Official Title:	**Alignment and Comfort Assessments using Non-Sliding Lingual Orthodontic Technique (BRIUS) and Conventional Bracket Systems**
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Study Design

This is a non-blinded single-center randomized clinical controlled pilot trial of growing orthodontic patients who underwent comprehensive multi-arch fixed orthodontic treatment for the first time. Subjects were randomized into one of two groups: BR lingual appliance (experimental intervention group) and LFFA (standard intervention group). The study was reviewed and approved by institutional review boards at the University at Buffalo Health Sciences (IRB # 00004055 - Appendix1). The study was also registered on the ClinicalTrials.gov Protocol Registration and Results System (ID# NCT04347018).

The patients were assessed for leveling an aligning by comparing their initial presentation prior to bonding (T1) with their alignment 18 weeks after bonding (T4).

Sample Population

Sample population included growing patients between 10 and 18 years of age, with full permanent dentition, and presented for orthodontic treatment at the University at Buffalo School of Dental Medicine (UBSDM) orthodontic clinic. Subjects were randomly allocated into one of two groups: BR and a LFFA group.

Participant Selection Criteria

The sample inclusion criteria were:

• Female and male 10 to 18 years old

• Mild to moderate case difficulty, defined by American Board of Orthodontics Discrepancy Index (DI) of 0 to 20

• Angle's Class I and Cl II (up to half cusp) molar and canine relationship.

• Fully erupted permanent dentition (excluding third molars).

• Mild to moderate crowding (7 mm or less).

• Good oral hygiene, determined by the orthodontist at each adjustment visit.

• Undergoing treatment with fixed orthodontic appliances in both jaws for a minimum of 6 months.

The exclusion criteria were:

Subjects were excluded if they had transposed, impacted, or missing teeth, previous history of orthodontic or orthognathic surgical treatments, treatments that involved tooth extractions or orthognathic surgery, systemic illness or craniofacial syndrome or disorder, missing appointments, and compromised oral hygiene. Subjects who had radiographic bone loss observed on the dental panoramic image were excluded. Additionally, any drugs that affect tooth movement used prior to the beginning of, or during the study would also exclude the subject.

Sample size

Sample size was calculated based on the results of Scott et al.34 that determined a standardized difference of 0.98 in the rate of tooth alignment within a period of 34 days would give a clinically relevant difference of 0.8 mm between two groups. For statistical power of 80% at a significance level of 0.05, 17 subjects were needed in each group for a total sample size of 34 subjects.

Study time points

Total observation duration for all study participants was 18 weeks from the first day of bonding maxillary and mandibular arches, which were both bonded on the same appointment.

Periodic records included intra-oral photos and an intra-oral scan for all subjects at the records appointment (T1), at 6 weeks – first adjustment visit (T2), at 12 weeks second adjustment (T3) and at 18 weeks third adjustment (T4). During each visit, in addition to the periodic records including intra-oral photos and scans, any broken brackets were repositioned for both groups.

Outcome Measures

There were two outcomes measured in this study, the effectiveness of tooth movement and patient comfort at 6, 12 and 18 weeks after appliance bonding.

A] Effectiveness of tooth movement:

1. Alleviation of crowding: Little's Irregularity Index (LII) which measures the alignment discrepancy in the five contact points of the lower anterior region was assessed between T1 and T4 for every patient. The scores were measures digitally by identifying the center of the mesial (CoM) and distal (CoD) contact points on each tooth at the same vertical level. The 3D slicer software was used to measure the horizontal distance between CoM and CoD of adjacent teeth in millimeters. The scores were then compared between the two groups (BR and LFFA) and comparisons were made in the different timepoints within each group.

2. Changes in 3D individual tooth positions: To assess the extent of movements achieved in all three planes for each maxillary and mandibular tooth from 6-6, digital model superimpositions were performed using 3D Slicer software (www.slicer.org Harvard University, Boston, MA, USA). Maxillary superimpositions were done based on the method described by Aliaga et al.35 using the palatal rugae. Mandibular superimposition was completed by overlaying the pre- and post-treatment digital models on the mucogingival junction which is a stable and reliable landmark according to a study by Ioshida et al.

B] Patient comfort level

Data obtained from the perceived comfort questionnaires was evaluated by identifying chronological pattern of any pain experienced as well as any other patterns according to the data obtained. The extent of comfort will be described by a percent at each time point, two-sample independent t-test will be done to compare the pain between the two groups.

