

Evaluation of adverse physiological events during Invisalign® treatment: part 1

Drs. Bridgette Jones Brooks, Bryan Keith Blankenship, and Jared Stasi explore the literature regarding clear aligners as compared to traditional braces

Experimental hypotheses

Based on an extensive review of the literature, the experimental hypotheses state that

1. Patients being orthodontically treated with Invisalign® experience less discomfort than patients being treated with traditional fixed appliances.
2. Patients being orthodontically treated with Invisalign experience fewer issues with periodontal health than patients being treated with traditional fixed appliances
3. Patients being orthodontically treated with Invisalign experience fewer issues with caries/demineralization periodontal health than patients being treated with traditional fixed appliances



Bridgette Jones Brooks, DMD, is a graduate of Spelman College with a Bachelors' degree in Psychology. She attended East Carolina University School of Dental Medicine where she obtained her Doctorate of Dental Medicine and then completed a General Practice Residency at Mountain Area Health Education Centers. She completed her orthodontic training at the Georgia School of Orthodontics where she received a certificate in Orthodontics and Dentofacial Orthopedics. She currently practices in the metropolitan Atlanta, Georgia, area.



Bryan Keith Blankenship, DDS, is an alumnus of The Ohio State University (DDS) and Bachelor's and Master's degrees in Microbiology. He is a graduate of the Georgia School of Orthodontics (Class of 2020). Dr. Blankenship currently practices orthodontics in Palm Coast, Florida.



Jared Stasi, DDS, earned a Bachelor of Science and his dental degree from Creighton University. He received a certificate in Orthodontics and Dentofacial Orthopedics from the Georgia School of Orthodontics (Class of 2020). Dr. Stasi currently practices orthodontics in Centennial, Aurora and Silverthorne, Colorado.

Disclosure: None of the authors has any financial interest in Invisalign® (Align Technology Inc.).

Educational aims and objectives

This article aims to study the differences in discomfort, periodontal health, or caries/demineralization experienced by patients who are being orthodontically treated with Invisalign® as compared to traditional fixed appliances.

Expected outcomes

Orthodontic Practice US subscribers can answer the CE questions on page XX or take the quiz online at orthopracticeus.com to earn 2 hours of CE from reading this article. Correctly answering the questions will demonstrate the reader can:

- Realize some basic benefits and challenges of clear aligner and braces orthodontic treatment.
- Realize what some studies have found regarding orofacial pain/discomfort with clear aligners or traditional braces.
- Realize what some studies report regarding maintain an appropriate level of oral hygiene with either clear aligners or traditional braces.
- Identify some challenges in avoiding dental caries and demineralization when using clear aligners or traditional braces.



Purpose/abstract

The aim of this study is to review the appropriate literature concerning adverse physiological events experienced by patients being treated with Invisalign appliances and comparing this literature to that of patients' adverse physiological events when undergoing fixed orthodontic appliance therapy.

Introduction/literature review

Invisalign removable orthodontic therapy was introduced in 1999 and serves as an alternative to traditional fixed orthodontic appliances. Invisalign claims to improve esthetics and to be more convenient for patients by allowing aligners to be removed during eating and drinking.¹ Patients treated with Invisalign have reported greater satisfaction during orthodontic therapy² and fewer negative impacts on their lives during the initial stages of their orthodontic treatment.³ As more adults are seeking orthodontic treatment, the popularity of clear aligners as a substitute for fixed orthodontic appliance therapy has increased.⁴

With the advent of Invisalign therapy, there has been a parallel increase in research regarding Invisalign treatment. Initially, research was done primarily in the areas of treatment efficacy, effectiveness, and oral hygiene.⁵ Significant research on the

gingival outcomes using Invisalign has also been conducted and evaluated.⁶ Studies have found varying psychosocial effects of Invisalign treatment.⁷ Few studies, however, have evaluated adverse effects of Invisalign use, including the effects of Invisalign treatment on patients' perceptions of pain and impacts on systemic health.

