Analysis of Upper Airway Functional and Dentofacial Changes during Non-Surgical Maxillary Expansion in Adults

by

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Abstract

Introduction: This analysis is part of an ongoing retrospective secondary pilot study on a randomized clinical trial. The purpose of this research project was to evaluate the effect of none-surgical maxillary expansion techniques on upper airway dimension and function, and skeletal and dental changes, using two different maxillary expanders: Moon and Dresden expanders.

Methods: A sample of thirteen patients were randomly allocated to either group A or group B. Patients in group A (N=5) received orthodontic treatment using an appliance called Dresden expander. Patients in group B (N=8) received orthodontic treatment using the Moon expander. Two sets of records were taken for each patient; before starting treatment (T_0) and after maxillary expansion completed (T_1). Records consisted of the following: clinical charting and diagnostic exams, intra-oral and extraoral photos, cone beam computer tomography (CBCT), nasal obstruction symptom evaluation (NOSE) questionnaires, and peak nasal inspiratory flow (PNIF). The changes on the upper airway dimension and function were evaluated using CBCT scans (using Dolphin software), PNIF (objective measurement), and NOSE questionnaire (subjective measure). The skeletal and dental changes were evaluated using various skeletal and dental landmarks in CBCT using Avizo software. For upper airway changes and skeletal and dental changes, one-way repeated measure mixed ANOVA tests and paired sample t-tests were conducted.

Results: For upper airway changes, from T_0 to T_1, no statistically significant differences were found between the Moon and the Dresden expander groups for nasopharynx volume (NPV), oropharynx volume (OPV), oropharynx minimal cross-sectional area (OPMCA), PNIF with both nostrils (PNIFBN), PNIF with left nostril blocked (PNIFLB), and PNIF with right nostril blocked

(PNIFRB), and NOSE questionnaires. Also, both expanders showed to have no significant effect on upper airway dimensions and function. For skeletal and dental changes, Moon expander resulted in buccal displacement of pulp chamber of tooth # 1.6, 2.6, and 2.4 ($p<0.05$). Dresden expander did not make any significant changes on the skeletal or dental landmarks after maxillary expansion. No other differences were found between the Dresden and Moon expander groups in transverse, vertical, and antero-posterior (A-P) directions ($P>0.05$).

Conclusion: The effect of microimplant-assisted rapid palatal expansion (MARPE) appliances on upper airway dimension and function in adults is yet to be determined and future randomized controlled clinical trial studies with larger sample size are needed. In terms of skeletal and dental changes, the only statistically significant change was in the Moon expander group in transverse (X) direction for pulp chamber of upper first molars and upper left first premolar. However, such changes may not be clinically significant. No significant differences were found between the two appliance designs in this analysis.

Preface

This thesis is an original work by Nikoo Habibnia. The research project was conducted at the orthodontics graduate clinic at the University of Alberta with the ethics approval from the Research Ethics Board (Pro00084145) from the University of Alberta on August 06, 2020. No part of this thesis has been previously published.

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Nomenclature

List of Abbreviations

RME	Rapid Maxillary Expansion	**MIP**	Minimum Inspiratory Pressure
RPE	Rapid palatal Expansion	**MEP**	Maximum Expiratory Pressure
SARPE	Surgically Assisted Rapid Palatal Expansion	**OEPF**	Oral Expiratory Peak Flow
MARPE	Microimplant-Assisted Rapid Palatal Expansion	**INF**	Inspiratory Nasal Flow
OSA	Obstructive Sleep Apnea	**NCW**	Nasal Cavity Width
CBCT	Three-dimensional Cone-Beam Computed Tomography	**PPV**	Palatopharyngeal Volume
NCV	Nasal cavity Volume	**GPV**	Glossopharyngeal Volume
MCA	Minimal Cross-sectional Area	**NLW**	Nasal Lateral Width
NPV	Nasopharynx Volume	**P1**	First Premolar
OPV	Oropharynx Volume	**P2**	Second Premolar
RMSV	Right Maxillary Sinus Volume	**M1**	First Molar
LMSV	Left Maxillary Sinus Volume	**M2**	Second Molar
NCA	Nasal Cavity Area	**NF**	Nasal Floor
NPA	Nasopharyngeal area	**HP**	Hard Palate
OPA	Oropharyngeal area	**HP5**	Hard Palate below 5mm
LPA	Laryngopharyngeal area	**LPV**	Laryngopharyngeal Volume
TAV	Total Airway volume	**P1NLW**	Coronary-level Lateral NLW at first premolar (P1) region
TAA	Total Airway Area	**P2NLW**	coronary-level lateral NLW at second premolar (P2) region
MIW	Maxillary Intermolar Width	**M1NLW**	Coronary-level Lateral NLW at first molar (M1) region
EMW	External Maxillary Width	**M2NLW**	Coronary-level Lateral NLW at second molar (M2) region)
PW	Palatal Width	**AR**	Acoustic Rhinometry
MW	Maxillary Width	**RPAV**	Retropalatal Airway Volume
HPAV	Hypopharyngeal Airway Volume	**RGAV**	Retroglossal Airway Volume

NFW	Nasal Floor Width	**NIPF**	Nasal Inspiratory Peak Flow
NOSE Questionnaire	Nasal Obstruction Symptom Evaluation (NOSE) Questionnaires	**TAD**	Temporary Anchorage Device
PNIF	peak nasal inspiratory flow	**PC16**	Pulp Chamber of tooth # 1.6
RGPF	Right Greater Palatine Foramen	**MBA16**	Mesio-Buccal Root Apex of tooth # 1.6
LGPF	Left Greater Palatine Foramen	**ALB16**	Buccal Alveolar Bone of tooth # 1.6
InfraOR	Right Infraorbital Foramen	**PC26**	Pulp chamber of tooth # 2.6
InfraOL	Left Infraorbital Foramen	**MBA26**	Mesio-Buccal Root Apex of tooth # 2.6
Mid-NPF	Mid-Nasopalatine Foramen	**ALB26**	Buccal Alveolar Bone of tooth # 2.6
FSR	Right Foramen Spinosum	**PC14**	Pulp chamber of tooth # 1.4
FSL	Left Foramen Spinosum	**PC24**	Pulp chamber of tooth # 2.4
FM	Foramen Magnum	**PC36**	Pulp chamber of tooth # 3.6
HCR	Right Hypoglossal Canal	**PC46**	Pulp chamber of tooth # 4.6
HCL	Left Hypoglossal Canal		

Chapter 1 - Introduction and Problem statement

1.1. Introduction

Angell introduced rapid maxillary expansion (RME) in 1860, it was popularized by Hass 100 years later and is routinely used in maxillary transverse deficiency and posterior crossbite management [1, 2]. It has been proposed that RME may also be indicated in patients with moderate arch length discrepancies[3] and those who might benefit from an increase in upper respiratory volume and airflow[4]. Different appliances have been introduced to facilitate maxillary expansion, ranging from simple removable acrylic appliances with a midline screw to bonded or banded expansion devices[2]. The most common design of RME is known as a tooth-borne expander, where the appliance has bands on upper first molars and sometimes either a band or a rest on upper first premolars and these teeth are main anchors for the device.

In growing patients, maxillary skeletal expansion is achieved by activating the expansion screw, which results in the separation of the midpalatal suture and the stimulation of new bone formation between the palatal bones at the suture level[5]. However, due to the forces applied to the abutment teeth during expansion, conventional tooth-borne RME may have potential dentoalveolar side effects such as root surface resorption and/or formation of pulp stones in abutment teeth[6], tipping of the teeth buccally and bending of the alveolar bone[7], anatomic defects close to the mesiobuccal root of maxillary first molars[4], and reduced buccal bone plate and bone dehiscence on the buccal aspect of anchorage teeth [8]. Age and skeletal maturation are important factors in determining the number of undesired side effects associated with RME. Although these side effects do seldomly occur and their long-term consequences are not always significant, in adults with maxillary transverse deficiency, using RME alone could have more dramatic consequences[9].

Conventionally, surgically assisted rapid maxillary expansion (SARPE) has been used to treat adult patients with maxillary transverse deficiency because of their skeletal maturity, pronounced interdigitation of the midpalatal suture (MPS), and age-related increase in rigidity and thickness of maxillary bone[10-12]. Studies have shown that adults' major resistance to maxillary expansion is not the midpalatal suture but the surrounding maxillary structures [13]. Therefore, more recently, a non-surgical bone-borne expansion technique called microimplant-assisted rapid palatal expansion (MARPE) was developed, which allows increased separation of the midpalatal suture in adults using bone-based anchorage into the palatal bones. Bone-borne expanders have been shown to reduce the adverse side effects of using RME alone, such as alveolar bending, dental buccal tipping, or bone loss around the abutment teeth [14, 15]. Research suggests that bicortical mini-implant anchorage may have higher stability, less chance of deformation and fracture, and could potentially result in a more parallel maxillary expansion [16].