Comfort level was assessed using an electronic survey instrument developed by Wu et al.37 (Appendix 2). This valid and reliable instrument used a VAS score to assess the overall comfort, comfort in the tongue, cheeks, lips, gingiva, and face and jaw.38 It also asked about the use of medications. The survey instrument was sent online to patients through QuestionPro (Austin, TX, USA). Each patient was instructed to complete and submit the survey daily, on the first seven days after their first visit (T1), second visit (T2), third visit (T3) and fourth visit (T4).

Procedure of the study

Subject Randomization

Prior to initiating sample recruitment, block randomization was carried out by a statistician who was not involved in recruiting or treating patients. Results of the randomization, whether BR or LFFA were written down on 34 different sheets of paper. Each sheet was then individually enclosed in opaque sequentially numbered envelopes. An envelope corresponding to the number of the sample joining the study would be opened to find out which group the new sample would fall into.

Subject recruitment process

Patients presented for treatment at the University at Buffalo orthodontic clinic were screened for eligibility by assessing their initial records. Initial records included the intraoral photographs and scans, panoramic x-rays and lateral cephalograms, following the standard of care. Individuals who fulfilled the inclusion criteria were invited to enrol in the trial during their consultation visit when the treatment options were discussed by their treating resident. The individuals who qualified for the study were given time to consider joining the study if they requested that.

Once the parent and child decided to enrol in the study, the parent or guardian signed a consent form for participation of their child in the study and the subjects signed an assent form for participation in the study.

Blinding

Principal investigator (MHA) and patients were able to recognize whether the appliance is bonded buccally (LFFA) or lingually (BR) hence blinding of subjects and principal investigator was not possible. Therefore, this study was an open label randomized controlled trial.

Treatment Group

The BR group went through treatment with the BRIUS appliance. The treatment was completed through a virtual treatment planning portal called the BRIUS Planner™. The final positions of each tooth was completed by a technician. Those movements were then adjusted if necessary and a final BRIUS plan was approved. BRIUS then sent an upper and a lower IM set in the final tooth positions. Along with the IM was an indirect bonding tray that was preloaded with non-prescription 2D® Lingual brackets from Forestadent (Pforzheim, Germany).

The LFFA group underwent treatment with 0.018 slot MBT prescription Pre-cemented 3M UNITEK Victory Series™ brackets (3M, Monrovia, CA, USA) which were bonded directly under adequate moisture control.

Bonding and treatment procedure in BRIUS™ Group

BR subjects were bonded using indirect bonding trays provided by the manufacturer, BRIUS™ (BRIUS, Plano, TX, USA). The bonding protocol recommended by the manufacturer was followed. Moisture control was accomplished using IsoVac (Zyris, Goleta, CA, USA) followed by prophylaxis, sandblasting of lingual surfaces of teeth with EtchMaster® Tips (Groman Dental, Margate, FL, USA) etching with 35% phosphoric acid Ultra-Etch (Ultradent, South Jordan, UT, USA) and bonding with Assure PLUS (Reliance Orthodontics, Itasca, IL). RelyX resin cement (3M Unitek, Monrovia, CA, USA) was applied to each bracket base.

Once bonding and conditioning was complete, the Rely X was loaded onto the brackets and the tray was inserted into the patient's mouth until the tray conforms to the shapes of all the teeth. Light cure unit was activated, and light was shined through the clear indirect bonding tray for 15 seconds on each tooth. The tray was then removed, and the brackets were light cured again for 15 seconds on each bracket to assure maximum cure of the cement underneath the brackets.

Subjects in the BR group were checked for broken brackets during each visit. Progression and tooth movement were observed, no adjustments were made to the appliance during the visits. Broken brackets were rebonded by cutting out a single tooth from the full arch template provided by the manufacturer. The same bonding protocol on the first visit was used for any rebonding procedures needed. Rebonding of broken brackets in BR subjects did not include any repositioning and the brackets were bonded back to their previous position. This was done by using the indirect bonding tray provided by BRIUS™ for the initial bonding.

Bonding and treatment procedure in Labial Full Fixed Appliance Group

Bonding for LFFA was performed by multiple providers. Bonding was done directly using Pre-cemented 3M UNITEK Victory Series™ 0.018-inch MBT brackets (3M, Monrovia, CA, USA) from permanent first molar to first molar and molar tubes on second molars as applicable. 3MUnitek Bands (3M, Monrovia, CA, USA) were placed on the first molars as needed. Treatment was provided by multiple providers and supervised by a faculty member.

Wire progression was started with 014-inch NiTi wire on the upper and the lower arches for 6 weeks followed by 016-inch NiTi for another 6 weeks and finally 16x22-inch NiTi for 6 weeks. The reason patients were seen every 6 weeks, unless emergency visits took place, was to allow every NiTi wire to fully express itself before stepping up to a heavier wire. No compensatory bends were made since only aligning NiTi wires were ligated to the brackets. Wires were ligated using 3M Unitek™ Alastik™(3M, Monrovia, CA, USA) elastomeric rings. In cases of bracket bond failure, brackets were re-bonded into the most appropriate position to promote the most efficient movement of teeth during alignment stage.

