The Effect of Upper Arch Expansion by clear aligners on Nasal Airway Volume in Children and Adults

by

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Abstract

Obstructive sleep apnea (OSA) affects more than 900 million people around the world (Benjafield et al., 2019). OSA occurs due to obstruction of the airway at different levels of the airway, including upper and lower pharyngeal constrictions due to narrow upper jaw and underdeveloped/backward positioned lower jaw. Treatment modalities of OSA include active oxygen infusion, oral appliances or surgical expansion of the upper arch and/or surgical advancement of the lower and upper jaws; however, these modalities have many challenges and complications (Benjafield et al., 2019; American Academy of Sleep Medicine, 2015; Schwengel et al., 2014; Yaggi et al., 2005). Previous research has shown that rapid maxillary expansion can improve the nasal airway, thereby improving OSA (Peppard et al., 2000; Cordasco et al., 2012; Mônego Moreira et al., 2017). Orthodontic appliances such as clear aligners can be used for slow maxillary expansion; however, the effect of this type of treatment on both the nasal airway volume and morphology has not been investigated. Therefore, the objective of this study was to investigate the effect of clear aligners on the nasal airway volume and morphology of pediatric patients undergoing maxillary expansion. In addition, a pilot study was conducted to investigate the effect of clear aligners on the volume of the nasal airway in adults.

We conducted a retrospective study on 13 pediatric patients (ages 6-13 years old). These patients had treatment of their malocclusion using clear aligners and their treatment involved upper arch expansion as well as initial and after treatment CBCTs (Cone Beam Computed Tomography) as part of their routine orthodontic records. We set up a control group of 8 children (7-12 years) without clear aligner treatment but having two CBCTs. Based on the treatment and control groups, we investigated whether pediatric patients treated with clear aligners had a significant increase in upper arch expansion and nasal airway volume and morphology. Secondly, we conducted a retrospective pilot study to investigate the effect of upper arch expansion using clear aligners in the adult population. We studied 6 adults (31-52 years) who were treated with clear aligners for maxillary expansion.

The results showed a significant increase in nasal airway volume as well as intermolar distance in the treatment group of pediatric patients, but not in the control group. No correlation was found between the changes in intermolar distance and nasal airway volume in the treatment group. In the adult population, the results suggest a trend of increased nasal airway volume after maxillary expansion with clear aligners, however, the results were not statistically significant. Further study with an increased sample size may confirm the suggested trends.

This work provides a method to investigate changes in nasal airway volume and morphology and demonstrates the potential for slow maxillary expansion with clear aligners to improve nasal airway parameters. This suggests that such treatment may be a possible solution to improve outcomes for OSA patients.

Keywords: obstructive sleep apnea (OSA), clear aligners, narrow upper jaw, cone-beam computed tomography systems (CBCT), intermolar distance, nasal airway volume

Preface

This thesis is an original work by Boyu Pan. The research project required the use of CBCT scan images of the nasal airway region. Therefore, this study has been approved by the University of Alberta Health Ethics Review Board: Pro 00047506. The CBCT scan data will be used anonymously.

In the third chapter of this thesis on the study of children, I was responsible for collecting, organizing, and conducting the patients' CBCT data, conducting the study, and editing the manuscript. Adelaide Lui assisted in collecting patient data in the local clinic for the study. Zamir Datoo, David Shaw, Kareem Ali, Delaney MacIntosh, and Mostafa Mohamed assisted in obtaining the results by applying our methods. Rabia Njie provided valuable advice on the methodology of our study. Delaney MacIntosh also helped to develop the methodology in the study. Dr. Westover and Dr. El-Bialy were the supervisory authors. They assisted in developing the methodology, analyzing the results and editing the manuscript.

In the third chapter of this thesis on adult research, I was responsible for collecting, organizing, and conducting research on patients' CBCT data as well as editing the manuscript. Adelaide Lui helped collect patient data in the local clinic. Dr. El-Bialy and Dr. Westover were the supervisory authors and were involved with concept formation, research analysis and manuscript edits.

Acknowledgments

First and foremost, I am grateful to my supervisors, Dr. Lindsey Westover and Dr. Tarek El-Bialy, who have helped me tremendously throughout my graduate studies in my life, my studies, and my research. I feel very fortunate to have received their patient and careful guidance. Their scientific research experience and knowledge of the field were crucial to the completion of this project. They are both excellent and are my role models, and I have learned a lot from them.

Finally, I would like to thank my family members my dad and mom. They are my strong backing, always behind me and giving me silently. At the same time, they are also one of my spiritual pillars.

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Chapter 1: Introduction

1.1 Background and Motivation

Obstructive sleep apnea (OSA) is one of the most common sleep disorders (Cerritelli et al., 2022). It affects people's sleep quality as well as their physical health. Besides causing depression and irritability (Schwengel et al., 2014), it can also lead to many serious health complications, such as stroke and cardiovascular disease (Yaggi et al., 2005; Peppard et al., 2000; Epstein et al., 2009).

Maxillofacial abnormalities are one of the causes of OSA problems in children, such as narrow intermolar spacing and narrowing of the maxilla and hypoplastic/posterior mandible (Schwengel et al, 2014). This results in airway obstruction at various levels of the airway. In clinical practice, the main methods of maxillary expansion orthodontic treatment include rapid maxillary expansion (RME), slow maxillary expansion (SME) and surgically assisted rapid maxillary expansion (SARME) (Ficarelli et al., 1978; Bell, 1982). These tooth-borne maxillary expansion treatments are common orthodontic treatments used to treat maxillofacial abnormalities (Görgülü et al., 2011; Farronato et al., 2011; Farronato et al., 2012; Leonardi et al., 2018; Maspero et al., 2019). These orthopedic expansion treatments are obtained by means of appliances that transmit forces to the teeth, which in turn lead to splitting of the midpalatal suture and a certain amount of widening of circummaxillary sutures (Lanteri et al., 2020).

In addition, some previous research has shown that RME can improve the nasal airway (De Felippe et al., 2009; Cordasco et al., 2012; Mônego Moreira et al., 2017). But, there have been cases of recurrence of maxillofacial abnormalities after RME therapy (Gurel et al., 2010) and RME can cause edema, pain, and ulcers in and around the palate. Alternatively, during the maxillary expansion treatment, the SME applies a milder force, which makes the entire treatment process more stable and provides more time for the bone formation of the intermaxillary structures (Bell, 1982; Hicks, 1978; Mew, 1983). Therefore, it is more physiological and more favored by doctors and patients (Martina et al., 2012). Compared to these traditional SME methods, clear aligners are safer, more hygienic, more comfortable and more aesthetically pleasing than other braces, such as traditional braces and ceramic braces (Lin et al., 2022; Sharma et al., 2021; White et al., 2017). However, the effect of maxillary arch expansion using clear aligners on the nasal airway in pediatric and adult patients has not been investigated.

The objective of this study was to investigate the effect of clear aligners on the nasal airway volume and morphology of pediatric patients undergoing maxillary expansion. In addition, a pilot study was conducted to investigate the effect of clear aligners on the volume of the nasal airway in adults.

1.2 Objectives

The study objectives were achieved through the following specific aims (SA):

SA1) Determine the possible 3D changes in the nasal airway volume and morphology after maxillary arch expansion with clear aligners using cone-beam computed tomography (CBCT) and compare the results of treatment to a control group without treatment.

SA2) Assess the maxillary intermolar distance changes associated with maxillary expansion using clear aligners in children.

SA3) Investigate statistical correlations between intermolar distance changes and changes in nasal airway volume in children.

SA4) Investigate the changes in the nasal airway volume in adults after upper arch expansion with clear aligners in a pilot study.

1.3 Thesis Outline

The research conducted in this these is presented as follows:

Chapter 1 provides a brief introduction to the research by describing the background and the motivation of the research. It also shows the research objectives in detail.

Chapter 2 provides a detailed background of the study as well as a review of the relevant literature.

Chapter 3 provides details of the study on the effect of the upper arch expansion by clear aligners on nasal airway volume in children (SA1 – SA3). The study methodology, data results and analysis, and discussion of data results are introduced in detail. Finally, conclusions are made regarding the effect of clear aligners on the nasal airway in children.

Chapter 4 provides details of the pilot study on the effect of the upper arch expansion by clear aligners on nasal airway volume in adults (SA4). The study methodology, the results, and statistical analysis are introduced. Finally, the effect of clear aligners on maxillary intermolar spacing and nasal airway volume in adults are discussed and conclusions are presented.

Chapter 5 provides the conclusions of the thesis and the analysis of its limitations and aspects that can be improved in the future.

Chapter 2: Literature Review

2.1 Obstructive Sleep Apnea

In recent years, obstructive sleep apnea (OSA) has become more and more well-known in the medical field and it has been also increasingly recognized by the public (Meier et al., 2003; Rask et al., 2021; Womack et al., 2002; Wong, 2002). In clinical practice, OSA is defined as a sleep disorder with more than or equal to five episodes per hour during sleep, which in turn leads to snoring during sleep, daytime sleepiness, interruption of breathing or waking up due to asphyxia (American Academy of Sleep Medicine, 2015). According to the survey, OSA occurs in at least 1%-4% of children (Lumeng et al., 2008). In addition, some physical characteristics of children, such as obesity, lymphatic tissue hypertrophy, and narrow upper and lower jaw bones, will make children more prone to OSA (Abulhamail et al., 2021). In the adult population, the prevalence of OSA increases with age, especially in those over 60 years of age, and obesity also increases the prevalence of OSA in adults (Qaseem et al., 2013; Balk et al., 2011; Qaseem et al., 2014; Balachandran et al., 2014). OSA affects at least 2-4% of adults (Epstein et al., 2009). In addition, in a worldwide survey, approximately 936 million people were found to have mild to severe OSA using the AASM 2012 diagnostic criteria and an apnoea-hypopnoea index threshold of 5 or more events per hour (Benjafield et al., 2019).

The high incidence of OSA makes it a daily problem for many people. This disease affects human health problems as well as the state of daily life. For example, it may cause emotional depression, irritability, breathing disorders, irregular sleep patterns, and a decline in human cognitive ability and memory (Schwengel et al., 2014). It also brings many complications, such as obesity, hypertension, stroke, and cardiovascular disease (Yaggi et al., 2005; Peppard et al., 2000; Epstein et al., 2009). In addition, and more seriously, untreated OSA is a risk factor for all-cause mortality, and the risk of death increases significantly as the severity of OSA increases (Yaggi et al., 2005). Given the enormous potential impact of untreated moderate to severe OSA on people's health, effective treatment is critical.

2.2 Maxillary expansion

In 1860, the concept of maxillary correction was first proposed by Angell (Haas, 1961). After more than a century of development, tooth-borne maxillary expansion is now a common orthodontic procedure for the treatment of children with maxillary hypoplasia (Görgülü et al., 2010). Two types of maxillary expanders are commonly used in clinical practice, the palatal acrylic (Haas-type) and the hygienic (Hyrax) dilator (Lanteri et al., 2020). Tooth-borne maxillary expansion can be rapid (RME) or slow (SME), depending on the length of correction and the amount of force applied. These two kinds of orthopedic expansion are achieved by using an appliance with a transverse screw as the active part to transmit lateral force to the upper and posterior teeth, which in turn causes the midpalatal suture (Fig. 2.1) to open and the circummaxillary suture to be widened by a certain amount (Starnbach et al., 1966; McNamara, 2006). RME is the expansion of the maxillary by a large and continuous corrective force in a short period of time. SME is to expand the maxillary through intermittent, relatively light and long-term corrective force. In addition, surgically assisted RME (SARME) is also an approach to expanding the maxillary, a treatment that combines orthodontic and surgical procedures (Koudstaal et al., 2005). Unlike RME and SME, which are mainly used in growing children and adolescents, SARME is mainly used in those who are fully developed (palatal suture is completely fused) (Ficarelli, 1978; Bell, 1982; Agarwal et al., 2010). Compared with RME and

SME, SARME is a more aggressive option and may cause bleeding or infection during treatment. SARME releases the area of resistance to expansion through the osteotomy procedure and activates the expander until the desired amount of expansion is achieved (Betts et al., 1995). The choice of any of these three methods depends primarily on the patient's age, malocclusion, and the specific state of the maxilla.

