SAFETY AND EFFICIENCY OF INVISALIGN IN MIXED DENTITION

By

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A THESIS PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
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Objective: To evaluate the safety and effectiveness of treatment with Invisalign in patients possessing mixed dentition who present with any combination of anterior crossbite, posterior crossbite, malalignment (crowding), spacing, and deep bite.

Materials and Methods: A multi-site clinical trial enrolled a total of 100 patients. Data were collected at baseline and 6 week intervals up to 24 weeks. Incisor alignment was measured using a modified Little's Index at baseline, week 12, and week 24. Deep bite and crossbite correction, gingival inflammation index (GI), plaque index (PI), decalcification index (DI), and quality of life surveys were recorded.

Results: A 35% reduction in the Little Index score on the upper arch and a 36% reduction on the lower arch from week 0 to week 24 occurred in subjects with malalignment. In subjects with spacing, a 59% reduction in the upper arch was observed. By week 24, 58% of the patients with anterior crossbites were corrected. In comparison, 50% of the patients with posterior crossbites were corrected. Mean bite depth improved 12%. No significant changes in GI, PI, or DI were observed. At week 24, 97% of patients experienced no impediment to speech, 98% showed no inhibition to eating, and 95% reported no need to take pain medication to ease discomfort.

Conclusion: Invisalign offers an esthetic modality to correct certain malocclusions in the mixed dentition

CHAPTER 1
INTRODUCTION

The late 1990s brought the advent of an orthodontic treatment modality that appeared to offer an esthetic alternative to traditional braces.[1] Manufactured by Align Technology, Inc., this treatment methodology consists of a sequenced application of clear polyurethane aligners that is promoted as an "invisible way to straighten teeth." [2] At the onset of Align's marketing program in 1999, the U.S. Food and Drug Administration (FDA) imposed a labeling requirement which contraindicated the Invisalign system for patients with unerupted second molars. But in December 2008, the FDA relaxed that restriction, thus enabling Align Technology to market its newly introduced Invisalign Teen product line to a younger demographic.[3]

Although the Invisalign system was not approved for patients with mixed dentition prior to 2009, the utilization of removable orthodontic appliances in children is not a new concept. In research conducted by Littlewood et al,[4] it was found that removable appliances have some advantage over conventional fixed appliances when used correctly to treat patients with mixed dentition. In particular, Littlewood opines that removable appliances can: (1) provide increased vertical and horizontal anchorage in the mixed dentition due to palatal coverage; (2) produce efficient overbite reduction in patients who are still experiencing dental and skeletal growth; (3) transmit forces to blocks of teeth; and (4) enable the patient to sustain hygienic cleanliness because they are removable.[4]

Several studies in adults have reported on the effectiveness of aligner movement.[5-7] All of these studies focused either on aligner material[8] or the ability of moving adult teeth without further practitioner intervention other than delivering aligners.[7] In a 2007 case report involving three patients, Boyd[9] deemed Invisalign as capable of effecting successful corrections of

moderate crowding, deep bites, and moderate Class II division 1 malocclusions, provided the patient complies with a minimum aligner usage of 22 hours per day.

Any appliance used to correct malocclusions may impact the quality of life of the patient. In a cohort study involving 217 children who received fixed orthodontic appliance therapy, Zhang et al[10] found that there was a significant deterioration in overall quality of life during treatment compared with pretreatment at one week and one month time intervals. Sergl et al[11] reported in a sample of 84 patients that severity of pain and discomfort experienced by the patients wearing fixed appliances was significantly higher than those treated with upper and/or lower removable appliances. In a multi-site trial examining quality of life and pain during the first week of treatment in adult patients with either fixed appliances or Invisalign, Miller et al[12] observed that Invisalign patients reported fewer negative impacts on overall quality of life and experienced less pain.

The purpose of this study was to evaluate the safety and effectiveness of treatment with Invisalign aligners in patients with mixed dentition who present with one or more of the following occlusion problems: (1) anterior crossbite; (2) posterior crossbite; (3) malalignment (crowding); (4) space closure; and (5) deep bite.

