western Institutional Review Board</td>
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SUMMARY

Patients seeking orthodontic treatment are commonly concerned with lengthy treatment duration and pain associate with the treatment. Due to increased number of adult orthodontic patients in the recent years, these concerns have become even more prevalent in the orthodontic offices. Hence, many clinicians are looking for the means to make orthodontic treatments shorter and less uncomfortable experience for their patients without compromising excellent clinical outcomes.

Increased patients’ pursuit for shorter and pain-free orthodontic treatment has also led to development of various products that promise to deliver these results. Manufacturing companies make strong claims of their products success even when supporting research data is limited. One of such products currently on the market is AcceleDent® Aura appliance from OrthoAccel Technologies Inc. (Houston, TX). The company claims that AcceleDent has potential to decrease pain associated with orthodontic treatment and decrease treatment time by 50%. Current available literature does not fully support these claims. Several studies have reported significant decrease in treatment time and pain during the treatment while other failed to see any difference when compared to control or sham device groups. The goal of our research is to contribute more to the existing conflicting literature on AcceleDent ability to affect tooth movement and pain during orthodontic treatment.

This was a randomized controlled trial that evaluated alignment of anterior teeth and pain levels patients undergoing orthodontic treatment with SureSmile. Thirty subjects were assigned into experimental group that used AcceleDent® Aura and 41 subjects were in control group treated with no additional appliance. Ten subjects were
dropped out from the study leaving 21 patients in experimental group and 40 patients in control group. Subjects assigned to AcceleDent group were instructed to use the device daily for 20 minutes, as recommended by OrthoAccel Technologies Inc. Compliance with device use was tracked throughout the treatment. Alignment of maxillary and mandibular anterior teeth was assessed from i-Tero scans obtained at the start of the treatment (T1), 3 months (T2), 6 months (T3), and at the end of the treatment or 12 months – whichever came first (T4). Pain intensity throughout the entire treatment was evaluated from subjects’ daily and weekly survey entries.

The results showed that mean values of irregularity index variable at follow up time points (T2, T3, and T4) were consecutively lower than at the beginning of the treatment. Within each group these differences were statistically significant with p-value <0.001. However, the mean difference in irregularity index were not statistically significant between the experimental and control groups. Pain level averages for day 1, day 2, and day 3 after each adjustment appointment were significantly lower in the experimental group when compared to control group during 3-6 months and 6 months until the end of the treatment (p-values= 0.006). The mean AcceleDent compliance was 78%. 
1. INTRODUCTION

1.1 Background

Some of the first attempts to accelerate tooth movement during orthodontic treatment were significantly invasive procedures called osteotomy and corticotomy (Köle, 1959). Osteotomy is a surgical cut through cortical and medullary bones; whereas, corticotomy is a surgical cut confined to the cortical bone (Sebaoun et al., 2008). When combined with orthodontic treatment, both of these procedures accelerate rate of tooth movement by activating rapid acceleratory phenomenon (RAP) through increased demineralization-remineralization of the surrounding bone (Sebaoun et al., 2008).

Decades later, Wilcko et al. (2001) modified and reintroduced this procedure to modern orthodontics under name periodontally accelerated osteogenic orthodontics (PAOO). Even though some of the orthodontic treatments combined with PAOO were accomplished 3-4 times faster than the conventional treatments, most patients and parents reported their unwillingness to undergo such an extensive surgical procedure to reduce treatment length (Wilcko et al., 2008, Uribe, et al., 2014). This is not surprising since pain has been reported as one of the biggest fears and apprehensions prior to treatment as well as the greatest dislikes during orthodontic treatment (O’Connor, 2000).

Consequently, less invasive procedures for accelerating tooth movement have become available. Chemical stimulations have been proposed as an adjunct to orthodontic treatment for accelerated tooth movement; however, these procedures have
been mainly investigated on animal models and require multiple, repeated local administrations (Nimeri et al., 2013). Micro-osseous perforations (MOPs), ultrasound, low-level light therapy (LLLT), and vibrations are amongst other procedures suggested to enhance orthodontic tooth movement (Nimeri et al., 2013). Thus far, vibration and LLLT have been the only methods that do not require an additional or prolonged office visit, but rather can safely be used at home. These methods became available with development of Orthopulse (Biolux Research Ltd., Vancouver, Canada) and AcceleDent (OrthoAccel Technologies Inc., Houston, TX) devices. Orthopulse was introduced in 2003 and uses LLLT, also known as photobiomodulation, to enhance tooth movement during orthodontic treatment (Shaughnessy et al., 2016). According to OrthoAccel website, the first AcceleDent prototype became available in 2008 and was designed to accelerate rate of tooth movement with a light force pulses that are transmitted through the roots of the teeth to the surrounding bone. Additionally, OrthoAccel claims that daily use of AcceleDent could alleviate pain that is commonly experienced during the orthodontic treatment. If these claims can be confirmed clinically, AcceleDent would be a true differentiator in orthodontic treatment since it could potentially help orthodontists' address the most common patients' concerns – pain and treatment time. However, current literature on AcceleDent is limited and reports conflicting data on its effectiveness. Additional clinical trials are necessary to determine the extent of AcceleDent impact on tooth movement and pain during orthodontic treatment.
1.2 **Specific Aims**

The primary aim of this study is to evaluate effect of AcceleDent® Aura device on arch alignment during orthodontic treatment with SureSmile. The second aim of the study is to evaluate if daily use of AcceleDent® Aura device has any effect on patients’ pain experience during orthodontic treatment with SureSmile.

1.3 **Null Hypotheses**

1. There are no statistically significant mean differences in the arch alignment associated with AcceleDent use in patients treated with SureSmile.

2. There are no statistically significant mean differences in pain level associated with AcceleDent use in patients treated with SureSmile.
2. REVIEW OF THE LITERATURE

2.1 Orthodontic Treatment Duration

Average orthodontic treatment duration is about two years; however, treatment length commonly varies from one to three and a half years depending on multiple factors (Marveas and Athanasiou, 2008; Skidmore et al., 2006). Some of the factors are evident prior to the start of the treatment, such as the difficulty of the case as determined by the severity of malocclusion based on Salzmann’s or ABO difficulty index, impacted teeth, need for extractions and surgery (Fink and Smith, 1992). Other factors cannot be determined until the patient starts treatment. These include patient’s individual biological characteristics and patient’s compliance with the treatment as determined by a number of broken appointments, broken brackets, oral hygiene, and rubber band wear (Beckwith et al., 1999; Skidmore et al., 2006; Alikhani, 2015). Practitioners also affect treatment duration by their ability to correctly diagnose the case, develop an appropriate treatment plan, and utilize suitable and efficient mechanics (Alikhani, 2015).

Prolong treatment with fixed orthodontic appliances can produce several pathological processes including enamel demineralization, root resorption, and periodontal disease (Talic, 2011). Additionally, prolonged treatment times require multiple office visits that can add on the burden to parents and patients due to the interferences with their school, extracurricular activities, and work schedules. A survey of 450 orthodontic patients and their parents reported their willingness to pay an additional fee if the length of their treatment can be reduced by 25-30% (Uribe et al.,
The same survey revealed that 70% of orthodontists are interested in implementing technologies to accelerate the rate of tooth movement (Uribe et al., 2014).

Indeed, many technologies and procedures have been developed to assist clinicians in providing more efficient treatment (Alikhani, 2015). These can generally be grouped into three categories – customized orthodontic treatment/appliances, surgical approach, and non-surgical approach (Uribe et al., 2014). Customized appliances were designed to minimize practitioner's errors during bracket positioning and wire bending; while surgical and non-surgical approaches primarily alter biological mechanisms that govern alveolar bone remodeling and tooth movement (Alikhani, 2015). The extent of invasiveness varies amongst these procedures. Naturally, patients and orthodontists are more likely to accept added procedure to their orthodontic treatment if it is less invasive (Uribe et al, 2014). SureSmile technology and mechanical stimulation in the form of vibrations are amongst the least invasive technologies currently available believed to impact orthodontic treatment duration.

2.2 **SureSmile Technology Effect on Orthodontic Treatment Duration**

SureSmile (OraMetrix, Inc., Richardson, TX) is a software technology that merges information from cone beam computed tomography (CBCT) and intraoral scan into a three-dimensional interactive program which can be utilized by clinicians as a diagnostic aid, patient education tool, and treatment appliance customization (Sachdeva, 2001; Sachdeva et al., 2005). In addition to the three-dimensional software, SureSmile utilizes robotic technology to bend sequential wires that will provide treatment outcomes set by a clinician for each patient (Sachdeva et al., 2005).
The SureSmile technology was designed to optimize the efficiency of orthodontic treatment by reducing diagnostic and treatment errors during orthodontic treatment (Sachdeva, 2001; Sachdeva et al., 2012). The largest reported study on SureSmile treatment efficiency evaluated a total of 9,390 SureSmile and 2,945 conventional patients and determined that average treatment time for SureSmile was 16 months and 24 months for conventional patients (Sachdeva et al., 2012). In addition to improved efficiency, the company claims that SureSmile technology increases the quality of orthodontic treatment. When categorized for the type of malocclusion and treatment choice, patients treated with SureSmile had lower American Board of Orthodontics Objective Grading System (ABO OGS) scores by 4.4 points (Saxe et al., 2010). Another study that compared 146 patients consecutively treated with either SureSmile or conventional braces also reported that cases finished with SureSmile had overall lower cast/radiographic evolution (CRE) score (Alford et al., 2011). Specifically, they reported that SureSmile technology performed superiorly in space closure and first order movements including teeth alignment and rotations correction (Alford et al., 2011). In addition to reaching more desirable finishes, these studies also reported that cases treated with SureSmile were on average finished 5.3 to 7 months earlier than patients with conventional braces (Saxe et al., 2010; Alford et al., 2011).

2.3 Cyclic Force Effect on Orthodontic Treatment Duration

Positive effects of mechanical stimulation in the form of vibration on bone fracture healing, sutural growth, and osteoporosis has been studied for decades. 24-50% increase in sutural width and 30-62% increase in sutural cell density were observed in
rat models subjected to a daily cyclic loading of 300mN, 4 Hz for 20 minutes (Vij and Mao, 2006). Similar significant changes in sutural growth were reported in rabbit models subjected to 1 Hz cyclic forces for 10 minutes daily or 8 Hz cyclic forces for 20 minutes daily (Kopher and Mao, 2003; Peptan et al., 2008). Application of mechanical stimulus of low magnitude and frequency ranging from 15 to 90 Hz in animal models also showed promising results towards osteoporosis intervention by increasing bone stiffness, bone strength, trabecular volume, and bone mineral content (Rubin et al., 2006; Rubin et al., 2002). Furthermore, improvements in bone quality and bone mineral density were reported in clinical trials (Thompson et al., 2014). Low-magnitude high-frequency vibration of 35 Hz for 20 minutes a day has additionally produced accelerated healing of fractured bone in rats (Leung et al., 2009). Mechanical testing of these healed fractured sites revealed 50.1% stronger bone than the control group (Leung et al., 2009).