In 2007, Allareddy, et al., conducted a comprehensive literature search of the Manufacturer and User Facility Device Experience (MAUDE) database (U.S. Food and Drug Administration) for pertinent medical reports associated with Align Technologies products. They found that there were 173 medical device reports from 2006-2016. Forty-five (26%) of these reports dealt with adverse physiological events associated with Invisalign therapy, and the nature of these events ranged from irritation of the tongue and lips to anaphylactic reactions.⁸

In recent years, Invisalign continues to introduce new products into the market, including Invisalign® First. Invisalign First is Phase 1 orthodontic treatment specifically targeting patients aged between 6 and 10 years.⁹ As this technology will begin to impact more of the consumer market, it seems logical and appropriate that more research is needed regarding possible complications that can be associated with

Invisalign treatment, especially side effects such as those highlighted in the Allareddy, et al., study.

Based upon informed consent and risk/benefit patient education presented by the dental practitioner prior to treatment, it then becomes the educated responsibility of the parents/patients to determine which treatment modality may be best suited for themselves and their children. Parameters, including pain experienced while undergoing treatment, changes in periodontal health, and caries experienced during treatment, will need to be thoroughly explored prior to the consumer making the best treatment modality decision.

Orofacial pain/discomfort

Orofacial pain encompasses many facets of pain in the head and neck region. It occurs within the trigeminal complex and encompasses dental pain (odontogenic), and hard tissue and soft tissue pain.¹⁰ With orthodontic treatment, patients are most likely to experience odontogenic pain. This pain is defined as being derived from the teeth and/or its supporting structures.¹¹ Inflammatory mediators are released when orthodontic forces are applied. These mediators not only aid in tooth movement, but also are associated with a pain-like sensation perceived by the patient. The perception varies among subjects, but in general, it has been described as beginning within a few hours of orthodontic treatment being initiated, peaking after 1 day, and subsiding within 7 days.¹² Pain perception can vary among individuals relative to factors such as gender and age, but adolescents (ages 14 to 17) reported more severe pain during orthodontic treatment when compared to preadolescents (ages 11 to 13) or adults (ages greater than 18).⁷

Most studies have focused on pain reported after separation of teeth for orthodontic banding or the bonding of traditional fixed orthodontic appliances.^{7,12} With the increased use of clear aligners, studies have also begun to compare pain experienced with Invisalign versus traditional fixed appliances. In a study of 60 adult orthodontic patients, Miller, et al.,⁴ found that significantly less pain was associated with Invisalign than with traditional fixed appliances during the first week of treatment. They also found that patients treated with Invisalign reported taking less pain medication during the first week of treatment than the fixed orthodontic appliance group. In another study, Shalish,



et al., compared patients' perception of recovery from pain/discomfort in the first few days after insertion of lingual fixed orthodontic appliances, or traditional fixed orthodontic appliances and Invisalign appliances. However, in this study, Invisalign patients not only reported more severe pain compared to patients with labial fixed appliances, but also reported the lowest level of oral symptoms.¹³ Fujiyama, et al., noted in a study of 145 cases that Invisalign may result in less pain/discomfort than fixed orthodontic appliances during initial stages, but care must be taken to avoid deformation of the Invisalign trays that could result in pain and discomfort.¹⁴

As mentioned earlier, many of the studies investigating pain/discomfort in Invisalign treatment and fixed orthodontic appliance treatment have targeted the early or initial phase of treatment, but few studies have targeted pain incurred during different time points during orthodontic treatment. White, et al., conducted a randomized prospective trial in which patients received orthodontic treatment with Invisalign or with traditional fixed appliances. They assessed patients during the week after bonding, and again after the first and second monthly adjustment. They found that patients being treated with fixed orthodontic appliances had more pain in the first week than the Invisalign group, and there were similar findings for subsequent adjustments with the Invisalign group experiencing less pain than the fixed group.¹⁵