CHAPTER 2
MATERIALS AND METHODS

A goal of 100 subjects was slated for inclusion in this study. This number was based on a minimum of 20 participants in each malocclusion group (deep bite, anterior crossbite, posterior crossbite, crowding, and spacing). Inclusion criteria required the participants to: (1) be not less than 7 nor more than 12 years of age; (2) be in good health; (3) have at least 4 permanent molars fully erupted; (4) have all 4 incisors; (5) have either an anterior crossbite, malalignment (crowding), posterior crossbite, spacing malocclusion, or deep overbite, or any combination thereof; (6) not have a malocclusion needing another appliance; and (7) be willing and able to comply with all procedures throughout the 24-week duration of the study.

Exclusion criteria consisted of the patient having: (1) significant periodontal problems; (2) active caries; (3) a severe Class III malocclusion that necessitates surgical correction; (4) a chronic daily use of any nonsteroidal anti-inflammatory or steroid medication; (5) used any investigational product within 4 weeks of the onset of the study; and (6) a medical condition that might cause, or exacerbate, a health risk as a result of participation in the study. Children who did not possess a full complement of teeth in the anterior segment were excluded as participants.

During the initial screening five northern Florida treatment sites, including the University of Florida, were utilized. Models from each treatment site were sent to the University of Florida for examination so as to ensure all participants fully complied with the inclusion criteria. Alginate impressions were taken and thereafter poured into stone models which, in turn, were subsequently utilized by Align Technology to fabricate the patient's polyurethane aligners. All patients were treatment planned and Clinchecks approved by a single practitioner (T.T.W.) Patients were seen at 6-week intervals to receive delivery of the next series of Invisalign aligners,

at which juncture additional study data were captured. The study coordinator supervised the aligner delivery and the data collection appointments at each treatment site.

The first appointment (week 0) included an intraoral clinical examination to assess, by means of visual inspection, the participant's tissue health and gingival recession. The first three aligners were delivered to the participants with instructions to wear each aligner for a period of 2 weeks before changing to the next aligner. Three additional aligners were subsequently delivered at 6-week intervals throughout the 24-week study period.

Study models of the upper and lower anterior teeth taken at weeks 0, 12, and 24 were scored with a modified Little's Index by one investigator (B.T.L.), who was trained and calibrated in this Index. Digital calipers were used to measure displacement of contact points, starting with the mesial of the lateral incisor and ending at the mesial of the contralateral lateral incisor. A modified Little's Index was utilized because a large number of subjects in this age group had primary canines that were exfoliating during the 24-week study period, thereby confounding the data.

Anterior and posterior crossbites were scored as either corrected (+) or not corrected (-) by the same trained and calibrated investigator (B.T.L.). A crossbite was deemed corrected when the affected tooth (teeth) repositioned into the appropriate buccal/lingual orientation when the casts were fully articulated.

Improvement in bite depth was measured as a vertical improvement in bite depth of the upper incisor relative to the lower incisal edge. Change in the bite depth was measured from the same teeth that were fully erupted at weeks 12 and 24. The upper incisal edge was marked on the lower incisor when the casts were fully articulated. Digital calipers were used to measure the distance from the line to the incisal edge to the nearest 0.1 mm.

Photographs and impressions for the study models were taken at the beginning of the study, at week 12, and at week 24 or earlier if the problem was corrected prior to week 24.

Qualitative survey assessments concerning the participants' "quality of life" perceptions were taken at weeks 6, 12, 18, and 24. The participants were asked to report any difficulties experienced while eating or talking; pain from aligner wear; or instances of pain caused by aligner wear that required analgesic medication. Questions were adapted from a previous questionnaire [12] that examined quality of life in adults.