These positive effects on sutural growth and bone turnover lead several investigators to examine the effect of cyclic forces effect on the rate of tooth movement (Vij and Mao, 2006; Kopher and Mao, 2003, Nishimura et al., 2008). The vibration of 60 Hz when applied once a week for 8 minutes produced 15% increase in the rate of tooth movement during maxillary molar expansion in rats (Nishimura et al, 2008). On the basis of these observations, OrthoAccel Technologies Inc. developed AcceleDent and consequently its newer model AcceleDent Aura. AcceleDent uses pulsatile technology with the frequency of 30 Hz and 0.25 N force that is transmitted to teeth and surrounding bone via an occlusal mouthpiece. According to OrthoAccel, the device is designed to affect bone turnover and tooth movement when used 20 minutes daily.
Although the exact mechanism of AcceleDent effect on the rate of tooth movement is unknown, animal models suggest that cyclic forces increase bone turnover by increasing osteoclasts formation and RANKL expression (Nishimura et al., 2008). Increased bone remodeling has been linked to increased tooth movement (Huang et al., 2014). AcceleDent received Food and Drug Administration (FDA) clearance as a class II medical device following the publication of several animal and clinical studies demonstrating no pathological effect on periodontinum (Nishimura et al., 2008; Kau, 2011). Radiographic evaluation of root lengths changes before and after orthodontic treatment in conjunction with AcceleDent reported changes in the range of -0.127 mm to -0.416 mm, which were not statistically significant (Kau, 2011). However, no long-term follow up studies are currently available.

Since AcceleDent emergence into the orthodontic market, several studies examined its effectiveness on the rate of tooth movement in human subjects. A small clinical trial of 14 patients treated with AcceleDent reported 2.1 mm and 3.0 mm per month movement of maxillary and mandibular teeth respectively (Kau et al., 2010). This was a 2 to 3 time fold increase compared to previously reported 1 mm average monthly tooth movement during conventional orthodontic treatment (Kau et al., 2010). Bowman (2014) also identified a positive effect of AcceleDent on tooth movement during mandibular arch leveling and aligning stages. Time for leveling and alignment in patients using AcceleDent device was reduced by 48 days and 27 days respectively when compared to the control group (Bowman, 2014). Similarly, Orton-Gibs and Kim (2015) observed that supplementing orthodontic treatment with AcceleDent cyclic forces helped reduce time in braces by 6.23 months. The positive effect of vibration was also
noted during maxillary canine retraction (Pavlin et al., 2015). In randomized clinical trail, the average monthly maxillary canine tooth movement into extraction space with AcceleDent was 0.37 mm greater than in control subjects (Pavlin et al., 2015). Even though these results were described as statistically significant, clinical significance of 0.37 mm per month increase of tooth movement is highly questionable. Contrary to these findings, several more recent studies noted no difference in tooth movement with vibration forces. One study evaluated the changes in the irregularity index and time required for initial and final anterior teeth alignment of patients treated with first premolar extraction (Woodhouse et al., 2015). Results of this trial showed no difference between AcceleDent device, sham device, or control group for any of the variables examined (Woodhouse et al., 2015). The most recent randomized prospective study evaluated the alignment of mandibular anterior teeth at 5, 8, and 10 weeks of orthodontic treatment and likewise reported no difference in the Little’s irregularity Index between AcceleDent and control groups (Miles and Fisher, 2016).

2.4 Pain During Orthodontic Treatment

Pain and discomfort are the most commonly encountered and disliked symptoms of orthodontic treatment (O’Connor, 2000; Kyrkanides et al., 2016). In one clinical study of 170 orthodontic patients, 97% of participants experienced pain during their treatment (Scheurer et al., 1996). Patients experienced the highest discomfort within the first 24 hours following appliances placement (Scheurer et al., 1996). Similarly, other studies found that pain during orthodontic treatment was quite common and reported by 81-95% of the patients (Jones and Chan, 1992; Bergius et al., 2000). For 30% of patients,
discomfort level during treatment was so severe that they considered withdrawing from their treatment (Otasevic at al., 2006). Interestingly, orthodontists tend to underestimate the amount of pain that their patients experience during orthodontic treatment, especially during post adjustment appointment period (Krukemeyer et al., 2009).

Orthodontic tooth movement causes pain due to the presence of numerous nociceptive fibers in the periodontal ligament that detect and transmit signals to the brain (Kyrkanides et al., 2016). Main constituents of pain cascade include compression of PDL that lead to changes in blood flow, the release of inflammatory mediators and neuropeptides, and hyperalgesia response (Krishnan, 2007). An individual's genetic makeup also impacts pain perception and tolerance (Okeson, 2015). Catechol-O-methyl transferase, an enzyme that influences individual's response to pain, varies in different individuals making them more or less susceptible to pain (Okeson, 2015). Additionally, patients perceive pain differently based on their age and gender, previous pain experiences, pain tolerance, anxiety levels, and the amount of force placed on the tooth (Scheurer et al., 1996; Okeson, 2015). Complexity and variations in pain perception amongst individuals have brought a challenge to researchers and clinicians to develop a product that would successfully manage discomfort during orthodontic treatment.

2.5 Cyclic Forces Effect on Pain During Orthodontic Treatment

Analgesics are commonly used for pain management. Non-steroidal anti-inflammatory drugs (NSAIDs) can help reduce pain during orthodontic tooth movement by reducing inflammatory response (Krishnan, 2007). However, reduction of inflammatory response also slowed down the rate of tooth movement (Krishnan, 2007).
Other analgesics such as aspirin and Tylenol did not affect tooth movement, but they were not as effective in pain reduction as Ibuprofen (Krishnan, 2007). Vibratory stimulation and plastic wafer occlusal therapy have been suggested as an alternative to managing orthodontic discomfort (Ottoson et al., 1981; Hwang et al., 1994).

Ottoson and colleagues were pioneers in evaluating the effect of vibration on pain of dental origin. They noted that vibration stimulation of 100 Hz partially or completely reduced dental pain in 91% of study participants (Ottoson et al., 1981). Hwang et al. (1994) reported that 56% of their patients noted benefit of using bite wafers for the management of orthodontic pain. However, Otasevic et al. (2006) argued that there are no positive effects of bite wafers on orthodontic pain. In their study, patients who used “Thera-chew wafers” reported experiencing significantly more pain in 10 days post 0.016" NiTi wire insertion (Otasevic et al., 2006). Marie et al. (2003) evaluate combined effect of vibration stimulation and bite wafers. They reported that patients using vibration stimulation transmitted through bite wafers apparatus for 15 minutes at orthodontic adjustment appointment experienced less pain during next three days (Marie et al., 2003). Interesting, they noted that, for most patients, vibrations were intolerable once discomfort was already present (Marie et al., 2003). However, the exact frequency produced by this appliance was not reported. Similarly to this appliance, AcceleDent combines effect of bite wafer and vibration stimulation. AcceleDent uses low frequency of 30Hz that is gentle and therefore could potentially be more tolerable than previously used appliance.

Available data on AcceleDent on the level of pain during orthodontic treatment is limited. Lobre et al. (2016) investigated effect of the micropulse device usage during
initial four months of orthodontic treatment and patient’s perception of pain. Patients were divided into two groups – experimental group that used micropulse device and control group (Lobre et al., 2016). During the initial four months of treatment, patients who used AcceleDent daily for twenty minutes during orthodontic treatment had significantly less pain than control studies (Lobre et al., 2016). The recent clinical trial reported no difference in pain experienced in orthodontic patients who used AcceleDent; however, patients in the experimental group reported less analgesic use than the control group (Miles and Fisher, 2016).
3. MATERIALS AND METHODS

3.1 Study Design

This was a randomized controlled trial that evaluated effect of AcceleDent® Aura device on arch alignment and pain during orthodontic treatment with SureSmile. All subjects were recruited and treated at three private orthodontic offices located in Grayslake, Antioch, and Gurnee in Illinois. The research protocol was approved by Western Institutional Review Board (WIRB) (Protocol # 2014-2264) (Appendix A).

All research data from the three private offices was de-identified prior to being available to principal investigator from the University of Illinois at Chicago Department of Orthodontics for analysis. UIC Office for the Protection of Research Subjects approved the protocol (#2015-0708) (Appendix B).

3.2 Subject Selection

Subjects recruitment was initiated via direct mailers and emails that were sent to the local communities and existing patients. Front desk staff in all three offices was trained to use a phone script to provide further information about the study to those who inquired about it (Appendix C). Two well-calibrated practitioners performed screening of all new patients seeking orthodontic treatment in their offices during period of January 2015-March 2016 to assess if patients would meet inclusion/exclusion criteria for the study. A screening template was utilized during all screening appointments for the study (Appendix D).
The following was inclusion criteria:

1. Healthy patient between age 10-40 years
2. Non-smoker
3. No NSAIDs and/or vitamin D supplement and/or bisphosphonates use during the treatment
4. Class I molar relationship
5. 6 mm or less of crowding
6. No anterior teeth missing in both maxillary and mandibular arches
7. No evidence of periodontitis or root resorption
8. Quadhelix expander is not required for treatment
9. Can be treated in 12 months as determined by orthodontist

The following was exclusion criteria:

1. Significant medical history
2. Smoker
3. Taking NSAIDs and/or vitamin D supplement and/or bisphosphonates during the treatment
4. Class II or class III molars
5. More than 6 mm of crowding
6. Require extraction to resolve crowding
7. One or more anterior teeth missing in both maxillary and mandibular arches
8. Has periodontitis or root resorption
9. Require quadhelix expander

If a patient qualified for the study based on inclusion/exclusion criteria, the doctor further introduced patients to the study by reading from the following script:

“Our office is doing a clinical study on a device called AcceleDent. The manufacturer says that AcceleDent affords the opportunity to finish treatment faster and potentially with less pain. Our study is to establish if this is true. If you would like to participate, here is what is in it for you:

• If you are randomly assigned for the group receiving AcceleDent, you will get the unit for free as long as you use is as instructed.
• If you are randomly assigned to the group not receiving the device, then you get the cash value as a reduction in your fee.”

Those patients who agreed to participate in the study were introduced to the office treatment coordinator who randomly assigned patients to experimental or control group. Randomization was completed by having patients draw a straw that signified either experimental or control group. At that time, each patient was assigned a unique de-identification code – e.g. s112225 and patients were ask to review and sign consent form (Appendix E). For participants age 12-17, both consent of legal guardian or parent and patient assent were obtained.