Periodontal health

As more teenagers and adults are beginning to use Invisalign for their orthodontic

treatment, more research is being done on the impact of Invisalign therapy and patient periodontal health and hygiene. Traditional fixed orthodontic appliances may make it more difficult for patients to maintain an appropriate level of oral hygiene. Periodontal health can be measured using many different parameters, including oral hygiene, bleeding on gingival probing, gingival inflammation, plaque index, gingival index, biofilm mass, papillary bleeding, and others.¹⁶ Miethke, et al., reported that patients treated with Invisalign may not have an increased risk of negative periodontal effects despite the trays remaining on the teeth throughout the day and night (exceptions are meals and sports) and cover both the teeth and gingiva.⁶

Azaripour, et al., studied the impact of treatment appliances on hygiene, periodontal health, and quality of life.² Patients' periodontal health and oral hygiene levels were assessed before and during orthodontic treatment with either traditional fixed appliances or Invisalign. Upon final assessment, there was a significant difference in the increase in bleeding and gingival inflammation when the traditional fixed appliances group and Invisalign group were compared with the Invisalign group demonstrating better gingival health. Rossini, et al., also sought to determine if clear aligner treatment has negative effects in periodontal health. They conducted a systematic review of the literature and were able to use five studies in their meta-analysis of the data to help answer this question. The results of the studies suggested that there were significantly less plaque, less bleeding on probing, better probing pocket depths, less plaque

biofilm mass, and better gingival index and papillary bleeding in the clear aligner groups when compared with the fixed appliance groups.¹⁶

Another periodontal assessment during Invisalign therapy and fixed orthodontic appliance therapy involves plaque biofilm levels. Low, et al.,¹⁷ found no significant difference in amounts of plaque biofilm among clear aligner wearers throughout their treatment when compared to fixed orthodontic appliance therapy patients. Levrini, et al., reported significantly different amounts of plaque biofilm between the Invisalign and fixed orthodontic appliance groups and also significantly different levels of bacteria in the plaque biofilm between the two groups, with the traditional fixed orthodontic appliance group having higher amounts of periodontal disease-causing bacteria in the biofilm.¹⁸

When comparing different fixed orthodontic appliance therapies relative to periodontal health parameters, self-ligating brackets have been reported to accumulate less plaque than elastomeric (rubber elastic) ligated traditional fixed appliances. Chibber, et al., studied the differences among the self-ligating brackets, Invisalign, and elastomerically ligated traditional fixed appliances and their effects on gingival index, papillary bleeding index, and plaque index.¹⁹ They found that although there were short-term significant differences between gingival index and papillary bleeding index between the clear aligner group and the self-ligating group and the elastomerically ligated group, there were no long-term significant differences between the three groups after 18 months.

Dental caries and demineralization

Since their inception in orthodontic treatment, it has been touted that clear aligners (Invisalign) are more hygienic than fixed orthodontic appliances. The ease of removing the trays during treatment for oral hygiene purposes is a major consideration. However, the evidence for clear aligners being more hygienic or caries-preventive has never been demonstrated. The design of the aligners prevents the normal, self-cleansing salivary flow, thus preventing the natural cleansing and remineralization of teeth.² Addition of composite attachments to the Invisalign trays may provide an increase in caries index and demineralization areas of the patient especially since the trays are designed to be worn for approximately 22-23 hours per day.

