Clear Aligner Adjunct Therapies: Effects on Patient Experience and Aligner Efficacy

Pranita Ramanan, DDS

A thesis submitted to the Department of Orthodontics and the Advanced Educated Committee of the Oregon Health & Science University School of Dentistry in partial fulfillment of the requirements for the Degree of Master of Science in Orthodontics.

Portland, Oregon
November 4, 2022

Clear Aligner Adjunct Therapies: Effects on Patient Experience and Aligner Efficacy

Pranita Ramanan, DDS

Master of Science in Orthodontics Research Advisory Committee:

Approved: _____ Date: _____

Jeffrey Nickel, DMD MSc PhD
Mentor
Associate Professor, Graduate Program Director
Department of Orthodontics
Oregon Health & Science University

Approved: _____ Date: _____

Laura Iwasaki, DDS MSc PhD
Committee Member
Professor, Chair
Department of Orthodontics
Oregon Health & Science University

Approved: _____ Date: _____

Howard Freedman, DDS
Committee Member
Assistant Professor, Director of Orthodontic Clinics
Department of Orthodontics
Oregon Health & Science University

Approved: _____ Date: _____

Hongseok An, DDS MSD FACP
Committee Member
Assistant Professor
Department of Restorative Dentistry
Oregon Health & Science University

Acknowledgements

Thank you to my thesis mentor, Dr. Jeffrey Nickel, for advising me throughout this project. I greatly appreciate your swift enthusiasm to guide me, and innovative suggestions to make sure I succeed.

Thank you to my thesis committee members, Dr. Laura Iwasaki, Dr. Howard Freedman, and Dr. Hongseok An for all your research guidance and support in my education.

Thank you to Dr. Dongseok Choi for all your statistical analyses and your unlimited patience in helping me interpret them.

Thank you to Dr. Daniel Leo for creating a tracking program for me on short notice. I am grateful for your time spent working back and forth with me to produce the best results.

Thank you to my husband, Ahmed Belal. Your unconditional support and encouragement are the reasons I have accomplished my dreams.

And lastly, thank you to all my friends and family who have been a part of this journey. I couldn't have made it through over a decade of education without you.

Table of Contents

Abstract

Objective: The purpose of this prospective pilot study was to assess if clear aligner adjunct therapies: "Chewies®" (Chew) or "PULSystem®" (Pul) affected reported pain, compliance, satisfaction or tray effectiveness.

Methods: With OHSU IRB oversight, subjects were recruited according to inclusion criteria of planned orthodontic therapy without the extraction of teeth, use of orthodontic elastics or interproximal tooth reduction during first four aligner trays, and a cervical vertebral maturation (CVM) index of ≥4. Subjects were randomly divided into 3 groups: Chew, Pul, and control (CG). Surveys were used to assess treatment pain, compliance, and satisfaction. Clear aligner efficacy was estimated by evaluating the difference in predicted and post-tray tooth positions.

Results: Ten subjects completed participation: Chew (N=3), Pul (N=4), and CG (N=3). Chew and Pul groups reported significantly lower levels of 'frustrating' pain ($p<0.01$ and $p<0.05$, respectively) and the Pul group reported significantly lower levels of 'strange' pain ($p<0.05$) when compared to the CG. The Pul group exhibited a significantly lower reported pain during the second week of aligner tray wear when compared to the first week during trays 1, 2, 3, and 4 compared to CG ($p<0.01$). All groups reported high compliance, and no significant group differences with respect to daily hours of tray use (Chew 20±2, Pul 22±1, and CG 21±2) and days per week of tray wear (Chew 7±0, Pul 7±0, and CG 6±1). All groups showed high satisfaction with aligner experience, with no significant group differences. There were no significant differences in tray efficacy between Chew, Pul, and CG.

Conclusions: Adjunct therapies may decrease pain intensity and duration, and influence tray efficacy in tooth movement.

I. Introduction

As the demand for orthodontic treatment has grown, the desire for more esthetic alternatives to traditional fixed appliances has also increased. Specifically, clear aligner therapy provides a removable esthetic alternative as well as other benefits including improved oral hygiene, fewer and shorter appointments, and fewer emergency visits.[1] Additionally, adults who were treated with clear aligners reported less pain and fewer negative impacts on their lives during the first week treatment when compared to those treated with fixed appliances.[2] These advantages not only contribute to the increasing demand of clear aligner therapy, but also their adjunctive therapies. Adjunctive therapies are available direct to consumers, often marketed with the claim that they aid in aligner treatment. Currently valued at a 2.85 billion dollar global market, clear aligners and their adjunctive therapies are a well desired treatment alternative to fixed orthodontic appliances.[3] As clear aligner adjunct therapies continue to be prescribed by clinicians, it is important to better understand these devices. Although literature shows clinical observations and patient reports, future research is needed to show the measurable effects clear aligner adjunct therapies may have on patient experience and treatment efficacy.

Clear aligner therapy utilizes clear plastic trays to provide tooth-moving forces, as well as tooth-colored attachments to improve dental retention.[4] Patients treated with clear aligner therapy must be carefully monitored to assess if their teeth are moving in the right direction, with respect to their determined treatment plan. The concept of accurately achieving predicted tooth positions is called "aligner tracking."[5] An assessment of clinically acceptable tracking includes the clear aligner tray presenting with a close-fit where the teeth are completely

seated.[4] If the actual position of the teeth does not match the predicted position, the treatment is considered to be not tracking. Tracking errors are noted when teeth are not seated within the plastic tray, forming a gap between the tooth and the tray.[6] Previous studies evaluated tracking by comparing the difference of actual and predicted tooth positions as a method to assess aligner treatment accuracy.[7, 8] A lack of clear aligner tracking will compromise the result of orthodontic treatment. Tracking problems can be attributed to a variety of reasons including the trays not being fully seated, a lack of tray compliance, distorted trays, broken or missing tray attachments, distortions in impression or scans, and restrictions of the tray material.

Clear aligner adjunct therapies have been created to overcome observed tracking problems and increase patient comfort during treatment. Examples of adjunctive therapies include commercial products such as "Chewies®" and "PULSystem®." These products are available to consumers on the market and used by orthodontists to aid in seating and removing clear aligners. Chewies (Dentsply Sirona Raintree Essix, Sarasota, FL) (Figure 1) are cotton-roll shaped styrene copolymer accessories which are prescribed to assist with fully seating clear aligner trays.[9] If a gap is visible between the tray and teeth, these log-shaped accessories can be used by patients to focus on an area to achieve tray-seating, with the aim of improving tracking.[9] Bowman et al. also described how this product was utilized to achieve specific dental movements and improve the predictability of orthodontic treatment.[9] PULSystem (PUL Technologies, San Francisco, CA) (Figure 2) is a hook-cushion hybrid made of polycarbonate and thermoplastic polyurethane. This appliance has been purported by the manufacturer to facilitate the seating of clear aligner trays by biting on the cushion, as well as aiding in aligner removal by using the hook to engage and remove the aligner.[10]

Dental pain and soreness are well-known side effects of orthodontic movement. Orthodontic pain has a reported prevalence of 72-100% and is thought of as a combination of ischemia, inflammation, and edema. [11, 12] Non-steroidal anti-inflammatory drugs (NSAIDs) are reported as the most successful way of reducing orthodontic pain by targeting the inflammatory mediators.[13] Biting pressure is also believed to cause a temporary displacement of teeth, alleviating orthodontic pressure and relieving pain. This phenomenon is referred to as the "bite wafer" effect.[14] Farzanegan et al. conducted a randomized clinical trial to evaluate the pain management in patients with fixed orthodontic appliances. The study found that both chewing gum and viscoelastic bite wafers are effective for pain reduction in orthodontic patients and can be recommended as suitable substitutes for ibuprofen.[15]

Clear aligner adjunct therapies have been observed to play a role in pain management in a similar manner. Penn, the founder of "Munchies", summarized an unpublished pilot study conducted by Sharp and Dove which focused on an dental-anatomy specific adjunct device ("Munchies", EOCA MD Pty Ltd, New South Wales, Australia). The unpublished study purportedly found that 70% of patients using the adjunct therapy with clear aligners reported pain relief induced by the "bite wafer effect".[14] This conclusion was referenced in a featured article published by the Postgraduate School of Dentistry (Double Bay, Australia) however, the pilot study was not found when the published literature was searched.[14] It is unclear how pain relief was measured and if a control group was used as comparison. The lack of peer-reviewed publications on clear aligner adjuncts warrants further investigation on orthodontic treatment effects.

The purpose of this study was to assess if clear aligner adjunct therapies on the market produce a clinically measurable effect on treatment comfort and efficacy of tooth movement. The findings of this study will allow orthodontists to better understand the effects adjunct therapies can have on clear aligner tray tracking and patient experience. The first aim of this study was to investigate if adjuncts affected reported pain in the first week of each tray (week 1), the last week of each tray (week 2), and overall pain after the first four trays used of comprehensive aligner treatment. A second aim was to test if adjuncts play a role in clear aligner treatment compliance and satisfaction. A third aim was to test if these adjuncts affected the efficacy of tooth movement by testing for group differences in clear aligner tracking. The null hypotheses are as follows:

1. There were no significant differences in overall and daily pain scores for i) cotton-roll shaped adjuncts ii) hook-cushion shaped adjuncts.
2. There were no significant differences in i) compliance and ii) satisfaction scores amongst adjunct and control groups.
3. There were no significant differences in tray efficacy/tooth movement amongst adjunct and control groups.

Figure 1. "Chewies", Dentsply Sirona Raintree Essix, Sarasota, FL. Image captured at OHSU Orthodontic Clinic.

Figure 2. "PULSystem", PUL Technologies, San Francisco, CA. Image downloaded from thepultool.com.

II. Materials and Methods

The protocol for this study was approved by the Oregon Health & Science University (OHSU) Institutional Review Board (Appendix A). This was a randomized prospective study that involved patients who presented to OHSU Orthodontics Clinic for orthodontic clear aligner treatment.

Subject Selection

Patients who presented for clear aligner treatment were screened for eligibility to participate in this study. Eligibility inclusion criteria were individuals between 18-75 years old and Cervical Vertebral Maturation (CVM) stage 4 and higher, who desired clear aligner treatment. [16] Additionally, each individual's treatment plan did not include elastic wear or interproximal tooth reduction (IPR) for the period of this research. Exclusion criteria were individuals whose treatment plan included inter-arch elastic wear for the period of this research (first four aligner trays) or dental extractions. Additional exclusion criteria included individuals with clenching/grinding habits, relatively very short clinical crowns, and females who were pregnant during treatment.

When patient records were evaluated for treatment planning, eligibility for participating in this study was also determined. Those who met the criteria were recruited for the study using the Subject Recruitment Script (Appendix B) during the treatment consultation appointment. Subject recruitment occurred at the Oregon Health & Science University School of Dentistry (OHSU) in Portland, OR. If the subject chose to participate, then informed consent (Appendix C) and survey data were

collected. If the patient declined participation, then any data collected for the purposes of the study were destroyed immediately.

Experimental Groups

This study focused on three groups A) cotton-roll shaped adjuncts (Chew, Figure 1), B) hook-cushion hybrid adjuncts (Pul, Figure 2), and C) no adjuncts (control). The cotton-roll shaped adjuncts were available in OHSU Orthodontics Department. The hook-cushion hybrid adjuncts were provided by the manufacturer for the purposes of this study. Both devices are also available direct-to-consumer on numerous online platforms. Participants were given their respective appliances, along with instructions on how to use them. Subjects had the option to keep the devices after the study.

Subjects were randomly assigned to Group Chew, Group Pul, or control (CG) group. Group Chew subjects were provided the cotton-roll shaped adjuncts with written instructions (Figure 3) on how to use these. Group Pul subjects were provided the hook-cushion hybrid adjuncts with written instructions (Figure 4) on how to use these, while (CG) subjects were provided no adjunct appliance. Subjects were also verbally instructed on how to use appliance, if applicable, and how to assess tray tracking.

Data Collection

The data collected for this study were: pre-treatment subject demographics including age, sex, and Angle's classification; pre-treatment and post-tray 4 (V2) survey responses (see below for details), and intra-oral digital scans.

Depression Survey: Patient Health Questionnaire-9 (PHQ9) (Appendix D)

The PHQ9 is a validated nine-question measure for depression severity in the past two weeks. Items were scored on a four-point Likert scale of "0 = not at all," "1 = several days," "2 = more than half the days," and "3 = nearly every day." The level of depression was defined by a total score of 0-4 for minimal depression, 5-9 for mild depression, 10-14 for moderate depression, 15-19 for moderately severe depression, and 20-27 for severe depression. [17, 18] The PHQ9 was developed by Kroenke et al. and downloaded from and internet site (Pfizer US Pharmaceuticals, New York, NY). [17, 19]

Anxiety Survey: General Anxiety Disorder-7 (GAD7) (Appendix E)

The GAD7 is a validated seven-question measure for anxiety severity in the past two weeks. Items were scored on a four-point Likert scale of "0 = not at all", "1 = several days", "2 = more than half the days", and "3 = nearly every day." The total scores were defined as 0-4 for minimal anxiety, 5-9 for mild anxiety, 10-14 for moderate anxiety, and 15-21 for severe anxiety. [20, 21] The GAD7 was developed by Spitzer et al. and downloaded from and internet site (Pfizer US Pharmaceuticals, New York, NY). [19, 21]

Somatization/Physical Symptoms: Patient Health Questionnaire-15 (PHQ15) (Appendix F)

The PHQ15 is a validated 15-question measure for somatic symptoms in the past four weeks. Items were scored on a three-point Likert scale of "0 = not bothered", "1 = bothered a little", and "2 = bothered a lot." The total scores were defined as 0-4 for minimal, 5-9 for mild, 10-14 for moderate, and 15-30 for severe levels of somatization. [22, 23] The PHQ15 was developed by Kroenke et al. and downloaded from and internet site (Pfizer US Pharmaceuticals, New York, NY). [19, 23]

Pain Survey (Appendix G)

The modified McGill Pain Questionnaire is a validated three-part survey to assess orthodontic pain.[24] The first part contained 15-items on various aspects of pain scored on a four-point Likert scale of "0 = no pain", "1 = mild pain", "2 = moderate pain", and "3 = severe pain." The second part asked subjects to mark the severity of their pain using a visual analog scale for the range "no pain" to "worst pain possible." Part three included a ranking of current pain level from "0 = no pain", "1 = little pain", "2 = moderate pain", "3 = bad pain", "4 = horrible pain", and "5 = extreme pain." [24, 25] This survey was be used to assess daily pain while subjects wore aligner trays as well as overall pain during the study.

Compliance Survey (Appendix H)

The compliance questionnaire is a two-part survey that was used to assess the subject's clear aligner wear compliance throughout the study. The first part (Appendix H1) was a daily question with a sliding bar from 0 to 24 hours a day. The second part (Appendix H2) was an overall assessment of daily and weekly wear with a similar sliding bar responses for hours per day and days per week, respectively. Additionally, any free response comments were collected at the end.

Satisfaction Survey (Appendix I)

The satisfaction questionnaire is a two-part survey that was used to assess subject satisfaction for the duration of the study that was modified from Miller et al. which in turn was adapted from validated Geriatric Oral Health Assessment Index.[2] The first part was derived from a validated survey to assess subject satisfaction while using aligners. It contained four items ranked on a five-point Likert scale of "1=never", "2=seldom",

"3=sometimes", "4=often", and "5=always." [2] The second part included five modified customer effort score survey questions used to assess other aspects of subject satisfaction. The items were scored on a seven-point Likert scale of "1=strongly disagree", "2=disagree", "3=somewhat disagree", "4=neutral", "5=somewhat agree", "6=agree", and "7=strongly disagree. For experimental Chew and Pul groups there were three additional items that assess subject satisfaction of the adjunct appliance and likelihood to recommend the appliance.