All subjects who participated in the study were compensated for their time and partaking in the study. Those subjects belonging to experimental group received
AcceleDent® Aura unit at no cost to them (a value of $600). Subjects in control group received a $600 discount towards their orthodontic treatment fee at the end of the study.

3.3 Sample

Seventy-one subjects were recruited for the study and randomly assigned into experimental group (30 subjects) and control group (41 subjects). Ten subjects were excluded from the study. Of these ten subjects, two discontinued treatment in the office and the rest were excluded due to their poor compliance with AcceleDent device use. Data from 21 subjects in the experimental group and 40 subjects in the control group were available for analysis. According to published orthodontic literature, at least 17 subjects per group (n=34) were required for the study to have a power of at least 80% with type error I at 0.05 (Pavlin et al., 2015; Miles and Fished, 2016).

3.4 Orthodontic Appliances

All brackets were bonded via indirect bonding technique. Posterior brackets were 0.018” slot, MBT prescription Victory Series (3M Unitek, Monrovia, California). Depending on participant’s esthetic concerns, either metal or ceramic brackets were chosen for anterior teeth. Anterior metal brackets were same as posterior – 0.018” slot, MBT prescription Victory Series (3M Unitek, Monrovia, California). Anterior ceramic brackets were 0.018” slot, MBT prescription Clarity™ ADVANCED Series (3M Unitek, Monrovia, California).

The following was wire sequence used:
• 0.016” x 0.022” Neo-Sentalloy Super-Elastic Nickel Titanium (Dentsply GAC, York, Pennsylvania)

• 0.016” x 0.016” SureSmile Copper Nickel Titanium (Cu-NiTi) (OraMetrix, Inc., Richardson, TX)

• 0.016” x 0.022” SureSmile Cu-NiTi (OraMetrix, Inc., Richardson, TX)

3.5 **AcceleDent® Aura**

AcceleDent® Aura (OrthoAccel Technologies Inc., Houston, TX) package was given to all subjects in the experimental group on a day of braces placement (Figure 1). The package included travel case, activator unit, custom fitted mouthpiece, power adaptor, USB extension cord, and user guide. Subjects received verbal and written instructions to use the device in the following manner:

• Twice a day on a day 0 (day of starting orthodontic treatment and/or each orthodontic adjustment)
  o 20 minutes prior to leaving office
  o 20 minutes prior to going to bed

• Twice a day on a day 1 (one day after starting orthodontic treatment and/or one day after each adjustment appointment)
  o 20 minutes in the morning
  o 20 minutes prior to going to bed

• Once a day after day 1
  o 20 minutes prior to going to bed
To track subjects’ compliance with AcceleDent use, they were instructed to bring their device with mouthpiece attached at each follow-up appointment. Compliance with appliance use was obtained via AcceleDent internal Universal Serial Bus (USB). Those subjects with lack of compliance, which was defined by consistent device use of 50% or less or 2 weeks without AcceleDent use, were removed from the study. Detailed FastTrac AcceleDent Usage Summary report was obtained from each subject’s device at the end of the treatment or the end of 12 months, whichever came first.

Figure 1. AcceleDent® Aura Device

3.6 **I-Tero Scans**

All subjects’ maxillary and mandibular teeth were scanned with i-Tero HD2.9 (Align Technology Inc.) intraoral scanner at four time points during their orthodontic treatment – T1, T2, T3, and T4.

- T1: Start of the treatment, prior to placement of any brackets
• T2: 3 months into the treatment. At this time, SureSmile scan and other records were taken. During T1 to T2 time period, subjects were wearing a light Nickel Titanium (NiTi) wires to achieve initial leveling and alignment
• T3: 6 months into the treatment. This usually coincided with patient’s first SureSmile wire check.
• T4: End of the treatment or 12 months into the treatment, whichever came first

Depending on available time during subjects’ office visits, either intraoral scans or alginate impressions of upper and lower arches were taken at T1, T2, T3, and T4. For the cases that had alginate impressions, models fabricated from the impressions were scanned with i-Tero scanner. All i-Tero scans were stored on the password protected office computers and identified according to subject’s unique identification number – e.g. s112225.

Available de-identified scans were collected and anterior teeth alignment at T1, T2, T3, and T4 was evaluated with Little’s irregularity index as previously described by Little (1975). Models were measured in OrthoCAD software version 3.5.0.38 (Cadent, Inc., Carlstadt, NJ) on one computer located at University of Illinois College of Dentistry. Plane to plane measurement feature in OrthoCAD was used to evaluate anterior teeth interproximal contact displacement of both maxillary and mandibular arches (Figure 2). Measurements were recorded in millimeters (mm). Prior to evaluation of anterior teeth contact points displacement, all scans were enlarged in OrthoCAD to three times of original magnification for total of magnification ranging from 320%-346% of the original
models (Figure 3). Five contact displacements measurements in millimeters were added to obtain Irregularity index.

Figure 2. Original size of study models in the OrthoCAD

Figure 3. Sample magnification and measurements
3.7 **Pain Survey**

To track level of pain during the orthodontic treatment, all subjects were asked to fill out a survey provided on www.surveymonkey.com (SurveyMonkey, San Mateo, California). Each participant created a unique user name and password to access the survey which consist of two questions. In the first question subjects wrote in their unique identification number (Figure 4). This number was provided to each patient at the initial appointment. In the second question, subjects reported their level of pain via visual analog scale (VAS) and family and child experience survey (FACES) with answer choices ranging from 0-10 (Figure 4). Detailed written instructions on how to access the survey and when to complete survey were given to each subject during bonding appointment. Additionally, email reminders were sent to all subjects when to complete the survey, which was at the following times:

- At the adjustment appointment (Day 0) before leaving from the office
- Days 1, 2, and 3 after each appointment
- Once a week until the next appointment

Furthermore, subjects were informed verbally and in written instruction that no pain relief medication is permitted during the study except acetaminophen when needed.
At the completion of treatment or 12 months, de-identified survey entries from each subject were exported from surveymonkey.com via excel document. The exported information contained subjects’ unique identification code, dates when answers were entered, and the subjects’ survey entries (Figure 5). All the responses were sorted as entered on the day 0, day 1, day 2, day 3, or weekly based on adjustment appointments dates for each subject (Figure 6).
Figure 6. Section of data exported from surveymonkey.com for subject S038145 with time period assigned

All the entries were analyzed in the following three time periods:

- **T1 period (start of the treatment to 3 months) pain entries**
  - Day 0
  - Day 1, day 2, day 3
  - Weekly

- **T2 period (3 months to 6 months) pain entries**
  - Day 0
  - Day 1, day 2, day 3
  - Weekly

- **T3 period (6 months to end of the treatment or 12 months, whichever came first) pain entries**
  - Day 0
  - Day 1, day 2, day 3
  - Weekly
3.8 Treatment Compliance

Subjects’ compliance with treatment was documented with collection of the following information:

- Oral hygiene status as recorded at subjects visit
  - A, B, C, grading system
    - A – excellent oral hygiene with minimal to no plaque and no gingival tissue swelling
    - B – mild plaque with mild gingival swelling
    - C – moderate to severe plaque with swollen and bleeding gingiva

- Compliance with AcceleDent use for those subjects in experimental group.
  - Those subjects with lack of compliance, which was defined by consistent device use of 50% or less or weeks without AcceleDent use, were removed from the study.
  - Detailed FastTrac AcceleDent Usage Summary report was obtained for each subject’s device at the end of the treatment or the end of 12 months, whichever came first.

3.9 Blinding

3.9.1 Blinding During Treatment

During their treatment, subjects were seen by either of the two practitioners, depending on doctor availability. Neither of the doctors was aware if the patient was assigned to experimental or control group. Clinical staff checked compliance with AcceleDent use without making doctors aware unless poor compliance was observed.
that warranted patient’s removal from the study. Subject blinding was not possible since they either had or did not have the AcceleDent unit.

3.9.2 Blinding During Model Measurement

To minimize bias during Little's irregularity index measurement, OrthoCAD models were measured in random order and principal investigator was unaware if subjects were assigned to experimental or control group until all measurements were completed.

3.10 Statistical Analysis

Intra-reliability of the principal investigator was evaluated with intra class correlation coefficient (ICC). Irregularity index of maxillary and mandibular anterior teeth was calculated for ten randomly selected i-Tero scans. Samples were measured at three different times, each 2 weeks apart. Mean differences in pain and irregularity indices between experimental and control groups were evaluated with independent student t-test. Paired t-test assessed mean difference in irregularity indices and pain levels at different time points within each group. The Shapiro-Wilk test was completed to assess if data was normally distributed. Statistical significance was set at 0.05. All statistical tests were completed in IBM SPSS Statistics for Windows version 22.0 (IBM Corp, Armonk, NY).
4. RESULTS

4.1. **Sample Distribution**

Data from sixty-one subjects were analyzed (Figure 7). The mean age and gender distribution of the subjects enrolled in the study are reported in Tables I and II. Pearson Chi-square test showed that there was no statistically significant difference in gender distribution between the experimental and control groups, p-value = 0.301. Similarly, independent student t-test shows no statistically significant differences in subjects’ age distribution between the two groups, p-value = 0.912 (Table III).

![Figure 7. Diagram of subject flow in the study](image)

<table>
<thead>
<tr>
<th>TABLE I. AGE DESCRIPTIVE STATISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Age (Years)</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
TABLE II. GENDER DISTRIBUTION OF THE SUBJECTS

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Frequency (n)</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Control</td>
<td>Female</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>Female</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>21</td>
</tr>
</tbody>
</table>

TABLE III. INDEPENDENT T-TEST FOR THE AGE MEAN DIFFERENCES

<table>
<thead>
<tr>
<th>Variable</th>
<th>Levene's Test</th>
<th>t-test for Equality of Means</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
</tr>
<tr>
<td>AGE (Years)</td>
<td>.004</td>
<td>.950</td>
</tr>
</tbody>
</table>

4.2. Arch Alignment

Alignment of maxillary and mandibular anterior teeth was assessed from the i-Tero scans obtained at the start of the treatment (T1), 3 months (T2), 6 months (T3), and at the end of the treatment or 12 months – whichever came first (T4). Data collection for this study extended to 12 months of subjects’ orthodontic treatment. T4 scans were collected at the end of the treatment if the treatment lasted less than 12 months. Even if the orthodontic treatment was not completed, T4 records for these subjects were collected at 12 months. At the end of 12 months, only 6 subjects in the control group and 2 subjects in the experimental group were not done with their
orthodontic treatment. These 8 subjects continued their treatment in the office; however, no further data was collected for the purpose of this project after 12 months. On average, T4 i-Tero scans were taken at 11.05 months in the control and 10.25 months into the treatment in the experimental group (Table IV). The mean times in months when the T2, T3, and T4 scans were obtained were not statistically significant between the groups (Table V).