The opening of the midpalate suture (MPS) has a predictable success rate until 12 years in both males and females[17]. However, after 12 years of age into adolescence and adulthood, MPS were in more advanced stages of sutural maturation (ranging from stage C to E)[17]. Although obliteration of the suture occurs during adolescence, a marked degree of ossification may not happen until the third decade of life. There is a significant amount of interindividual variations with regards to the start of suture closure[18]. Therefore, there are variabilities in developmental stages of fusion of the MPS, regardless of the patient's chronological age and sex[17]. For instance, a few case reports have reported the absence of MPS ossification in adults aged 27[18], 54[19], and 71[20] years old. As a result, understanding individual variabilities in the maturation of the MPS can have a significant impact in identifying patients in late adolescence or young adulthood who could benefit from RME or MARPE alone as a less invasive alternative treatment to SARPE procedure[21].

Nowadays, the increased awareness of obstructive sleep apnea (OSA) in children and adults has resulted in more studies evaluating the effect of maxillary expansion appliances and their impact on upper airway dimensions, using three-dimensional cone-beam computed tomography (CBCT). OSA is a chronic condition that can affect both children and adults. Symptoms of this condition include repetitive episodes of a complete or partial collapse of the upper airway during sleep and a reduction in airway flow[22]. Patients are usually awakened during sleep due to the collapsed airway and the increased breathing efforts[22]. Patients with a considerable amount of airway obstruction could shift towards mouth breathing[23]. In 1996, the first use of RME to manage OSA on a 22-year-old patient with maxillary transverse deficiency (apnea-hypopnea index (AHI) changed from 22/h to 4/h) was reported[24]. After that, many studies started to focus on the effect of RME on children with OSA[25]. However, only a limited number of studies[26-29] have evaluated the effect of MARPE appliances on the upper airway in adults.

According to the American Academy of Sleep Medicine's (AASM) manual of sleep disorders, the criteria for diagnosis of OSA in adults require either signs or symptoms (such as sleepiness, fatigue, snoring, insomnia, nocturnal respiratory disturbances, or observed apnea) or medical and psychiatric disorders (such as hypertension, coronary artery disease, cognitive dysfunction, or mood disorder)[30]. These should be coupled with five or more obstructive respiratory events (i.e. Obstructive and mixed apnea, hypopneas, respiratory effort-related arousals) per hour of sleep during Polysomnography(PSG)[30]. Alternatively, if the AHI is ≥15/h, that would satisfy the criteria[30].

The shape and dimension of the upper airway have been linked to OSA [31]. Research suggests that RME could increase nasal permeability, nasal width, nasal cross-section area and volume, enlarge the palatal space and, therefore, reduce airway resistance[32], [33 34], [35], [36]. Reduction in airway resistance could decrease negative pressure during ventilation, which may benefit some patients with OSA[37]. In addition, enlargement of the palatal space creates more space for the tongue function, improves the tongue posture, and facilitates an increase in airway space in the oropharynx due to an anterior repositioning of the tongue base[38].

Current treatments for OSA in adults are based on symptoms and severity of the syndrome. Continuous positive airway pressure (CPAP) is the first line of treatment when the AHI is ≥15 events per hour[39]. It must be noted that over 50% of the patients cannot tolerate it. Surgical management includes tonsillectomy, tracheostomy, or maxillomandibular advancement surgery. However, such surgical interventions are invasive, and therefore, adult patients try to avoid them due to their potential morbidity [39]. Consequently, it is crucial to explore the effect of non-surgical maxillary expansion on an adult's upper airway dimensions and function. Such studies could help adults with OSA have a less invasive treatment modality for their condition if they qualify. Specific phenotyping of this subgroup is still elusive.

Morphology of the MPS has been studied using occlusal radiographs [40], histology[18, 41], and CBCT imaging[42]. Occlusal radiographs are not reliable due to the overlying images of the nasomaxillary soft tissue that could lead to a false interpretation[20]. Histology is unavailable for living persons unless another reason for a nearby surgical intervention exists. In contrast, CBCT has shown to be a promising tool to evaluate the maturation stage of the maxillary suture and predictability of the outcome of RME appliances before treatment[17]. CBCT is also a valuable tool for assessing skeletal and dental changes and upper airway dimensions after maxillary expansion.

Regarding upper airway function, when evaluating the effect of maxillary expanders on respiratory performance, functional respiratory parameters should be included and combined with anatomical examinations of the upper airway[43]. Peak nasal inspiratory flow (PNIF), an objective measurement, is an easy-to-use and inexpensive medical device that directly measures the nasal airflow during maximal inspiration and has demonstrated good reproducibility and internal consistency in different studies[44, 45]. In addition, the nasal obstruction symptom evaluation (NOSE) questionnaire, which is a validated subjective measure, is used to evaluate nasal obstruction and has demonstrated adequate reliability, reproducibility, and internal consistency[46].

There are many designs of MARPE available in the market, and different designs of expanders have different stress distributions, stability, and displacement[16]. However, there is a lack of comparison between the different designs, making the clinical choice for the best type of appliance difficult [16]. In addition, to date, there is no conclusive evidence showing the effect of MARPE on improving the upper airway dimension and function in young adults. As a result, the purpose of this research project is to evaluate the effect of none-surgical maxillary expansion techniques on upper airway dimension and function, and skeletal and dental effects, using two different maxillary expanders: Moon and Dresden expanders. The changes on the upper airway dimension and function are evaluated using CBCT scans, PNIF (objective measurement), and NOSE questionnaire (subjective measure). The skeletal and dental changes will be evaluated using various skeletal and dental landmarks in CBCT using Avizo software.

1.2. Research Questions and Hypothesis

Primary questions:

1. Are there differences in nasopharynx volume, oropharynx volume, oropharynx minimal cross-sectional area, peak nasal inspiratory flow for both nostrils, peak nasal inspiratory flow with right nostril blocked, peak nasal inspiratory flow with left nostril blocked, and NOSE questionnaires, from pre-treatment (T_0) to post-treatment (T_1), between the Dresden and the Moon appliances?
2. Within each treatment group (Moon and Dresden group), are there any significant changes in nasopharynx volume, oropharynx volume, oropharynx minimal cross-sectional area, peak nasal inspiratory flow for both nostrils, peak nasal inspiratory flow with right nostril blocked, and peak nasal inspiratory flow with left nostril blocked, from T_0 to T_1?

Hypothesis:

For upper airway analysis, the following hypothesis were evaluated:

1) H_0: There are no differences in the **nasopharynx volume**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **nasopharynx volume**, from T_0 to T_1, of at least one of the appliances is different from the other.
2) H_0: There are no differences in the **oropharynx volume**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **oropharynx volume**, from T_0 to T_1, of at least one of the appliances is different from the other.
3) H_0: There are no differences in the **oropharynx MCA**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **oropharynx MCA**, from T_0 to T_1, of at least one of the appliances is different from the other.
4) H_0: There are no differences in the **PNIFBN, PNIFLB, PNIFRB**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **PNIFBN, PNIFLB, PNIFRB**, from T_0 to T_1, of at least one of the appliances is different from the other.
5) H_0: There is no interaction between appliance type and time (PrePost) on upper airway (NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB). H_a: There is an interaction between appliance type and time (PrePost) on upper airway (NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB).
6) H_0: There is no difference in the median NOSE questionnaire answers in patients treated with either Moon or Dresden expander. H_a: There is a difference in the median NOSE questionnaire answers in patients treated with either Moon or Dresden expander.
7) H_0: Within each treatment group, there are no statistically significant changes on upper airway for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, from T_0 to T_1. H_a: Within each treatment group, there are statistically significant changes on upper airway for NPV, OPV, OPMCA, PNIFBN, PNIFLB, and PNIFRB, from T_0 to T_1.

Secondary questions:

1. Are there differences in the mean orthogonal distances (*mm*) of the selected skeletal and dental landmarks, from T_0 to T_1, in the transverse, vertical, and antero-posterior directions between the Dresden and the Moon appliances?
2. Within each treatment group (Moon and Dresden group), are there any significant changes in the mean orthogonal distances (*mm*) of the selected skeletal and dental landmarks from T_0 to T_1, in the transverse, vertical, and antero-posterior directions?

Selected skeletal and dental landmarks are the following: *Right and Left greater palatine Foramen, right and left infraorbital foramen, mid-nasopalatine foramen, right and left foramen spinosum, foramen magnum, right and left hypoglossal canal, pulp chamber of tooth # 1.6, 2.6, 1.4, 2.4, 36, 46, mesio-buccal root apex of tooth # 1.6 and 2.6, and buccal alveolar bone of tooth # 1.6 and 2.6.*

Hypothesis:

For skeletal and dental changes, the following hypothesis were evaluated:

1) H_0: There are no differences in the mean orthogonal distances (*mm*), from T_0 to T_1, in the transverse (X), vertical (Z), and A-P (Y) directions between the Dresden and the Moon appliances. H_a: The mean orthogonal distances, from T_0 to T_1, in the transverse, vertical, and A-P directions of at least one of the appliances is different from the others.
2) H_0: There is no interaction between appliance type and time (PrePost) on the mean orthogonal distances. H_a: There is an interaction between appliance type and time on the mean orthogonal distances.
3) H_0: Within each treatment group, there are no statistically significant changes on the mean orthogonal distances from T_0 to T_1 in the transverse, vertical, and antero-posterior directions. H_a: Within each treatment group, there are statistically significant changes on the mean orthogonal distances from T_0 to T_1 in the transverse, vertical, and antero-posterior directions.