Cariogenic, sugar, and carbohydrate-based drinks can significantly affect the

Parameters, including pain experienced while undergoing treatment, changes in periodontal health, and caries experienced during treatment, will need to be thoroughly explored prior to the consumer making the best treatment modality decision.

patients' dental health if a significant consumption of these fluids occurs during Invisalign in the absence of adequate dental and gingival cleansing resulting in an increase in acid-producing plaque.²⁰ While it is standard operating procedure to instruct patients in proper oral hygiene and in avoidance of wearing the trays while eating or drinking, patients are too often noncompliant to these suggestions, and the resultant side effects concerning dental and gingival health can become problematic. Several articles have shown the effects of caries and demineralization with clear aligner appliances.²¹ Nontypical areas of decalcification generally cleansed with saliva, such as cusp tips and incisal edges, have been associated with higher caries indices when aligners are worn during food and drink consumption.²² Regardless of the appliances used in orthodontic therapy, patient education is a must especially in high-caries risk and poor oral hygiene patients.

Interproximal reduction (IPR): adjunct in Invisalign therapy and its impact upon oral health

Interproximal reduction (IPR), also known as interproximal enamel reduction (IER), involves removing enamel from the interproximal surfaces of teeth. This technique provides an alternative to extraction treatment by allowing for reduction of tooth mass and the resultant increase in interproximal space²³ and is a technique frequently used during Invisalign treatment. Both anterior and posterior teeth may be designated for IPR, with as much as 7 mm of total interproximal reduction possible in the posterior teeth (premolar and first molar region) and another 2.5 mm of reduction in the anterior teeth (cuspid to cuspid). It also has been suggested that IPR can reduce treatment time by removing the exact amount of tooth structure needed to resolve crowding in cases where it is used.²⁴ IPR can be done

using several techniques, including air-rotor stripping (ARS) with diamond or carbide burs, handpiece-mounted diamond discs, and motor- or hand-driven interproximal diamond strips.

Some have suggested that IPR abrades the enamel surface of the designated teeth, resulting in dental surfaces that are more susceptible to plaque and bacterial accumulation.²⁵ Different IPR instruments have been found to produce different amounts of enamel surface abrasion, with diamond burs creating the roughest surface and diamond discs creating the least abrasion (as measured by nanotopography).²⁶ Polishing is a strategy that is used to reduce this surface roughness and reportedly restores the tooth to a surface that is smoother than untreated enamel.²⁴

Several authors have studied the risks of IPR on caries formation and ways to mitigate this risk. Twesme, et al., found that there was an increase in demineralization of tooth structure when IPR was performed using an air-rotor device, but when topical fluoride was applied after the procedure, the penetration of the lesion was diminished.²⁷ Polishing is a strategy that can be used to reduce surface roughness of the enamel and reportedly restores the tooth to a surface that is smoother than untreated enamel.²⁴ Several other studies determined that there is not an increased caries risk associated with IPR.^{23,24,25} To summarize, IPR as an adjunct in Invisalign therapy is a viable non-extraction procedure, but the clinician must be judicious in its use so as not to result in patient pain, discomfort, or reduction in acceptable periodontal and dental health.

Materials and methods

A variety of methods and materials were used in the selected studies for this systematic review. Many studies of orofacial pain have utilized self-report questionnaires^{4,7,12,13,14,15} and visual analog scales^{12,14,15} in

the assessment of pain, while others had patients completed a diary of their experience with the fixed orthodontic appliances and Invisalign trays. When assessing periodontal changes, clinical examinations were often performed using various indices, including plaque index, gingival index, bleeding on probing, papillary index, periodontal bleeding index, and periodontal probing depths.^{2,6} Several studies were structured as clinical trials with differing levels of blinding and controls.^{18,19} Other studies analyzed the aligners or aligner materials directly using Polymerase Chain Reaction and Scanning Electron Microscope,^{17,18} and one study used a systematic review for comparison of the two different orthodontic treatment modalities.¹⁶ Caries and demineralization were often assessed using radiographs and clinical examination of patients who had undergone IPR in the past.^{23,24,25} For some of the in-vitro studies, extracted teeth were treated with IPR directly and demineralization was simulated in the lab.^{26,27}

Data analysis and results

Orofacial pain^{4, 13,14,15}

A total of four studies addressed orofacial pain. Among these four studies, all are prospective in nature, and all studies evaluated patients' experience with the treatment longitudinally. All of the four studies used only adult patients. The sample sizes in these studies ranged from 41 to 145. The age of the sample of patients selected in these studies ranged from 18 to 60 years with a mean age of 28. A total of 32% of all participants in these four studies are male (67 patients). A total of 67.6% of all participants in these four studies are female (140 patients). The follow-up time of patients after the procedure in these studies ranged from 1 to 60 days. Among those six studies, four studies used a self-reported questionnaire to understand the experience of patients and four studies used a visual analog scale to measure pain level experienced by patients.