**TABLE IV. DESCRIPTIVE STATISTICS FOR THE EXPERIMENTAL AND CONTROL GROUPS SCAN TIMES (MONTHS)**

<table>
<thead>
<tr>
<th>I-Tero Scans</th>
<th>Groups</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Std. Error Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scan-T2</td>
<td>Control</td>
<td>40</td>
<td>3.14</td>
<td>.80</td>
<td>.13</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>21</td>
<td>3.15</td>
<td>.56</td>
<td>.12</td>
</tr>
<tr>
<td>Scan-T3</td>
<td>Control</td>
<td>40</td>
<td>6.33</td>
<td>.88</td>
<td>.14</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>20</td>
<td>6.18</td>
<td>.91</td>
<td>.20</td>
</tr>
<tr>
<td>Scan-T4</td>
<td>Control</td>
<td>40</td>
<td>11.05</td>
<td>1.54</td>
<td>.24</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>21</td>
<td>10.25</td>
<td>1.75</td>
<td>.38</td>
</tr>
</tbody>
</table>

**TABLE V. INDEPENDENT T-TEST FOR THE MEAN T2, T3, AND T4 SCAN TIMES (MONTHS)**

<table>
<thead>
<tr>
<th>I-Tero Scans</th>
<th>Levene’s Test</th>
<th>t-test for Equality of Means</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
<td>t</td>
</tr>
<tr>
<td>Scan-T2</td>
<td>Equal variances assumed</td>
<td>3.15</td>
<td>.081</td>
</tr>
<tr>
<td>Scan-T3</td>
<td>Equal variances assumed</td>
<td>.01</td>
<td>.932</td>
</tr>
<tr>
<td>Scan-T4</td>
<td>Equal variances assumed</td>
<td>.62</td>
<td>.434</td>
</tr>
</tbody>
</table>

Intra-operator reliability for irregularity index measurements was tested with ICC.
ICC with intra-reliability (>0.90) and 95% confidence interval (CI) ranging from [0.921 to 0.999] indicates good reliability of the method used in the study. The Shapiro-Wilk test revealed normal distribution for the majority of the variables involved in this study. A total of 59 mandibular arches and 54 maxillary arches irregularity indices were analyzed. Two maxillary arches and seven mandibular arches were not measured due to one or more missing or unerupted anterior teeth at the time of the initial i-Tero scans.

Mean irregularity index values at T1, T2, T3, and T4 for all upper and lower arches were calculated and recorded in Tables VI and VII. Independent t-test revealed that there was no statistically significant difference in mean irregularity indices at the beginning of the treatment between experimental and control groups for either upper or lower arches. The p-values for upper and lower arches irregularity indices at T1 were 0.954 and 0.216 respectively. Within each experimental and control groups, mean values of maxillary and mandibular irregularity indices at follow up time points (T2, T3, and T4) were lower and consecutively smaller than the initial (T1) (Figure 8). Paired t-test showed that these differences were statistically significant with p-value < 0.001 (Table VIII and IX). However, independent student t-test showed that mean differences in irregularity indices between the experimental and control groups at each time point and their differences were not statistically significant, p-value > 0.05 (Table X and XI). Based on these results, the first null hypothesis was accepted. There were no statistically significant mean differences in the arch alignment associated with AcceleDent use in patients treated with SureSmile.
### TABLE VI. DESCRIPTIVE STATISTICS FOR THE CONTROL GROUP
IRREGULARITY INDEX (mm)

<table>
<thead>
<tr>
<th>Irregularity Index</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 Lower arch</td>
<td>39</td>
<td>4.19</td>
<td>2.16</td>
<td>.35</td>
</tr>
<tr>
<td>Upper arch</td>
<td>33</td>
<td>4.54</td>
<td>1.99</td>
<td>.35</td>
</tr>
<tr>
<td>T2 Lower arch</td>
<td>39</td>
<td>2.05</td>
<td>1.29</td>
<td>.21</td>
</tr>
<tr>
<td>Upper arch</td>
<td>33</td>
<td>1.92</td>
<td>.87</td>
<td>.15</td>
</tr>
<tr>
<td>T3 Lower arch</td>
<td>38</td>
<td>1.38</td>
<td>1.14</td>
<td>.18</td>
</tr>
<tr>
<td>Upper arch</td>
<td>32</td>
<td>1.19</td>
<td>.81</td>
<td>.14</td>
</tr>
<tr>
<td>T4 Lower arch</td>
<td>39</td>
<td>.62</td>
<td>.51</td>
<td>.11</td>
</tr>
<tr>
<td>Upper arch</td>
<td>33</td>
<td>.53</td>
<td>.64</td>
<td>.14</td>
</tr>
</tbody>
</table>

### TABLE VII. DESCRIPTIVE STATISTICS FOR THE EXPERIMENTAL GROUP
IRREGULARITY INDEX (mm)

<table>
<thead>
<tr>
<th>Irregularity Index</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 Lower arch</td>
<td>21</td>
<td>5.01</td>
<td>2.83</td>
<td>.62</td>
</tr>
<tr>
<td>Upper arch</td>
<td>20</td>
<td>4.51</td>
<td>1.95</td>
<td>.44</td>
</tr>
<tr>
<td>T2 Lower arch</td>
<td>21</td>
<td>2.30</td>
<td>1.11</td>
<td>.24</td>
</tr>
<tr>
<td>Upper arch</td>
<td>20</td>
<td>2.08</td>
<td>1.10</td>
<td>.25</td>
</tr>
<tr>
<td>T3 Lower arch</td>
<td>20</td>
<td>1.32</td>
<td>.48</td>
<td>.11</td>
</tr>
<tr>
<td>Upper arch</td>
<td>19</td>
<td>1.28</td>
<td>.81</td>
<td>.18</td>
</tr>
<tr>
<td>T4 Lower arch</td>
<td>21</td>
<td>.66</td>
<td>.50</td>
<td>.11</td>
</tr>
<tr>
<td>Upper arch</td>
<td>20</td>
<td>.60</td>
<td>.61</td>
<td>.14</td>
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</table>
TABLE VIII. PAIRED T-TEST FOR TIME POINTS MEAN DIFFERENCES IN THE IRREGULARITY INDICES (mm) IN THE CONTROL GROUP

<table>
<thead>
<tr>
<th>Irregularity Index</th>
<th>Paired Differences</th>
<th>Mean</th>
<th>SD</th>
<th>Std. Error</th>
<th>95% CI of the Difference</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pair 1 T2 - T1 lower arch</td>
<td></td>
<td>-2.14</td>
<td>1.67</td>
<td>.27</td>
<td>-2.68 -1.60</td>
<td>-8.00</td>
<td>38</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 2 T3 - T1 lower arch</td>
<td></td>
<td>-2.85</td>
<td>1.88</td>
<td>.31</td>
<td>-3.47 -2.23</td>
<td>-9.31</td>
<td>37</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 3 T4 - T1 lower arch</td>
<td></td>
<td>-3.56</td>
<td>2.03</td>
<td>.33</td>
<td>-4.22 -2.91</td>
<td>-10.95</td>
<td>38</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 4 T3 - T2 lower arch</td>
<td></td>
<td>-0.68</td>
<td>.52</td>
<td>.08</td>
<td>-.85 -.51</td>
<td>-8.18</td>
<td>37</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 5 T4 - T2 lower arch</td>
<td></td>
<td>-1.43</td>
<td>1.05</td>
<td>.17</td>
<td>-1.77 -1.09</td>
<td>-8.46</td>
<td>38</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 6 T4 - T3 lower arch</td>
<td></td>
<td>-0.77</td>
<td>.89</td>
<td>.14</td>
<td>-.106 -.48</td>
<td>-5.35</td>
<td>37</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 7 T2 - T1 upper arch</td>
<td></td>
<td>-2.62</td>
<td>1.83</td>
<td>.32</td>
<td>-3.27 -1.97</td>
<td>-8.21</td>
<td>32</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 8 T3 - T1 upper arch</td>
<td></td>
<td>-3.41</td>
<td>1.85</td>
<td>.33</td>
<td>-4.08 -2.74</td>
<td>-10.43</td>
<td>31</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 9 T4 - T1 upper arch</td>
<td></td>
<td>-4.01</td>
<td>2.00</td>
<td>.35</td>
<td>-4.72 -3.30</td>
<td>-11.52</td>
<td>32</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 10 T3 - T2 upper arch</td>
<td></td>
<td>-.75</td>
<td>.56</td>
<td>.10</td>
<td>-.95 -.55</td>
<td>-7.66</td>
<td>31</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 11 T4 - T2 upper arch</td>
<td></td>
<td>-1.39</td>
<td>.66</td>
<td>.12</td>
<td>-1.62 -1.15</td>
<td>-12.03</td>
<td>32</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 12 T4 - T3 upper arch</td>
<td></td>
<td>-.65</td>
<td>.64</td>
<td>.11</td>
<td>-.88 -.42</td>
<td>-5.80</td>
<td>31</td>
<td>.000*</td>
</tr>
</tbody>
</table>

* Statistically significant mean difference
### TABLE IX. PAIRED T-TEST FOR TIME POINTS MEAN DIFFERENCES IN THE IRREGULARITY INDICES (mm) IN THE EXPERIMENTAL GROUP

<table>
<thead>
<tr>
<th>Irregularity Index</th>
<th>Paired Differences</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Std. Error Mean</td>
<td>95% CI of the Difference Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Pair 1</td>
<td>T2 - T1 lower arch</td>
<td>-2.70</td>
<td>2.44</td>
<td>.53</td>
</tr>
<tr>
<td>Pair 2</td>
<td>T3 - T1 lower arch</td>
<td>-3.72</td>
<td>2.82</td>
<td>.63</td>
</tr>
<tr>
<td>Pair 3</td>
<td>T4 - T1 lower arch</td>
<td>-4.34</td>
<td>2.98</td>
<td>.65</td>
</tr>
<tr>
<td>Pair 4</td>
<td>T3 - T2 lower arch</td>
<td>-1.03</td>
<td>1.11</td>
<td>.25</td>
</tr>
<tr>
<td>Pair 5</td>
<td>T4 - T2 lower arch</td>
<td>-1.64</td>
<td>1.29</td>
<td>.28</td>
</tr>
<tr>
<td>Pair 6</td>
<td>T4 - T3 lower arch</td>
<td>-0.67</td>
<td>.43</td>
<td>.10</td>
</tr>
<tr>
<td>Pair 7</td>
<td>T2 - T1 upper arch</td>
<td>-2.43</td>
<td>1.51</td>
<td>.34</td>
</tr>
<tr>
<td>Pair 8</td>
<td>T3 - T1 upper arch</td>
<td>-3.33</td>
<td>1.71</td>
<td>.39</td>
</tr>
<tr>
<td>Pair 9</td>
<td>T4 - T1 upper arch</td>
<td>-3.92</td>
<td>2.03</td>
<td>.46</td>
</tr>
<tr>
<td>Pair 10</td>
<td>T3 - T2 upper arch</td>
<td>-.85</td>
<td>.77</td>
<td>.18</td>
</tr>
<tr>
<td>Pair 11</td>
<td>T4 - T2 upper arch</td>
<td>-1.49</td>
<td>1.21</td>
<td>.27</td>
</tr>
<tr>
<td>Pair 12</td>
<td>T4 - T3 upper arch</td>
<td>-.70</td>
<td>.65</td>
<td>.15</td>
</tr>
</tbody>
</table>