Chapter 2 - Analysis of Nasal Functional Changes and Skeletal and Dental changes during Non-Surgical Maxillary Expansion in Children and Adults: A Scoping Review

2.1. Introduction

Maxillary transverse deficiency is a common orthodontic condition associated with narrow palate and posterior crossbite. Some individuals with these characteristics could also suffer from narrowing of the upper airway and obstructive sleep apnea (OSA) [47]. Growing patients with maxillary transverse deficiency are commonly treated with rapid maxillary expansion (RME) appliances. RME works by expanding the maxillary arch through separating the midpalatal suture[47].

OSA is a chronic sleep breathing condition that could affect both children and adults[22]. Signs of this condition include repetitive episodes of complete or partial collapse of the upper airway during sleep and a reduction in airway flow[22]. Individuals are usually awakened during sleep due to the collapsed airway and the increased breathing efforts[22]. Individuals with a considerable amount of upper airway obstruction could shift towards continuous mouth breathing[23].

Specific upper airway shapes and dimensions have been linked to OSA [31]. Nowadays, the increased awareness in OSA in children and adults have resulted in more studies evaluating the effect of maxillary expansion appliances on upper airway dimensions, using three-dimensional Cone-Beam Computed Tomography (CBCT). Research suggests that RME could result in an increase in nasal permeability, nasal width, nasal cross section area and volume, enlargement of the palatal space and therefore, a potential reduction in airway resistance[32, 33, 34, 35, 36]. Reduction in upper airway resistance could result in less negative pressure during ventilation, which is very beneficial in patients with OSA[37]. In addition, enlargement of the palatal space creates more space for the tongue, which in turn could improve the tongue posture and may facilitate an increase in oropharyngeal airway space[38].

In patients over 17 years of age with maxillary transverse deficiency, using a standard RME approach could have some potential adverse effects such as tipping and extrusion of the molars, potential relapse, and gingival recession[9]. Previously, the gold standard to treat maxillary transverse deficiency in adults was through surgically-assisted rapid palatal expansion (SARPE). More recently, a novel non-invasive technique called microimplant-assisted rapid palatal expansion (MARPE) has been proposed, which allows separation of the midpalatal suture in some adults using bone anchorage in the palate. In this technique, the forces are applied directly into the bone and not through anchorage teeth. Since this is a new technique, to date, there is no conclusive evidence showing the effect of MARPE on improving OSA signs and symptoms.

Current treatments for OSA in adults are based on symptoms and severity of the syndrome. Continuous positive airway pressure (CPAP) is the first line of treatment when the apnea hypopnea index (AHI) is ≥15 events per hour, while over 50% of the patients cannot tolerate it[39]. Surgical treatments include tonsillectomy, tracheostomy, or maxillomandibular advancement surgery. However, such surgical interventions are invasive and therefore, adult patients try to avoid them due to their potential morbidity [39]. Therefore, it is crucial to explore the effect of non-surgical maxillary expansion on adult's upper airway, as the result of such studies could help adults with OSA to have a less invasive treatment modality for their condition if qualified.

Recently, upper airway dimension evaluation is commonly done using CBCT imaging. In addition to CBCT imaging, various objective and subjective measurements have been proposed for the evaluation of OSA signs and symptoms during RME such as polysomnography (PSG), minimum inspiratory pressure (MIP), maximum expiratory pressure (MEP), oral expiratory peak flow (OEPF), inspiratory nasal flow (INF) (objective measurement)[48], and nasal obstruction symptom evaluation (NOSE) questionnaires (subjective measurements) [49]. Aquastic rhinometry [1] and apnea/hypopnea index (AHI) [43] are other modalities of airway evaluation discussed in different studies assessing RME effects.

To date, multiple systematic reviews have been published regarding the effect of RME or MARPE appliances on upper airway dimensions and skeletal and dental changes. For instance, in systematic reviews conducted by Alyessary et al[50] and Baratieri et al[51], they evaluated the effect of RME appliance on airway dimensions and breathing in patients younger than 17 years of age. They reported an increase in nasal cavity width and a decrease in airway resistance after using RME appliance[50, 51]. In another systematic review and metal analysis conducted by Buck et al (2017)[52], they included studies (17 studies) that followed up patients at least eight months post expansion. They concluded that RME in growing patients (younger than 18 years of age) with maxillary transverse deficiency is potentially associated with an increase in nasal cavity volume and total upper airway volume, velopharynx volume, nasopharynx volume, oropharynx volume, and hypopharynx volume in short and long-term[52]. In a systematic review conducted by Arqub et al (2021)[53], they evaluated the effect of tooth-borne, tooth-bone-borne, and bone-borne micro-implant assisted rapid maxillary expansion appliances on upper airway dimensions and function in patients 10-17 years of age. Based on their included studies (three studies) [1, 28, 54], they concluded that MARPE did not lead to significant changes on upper airway volume and minimal cross-sectional area, regardless of its design and reported that the influence of MARPE appliances on breathing is still unclear[53]. In another systematic review and metal analysis conducted by Kapetanovic et al (2021)[55], they evaluated the skeletal and dental changes after using MARPE appliances in late adolescents and adults (≥ 16 years of age) [55]. They included eight articles[27, 56-62], and concluded that MARPE is a successful treatment modality for patients with maxillary transverse deficiency and could induce both skeletal (2.33 mm) and dental (6.55 mm) maxillary expansion. However, according to this systematic review, out of the eight articles, seven had serious risk of bias, one had moderate risk of bias, and the GRADE quality of evidence was found to be very low[55]. Therefore, the results of such studies should be interpreted with caution.

To the best of our knowledge, no scoping review has been conducted to map the available literature on the effect of MARPE on upper airway dimensions. It is important to note that although there are multiple studies available in the literature that only focused on the skeletal and dental effect of MARPE appliances [58, 59, 63-81], there are limited literature available on the effect of such appliances on upper airway dimensions (especially in adult patients), and that is the main focus of this review. Therefore, the purpose of this scoping review was to map what we currently know about the effect of MARPE on upper airway dimensions and skeletal and dental changes, and to identify gaps surrounding this topic. There are different designs of MARPE available in the market with different names such as mini-implant-assisted rapid maxillary expander (MARME)[82], bone-anchored maxillary expander (BAME), tooth-bone-anchored expanders (MSE)[74]. In this review, all bone-anchored expanders are referred to as microimplant-assisted rapid palatal expansion (MARPE) appliances.

2.2. Methods

This scoping review was completed following Arksey and O'Malley's scoping review framework[83].

2.2.1. Research question

A scoping review of human studies that evaluated the effect of MARPE on upper airway dimensions and skeletal and dental changes was undertaken.

2.2.2. Identifying relevant studies

The PICO statement (population, Intervention, comparison, outcome) of this scoping review are summarized in Table 2.4, Appendix 1.

Inclusion criteria- The final articles selected were those whose main objective was to evaluate the effect of MARPE on upper airway dimensions. These articles could also report the skeletal and dental effects of MARPE, but that was not mandatory to be included in the study. Studies that compared MARPE and RME appliances and their effects on upper airway dimensions were also included. Only Randomized Controlled Trial studies were selected. In terms of imaging, included studies had to have CBCT as their imaging modality for evaluation of upper airway dimensions and skeletal and dental changes. In addition to CBCT, included studies could also have evaluated upper airway function as part of their evaluation, but that was not mandatory. Studies with and without a control group were chosen and only those with English language (or translated to English) were considered. No age limitation was considered for this review.

Exclusion criteria- Studies comparing SARPE with MARPE, those that only evaluated different MARPE designs, those that only considered MARPE in conjunction with SARPE, papers that used other diagnostic imaging tools than CBCT imaging were not considered. Any study other than RCTs such as reviews, systematic reviews and meta-analysis, book chapters, case reports, personal opinions, letters, conference abstracts were excluded. Patients with syndromic characteristics, systemic diseases, and those who previously had maxillary expansion were also excluded.

Comprehensive electronic search for the following four databases were developed: PubMed, MEDLINE, EMBASE, and Web of Science. Grey literature search was also completed using google scholars. In addition, the reference list of the selected papers and repeated author names were screened for any potentially missed paper. The search was carried out on May 02, 2021. The end date for all database searches was Aug 30, 2021. All search results were exported to Rayyan Software[84] (Qatar Computing Research Institute, Doha, Qatar) and duplicates were excluded.

2.2.3. Study selection

Study selection was carried out in two phases. In phase I, two reviewers (NH and AT) independently evaluated the articles by only reading the titles and abstracts using Rayyan Software[84] and the blind option was selected. Any study that did not fulfill the criteria was excluded. In phase II, the articles were screened in full text by the same reviewers and if any disagreement developed, the third reviewer (AH) was consulted. Final selections were reviewed one last time by the first reviewer (NH).

2.2.4. Charting of the data

The data were extracted by the first reviewer (NH) and articles were listed as authors, year of publication, country, sample size, patient's age range, type of appliances, control groups, type of airway evaluation (ie. volume, minimum cross-sectional area (MCA), oxygen saturation, ect), type of skeletal and dental evaluation, different time points, diagnostic radiographs, software used, and main findings. The second reviewer (AT) cross checked all the collected information for accuracy.