Patients were scanned at the start of each visit with an iTero scanner (Align Technology, San Jose, CA, USA) to be able to evaluate movements of teeth between visits, between groups and before and after alignment.

Study model superimposition methods

The steps for performing superimpositions were as follows:

Step 1:

Pre-orientation (Figure 3) – The model was loaded onto the 3D slicer software to ensure every model was oriented the same way in the viewing pane of the software. In other words, the right side of the model would be displayed when “right view” button was clicked, and the left side of the model would be displayed when the “left view” button was clicked.

Step 2:

Orientation (Figure 4) – The models were oriented within digitally constructed sagittal, axial and coronal planes around which dental models could be transformed. In the sagittal plane, the midpalatine raphe and midpalatine suture were centered along the sagittal plane. In the

coronal plane, the buccal cusp of the second premolar was coincident with the coronal plane. In the axial plane, the incisal edges of the central incisors and the buccal cusps of the first molars contacted the occlusal plane evenly.

Step 3:

Approximation (Figure 5) – The T1 and T4 models were “approximated” using corresponding landmarks, the mesiobuccal cusp tips and the buccal cusp tips of the second premolars. This step helped reduce rotations during the registration step.

Step 4:

Registration (Figure 6) – At least five corresponding landmarks were identified on the T1 and T4 models. Then, a region of interest (ROI) was created around those landmarks with a 20 mm diameter at each landmark. The landmarks began from the most posterior point of the incisive papilla, included the second and third palatal rugae and the most posterior landmark for superimposition extended 10 mm beyond the most medial points on the most posterior palatal rugae.

More landmarks were selected if the intraoral scan did not extend 10 mm posterior to the most posterior palatal rugae. The landmarks were restricted to the palatal rugae structures and the ROI was away from the marginal gingiva of the teeth. The two models were then overlayed according to the point where the two ROIs coincide on the T1 and T4 models, and changes were then computed. This creates a final “registration model” which shows the movements completed during treatment. The models were verified for the presence of any aberrant movements that did not match with the mechanics of treatment. If there were movements (yaw, roll, pitch) present in the registration model when compared to the oriented model that did not correspond to what was actually done, the registration step was repeated until it only represented movements achieved during the treatment at T4.

Step 5:

Distance measurement (Figure 7) – Corresponding landmarks were identified on T1 oriented model and the T4 registered model. The distance between each landmark was then measured. Once the software was requested to measure the distance between two points, the distance was automatically measured in the x, y and z planes as well as an overall 3D vector.

The landmarks on each tooth were as follows:

• Upper and lower central and lateral incisors: The center of the incisal edge mesio-distally and bucco-lingually

• Upper and lower canines: the highest point on the cusp tip. If there was cusp wear, then it is the center of the worn canine cusp.

• Upper and lower premolars: the highest points on the buccal cusp tips. If there was cusp wear, then it is the center of the worn buccal cusp.

• Upper and lower first molars: the highest points on the mesiobuccal cusp tips. If there was cusp wear, then it is the center of the worn mesiobuccal cusp.

All these analyses were completed by a single examiner (MHA) who was calibrated by an expert at using the software. Intra-examiner reliability was done on randomly selected two weeks after initial analyses were completed

Statistical Analysis

All tooth movement data were assessed for normality with the Shapiro-Wilks test. Sample sizes were relatively small in both the BR and FFA groups, so the power of this test to correctly identify non-normal distributions is likely low. Therefore, t-tests for differences between groups were performed where appropriate along with the Mann-Whitney nonparametric tests. The difference in between group continuous questionnaire outcomes and continuous demographic data were also evaluated for significance with the Mann-Whitney test. The within group tests for the paired differences in T1 and T4 values of Little's Irregularity Index were done with the Wilcoxon signed rank test. Categorical questionnaire outcome and categorical demographics data associations with the BR and FFA groups were tested for independence using Fisher's exact test, since there were instances of low (< 5) or and zero cell counts. A post hoc power to sample size analysis using Little's Irregularity Index data was also performed under an assumption of normality. The estimated effect size used was determined by first calculating the mean of the paired T1 to T4 differences in both the BR and FFA groups, and then taking the difference between these group means. The standard deviation for the sample size calculations was taken as the pooled value of the standard deviations of both groups' paired differences. All statistical analysis was performed using R (v4.0.4) through RStudio (v.461).