The Plaque Index was assessed using the Turesky modification of the Quigley-Hein Plaque Index (PI).[13] The Gingivitis Index (GI) was assessed at each visit using the Papillary Bleeding Score of Loesche.[14] The Decalcification Index (DI) was assessed visually and tactilely with a dental explorer and scored by using a modified version of the white spot lesion index of Gorelick et al.[15] All assessments were made by the same examiner (J.C.).

The paired *t*-test was utilized to compare changes in PI, GI, and DI from week 0 to week 24. The paired *t*-test was also used to compare groups for deep bite and modified Little's Index. The Wilcoxon rank sum test was used to compare ages, malocclusion categories, and correction of anterior and posterior crossbites. McNemar's test with continuity correction was used to calculate significance for changes in the quality of life variables over time.

CHAPTER 3
RESULTS

A total of 100 participants with mixed dentition participated in the study. The participants were comprised of 47 females and 53 males, all of whom had any combination of occlusal problems which included anterior crossbite, upper and/or lower crowding (malalignment), posterior crossbite, upper and/or lower anterior spacing, and deep overbite (Fig 3-1.)

The mean age of the 100 participants was 9.5 years, with a racial composition of 85 whites, 10 Hispanics, 4 blacks, and 1 mixed race. Five northern Florida treatment sites were utilized, including the University of Florida (UF), Gainesville (GV), Ocala (OC), Orange Park, and Jacksonville (JX) (Fig 3-2). The Institutional Review Board of the University of Florida approved the study, and informed consent was obtained from all participants.

The intraoral health of subjects were assessed by means of a plaque index, gingival index, and decalcification index. As shown in Table 3-1, there were no statistical differences ($p>.05$) between week 0 and week 24.

Table 3-2 depicts both the percentage and the number of patients with anterior and posterior crossbites that corrected by either week 12 or week 24. By week 24, 15 patients (57.7 %) with anterior crossbites were corrected. In comparison, 11 patients (50.0 %) with posterior crossbites were corrected during this same time span. Wilcoxan rank sum tests were used to test for differences between the ages of subjects or the total number of occlusal problems for those subjects whose crossbites were either corrected or not corrected. No significant differences were found between the groups ($p>.05$).

Table 3-3 describes the subject population with and without deep bite. In the deep bite group, there was a 10.8% change by week 12, and a 12.6% change by week 24. (Table 3-4).

Table 3-5 shows the mean Little's Index values for all patients with spacing and crowding (malalignment) in both the upper or lower jaws and associated p-values. Malalignment is defined in this study as being inclusive of crowding, yet additionally contains those patients whose teeth were poorly aligned but did not necessarily have crowding. Subjects with crowding showed a 35.5% reduction in the Little's Index score on the upper arch and a 35.8% reduction on the lower arch from week 0 to week 24. In subjects with spacing, a 58.6% reduction in the upper arch was observed. The lower arch also had a reduction in values, but did not meet a level of significant change ($p>.05$). (Table 3-6)

As a means of measuring the impact on the quality of life subjects were given questionnaires at 6 week intervals. The percentage reporting problems talking decreased from 13% (13 out of 97) at week 6 to 3% (3 out of 89) at week 24. A similar percentage decrease was observed in those subjects having problems eating, being reduced from 8% (8 out of 97) to 1 % (1 out of 89). The percentage of participants who reported pain with aligner use was 46% (45 out of 97) at week 6, which thereafter dropped to 21% (19 out of 89) by week 24. For those subjects who required analgesic medication to relieve their pain, 30% (29 out of 97) required medication at week 6, dropping significantly to 4% (4 out of 89) by week 24. (Fig 3-3)

P values calculated from McNemar's test with continuity correction showed significant changes ($P<.05$) from week 6 to week 12 for subjects reporting problems talking, pain, and medication usage for pain. There was also a significant change in medication usage from week 12 to week 18 (Table 3-7).

Table 3-1. PI, GI, and DI mean scores at week 0 and week 24 with associated standard error and P values. P values calculated with paired t test (N=80).