2.3. Results

2.3.1. Study selection

In phase I, 826 citations were identified using four databases: PubMed (444), EMBASE (185), MEDLINE (105), and Web of Science (92). After duplicates were removed, 569 articles remained. After comprehensive evaluation of the titles and abstracts, 520 articles were excluded from this scoping review and 49 articles remained for phase II evaluation. From the google scholar search, 8 articles were retrieved, out of which 3 articles met the inclusion criteria. Therefore, in phase II, there was a total of 52 articles to be evaluated for full text review. The references of the included studies were also assessed for potential related articles. Only 7 articles were finally included in this scoping review after thorough text evaluation. The PRISMA flow diagram of literature search, selection criteria, inclusion and exclusion of studies is summarized in Figure 2.1, Appendix 1.

2.3.2. Study characteristics

The main outcome of included studies, type of appliances used, portion of the upper airway analyzed, type of skeletal and dental evaluation, diagnostic tests, and the software used for each analysis is summarized in Table 2.1, Appendix 1.

The selected studies were grouped into three age categories: studies that only focused on children (≤ 17 years of age) [85, 1, 86], adults (>17 years of age) [26, 27], and those with samples composed of both adults and children [28], [29].

The studies that included children only were published between 2015 and 2021 and were conducted in USA [85, 86] and Canada [85, 1, 86]. Type of appliances used were MARPE and RME. Two of these studies [1, 85] had controls. All studies had CBCT imaging. Dolphin software was used in two of the included studies[85, 86], while the third study used acoustic rhinometry (AR) and the AVIZO software [1].

The upper airway compartments that were evaluated in pediatric studies are as follows: three studies explored nasal cavity volume (NCV)[1, 85, 86], two explored minimal cross-sectional area (MCA) [1, 85], two focused on nasopharynx volume (NPV) and oropharynx volume (OPV) [85, 86], one study evaluated right and left maxillary sinus volume (RMSV, LMSV) [86], and one study explored nasal cavity area (NCA), nasopharyngeal area (NPA), oropharyngeal area (OPA), laryngopharyngeal area (LPA), and total airway volume and area (TAV, TAA) [85].

The skeletal and dental evaluations in pediatric studies are as follows: two studies explored maxillary intermolar width (MIW), external maxillary width (EMW), and palatal width (PW) [85], [86], one study focused on maxillary right and left first molar buccal Inclination [86], one study evaluated the skeletal and dental effect of MARPE using 12 points: the point where lateral and inferior walls of the nasal cavity connect in the xz dimension parallel to the apices of the roots of the upper cuspids (points 1 and 2) , upper first bicuspids (points 3 and 4) , upper second bicuspids (points 5 and 6), and upper first molars (points 7 and 8), points where the base of each inferior nasal concha meets the lateral wall of the nasal cavity in the xz dimension parallel to the apices of the roots of the upper cuspids (points 9 and 10), and the most superficial points of the infra-orbital canals in the xy dimension parallel to the level of the inferior conchae (points 11 and 12)[1].

The studies in adults were published between 2018 and 2020 and were conducted in Korea[27] and China [26]. Type of appliances used was MARPE in both studies, and no control was used. Software used were Dolphin[26] and OnDemand3D software[27].

The areas of upper airway that were evaluated in adult studies are as follows: two studies explored NCV and NPV[26, 27], one study evaluated total airway volume (TAV), cross-sectional area of airway on anterior (ANS-perp), middle (choanae), and posterior (C3)[26], and one study[27] evaluated the retropalatal airway volume, retroglossal airway volume, hypopharyngeal airway volume, minimal cross-sectional area (MCA) (nasal cross-sectional height (ANS), nasal cross-sectional width (ANS), nasal cross-sectional height (midpoint), nasal cross-sectional width (midpoint), nasal cross-sectional height (PNS), nasal cross-sectional width (PNS)) , height of nasopharyngeal airway, height of retropalatal airway, height of retroglossal airway, height of hypopharyngeal airway volume, Latero-lateral distance (PNS), anteroposterior distance (PNS), latero-lateral distance (uvula), anteroposterior distance (uvula), antero-lateral distance (epiglottis), anteroposterior distance (epiglottis), cross-sectional area (PNS), cross-sectional area (uvula), cross-sectional area (epiglottis).

The skeletal and dental evaluations in adult studies are as follows: one study evaluated the nasal lateral width (NLW) , nasal floor width (NFW), maxillary width (MW), zygomatic bone width, temporal bone width, and palate thickness [26]. one of the adult studies did not evaluate skeletal and dental changes after maxillary expansion and only focused on airway changes [27].

The studies with samples composed of both adults and children were published between 2019 and 2020, and were conducted in USA[28], Brazil [28], and China [29]. Two of the studies used MARPE only [28], [29]. No control was used in any of these studies. One study used Dolphin software [29] and one study used analogue manometer for respiratory muscle strength measurement, ASSESS expiratory peak flow meter device to measure maximum airflow, and In Check Nasal device to evaluate nasal inspiratory peak flow [28].

The areas of upper airway that were evaluated in studies composed of both adults and children are as follows: one study explored minimum inspiratory pressure (MIP), maximum expiratory pressure (MEP), oral expiratory peak flow (OEPF), inspiratory nasal flow (INF), and nasal cavity width (NCW) [28], and one study focused on upper airway volume (NPV, palatopharyngeal volume (PPV), glossopharyngeal volume (GPV), OPV, TAV); upper airway area (MCA for Oropharynx, palatopharynx, glossopharynx, PNS plane cross section area, SP plane cross-section area, and C3 pi plane cross-section area); and upper airway length (nasal lateral width (NLW), coronary-level lateral NLW at first premolar (P1) region (P1NLW), coronary-level lateral NLW at second premolar (P2) region (P2NLW), coronary-level lateral NLW at first molar (M1) region (M1NLW), coronary-level lateral NLW at second molar (M2) region)(M2NLW)) [29].

The skeletal and dental evaluations in studies composed of both adults and children are as follows: one study evaluated midpalatal suture opening, alveolar bone width, interdental distance (mid-fossae of R and L upper first molars and premolars), and tooth inclination (long axis of first premolars and molars to the palatal base of the maxilla)[28], and one study focused on the lateral maxillary expansions of the P1 , P2, M1, M2 , and transverse skeletal expansion with linear measurements at three different levels: nasal floor (NF), hard palate (HP), and hard palate below 5mm (HP5) [29].

2.3.3. Synthesis of results

A. Pediatric studies

Upper Airway Changes

In pediatric studies, study by Mehta S. et al [85] evaluated the effect of MARPE and RPE in 3 time points: T_1: pre-treatment; T_2: immediately after maxillary expansion completed; and T_3: two years and eight months after expansion completed. They reported a statistically significant increase ($P< 0.005$) in upper airway volume (NCV (14.4 % for MARPE and 11.5 % for RPE), NPV (21.8% MARPE, 24.1% RPE), OPV (19.2 % MARPE, 26.4 % RPE), NPA (22.7 % MARPE, 29.8% RPE), TAV (20.5 % MARPE, 25.5% RPE), TAA (TAA; 8.1% MARPE, 16.9% RPE), MCA (20.3% MARPE, 21.7% RPE)) in both MARPE and RPE groups in short term. No significant increase in lower airway volume (Laryngopharyngeal volume (LPV)) was noted. The control group showed no significant change in the parameters from T_1 to T_2. Shortly after maxillary expansion, no significant difference was found between the MARPE and RPE groups. However, in long term (two years and eight months after expansion), MARPE showed to lead to a significant increase in the NPV (44.3 % increase in MARPE vs. 29% increase in RPE) compared to RPE. Also, no significant increase on TAV noted in the long term. All other upper airway parameters that increased in short term, also showed an increase in long term in this study. In the control group, from T_1 to T_3, there was a statistically significant increase in the NCV (29.4%), NCA (39.5%), NPV (35.6%), OPV (40.7%), TAV (39%), and MCA (59.3%).

The study by Kavand G. et al [86] also supported these findings. They evaluated effect of MARPE and RPE in two time points: T_1: pre-treatment; and T_2: 3 months post expansion and found an increase in NCV (12.5% in RPE and 16.1% in MARPE) and NPV (21.8% in RPE, 20.0% in MARPE) using MARPE and RPE. However, no significant changes in OPV noted after expansion. The study by Kabalan O. et al[1];however, reported no significant changes in NCV and MCA after using MARPE and RPE. They evaluated the effect of MARPE and RPE in two time points: T_1: pre-treatment; and T_2: 6 months post expansion.

Skeletal and Dental Changes

In pediatric studies, study by Mehta S. et al[85] reported an increase in MIW (10.7% for MARPE and 14.3% for RPE), EMW(2.8% for MARPE, 3.3% for RPE), and PW(10.4% for MARPE, 6.4% for RPE) in short term (immediately after expansion (T_2)). The control group showed no significant changes in the parameters from T_1 to T_2. In the short term, no significant difference was noted between the MARPE and RPE groups. However, in long term, MARPE resulted in a more significant increase in PW (9.3% for MARPE Vs. 4.8% for RPE) compared to RPE. At T_2, the amount of MIW was greater in RPE (14.3%) compared to MARPE (10.7%). However, in long term for MIW, there was no significant difference between MARPE (12.4%), RPE (9.9%) and control groups (8.6%). In the control group, from T_1 to T_3, there was a significant increase in MIW (8.6%), and PW (3.7%).