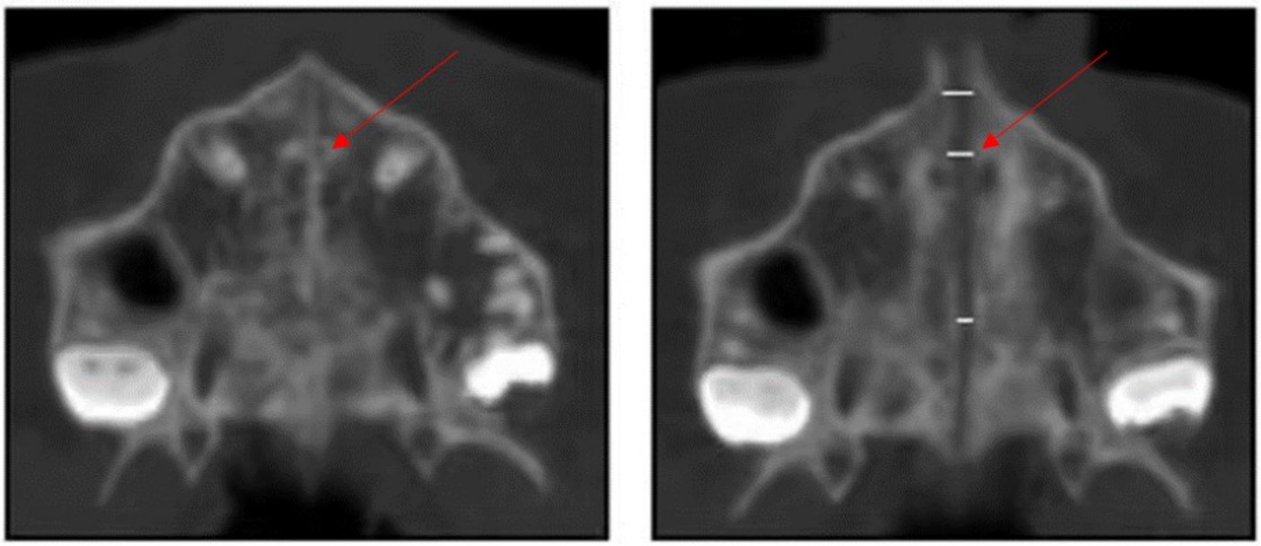


Fig. 2.1 Midpalatal suture. (left) before RME treatment. (right) after RME treatment. (Angelieri et al., 2013)

In clinical studies, Gurel et al. (Gurel et al., 2010) found a large number of recurrences of maxillary narrowing after RME. In addition, some studies pointed out some disadvantages of RME, such as the palate and surrounding pain, edema, ulcers and incisal diastema in patients. Compared with RME and SARME, the maxillary expansion treatment process of SME is slower, more stable and the applied expansion force is also smaller and gentler. SME enhances bone formation in intermaxillary structures due to less intervening force (Bell, 1982; Hicks, 1978; Mew, 1983). However, these traditional SME treatments are not aesthetically pleasing compared to the clear aligners orthodontic treatment. As an orthodontic appliance for orthodontic treatment, clear aligners (Fig. 2.2) are gaining more and more attention from orthodontic patients because of their aesthetic, removable and portable advantages (Womack et al., 2002; Wong, 2002). A study has shown that clear aligners in orthodontic treatment can also allow for expansion of the upper arch (Morales-Burruezo et al., 2020). Clear aligners are transparent braces that are virtually invisible when placed on the teeth. They are flexible plastic appliances made of polyurethane resin. During clear aligners orthodontic treatment, orthodontists regularly customize new clear aligners for the patient to achieve the final orthodontic plan. Therefore, it has good adaptability for patients.

Fig. 2.2 Clear aligners (from: https://www.goldenstatedentistry.com/blog/straighten-your-teeth-with-invisalign-clear-aligners)

2.3 Cone Beam Computed Tomography

When analyzing a three-dimensional (3D) model structure such as craniofacial anatomy, two-dimensional (2D) imaging technology such as panoramic radiographs provide only a planar projection and do not adequately represent the 3D geometry (Suomalainen et al., 2015). Using a 2D measurement tool to quantify a 3D geometry may lead to problems such as landmark identification errors and errors in measurement data (Major et al., 1994). The use of 3D technology makes up for the deficiencies of 2D technology in analyzing 3D models. Computed tomography (CT) is still widely used in clinical practice today to obtain the required 3D information in many applications (Armistead et al., 1989). But in the field of dentistry, it is limited by the disadvantages of high cost, limited access, and high radiation dose (Venkatesh et al., 2017; Silva et al., 2008).

The cone-beam CT (CBCT) is also 3D imaging, but it provides high-resolution 3D imaging, diagnostic reliability analysis and risk assessment (Silva et al., 2008; Mozzo et al., 1998; Yamamoto et al., 2003). In addition, its radiation dose is much lower than the radiation dose of traditional CT to the subject. Therefore, CBCT is widely used in both clinical and in scientific research (Suomalainen et al., 2015; Venkatesh et al., 2017). Based on CBCT which has high resolution and can be marked in 3D coordinates, it can be used for orthodontic surgery planning simulation, maxillofacial skeletal analysis, maxillary and tooth status analysis in orthodontic surgery, and to get 3D views of the upper airways (Silva et al., 2008).

Regarding the working principle of CBCT, it uses a rotating imaging device that moves around the patient's head. The scanner records 150 to 600 different x-ray scans. A powerful computer then processes these scans and creates a virtual model of the area under study (Scarfe et al., 2008). The resolution of CBCT imaging is determined by voxels, the size of which depends mainly on the size of the pixels on the area detector. The resolution of the area detector is a sub-millimeter (ranging from 0.09 mm to 0.4 mm) (Scarfe et al., 2008). This is why CBCT usually provides isotropic voxel resolution in three dimensions.

2.4 Isolating the Nasal Airway

The human respiratory airway can be divided into four main parts: the nasal cavity, the nasopharynx, the left maxillary sinus and the right maxillary sinus (Fig. 2.3) (Lanteri et al., 2020). The nasal cavity is connected to the pharynx region. The pharynx contains three regions: the nasopharynx, oropharynx and laryngopharynx (Fig. 2.4).

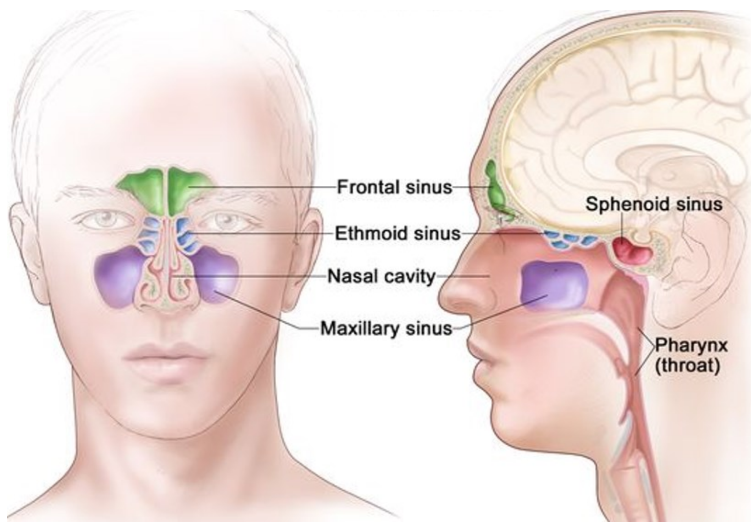


Fig. 2.3 Anatomy of the nasal cavity and paranasal sinuses (from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/paranasal-sinus)

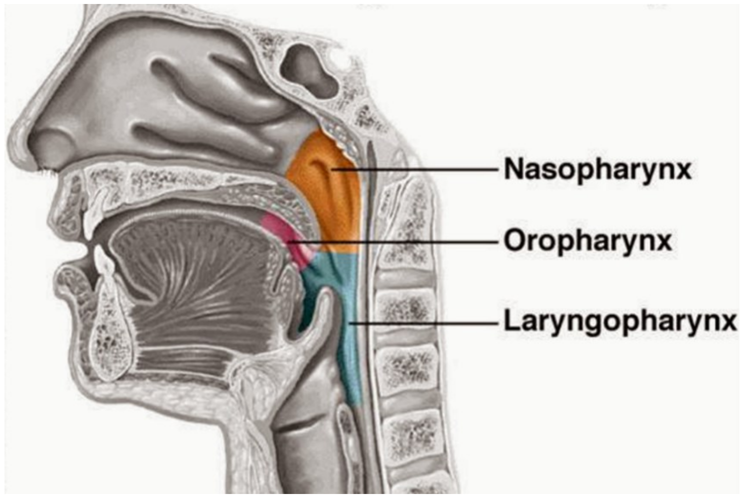


Fig. 2.4 Anatomy of the region of the pharynx (from: https://smallcollation.blogspot.com/2013/04/pharynx.html#gsc.tab=0)

Lanteri et al. (Lanteri et al., 2020) suggested that the nasopharynx and nasal cavity can be defined based on the sagittal and coronal planes. They suggest the following method regarding the segmentation of the nasopharynx and nasal cavity. Regarding the segmentation of the nasopharynx, a straight line is used to connect the point S (sella) and the point PNS (posterior nasal spine) on the Sagittal plane to segment the connection between the nasopharynx and the nasal cavity, connecting the point S and the point CV2tp (the tip of the odontoid process) to form the posterior line of the nasopharynx, in addition, the bottom line of the nasopharynx is defined by the point CV2tp connecting the point PNS (Lanteri et al., 2020). Regarding the segmentation method of the nasal cavity, they (Lanteri et al., 2020) proposed that the bottom boundary of the nasal cavity is determined by the straight line connecting the point PNS and the point ANS (anterior nasal spine). The boundary of the anterior part of the nasal cavity is determined by two connected lines, which are the line connecting the point ANS and the point TNB (the tip of the nasal bone) and the line connecting the point TNB and the point N (nasion). Its top limit is determined by a straight line connecting points S and N (Fig. 2.5).

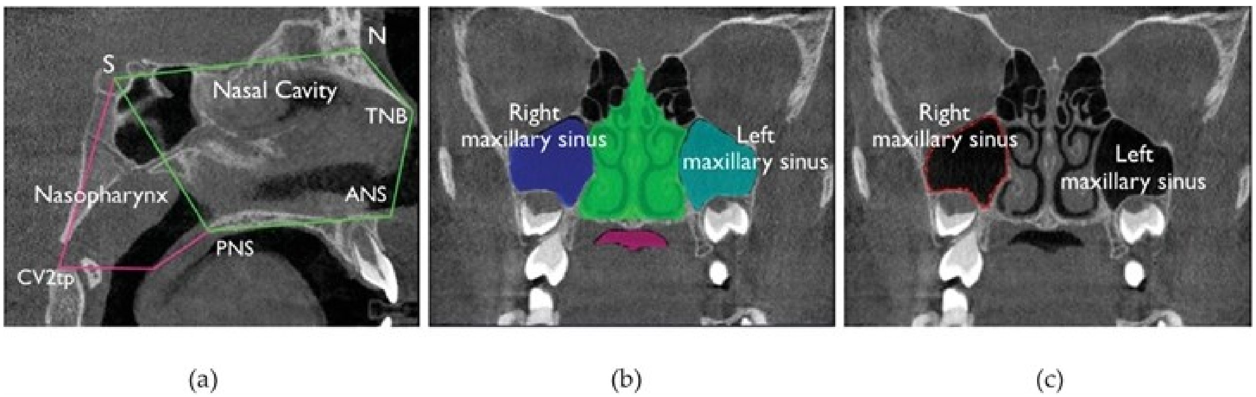


Fig. 2.5 Visual explanation of planes and points used on the different cone-beam computed tomography (CBCT) axis for performing volume segmentation of the respiratory segments analyzed: Nasal cavity, maxillary sinuses, and rhinopharynx. (a) sagittal view, (b) (c) coronal views (Lanteri et al., 2020). (N (nasion), TNB (the tip of the nasal bone), ANS (anterior nasal spine), PNS (posterior nasal spine), S (sella), CV2tp (the tip of the odontoid process))

In some studies (Cordasco et al., 2012; Kim et al., 2018), they suggested that the lower part is the area more affected by maxillary expansion treatment compared to the upper part of the nasal airway, and therefore the lower part should be the main consideration when studying the effect of maxillary expansion treatment on the nasal airway. So, in their study, A line passing through the red dot on the lower edge of the right middle nasal turbinate was created to cut off the upper part (Fig. 2.6).