Angle's Classification

The subjects were identified as Class I, II, or III dental malocclusion using Angle's classification of malocclusion. [26]

Intra-oral Pre-treatment Scan

Pre-treatment scans were captured using an iTero® intra-oral scanner optical impression device (Model: iTero Element, Align Technology, San Jose, CA). The scans were sent to a company (Align Technology, San Jose, CA) for treatment planning overseen by OHSU clinical personnel. These scans were downloaded from the company database.

Intra-oral Post-Tray4 Scan

Post- tray 4 (Visit 2) scans were captured using an intra-oral scanner (Mode: iTero Element, Align Technology, San Jose, CA or Model: S1AP, S2AP, 3Shape Trios, Copenhagen, Denmark). The scans were downloaded and imported to digital dental model software (*Ortho Insight 3D® Motionview Software LLC, Hixon, TN)* for analysis.

Subject Activities

Subject surveys were utilized for data collection of PHQ-9, GAD-7, PHQ-15, reported pain, satisfaction, and compliance. Surveys were provided to the subjects via an online platform, approved for use at OHSU (Qualtrics, Provo, UT). Surveys were completed at OHSU or at each subject's home. Subjects' study activities were categorized as the following:

- **Records appointment**
    - Treatment records screened for potential subject eligibility
- **Consultation appointment**
    - Subject recruitment script and subject consent form (Appendix B and C)
    - Pre-treatment Data Collection - PHQ9, GAD, and PHQ15 Qualtrics surveys (Appendix J)
- **Visit (V) 1: Delivery appointment –**
    - Appliance Instructions – Provided instruction forms, if applicable (Figures 3, 4, 5)
    - Quick Response (QR) code provided to access daily surveys (Figure 6)
- **Between V1 and V2 appointments (Eight weeks) -**
    - Subjects wore each tray for two weeks
    - Daily pain, compliance, and satisfaction surveys completed (Appendix K)
    - Reminders were sent if no survey data were collected in a 48-hour window
- **V2 (post-tray 4) appointment** –
    - Progress assessment intraoral scan was captured
    - V2 PHQ-9, GAD-7, and PHQ-15 online surveys (Appendix J)
    - Overall pain, compliance and satisfaction surveys completed (Appendix L).

Data Analysis of Treatment Efficacy

Treatment efficacy was determined by assessing the differences in position of the canines and incisor teeth when compared to predicted positions of the teeth after Tray 4. The subject's intra-oral scans from V2 (post trays 4) were downloaded as a Steriolithography (STL) file and labeled as "post". Maxillary (MX) occlusal and mandibular (MD) occlusal views were each derived as a portable network graphics (png) file, giving a two-dimensional view of the occlusion. The predicted occlusal positions for timepoint tray 4 were captured as png files from a cloud-based commercial software (*ClinCheck Pro® 6.0, Align Technology, San Jose, CA)* used for clear aligner treatment planning. These images were labeled as "Pred." Each subject had a total of four png files: MXPost, MXPred, MDPost, and MDPred. This study had a total of 40 png images.

Images were analyzed using a custom-built computer program (MATLAB *2019, The MathWorks Inc., Natick, Massachusetts)*. The computer program was developed to quantify tooth movement after the wearing of trays 1-4, for comparison with predicted movement using the four image files for each subject. On each image four pre-measured reference points were added to allow the computer program to calibrate for scale differences between predicted and post-tray 4 images (Figure 7). Following the scaling protocol, the custom computer program provided prompts to identify sequential images for digitization (Appendix M). The program calculated the difference between actual and predicted tooth positions by providing a ΔX and ΔY absolute values for 3 points on each of the canines and incisors. The points chosen were those that were reproducible on the distal-occlusal surface, mesial-occlusal surface, and cingulum area of each tooth (Appendix M). ΔX values represented a change parallel to the

transverse axis of the dental arch (horizontal axis of the image) and ΔY values represented a change parallel to the anteroposterior axis (vertical axis of the image) (Figure 7). Absolute values were averaged for each tooth, creating ΔX and ΔY averages that were utilized to estimate the tooth position differences between post-tray 4 and predicted treatment images. The detailed steps can be found in the scan labeling protocol in Appendix N.

Statistical Analysis

Means, standard deviations, and ranges were calculated for PHQ9, GAD7, PHQ15, pain, compliance, and satisfaction total scores. ANOVA and Tukey's post hoc tests determined if there were significant group differences in pre-treatment vs. post-tray 4 survey data and post-tray 4 vs. predicted tooth position differences. Kruskal-Wallis tests were used to test for group differences in reported compliance. T-tests were used to analyze for group differences in reported daily pain, and Chi-squared tests were used to identify group differences in overall pain and satisfaction. Statistical significance was set at $\alpha = 0.05$. Effect size and power were calculated for the sample. Intraclass correlation coefficient was calculated to determine intra-rater reliability. Software was used for statistical analyses (R version 4.2.1 (2022-06-23), R Core Team, Auckland, New Zealand) and graphical figures (Microsoft® Excel version 16.38, Microsoft Corporation, Redmond, Washington).

CAAT Study

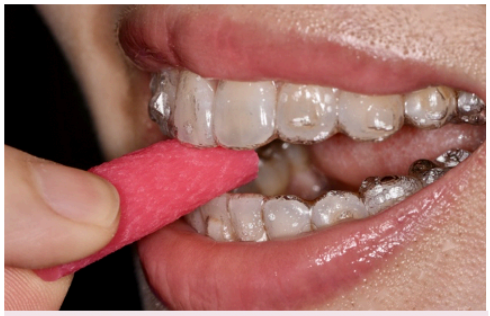
Thank you for volunteering to be a part of our project.

Today you were provided with **4 clear aligner trays**. Please make sure to:

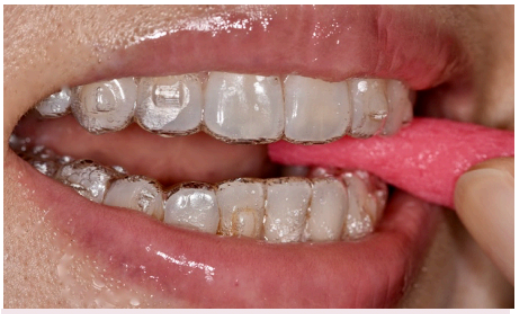
- Wear the trays at least **22 hours** a day.
- Wear each tray for **14 days**.
- Use the **Chewies** when seating your trays.
- Complete the **daily survey.**

How to use the Chewies:

When **seating** the aligner trays, use the Chewies by biting on the appliance. **Bite solidly between your teeth for 10-15 seconds, release, and repeat.** Move from your front teeth and work your way to your back teeth. If you see a gap in the tray, make sure to chew on the chewies until the tray is seated all the way.



Bite down in the front to seat the tray all the way.



Bite around to the back to seat the tray all the way.

Images captured at OHSU Orthodontics and used with patient's permission.

Figure 3. Instruction handout for Chew group.

CAAT Study

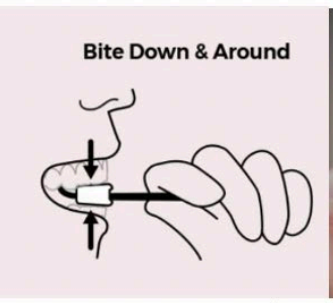
Thank you for volunteering to be a part of our project.

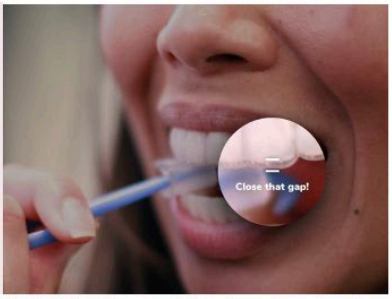
Today you were provided with **4 clear aligner trays**. Please make sure to:

- Wear the trays at least **22 hours** a day.
- Wear each tray for **14 days**.
- Use the **PulSystem** when seating your trays.
- Complete the **daily survey.**

How to use the PulSystem:

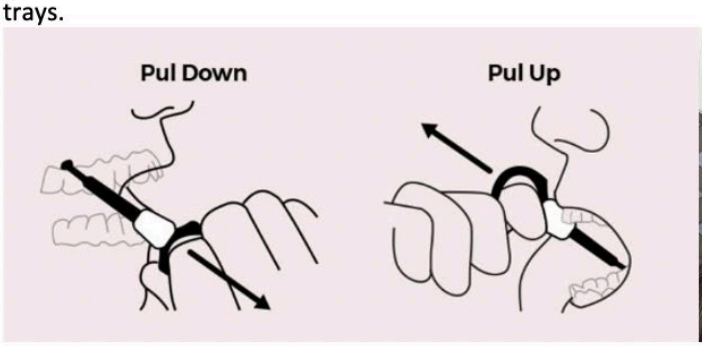
When **seating** the aligner trays, use the PulSystem by biting on the end of the appliance. **Bite solidly between your teeth for 10-15 seconds, release, and repeat.** Move from your front teeth and work your way to your back teeth. If you see a gap in the tray, make sure to bite on the PulSystem until the tray is seated all the way.





Images included with permission from thepultool.com

When **removing** the aligner trays, use the hook of the PulSystem to engage and remove the trays.



Images included with permission from thepultool.com

Figure 4. Instruction handout for Pul group.

CAAT Study

Thank you for volunteering to be a part of our project.

Today you were provided with **4 clear aligner trays**. Please make sure to:

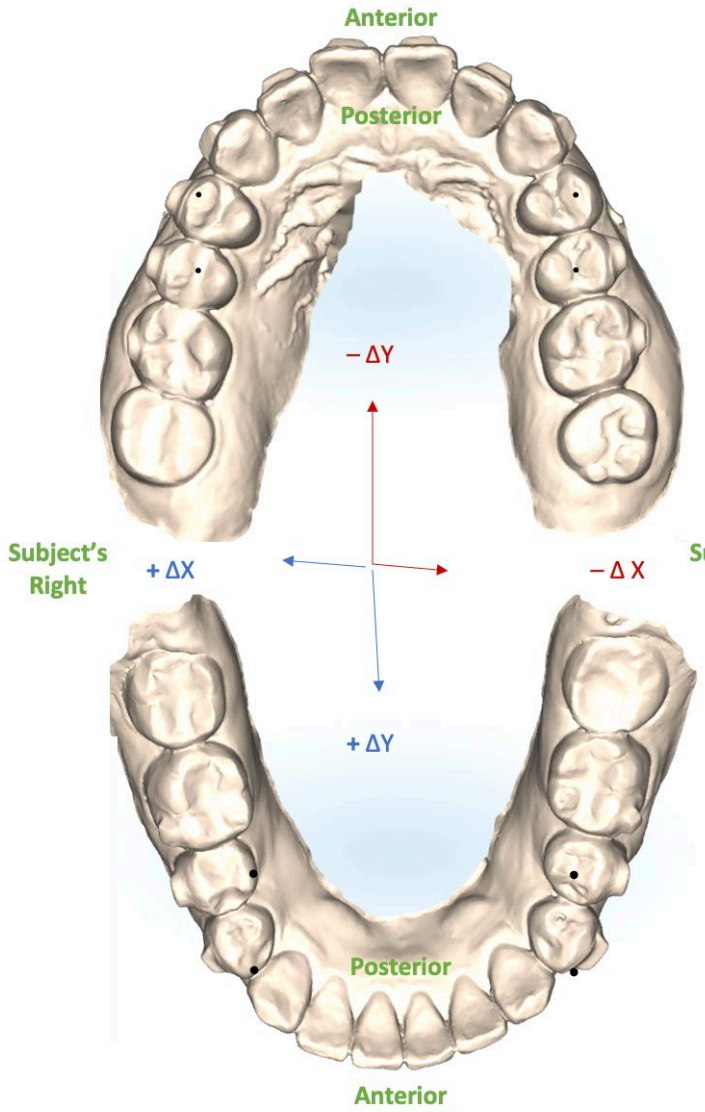
- Wear the trays at least **22 hours** a day.
- Wear each tray for **14 days**.
- Complete the **daily survey.**

Figure 5. Instruction handout for control group.

CAAT Study

Please complete your daily survey!

Figure 6. Quick Response (QR)



For upper teeth:

+ΔX = image's left/subject's right
-ΔX = image's right/subject's left
+ΔY = top of image/ anterior of teeth
-ΔY = bottom of image/posterior of teeth

For lower teeth:

+ΔX = image's left/subject's right
-ΔX = image's right/subject's left
+ΔY = top of image/ posterior of teeth
-ΔY = bottom of image/anterior of teeth

Figure 7. Prediction and Post-tray 4 Image Orientation.

III. Results

Eleven subjects met inclusion criteria, gave informed consent, and were enrolled in the study. One subject was not included in the study due to insufficient survey responses. Subjects were randomly assigned to three groups. Three subjects were assigned to the Chew group, four subjects to the Pul group, and three subjects to the control group (CG). Mean age ± standard deviation for the groups at study enrollment were 49 ± 23 years for Chew, 54 ± 12 years for Pul, and 43 ± 10 years for the CG. There were no significant age differences between the groups (p=0.65, Table 1). The percent of females in each group was 100% female for the Chew group, 75% female for the Pul group, and 100% female for the CG (Table 1). The percent of Angle's class II vs. class I malocclusion in each group was 67% vs. 33% in the Chew group, 25% vs 75% in the Pul group, and 0% vs. 100% in the CG (Table 1).

PHQ-9, GAD-7, and PHQ-15 Survey Analysis (Table 2)

Pre-treatment and post-tray 4 PHQ-9 scores were not significantly different between Chew, Pul, and control groups (p=0.16 and p=0.27, respectively, Figure 8). All three groups' pre- and post-tray 4 mean scores indicated minimal depression (Chew group pre: 0±0 and post: 1±1, Pul group pre: 4±3 and post: 5±3, CG pre: 3±4 and post: 3±3).

Pre-treatment and post-tray 4 GAD-7 scores were not significantly different between Chew, Pul, and control groups (p=0.34 and p=0.19, respectively, Figure 9). Chew and control groups' pre- and post-tray mean scores indicated minimal anxiety, while the Pul group's mean scores indicated mild anxiety (Chew group pre: 1±2 and post: 2±4, Pul group pre: 6±4 and post: 7±5, CG pre: 4±3 and post: 4±6).

There were significant differences in pre-treatment PHQ15 scores between Chew and Pul groups compared to the control group ($p<0.001$ and $p<0.05$, respectively, Figure 10). Post-tray 4 PHQ-15 scores were not significantly different between Chew, Pul, and control groups ($p=0.08$ and $p=0.24$, respectively, figure 10). The Chew group's pre and post-tray, as well as the Pul group's pre-treatment mean PHQ-15 scores indicated minimal somatization. The Pul group's post-tray, and the CG's pre- and post-tray mean scores indicated mild somatization. (Chew group pre: 2±2 and post: 3±3, Pul group pre: 4±1 and post: 5±4, CG pre: 8±3 and post: 8±1).

Pain Analysis

All groups reported overall low levels of pain during Trays 1 through 4 (Table 3). Although the Chew and Pul groups reported lower levels of pain when compared to the control group, the differences were not statistically significant ($p=0.69$). The modified McGill pain questionnaire measured the intensity of various aspects of pain by using the following terms: pressure, sore, aching, throbbing, tight, cutting, burning, tingling, pulling, dull, uncomfortable, strange, frustrating, annoying, and miserable. Compared to the control group, the Chew and Pul groups reported significantly lower levels of 'frustrating' pain ($p<0.01$ and $p<0.05$, respectively) and the Pul group reported significantly lower levels 'strange' pain ($p<0.05$) (Figure 11). Although not statistically significant, the Chew and Pul groups reported lower levels of 'uncomfortable' and 'tight' pain compared to the control group (Figure 11).