The study by Kavand G. et al [86] showed a statistically significant increase ($P < 0.05$) in EMW(increase by 3.5 % for RME and 2.7% for MARPE) , PW (6.5% for RME and 10.1% for MARPE), and MIW(10.3% for RME and 7.3 % for MARPE at level of central fossae) in both RME and MARPE groups. They reported no significant differences in terms of skeletal and dental expansion between the RME and MARPE groups, except that there was a significantly larger amount of buccal tipping of maxillary right first molar using RME (2.8 % for RME vs. 0.4% for MARPE) compared to MARPE. Study by Kabalan O. et al [1] showed no correlation between skeletal changes and the amount of airway intake after maxillary expansion ($P > 0.05$) and no significant skeletal and dental expansion noted compared to the control group.

B. Adult studies

Upper Airway Changes

In adult studies, the study by Kim S-Y. et al [26], they evaluated effect of MARPE in three time points: T_0: pre-treatment; and T_1: immediately after maxillary expansion completed, and T_2: one year after expansion completed. They showed a statistically significant increase ($P<0.05$) in NCV (at T_1: 1061.6 mm^3 increase), with further increase after one year (T_2: an additional increase of 648.6 mm^3). They also found a statistically significant increase in NPV (increase of 942.4 mm3 from T_0 to T_2). However, the increase in NCV was found to be more than the increase in NPV (the NCV increased by 9.99%, 5.5%, and 15.4% from T_0 to T_1, T_1 to T_2, and T_0 to T_2, respectively while the NPV increased by 6.4%, 4.1%, and 10.5%, respectively). TAV also increased from T_0 to T_2 (2652.6 mm^3 increase). There was also an increase in cross-sectional area of airway on anterior (ANS-perp) and middle (choanae) segments after expansion (31.3%, 9.5% respectively), but no significant changes found on the cross-sectional area of the posterior segment of the airway (C3) (6.1% increase) [26]. Similarly, in the study conducted by Li et al [27], they evaluated effect of MARPE at two time points: T_1: pre-treatment; and T_2: immediately after maxillary expansion completed. They reported an increase in NCV and dimension (16.2%) and NPV and dimension (14.1%) after maxillary expansion. They also found that enlargement of the PNS after expansion contributed to the increase in NPV. They reported no statistically significant changes on RPAV, RGAV, HPAV, and MCA. Therefore, overall, no changes on the inferior section of the upper airway and MCA were found.

Skeletal and Dental Changes

In the study conducted by Li et al [27], they reported a significant expansion of nasal lateral width (NLW) (6.9%), nasal floor width (NFW) (7.5%), maxillary (3%), zygomatic (0.5 %) , and temporal (0.6%) bone widths ($P< 0.001$). The results showed that the increase in maxillary width is negatively affected by thickness of the hard palate (HP). No clear association was found between vertical skeletal patterns (hyperdivergent, normodivergent, and hypodivergent) and changes of upper airway after MARPE due to the complex structures involved.

C. Studies composed of both adults and children

Upper Airway Changes

In studies composed of both adults and children, Storto C.J. et al [28] evaluated effect of MARPE in three time points for airway: T_0: pre-treatment; T_1: immediately after maxillary expansion completed, and T_2: five months after expansion completed. They reported that minimum inspiratory pressure (MIP) showed a clinically significant improvement of 20% between T_0 and T_2 (5 months after expansion). Maximum expiratory pressure (MEP) had a 10% increase from T_0 and T_1, but no further changes noted at T_2. Nasal inspiratory peak Flow increased significantly between T_0 - T_1 and T_1- T_2 (30.45% and 30.28%, respectively). Oral expiratory peak flow (OEPF) significantly increased between T_0 - T_1 and T_1- T_2 (25% and 40 %, respectively) in patients who initially presented with low airflow (had lower values than 100% and sign of airway obstruction). Those with satisfactory initial airflow also showed a significant increase from T_0 to T_2 (20%). Nasopharynx volume (NPV) also showed a significant improvement (from 16,058 (+/- 2171.98) to 21,835.55 (+/-1937.64) mm3). They also reported a significant increase ($P<0.05$) in nasal cavity width (NCW) ($P< 0.05$) [28]. Pearson correlation and linear regression analyses was also completed to evaluate if there is any correlation between airway volume and MIP and MEP values. The results showed a strong positive correlation between airway volume and nasal inspiratory peak Flow (NIPF) ($r^2= 0.9804$; $P < 0.01$), Oral Expiratory Peak Flow (OEPF) ($r^2 = 0.9364$; $P< 0.01$), and MIP ($r^2 = 0.9482$; $P< 0.01$), which means that an increase in the airway volume had a positive effect in airflow (NIPF and OEPF) and muscular strength during MIP. There was no correlation between the airway volume and MEP ($r^2 = 0.0016$; $P> 0.05$)[28].

Yi F. et al [29] evaluated effect of MARPE in two time points: T_0: pre-treatment; and T_1: three months after maxillary expansion completed. They reported that after using MARPE appliance, there was a statistically significant increase ($P< 0.005$) in NPV (increased by 502 mm^2 (8.48%)). They also found an increase ($P<0.001$) in nasal lateral width (NLW) (by 1.63 mm (6.61%)), nasal lateral width at first premolar (P1NLW) (by 3.00 mm (8.76%)), nasal lateral width at second premolar (P2NLW) (by 1.48mm (3.72%)), nasal lateral width at first molar (M1NLW) (by 1.54mm (3.33%)), and nasal lateral width at second molar (M2NLW) (by 1.35mm (3.11%)). No significant changes found in palatopharyngeal volume (PPV), glossopharyngeal volume (GPV), oropharynx volume (OPV), and total airway volume (TAV).

Skeletal and Dental Changes

In studies composed of both adults and children, Storto C.J. et al [28] reported a statistically significant increase ($P<0.05$) in midpalatal suture opening (4.7 mm at level of P1 and 4mm at M1), interdental distance (3.59mm at P_1 and 5.34 mm at M_1), tooth inclination for upper first molar

(3.61mm), and alveolar bone width (3.59 mm at P_1 and 3.88 at M_1). The tooth inclination for upper first premolars was not statistically significant (1.83 mm of change (P=0.173)).

Yi F. et al [29] reported a statistically significant ($P< 0.05$) increase in width of midpalate, nasal floor (NF), hard palate (HP), hard palate below 5 mm (HP5). The midpalatal width change from pre-expansion to post-expansion was 2.19 mm at PM1, 1.45 mm at P2, 1.25 at M1, 0.93 at M2. The nasal floor changes were 1.97 at P1, 2.11 at P2, 1.77 at M1, and 1.45 at M2. The hard palate changes were 2.64 at P1, 2.06 mm at P2, 1.67 at M1, and 1.58 at M2. HP5 changes were 2.97 at P1, 2.23 at P2, 1.76 at M1, 1.69 at M2. Finally, the buccal cusp changes were 3.14 mm at P1, 3.61 at P2, 3.92 at M1, and 3.61 at M2. For both MP and HP5, the bone expansion from P1 to M2 gradually decreased, which indicated there is more expansion in anterior region compared to posterior region. Overall, bone expansion, alveolar expansion, dental expansion was 73.00%, 26.00% and 1.00% of the total expansion respectively at P1 region, 40.17%, 21.61% and 38.22 of the total expansion respectively at P2 region, 31.89%, 13.01% and 55.10% of the total expansion respectively at M1 region, and 25.76%, 21.05% and 53.19% of the total expansion respectively at M2 region. This study also reported a more horizontal skeletal expansion with MARPE compared to the reverse "V" pattern expansion seen with RME appliances.

2.4. Discussion

2.4.1. Upper airway changes

The objective of this scoping review was to map what we currently know about the effect of MARPE on upper airway and skeletal and dental changes, and to identify gaps in this topic. There are significant methodological differences between the included studies which makes a direct comparison between the results difficult. However, there are some consistent findings between these studies. The increase in nasal cavity volume (NCV) after using MARPE and RPE was consistently reported by included studies [85,86,26,1, 27]. Overall, their results showed an increase in NCV from 14.4% [85] up to 16.2% [27] for MARPE and between 11.5% [85] to 12.5% [86] for RPE group. However, these differences may not be considered clinically relevant. Further supporting this interpretation, one study showed no significant changes in NCV after expansion for either MARPE or RPE appliances[1]. A summary of the most common upper airway portions used in the included studies is shown in Table 2.2, Appendix 1. The increase in nasopharynx volume (NPV) after using MARPE and RPE was also reported by multiple included studies [85,86,26,27, 28, 29]. Overall, results showed an increase in NPV from 8.48% [29] to 21.8 % [85] for MARPE and from 21.8% [86] to 24.1%[85] for RPE groups.