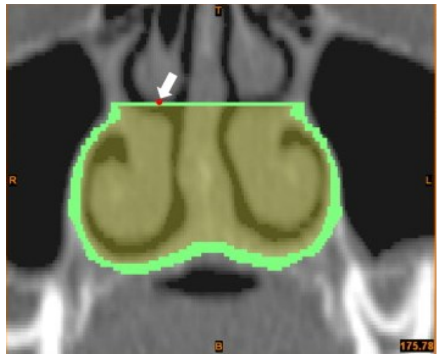


Fig. 2.6 Definition of the upper edge of the nasal airway in a study (Cordasco et al., 2012)

When segmenting the nasal airway, the following points should be noted as possible causes of errors. The nasal airway is not a constant, static structure, but can be affected by many factors that can change the nasal airway volume. Allergy and inflammation can affect the nasal airway and cause changes in nasal airway volume (Nathan et al., 2005; Trudo et al., 1998; Tsuiki et al., 2005). In addition, the nasal airway morphology can be affected differently when a person is in different body positions. For example, the nasal airway will be subjected to greater resistance when in a supine position than an upright position (Van Holsbeke et al., 2014). Therefore, the variable needs to be controlled in the study. The impact of this aspect on the study needs to be minimized by having all patients in the same position when CBCT data are collected from them.

2.5 Summary

The above review describes in various aspects of obstructive sleep apnea (OSA), maxillary expansion, cone beam computed tomography, nasal airway anatomy and nasal airway change. This allows a more detailed description of the background and relevant information of the study. In the next chapters, 3D modeling, statistical analysis, and other methods will be used to study how upper arch expansion by clear aligners can affect the nasal airway volume in children and adults.

Chapter 3: The Effect of Upper Arch Expansion by Clear Aligners on Nasal Airway Volume in Children

(This chapter has been prepared as a manuscript to be submitted to the journal of Angle Orthodontist)

3.1 Abstract

Objective

To investigate the effect of orthodontic treatment using clear aligners on the nasal airway volume and intermolar distance of pediatric patients undergoing maxillary expansion.

Materials and Methods

Cone-beam computed tomographic (CBCT) radiographs were taken as part of diagnostic records of 13 children (6-13 years) with constricted maxilla (experimental group) who had been treated with clear aligners expansion treatment for around 1 year. There was also a control group of 8 children (7-12 years) who had no treatment, their CBCTs were taken for diagnostic records, however, they did not pursue treatment in time and were analyzed to compare the possible effects of clear aligners on nasal airway volume. The changes in nasal airway volume and intermolar distance were compared and analyzed between the experimental and control groups. Correlation analysis between nasal airway volume and intermolar distance changes was also performed.

Results

Compared with the control group, the nasal airway volume of the patients in the experimental group showed a significant increase ($p<0.001$), and the intermolar distance also increased significantly ($p<0.001$).

Conclusion

This study showed that orthodontic maxillary expansion using clear aligners can increase maxillary intermolar width and increase nasal airway volume in children with constricted maxillae.

3.2 Introduction

It is estimated that obstructive sleep apnea (OSA) affects more than 900 million people around the world (Benjafield et al., 2019). Clinically, OSA is defined as no less than five sleep disturbances per hour during sleep, resulting in snoring, daytime sleepiness, interrupted breathing, or arousal from choking (American Academy of Sleep Medicine, 2015). This sleep problem affects the quality of human daily life and physical health. It can lead to irritability, depression, irregular sleep patterns, and cognitive and memory decline in humans (Schwengel et al., 2014). In addition, it may bring many complications, such as hypertension, stroke, or cardiovascular disease, among others (Yaggi et al., 2005; Peppard et al., 2000; Epstein et al., 2009).

One of the causes of OSA in children is maxillofacial abnormalities, such as narrow maxilla and hypoplastic/posterior mandible (Schwengel et al, 2014). This results in airway obstruction at various levels of the airway. Currently, in clinical practice, the main methods of maxillary expansion include rapid maxillary expansion (RME), slow maxillary expansion (SME) and surgically assisted rapid maxillary expansion (SARME) (Ficarelli et al., 1978; Bell, 1982). Some previous research (Peppard et al., 2000; Cordasco et al., 2012; Mônego Moreira et al., 2017) has shown that RME can improve the nasal airway. However, there have been cases of recurrence after RME therapy (Gurel et al., 2010) and RME can cause edema, pain, and ulcers in and around the palate. Alternatively, SME exerts milder forces during maxillary expansion treatment, which makes the whole treatment process more stable and gives more time for bone formation in the intermaxillary structure (Bell, 1982; Hicks, 1978; Mew, 1983). Therefore, it is more physiological and more favored by doctors and patients (Martina et al., 2012).

Compared to traditional SME treatments, orthodontic maxillary expansion using clear aligners could be considered a safer, more hygienic, more comfortable and more aesthetically pleasing modality than other fixed appliances or bulky removable screw carrying appliances (Djeu et al., 2005). However, the effect of clear aligners on the nasal airway in pediatric patients has not been investigated. The objective of this study was to investigate the effect of clear aligners on the nasal airway volume and morphology of pediatric patients undergoing maxillary expansion. Further, the effect of clear aligners on intermolar distance and its correlation with nasal airway volume were also investigated in this study.

The study objectives were achieved through the following specific aims (SA):

SA1) Determine the possible 3D changes in the nasal airway volume and morphology after maxillary arch expansion with clear aligners using cone-beam computed tomography (CBCT) and compare the results of treatment to a control group without treatment.

SA2) Assess the maxillary intermolar distance changes associated with maxillary expansion using clear aligners in children.

SA3) Investigate statistical correlations between intermolar distance changes and changes in nasal airway volume.

3.3 Method

Participants:

The records of the experimental group were composed of n = 13 pediatric patients (5 males, 8 females) with a mean age of (9.45±1.78 years [mean ± SD]) (range: 6–13 years) (By calculation, the treatment group sample size for a paired t-test was found to be 5.). At the first, they were retrieved from the local orthodontic clinic records that use this treatment as a routine treatment. All participants underwent SME using Invisalign child clear aligners (Align Technology, San Jose, CA, USA) as part of their orthodontic treatment plan with a mean treatment time of (13.26±2.35 months [mean ± SD]) (range: 9-18 months). All participants had a CBCT at the start of treatment (T1) and another CBCT at the end of treatment (T2) as part of their clinical treatment protocol. Some patients had two CBCTs as part of their proposed treatment but did not start treatment at T1 due to either financial or personal reasons. They came back for treatment at similar T2 to the experimental group and were considered the control group. The control group consisted of (n = 8; 5 males, 3 females) with a mean age of (9.95±1.49 years [mean ± SD]) (range: 7–12 years) without any treatment were identified as the control group. The Control group had a CBCT at time T1 and another CBCT at time T2 with a mean time between scans of (12.12±2.56 months [mean ± SD]) (range: 9-17 months). The CBCT scans for both groups were performed for clinical diagnosis and treatment planning using the i-CAT FLX V-Series (the model number is 1.009 9472) scanner. The pixel size of these CBCT scan images was 0.3 mm with a resolution of 536×536 pixels per slice. The number of slices for the CT scan data sets was 440 and the slice thickness was 0.3 mm. Approval by the University of Alberta Health Ethics

Review Board (protocol number: Pro 00047506) with consent to use the data anonymously. All patients signed consent for their records to be used for research purposes.

Nasal airway volume

The method utilized in this research project is similar to the previously published protocol (Alsufyani et al., 2016). In summary, to create 3D nasal airway models from the CBCT scan images, the scans were imported into Materialise Mimics (Materialise®, Leuven, Belgium) (Fig. 3.1-a). A color mask was created by thresholding in Mimics® to represent the nasal airway (Fig. 3.1-b). Then, manual segmentation was used to remove unnecessary features such as the frontal sinus, maxillary sinus, pharynx, etc. to isolate the nasal airway model (Fig. 3.1-c). The starting point of the anterior nasal airway boundary was defined as the most anterior slice where the boundary was closed (Fig. 3.2-a). As shown in figure (Fig. 3.2-b), the posterior boundary of the nasal airway was identified as the most posterior slice where the two parts are connected. (Fig. 3.2-b). The upper part belongs to the nasopharynx region, while the lower part belongs to the laryngopharynx region. Finally, the 3D nasal airway model was exported as an STL file.

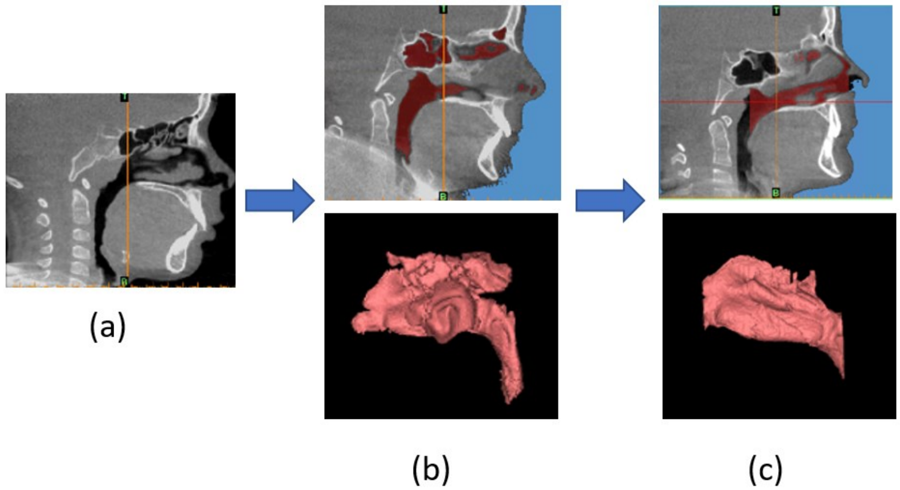
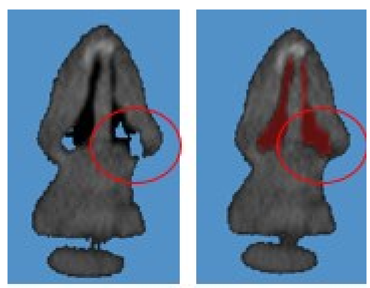
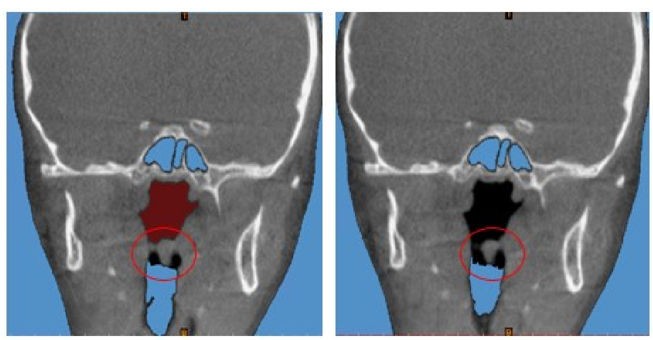


Fig. 3.1 (a) Importing CBCT scan images into Mimics®. (b) Creating a red color mask. (c) The nasal airway model.



(a)



(b)

Fig. 3.2 Definition of anterior and posterior nasal airway boundaries.

The T1 and T2 nasal airway 3D models were imported into Geomagic® ControlTM 2015 (3D

Systems, South Carolina, USA). The models were cleaned to remove spikes using the tool available in the software. The two models (T1 and T2) were aligned using the best-fit alignment function with T1 as the reference model and T2 as the floating (test) model. (Fig. 3.3). The best-fit alignment is a built-in function that minimizes the distance between reference and test models by means of an iterative closest point algorithm. After aligning the models, there was imperfect alignment at the anterior and posterior boundary parts (Fig. 3.4) so the edges were trimmed with planes to ensure perfectly aligned boundaries (Fig. 3.5). Under the trim with the plane tool, the position and the angle of the plane can be set to cut off the model to ensure that there is no excess at the anterior and posterior boundary parts of the T1 and T2 models.