Daily reported pain was consolidated into weekly averages for each subject. This allowed group comparisons of pain levels during wear of each aligner (trays 1-4) for the first

week compared to the second week. The Pul group showed a significant decrease in reported pain from the first week to the second week of aligner tray wear compared to the control group ($p<0.01$, Figure 12).

Compliance Analysis (Table 4)

All groups reported high compliance of days/week and hours/day of aligner wear, with no significant difference between Chew and Pul relative to CG (Chew: $p=0.23$ and $p=0.49$; Pul: $p=1.0$ and $p=0.17$, respectively). Chew reported 20 ±2 hours/day and 7 ±0 days/week, Pul reported 22 ±1 hours/day and 7 ±0 days/week, and the control reported 21 ±2 hours/day and 6 ±1 days/week compliance.

Satisfaction Analysis (Table 5)

Chew and Pul groups reported higher likelihoods to recommend aligner treatment and higher satisfaction with the aligner experience compared to the control group, although the differences were not statistically different ($p=0.10$ and $p=0.51$, respectively). Adjunct-use groups reported high likelihoods to recommend their appliances; the Chew group score was 7/10 and the Pul group score was 9/10.

Efficiency Analysis

The efficacy measurement was defined by differences between predicted tooth position vs. actual tooth position post-tray 4. Anteroposterior and transverse linear differences between predicted (ClinCheck Pro®) tooth positions points and post-tray 4 tooth

positions were computed for 3 points per tooth for the maxillary and mandibular anterior teeth by group (Tables 6 and 7). There were no significant differences between groups with respect to the x-axis (anteroposterior) tooth positions of mandibular and maxillary anterior teeth (Figure 13). There were no significant differences between groups with respect to the y-axis (anteroposterior) tooth positions of mandibular and maxillary anterior teeth. (Figure 14).

Intra-rater reliability was determined for the tooth tracking measurements. Intraclass correlation coefficient (ICC) was 0.82, indicating good reliability, as defined by ICC>0.75.[27] Given the low number of subjects recruited, the observed powers of all groups were less than 0.80 (Chew: 0.06 and Pul: 0.12). Based on the pilot data of efficacy of tooth movement, there was a medium effect size (Chew: 0.4; Pul: 0.5), indicating the potential for clinically significant findings when sufficient numbers of subjects participate. A power analysis indicated a required sample size of 56 subjects for Chew and 33 subjects for Pul to achieve a β of 0.80.

Table 1. Subject Demographics: Mean age, sex and malocclusion distribution. No significant age differences were found between the groups (p=0.65).

	Chew (N=3)	Pul (N=4)	CG (N=3)
Mean (Standard Deviation) Age in years at start of study	49 (23)	54 (12)	43 (10)
Number of Females (percent)	3 (100%)	3 (75%)	3 (100%)
Number of Males (percent)	0 (0%)	1 (25%)	0 (0%)
Number of Class I Malocclusions (percent)	1 (33.3%)	1 (25%)	3 (100%)
Number of Class II Malocclusions (percent)	2 (66.7%)	3 (75%)	0 (0%)

Table 2. Mean (Standard Deviation) total scores for surveys pre and post-tray 4 and category for each mean total score. Pre-treatment and post-tray 4 PHQ-9 scores were not significantly different between Chew, Pul, and control groups (p=0.16 and p=0.27, respectively). Pre-treatment and post-tray 4 GAD-7 scores were not significantly different between Chew, Pul, and control groups (p=0.34 and p=0.19, respectively). There were significant differences in pre-treatment PHQ15 scores between Chew and Pul groups compared to the control group (p<0.001 and p<0.05, respectively). Post-tray 4 PHQ-15 scores were not significantly different between Chew, Pul, and control groups (p=0.08 and p=0.24, respectively).

	Chew (N=3)	Pul (N=4)	CG (N=3)
PHQ9 Score			
Pre-Tx	0 (0) minimal	4 (3) minimal	3 (4) minimal
Post-Tx	1 (1) minimal	5 (3) minimal	3 (3) minimal
GAD7 Score			
Pre-Tx	1 (2) minimal	6 (4) mild	4 (3) minimal
Post-Tx	2 (4) minimal	7 (5) mild	4 (6) minimal
PHQ15 Score			
Pre-Tx	2 (2)*** minimal	4 (1)* minimal	8 (3) mild
Post-Tx	3 (3) minimal	5 (4) mild	8 (1) Mild

Note: $^{***}p \leq 0.001$, $^{**}p \leq 0.01$, $^{*}p \leq 0.05$

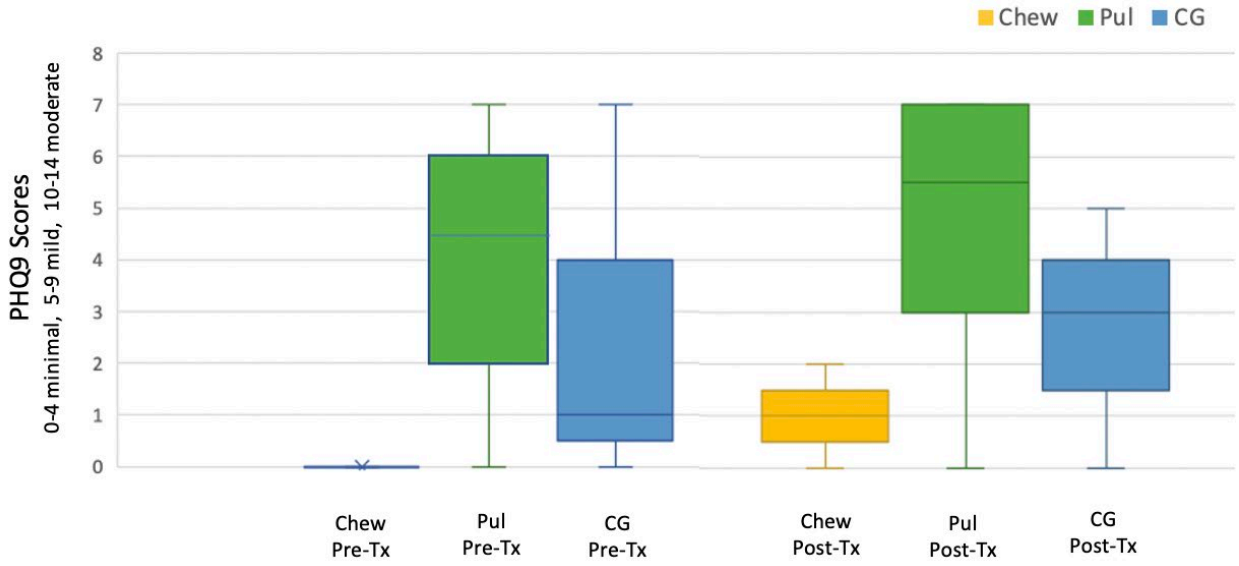


Figure 8. Pre and post-tray 4 Patient Health Questionnaire-9 total scores. Lines in box plot indicate median value for the data set. Pre-treatment and post-tray 4 PHQ-9 scores were not significantly different between Chew, Pul, and control groups (p=0.16 and p=0.27, respectively).

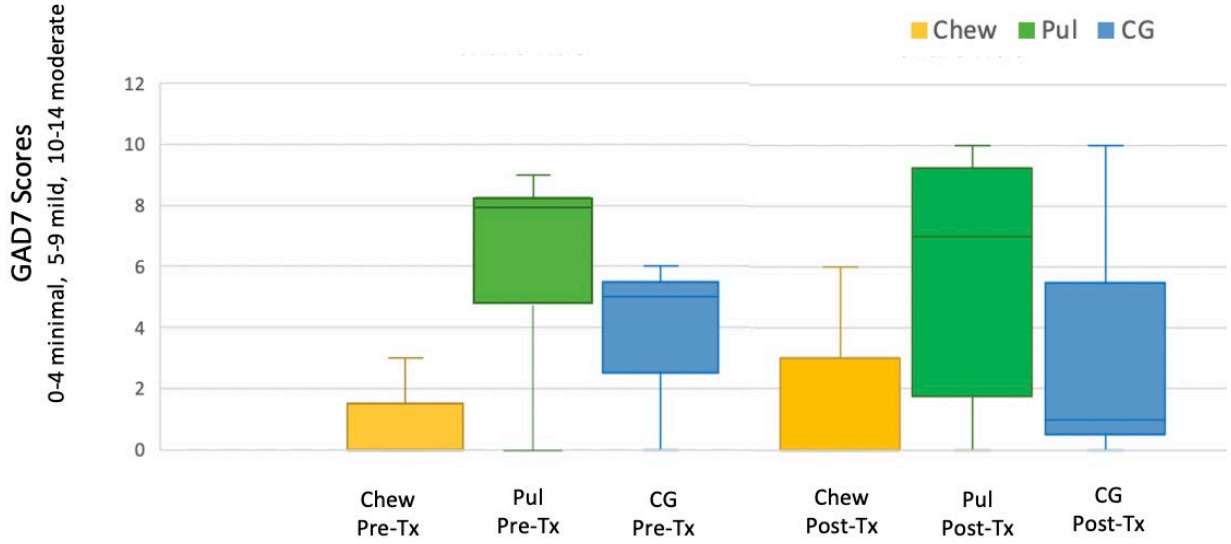


Figure 9. Pre and post-tray 4 General Anxiety Disorder-7 total scores. Lines in box plot indicate median value for the data set. Pre-treatment and post-tray 4 GAD-7 scores were not significantly different between Chew, Pul, and control groups (p=0.34 and p=0.19, respectively).

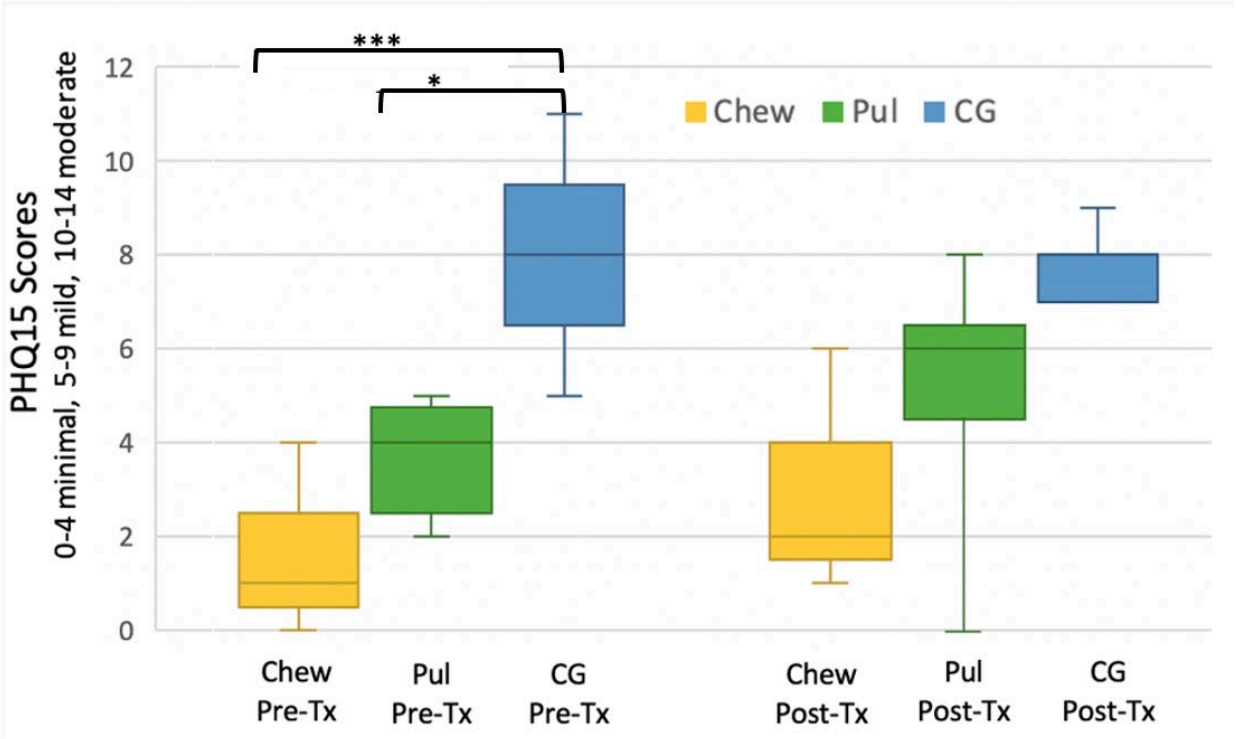


Figure 10. Pre and post-tray 4 Patient Health Questionnaire-15 total scores. Lines in box plot indicate median value for the data set. There were significant differences in pre-treatment PHQ15 scores between Chew and Pul groups compared to the control group ($p<0.001$ and $p<0.05$, respectively). Post-tray 4 PHQ-15 scores were not significantly different between Chew, Pul, and control groups ($p=0.08$ and $p=0.24$, respectively).
Note: $^{***}p \leq 0.001$, $^{**}p \leq 0.01$, $^{*}p \leq 0.05$

Table 3. Overall reported pain. All groups reported overall low levels of pain during trays 1-4. Although Chew and Pul groups reported lower levels of pain when compared to the control group, the differences were not statistically significant ($p=0.687$).