Although there are limited number of studies that evaluated the effect of MARPE on upper airway (especially on adults), there is, however, a considerable amount of literature focusing on the effect of RME alone on upper airway dimensions in younger patients (17 years and younger). Almuzian M. et al [87] evaluated the effect of RME on nasopharyngeal airway using CBCT imaging in patients 10 to 16 years of age, and found a statistically significant increase in NPV after expansion (15.2% in males and 12% in females). Similarly, study by Lotfi V. et al [88] focused on two different expansion protocols for RME (group A: 0.8 mm expansion per day (4 turns) and group B: 0.5 mm per day (2 turns)) and their effect on upper airway in patients 12 to 16 years of age. They reported a clinically significant increase in NCV and NPV in both groups (more in group A compared to group B). For NCV, group A had a mean increase of 2705.47mm^3 and group B had a mean increase of 1054.92mm^3. For NPV, group A had a mean increase of 456.24mm^3 and group B had a mean increase of 103.29mm^3. Similarly, Smith T. et al [89] reported an increase in NCV and NPV after using RME in patients 8-15 years of age (an increase of 15.2% for NCV and 16.2% for NPV,). Zeng et al [90] also reported a significant increase in lower part of NCV (8.1% increase), but no significant changes were found in NPV in patients 10-15 years of age after using RME.

Oropharynx volume (OPV) was another part of the airway that was evaluated in three of the included studies, where only one study showed a significant increase in OPV (19.2 % in MARPE, 26.4 % in RPE)[85], while the remaining two articles showed no significant changes [86],[29]. Minimal cross-sectional area (MCA) was also evaluated by two of the included studies [1,27], where both reported no significant changes after using MARPE. There is, however, inconsistent evidence in literature regarding OPV and changes on the airway cross-sectional area after using MARPE and RME appliances. Gianoni-Capenakas S et al [49] evaluated the effect of RME on OPV and MCA in patients 11 to 17 years of age using CBCT imaging, and found a statistically significant increase in both (18% and 23%, respectively). Zhao et al[91] , however, reported no significant increase in OPV, MCA, retroglossal airway length or volume, retropalatal airway length after RME in patients 12.8 +/- 1.85 years old. They found a significant increase in retropalatal airway volume ($P<0.011$)[91]. However, study by Li et al [27] was one of the included studies that reported no changes on retropalatal airway volume (RPAV), retroglossal airway volume (RGAV), hypopharyngeal airway volume (HPAV) after using MARPE. It is important to note that the study by Li et al (2020) was conducted in adults, whereas study by Zhao et al (2010) was done in children.

Total Airway Volume (TAV) is another upper airway portion that was discussed by three of the included studies [85,26,29], two of which found an increase in TAV[85,26], while the third study reported no changes [29]. Similarly, study by Fastuca R.et al [43] used Haas-type expander in patients 8.3 ±0.9 years and reported an increase in TAV (change of 175.8 mm^3 (CI: 91.5-253.3)). Fastuca R.et al also used polysomnography (PSG) examination as a functional respiratory parameter and reported a clinically significant increase ($p<0.05$) in oxygen saturation (SpO2: mean+/- SD= 5.72±1.95 % from T_0 to T_1)) and apnea/hypopnea index (AHI: mean+/- SD= -3.56±1.32 from T_0 to T_1). They concluded that when evaluating the effect of RME on the respiratory performance, in order to achieve a more reliable conclusion, functional respiratory parameters (such as PSG) should be included and combined with anatomical examinations of the airway (such as evaluating nasopharynx volume) [43]. Such studies, however, are not commonly done. Therefore, studies that only focus on the anatomical investigations of the RME on airway volume might be limited in their conclusions. All of the studies included in this scoping review only evaluated the anatomical parts of the airway except one conducted by Storto C.J et al[28], which combined both anatomical examinations (Nasopharynx volume and nasal cavity width) and functional respiratory parameters (such as Minimum Inspiratory Pressure (MIP), Maximum Expiratory Pressure (MEP), oral expiratory peak flow, and Nasal Inspiratory peak flow). Their result showed a statistically significant increase in respiratory muscle strength (MIP, MEP), OEPF, NPV, and NCW after using MARPE appliance. They also reported a significant enlargement of the nasal cavity, alveolar bone, and interdental widths at the premolar and molar region, and concluded that skeletal changes by MARPE affect airway volume and significant improvement of muscle strength and nasal and oral peak flow. Pearson correlation and linear regression analyses data also showed that an increase in the airway volume had a positive effect in airflow (NIPF, OEPF) and muscular strength during maximum inspiratory pressure (MIP). No correlation was found between the airway volume and MEP[28].

Long term studies are important in determining the effect of the appliance after the potential relapse period, while only three of the included studies in this review were long-term studies[85 26, 28]. Research by Davami et al[66] showed that the findings could be altered by relapse when looking at expansion groups in long-term and this alteration might change the primitive results of expansion[66]. For example, study by Mehta et al reported that although the TAV increased in short term (20.5 % for MARPE, 25.5% for RPE), no significant increase on TAV noted in the long term (after 2 years and 8 months).

2.4.2. Skeletal and dental changes

A summary of the most common skeletal and dental landmarks that were used in included studies of this scoping review is shown in Table 2.3, Appendix 1. Maxillary intermolar width (MIW) was reported by two of the included studies [85,86], where both studies showed an increase after using MARPE and RPE. External maxillary width (EMW) and palatal width (PW) were also reported by two of the included studies and both showed an increase after using MARPE and RPE[85,86]. Midpalatal suture opening is another landmark that was reported by two of the included studies [28,29] after using MARPE in adult patients and both showed an increase. Both studies indicated that when using MARPE appliance, there is more expansion in anterior region (first premolar region) compared to posterior region (molar region)[28,29].

Tooth inclination and buccal cusp changes were also discussed by two of the included studies (both used MARPE only) [28,29], and both found more buccal cusp changes for upper first molars (3.61 mm change in both studies) compared to premolars (1.83 mm in study by Storto et al and 3.14 mm in study by Yi et al). These findings are consistent with the conclusions from other studies. Study by Zhao et al[91] also reported the mean percentage increase of molar-to-molar width of 10.7% ± 10.96% (3.3 to 3.10 mm) after using RME in patients 12.8 +/- 1.85 years. Davami et al [66] evaluated the long-term effect (T1: before treatment; T2: when treatment was completed (average of 2 years)) of RPE and MARPE on skeletal and dental landmarks in patients 11-17 years old. They reported that in both groups, the greatest lateral crown and alveolar bone displacement was in the first molar region (5.28 mm for MARPE and 4.38 for RPE group). The greatest alveolar bone displacement was also reported to be at the M1 region (1.74 mm for MARPE and 3.11 mm for RPE). They also showed that the posterior skeletal expansion was greater in posterior region (1.91 mm for MARPE and 1.96mm for RPE) than anterior region (1.32 mm for MARPE and less than 1mm for RPE). The result of this study showed that in long-term, there was no significant difference in the skeletal and dental changes in transverse, anterior-posterior, and vertical planes between the RPE and MARPE groups [66]. The result reported from Davami et al showed more posterior expansion than anterior expansion, which is different from most of the previously reported studies that found either a nearly parallel expansion in bone-anchored expanders or more anterior skeletal expansion than posterior expansion (such as the results reported by two of the included studies in this review [48,29]). Such inconsistency between results could be due to the fact that the study by Davami et al has taken the role of relapse into account since they evaluated expansion almost 2 years after using RME and MARPE appliances, whereas in the study by Storto et al and Yi et al, relapse was not considered. Another reason for such discrepancy could be attributed to the appliances. In the study by Storto et al and Yi et al, both used 4 miniscrews paramedial to the mid-palatal suture, whereas the study by Davami et al used Dresden expander with 2 miniscrews on the alveolar bone area.

Asymmetric expansion is also discussed in the literature when using RPE or MARPE appliances. Study by Canan et al [92] evaluated skeletal and dental effects by comparing a tooth-borne expander (RPE), a bone-borne expander (four miniscrews), and a hybrid expander (with 2 miniscrews and bands on upper first molars) using CBCT imaging on patients between 12-15 years of age. In each group, the expansion screws were activated by 2 quarter turns per day and expansion was evaluated at three time points (T_0: before expansion; T_1: after expansion completed; and T_2: 6 months after treatment). In RPE and hybrid groups, the right first molar moved more buccally than in the bone-borne group and this difference increased after retention. At the level of premolars, expansion was achieved for all three groups, while the amount of expansion in the bone-borne group was less than tooth-borne group[92]. Overall, similar skeletal and dental effects were reported for all three groups, with the exception that the bone-borne expander had less amount of expansion on the right side. This was attributed to different designs of bone-borne expanders with different locations where miniscrews are inserted, different force distributions, and activation protocols[92]. According to Elkenawy et al[79] such asymmetrical expansion could also be explained by the individual bone density of the maxillary sutures and the surrounding structures and potentially the differences in bone morphology on each side of the suture. However, the true reason for such asymmetries needs to be further studied [79]. Elkenawy et al also reported in their study, that out of 31 patients, 16 patients had a statistically significant asymmetric expansion. In these asymmetric expansion cases, one half of anterior nasal spine (ANS) moved more than the contralateral half by 2.22 mm[79].