Variable	*Week 0 (T0)*	*Week 24 (T2)*	*Mean Change(T0-T2)*	*P value*
PI upper	0.992(SE .0761)	1.057(SE .0902)	-0.0656	0.57
PI lower	0.886(SE .0848)	0.787(SE .0859)	0.0993	0.40
GI upper	1.332(SE .0420)	1.310(SE .0420)	0.0218	0.69
GI lower	1.379(SE .0431)	1.306 (SE .0414)	0.0732	0.17
DI upper	0.031(SE .0117)	0.0139(SE .0047)	0.0172	0.17
DI lower	0.007(SE .0040)	0.005(SE .0031)	0.0020	0.70

Table 3-2. Anterior and posterior crossbite correction with 95% confidence intervals for patients +/- 5 weeks of designated time point

Anterior and Posterior Crossbite Correction within 5 weeks of time point			
	Corrected/ Total	*% Corrected*	*95% Confidence Interval*
Anterior Crossbite			
Week 12	5 of 29	17.20%	(5.8%-35.8%)
Week 24	15 of 26	57.70%	(36.9%-76.6%)
Posterior Crossbite			
Week 12	2 of 23	8.70%	(1.1%-28.0%)
Week 24	11 of 22	50.00%	(28.2%-71.8%)

Table 3-3. Mean bite depth for patients with deep bite and those without measured within 5 weeks of time point.

	Mean Bite Depth (mm)					
	W/O deep bite			*W Deep bite*		
	N	*Mean*	*Std error*	*N*	*Mean*	*Std error*
Week 0	57	1.62	0.203	43	4.7	0.159
Week 12	54	1.66	0.208	40	4.18	0.168
Week 24	52	1.89	0.161	35	4.05	0.195

Table 3-4. Change in bite depth between time points. P- value calculated with paired t-tests using mean change between time points.

Deep bite change in subjects with Deep Bite within 5 weeks of time point			
Time Period	*Mean change (mm)*	*% change*	*P value*
0 to 12 weeks	0.561	10.80%	0.0003
12 to 24 weeks	0.08	2.18%	0.062
0 to 24 weeks	0.634	12.62	0.0005

Table 3-5. Mean Modified Little's Index values (mm) for different combinations of crowding/spacing with associated standard errors at week 0 (T1), week 12 (T2), and week 24 (T3). P values calculated using paired t-test.

	T0	*T1*	*T2*	*P value(T0-T1)*	*P value (T1-T2)*	*P value (T0-T2)*
Upper Crowding/Spacing	6.26 (SE 0.365)	4.43 (SE 0.302)	3.02 (SE 0.234)	<.0001	<.0001	<.0001
Upper crowding	6.22 (SE 0.454)	4.60 (SE 0.388)	3.16 (SE 0.285)	<.0001	<.0003	<.0001
Upper spacing	6.41 (SE 0.553)	4.05 (SE 0.404)	2.68 (SE 0.381)	<.0001	<.0001	<.0001
Lower Crowding/Spacing	3.15 (SE 0.164)	2.40 (SE 0.137)	1.91 (SE 0.147)	<.0001	<.0001	<.0001
Lower Crowding	3.22 (SE 0.169)	2.44 (SE 0.136)	1.99 (SE 0.150)	<.0001	<.0001	<.0001
Lower Spacing	1.99 (SE 0.512)	0.78 (SE 0.394)	0.61 (SE 0.288)	0.17	0.58	0.13

Table 3-6. Mean percentage change between week 0-week 12 (T0-T1), week 12-week 24 (T1-T2), and week 0-week 24 (T1-T2). Number (N) of patients in category next to percentage.