	Chew (N=3)	Pul (N=4)	CG (N=3)
No Pain	33%	50%	0%
Little Pain	67%	50%	100%
Moderate Pain	0%	0%	0%
Bad Pain	0%	0%	0%
Horrible Pain	0%	0%	0%
Extreme Pain	0%	0%	0%

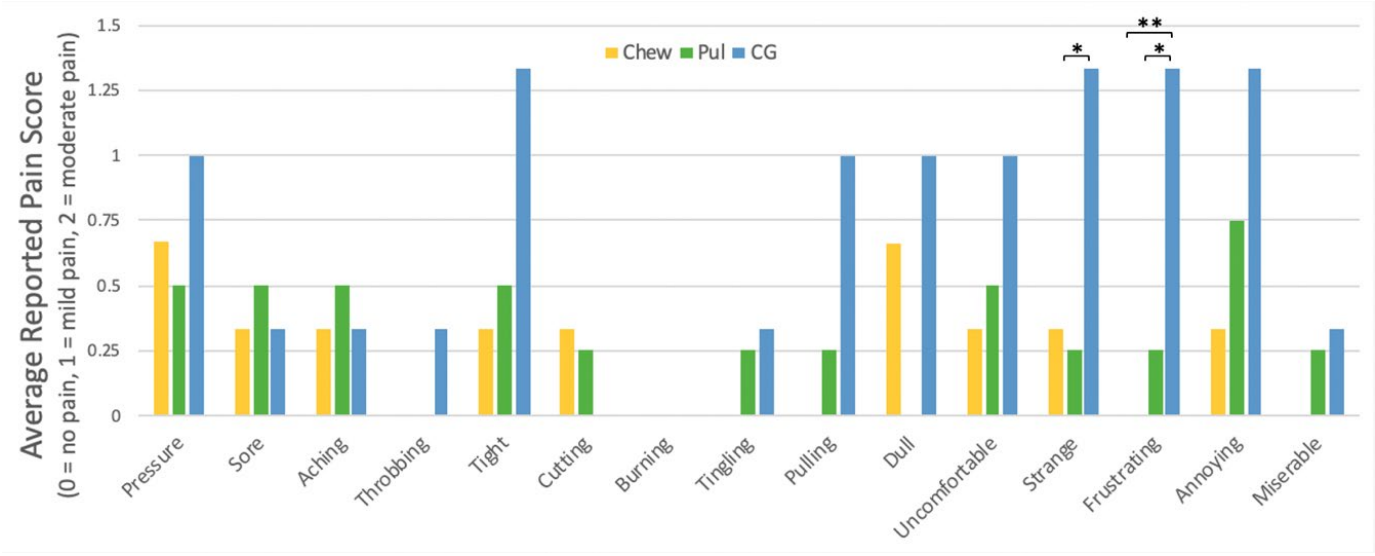


Figure 11. Overall average reported pain scores from modified McGill pain questionnaire for the three groups. When compared to the control group, Chew and Pul groups reported significantly lower levels of 'frustrating' pain ($p<0.01$ and $p<0.05$, respectively) and the Pul group reported significantly lower levels 'strange' pain ($p<0.05$).
Note: $^{***}p \leq 0.001$, $^{**}p \leq 0.01$, $^{*}p \leq 0.05$

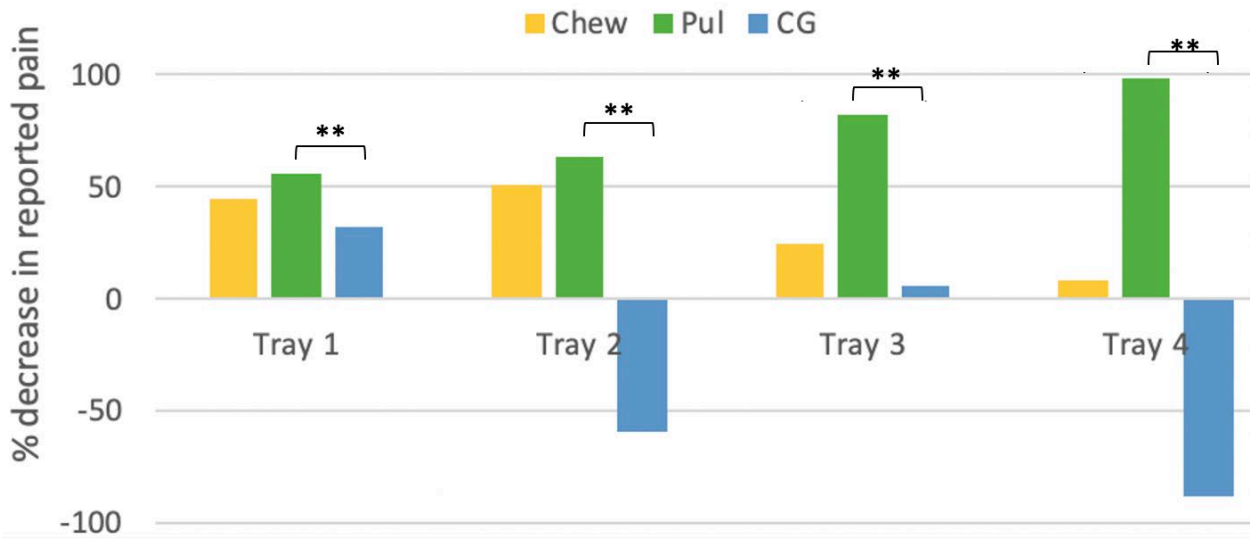


Figure 12. Average percent decreases in reported daily pain between weeks 1-2 of each aligner tray wear for three groups. The Pul group showed a significant decrease in reported pain from the first week to the second week of aligner tray wear compared to the control group for all four trays ($p<0.01$).
Note: $^{***}p \leq 0.001$, $^{**}p \leq 0.01$, $^{*}p \leq 0.05$

Table 4. Overall reported compliance. All groups reported high compliance of days/week and hours/day of aligner wear, with no significant differences between Chew and Pul groups relative to CG (Chew: p=0.23 and p=0.49; Pul: p=1.0 and p=0.17, respectively).

	Chew (N=3)	Pul (N=4)	CG (N=3)
Days worn per week			
Mean (SD)	7 (0)	7 (0)	6 (1)
Median [Min, Max]	7 (7, 7)	7 (7, 7)	7 (5, 7)
Hours worn per day			
Mean (SD)	20 (2.)	22 (1)	21 (2)
Median [Min, Max]	20 (18, 22)	23 (20, 23)	20 (20, 23)

Table 5. Overall reported satisfaction. The Chew and Pul groups reported higher likelihoods to recommend aligner treatment and a higher satisfaction with aligner experience compared to the control group, although the difference is not statistically different (p=0.10 and p=0.51, respectively). Chew and Pul reported high likelihoods to recommend their adjunct appliances.

	Chew (N=3)	Pul (N=4)	CG (N=3)
I would recommend aligner treatment to a friend.			
Strongly Disagree	0%	0%	0%
Somewhat Disagree	0%	0%	0%
Neither Agree or Disagree	0%	0%	33%
Somewhat Agree	0%	25%	67%
Strongly Agree	100%	75%	0%
I am satisfied with my aligner experience.			
Strongly Disagree	0%	0%	0%
Somewhat Disagree	0%	0%	0%
Neither Agree or Disagree	0%	0%	33%
Somewhat Agree	0%	25%	33%
Strongly Agree	100%	75%	33%
How likely are you to recommend the adjunct appliance out of 10?			
	7 ± 5	9 ± 1	

Table 6. Mandibular anterior tooth position efficacies, showing means and standard deviations for average ΔX (transverse) and ΔY (anteroposterior), where positive and negative ΔX values indicate differences to the left and right of the subject, respectively, and positive and negative ΔY values differences indicate anterior and posterior, respectively.

	chewy				pul				control			
	delta x		delta y		delta x		delta y		delta x		delta y	
	average	Stdev	average	Stdev	average	Stdev	average	Stdev	average	Stdev	average	Stdev
LL3	-0.07	0.17	0.10	0.21	0.05	0.18	0.18	0.21	0.04	0.25	0.08	0.26
LL2	-0.04	0.07	-0.03	0.15	0.08	0.12	0.02	0.03	0.02	0.17	-0.04	0.10
LL1	0.09	0.98	0.02	0.06	0.08	0.13	0.11	0.12	0.09	0.12	0.05	0.04
LR1	-0.08	0.07	-0.14	0.14	-0.09	0.14	0.02	0.06	0.01	0.23	0.05	0.26
LR2	-0.11	0.23	-0.16	0.25	-0.24	0.3	-0.08	0.24	0.11	0.25	0.00	0.23
LR3	-0.09	0.20	-0.07	0.28	-0.13	0.24	-0.29	0.22	-0.05	0.16	-0.06	0.08

Table 7. Maxillary anterior tooth position efficacies, showing means and standard deviations for average ΔX (transverse) and ΔY (anteroposterior), where positive and negative ΔX values indicate differences to the left and right of the subject, respectively, and positive and negative ΔY values differences indicate posterior and anterior, respectively.

	chewy				pul				control			
	delta x		delta y		delta x		delta y		delta x		delta y	
	average	Stdev	average	Stdev	average	Stdev	average	Stdev	average	Stdev	average	Stdev
UR3	-0.02	0.13	-0.08	0.05	0.00	0.06	-0.07	0.14	0.12	0.21	0.11	0.05
UR2	0.02	0.08	-0.02	0.12	-0.09	0.09	-0.01	0.22	0.05	0.16	0.05	0.05
UR1	-0.06	0.05	0.07	0.25	-0.01	0.04	-0.14	0.12	0.02	0.06	-0.02	0.03
UL1	-0.27	0.15	-0.16	0.21	-0.20	0.20	-0.21	0.29	-0.11	0.10	-0.21	0.16
UL2	-0.32	0.26	-0.39	0.09	-0.27	0.37	-0.30	0.20	-0.20	0.11	-0.16	0.13
UL3	-0.34	0.09	-0.11	0.06	-0.21	0.26	-0.19	0.32	-0.16	0.16	-0.12	0.12

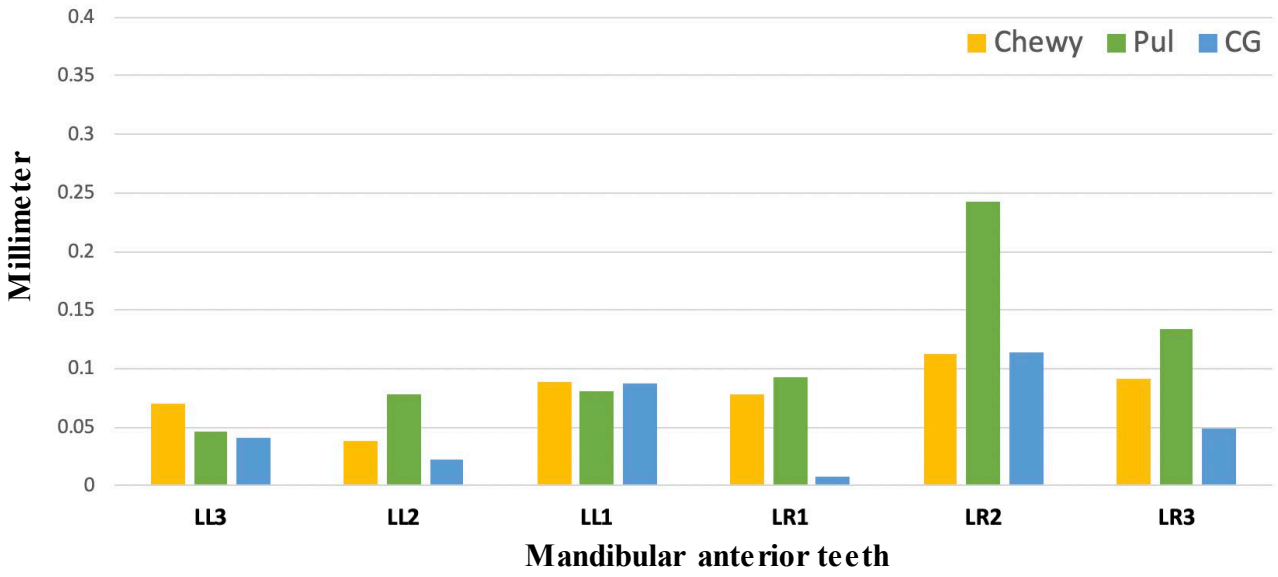


Figure 13a. Mandibular anterior teeth absolute value differences in the x-axis for predicted tooth positions points and post-tray 4 tooth position. There were no significant difference between groups in transverse tooth positions.

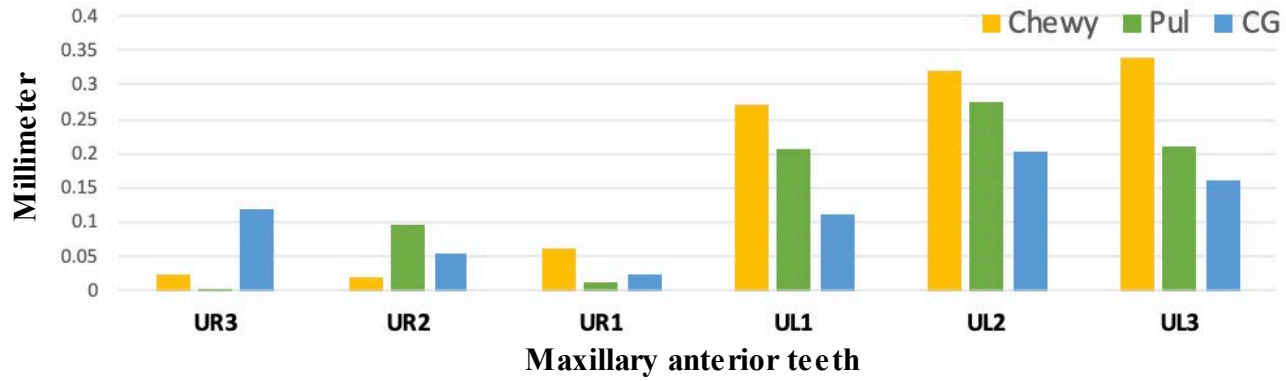


Figure 13b. Maxillary anterior teeth absolute value differences in the x-axis for predicted tooth positions points and post-tray 4 tooth position. There were no significant difference between groups in transverse tooth positions.

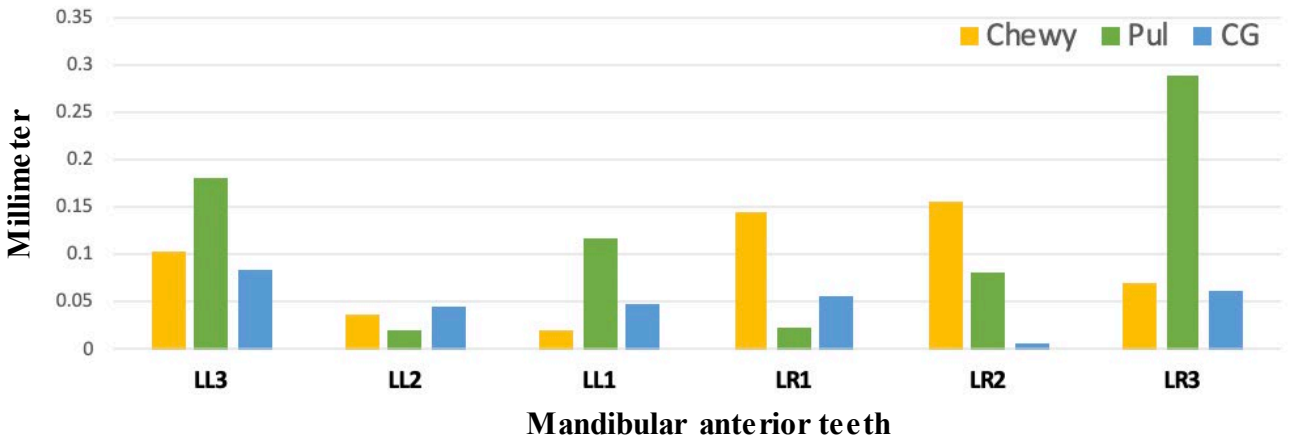


Figure 14a. Mandibular anterior teeth absolute value differences in the y-axis for predicted tooth positions points and post-tray 4 tooth position. There were no significant differences between groups with respect to the anteroposterior tooth positions.

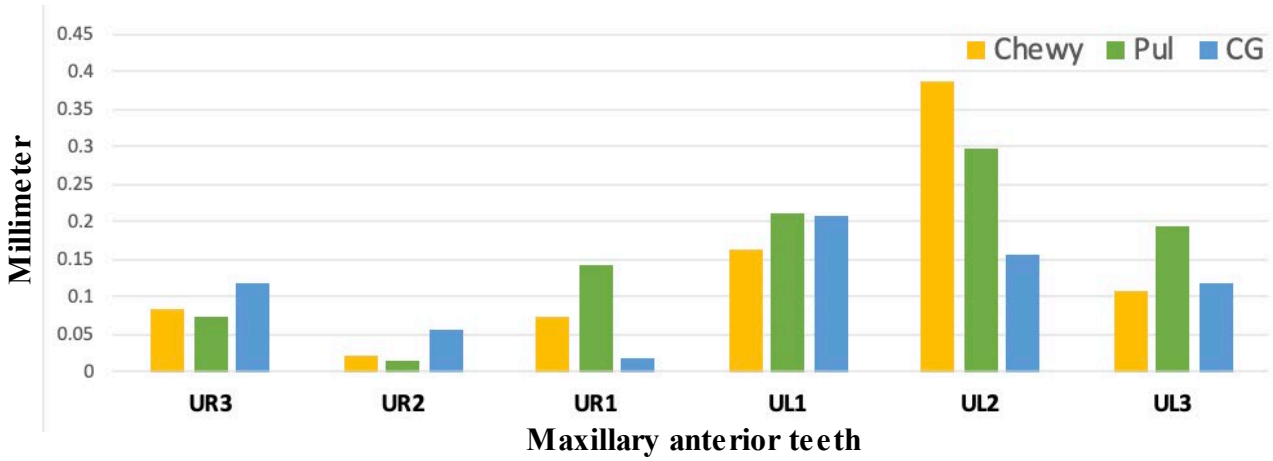


Figure 14b. Maxillary anterior teeth absolute value differences in the y-axis for predicted tooth positions points and post-tray 4 tooth position. There were no significant differences between groups with respect to the anteroposterior tooth positions.