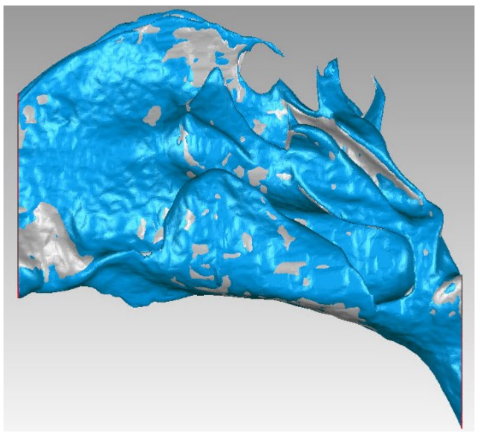
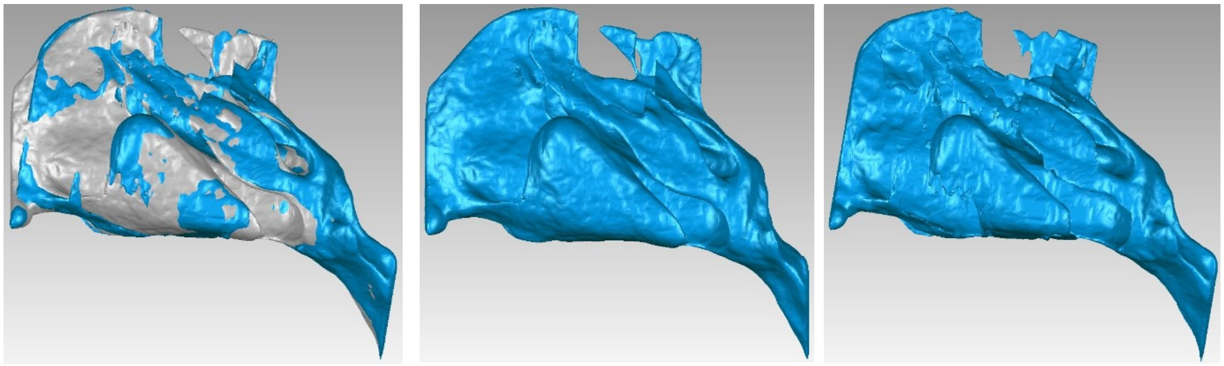


Fig. 3.3 The Time-1 model and Time-2 model after best-fit alignment (The grey color represents the Time-1 model (Reference) and the blue color represents the Time-2 (Test)).



(a) (b) (c)

Fig. 3.4 The model needed to be cut off some extra parts. (a) both overlapped. (b) T1 model. (c) T2 model.

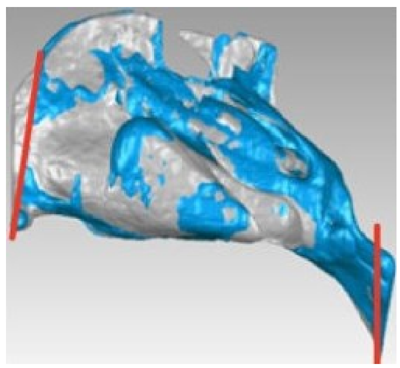


Fig. 3.5 Trim in Geomagic®

The geometrical deviations between the T1 and T2 models were determined by conducting a 3D deviation analysis in Geomagic®. This provides a deviation map that can give a visual and quantitative representation of the degree of difference between the surfaces of the models (Fig. 3.6). The deviation map shows both positive and negative deviation areas. This indicates that the surface of the test model (T2 model) is above or below the reference model (T1 model). The lower threshold value for the deviation color map was set to ±0.3mm indicating that any areas with deviations within these limits would be considered negligible and colored green. The upper threshold value for the deviation color map was set to ±5.0mm, which captured the largest deviations between the models where there were corresponding points. The root mean square

(RMS) error, the maximum upper deviation, and the maximum lower deviation were also output as outcome metrics from the 3D deviation analysis. In addition, the volume and surface area of the nasal airway models can be measured in Geomagic®.

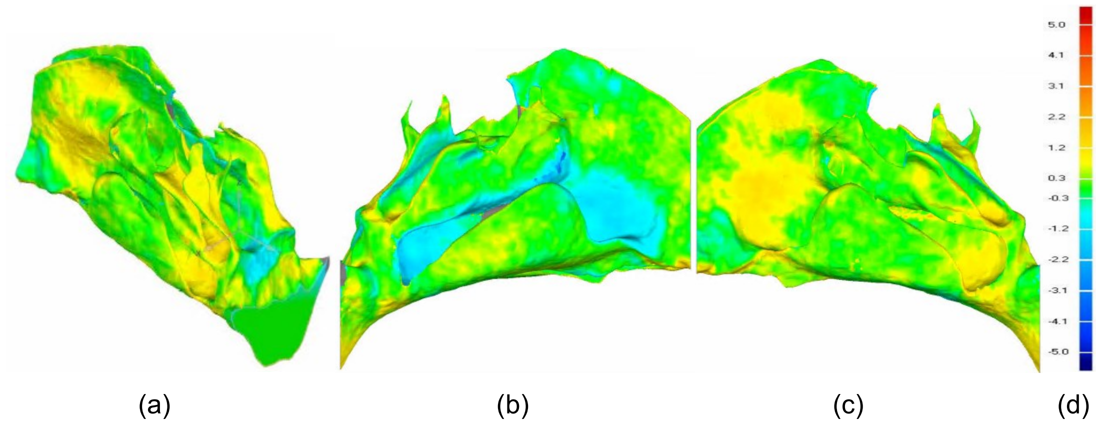


Fig. 3.6 3D deviation map comparing the nasal airway models at times T1 and T2. (a) Isometric. (b) Left. (c) Right. (d) deviation scale in mm.

Intermolar distance

Measuring the amount of expansion of the actual maxillary intermolar distance. The age of our pediatric patients was mainly distributed between 7-12 years old, and the first permanent molar in the maxillary was usually completed its eruption before that (Ekstrand et al., 2003). Therefore, we took the distance between the first permanent molar as the target of our study.

To create 3D models from these CBCT scan images, the scans were imported into Materialise Mimics (Fig. 3.7-a). A color mask was created in Mimics® to represent the skull and cervical bone (Fig. 3.7-b). Then, segmentation is done in Mimics® to remove unnecessary parts, like cervical bone and lower jaw bone to isolate the maxillary teeth (Fig. 3.7-c). The maxillary teeth model needs to be smoothed in MIMICS to remove some noises. Finally, the 3D maxillary teeth model was exported as an STL file.

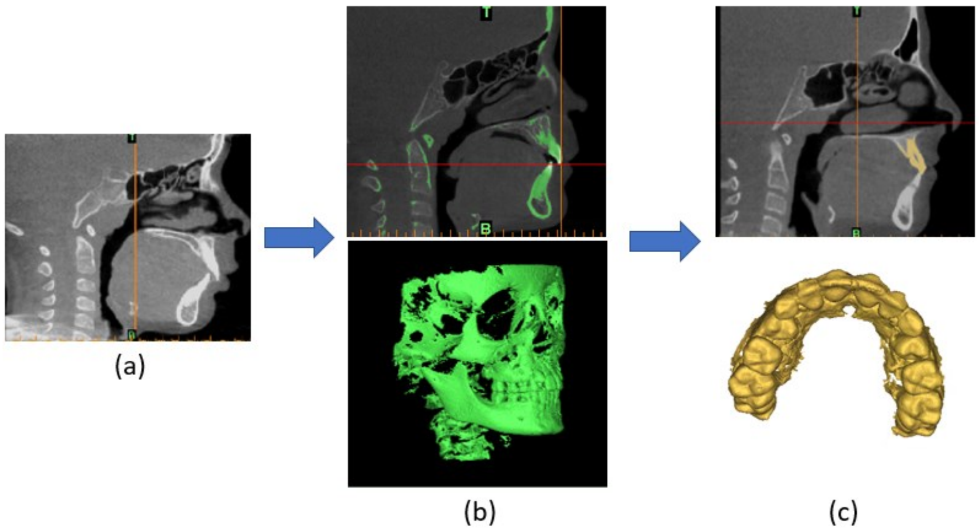


Fig. 3.7 (a) Importing CBCT scan images into Mimics®. (b) Creating a color mask to represent the bone in CBCT scan images. (c) The maxillary teeth model.

To find the difference between T1 intermolar distance and T2 intermolar distance, both T1 and T2 maxillary teeth models were imported into Geomagic® Control^{TM} 2015. In order to continue to remove some noise around the maxillary teeth model, the tool in Geomagic® was used to remove spikes with larger angle deficiency to smooth the model. Then, the distance between the central fossae of the first permanent molars of the upper arch was measured as the intermolar distance (Fig. 3.8) by using the measurement tool in Geomagic®.

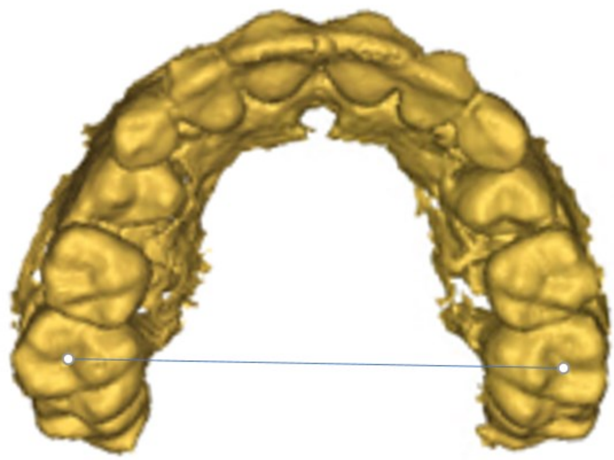


Fig. 3.8 The distance between the central fossae of the first permanent molars of the upper arch

Statistical analysis

Nasal airway volume:

The T1 and T2 nasal airway volumes of patients in the treatment group or control group were compared using a Paired-Samples T-Test to assess differences, respectively. The nasal airway volume changes of all participants in the treatment group and control group are compared using an Independent T-test to assess differences. $p<0.05$ is considered significant.

Paired patients are the participants in the treatment group and the participants in the control group of the same sex, similar ages and similar duration of monitoring. There were 4 paired groups of patients of the same sex, very similar ages and duration of monitoring in the study. This allowed us to investigate the effect of clear aligners on the nasal airways of pediatric patients from a different perspective.

To test the reliability of this study, intra-reliability research and inter-reliability research were investigated. For inter-reliability, first, individual researchers' segmentation of particular models was compared. Researcher A, researcher B and researcher C each performed segmentation of the T1 nasal airway model of Participant 1. Then, researcher A, researcher B and researcher C segmented both the T1 and T2 nasal airway models of Participant 14 separately. The results (the T1 nasal airway model of Participant 1 and the T1 and T2 nasal airway models of Participant 14) from these 3 researchers were analyzed by intraclass correlation coefficient (ICC). And, the volume changes between the two models of Participant 14 were calculated by each researcher. For intra-reliability research, researcher A repeated 3 times the T1 nasal airway segmentation of Treatment 3 (each time at 2-week intervals to minimize the effect of recency bias).

Intermolar distance:

The T1 and T2 intermolar distances of patients in the treatment group or control group were compared using a Paired-Samples T-Test to assess differences, respectively. The intermolar distance changes of all participants in the treatment group and control group are compared using an Independent T-test to assess differences. (The CBCT scans of Participant 13 are too poor to get the dental model in MIMICS. Therefore, the intermolar distance could not be obtained.)

Same to the nasal airway study, there were 4 paired groups of patients of the same sex, very similar ages and duration of monitoring in the study.

To test the reliability of the distance measurement results, intra-reliability research and inter-reliability research were added. For inter-reliability research, researcher A, researcher D and researcher E each measured the distance between the first permanent molars of 4 treatment patients. The results from all three researchers were analyzed by the intraclass correlation coefficient (ICC). For intra-reliability research, researcher A repeated 3 times on measuring the distance between the first permanent molars of the same 4 treatment patients (each time at 1-week intervals to ensure that the details of the previous segmentation were forgotten). The results of all three measurements were analyzed by the intraclass correlation coefficient (ICC).