* Statistically significant mean difference
### TABLE X. INDEPENDENT T-TEST FOR TIME POINTS MEAN DIFFERENCES IN THE IRREGULARITY INDICES (mm) BETWEEN THE GROUPS

<table>
<thead>
<tr>
<th>Irregularity Index</th>
<th>Levene’s Test</th>
<th>t-test for Equality of Means</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2-T1 lower arch</td>
<td>8.45</td>
<td>.005*</td>
</tr>
<tr>
<td>T2-T1 upper arch</td>
<td>2.55</td>
<td>.116</td>
</tr>
<tr>
<td>T3-T1 lower arch</td>
<td>7.79</td>
<td>.007*</td>
</tr>
<tr>
<td>T3-T1 upper arch</td>
<td>.08</td>
<td>.776</td>
</tr>
<tr>
<td>T4-T1 lower arch</td>
<td>6.05</td>
<td>.017*</td>
</tr>
<tr>
<td>T4-T1 upper arch</td>
<td>.80</td>
<td>.779</td>
</tr>
<tr>
<td>T3-T2 lower arch</td>
<td>9.52</td>
<td>.003*</td>
</tr>
<tr>
<td>T3-T2 upper arch</td>
<td>.95</td>
<td>.335</td>
</tr>
<tr>
<td>T4-T2 lower arch</td>
<td>1.02</td>
<td>.318</td>
</tr>
<tr>
<td>T4-T2 upper arch</td>
<td>3.77</td>
<td>.058</td>
</tr>
<tr>
<td>T4-T3 lower arch</td>
<td>2.92</td>
<td>.093</td>
</tr>
<tr>
<td>T4-T3 upper arch</td>
<td>.00</td>
<td>.995</td>
</tr>
</tbody>
</table>

* Statistically significant mean difference
### TABLE XI. INDEPENDENT T-TEST FOR EACH TIME POINT MEAN IRREGULARITY INDICES (mm) BETWEEN THE GROUPS

<table>
<thead>
<tr>
<th>Irregularity Index</th>
<th>Levene's Test</th>
<th>t-test for Equality of Means</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
</tr>
<tr>
<td>T1 Lower arch</td>
<td>3.26</td>
<td>.076</td>
</tr>
<tr>
<td>T1 Upper arch</td>
<td>.01</td>
<td>.912</td>
</tr>
<tr>
<td>T2 Lower arch</td>
<td>.37</td>
<td>.548</td>
</tr>
<tr>
<td>T2 Upper arch</td>
<td>.91</td>
<td>.346</td>
</tr>
<tr>
<td>T3 Lower arch</td>
<td>3.80</td>
<td>.056</td>
</tr>
<tr>
<td>T3 Upper arch</td>
<td>1.13</td>
<td>.293</td>
</tr>
<tr>
<td>T4 Lower arch</td>
<td>.122</td>
<td>.729</td>
</tr>
<tr>
<td>T4 Upper arch</td>
<td>.02</td>
<td>.898</td>
</tr>
</tbody>
</table>
4.3. **Pain Level**

Subjects' pain levels during the entire treatment were collected from surveymonkey.com and analyzed. These contained weekly survey entries and entries on days 0, 1, 2, 3 after each appointment. Results were analyzed in three time periods:

- **T1** (period between 0-3 months)
- **T2** (period between 3-6 months)
- **T3** (period between 6-12 months or end of treatment, whichever came first).
Thirteen subjects in the control group and four subjects in the experimental group were absolutely non-complaint with survey entries; therefore, these could not be included in the pain data analysis. Survey entries of 31 and 17 subjects in control and experimental groups respectively were analyzed.

Seventy-five percent of subjects in the control group did not have any pain on the day of their adjustment appointments (day 0) throughout the treatment. The rest of the subjects in the control group reported minimal pain ranging between 1 and 4, and only two subjects reported more severe pain of 7. In the experimental group, 76% of subjects also did not have any pain on the days 0. The rest of the subjects had minimal pain ranging from 1 to 3. Weekly entries revealed that participants in both groups predominantly did not have pain at all and occasionally experienced minimal pain ranging from 0 to 3.

Table XII shows pain descriptive statistics for the initial 3 days post adjustment appointment during T1, T2, and T3 for both experimental and control groups. Paired t-test revealed that differences in pain level averages during the 3 days post adjustment appointments were statistically significant between T1 and T3 (p=0.000) as well as T2 and T3 (p=0.004) time periods in the control group (Table XIII). However, there was no statistically significant difference in the pain level averages differences between T1 and T2 periods (p=0.152). In the experimental group, paired t-test showed that differences in the pain level averages were statistically significant for all time periods with p-value ranging from 0.001 to 0.017 (Table XIV).

Pain level averages for day 1, day 2, and day 3 of each adjustment appointment were significantly lower (p= 0.006) in the experimental group when compared to control
group during T2 (3-6 months) and T3 (6 month to the end of treatment or 12 months) (Figure 9 and Table XV). Based on these values, the second null hypothesis was rejected. There were statistically significant mean differences in pain level associated with AcceleDent use in patients treated with SureSmile during 3-6 months and 6 months until the end of the treatment.

TABLE XII. PAIN DESCRIPTIVE STATISTICS FOR THE CONTROL AND EXPERIMENTAL GROUPS

<table>
<thead>
<tr>
<th>Pain Level Average</th>
<th>Groups</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Control</td>
<td>31</td>
<td>3.69</td>
<td>2.38</td>
<td>.43</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>17</td>
<td>3.69</td>
<td>2.54</td>
<td>.62</td>
</tr>
<tr>
<td>T2</td>
<td>Control</td>
<td>30</td>
<td>2.95</td>
<td>2.02</td>
<td>.37</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>17</td>
<td>1.36</td>
<td>1.40</td>
<td>.34</td>
</tr>
<tr>
<td>T3</td>
<td>Control</td>
<td>30</td>
<td>1.70</td>
<td>1.56</td>
<td>.29</td>
</tr>
<tr>
<td></td>
<td>AcceleDent</td>
<td>16</td>
<td>.66</td>
<td>.85</td>
<td>.21</td>
</tr>
</tbody>
</table>

TABLE XIII. PAIRED T-TEST FOR TIME POINTS MEAN DIFFERENCES IN THE PAIN LEVELS IN THE CONTROL GROUP

<table>
<thead>
<tr>
<th>Pain Level Average</th>
<th>Paired Differences</th>
<th>Mean</th>
<th>SD</th>
<th>Std. Error Mean</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pair 1 T2 - T1</td>
<td>-.75</td>
<td>2.75</td>
<td>.51</td>
<td>-1.80</td>
<td>.29</td>
<td>-1.47</td>
<td>28</td>
<td>.152</td>
</tr>
<tr>
<td>Pair 2 T3 - T1</td>
<td>-2.02</td>
<td>1.99</td>
<td>.36</td>
<td>-2.77</td>
<td>-1.28</td>
<td>-5.56</td>
<td>29</td>
<td>.000*</td>
</tr>
<tr>
<td>Pair 3 T3 - T2</td>
<td>-1.23</td>
<td>2.06</td>
<td>.39</td>
<td>-2.02</td>
<td>-.43</td>
<td>-3.16</td>
<td>27</td>
<td>.004*</td>
</tr>
</tbody>
</table>

* Statistically significant mean difference
TABLE XIV. PAIRED T-TEST FOR TIME POINTS MEAN DIFFERENCES IN THE PAIN LEVELS IN THE EXPERIMENTAL GROUP

<table>
<thead>
<tr>
<th>Pain Level Average</th>
<th>Paired Differences</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std. Deviation</td>
<td>Std. Error Mean</td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Pair 1 T2 - T1</td>
<td>-2.02</td>
<td>2.85</td>
<td>.71</td>
<td>-3.54</td>
<td>-.50</td>
</tr>
<tr>
<td>Pair 2 T3 - T1</td>
<td>-2.88</td>
<td>2.64</td>
<td>.68</td>
<td>-4.34</td>
<td>-1.41</td>
</tr>
<tr>
<td>Pair 3 T3 - T2</td>
<td>-.74</td>
<td>1.06</td>
<td>.27</td>
<td>-1.33</td>
<td>-.16</td>
</tr>
</tbody>
</table>

* Statistically significant mean difference

TABLE XV. INDEPENDENT T-TEST FOR THE MEAN PAIN LEVEL AT EACH TIME POINT BETWEEN THE GROUPS

<table>
<thead>
<tr>
<th>Pain Level Average</th>
<th>Levene's Test</th>
<th>t-test for Equality of Means</th>
<th>95% Confidence Interval of the Difference</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
<td>t</td>
<td>df</td>
</tr>
<tr>
<td>T1 Equal variances assumed</td>
<td>.18</td>
<td>.672</td>
<td>-.01</td>
<td>46</td>
</tr>
<tr>
<td>T2 Equal variances assumed</td>
<td>1.76</td>
<td>.192</td>
<td>2.87</td>
<td>45</td>
</tr>
<tr>
<td>T3 Equal variances not assumed</td>
<td>4.53</td>
<td>.039*</td>
<td>2.92</td>
<td>43.95</td>
</tr>
</tbody>
</table>

* Statistically significant mean difference
4.4. **Compliance**

The average oral hygiene of all subjects participating in the study was B, which was defined as mild plaque with mild gingival swelling. Eight subjects were non-compliant with device use and were excluded from the study. These subjects either did not use the device for weeks or had consistent device use of 50% or less. The mean AcceleDent compliance of the remaining 21 subjects in the study was 78%, with minimum to maximum range from 53.5% to 99%.

Figure 9. Cluster bar chart showing differences in pain level averages in the control and experimental groups
5. DISCUSSION

5.1. **Result Analysis**

5.1.1. **Arch Alignment**

Several previous studies evaluated effects of AcceleDent device on tooth movement during orthodontic treatment. Pavlin et al. (2015) assessed the monthly rate of maxillary canine movement during retraction into a premolar extraction space. Bowman (2016) analyzed effect of AcceleDent device in class II patient requiring maxillary molar distalization with TAD supported distal jet appliance. Other orthodontic literature predominantly either compared tooth movement between AcceleDent and non-AcceleDent groups during the initial leveling and alignment via Little’s irregularity index or evaluated time require to accomplish full engagement of large rectangular NiTi or SS wires (Kau et al., 2010; Bowman, 2014; Woodhouse et al., 2015; Miles and Fisher, 2016). Similarly, this study utilized Little’s irregularity index was used to evaluate alignment of anterior teeth at different time points during up to 12-month orthodontic treatment with SureSmile.