Periodontal health^{2,6,16,17,18,19}

A total of six studies addressed periodontal health. Among these six studies two are a prospective cohort, one cross-sectional study, one RCT by design, and one study is a systematic review of literature. All studies used adult patients. Three studies also utilized adolescent patients. The sample sizes in these studies ranged from 11 to 63. The age of the sample of patients selected in these studies ranged from 11 to

63 years. The average of the two studies reporting patients' age means was 24 years old. A total of 41% of all participants in these 5 studies are male (135 male). A total of 59% of all participants in these 5 studies are female (199 female). The follow-up time of patients after the procedure in these studies ranged from 1 to 14 days. Periodontal health outcomes (periodontal health) were measured in these studies by using plaque index, gingival index, bleeding on probing, papillary index, periodontal bleeding index, and periodontal probing depths.


Caries^{21, 24, 25, 26, 27}

A total of five studies addressed the issue of caries. Among these one study is a case report, one study followed patients longitudinally, and one study involved radiography and imaging. A total of four studies used adult patients, and two studies utilized premolars. The sample sizes in these studies

ranged from 40 to 61. The age of the sample of patients selected in these studies ranged from 19-70 years of age. A total of 60% of all participants in these five studies are male (126 patients). A total of 40% of all participants in these five studies are female (83 patients). The follow-up time of patients after the procedure in these studies ranged from 1 to 10 years. Caries were measured per radiographic assessment.

Part 2 of this article will continue with the Discussion and Findings of the studies and some conclusions regarding orofacial pain, periodontal health, and caries/demineralization.

Acknowledgments

The authors would like to extend their appreciation to Dr. Harish Parihar (the biostatistician) and Dr. John Stockstill, Professor and Director of Dental Research at the Georgia School of Orthodontics, for their valuable guidance and contributions to this article. 