Three of the included studies in this review compared the effect of MARPE and RPE[85,1,86]. All three studies were conducted on patients younger than 17 years of age. Overall, all three studies concluded that there were no significant differences between the two groups after expansion. However, one of the long-term studies (2 years and 8 months) by Mehta et al[85] reported that although there were no significant differences between the two groups in short term, MARPE showed to lead to a significant increase in the NPV (44.3 % increase in MARPE vs. 29% increase in RPE) compared to RPE in long term. The study by Kavand et al[86] also reported no significant differences between RME and MARPE groups, except for the significantly larger increase in buccal inclination of the maxillary right first molar after RME.

2.4.3. Limitations

The main shortcoming of this scoping review is the limited number of existing studies and the heterogeneity in terms of methodology among the included studies. Consistent methodology is needed to evaluate upper airway dimensions to be able to compare the results of different studies. In addition, only one of the included studies evaluated both anatomical parts of upper airway and functional changes[28]. When evaluating the effect of RME on the respiratory performance, to achieve a more reliable conclusion, functional respiratory parameters should be included and combined with anatomical examinations of the airway [43]. It is important to note that dimensional changes of upper airway do not necessarily imply functional improvements in airway. Therefore, studies that only focus on the anatomical investigations of the RME or MARPE on airway volume might be limited in their conclusions.

2.5. Conclusions

In summary, this scoping review provides an insight of the current knowledge available regarding MARPE effect on upper airway dimensions and skeletal and dental changes. Although there is conflicting and limited evidence available for upper airway dimensional analysis using MARPE (especially in adults), considerable progress has been made in this area of research which made it crucial to put together a critical appraisal of this field and to discuss potential gaps in this topic to help improve our knowledge in this area of research.

For upper airway changes, the consensus among majority of the included studies was that regardless of the design of the appliance, MARPE and RME resulted in a statistically significant increase in nasal cavity volume, nasopharynx volume, and total airway volume. There is, however, inconsistent evidence regarding oropharynx volume and minimal cross-sectional areas. Table 2.2 (Appendix 1) summarizes the most common upper airway compartments that were discussed in included studies and the changes that were reported by each study.

For skeletal and dental changes, the consensus among the included studies was that regardless of the design of the appliance, MARPE and RME resulted in a statistically significant increase in maxillary intermolar width, external maxillary width, palatal width, nasal lateral width, nasal floor width, and tooth inclination and buccal cusp changes on upper molas and premolars. Table 2.3 (Appendix 1) summarizes the most common skeletal and dental changes that were discussed in included studies, and the changes that were reported by each study.

2.6. Practice points

This scoping review shows that:

1. There is limited and conflicting evidence in the literature, focusing on the effect of MARPE on upper airway dimensions.
2. The most common upper airway portions that are investigated in studies involving MARPE are nasopharynx volume (NPV-6 studies), nasal cavity volume (NCV-5 studies), oropharynx volume (OPV-3 studies), total airway volume (TAV-3 studies), and minimal cross-sectional area (MCA-3 studies).
3. The most common skeletal and dental landmarks that are investigated in included studies are maxillary intermolar width (MIW), external maxillary width (EMW), palatal width (PW), midpalatal suture opening, nasal lateral width (NLW), nasal floor width (NFW), and tooth inclinations and buccal cups changes of maxillary molars and premolars.

2.7. Research agenda

1. Consistent methodology is needed to evaluate upper airway dimensions to be able to compare the results of different studies.
2. There are only three long-term studies [26, 28, 85] evaluating the effect of MARPE on upper airway dimensions and skeletal and dental changes. More long-term studies are needed to consider the effect of relapse after maxillary expansion.
3. Future studies combining functional respiratory parameters (such as PSG) with anatomical examinations of the airway are recommended.

4. Studies on MARPE appliances in adults, with inclusion criteria of adult patients with OSA and maxillary transverse deficiency are recommended to directly evaluate the effect of MARPE on upper airway of these individuals.
5. Asymmetric expansion is another topic that could be investigated further in the literature, especially in adult population after using MARPE appliances. It has been proposed [79] that asymmetrical expansions could be explained by the individual bone density of the maxillary sutures and the surrounding structures and potentially the differences in bone morphology on each side of the suture. However, the true reason for such asymmetries needs to be further studied [79].
6. Finally, tongue posture was not discussed in any of the included studies. It has been proposed that after maxillary expansion, enlargement of the palatal space creates more space for the tongue, which in turn could improve the tongue posture and facilitate an increase on airway space in the oropharynx [38]. This is another important area that could be investigated in future studies using MARPE appliances.

Chapter 3 - Upper Airway Changes

3.1. Methods

This analysis is part of an ongoing retrospective secondary pilot study on a randomized clinical trial with a sample size of thirteen, with five patients in the Dresden expander group (group A) and eight patients in the Moon expander group (group B). The study was conducted at the orthodontics graduate clinic at University of Alberta with the ethics approval from the Research Ethics Board (Pro00084145) from the University of Alberta.

3.1.1. Inclusion and exclusion criteria

The inclusion criteria were as follows: patients must be 17 years of age or older with a maxillary transverse deficiency of at least 5 mm and unilateral or bilateral posterior crossbite. Maxillary transverse deficiencies were calculated by measuring (using calipers) the difference between palatal cusps of maxillary first molars and central fossa of mandibular first molars. A 20% over-correction was then added to the total amount of expansion needed to account for any relapse. Exclusion criteria included patients who had any systemic disease or syndromic patients, previous orthodontic treatment, or maxillary expansion, patients with large tori or canted maxillary palatal planes.

A person external to the research project randomly assigned patients to either treatment group using a random number generator. The demographic characteristic of subjects is summarized in Table 3.1.

Table 3.1. Subject Demographics

Appliance	n	Mean age ± SD	Age range	# Of Male participants	# Of Female participants
Dresden (Group A)	5	21.58 ± 4.88	17.1-27.9	2	3
Moon (Group B)	8	24.24 ± 6.87	17.1-33.5	3	5

3.1.2. Experimental design

Two sets of records were taken for each group: 1. Before treatment (T_0) and 2. After maxillary expansion was completed and diastema formed between tooth # 1.1 and 2.1 (any size of diastema) (T_1). For each patient orthodontic clinical charting and diagnostic exams, intra-oral and extraoral photos, Cone Beam Computer Tomography (CBCT), nasal obstruction symptom evaluation (NOSE) questionnaires, and peak nasal inspiratory flow (PNIF) test were available. CBCTs were taken using I-CAT New generation Machine (a large field of view 16 x 13.3 cm, voxel size 0.30 mm, 120 kVp, 18.54 mAS, and 8.9 seconds). Patients were positioned so that the Frankfort horizontal plane was parallel to the floor. Patient's head was stabilized using strips to ensure that their head and neck are still during CBCT scans. They were asked to maintain maximum intercuspation with their tongue touching behind the upper central incisors and avoid any swallowing during the scanning. The scans were stored in DICOM files and were coded for blinding purposes. The CBCTs were assessed using Dolphin 3D® software (version 11.95, Chatsworth, CA, USA). All CBCT images were taken by one of the two radiology technicians at the University of Alberta.

Patients in group A received orthodontic treatment using an onplant-anchored expansion appliance called Dresden expander. This appliance consists of onplants located between upper second premolars and first molars, 9mm away from the mid-palatal suture. Model casts were obtained from the patients and the appliances were fabricated by the laboratory at the University of Alberta. Appliances were placed in the patient's mouth under local anesthetic (2% lidocaine, 1:100,000 epinephrine, 1 carpule). Once the appliance was positioned, two temporary anchorage devices (TADs) of 9-11 mm in length were inserted to hold the appliance in place (one on each side of the palatal alveolar bone). The activation protocol for Dresden expander was one turn per day since the day of insertion, which results in 0.25 mm per day maxillary expansion. During the first appointment, the Dresden expander was inserted and the brackets on lower teeth were bonded. Patients were then instructed on how to complete the NOSE questionnaires and initial PNIF measurements were also taken by one calibrated examiner. Patients started activating the appliance one turn per day as per instructions given to them.

Patients in group B received orthodontic treatment using the Moon expander. Model casts were obtained from the patients and the appliances were fabricated by the laboratory at the University of Alberta. The appliances were cemented to maxillary first molars using "reliance ultra-band-lok®" adhesive. Under local anesthetic (2% lidocaine, 1:100,000 epinephrine, 1 carpule) four temporary anchorage devices (TADs) of 11-13mm in length were inserted (two on each side of the mid palatal suture). The activation protocol for Moon expander was two turns per day since the day of insertion, which results in 0.3 mm per day maxillary expansion. During the first appointment, the Moon expander was inserted and the brackets on lower teeth were bonded. Patients were instructed on how to complete the NOSE questionnaires and initial PNIF measurements were also taken by one calibrated examiner. Patients started activating the appliance two turns per day as per instructions given to them.

Prior to TAD placements, patients in both treatment groups received a chlorohexidine rinse (0.12%) for 2 minutes and all TADS were placed by one orthodontist. Both treatment groups received a minimum of 5mm total activation or until the maxillary transverse deficiency was fully corrected and the palatal cusps of maxillary molars met the buccal cusps of mandibular molars based on McNamara protocol[93]. Once expansions completed (5-10 mm of expansion depending on the patients' need) and diastema formed between the top two front teeth (any size of diastema), a second set of records were taken, and brackets were placed on upper teeth. Both appliances were kept in the mouth inactive for six months after expansion for stability period. Dresden and Moon expanders are showcased in Figure 3.1.