Irregularity index was initially developed by Little (1975) for evaluation of orthodontic relapse of anterior teeth in the lower arch only. Since then, the use of the index has been expanded in the orthodontic literature to include maxillary arch anterior teeth and to evaluate performance of different systems (e.g. wires and brackets) on tooth alignment during the orthodontic treatment (Burns et al., 2014). In this study, Little’s irregularity index was used to evaluate anterior teeth movements in both upper and lower arches. All previous AcceleDent studies only evaluate lower teeth alignment
and they used plaster models to calculate the index. However, this study used digital models that were enlarged to a well-defined magnification prior to completion of any measurements. This enabled principal investigator to better visualize and more reliably select all anterior teeth contact points.

Scans of maxillary and mandibular arches were obtained at the start of the treatment (T1), 3 months (T2), 6 months (T3), and at the end of the treatment or 12 months – whichever came first (T4). Data revealed that all scans were not taken at exactly 3, 6, and 12 months into the treatment for every subject. This was expected for the T4 scans since the patients that completed their treatment prior to 12 months had their final scans at the time their braces were removed. Even though there were some differences in the times when the scans were taken at T2, T3, and T4, these differences were shown not to be statistically significant.

Evaluation of the scans revealed that irregularity index values became progressively smaller over the course of the treatment. This is not surprising, as more alignment should be achieved as orthodontic treatment progresses. These differences in irregularity indices were statistically significant between the four time points within each tested group. However, there were no statistically significant mean differences in irregularity indices at any time points between the experimental and control groups. These findings were similar to that of Miles and Fisher (2016) who reported no difference in mandibular irregularity indices during the initial 10 weeks of orthodontic treatment. Similarly, Woodhouse et al. (2015) concluded that AcceleDent did not have any effect on increasing rate of tooth movement due to no difference in irregularity index values or time required to reach initial and final alignment of mandibular anterior teeth.
However, it important to note that in all the studies, including the present investigation, patients in control and experimental groups were seen at the same time intervals between the appointments. This scheduling pattern could have negatively impacted AcceleDent group device since tooth movement could have been achieved earlier in the experimental group without detection. Wires in the AcceleDent groups could have been passive for days or even weeks before the scans were acquired. Since both groups had the same interval between their adjustment appointments (6-8 weeks) and there was no difference in irregularity index values, one can conclude that in this setting there were no differences in rate of tooth movement either. Nevertheless, the possibility of more frequent adjustments (e.g. 3-4 weeks) in patients with AcceleDent should be further investigated.

5.1.2. Pain

While effects of AcceleDent device on pain levels during orthodontic treatment were previously investigated, this was the first study that followed patients for up to 12 months. Lobre et al. (2016) documented pain during the initial four months of the treatment, whereas, Miles and Fisher (2016) followed their patients’ pain experiences for only one week. These two studies reported inconsistent conclusions. Lobre et al. (2016) reported that overall pain during the initial four months of orthodontic treatment was significantly lower in the AcceleDent group. All of the patients in the study experienced highest level of pain the first week after the adjustment appointments, but these peaks were significantly reduced in experimental group (Lobre et al., 2016). Although promising, these data should be interpreted with caution due to several
drawbacks in the study design. Subjects recorded their survey responses in paper diaries; therefore, instigators would not have known precisely when the survey responses were entered since the non-complaint patients could have retroactively entered the data. Additionally, this paper did not report age and gender of the patients enrolled in the study even though it was mentioned that this was data was collected. Differences in age and gender distribution in the two groups could have affected the outcomes of the investigation. A more recent study by Miles and Fisher (2016) reported no difference in pain between the two groups. Interestingly, despite no differences in pain, patients with AcceleDent device reported using less analgesic medication. The pain levels were, however, only evaluated during the first week of orthodontic treatment. This study also used paper charts for survey data entry.

In the current study, subjects completed VAS type pain rating survey at day 0, day 1, day 2, and day 3 after each adjustment appointment and then weekly until the following appointment for up to 12 months. Subjects utilized online surveys to document their responses. The main advantage for using an online survey is that date and time of surveys responses was accurately recorded in the real time and could not be altered by subjects. Additionally, subjects received email reminders to enter their survey responses when required. There was no statistical difference in age and gender between the two groups. Having uniform distribution of subjects based on their age and gender in both groups is crucial for pain data interpretation as these two factors could affect individual’s perceived pain (Okeson, 2015).

Our data revealed that majority of subjects (75% in control and 76% in experimental group) did not have any pain during day 0 and weekly between their
orthodontic adjustment appointments. The rest of the subjects had minimal pain ranging from 1-4 on a scale 1-10. Only two subjects reported severe pain of 7 on a day of their adjustment appointment (day 0). Previous research on pain intensity during orthodontic treatment showed that pain emerges about 4 hours and peaks at 24 hours after new wire placement (Krishnan, 2007). Low day 0 pain scores reported by the patients in this study would be expected since they were asked to fill out survey shortly after wire placement and prior to leaving the office that day. Also, it is not surprising that majority of the patients did not have any pain during weeks in between their appointments as these results are in agreement with the existing orthodontic literature (Krishnan, 2007).

Day 1, day 2, and day 3 pain entries were analyzed jointly. Statistical analysis revealed that there was no difference in average pain levels between the two groups from the start of the treatment to 3 months into the treatment. The average reported pain during this time period was exactly the same between the two groups – 3.69. From 3 months to the end of observation period, subjects in the experimental group had significantly less pain during these three days. Even though these differences showed to be statistically significant, the mean of the pain during these periods in both groups was low. Average pain levels for experimental group during 3-6 and 6 months to the end of the treatment (or 12 months) were 1.36 and 0.66 respectively. For control groups these numbers were 2.95 for 3-6 months and 1.7 for period between 6 months and the end of treatment (or 12 months). Value of pain levels decreased as treatment progressed for both experimental and control groups. These differences were significant for all time periods in the experimental groups and only significant from 3-6 and 6 months to the end of the treatment (or 12 months) in the control group.
Data in this study revealed that AcceleDent has potential to reduce discomfort level during orthodontic treatment after initial 3 months of the treatment. It is not possible to determine exact reasoning why pain level during the initial 3 months of the treatment was the same between the two groups. One could assume that patients need some time to get used to the device and become comfortable with using it. Another contributing factor could have been that teeth movement during the initial 3 months was more extensive than the movement during any other time during the treatment. This was supported with irregularity index differences that showed the greatest change between initial and 3 months scans. The mean difference in irregularity indices between T1 and T2 periods was -2.14 mm in control and -2.70 mm in experimental groups. The differences in irregularity index values for other time periods (T2-T3 and T3-T4) were only -1 mm or less than -1 mm.

5.1.3. AcceleDent Compliance

Good compliance with AcceleDent use is critical to properly evaluate device effect on orthodontic tooth movement and pain. However, only few studies assessed AcceleDent compliance data. Woodhouse et al. (2015) reported that AcceleDent usage data obtained from devices’ USB was unreliable; therefore, they were unable to determine compliance for their subjects. However, they did not provide clarification of their conclusion on compliance data unreliability. Kau et al. (2010) reported differences in patients’ self-reported journal compliance (80%) and device reported compliance (67%). They contributed these differences to patient’s compliance overestimation and not device data collection unreliability.
In this study, an attempt was made to closely monitor AcceleDent device compliance at each subject’s appointment. Those subjects that did not meet compliance criteria defined at the beginning of the study were excluded. Many of the AcceleDent units used in this study failed to properly sync dates when the device was used. Due to encountered errors with dates syncing, this study was unable to report compliance in specific time periods (0-3, 3-6, and 6-12 months). Instead, the average compliance throughout the entire observation period was analyzed. On average, compliance with AcceleDent use throughout the entire treatment was 78%, with the range of 53.5% to 99%. Compliance in our study was marginally superior than that described by Miles and Fisher (2016) who reported average compliance of 73.8% and diverse range from 27% to 100%. These differences could be attributed to exclusion of non-complaint patients in the current investigation while the other study did not exclude any patients based on non-compliance. One should be aware that all compliance data should be interpreted with caution due to the lack of indicators that confirm intraoral use of AcceleDent device. Even if the percentage shows high compliance with device use, currently there is truly no reliable way to determine that device was actually used intraorally.

5.2. **Study Limitations**

The principal investigator did not have any direct contact with subjects enrolled in the study. All data was documented and collected in the three private offices in Illinois. Therefore, the accuracy and availability of the data was dependent on the office staff and clinicians following the approved research protocol. Digital models available to principal investigator for the measurement of irregularity indices were from either direct
intraoral scans or scan of models fabricated from the intraoral alginate impressions. Therefore, quality of impressions, model fabrication, time lapse between impression taking and model pouring could have influence accuracy of the available models.

Subjects in the study were not blinded because they either had or did not have the AcceleDent device. This would not have any effect on arch alignment; however, it could have introduced some bias in the experimental group pain evaluation if subject had expectations that the device could affecting their discomfort level during the treatment. However, sham device was not included in this study because it would essentially serve as bite wafer and previous research showed inconsistent data on effect of bite wafers on pain perception during orthodontic treatment (Hwang et al., 1994; Otasevic et al., 2006).

Additionally, the study lacked clear instructions on use and documentation of pain medication. Even though patients were instructed not to use NSAIDs such as Advil and Ibuprofen, they were allowed to take acetaminophen for pain. However, patients were no required to report the times and amounts of the medication taken. Furthermore, more accurate pain level evaluations would have been obtained if subjects were specifically instructed to complete survey prior to taking any pain medication.

Several subjects and the private office staff reported mechanical difficulties with several AcceleDent Aura devices. These included problems with device charging and holding charge, device malfunctioning, and inaccurate syncing dates when the device was used. This could had been a factor in exclusion of eight subjects from the study due to the poor compliance with the device use and 78% average compliance of the remaining subject in the experimental groups. Finally, due to the lack of indicators that
confirm intraoral use of AcceleDent device, there was no reliable way to determine if the patients actually used the device properly.

5.3. Future Studies

This study showed that AcceleDent device did not have any effect on the rate of alignment of anterior teeth in maxillary and mandibular arches; however, the effect of the device during other orthodontic tooth movements should be further investigated. These could include evaluation of vibration on tooth movements during expansion, closing of maxillary and mandibular extraction spaces with retraction or protraction, and intrusion/extrusion of teeth. Future investigations should also explore if patients using AcceleDent device during orthodontic treatment could be seen in the shorter time intervals than those patients without the device.