REFERENCES

- Phan X, Ling PH. Clinical limitations of Invisalign. *J Can Dent Assoc.* 2007;73(3):263-266.
- 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;15:69.
- Miethke R, Vogt S. A comparison of the periodontal health of patients during treatment with the Invisalign system and with fixed orthodontic appliances. *J Orofac Orthop.* 2005;66(3):219-229.
- Miller K, McGorray S, Womack R, et al. A comparison of treatment impacts between Invisalign aligner and fixed appliance therapy during the first week of treatment. *Am J Orthod Dentofacial Orthop.* 2007;131(9):302.
- Gu J, Tang J, Skulski B, et al. Evaluation of Invisalign treatment effectiveness and efficiency compared with conventional fixed appliances using the Peer Assessment Rating index. *Am J Orthod Dentofacial Orthop.* 2017;151(2):259-266.
- Miethke R and Brauner K. A comparison of the periodontal health of patients during treatment with the Invisalign system and with fixed lingual appliances. *J Orofac Orthop.* 2007;68(3):223-231.
- Brown D, Moerenhout R. The pain experience and psychological adjustment to orthodontic treatment of preadolescents, adolescents, and adults. *Am J Orthod Dentofacial Orthop.* 1991;100(4):349-356.
- Allareddy V, Nalliah R, Lee M, Rampa S, Allareddy V. Adverse clinical events reported during Invisalign treatment: Analysis of the MAUDE database. *Am J Orthod Dentofacial Orthop.* 2017;152(5):706-710.
- Blevins, R. Phase I orthodontic treatment using Invisalign First. 2019. *J Clin Orthod.* 52(3):73-83.
- Kandasamy S, Greene C, Rinchuse D, Stockstill J. *TMD and Orthodontics.* Springer International Publishing Company: New York, NY; 2016.
- Renton T. Dental (Odontogenic) Pain. *Rev Pain.* 2011;5(1):2-7.
- Sandhu S, Leckie G. Orthodontic pain trajectories in adolescents: Between-subject and within-subject variability in pain perception. *Am J Orthod Dentofacial Orthop.* 2016;149(4):491-500.
- Shalish M, Cooper-Kazaz R, Ivgil et al. Adult patients' adjustability to orthodontic appliances. Part I: a comparison between Labial, Lingual, and Invisalign. *Eur J Orthod.* 2011;34(6):724-730.
- Fujiyama K, Honjo T, Suzuki M, Matsuoka S, Deguchi T. Analysis of pain level in cases treated with Invisalign aligner: comparison with fixed edgewise appliance therapy. *Prog Orthod.* 2014;15(1):64.
- White D, Julien K, Jacob H, Campbell P, Buschang P. Discomfort associated with Invisalign and traditional brackets: A randomized, prospective trial. *Angle Orthod.* 2017;87(6):801-808.
- Rossini G, Parrini S, Castrolforio T, Deregius A, Debernardi C. Periodontal health during clear aligners treatment: a systematic review. *Eur J Orthod.* 2014;37(5):539-543.
- Low B, Lee W, Seneviratne C, Samaranayake L, Hagg U. Ultrastructure and morphology of biofilms on thermoplastic orthodontic appliances in 'fast' and 'slow' plaque formers. *Eur J Orthod.* 2010;33(5):577-583.
- Levrini L, Mangano A, Montanari P, Margherini S, Caprioglio A, Abbate G. Periodontal health status in patients treated with the Invisalign system and fixed orthodontic appliances: A 3 months clinical and microbiological evaluation. *Eur J Dent.* 2015. 9(30):404-410.
- Chibber A, Agarwal S, Yadav S, Kuo C, Upadhyay M. Which orthodontic appliance is best for oral hygiene? A randomized clinical trial. *Am J Orthod Dentofacial Orthop.* 2018;153(2):175-183.
- Moshiri M, Eckhart J, McShane P, German D. Consequences of poor oral hygiene during clear aligner therapy. *J Clin Orthod.* 2013;47(8):494-498.
- Birdsall, J and Robinson, S. A case of severe caries and demineralization in a patient wearing an essix-type retainer. *Prim Dent Care* 2008. 15(2):59-61.
- Sheridan, John J., et al. Avoiding demineralization and bite alteration from full-coverage plastic appliances. *J Clin Orthod.* 2001;35(7):444.
- Zachrisson B, Minster L, Øgaard B, Birkhed D. Dental health assessed after interproximal enamel reduction: Caries risk in posterior teeth. *Am J Orthod Dentofacial Orthop.* 2011;139(1):90-98.
- Jarjoura K, Gagnon G, Nieberg L. Caries risk after interproximal enamel reduction. *Am J Orthod Dentofacial Orthop.* 2006;130(1):26-30.
- Zachrisson B, Nyøgaard L, Mobarak K. Dental health assessed more than 10 years after interproximal enamel reduction of mandibular anterior teeth. *Am J Orthod Dentofacial Orthop.* 2007;131(2):162-169.
- Meredith L, Farella M, Lowrey S, Cannon R, Mei L. Atomic force microscopy analysis of enamel nanotopography after interproximal reduction. *Am J Orthod Dentofacial Orthop.* 2017;151(4):750-757.
- Twesme D, Firestone A, Heaven T, Feagin F, Jacobson A. Air-rotor stripping and enamel demineralization in vitro. *Am J Orthod Dentofacial Orthop.* 1994;105(2):142-152.