	Change(T0-T1)	*Change(T1-T2)*	*Change(T0-T2)*
Upper Crowding/Spacing	28.1% (N=77)	13.4% (N=77)	42.1% (N=73)
Upper crowding	25.7% (N=55)	9.9% (N=49)	35.5% (N=52)
Upper spacing	34.3% (N=23)	22.0% (N=22)	58.6% (N=22)
Lower Crowding/Spacing	18.0% (N=74)	14.9% (N=66)	37.2% (N=68)
Lower Crowding	16.0% (N=70)	15.3% (N=62)	35.8% (N=64)
Lower Spacing	52.5% (N=4)	8.6% (N=4)	61.2% (N=4)

Table 3-7. P values between weeks for problems talking with aligners, eating with aligners, pain due to aligners, and pain resulting in medication usage.

P values from McNemar's test with continuity correction				
	Talking	*Eating*	*Pain*	*Medication*
Wk 6 to 12	0.0055	1	0.0003	0.008
Wk 12 to 18	1	0.07	1	0.0265
Wk 18 to 24	1	1	0.8	1

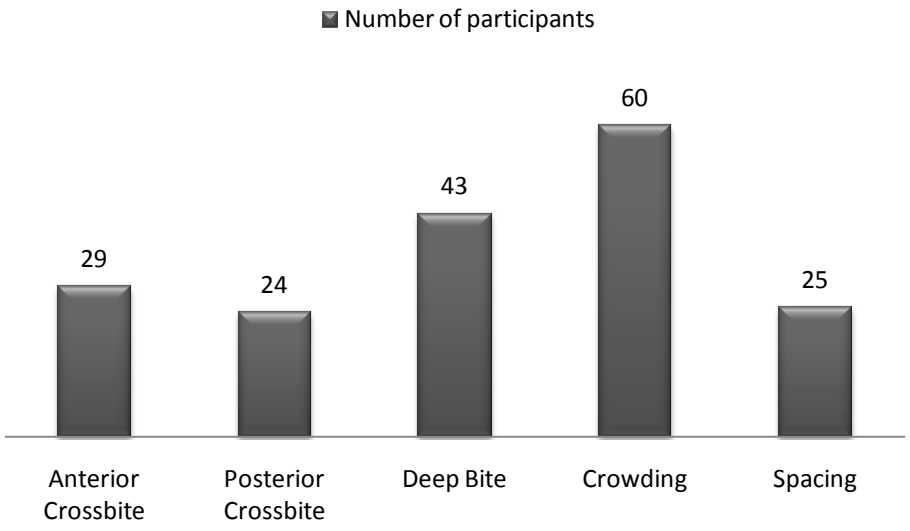

Figure 3-1. Malocclusion Categories with number of participants. Subjects can have more than one malocclusion type.

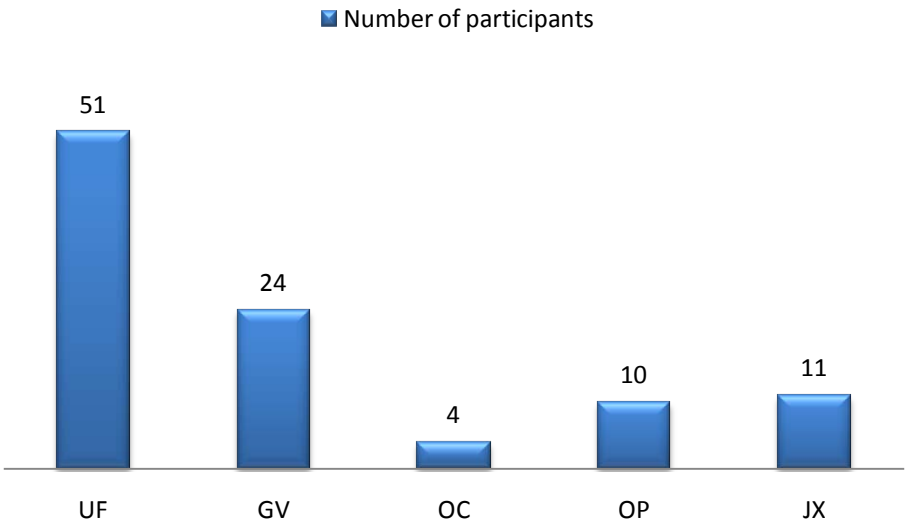

Figure 3-2 Treatment site locations and number of participants.