IV. Discussion

The aim of this study was to evaluate if clear aligner adjunct therapies affected subject's treatment experience and efficacy. Experience was assessed by subject's reported pain, compliance, and satisfaction. Treatment efficacy was estimated by comparing actual tooth positions to those predicted during treatment planning. Designing a prospective study was critical to control treatment prescription and adequately evaluate our variables, but proved difficult for subject recruitment within the targeted timeframe of nine months. The number of subjects enrolled was insufficient for clinical application of our findings. However the data collected shows direction for future investigation.

Remarkable emotional or physical stresses can alter one's perception of pain.[28, 29] For this reason, it was important to collect pre-treatment depression, anxiety, and somatization information which may play a role in orthodontic pain interpretation. The pre-treatment data were also measured after tray 4 to ensure that no significant changes occurred during the time of this study. Mean PHQ-9 and GAD-7 scores showed no significant differences between groups and timepoints. This indicated that depression and anxiety were unlikely to contribute to pain level differences. The Chew group had a significantly higher mean PHQ-15 score at pre-treatment, when compared to the Pul and control groups ($p<0.001$ and $p<0.05$, respectively). However, mean post-tray 4 PHQ-15 scores showed no significant differences in somatization scores across all three groups. Although somatization scores displayed variance pre-treatment, it is of value to note that all scores were either "minimal somatization" or "mild somatization."

When asked to assess overall pain during the first four trays of treatment, all three groups reported low levels with no significant difference. However, when asked to rate the

intensity of different aspects of pain, both Chew and Pul groups reported significantly lower levels of 'frustrating' pain ($p<0.01$ and $p<0.05$, respectively), and Pul group reported significantly lower levels 'strange' pain ($p<0.05$) compared to the control group. Chew and Pul groups also described lower levels of 'uncomfortable' and 'tight' pain when compared to the control group, though not significantly different. In addition, the rate of decrease in daily pain was analyzed across the three study groups. Pul group exhibited significantly decreased reported pain from the first week to the second week of aligner tray wear when compared to the control group ($p<0.01$). These findings warrant future examination of all aspects of pain with an increased sample size and standardized PHQ-15 scores, to determine whether adjunct therapies aid in clinically improved comfort during aligner therapy.

Chewing forces have been shown to aid in inflammatory pain relief during orthodontic movement. [12, 15] The findings of this study corroborate this and show that adjunct appliances decreased the intensity of reported pain. Furthermore, this research exhibits that use of clear aligner adjuncts, such as hook-cushion hybrid adjuncts (PULsystem), may decrease reported pain at a faster rate during orthodontic treatment compared to aligner treatment without the use of adjuncts. An adjunct therapy that decreases pain intensity and duration would have important clinical relevance in clear aligner treatment. Future research is needed to substantiate this discovery.

Adjunct therapies did not increase or decrease subject willingness to comply or satisfaction with treatment. Chew, Pul, and control groups showed high compliance of aligner tray wear with no significant differences. Chew, Pul, and control groups also showed high satisfaction with aligner treatment. Although Chew and Pul reported higher likelihoods to

recommend aligner treatment and higher satisfaction with aligner experience than the control group, the differences were not statistically different.

Clear aligner efficacy in tooth movement was estimated by evaluating the differences amongst predicted vs. post-tray 4 tooth positions. Predicted and actual tooth positions were not significantly different for all three groups. The interpretation of the data should be done with caution given that the method used to evaluate tray efficacy has limitations. Firstly, two-dimensional images were used to analyze dental movements. It was difficult to ensure that the same projection angle relative to the occlusal plane. A minor difference in the angle between the two images would cause magnification and rotation discrepancies. Secondly, the occlusal view of the dentition limited evaluation to the anteroposterior (y-axis) and transverse (x-axis) positions of the teeth. The vertical position of the teeth is another dimension in which tracking is vital, and these missing data may have contributed to additional errors in the tracking data. Thirdly, prediction scans (ClinCheck Pro®) lacked dental anatomy when compared to the post-tray 4 scans. This made it difficult to assess distinct, reproducible dental features when labeling points on the images.

Future investigations should utilize superimposition of three-dimensional predicted and post-tray 4 scans, in order to avoid the limitations of the technique used in the current study. This method facilitates control for magnification error in three planes of space. Literature has compared the efficacy of clear aligner treatment and found that it is not accurate at bodily dental movement, expansion, extrusion, and torque expression.[30-33] Three-dimensional superimposition of study files would have facilitated an examination of the ability of clear aligner adjunct therapies to improve efficacy of specific dental movements.

The small sample size was the greatest limitation of this research. With a larger subject pool, subjects' pre-treatment survey data could have been considered when randomly distributing subjects into groups. This would have controlled for group difference in pre-treatment and post-tray 3 depression, anxiety, and somatization scores. Additionally, power analysis and significant differences would have been more clinically relevant. In addition, due to the daily time commitment from subjects and the programmatic time constraints, this study investigated a limited sequence of aligner trays. An extended study that allowed for more treatment trays may have shown more applicable tracking efficiency outcomes. It is also likely that four trays is not enough time to show patient treatment satisfaction differences. Additionally, subjects did not report if they used additional pain-relieving medications to treat orthodontic-associated discomfort. These data should be collected and reported in future studies to confirm that pain relief can be attributed to adjunct use.

V. Conclusions

In this prospective clinical pilot study, the following conclusions were made:

1. i. Cotton-roll shaped adjuncts were associated with significantly lower scores of frustrating pain compared to a control group.

   ii. Hook-cushion hybrid adjuncts showed significantly lower scores of frustrating and strange pain, and faster decreases in pain during early aligner tray wear compared to a control group.

2. i. There were no significant differences between adjunct and control groups in aligner wear compliance.

   ii. Although adjunct groups reported higher satisfaction compared to control, there were no significant differences between groups.

3. There were no significant differences between adjunct and control groups in clear aligner tracking efficacy.

VI. Comprehensive Literature Review

Clear Aligner Therapy

Clear aligners are removable tooth positioning appliances fabricated from plastic. They are designed to form a tight-fit around dentition and sequentially displace them into a more desired position. Although once used to treat mild malocclusions, novel approaches have allowed clear aligners to be utilized for a greater range of malocclusion.[4]. As demand for clear aligner therapy increases, research allows us to understand the benefits and restrictions of this modality.

Clear Aligner Fabrication

Aligner trays can be fabricated manually, digitally, or a combination of the both. The manual technique utilizes multiple models, separation of teeth, reposition of teeth in wax, and suctioning vacuum-formed aligners.[1] Digitally, CAD-CAM technology allows virtual dental repositioning and sequencing of orthodontic movement. Once the orthodontic stages are set, stereolithography files are produced and the aligners are 3D printed.[1] Clear aligners may also be fabricated using a combination of both techniques. For example, orthodontists may digital treatment plan orthodontic movements and then 3D print models to use for manual fabrication of the vacuum-formed aligners. Aligners can be fabricated in varying thickness, commonly being 0.02, 0.025, or 0.030 inch trays.[1] For Invisalign specifically, it was reported that trays varied from 0.566 to 0.644 mm thickness.[34]

Clear Aligner Biomechanics

In order to achieve dental movements, aligner trays must have a relatively high stiffness in order to clasp dentition and apply an orthodontic force. Aligners utilize tooth-colored

composite attachments to provide a handle for trays to better grip onto.[4]. Attachment size, shape, and location can vary depending on the goal movement to be achieved, such as extrusion, intrusion or rotation. These additions allow clear aligner therapy to better apply force as well. Aligner trays can vary in shape and thickness to create different forces through pressure points and power ridges. [1] Clear aligner treatment may also utilize bondable buttons/hooks, elastics, temporary anchorage devices, and other appliances to successful correct malocclusions. On average, Invisalign prescribes each aligner to include 0.25 to 0.33mm of movement.[32]

Due to their removable nature, aligner trays must be carefully monitored to ensure successful tracking of treatment. An assessment of clinically acceptable tracking includes the clear aligner tray presenting with a close-fit where the trays are completely seated.[4] A lack of clear aligner tracking will compromise the result of orthodontic treatment. Tracking problems can be attributed to a variety of reasons, including the trays not being fully seated when worn by the patient, a lack of tray compliance, distorted trays, and broken or missing tray attachments.

Effectiveness of Clear Aligners

Clear aligner therapy is a relatively novel appliance in orthodontics. Naturally, literature shows varying conclusions on aligner effectiveness and efficiency, some of which directly contradict each other. As the technology continues to develop, further research must be conducted to clarify these results.

Borda et al. assessed teenagers undergoing orthodontic treatment and found that fixed appliance therapy had more treatment and emergency visits when compared to clear aligner

treatment. Additionally, they found that clear aligner treatment had improved alignment, overjet, and occlusion when compared to that of fixed appliances.[35] However, a systematic review conducted by Ke et al. concluded that aligners were less effective as improving occlusion and in facilitating torque dental movements when compared to fixed appliances.[30]

Buschang et al. explored total treatment time in both treatment modalities and found that aligner patients spent 67% less time in treatment, attributed to fixed appliances requiring more time in the finish and detail stage.[36] They also concluded that clear aligner patients required less chair time during their appointments.[36]

A systematic review focused on the effectiveness of Invisalign treatment concluded that aligners were successful at leveling, tipping, and derotating teeth, but ineffective with bodily movement and expansion.[31] Kravitz et al. considered anterior Invisalign effectiveness and found that extruding anterior teeth was the less accurate movement of aligners, while lingual constriction was the most accurate.[32] Roughly a decade later, they investigated Invisalign's effectiveness in full dentition treatment and found that buccal-lingual crown tip was the most effective movement.[33]

Patient Satisfaction and Compliance

Miller et al. conducted a prospective, longitudinal cohort study involving 60 adult orthodontic patients (33 with Invisalign aligners, 27 with fixed appliances) and investigated functional, psychosocial, and pain-related outcomes. They found that those treated with aligners reported less pain and fewer negative impacts on their lives during the first week of orthodontic treatment when compared to fixed appliances.[2] Ke et al. found clear aligner treatment to have a significantly shorter treatment time when compared to fixed treatment.[30]

Fixed appliances are a well-known bacterial plaque trap, increasing the risk of caries and periodontal disease. Azaripour et al. investigated patients of both treatment modalities and found that those treated with fixed appliances reported significantly more gingival irritation. Those treated with clear aligners reported increased quality of life, less laughing inhibition, less change to eating habits, and increased dental brushing frequency.[37]

As mentioned previously, a large factor in clear aligner treatment success is compliance with tray wear to ensure expression of dental movement. Timm et al. aimed to investigate the factors that may influence aligner wear compliance. Although other literature state the females tend to be more compliant than males, they concluded that males were significantly more compliant, along with those who did not have previous orthodontic treatment.[38] In a subsequent article, Timm el al. found that with the introduction of electronic reminders, poor compliance decreased from 24.47% to 9.32%.[39]

Current Clear Aligner Market

As of 2021, the global clear aligner market was estimated at $2.85 billion USD with a projection to grow to $10.04 billion by the end of 2028.[3] The increased demand for esthetic treatment and technological development play a large role in this prediction, despite the current economic climate and high cost of treatment. Global Market Insights estimate most aligners costing $4,000-5,000 a case.[40] Surveys show that the increase in adults seeking treatment is attributed to the availability of clear aligner therapy and lingual braces.(fortune) Currently, the market is majorly dominated by Align Technology, Inc. (Invisalign) and Institut Straumann AG (ClearCorrect).[3]

Clear Aligner Adjunct Therapies

Clear aligner adjunct appliances have been developed in hopes of overcoming tracking problems, facilitating dental movements, and reducing pain. A few adjunct appliances on the market include Chewies, PULSystem, Movemints, Outie Tool, Munchies, and Orthokey. The role these adjunct appliances have in pain management is described in the "Pain Management in Orthodontics" section of this paper.

Chewies are cotton-roll styrene copolymers that were made the help patients seat their clear aligner trays. Bowmen et al., the inventor of Chewies, describes the following appliance prescription to aid in seating aligner trays: "the patient bites down repeatedly on the soft Chewies, each the size of a cotton roll, for several minutes a day to help seat the aligners, especially as each new pair is started. Chewies are also prescribed when an air gap develops at the incisal edges. In that case, the Chewie should be positioned directly over the affected region to focus the chewing forces, with the patient holding the device solidly between the teeth for 10-15 seconds, releasing, and repeating for about five minutes twice a day."[9] The article also describes Chewie use to address anterior open bites by biting on the appliance to increase intrusive posterior forces.[9] It is important to note that this article is based on anecdotes and further research is needed to confirm these theories.

The PULSystem is a hook-cushion hybrid appliance made of polycarbonate and thermoplastic polyurethane.[10] This appliance combines the benefits of the chewy-like seating appliance with a removing hook, to allow patients to improve both tray seating and removal. Clear aligner trays must be frequently removed for patients to eat, drink, or clean their teeth. Since clear aligner trays have a high stiffness and tight dental fit to express dental movements,

patients may find it difficult the remove their trays and the PULSystem is marketed to decrease the difficulty.

Pain in Orthodontics

Dental pain is a well-known side effect of orthodontic treatment and not only includes the sensation of pain, but also the perception and interpretation of the pain. Orthodontic pain has a reported prevalence of 72-100% and is thought of as a combination of ischemia, inflammation, and edema. [11, 12] To better understand orthodontic pain, one must understand pain pathways and management.

Cellular Components of Orthodontic Pain

When a dentition undergoes orthodontic movement, the side of the root that is 'pulled' experiences tension and the side the force is 'pushing' towards experiences compression and thus ischemia. The local ischemia causes the release of nitric oxide from periodontal cells and triggers the neural pathway of pain sensation. Additionally, recruited leukocytes release chemotaxins and inflammatory mediators to stimulate blood vessel dilation and local inflammation. [11] This process ultimately leads to M1 macrophage promotion of bone resorption and successful alveolar remodeling.[41] As local inflammation intensifies, the pain sensation pathways are further stimulated.

Neural Components of Orthodontic Pain

Nociception, or the sensation of pain, occurs with the stimulation the spinothalamic pain pathway. This pathway utilizes myelinated Að-nerve fibers (fast pain sensation) and unmyelinated C-nerve fibers (delayed pain sensation). [42] These fibers are activated through noxious stimuli and once the pain threshold is reached, they trigger a cascade of events. Once

the two afferent nerve fibers are stimulated, the dorsal horn of the spinal cord is activated and signals the central nervous system.[42] In orthodontics, the neurons activated are in the trigeminal ganglia and synapse at the trigeminal nucleus caudalis of the medulla oblongata and ultimately the nucleus caudate of the thalamus. From here, the thalamus projects to other areas of the pain instigating pain perception.[11]

Interpretation of Orthodontic Pain

Once nociception is processed in other areas of the cortex, unpleasant feelings generate. Pain from tooth movement can be described as dull, sore, pressure and uncomfortable.[11] Facial muscles can be stimulated to produce expressions of discomfort, such as grimacing and closing eyelids.[11] In rats, it has been show that orthodontic movement causes emotional stress indicated by increased anxiety, discomfort, and aggression, as well as decreased explorative behaviors.[43] It is likely that orthodontic patients experience similar emotional stresses.