Correlation analysis

To find the relations between the change in intermolar distance and the change in nasal airway volume, a correlation statistical analysis was created for the treatment and control groups, respectively. In the treatment group and the control group, the nasal airway volume change values and intermolar distance change values for each patient will be used as analysis values. The main result of a correlation is called the correlation coefficient (or "r").

3.4 Results

Nasal Airway Volume

Table 3.1 and Table 3.2 display the nasal airway volume changes of both the treatment group and control group. The results showed that the average volume change was 16.24% and -6.12% in the treatment and control groups, respectively. The results of the Paired-Samples T-Test between the T1 and T2 of the treatment group showed a significant increase in nasal airway volume with the clear aligners treatment ($p<0.001$). However, the results of the paired t-test between the T1 and T2 CBCTs showed no significant change in nasal airway volume in the untreated control group ($p=0.136$). In addition, the results of the Independent T-Test showed that there is a significant difference between the treatment group and the control group ($p<0.0001$).

Deviation maps for each patient in the treatment and control groups are shown in Fig. 3.9 and

Fig. 3.10, respectively, showing isometric, left, and right views of the nasal airway. The green areas of the deviation map represent regions where the deviation between the T1 nasal airway model and T2 nasal airway model surfaces are small (< 0.3 mm), whereas the dark red/blue areas represent regions with larger deviations (> 5.0 mm). The positive deviation values indicate that the T2 nasal airway model is above the T1 nasal airway model (outward deviation/increase) and negative deviation values indicate that the T2 nasal airway model is beneath the T1 nasal airway model (inward deviation/decrease). Based on the Deviation maps for the treatment group and the control group, the treatment group nasal airway models have more yellow and red areas and fewer blue areas than the control group models. This means that the nasal airway volume in the treatment group has more volume increase areas and fewer volume decrease areas compared to the control group.

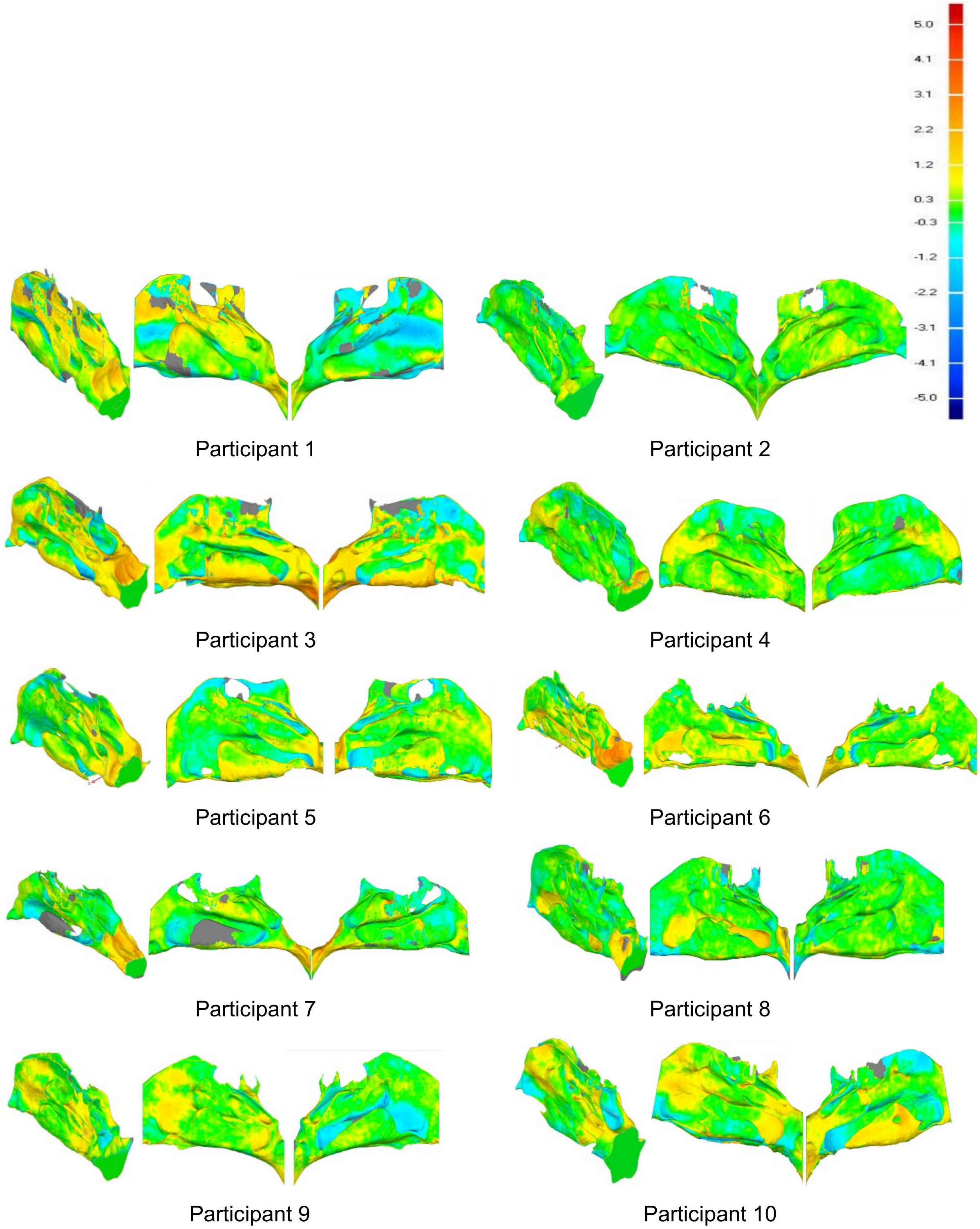
Table 3.1 Nasal airway volume changes in the treatment group

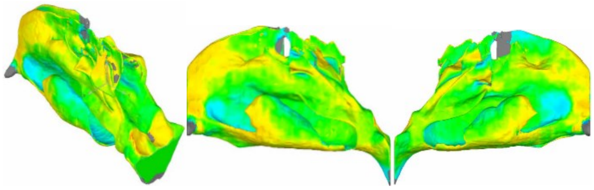
Patient	Sex(M/F)	Nasal airway volume Time-1 (mm^3)	Nasal airway volume Time-2 (mm^3)	Difference (mm^3)	Difference (%)
Participant 1	F	8336.6	9228.0	891.4	10.69%
Participant 2	F	8612.8	9394.1	781.3	9.07%
Participant 3	M	12157.5	14838.6	2681.1	22.05%
Participant 4	F	7844.9	8746.6	901.7	11.49%
Participant 5	F	7259.1	8199.4	940.3	12.95%
Participant 6	M	9996.4	13079.4	3083.0	30.84%
Participant 7	M	8762.9	9854.0	1091.1	12.45%
Participant 8	F	14167.8	16144.5	1976.7	13.95%
Participant 9	F	13444.7	14462.4	1017.7	7.57%
Participant 10	M	12410.1	14060.5	1650.4	13.30%

Participant 11	F	13615.2	14874.6	1259.4	9.25%
Participant 12	F	11269.2	13564.2	2295.0	20.37%
Participant 13	M	10053.1	13782.4	3729.3	37.10%
Average					16.24%
Standard error		659.9	773.5		

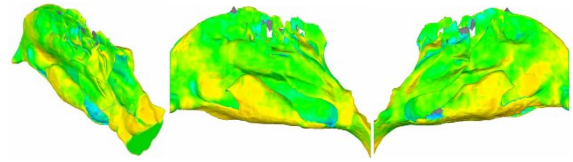
Table 3.2 Nasal airway volume changes in the control group

Patient	Sex(M/F)	Nasal airway volume Time-1 (mm^3)	Nasal airway volume Time-2 (mm^3)	Difference (mm^3)	Difference (%)
Control 1	F	10594.5	8171.6	-2422.9	-22.87%
Control 2	M	11747.0	10680.7	-1066.3	-9.08%
Control 3	F	13779.9	14487.7	707.8	5.14%
Control 4	M	9625.4	9384.7	-240.7	-2.50%
Control 5	M	17251.3	16758.6	-492.7	-2.86%
Control 6	F	13604.4	13313.7	-290.7	-2.14%
Control 7	M	13842.8	14282.9	440.1	3.18%
Control 8	M	20121.4	16525.6	-3598.8	-17.87%
Average					-6.12%
Standard error		1144.5	1062.6		

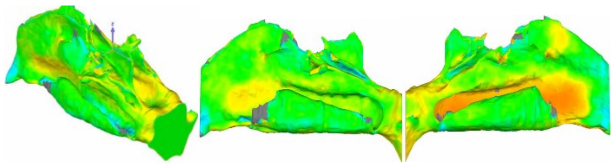

5.0
4.1
3.1
2.2
1.2
0.3
-0.3
-1.2
-2.2
-3.1
-4.1
-5.0
Participant 1
Participant 2
Participant 3
Participant 4
Participant 5
Participant 6
Participant 7
Participant 8
Participant 9
Participant 10



Participant 11

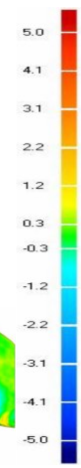


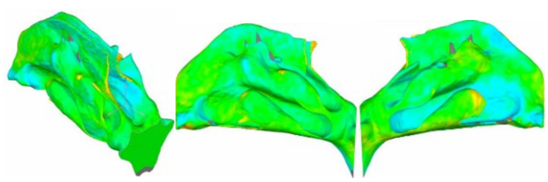
Participant 12



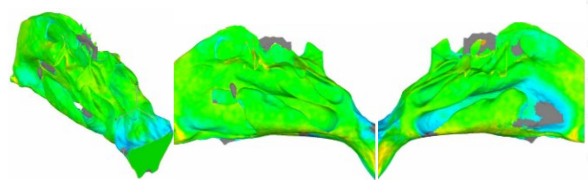
Participant 13

Fig. 3.9 Deviation maps of each patient in the treatment group (isometric view, left view and right view of the nasal airway) and the deviation map scale in millimeter

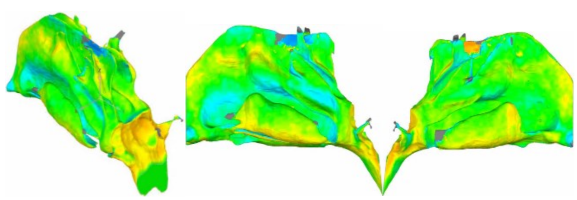




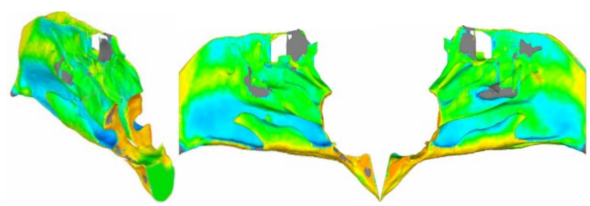
Control 1



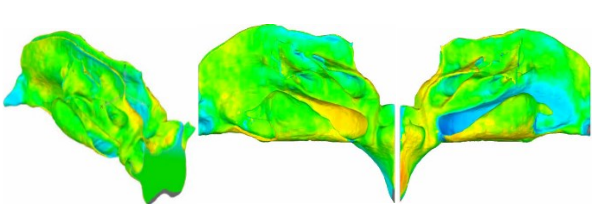
Control 2



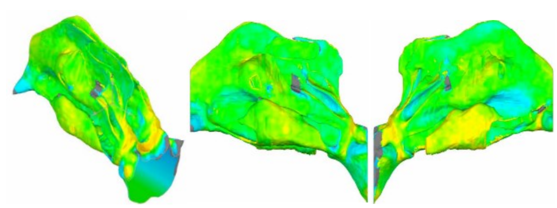
Control 3



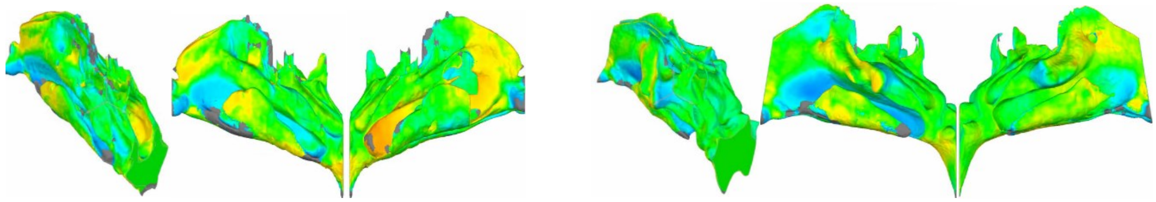
Control 4



Control 5



Control 6



Control 7 Control 8

Fig. 3.10 Deviation maps of each patient in the control group (isometric view, left view and right view of the nasal airway) and the deviation map scale in millimeter

Fig. 3.11 shows the comparison of the difference in mean nasal airway volume between the treatment group and the control group at T1 and T2, and also includes the analysis of standard errors. This demonstrates the increase in nasal airway volume in patients treated with clear aligners and, conversely, the decrease in nasal airway volume in untreated patients. The results also show that the standard error of each group of data is small and therefore the data are stable. Fig. 3.11 shows that the control group had a much higher volume than the treatment group at T1. The reason may be due to the fact that the control group had a larger percentage of males than the treatment group. From Table 3.1 and Table 3.2, it can be seen that the nasal airway volume at T1 was generally larger in males than in females.