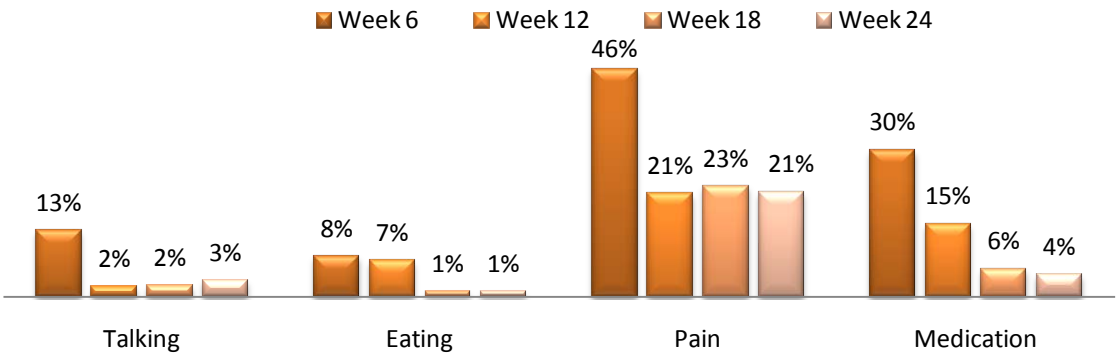

Figure 3-3. Percentage of subjects reporting pain with aligner use, having pain requiring medication usage for pain relief, problems talking due to aligners, and problems eating due to aligners.

CHAPTER 4
DISCUSSION

No previous studies have been undertaken on the use of Invisalign therapy in patients in the mixed dentition. The purpose of this study was to evaluate the effectiveness of treatment with Invisalign aligners in patients with mixed dentition vis-à-vis those malocclusions that are most prevalent in this age group.

Plaque Index scores in this study [upper 1.057 (SE .0902), lower 0.787 (SE .0859) at week 24] were less than those reported elsewhere in the literature,[16] while Gingival Inflammation scores [1.310 (SE.0420) upper, 1.306 (SE .0414) lower at week 24], and DI scores [0.0139 (SE .0047) upper and .002 (SE.0031) lower at week 24] were in the range of scores reported by patients who did not have appliances.[15-16] The low plaque index scores might correlate to a shorter observation period, or perhaps to a keener group of subjects devoted to oral hygiene than participants involved in other research. Previous studies by Naranjo et al[17] and Lee et al[18] have established the increased prevalence of plaque after placement of fixed orthodontic appliances. In our study there were no significant differences for plaque index (PI), papillary bleeding score (GI), and decalcification index (DI) between the values obtained at week 0 and later at week 24 for either the upper or the lower arch. This is significant inasmuch it has been reported in the literature that white spot lesions can be seen in 50% of the patients on at least one tooth after treatment with fixed appliances.[15] Oral hygiene maintenance appears to be easier to obtain in the Invisalign system, possibly due to the removable nature of the appliance, which allows for easier access during plaque removal.[19]

A dearth of quality studies regarding correction of posterior crossbite exists in the literature.[20-21] Previous studies have reported self correction of posterior crossbites in the mixed dentition to be as high as 45% (9 out of 20 patients)[22] to as low as no self correction (0 out of

15).[23] Nonetheless, orthodontic correction of crossbites is widely utilized. McNally et al reported correction of posterior crossbite by intermolar expansion using either a quadhelix or expansion arch at 12 weeks, with a mean expansion of 4.54 mm and 5.09 mm, respectively, at the molars. Petrén et al[23] reported an average treatment time of 4.8 months to correct posterior crossbite using a quadhelix. Kennedy et al[24] estimates the time to correct a posterior crossbite to be between two to six weeks. In this study, correction of anterior and posterior crossbites at week 24 was 57.7% (95% CI (36.9%-76.6%) and 50% (95% CI (28.2%- 71.8%), respectively. It should be noted that a few patients were not finished with their prescribed number of aligners by the week 24 benchmark. As a result, the correction effectiveness likely would increase if the patients were followed out over a longer period for further observation. Moreover, it would appear that, relative to other studies, the mean time to correct a crossbite is longer using the Invisalign appliance versus more conventional appliances, such as the quadhelix.[25]