While pain can induce distress, emotional stresses, such as depression, can also alter the perception of pain. Thompson et al. conducted a meta-analysis of 32 studies and concluded that the modality of the pain is a factor on if depression affected pain interpretation. Specifically, they found that depression lead to a decreased pain threshold (increased pain) during ischemic-induced pain, such as that seen in orthodontics.[28] Anxiety can also alter pain interpretation. Hermesdorf et al. found that among depressed patients, the increased severity of anxiety symptoms served as a predictor for increased pain sensitivity.[29] Decreased pain threshold can lead to allodynia, pain by nonpainful stimuli, and hyperalgia, painful stimuli hurt

even more. The intricate relationship of nociception and psychology is complex, and important in pain management.

Gate Control Theory

Pressure, vibration, and other kinds of sensation play a role in decreasing pain perception. This can be demonstrated when one experiences acute pain, such as a paper cut. The painful sensation decreases when the finger is shaken, rubbed, or run under cold-water, all reactions humans may immediately do after a painful stimulus. This phenomenon can be explained through Gate Control Theory. The non-noxious stimuli, such as rubbing, stimulate mylineated Aß-nerve fibers. These fibers meet nociceptive nerves at a "gate" in the dorsal root ganglion and inhibit the pain transmission to the central nervous system.[44]

Pain Management in Orthodontics

To manage the pain during orthodontics, the cellular or neural aspects of the pain pathway must be target. NSAIDs are reported as the most successful way of reducing orthodontic pain by targeting the inflammatory mediators.[13] It is also believed that displacing teeth facing orthodontic forces can temporarily resolve the ischemic area and lead to pain relief.[12] Farzanegan et al. investigated this concept by conducting a randomized clinical trial to evaluate the pain management in patients with fixed orthodontic appliances. The study found that both chewing gum and viscoelastic bite wafers are effective for pain reduction in orthodontic patients and can be recommended as suitable substitutes for ibuprofen.[15]

Biting pressure is believed to cause a temporary displacement of teeth, causing a "Gate Control" effect by stimulating non-nociceptive nerve fibers. In turn, this decreases perceived pain. This phenomenon is also referred to as the "Bite Wafer Effect." Additionally, chewing

forces are believed to induce normal vascular and lymphatic flow, which In turn relieves the inflammatory pain.[45] Clear aligner adjunct therapies have been observed to play a role in pain management in a similar manner. Penn, the founder of "Munchies", summarized a pilot study conducted by Sharp A. and Dove E. which focused on the anatomically specific adjunct device ("Munchies", EOCA MD Pty Ltd, New South Wales, Australia). The study found that 70% of patients using the adjunct therapy with clear aligners reported pain relief.[14] They found the ideal prescription for Munchies to be 3-4 minutes of posterior chewing every 6-8 hours in order to find pain relief. [14] The methods and data from the pilot study were not found during this literature review. Reported conclusions are unclear whether pain relief experience was compared to a control group.

VII. References

1. Tamer I, Oztas E, Marsan G. Orthodontic Treatment with Clear Aligners and The Scientific Reality Behind Their Marketing: A Literature Review. Turk J Orthod 2019;32(4):241-46.
2. Miller KB, McGorray, S. P., Womack, R., Quintero, J. C., Perelmuter, M., Gibson, J., Dolan, T. A., & Wheeler, T. T. . A comparison of treatment impacts between Invisalign aligner and fixed appliance therapy during the first week of treatment. . American journal of orthodontics and dentofacial orthopedics 2007;131(3):302.
3. . Clear aligners market size, Share, growth: Global forecast [2028. Market Research Report Fortune Business Insights. Fortune Business Insights; 2021.
4. Proffit WR, Fields, H. W., & Sarver, D. M. . Contemporary orthodontics. Sixth ed. St. Louis, Mo: Mosby Elsevier; 2007. p. 290, 316-19.
5. Hansa I, Katyal V, Ferguson DJ, Vaid N. Outcomes of clear aligner treatment with and without Dental Monitoring: A retrospective cohort study. American Journal of Orthodontics and Dentofacial Orthopedics 2021;159(4):453-59.
6. Bowman SJ. Improving the predictability of clear aligners. Seminars in Orthodontics 2017;23(1):65-75.
7. D'Antò V, Bucci R, De Simone V, et al. Evaluation of Tooth Movement Accuracy with Aligners: A Prospective Study. Materials 2022;15(7):2646.
8. Al-Nadawi M, Kravitz ND, Hansa I, et al. Effect of clear aligner wear protocol on the efficacy of tooth movement:A randomized clinical trial. The Angle Orthodontist 2020;91(2):157-63.
9. Bowman SJ, Celenza F, Sparaga J, et al. Creative adjuncts for clear aligners, part 2: Intrusion, rotation, and extrusion. J Clin Orthod 2015;49(3):162-72.
10. THEPULTOOL®.
11. Long H, Wang Y, Jian F, et al. Current advances in orthodontic pain. Int J Oral Sci 2016;8(2):67-75.
12. Furstman L BS. Clinical considerations of the periodontium. . American journal of orthodontics and dentofacial orthopedics 1972;61:138-55.
13. Ngan PW HU, Yin C. . The effect of ibuprofen on the level of discomfort in patients undergoing orthodontic treatment. . American journal of orthodontics and dentofacial orthopedics 1994;106:88-95.
14. Penn D. The Bite Wafer Effect: The Use of a Viscoelastic Appliance in the Management of Orthodontic Pain with Sequential Aligner Therapy. PG Dental School; 2016.
15. Farzanegan F, Zebarjad SM, Alizadeh S, Ahrari F. Pain reduction after initial archwire placement in orthodontic patients: a randomized clinical trial. Am J Orthod Dentofacial Orthop 2012;141(2):169-73.
16. McNamara JA, Jr., Franchi L. The cervical vertebral maturation method: A user's guide. Angle Orthod 2018;88(2):133-43.
17. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16(9):606-13.
18. Kurt Kroenke MD RL, Spitzer M. . The PHQ-9 : A New Depression Measure. . Psychiatr Ann [Internet] 2002(32):1-7.
19. PfizerInc. "https://www.phqscreeners.com/terms".

20. Lowe B, Decker O, Muller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. Med Care 2008;46(3):266-74.
21. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166(10):1092-7.
22. Kocalevent RD, Hinz A, Brahler E. Standardization of a screening instrument (PHQ-15) for somatization syndromes in the general population. BMC Psychiatry 2013;13:91.
23. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. Psychosom Med 2002;64(2):258-66.
24. Iwasaki LR, Freytag LE, Schumacher CA, Walker MP, Williams KB. Validation of a modified McGill Pain Questionnaire for orthodontic patients. Angle Orthod 2013;83(5):906-12.
25. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30(2):191-97.
26. Angle EH. Classification of Malocclusion Dental Cosmos 1899;41(3):248-64.
27. Koo TK LM. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. Journal of Chiropractic Medicine. 2016;15(2):155-63.
28. Thompson T, Correll CU, Gallop K, Vancampfort D, Stubbs B. Is Pain Perception Altered in People With Depression? A Systematic Review and Meta-Analysis of Experimental Pain Research. J Pain 2016;17(12):1257-72.
29. Hermesdorf M, Berger K, Baune BT, et al. Pain Sensitivity in Patients With Major Depression: Differential Effect of Pain Sensitivity Measures, Somatic Cofactors, and Disease Characteristics. J Pain 2016;17(5):606-16.
30. Ke Y, Zhu Y, Zhu M. A comparison of treatment effectiveness between clear aligner and fixed appliance therapies. BMC Oral Health 2019;19(1):24.
31. Papadimitriou A, Mousoulea S, Gkantidis N, Kloukos D. Clinical effectiveness of Invisalign® orthodontic treatment: a systematic review. Progress in Orthodontics 2018;19(1):37.
32. Kravitz ND, Kusnoto B, BeGole E, Obrez A, Agran B. How well does Invisalign work? A prospective clinical study evaluating the efficacy of tooth movement with Invisalign. Am J Orthod Dentofacial Orthop 2009;135(1):27-35.
33. Haouili N, Kravitz ND, Vaid NR, Ferguson DJ, Makki L. Has Invisalign improved? A prospective follow-up study on the efficacy of tooth movement with Invisalign. Am J Orthod Dentofacial Orthop 2020;158(3):420-25.
34. Mantovani E, Parrini S, Coda E, et al. Micro computed tomography evaluation of Invisalign aligner thickness homogeneity. Angle Orthod 2021;91(3):343-48.
35. Borda AF, Garfinkle JS, Covell DA, et al. Outcome assessment of orthodontic clear aligner vs fixed appliance treatment in a teenage population with mild malocclusions. Angle Orthod 2020;90(4):485-90.
36. Buschang PH, Shaw SG, Ross M, Crosby D, Campbell PM. Comparative time efficiency of aligner therapy and conventional edgewise braces. Angle Orthod 2014;84(3):391-6.
37. Azaripour A, Weusmann J, Mahmoodi B, et al. Braces versus Invisalign®: gingival parameters and patients' satisfaction during treatment: a cross-sectional study. BMC Oral Health 2015;15(1):69.
38. Timm LH, Farrag G, Baxmann M, Schwendicke F. Factors Influencing Patient Compliance during Clear Aligner Therapy: A Retrospective Cohort Study. Journal of Clinical Medicine 2021;10(14):3103.

39. Timm LH, Farrag G, Wolf D, Baxmann M, Schwendicke F. Effect of electronic reminders on patients' compliance during clear aligner treatment: an interrupted time series study. Scientific Reports 2022;12(1):16652.
40. . Clear Aligners Market Size Competitive Market Share & Forecast, 2022 – 2030. Global Market Insights; 2022. p. 105.
41. He D, Kou X, Yang R, et al. M1-like Macrophage Polarization Promotes Orthodontic Tooth Movement. Journal of Dental Research 2015;94(9):1286-94.
42. Yam MF, Loh YC, Tan CS, et al. General Pathways of Pain Sensation and the Major Neurotransmitters Involved in Pain Regulation. Int J Mol Sci 2018;19(8).
43. Yozgatian JH, Zeredo JL, Hotokezaka H, et al. Emotional stress- and pain-related behaviors evoked by experimental tooth movement. Angle Orthod 2008;78(3):487-94.
44. Merrick MA. 8 - Therapeutic Modalities As an Adjunct to Rehabilitation. In: Andrews JR, Harrelson GL, Wilk KE, editors. Physical Rehabilitation of the Injured Athlete (Fourth Edition). Philadelphia: W.B. Saunders; 2012. p. 104-42.
45. LW W. Pain and cooperation in orthodontic treatment. Journal of Clinical Orthodontics 1984;18:572-5.

VIII. Appendices

Appendix A. Oregon Health & Science University Institutional Review Board approval.

OREGON HEALTH & SCIENCE UNIVERSITY

IRB MEMO

Research Integrity Office
3181 SW Sam Jackson Park Road - L106RI
Portland, OR 97239-3098
(503)494-7887 irb@ohsu.edu

APPROVAL OF SUBMISSION

May 24, 2021

Dear Investigator:

On 5/24/2021, the IRB reviewed the following submission:

IRB ID:	STUDY00022928
Type of Review:	Initial Study
Title of Study:	Clear Aligner Adjunct Therapies: Effects on Tray Efficacy and Patient Experience
Principal Investigator:	Sohyon Kim
Funding:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• PHQ-15_2013-05-12-1.pdf • PHQ-9_2013-05-12-1.pdf • GAD-7_2013-05-12-1.pdf • HIPAA- Prep to Research Form _.docx • CAAT Study - Recruitment Scrupt.docx • Appliance Handouts.pdf • Compliance Survey.pdf • Modified McGill Pain Questionnaire.pdf • Satisfaction Survey.pdf • CAAT Study Protocol • Consent and Authorization Form

The IRB granted final approval on 5/24/2021. The study is approved until 5/23/2022.

Review Category: Expedited Category # 1, 4, 5, 7

Copies of all approved documents are available in the study's **Final** Documents (far right column under the documents tab) list in the eIRB. Any additional documents that require an IRB signature (e.g. IIAs and IAAs) will be posted when signed. If this applies to your study, you will receive a notification when these additional signed documents are available.

Ongoing IRB submission requirements:

Version Date: 06/30/2016 Page 1 of 2

- Six to ten weeks before the expiration date, you are to submit a continuing review to request continuing approval.
- Any changes to the project must be submitted for IRB approval prior to implementation.
- Reportable New Information must be submitted per OHSU policy.
- You must submit a continuing review to close the study when your research is completed.

Guidelines for Study Conduct

In conducting this study, you are required to follow the guidelines in the document entitled, "Roles and Responsibilities in the Conduct of Research and Administration of Sponsored Projects," as well as all other applicable OHSU IRB Policies and Procedures.

Requirements under HIPAA

If your study involves the collection, use, or disclosure of Protected Health Information (PHI), you must comply with all applicable requirements under HIPAA. See the HIPAA and Research website and the Information Privacy and Security website for more information.

IRB Compliance

The OHSU IRB (FWA00000161; IRB00000471) complies with 45 CFR Part 46, 21 CFR Parts 50 and 56, and other federal and Oregon laws and regulations, as applicable, as well as ICH-GCP codes 3.1-3.4, which outline Responsibilities, Composition, Functions, and Operations, Procedures, and Records of the IRB.

Sincerely,

The OHSU IRB Office

Version Date: 06/30/2016 Page 2 of 2

Appendix B. Subject recruitment script.

CAAT Study

Clear Aligner Adjunct Therapies: Effects on Tray Efficacy and Patient Experience

Participant Recruitment Script

My name is _____ and I want to speak to you about the opportunity to volunteer in the CAAT study. This study is run here in the OHSU Orthodontics Department and we think you would be a great candidate for it. It is completely voluntary and you may choose to leave the study at any time.

This study will be for the first 4 trays of your treatment. If you choose the participate, we may or may not give you an additional appliance to use with your trays. You will be asked to complete survey questions before, during, and after wearing the first 4 trays of your treatment. At the following appointment, we will do an additional iTero scan that will help us track your teeth after 4 trays of treatment. Does this sound like something you may be interested in?

If yes → I have a consent form here that we can go through together.

If no → Thank you for your time.

Appendix C. Subject consent form.

OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: _____

CLINICAL RESEARCH CONSENT AND AUTHORIZATION
SUMMARY OF KEY INFORMATION ABOUT THIS STUDY

TITLE: Clear Aligner Adjunct Therapies: Effects on Tray Efficacy and Patient Experience (CAAT Study)
PRINCIPAL INVESTIGATOR: Sohyon "Michelle" Kim, DMD, MS *(503) 494-5703*

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE:
The purpose of the study is to learn [more about adjunct therapies devices have a clinically measurable effect on clear aligner tray efficacy and patient satisfaction We are hoping to find out by using survey questionnaires and progress assessment scans.

DURATION:
Your participation in the study will consist of 2 visits over the next 2 months that are combined with your scheduled visits. It will add an additional 20 minutes to each appointment. We will ask to follow your health through the use of surveys during the use of your first 4 trays,

PROCEDURES:
If you decide to participate, you will be asked to answer survey questions and undergo a progress assessment iTero scan.

RISKS: This is a minimal risk study.

BENEFITS: You will not directly benefit from taking part in this research.

ALTERNATIVES: You may choose not to participate in this study, or participate in another study if one is available.