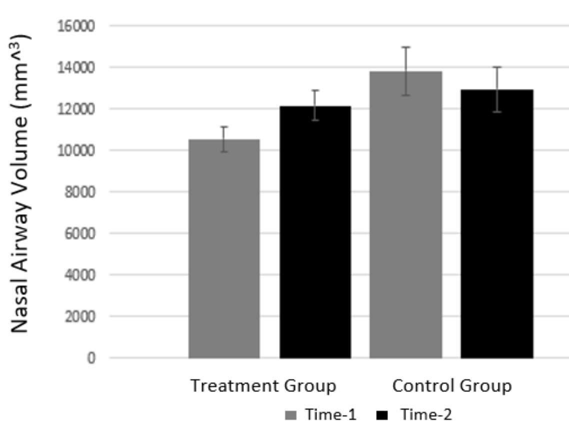


Fig. 3.11 Mean & Standard Error (the comparison of the difference in nasal airway volume between the treatment group and the control group at T1 and T2)

Nasal airway analysis of paired patients

There are 4 sets of matching groups in Table 3.3. The amount of nasal airway volume change in each group is compared between treated and untreated patients. It can be seen more visually that the treated patients had a significant increase in nasal airway volume compared to the untreated patients (of the same sex, similar age and similar monitoring time), while the untreated patients had a continuous decrease in nasal airway volume. The same findings can also be seen in the deviation maps from Fig. 3.9 and Fig. 3.10.

Table 3.3 Paired Groups (nasal airway)

(a) Paired group 1

	(sex, age, time period)	Nasal Airway Volume (Time-1)	Nasal Airway Volume (Time-2)	Volume Change (%)
Participant 1	(F, 8.28 years, 11.96 months)	8336.6	9228.0	10.69%
Control 1	(F, 8.17 years, 10.61 months)	10594.5	8171.6	-22.87%

(b) Paired group 2

	(sex, age, time period)	Nasal Airway Volume (Time-1)	Nasal Airway Volume (Time-2)	Volume Change (%)
Participant 8	(F, 12.57 years, 11.50 months)	14167.8	16144.5	13.95%
Participant 9	(F, 12.33 years, 13.57 months)	13444.7	14462.4	7.57%

Control 6	(F, 11.03 years, 11.93 months)	13604.4	13313.7	-2.14%

(c) Paired group 3

	(sex, age, time period)	Nasal Airway Volume (Time-1)	Nasal Airway Volume (Time-2)	Volume Change (%)
Participant 7	(M, 10.28 years, 11.76 months)	8762.9	9854.0	12.45%
Participant 13	(M, 10.04 years, 11.04 months)	10053.1	13782.4	37.10%
Control 5	(M, 10.44 years, 10.05 months)	17251.3	16758.6	-2.86%
Control 8	(M, 11.06 years, 10.81 months)	20121.4	16525.6	-17.87%

(d) Paired group 4

	(sex, age, time period)	Nasal Airway Volume (Time-1)	Nasal Airway Volume (Time-2)	Volume Change (%)
Participant 3	(M, 9.86 years, 12.42 months)	12157.5	14838.6	22.05%
Participant 13	(M, 10.04 years, 11.04 months)	10053.1	13782.4	37.10%
Control 2	(M, 8.68 years, 11.40 months)	11747.0	10680.7	-9.08%

Reliability research of nasal airway volume

Table 3.4 and Table 3.5 display the results of reliability research for nasal airway volume.

Table 3.4 Inter-reliability research for nasal airway segmentation

(a)

Model	Comparison	Volume Difference (%)	Surface Area Difference (%)
Participant 1 (T1)	Researcher A&B	2.73%	0.49%
Participant 1 (T1)	Researcher A&C	10.01%	1.22%
Participant 1 (T1)	Researcher B&C	7.48%	1.72%
Participant 14 (T1)	Researcher A&B	3.61%	0.51%
Participant 14 (T1)	Researcher A&C	9.07%	1.33%
Participant 14 (T1)	Researcher B&C	12.23%	2.78%
Participant 14 (T2)	Researcher A&B	2.24%	0.36%
Participant 14 (T2)	Researcher A&C	9.81%	1.26%
Participant 14 (T2)	Researcher B&C	10.93%	5.10%
Average		7.57%	1.64%

(b)

	Participant #14 volume change
Researcher A	0.62%
Researcher B	-0.71%
Researcher C	0.76%

Based on Table 3.4-a, there was a 7.57% average difference between the nasal airway volume results obtained by the three researchers. However, the data in Table 3.4-b show that the nasal airway volume changes result for Participant 14, the three researchers obtained extremely similar results. And the ICC of the inter-reliability research is 0.960.

Table 3.5 Intra-reliability research for nasal airway segmentation

Comparison	Volume Difference (%)	Surface Area Difference (%)
Model A&B	-0.26%	0.03%
Model A&C	1.22%	0.16%
Model B&C	1.48%	0.18%
Average	0.99%	0.12%

Based on the results in Table 3.5, the researcher's error due to his own factors is extremely small.

Based on the inter-reliability and intra-reliability research, the results show that the nasal airway volume results obtained in this study are stable and reliable.

Intermolar Distance

Table 3.6 and Table 3.7 display the intermolar distance changes of each patient in the treatment group and control group, respectively.

Table 3.6 Intermolar (the maxillary first permanent molars) distance changes in the treatment group

Patient	Sex(M/F)	Intermolar distance Time-1 (mm)	Intermolar distance Time-2 (mm)	Difference (mm)
Participant 1	F	40.3	41.7	1.4
Participant 2	F	46.0	49.2	3.2
Participant 3	M	46.0	48.6	2.6

Participant 4	F	41.8	44.2	2.4
Participant 5	F	41.8	45.1	3.3
Participant 6	M	43.3	46.2	2.9
Participant 7	M	47.5	52.3	4.8
Participant 8	F	42.6	44.4	1.8
Participant 9	F	43.6	45.6	2.0
Participant 10	M	49.7	50.7	1.0
Participant 11	F	47.3	47.7	0.4
Participant 12	F	44.7	47.3	2.6
Participant 13	M	N/A	N/A	N/A
Average		44.550	46.917	2.367
Standard Error		0.809	0.864	

The results of the Paired-Samples T-Test between the T1 and T2 groups showed a significant increase in intermolar distance with the clear aligners treatment ($p<0.001$).

Table 3.7 intermolar (the maxillary first permanent molars) distance changes in the control group

Patient	Sex(M/F)	Intermolar distance Time-1 (mm)	Intermolar distance Time-2 (mm)	Difference (mm)
Control 1	F	43.5	47	3.5
Control 2	M	44.7	44.7	0
Control 3	F	47.1	47.3	0.2
Control 4	M	43.7	43.8	0.1
Control 5	M	46.3	46.7	0.4
Control 6	F	46.3	46.6	0.3
Control 7	M	44.9	45	0.1
Control 8	M	44.7	45.5	0.8

Average		45.150	45.825	0.675
Standard Error		0.428	0.416	

The results of the Paired-Samples T-Test between the T1 and T2 groups showed no significant increase in molar spacing in the untreated control group (p=0.146). The results of the Independent T-Test showed that there is a significant difference between the treatment group and the control group (p=0.0053).

All the above intermolar distance data reflect that clear aligners treatment can result in a significant increase in intermolar distance in children.

Fig. 3.12 shows the comparison of the difference in mean intermolar distance between the treatment group and control group at T1 and T2, and also includes the analysis of standard errors. From this figure, it is apparent that the increase in intermolar distance was higher in the treatment group than in the control group. In the control group, the increase in intermolar distance was small and almost unchanged. The standard error values for each group are small, so the data are stable.

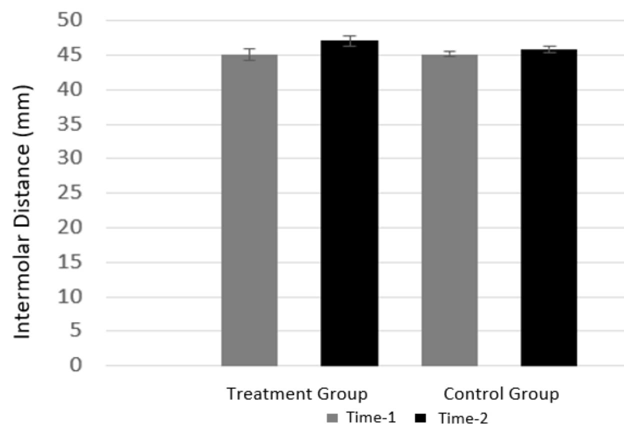


Fig. 3.12 Mean & Standard Error (the comparison of the difference in intermolar distance between the treatment group and control group at T1 and T2)

Intermolar distance analysis of paired patients

There are 4 sets of matching groups in Table 3.8. The amount of intermolar distance change in each group is compared between treated and untreated patients. With the exception of the paired group 1 of outliers, it shows that the intermolar distance increased more in treated patients compared to untreated patients (same sex, similar age and similar monitoring time).

Table 3.8 Paired Groups (intermolar)

(a) Paired group 1

	(sex, age, time period)	Intermolar Distance (Time-1) (mm)	Intermolar Distance (Time-2) (mm)	Distance Change (mm)
Participant 1	(F, 8.28 years, 11.96 months)	40.3	41.7	1.4
Control 1	(F, 8.17 years, 10.61 months)	43.5	47	3.5

(b) Paired group 2

	(sex, age, time period)	Intermolar Distance (Time-1) (mm)	Intermolar Distance (Time-2) (mm)	Distance Change (mm)
Participant 8	(F, 12.57 years, 11.50 months)	42.6	44.4	1.8
Participant 9	(F, 12.33 years, 13.57 months)	43.6	45.6	2.0
Control 6	(F, 11.03 years, 11.93 months)	46.3	46.6	0.3

(c) Paired group 3

	(sex, age, time period)	Intermolar Distance (Time-1) (mm)	Intermolar Distance (Time-2) (mm)	Distance Change (mm)
Participant 7	(M, 10.28 years, 11.76 months)	47.5	52.3	4.8
Participant 13	(M, 10.04 years, 11.04 months)	N/A	N/A	N/A
Control 5	(M, 10.44 years, 10.05 months)	46.3	46.7	0.4
Control 8	(M, 11.06 years, 10.81 months)	44.7	45.5	0.8

(d) Paired group 4

	(sex, age, time period)	Intermolar Distance (Time-1) (mm)	Intermolar Distance (Time-2) (mm)	Distance Change (mm)
Participant 3	(M, 9.86 years, 12.42 months)	46.0	48.6	2.6

Participant 13	(M, 10.04 years, 11.04 months)	N/A	N/A	N/A
Control 2	(M, 8.68 years, 11.40 months)	44.7	44.7	0

Reliability research of intermolar distance

Table 3.9 and Table 3.10 display the results of reliability research for intermolar distance.

The ICCs of the inter-reliability and the intra-reliability research results are 0.888 and 0.992, respectively.

Based on the inter-reliability and intra-reliability research, the results show that the intermolar distance results obtained in this study are reliable.