Evidence-based guidance regarding deep bite correction in children is lacking in the literature.[26] In this study, bite depth correction showed a mean improvement of only 13% at the conclusion of week 24. It appears bite depth correction with Invisalign in the mixed dentition patient is an unpredictable movement. These values are in agreement with Kravitz,[7] who found that only 43% of projected anterior intrusion was achieved. This study suggests that significant correction of deep overbites with polyurethane aligners is a more difficult movement to achieve. In the transitional dentition, factors such as short crown height, erupting permanent teeth, and missing or loose deciduous teeth all contribute to the problem of placing the correct biomechanical force to intrude the incisors. This is a problem clinician's encounter with any appliance in the transitional dentition.

Alignment of the dentition in adult patients treated with Invisalign was reported by Kuncio[5] to have comparable alignment scores to traditional braces. In this study subjects with crowding showed a 35.5% reduction in the Little's Index score on the upper arch and a 35.8% reduction on the lower arch from week 0 to week 24. In subjects with spacing, a 58.6% reduction in the upper and 61.2% reduction in the lower arch was observed. The low number of subjects categorized as having spacing on the lower arch no doubt contributed to this value lacking statistical significance. Nonetheless, improvement was noted in both arches, with reduction of the Little's Index score greater in the spacing subjects. Patients may have experienced even greater reduction in the Little's Index score beyond week 24. Thus it appears the Invisalign System can effect improvement in alignment scores in patients with mixed dentition.

Quality of life measures for the aligners previously were assessed by Nedwed et al[27] in an adult population with findings that showed: 44% of patients experienced no speech impairment; 34 % had no pain; 54% experienced mild pain while wearing aligners; and, 44% of the patients reported difficulty in chewing. These numbers are slightly higher than reported in this study, which perhaps implies a greater adaptability of the mixed dentition patient to treatment. In contrast, Miller et al[12] showed that the patients treated with Invisalign had quality of life values that returned to near baseline levels by day 7. He also showed that subjects in the fixed appliance group took more pain medications than those in the Invisalign group at days 2 and 3.[12] In his survey of 357 adolescents, Bernabe et al[28] found 38.7% of respondents reported quality of life to be severely affected with fixed appliances, versus only 20% who had exclusively used removable appliances. These values are in general agreement with our findings.

As with other removable appliances, compliance was an issue in this study. Both Boyd[29] and Phan[30] noted that adult patients who fail to wear the aligners at least 22 hours per day are unlikely to achieve desired results. Lindaurer et al[31] found that one in six patients lost their prescribed essix retainers, with the majority of those losses being ascribed to the clear and removable nature of the essix retainer--properties that are similar to Invisalign aligners. Petren[23] found one third of the patients who utilized a removable plate for posterior crossbite correction to be non-complaint. Compliance likely played a role in the large standard deviations in this study. Future studies are needed in this area, possibly utilizing non-patient reported compliance measures, such as compliance indicators on Invisalign Teen.

CHAPTER 5
CONCLUSIONS

Invisalign treatment in mixed dentition yielded varied treatment results.

The following conclusions can be made:

1. Gingival and tooth health showed no change form baseline to week 24 indicating that Invisalign offers a hygienic modality of treatment for patients in the mixed dentition.

2. Little's Index scores were reduced in the majority of subjects.

3. Correction of anterior and posterior crossbite was effective in approximately 50% of the cases through 24 weeks.

4. Deep bite correction is difficult movement using aligners in mixed dentition.

5. Quality of life was not impacted for the majority of the mixed dentition patients who were treated with the Invisalign system.

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