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

END OF CONSENT SUMMARY

OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: STUDY00022928

Research Consent and Authorization Form

TITLE: Clear Aligner Adjunct Therapies: Effects on Tray Efficacy and Patient Experience (CAAT Study)

PRINCIPAL INVESTIGATOR: Sohyon "Michelle" Kim, DMD, MS (503) 494-5703

CO-INVESTIGATORS: Pranita Ramanan, DDS (925) 452-7234

WHO IS PAYING FOR THE STUDY?: N/A

WHO IS PROVIDING SUPPORT FOR THE STUDY?: Oregon Health & Science University, School of Dentistry

DO ANY OF THE RESEARCHERS HAVE A CONFLICT OF INTEREST WITH THIS STUDY?: No

WHY IS THIS STUDY BEING DONE?:
You have been invited to be in this research study because you are receiving Invisalign treatment at the OHSU Department of Orthodontics. The purpose of this study is to see if adjunct therapies devices have a clinically measurable effect on clear aligner tray efficacy and patient satisfaction. This study will require two additional visits after today that will occur during the same time as your appointments. It will add a maximum of additional 20 minutes to the appointments. While using the trays, you will be asked to answer a few survey questions every day.

WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?

Activity	Purpose
Records	Records were collected for the purpose of elective Invisalign treatment. These records were evaluated to see if you are eligible for the research study.
Consultation (+20 minutes)	Patient Recruitment, Consent Discussion, Medical History and Medications, and Baseline Surveys collected

Delivery Appointment (+20 minutes)	Provide Instructions for appliance. Provide link for surveys.
4-Trays-Later Appointment (+20 minutes)	Rescan for Invisalign Progress Assessment

Daily survey questions will ask about treatment compliance, pain/discomfort, and satisfaction. It should take no more than 10 minutes to complete.

WILL I RECEIVE RESULTS FROM THE [TESTING] IN THIS STUDY?

We will give you the results of your Invisalign Progress Assessment scan.

If we discover information that is important for your health care, either in this study or in the future, we will contact you and ask if you want to know the results. If you choose to receive the results, you may need to have the test repeated in a non-research laboratory.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?:
The is a minimal risk study, Known risks include:

- You may be temporarily uncomfortable during the iTero Progress Assessment scan. If this occurs, you can inform the treating provider and adjustments can be made.
- You may feel frustrated by the number and frequency of survey questions. You may refuse to answer any of the questions that you do not wish to answer.

WHO WILL SEE MY PERSONAL INFORMATION?:
We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. [*If there are special precautions this study is taking to achieve this, describe here, e.g., collecting data anonymously or coding samples immediately so they are never identified.*]
We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE? and the WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

Under Oregon law, suspected child or elder abuse must be reported to appropriate authorities.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT? Study information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?:
There will be no cost to you or your insurance company to participate in this study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?:
If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact one of the study investigators

If you are injured or harmed by the study procedures, you will be treated. OHSU does not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.
If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

WHERE CAN I GET MORE INFORMATION?:
If you have any questions, concerns, or complaints regarding this study now or in the future, contact **Dr. Sohyon "Michelle" Kim** (503) 494-5703 **or Dr. Pranita Ramanan** (925) 452-7234.

This research has been approved and is overseen by an Institutional Review Board ("IRB"), a committee that protects the rights and welfare of research subjects. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.

- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

WHAT ARE MY RESPONSIBILITIES IN THIS STUDY?
If there are important instructions for the subject to follow during the study, list them here. Do not state 'you are required', or 'you must'. You may say 'You should' or 'We will ask you to…'

DO I HAVE TO TAKE PART IN THIS STUDY?
Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your provider.

The participation of OHSU students or employees in OHSU research is completely voluntary and you are free to choose not to serve as a research subject in this protocol for any reason. If you do elect to participate in this study, you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator's department, or your grade in any course.

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER?
If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. You can choose to withdraw from some or all of the optional parts of this study without withdrawing from the whole study. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Sohyon Michelle Kim
OHSU School of Dentistry
SDORTHO
2730 SW Moody Ave,
Portland, OR 97201
Email: kimmiche@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If in the future you decide you no longer want to participate in this research, we will remove your name and any other identifiers from your samples and information, but the material will not be destroyed and we will continue to use it for research.

You may be removed from the study if you cannot follow study instructions or if you are female and become pregnant.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Subject Printed Name	Subject Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Appendix D. *Depression PHQ9 survey downloaded from Pfizer Inc.[19], validated by Kroenke et al. [17]*

Patient Health Questionnaire - 9

Over the last 2 weeks, how often have you been bothered by the following problems?
Please place a check mark in the box to indicate your answer.

		Not at all	Several days	More than half the days	Nearly every day
		0	1	2	3
1.	Little interest or pleasure in doing things	☐	☐	☐	☐
2.	Feeling down, depressed, or hopeless	☐	☐	☐	☐
3.	Trouble falling or staying asleep, or sleeping too much	☐	☐	☐	☐
4.	Feeling tired or having little energy	☐	☐	☐	☐
5.	Poor appetite or overeating	☐	☐	☐	☐
6.	Feeling bad about yourself – or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
7.	Trouble concentrating on things, such as reading the newspaper or watching television	☐	☐	☐	☐
8.	Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	☐	☐	☐	☐
9.	Thinking that you would be better off dead or of hurting yourself in some way	☐	☐	☐	☐
TOTAL SCORE =					

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?			
Not difficult at all	Somewhat difficult	Very Difficult	Extremely difficult
☐	☐	☐	☐

Appendix E. Anxiety GAD7 survey downloaded from Pfizer Inc.[19], validated by Löwe et al.[20]

GAD - 7

Over the last 2 weeks, how often have you been bothered by the following problems? Place a check mark in the box to indicate your answer.

		Not at all	Several days	More than half the days	Nearly every day
		0	1	2	3
1.	Feeling nervous, anxious or on edge	☐	☐	☐	☐
2.	Not being able to stop or control worrying	☐	☐	☐	☐
3.	Worrying too much about different things	☐	☐	☐	☐
4.	Trouble relaxing	☐	☐	☐	☐
5.	Being so restless that it is hard to sit still	☐	☐	☐	☐
6.	Becoming easily annoyed or irritable	☐	☐	☐	☐
7.	Feeling afraid as if something awful might happen	☐	☐	☐	☐
TOTAL SCORE =					

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?			
Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

Appendix F. *Somatization/Physical Symptoms PHQ15 survey downloaded from Pfizer Inc.[19], validated by Kocalevent et al.[22]*

Patient Health Questionnaire-15: Physical Symptoms

During the last 4 weeks, how much have you have been bothered by any of the following problems? Please place a check mark in the box to indicate your answer.

		Not bothered	Bothered a little	Bothered a lot
		0	1	2
1.	Stomach pain	☐	☐	☐
2.	Back pain	☐	☐	☐
3.	Pain in your arms, legs, or joints (knees, hips, etc)	☐	☐	☐
4.	Menstrual cramps or other problems with your periods [women only]	☐	☐	☐
5.	Headaches	☐	☐	☐
6.	Chest pain	☐	☐	☐
7.	Dizziness	☐	☐	☐
8.	Fainting spells	☐	☐	☐
9.	Feeling your heart pound or race	☐	☐	☐
10.	Shortness of breath	☐	☐	☐
11.	Pain or problems during sexual intercourse	☐	☐	☐
12.	Constipation, loose bowels, or diarrhea	☐	☐	☐
13.	Nausea, gas, or indigestion	☐	☐	☐
14.	Feeling tired or having low energy	☐	☐	☐
15.	Trouble sleeping	☐	☐	☐
TOTAL SCORE =				

Appendix G1. Daily pain survey modified McGill Pain Questionnaire validated for orthodontic patients by Iwasaki et al.[24]

Modified McGill Pain Questionnaire (daily)

(Validated for orthodontic patients by Iwasaki et. al in Angle Orthodontist Vol 83, No 5, 2013)

The words below are sometimes used to explain how your mouth feels while you have clear aligners. Mark the column to indicate the level of pain you feel for each word.

	0 No Pain	1 Mild	2 Moderate	3 Severe
Pressure				
Sore				
Aching				
Throbbing				
Tight				
Cutting				
Burning				
Tingling				
Pulling				
Dull				
Uncomfortable				
Strange				
Frustrating				
Annoying				
Miserable				

Mark along this line to indicate how bad your pain is – the left of the line means no pain at all and the right end means worst pain possible.

No Pain ---------- Worst Pain Possible

Mark the space that best indicates your level of pain right now – only mark one.

0	No Pain	
1	Little Pain	
2	Moderate Pain	
3	Bad Pain	
4	Horrible Pain	
5	Extreme Pain	

Appendix G2. Overall pain survey modified McGill Pain Questionnaire validated for orthodontic patients by Iwasaki et al.[24]

Modified McGill Pain Questionnaire (overall)

(Validated for orthodontic patients by Iwasaki et. al in Angle Orthodontist Vol 83, No 5, 2013)

The words below are sometimes used to explain how your mouth feels while you have clear aligners. Mark the column to indicate the level of pain you feel for each word **for your treatment overall**.

	0 No Pain	1 Mild	2 Moderate	3 Severe
Pressure				
Sore				
Aching				
Throbbing				
Tight				
Cutting				
Burning				
Tingling				
Pulling				
Dull				
Uncomfortable				
Strange				
Frustrating				
Annoying				
Miserable				

Mark along this line to indicate how bad your pain was **throughout your treatment** – the left of the line means no pain at all and the right end means worst pain possible.

No Pain ---------- Worst Pain Possible

Mark the space that best indicates your level of pain **throughout treatment** – only mark one.

0	No Pain	
1	Little Pain	
2	Moderate Pain	
3	Bad Pain	
4	Horrible Pain	
5	Extreme Pain	

Appendix H1. *Daily compliance survey.*

Compliance Survey (daily)

Date? _____

How many hours did you wear your aligners? _____

Additional Comments:

Appendix H2. *Overall compliance survey.*

Compliance Survey (overall)

On average, how many hours a day did you wear your aligners? ____

On average, how many days a week did you wear your aligners? ____

Additional Comments:

Appendix I1. *Daily satisfaction survey modified from Miller et al.[2] which is adapted from validated Geriatric Oral Health Assessment Index.*

Satisfaction Survey (daily)

Satisfaction Survey modified from that used in Miller et al. (2007). Adapted from the well-validated Geriatric Oral Health Assessment Index

1.Did you have trouble biting or chewing food?
Never Seldom Sometimes Often Always

2.Did your teeth or aligners prevent you from speaking the way you wanted?
Never Seldom Sometimes Often Always

3.Were you able to eat without feeling discomfort?
Never Seldom Sometimes Often Always

4.Did your aligners cause discomfort to your cheeks, lips, or tongue?
Never Seldom Sometimes Often Always

Additional Comments:

Appendix I2. Overall satisfaction survey modified from Miller et al.[2] which is adapted from validated Geriatric Oral Health Assessment Index. Customer Effort Score survey questions modified for adjunct aligner therapies.

Satisfaction Survey (overall)

Satisfaction Survey modified from that used in Miller et al. (2007). Adapted from the well-validated Geriatric Oral Health Assessment Index

1.Did you have trouble biting or chewing food?
Never Seldom Sometimes Often Always

2.Did your teeth or aligners prevent you from speaking the way you wanted?
Never Seldom Sometimes Often Always

3.Were you able to eat without feeling discomfort?
Never Seldom Sometimes Often Always

4.Did your aligners cause discomfort to your cheeks, lips, or tongue?
Never Seldom Sometimes Often Always

Additional Comments:

Customer Effort Score Survey

5.I would recommend aligner treatment to a friend.
Strongly Disagree | Disagree | Somewhat Disagree | Neutral | Somewhat Agree | Agree | Strongly Agree

6.I am satisfied with my aligner experience.
Strongly Disagree | Disagree | Somewhat Disagree | Neutral | Somewhat Agree | Agree | Strongly Agree

7.It was easy to seat my aligner trays.
Strongly Disagree | Disagree | Somewhat Disagree | Neutral | Somewhat Agree | Agree | Strongly Agree

8.It was easy to remove my aligner trays.
Strongly Disagree | Disagree | Somewhat Disagree | Neutral | Somewhat Agree | Agree | Strongly Agree

9.I am confident my aligner trays were tracking.
Strongly Disagree | Disagree | Somewhat Disagree | Neutral | Somewhat Agree | Agree | Strongly Agree

Only for Experimental groups →

10.How often did you use the chewies/pultool?

Never
Few times a week
Every day
Multiple times a day
Other: ____

11.How likely are you to recommend chewies/pultool?
0 1 2 3 4 5 6 7 8 9 10
Not Likely — Very Likely

12.How likely are you to continue to use the chewies/pultool?
0 1 2 3 4 5 6 7 8 9 10
Not Likely — Very Likely

Additional Comments:

Appendix J. *Consultation appointment survey as formatted in Qualtrics (pre-treatment survey).*

CAAT Study

Your Name:

Over the last two weeks, how often have you been bothered by the following problems?

	Not at all	Several days	More that half the days	Nearly every day
Little interest or pleasure in doing things	O	O	O	O
Feeling down, depressed, or hopeless	O	O	O	O
Trouble falling or staying asleep, or sleeping too much	O	O	O	O
Feeling tired or having little energy	O	O	O	O
Poor appetite or overeating	O	O	O	O
Feeling bad about yourself--or that you are a failure or have let yourself or your family down	O	O	O	O
Trouble concentrating on things, such as reading the newspaper or watching television	O	O	O	O
Moving or speaking so slowly that other people could have noticed? Or the opposite--being so fidgety or restless that you have been moving around a lot more than usual	O	O	O	O
Thinking that you would be better off dead or hurting yourself in some way	O	O	O	O

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- O Not difficult at all
- O Somewhat difficult
- O Very difficult
- O Extremely difficult

CAAT Study

Over the last two weeks, how often have you been bothered by the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious, or on edge	O	O	O	O
Not being able to stop or control worrying	O	O	O	O
Worrying too much about different things	O	O	O	O
Trouble relaxing	O	O	O	O
Being so restless that it is hard to sit still	O	O	O	O
Becoming easily annoyed or irritable	O	O	O	O
Feeling afraid as if something awful might happen	O	O	O	O

If you checked off any above problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- O Not difficult at all
- O Somewhat difficult
- O Very difficult
- O Extremely difficult

CAAT Study

During the last 4 weeks, how much have you been bothered by any of the following problems?

	Not bothered	Bothered a little	Bothered a lot
Stomach pain	O	O	O
Back pain	O	O	O
Pain in your arms, legs, or joints (knees, hips, etc)	O	O	O
Menstrual cramps or other problems with your periods (If Not Applicable, please select "Not bothered")	O	O	O
Headaches	O	O	O
Chest pain	O	O	O
Dizziness	O	O	O
Fainting spells	O	O	O
Feeling your heart pound or race	O	O	O
Shortness of breath	O	O	O
Pain or problems during sexual intercourse	O	O	O
Constipation, loose bowels, or diarrhea	O	O	O
Nausea, gas, or indigestion	O	O	O
Feeling tired or having low energy	O	O	O
Trouble sleeping	O	O	O

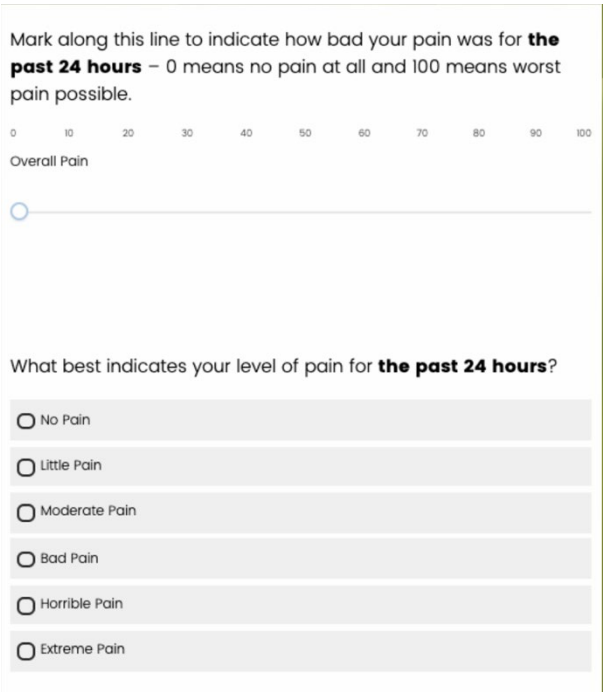
Appendix K. *Between V1 and V2 appointments survey as formatted in Qualtrics (daily survey).*

CAAT Study

Your name:

The words below are sometimes used to explain how your mouth feels while you have clear aligners. Mark the column to indicate the level of pain you felt for each word for **the past 24 hours**.