Table 3.9 Inter-reliability research for intermolar distance

Patient	Intermolar distance change (mm) (researcher A)	Intermolar distance change (mm) (researcher D)	Intermolar distance change (mm) (researcher E)
Participant 1	1.4	2.1	1.1
Participant 2	3.2	3.0	3.7
Participant 3	2.6	2.5	1.6
Participant 4	2.4	2.7	2.7

Table 3.10 Intra-reliability research for intermolar distance

Patient	Intermolar distance change (mm) (Measurement 1)	Intermolar distance change (mm) (Measurement 2)	Intermolar distance change (mm) (Measurement 3)
Participant 1	1.4	1.3	1.5
Participant 2	3.2	2.9	3.3
Participant 3	2.6	2.5	2.6
Participant 4	2.4	2.5	2.4

Correlation analysis

Fig. 3.13 and Fig. 3.14 show the correlation analysis between the change in nasal airway volume and the change in intermolar distance of the patients in the treatment and control groups, respectively.

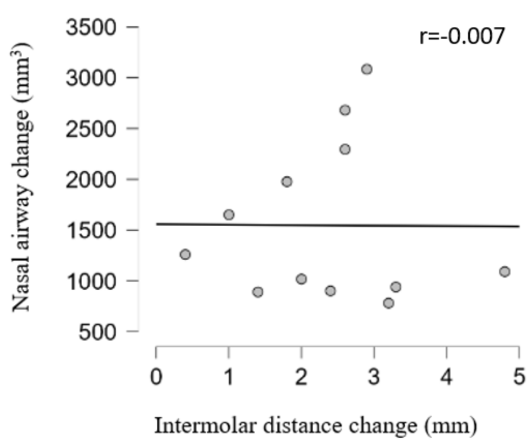
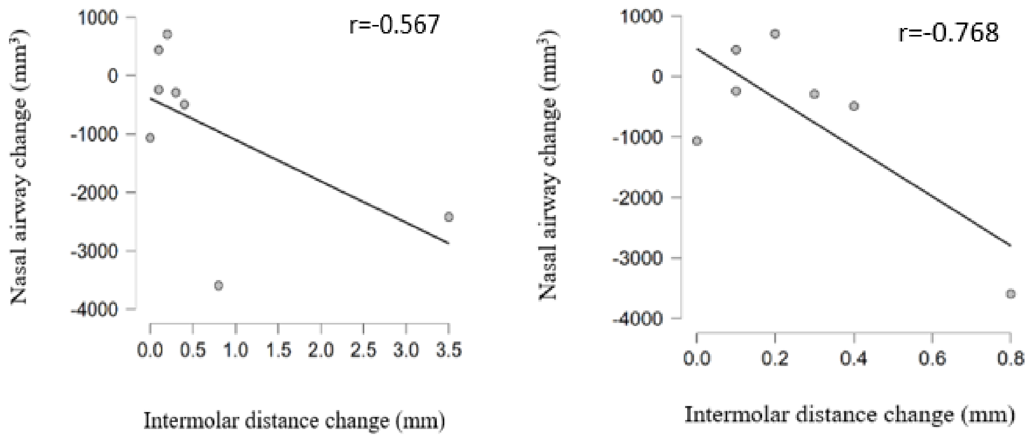


Fig. 3.13 Correlation analysis in the treatment group (intermolar distance change & nasal airway volume change)

In the treatment group, there was no obvious correlation between the change in intermolar distance and the change in nasal airway volume by the patients after treatment with clear aligners.



(a) all control patients (b) without Control 1

Fig. 3.14 Correlation analysis in the control group (intermolar distance change & nasal airway volume change)

In the control group (Fig. 3.14-a), there was a negative correlation between the change in intermolar distance and the change in nasal airway volume. With a small increase in intermolar distance, there was a concomitant decrease in nasal airway volume. When we remove the outlier (Fig. 3.14-b), the new regression analysis shows that the negative correlation is even stronger.

3.5 Discussion

In this paper, we show the effect of clear aligners in children. With clear aligners treatment, the patient's intermolar distance was significantly expanded and the volume of the nasal airway was significantly increased. Studying the effect of clear aligners on the intermolar distance and nasal airway volume will help orthodontists to develop better treatment plans. So that more people who suffer from sleep apnea obstruction can escape from their pain. In some previous studies (De Felippe et al., 2009; Cordasco et al., 2012; Mônego Moreira et al., 2017), the effects of RME on nasal volume have been studied. De Felippe et al. used three-dimensional morphometric analysis and acoustic rhinometry to evaluate the maxillary dental arches and nasal cavities and concluded that RME resulted in a significant expansion of the palate and a significant increase in nasal airway volume (De Felippe et al., 2009). Cordasco et al reported that RME increased the nasal airway cavity size in children (Cordasco et al., 2012). Moreover, Moreira et al. found the effect of two RME methods of Hyrax and Haas appliances on the nasal airway (Mônego Moreira et al., 2017). Both appliances can significantly increase nasal cavity dimensions in children. Our study is the first to use clear aligners as a study to see how it affects the nasal airway.

Regarding the segmentation of the nasal airway model, some apical regions of the nasal airway are often connected to the sinus parts, which causes a lot of trouble for the segmentation of the model. Therefore, we drew on the experience of previous studies (Cordasco et al., 2012; Kim et al., 2018). Since the lower part of the nasal airway is more affected by maxillary expansion compared to the upper part (Cordasco et al., 2012; Kim et al., 2018). Therefore, we removed the indeterminate apical parts of the nasal airway which could be both the sinus and the nasal airway as much as possible to control for study stability.

In the previous study, Cordasco et al (Cordasco et al., 2012) reported that RME can increase by about 8% nasal airway volume in children. However, our research shows an average increase of 15% in nasal airway volume in the treatment group. The data in their study is a mean age of 9.70±1.41 years, similar to our data (which is a mean age of 9.45±1.78 years). But their treatment time was 7 months, which is less than our study treatment with an average of 13.26 months. This may be one of the reasons why their volume increase is smaller than ours.

In the treatment group, there is no correlation between the change in intermolar distance and the change in nasal airway volume was found. But, in Fig. 3.13, a positive correlation line consisting of points from 6 patients can be identified. There is also a near-horizontal correlation curve consisting of points from the other 6 patients. The reason for this will be investigated in the future.

Although there are important new findings revealed by our study, there are also limitations. Due to the difficulty of collecting data on untreated patients in the control group, there were only 8 in the control group in this study. Also based on Fig. 3.11, the mean nasal airway volume at T1 in the control group was slightly larger than the mean nasal airway volume at T1 in the treatment group. Based on the available data and results, it may be due to the fact that the mean age of the control group (9.95 years) was greater than that of the treatment group (9.45 years). In addition, it may also be that the control group had a larger percentage of males than the treatment group. Therefore, the database of the control group needs to be expanded, and then the reasons for this need to be further explored in future studies.

3.6 Conclusion

This study fills an important gap in the literature by examining the effects of clear aligners treatment on sleep apnea obstruction in children. The effect of clear aligners treatment on intermolar distance and nasal airway volume was found. The presence of an untreated control group made the results of the study more convincing. The results showed a significant increase in both maxillary intermolar distance and nasal airway volume in the treatment group, while in the control group there was no significant increase in either. Thus, this study confirms that clear aligners treatment is effective in increasing nasal airway volume and expanding the maxillary intermolar distance in children.

Chapter 4: The Effect of Upper Arch Expansion by Clear Aligners on Nasal Airway Volume in Adults

4.1 Introduction

Obstructive sleep apnea (OSA) is a common chronic condition that affects not only children, but many adults as well. It affects at least 2-4% of adults (Epstein et al., 2009). With the improvement of medical technology and living standards, it is being taken more and more seriously. Slightly different from children, in adults, the main risks for OSA are obesity (especially in those with upper body obesity), smoking, alcohol consumption, and poor physical fitness (Partinen et al., 1992). OSA not only affects people's sleep quality at night, but it also makes people feel poorly during the day. For example, during the daytime, they feel physically tired, have difficulty concentrating, have reduced cognitive ability, and are cranky (Yaggi et al., 2005). Also, OSA will lead to many diseases and complications such as stroke, hypertension and consequent cardiovascular diseases (Yaggi et al., 2005; Peppard et al., 2000). Stroke is the second leading cause of death worldwide and the leading cause of long-term disability (Yaggi et al., 2005). Several studies have shown that the prevalence of OSA in stroke patients is over 60%, compared to 4% in the middle-aged adult population (Mohsenin et al., 1995; Dyken et al., 1996; Bassetti et al., 1999; Young et al., 1993). OSA will seriously affect people's health and even affect the life safety of some elderly people.

Current treatments for OSA in the adult population include lifestyle changes to make weight lighter, positive airway pressure, oral appliance therapy, and surgery (tracheostomy and maxillomandibular advancement surgery, etc.) (Semelka et al., 2016; Chang et al., 2019). In oral appliance therapy, some studies have found that some RME appliances can expand the nasal airway by dilating the oral maxillary, thereby improving OSA in adults (Cordasco et al., 2012; Mônego Moreira et al., 2017). However, the relatively mild and stable method of SME is preferred by patients and physicians over RME, which can cause edema, pain, ulceration and the potential for recurrence (Rosvall et al., 2009). Orthodontic maxillary expansion using clear aligners, which are more aesthetically pleasing when worn, is a type of RME and is very popular nowadays. There are no studies on whether clear aligners can increase the volume of the nasal airway and thus improve OSA in adults. Our previous study showed that clear aligners treatment is effective in expanding the maxillary intermolar width and thus increasing nasal airway volume. So, we decided to conduct a similar study (a pilot study) in adults to see if clear aligners could also significantly increase nasal airway volume in adults and thus improve their OSA problems.

The pilot study objective:

Determine the possible 3D changes in the nasal airway volume and morphology after maxillary arch expansion with clear aligners using cone-beam computed tomography (CBCT).

4.2 Method

Participants:

A sample of n = 6 adult patients (3 males, 3 females) with a mean age of (37.42±6.54 years [mean ± SD]) (range: 31–52 years) at the first visit was identified from a local orthodontic clinic for the treatment group of this study. All participants used clear aligners as part of their orthodontic treatment plan with a mean treatment time of (33.84±10.47 months [mean ± SD]) (range: 16-51 months). All participants had a CBCT at the start of treatment (T1) and another

CBCT at the end of treatment (T2) as part of their clinical protocol. The CBCT scans for all patients were performed for clinical use on the i-CAT FLX V-Series (the model number is 1.009 9472) scanner. The pixel size of these CBCT scan images was 0.3 mm with a resolution of 536×536 pixels per slice. The number of slices for the CT scan data sets was 440 and the slice thickness was 0.3 mm. Approval by the University of Alberta Health Ethics Review Board with consent to use the data anonymously.

Table 4.1 Adult participants' information

Patient	Sex(M/F)	Age (years)	Treatment time (total) (months)
Adult 1	M	33.15	39.72
Adult 2	F	36.68	26.22
Adult 3	F	51.38	50.23
Adult 4	M	31.37	33.77
Adult 5	M	37.10	36.30
Adult 6	F	34.85	16.79
Average		37.42	33.84

Nasal airway volume

The process of building, segmenting and comparing the adult nasal airway models are almost the same as that of the pediatric nasal airway model.

To create 3D nasal airway models from the CBCT scan images, the scans were imported into Materialise Mimics (Materialise®, Leuven, Belgium). Them, manual segmentation in Mimics®

to remove unnecessary features such as the frontal sinus, maxillary sinus, pharynx, etc. to isolate the nasal airway model. The anterior and posterior boundary of the nasal airway were defined the same as in the pediatric study. Finally, the 3D nasal airway model was exported as an STL file.

The STL files of nasal airway 3D models were imported into Geomagic® ControlTM 2015 (3D Systems, South Carolina, USA). First, they were cleaned to remove spikes in Geomagic®. The models (T1 and T2) were aligned using the best-fit alignment function. The best-fit alignment is a built-in function that minimizes the distance between two models by means of an iterative closest point algorithm. After aligning the models, there were some imperfect alignment parts at the anterior and/or posterior boundary parts, so the edges were trimmed with planes to ensure perfectly aligned boundaries. Under the trim with the plane tool, the position and the angle of the plane can be set to cut off the model to ensure that there is no excess at the anterior and posterior boundary parts of the aligned models.

The geometrical deviations between the aligned models (T1 and T2) were determined by conducting a 3D deviation analysis in Geomagic®. This provides a deviation map that can give a visual and quantitative representation of the degree of difference between the surfaces of the models. In addition, the volume of the nasal airway models can be measured in Geomagic®.