Additionally, the effect of different vibration frequencies on tooth movement and pain should be explored. Recently developed device called VPro5 from Propel Orthodontics LLC (Ossining, NY), which uses different frequency and is used only 5 minutes a day, should be compared with the AcceleDent device. This study demonstrated that differences in pain during orthodontic treatment exist between the groups; however, the future investigations should attempt to replicate this study with larger sample size that would allow categorization of subjects by gender and age. Future pain studies should possibly include sham device and importantly subjects should keep a log of analgesic medication type and dose taken during the observation period.
6. CONCLUSION

The objective of this study was to evaluate if AcceleDent had any effect on arch alignment and pain experience during the orthodontic treatment with SureSmile. Two null hypothesis were tested.

- The study accepts the first null hypothesis that there are no statistically significant mean differences in the arch alignment associated with AcceleDent use in patients treated with SureSmile. There was no statistically significant mean differences in the alignment of anterior maxillary and mandibular anterior teeth between experimental and control groups at any time points measured during the treatment.

- The study rejects the second null hypothesis that there are no statistically significant mean differences in pain level associated with AcceleDent use in patients treated with SureSmile. The AcceleDent device did not have statistically significant effect on mean pain level between the two groups during initial three months of the treatment. However, after the 3\textsuperscript{rd} month until the end of the orthodontic treatment, patients who used AcceleDent device reported significantly less pain during day 1, day 2, and day 3 after their adjustment appointments.

- Since AcceleDent group reported decreased pain during the majority of their orthodontic treatment, patients using this device could possibly be seen on more frequent intervals; therefore, theoretically, the total treatment time could also be reduced since more frequent appointment could lead to less total treatment time.
CITED LITERATURE


Rubin, C., Turner, A.S., Muller, R., Mittra, E., McLeod, K., Lin, W., and Qin, Y.: Quantity and quiliaty of trabecular bone in the femur are enhanced by strongly anabolic, noninvasive mechanical intervention. J Bone Miner Res. 17;349-357:2002.


APPENDICES
APPENDIX A

Western Institutional Review Board*
1019 39th Avenue SE Suite 120 | Puyallup, WA 98374-2115
Office: (360) 252-5500 | Toll Free: (800) 952-4789
www.wirb.com

Certificate of Approval

THE FOLLOWING WERE APPROVED

INVESTIGATOR: Terry Sellke DDS, MS
30 North Slusser Street
Grayslake, Illinois 60030

BOARD ACTION DATE: 01/19/2015

AMOUNT: 5

STUDY APPROVAL EXPIRES: 01/19/2016

WIRB PRO NUM: 1150957

STUDY NUM: 115356

ONLINE TRACKING: 20142264

INVEST NUM: 115356

W0 NUM: 1-860811-1

CONTINUING REVIEW: Annually

SITE STATUS REPORTING: Annually

INST. NUM:

SPONSOR: Sellke and Reily LTD

PROTOCOL NUM: AD-SMILE11012014

AMEND PRO. NUM:

The effect of AcceleDent application on discomfort level and rate of tooth movement in orthodontic treatment with SureSmile

APPROVAL INCLUDES:
Investigator
Braces Informed Consent #12532213.0 - As Submitted
Pain Scale #12724596.0 - As Submitted
Protocol (10-30-2014)
Screening Requirements for Study #12578735.0 - As Modified
Consent Form [S0]
Financial Disclosure Form (10-27-2014) Sellke

WIRB APPROVAL IS GRANTED SUBJECT TO:
The Board requires that all adult subjects must be able to consent for themselves to be enrolled in this study. This means that you cannot enroll incapable subjects who require enrollment by consent of a legally authorized representative.

The Board determined that the device as used in this research study is a non-significant risk device.

WIRB HAS APPROVED THE FOLLOWING LOCATIONS TO BE USED IN THE RESEARCH:
Drs. Sellke and Reily, LTD, 30 North Slusser, Grayslake, Illinois 60030
Drs. Sellke and Reily, LTD, 1138 South Main Street, Route 83 and 173, Antioch, Illinois 60002
Gurnee Orthodontics, 101 S Greenleaf Ave, Gurnee, Illinois 60031

If the PI has an obligation to use another IRB for any site listed above and has not submitted a written statement from the other IRB acknowledging WIRB’s review of this research, please contact WIRB’s Client Services department.

ALL WIRB APPROVED INVESTIGATORS MUST COMPLY WITH THE FOLLOWING:

1. Conduct the research in accordance with the protocol, applicable laws and regulations, and the principles of research ethics as set forth in the Belmont Report.

2. Although a participant is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the investigator should make a reasonable effort to ascertain the reason, while fully respecting the participant’s rights.

IF YOU HAVE ANY QUESTIONS, CONTACT WIRB AT 1-800-562-4789

This is to certify that the information contained herein is true and correct as reflected in the records of the Western Institutional Review Board (WIRB), DHHS/CFDA parent organization number IORG 0000432, IRB registration number IRB00000533. WE CERTIFY THAT WIRB IS IN FULL COMPLIANCE WITH GOOD CLINICAL PRACTICES AS DEFINED UNDER THE U.S. FOOD AND DRUG ADMINISTRATION (FDA) REGULATIONS, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) REGULATIONS, AND THE INTERNATIONAL CONFERENCE ON HARMONISATION (ICH) GUIDELINES.

Board Action: 01/19/2015; Study: 1150957
Copyright © 2013 Western Institutional Review Board, Inc. All rights reserved.
3. Unless consent has been waived, conduct the informed consent process without coercion or undue influence, and provide the potential subject sufficient opportunity to consider whether or not to participate. (Due to the unique circumstances of research conducted at international sites outside the United States and Canada where WIRB approved materials are translated into the local language, the following requirements regarding consent forms bearing the WIRB approval stamp and regarding certification of translations are not applicable.)
   a. Use only the most current consent form bearing the WIRB "APPROVED" stamp.
   b. Provide non-English speaking subjects with a certified translation of the approved consent form in the subject's first language. The translation must be approved by WIRB unless other arrangements have been made and approved by WIRB.
   c. Obtain pre-approval from WIRB for use of recruitment materials and other materials provided to subjects.

4. Enrollment of limited readers and non-readers: unless consent has been waived or the protocol excludes enrollment of limited readers or non-readers, involve an impartial witness in the consent process when enrolling limited or non-readers and document the participation of the impartial witness using the designated signature lines on the WIRB-approved consent form. In the absence of designated signature lines, download the WIRB standard impartial witness form from www.wirb.com.

5. Obtain pre-approval from WIRB for changes in research.

6. Obtain pre-approval from WIRB for planned deviations and changes in research activity as follows:
   - If the research is federally funded, conducted under an FWA, or is a clinical investigation of a drug or biologic, then all planned protocol deviations must be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects ([DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].)
   - However, if the research is a clinical investigation of a device and the research is not federally funded and not conducted under an FWA, then only planned protocol deviations that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data should be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects ([DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].)

The reason for these different requirements regarding planned protocol deviations is that the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) drug and biologic divisions have adopted the regulatory interpretation that every planned protocol deviation is a change in research that needs prior IRB review and approval before implementation; however, the FDA device division operates under a distinct regulation (21 CFR 812.150(a)(4)).

Deviations necessary to eliminate apparent immediate hazards to the human subjects should be reported within 10 days.

7. Report the following information items to the IRB within 5 days:
   a. New or increased risk
   b. Protocol deviation that harmed a subject or placed subject at risk of harm
   c. Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a subject
   d. Audit, inspection, or inquiry by a federal agency
   e. Written reports of federal agencies (e.g., FDA Form 483)
   f. Allegation of Noncompliance or Finding of Noncompliance
   g. Breach of confidentiality
   h. Unresolved subject complaint
   i. Suspension or premature termination by the sponsor, investigator, or institution
   j. Incarceration of a subject in a research study not approved to involve prisoners
   k. Adverse events or IND safety reports that require a change to the protocol or consent
   l. State medical board actions
   m. Unanticipated adverse device effect
   n. Information where the sponsor requires prompt reporting to the IRB

Information not listed above does not require prompt reporting to WIRB.

Please go to www.wirb.com for complete definitions and forms for reporting.

8. Provide reports to WIRB concerning the progress of the research, when requested.

9. Ensure that prior to performing study-related duties, each member of the research study team has had training in the protection of human subjects appropriate to the processes required in the approved protocol.
APPENDIX A (Continued)

Federal regulations require that WIRB conduct continuing review of approved research. You will receive Continuing Review Report forms from WIRB. These reports must be returned even though your study may not have started.

DISTRIBUTION OF COPIES:
Contact, Company
Terry Sellke DDS, MS, Sellke and Reily LTD
Julie Myrdal, Sellke and Reily LTD
APPENDIX B

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Notice of Determination of Human Subject Research

June 30, 2015

*20150708
-91044-1*

20150708-91044-1

Milena Bulic
Orthodontics
801 S. Paulina St.
M/C 841
Chicago
Phone: (312) 996-7138 / Fax: (312) 996-0873

RE: Protocol # 2015-0708
The Effect of AcceleDent Application on Discomfort Level and Rate of tooth Movement in Orthodontic Treatment with SureSmile

Sponsor: None

Dear Milena Bulic:

The UIC Office for the Protection of Research Subjects received your “Determination of Whether an Activity Represents Human Subjects Research” application, and has determined that this activity DOES NOT meet the definition of human subject research as defined by 45 CFR 46.102(f).

You may conduct your activity without further submission to the IRB.

If this activity is used in conjunction with any other research involving human subjects or if it is modified in any way, it must be re-reviewed by OPRS staff.
Phone Etiquette for Study

When patients call and are interested in participating in the study because they have heard about it from the direct mailer or some other venue. We are to follow the following scripting. We are not permitted to share with them if they are or are not eligible for the study, since they have called our office they are interested in orthodontic treatment and the doctor will see them and acknowledge at that consultation appointment if they are an eligible candidate at that time. However if they have not had a dental cleaning and checkup in a very long time, it's always a good idea to encourage them to schedule that appointment because starting treatment would be on hold until after that appointment is taken care of.

This research study involves an FDA approved appliance called AcceleDent. AcceleDent claims to reduce treatment time and pain levels and we are conducting a study to measure and compare the speed of treatment and level of discomfort between two groups with and without the AcceleDent unit. The decision to participate or not to participate does not change the standard of care that you will receive. All participants will receive a financial reward of $600 for successfully completing the study. Would you like to schedule a complimentary orthodontic consultation?

At the consultation, the same standard of care is followed and the doctor will share with the TC if the patient meets the study criteria and can move forward to the next step. Once the doctor’s portion is complete then the TC will follow the screening requirement process for the study (see that document).
APPENDIX D

Screening Requirements for Study:

To see if you might qualify for this study, I need to ask you some questions about your health history and present condition. Some of these questions may be sensitive. You do not have to answer any questions you do not want to answer. You may stop this interview at any time. If you do not qualify for this study, the information you give me will be immediately shredded.