	0 - No Pain	1 - Mild	2 - Moderate	3 - Severe
Pressure	O	O	O	O
Sore	O	O	O	O
Aching	O	O	O	O
Throbbing	O	O	O	O
Tight	O	O	O	O
Cutting	O	O	O	O
Burning	O	O	O	O
Tingling	O	O	O	O
Pulling	O	O	O	O
Dull	O	O	O	O
Uncomfortable	O	O	O	O
Strange	O	O	O	O
Frustrating	O	O	O	O
Annoying	O	O	O	O
Miserable	O	O	O	O



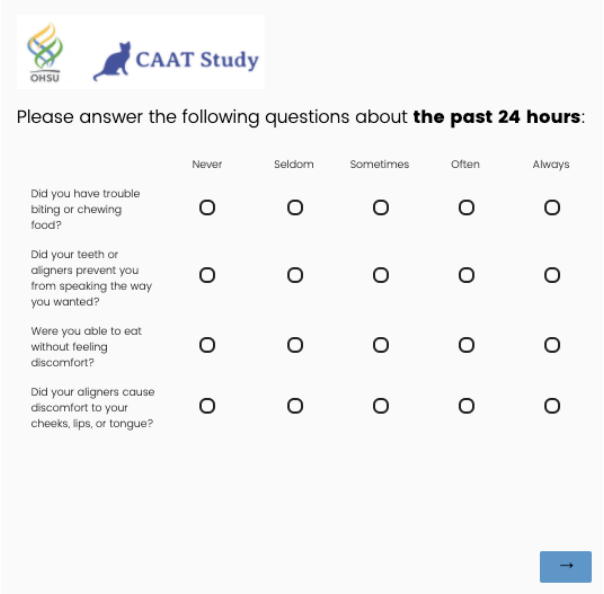
Mark along this line to indicate how bad your pain was for **the past 24 hours** – 0 means no pain at all and 100 means worst pain possible.

0 10 20 30 40 50 60 70 80 90 100

Overall Pain

What best indicates your level of pain for **the past 24 hours**?

- No Pain
- Little Pain
- Moderate Pain
- Bad Pain
- Horrible Pain
- Extreme Pain

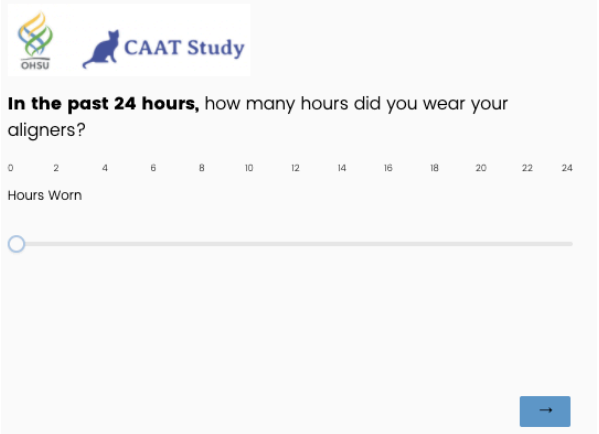


CAAT Study

Please answer the following questions about **the past 24 hours**:

	Never	Seldom	Sometimes	Often	Always
Did you have trouble biting or chewing food?	O	O	O	O	O
Did your teeth or aligners prevent you from speaking the way you wanted?	O	O	O	O	O
Were you able to eat without feeling discomfort?	O	O	O	O	O
Did your aligners cause discomfort to your cheeks, lips, or tongue?	O	O	O	O	O

→



CAAT Study

In the past 24 hours, how many hours did you wear your aligners?

0 2 4 6 8 10 12 14 16 18 20 22 24

Hours Worn

→

Appendix L. *V2: 4-Trays-Later appointment survey as formatted in Qualtrics (overall values).*

CAAT Study

The words below are sometimes used to explain how your mouth feels while you have clear aligners. Mark the column to indicate the level of pain you felt for each word for your treatment **overall**.

	0 - No Pain	1 - Mild	2 - Moderate	3 - Severe
Pressure	O	O	O	O
Sore	O	O	O	O
Aching	O	O	O	O
Throbbing	O	O	O	O
Tight	O	O	O	O
Cutting	O	O	O	O
Burning	O	O	O	O
Tingling	O	O	O	O
Pulling	O	O	O	O
Dull	O	O	O	O
Uncomfortable	O	O	O	O
Strange	O	O	O	O
Frustrating	O	O	O	O
Annoying	O	O	O	O
Miserable	O	O	O	O

Mark along this line to indicate how bad your pain was **throughout** your treatment – 0 means no pain at all and 100 means worst pain possible.

0 10 20 30 40 50 60 70 80 90 100

Overall Pain

What best indicates your level of pain **throughout** treatment?

- O No Pain
- O Little Pain
- O Moderate Pain
- O Bad Pain
- O Horrible Pain
- O Extreme Pain

→

CAAT Study

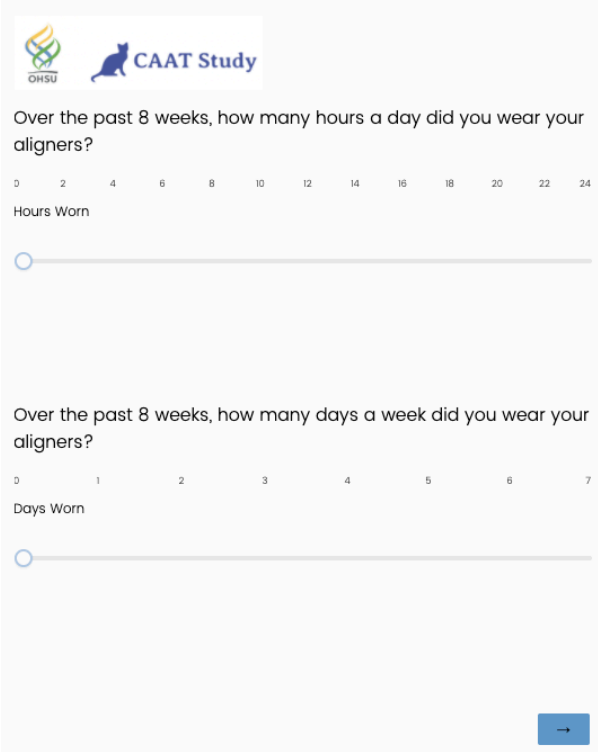
Please answer the following questions about the past 8 weeks of treatment:

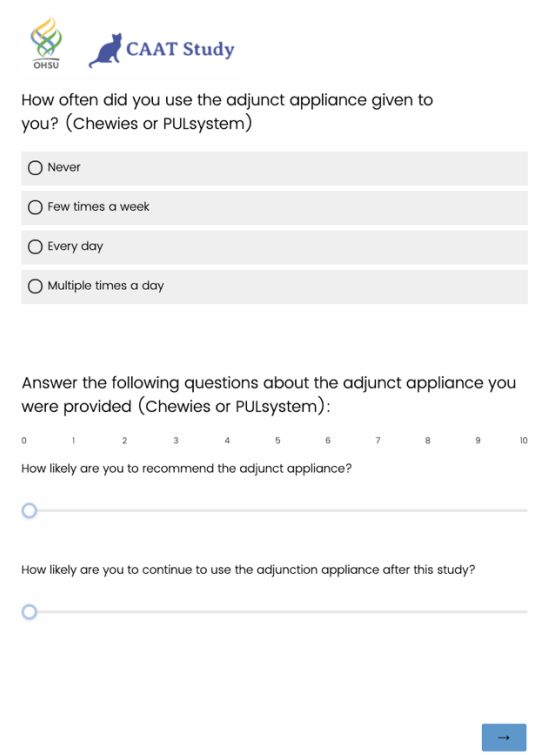
	Never	Seldom	Sometimes	Often	Always
Did you have trouble biting or chewing food?	O	O	O	O	O
Did your teeth or aligners prevent you from speaking the way you wanted?	O	O	O	O	O
Were you able to eat without feeling discomfort?	O	O	O	O	O
Did your aligners cause discomfort to your cheeks, lips, or tongue?	O	O	O	O	O

Please answer the following questions:

	Strongly Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Strongly agree
I would recommend aligner treatment to a friend.	O	O	O	O	O
I am satisfied with my aligner experience.	O	O	O	O	O
It was easy to seat my aligner trays.	O	O	O	O	O
It was easy to remove my aligner trays.	O	O	O	O	O
I am confident my aligner trays were tracking.	O	O	O	O	O

→



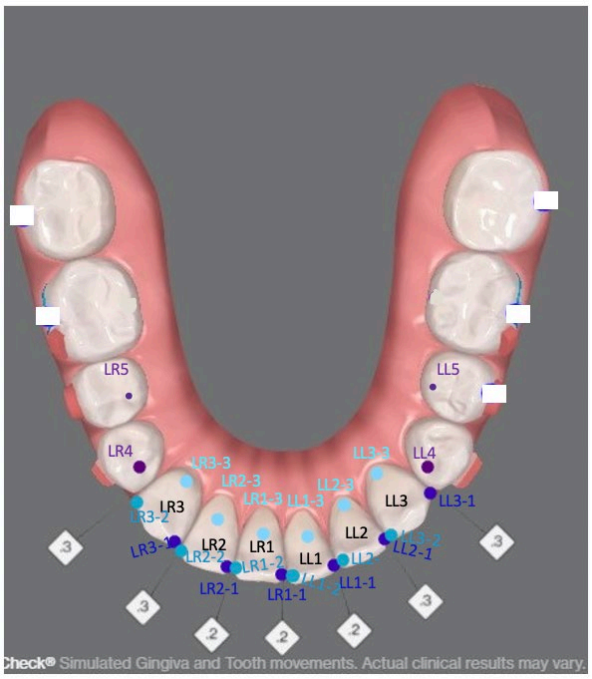


Appendix M. *MatLab software prompts.*

```
%This program is used to track teeth moving

%The following is used find the relation between Pixels and millimeters
%with head X-rays. Since every image keeps the same relation, we can find
%the ratio before hand.
clear; clc; close all
SubjID=input('Please type in the subject ID: ','s')
JawType=input('Is this a upper Jaw(MX) or a lower jaw(MD)? : ','s');
Dist12=input('Please type in the distance between the second premolars: ');
Dist14=input('Please type in the distance between the left second premolar and the left first premolar: ');
%RulerL=str2double(RulerLength);
XX=[]; %to store x value on lateral plane in pixels under the windows graphical system
YY=[]; %to store y value on lateral plane in pixels
ZZ=[]; %to store z value on AP plane in pixels

XXX=[]; %to store x value on lateral plane in millimeter under anatomical coordinate system
YYY=[]; %to store y value on lateral plane
ZZZ=[]; %to store z value on AP plane

FileName1=[SubjID,JawType,'Post.png'];
```

Appendix N. *Labeling protocol for labeling teeth in MatLab.*

S001MD**Pred**

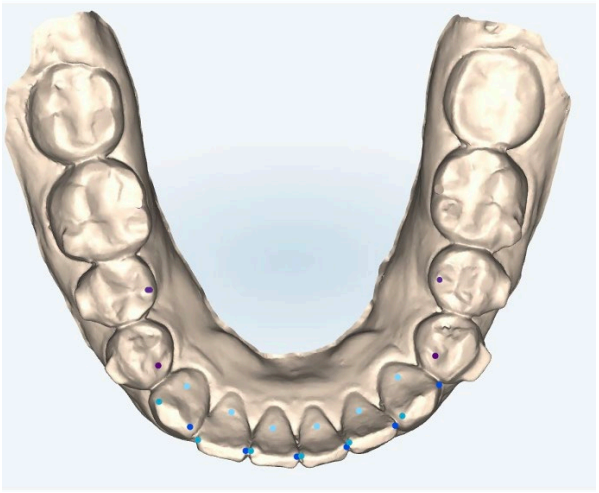


1. Mark 4 points to orient the picture in this clockwise order:
   a. Reference point LL5 **(Pred-LL5)**
   b. Reference point LL4 **(Pred-LL4)**
   c. Reference point LR4 **(Pred-LR4)**
   d. Reference point **(Pred-LR5)**

2. Mark the 6 anterior teeth in the following order. Each tooth requires 3 measurements made in a clockwise order
   a. **LL3**
      i. Distal point **(Pred-LL3-1)**
      ii. Mesial point **(Pred-LL3-2)**
      iii. Cingulum point **(Pred-LL3-3)**
   b. **LL2**
      i. Distal point **(Pred-LL2-1)**
      ii. Mesial point **(Pred-LL2-2)**
      iii. Cingulum point **(Pred-LL2-3)**
   c. **LL1**
      i. Distal point **(Pred-LL1-1)**
      ii. Mesial point **(Pred-LL1-2)**
      iii. Cingulum point **(Pred-LL1-3)**

      crossing midline
   d. **LR1**
      i. Mesial point **(Pred-LR1-1)**
      ii. Distal point **(Pred-LR1-2)**
      iii. Cingulum point **(Pred-LR1-3)**
   e. **LR2**
      i. Mesial point **(Pred-LR2-1)**
      ii. Distal point **(Pred-LR2-2)**
      iii. Cingulum point **(Pred-LR2-3)**
   f. **LR3**
      i. Mesial point **(Pred-LR3-1)**
      ii. Distal point **(Pred-LR3-2)**
      iii. Cingulum point **(Pred-LR3-3)**

S001MD**Post**



1. Mark 4 points to orient the picture in this clockwise order:
   a. Reference point LL5 **(Post-LL5)**
   b. Reference point LL4 **(Post-LL4)**
   c. Reference point LR4 **(Post-LR4)**
   d. Reference point **(Post-LR5)**

2. Mark the 6 anterior teeth in the following order. Each tooth requires 3 measurements made in a clockwise order
   a. **LL3**
      i. Distal point **(Post-LL3-1)**
      ii. Mesial point **(Post-LL3-2)**
      iii. Cingulum point **(Post-LL3-3)**
   b. **LL2**
      i. Distal point **(Post-LL2-1)**
      ii. Mesial point **(Post-LL2-2)**
      iii. Cingulum point **(Post-LL2-3)**
   c. **LL1**
      i. Distal point **(Post-LL1-1)**
      ii. Mesial point **(Post-LL1-2)**
      iii. Cingulum point **(Post-LL1-3)**

      crossing midline
   d. **LR1**
      i. Mesial point **(Post-LR1-1)**
      ii. Distal point **(Post-LR1-2)**
      iii. Cingulum point **(Post-LR1-3)**
   e. **LR2**
      i. Mesial point **(Post-LR2-1)**
      ii. Distal point **(Post-LR2-2)**
      iii. Cingulum point **(Post-LR2-3)**
   f. **LR3**
      i. Mesial point **(Post-LR3-1)**
      ii. Distal point **(Post-LR3-2)**
      iii. Cingulum point **(Post-LR3-3)**