Statistical analysis

The T1 and T2 nasal airway volumes of adult patients were compared using a Paired-Samples T-Test to assess differences. $P<0.05$ is considered there is a statistically significant difference between the two groups. In addition, a bar chart with standard error bars was used to compare the two groups (T1 and T2).

4.3 Results

Table 4.2 displays the nasal airway volume changes of those 6 adult patients. The results showed that the average volume change was 12.71%. The results of the Paired-Samples T-Test between the T1 and T2 didn't show a significant increase in nasal airway volume with the clear aligners treatment (p=0.071).

Table 4.2 Nasal airway volume changes

Patient	Sex(M/F)	Nasal airway volume Time-1 (mm^3)	Nasal airway volume Time-2 (mm^3)	Difference (mm^3)	Difference (%)
Adult 1	M	20054.2	21620.6	1566.4	7.81%
Adult 2	F	19164.3	23791.5	4627.2	24.14%
Adult 3	F	21816.7	27796.3	5979.7	27.41%
Adult 4	M	24683.2	24995.9	312.7	1.27%
Adult 5	M	23739.9	22729.9	-1010	-4.25%
Adult 6	F	17597.4	21094.8	3497.4	19.87%
Average		21176.0	23671.5	2495.6	12.71%
Standard deviation		2496.5	2255.2		

Deviation maps for each adult patient are shown in Fig. 4.1, showing isometric, left, and right views of the nasal airway model. Same to the pediatric study, the green areas of the deviation map represent regions where the deviation between the T1 nasal airway model and T2 nasal airway model surfaces are small (< 0.3 mm), whereas the dark red/blue areas represent regions with larger deviations (> 5.0 mm). The positive deviation values indicate that the T2 nasal airway model is above the T1 nasal airway model (outward deviation/increase) and negative deviation values indicate that the T2 nasal airway model is beneath the T1 nasal airway model (inward deviation/decrease).

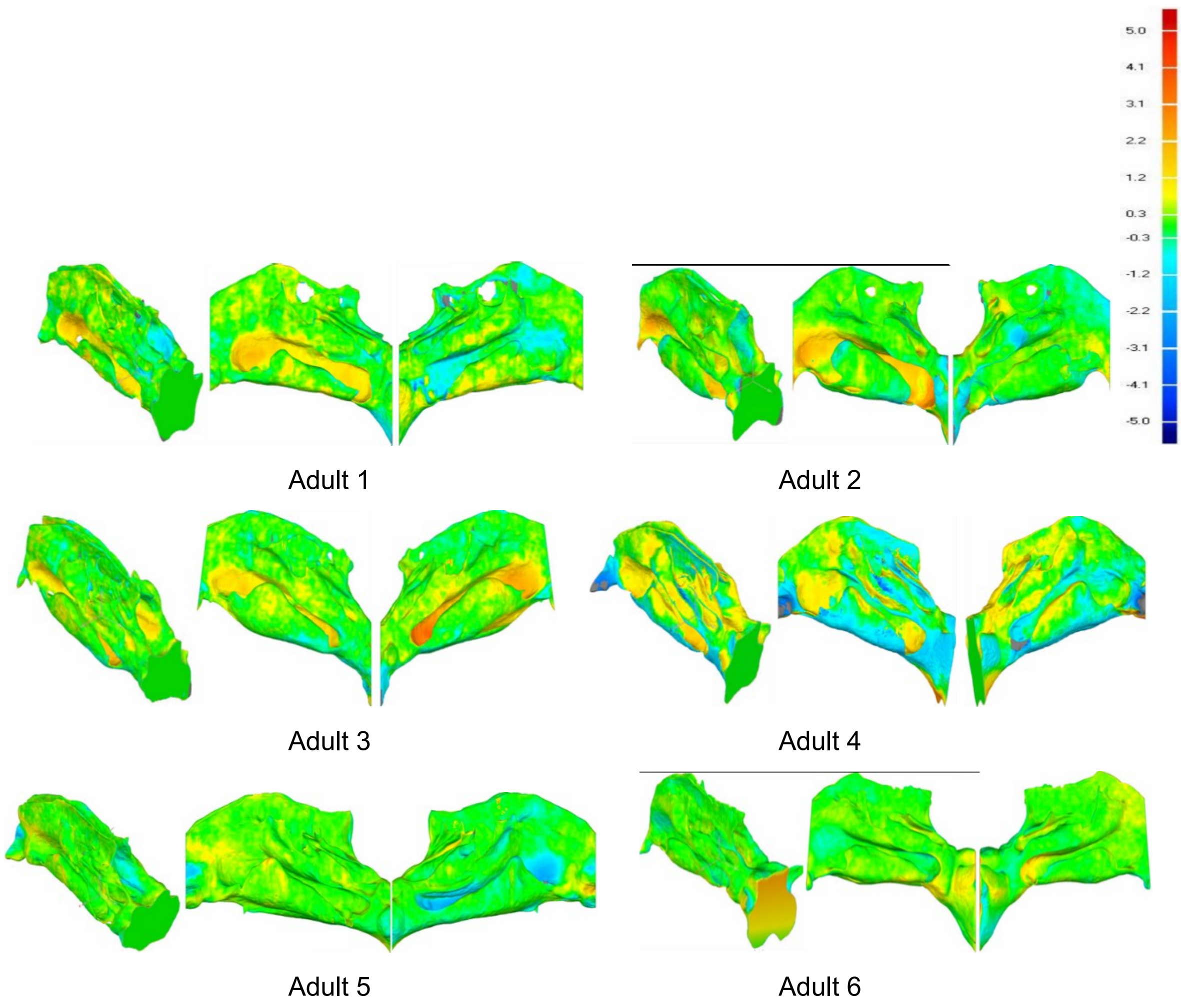


Fig. 4.1 Deviation maps of each adult patient (isometric view, left view and right view of the nasal airway) and the deviation map scale in millimeter

Fig. 4.2 shows a comparison of the differences in mean nasal airway volumes at T1 and T2 in six adult patients, which also includes an analysis of standard errors. Based on the standard error bars in Fig. 4.2, it can be seen that the error of the data is not very large and the data is relatively stable. In addition, the lowest point of the standard error bar of T2 is slightly higher than the highest point of the standard error bar of T1, which is an evidence of a difference between the two groups.

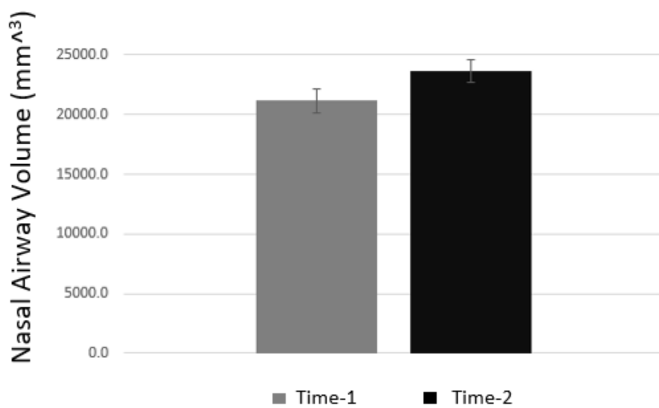


Fig. 4.2 Mean & Standard Error (the comparison of the differences in nasal airway volume between T1 and T2 in six adult patients)

4.4 Discussion

The current pilot study showed that there was an increase in volume after clear aligners treatment, but it was not significant. There were three men and three women in the six patient data collected at the local clinic. The reason for this is that the ratio of men to women in the study is 1:1 as much as possible, so the sex factor does not have any influence on the results of the study. This is because in the pediatric study we found that the nasal airway volume may be different in men and women. For a few specific data results in this pilot study, such as a 1.27% increase in nasal airway volume in Adult 4 and a decrease in nasal airway volume in Adult 5, this may be due to the variable nature of the nasal airway. If a person has rhinitis or allergic attacks, the volume of the nasal airway will decrease, causing the obstruction (Nathan et al., 2005). The particular results of these two patients may also be the reason for a P-value slightly greater than 0.05 in the statistical analysis. In addition, the p-value of 0.071 is very close to the significance and probably just means we don't have a large enough sample size. Therefore, at this point, it is likely that maxillary expansion performed by clear aligners will result in a significant increase in nasal airway volume in adults.

In a previous study, Kim et al. found a significant increase in the anterior nasal cavity and total nasal airway volume in adults after maxillary expansion with nonsurgical miniscrew-assisted rapid maxillary expansion (MARME) ($p<0.05$) (Kim et al., 2018). So I hypothesized that clear aligners, also used as a maxillary expansion treatment, would also result in a significant increase in nasal airway volume in adults, thus improving OSA in adults. But in another previous study, Horani et al. found no significant changes in the mean airway volume of the nasal cavity in adults after orthodontics treatment with non-extraction clear aligner therapy (Horani et al., 2021). In the future, we will continue to collect data at the local clinic in a 1:1 male-to-female ratio, thus expanding the number of data and investigating how the clear aligner affects the nasal airway in adults. Based on the existing 6 patient results, a sample size calculation was performed and we needed a total of 10 patients. We will also try to collect patients who are not treated with clear aligners at the local clinic to create a control group to make the study more convincing. In addition, we will also conduct a study of the intermolar distance in this adult study as we did in the pediatric study. This will be considered as an important indicator to investigate whether there is a significant increase in maxillary intermolar distance with the clear aligners treatment and the correlation between intermolar distance change and nasal airway volume change.

4.5 Conclusion

Based on the analysis of CBCT scans from six patients, no statistically significant increase in nasal airway volume was found in adults treated with clear aligners in this pilot study. However, there was a mean increase in nasal airway volume of 12.71%.

Chapter 5: Conclusion

This thesis fills an important gap in the literature by examining the effects of clear aligners treatment on nasal airway volume and morphology in children and adults. This work has important applications for future clinical studies evaluating clear aligners as a potential treatment for obstructive sleep apnea (OSA). The study found that clear aligners maxillary expansion significantly increased maxillary intermolar distance and significantly increased nasal airway volume in children. In the pilot study in adults, the study found an increase in nasal airway volume of 12.71% through maxillary expansion of the clear aligners, though the differences were not significant with the small sample studied. In the clinical aspect, the results of this research provide invaluable information for orthodontists and patients. Clear aligners can be a better option for doctors and patients in dilating the intermolar or expanding the nasal airway than the more invasive surgical and RME orthodontic treatments, as well as the aesthetically unpleasant SME orthodontic treatment.

The study has also made a great contribution to biomedical and engineering aspects. The study has provided some new ideas for future researchers regarding nasal airway segmentation. In addition, since the patients in this study were treated with Invisalign clear aligners, Invisalign will likely have more marketing points such as a significant increase in nasal airway volume, which will likely attract more consumers to Invisalign and thus capture a larger market share.

There are some limitations in this study, such as the ratio of male to female in the treatment and control groups should be controlled to 1:1 respectively in the pediatric study to control for potential sex-differences in natural growth or response to SME. Further, the adult study was limited by the small sample size, as already mentioned before, however, it provided an important pilot dataset. Therefore, in the future, we will continue to expand the sample size of the pediatric and adult studies by a 1:1 male to female ratio. Also, for adult studies that lack a control group, we will collect samples at the local clinic to create a control group whenever possible. Moreover, it has been mentioned before that the nasal airway is affected by many factors, some of which are difficult to control. When collecting CBCT scans from participants, we did not confirm whether they were suffering from allergies or rhinitis. This will affect the results of our data. In addition, since many parts of the upper part of the nasal airway are connected to the sinus, in the study we removed some uncertain upper parts connected to the sinus in order to minimize the error. Although the lower part of the nasal airway is mainly affected by the maxillary expansion of the clear aligners. However, this inevitably still produces some errors in the data results.

Finally, based on the research experience of these studies above and knowledge of related fields, there are many areas that can be explored and studied in the field of biomedical engineering and dental. Future work may investigate (1) the effect of clear aligners on the mandible and the intermolar distance of the mandible, (2) whether other brands of clear aligners orthodontic treatment can also significantly increase the nasal airway, (3) whether Invisalign maxillary expansion can effectively improve OSA problems, and (4) the morphology and size differences of the nasal airway in men and women.

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