Do I have your permission to proceed?
1. Are you in good health?
2. Do you have periodontitis?
3. Do you smoke?
4. Do you take Advil or other NSAIDs, like ibuprofen?
5. Do you take a Vitamin D supplement?
6. Do you take bisphosphonates?

Thank you for answering these questions.

If they qualify: Based on this information you qualify to participate in the study and your files will be kept encrypted and secure till the end of the study which we anticipate the date of June 2017. Is it ok with you if we use your information that we collect from this study for possible future studies?

If they do NOT qualify: I’m sorry you do not qualify for participation in this study and the information you gave me will be immediately shredded.
APPENDIX E

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: The effect of AcceleDent application on discomfort level and rate of tooth movement in orthodontic treatment with SureSmile

PROTOCOL NO.: AD-SMILE11012014
WIRB® Protocol #20142264

SPONSOR: Sellke and Reily LTD.

INVESTIGATOR: Terry Sellke, DDS, MS
30 North Slusser Street
Grayslake, Illinois 60030
United States

STUDY-RELATED PHONE NUMBER(S): Terry Sellke, DDS, MS
847-223-2894
847-204-8127 (24 Hours)

SUB-INVESTIGATOR: Donald Reily, DDS, MS

STUDY COORDINATOR: Julie Myrdal

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

In this consent form, “you” always refers to the subject. If you are a parent or legal guardian, please remember that “you” refers to the study subject.

You are being asked to be a subject in a research study involving an FDA approved appliance called AcceleDent. AcceleDent will be used in addition to SureSmile treatment in selected subjects. SureSmile is a treatment system involving robotically bent wires to straighten teeth and is approved by the U.S. Food and Drug Administration (FDA). The procedures used are standard of care. The experimental part of this study is to compare the use of the AcceleDent versus no use of AcceleDent treatment to see if it shortens the time it takes to straighten your teeth and if it reduces your pain in orthodontic treatment with SureSmile.
APPENDIX E (Continued)

The study doctor, Dr. Terry Sellke, DDS, MS, and his partner, Dr. Donald Reily DDS, M.S., will be responsible for carrying out the research procedures for all subjects in the study. You will be in this study for about 1 year. There will be 100 subjects in the study.

We ask that you read this consent form and ask any questions you may have before agreeing to be a research subject. Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future relationship with Dr. Sellke and Reily, LTD or Gurnee Orthodontics or individuals involved in this study. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

**What is the purpose of this research?**

The goal of this study is to compare the effectiveness of an AcceleDent appliance used in addition to standard SureSmile treatment. We will be measuring the speed of treatment, the level of discomfort, and the treatment results in a sample of patients using versus not using an AcceleDent appliance.

**What procedures are involved?**

If you agree to participate in this study, you will be randomly assigned to either the control or AcceleDent group. You will have an equal chance of being in each group.

The treatment procedures that will be used incorporating SureSmile treatment will be identical between the two groups. The only variable that will be studied is the effectiveness of AcceleDent 1) in moderating discomfort when using SureSmile wires and 2) in reducing the time required to successfully treat the subject with SureSmile technology.

Subjects in the group using AcceleDent will be required to use the device for a 20 minute period in the orthodontist’s office after each adjustment, that evening, morning and night on the second and third days, and daily thereafter until the next appointment. This process will be repeated after each appointment until treatment is completed.

Patients who agree to participate in the study will be asked to respond to a short email questionnaire assessing their discomfort level one day, two days, three days, and weekly after each appointment.

iTero scans of the teeth will be taken during the study at the following times:

- Before treatment begins
- Approximately 8 - 10 weeks after appliances are placed
- Approximately 5 - 6 months into treatment
- At the end of treatment or at 12 months into treatment, whichever comes first

iTero scans involve an FDA approved digital scanning device to create 3D digital models of the teeth. This painless, non-invasive process involves no injections or harmful actions.
What are the potential risks and discomforts?

The possible risks and discomforts you might experience during this study include:

- Those that patients may have while receiving SureSmile treatment
- The inconvenience in the AcceleDent group of using the device at the prescribed times
- That the AcceleDent device does not provide a reduction in discomfort nor faster treatment
- Loss of confidentiality

If at any time you wish to withdraw from the study, you may do so.

There may be risks or side effects which are unknown at this time.

Are there benefits to taking part in the research?

The potential benefits of your participation in this study include:

- The possibility of reduced treatment time and treatment discomfort with the AcceleDent group.
- Information learned from this study may help patients in the future.

What are the costs and payments for participating in this research?

There are no additional costs involved for participating in this research. You will receive a free orthodontic evaluation. This is a standard practice of the study doctors, whether you are in a study or not.

Participants who complete the study will receive a $600 credit on their treatment fee. There will be no additional treatment fees for these participants.

Are there alternative treatments?

Absolutely! If you do not desire to participate in the study, your orthodontic treatment will proceed as usual with other SureSmile cases. You do not have to be in this study to receive orthodontic treatment with SureSmile.

What about privacy and confidentiality?

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The investigators, Dr. Terry A. Sellke and Dr. Donald J. Reily must get your authorization (permission) to use or give out any health information that might identify you. However, it is the intent of this study to de-identify your records to prevent access to private information that could
APPENDIX E (Continued)

identify your records as yours. This means that the investigators will hold a key that links your personal health information to your identity.

What information may be used and given to others?

If you choose to be in this study, the investigator and sub-investigator will get personal information about you. This may include information that might identify you. They may also get information about your health including:

- Past and present medical and dental history
- Research records and photographs
- Records relating to phone calls made as part of this research
- Records about your study visits
- Records about the study devices

Who may use and give out information about you?

De-identified information about your health may be used and given to others by the co-investigators and staff. They might see the research information during and after the study.

Who might get this information?

Your information may be given to the sponsor of this research, Dr. Terry A. Sellke, DDS, MS.

Information about you and your health might also be given to:

- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- The Western Institutional Review Board® (WIRB®)

Why will this information be used and/or given to others?

De-identified information will be used to assess study outcomes. Consultants and the organizations listed above may analyze and evaluate the results of the study as well as visit the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

The information may be reviewed by WIRB®. WIRB is a group of people who perform independent review of research as required by regulations.
What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health and mental health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

Yes, but this permission will not stop automatically.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to Dr. Terry A. Sellke, DDS, MS. If you withdraw your permission, you will not be allowed to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

Your information will be de-identified to the best of our ability before dissemination to any other party. There is little risk that your private health information can be identified as yours. However, there is a risk that your health information will be given to others without your permission.

What if I am injured as a result of my participation?

In the unlikely event of injury related to this research study, treatment will be made available through Dr. Sellke and Reilly, LTD. However, you or your third party payer, if any, will be billed for this treatment. You do not give up any legal rights by signing this consent form and taking part in the study.

Who will provide the source of funding?

Funding for this research study will be provided by Dr. Terry A. Sellke, DDS, MS.

Is there a financial disclosure?
Dr. Sellke receives speaking fees. If you have any questions about this, feel free to ask him.
Will I receive new information about this study?

During the course of the study, you will be informed of any new findings such as changes in the risks or benefits resulting from participation in this research study or new alternatives to participation that might change your decision to be in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

What will happen if I decide not to participate?

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits as related to your treatment.

Your participation in this study may be stopped at any time by the investigator or the sponsor without your consent for any reason, including if it is in your best interest or you do not consent to continue in the study after being told of changes in the research that may affect you.

Who should I contact if I have questions?

If you have any questions concerning your participation in this study, if you have questions, concerns or complaints about the research, or if at any time you feel you have experienced a research-related injury, contact:

Dr. Terry A. Sellke at 847-223-2894 or 847-204-8127 (24 Hours).

If you have any questions about your rights as a research subject, or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research. WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will be given a signed and dated copy of this consent form.
APPENDIX E (Continued)

Signature of Subject or Parent/Legal Guardian

Consent and Assent Instructions:
Consent: Subjects 18 years and older must sign on the subject line below
For subjects under 18, consent is provided by the Parent/Legal Guardian
Assent: Is required for subjects ages 12 through 17 years using the Assent Section below

I have read the information in this consent form (or it has been read to me). I have been given an opportunity to ask questions and my questions about the study and my (my child’s) participation in it have been answered to my satisfaction. I agree to (allow my child to) participate in this research.

I authorize the use and disclosure of my (my child’s) health information to the parties listed in the authorization section of this consent for the purposes described above.

By signing this consent form, I have not given up any of my/my child’s legal rights.

Printed Name of Subject

CONSENT SIGNATURE:

Signature of Subject (18 years and older) Date

Signature of Parent/Legal Guardian
(when applicable) Date

Printed Name of Parent/Legal Guardian Date

Signature of Person Conducting Informed Consent Discussion Date

Printed Name of Person Conducting Informed Consent Discussion Date

Signature of Witness Date

Printed Name of Witness
APPENDIX E (Continued)

ASSENT SIGNATURES, For Subjects Ages 12 through 17 years:

Assent:
This research study has been explained to me and I agree to be in this study.

Subject’s Signature for Assent     Date     Age (years)

I confirm that I have explained the study to the extent compatible with the subject’s understanding, and that the subject has agreed to be in the study.

Signature of Person Conducting Assent Discussion     Date

---------------------------------- Use the following only if applicable ----------------------------------

If this consent form is read to the subject because the subject (or parent/legal guardian) is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject (or the subject’s parent/legal guardian). The subject (or the subject’s parent/legal guardian) freely consented to be in the research study.

Signature of Impartial Witness     Date

Printed Name of Impartial Witness

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling subjects who do not speak English.
VITA

NAME: Milena Bulic

EDUCATION:
B.S., Biology, Park University, Parkville, MO, 2008
B.A., Chemistry, Park University, Parkville, MO 2008
D.D.S., University of Illinois at Chicago, Chicago, IL, 2014
M.S., University of Illinois at Chicago, Chicago, IL, 2017 (anticipated)
Specialty Certificate, Orthodontics, University of Illinois at Chicago, Chicago, IL, 2017 (anticipated)

HONORS:
- Pierre Fauchard Academy Award
- ISDS Foundation David Shapiro Memorial Scholarship
- ISDS Foundation Best Basic Science Poster Presentation Award
- American Institute of Orthodontic Research Award
- Delta Dental of Illinois Foundation Outstanding Dental Student
- NAIA Volleyball All-America Scholar Athlete
- Burton W. Scheib Pre-Medical/Dental Prize
- Chemistry and Biology Department Honors
- Professor L. A. Robbins Science Memorial Award
- American Chemistry Society Freshman of the Year

PROFESSIONAL MEMBERSHIP:
- American Association of Orthodontists
- American Dental Association
- Illinois State Dental Society
- Illinois Society of Orthodontists
- Chicago Dental Society