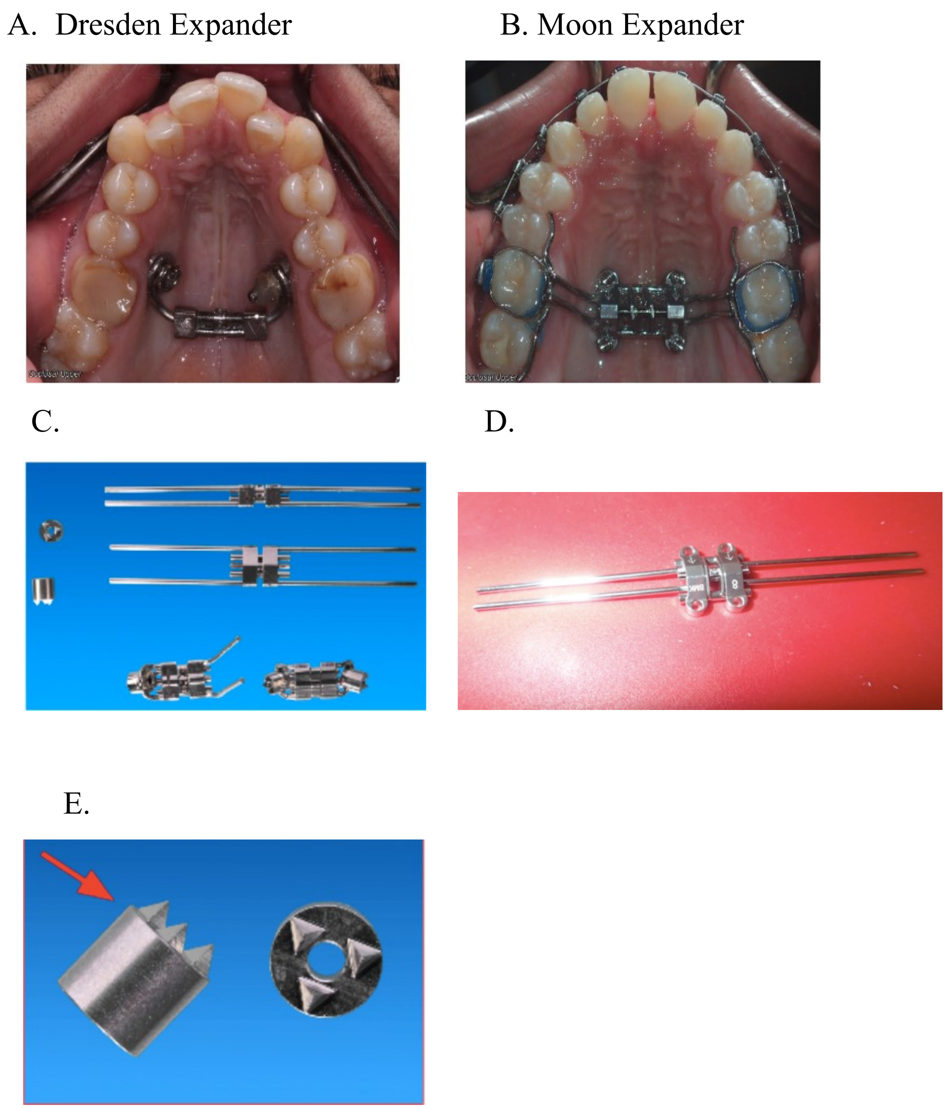


Figure 3.1 A. Dresden Expander. B. Moon Expander. C. Top appliance: Moon Expander, bottom appliance: Dresden Expander. D. Moon Expander. E. Components of Dresden Expander

3.1.3. Method used for analysis of nasopharynx and oropharynx

After all the CBCT data were collected, the images were stored as DICOM files and patient codes were assigned to each patient for blinding purposes. Analysis of nasopharynx and oropharynx was completed using objective and subjective measurements. Objective measurements were done using CBCT scans (Dolphin 3D® software) and peak nasal inspiratory flow (PNIF) measurements. The subjective measurements were done using NOSE questionnaires. Analysis and measurements of the nasopharynx and oropharynx were done by one calibrated and trained examiner. Each measurement was done three times, and an average of the three values was taken. The protocol used for analysis of nasopharynx and oropharynx is similar to the ones previously described in the literature[86, 89].

3.1.4. Head Orientation of the CBCT scans in Dolphin software prior to nasopharynx and oropharynx measurements

Prior to landmark identification, to make sure all the scans were being measured in the same orientation, the "orientation calibration" button was selected, and the scans were oriented in two planes (Figure 3.2, A and B).

1. Frontal view: the horizontal reference line was fixed through right and left orbitale. The mid-sagittal perpendicular plane was fixed through Anterior Nasal Spine (ANS) and Menton.
2. Right lateral view: the horizontal reference line was fixed through the Frankfort Horizontal plane (from porion to right orbitale). The coronal plane was fixed through the furcation point of maxillary right first molar.

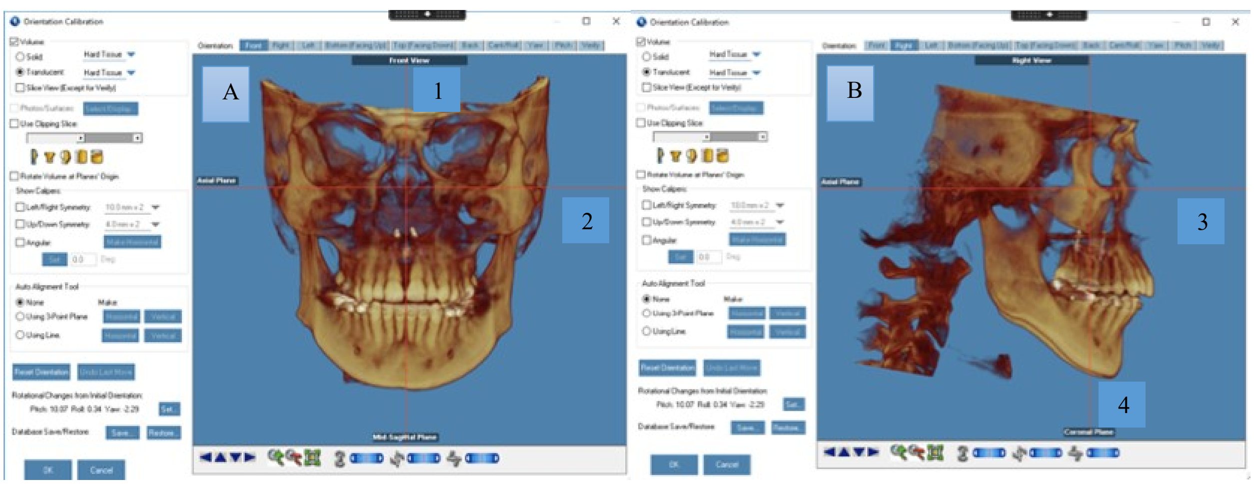


Figure 3.2 Head orientation of the CBCT scans. (A) Frontal view. (B) Sagittal View. Images were oriented based on (1) Skeletal midline, (2) Lower border of the orbit, (3) Frankfort horizontal plane, and (4) Line passing through furcation of maxillary first molars[86,89]

3.1.5. Landmarks and measurements of the nasopharynx and oropharynx in CBCT scans

Boundaries of nasopharynx and oropharynx are described in Table 3.2 and showcased in Figure 3.3. All the landmarks were identified in the mid-sagittal plane by selecting the sagittal view and the "Home" Button. This was to ensure that landmark selections were consistent between different CBCTs. A grey value (HU) of 500 was used for all the patients in this study, as it was found to be the ideal grey value that allowed complete filling of the airway spaces. The selected areas were then populated using "seed points", and the software automatically filled the airway volume (mm^3) using pink color. For oropharynx, in addition to airway volume, the minimal cross-sectional area (MCA) in mm^2 (Grey color) was identified by the software (Figure 3.4). This was done by first selecting the upper and lower boundaries of the oropharynx (dotted red lines), followed by enabling the MCA function of the software. Nasopharynx volume (NPV), oropharynx volume (OPV) and oropharynx minimal cross-sectional area (OPMCA) were recorded. This process was repeated three times for each CBCT scan at T_0, and three times at T_1, and the scans were randomly analyzed to allow for a blinded assessment. An average of the three measurements at each time point was taken and used as a final value.

Table 3.2. Description of the upper airway boundaries in CBCT scans [86,89].

Airway Areas	Anterior boundary	Superior boundary	Posterior boundary	Inferior boundary
Nasopharynx volume, mm^3	Line extending from posterior nasal spine (PNS) to mid-sella (S)	mid-sella (S)	Line extending from mid-sella (S) to tip of odontoid process	Line extending from tip of odontoid process to PNS
Oropharynx volume, mm^3	Line extending from PNS to menton (M)	Line extending from PNS to tip of odontoid process	Line extending from tip of odontoid process to the most anterior-inferior point of the cervical vertebra 3 (CV3)	Line extending from the anterior-inferior point of the cervical vertebra 3 (CV3) to Menton

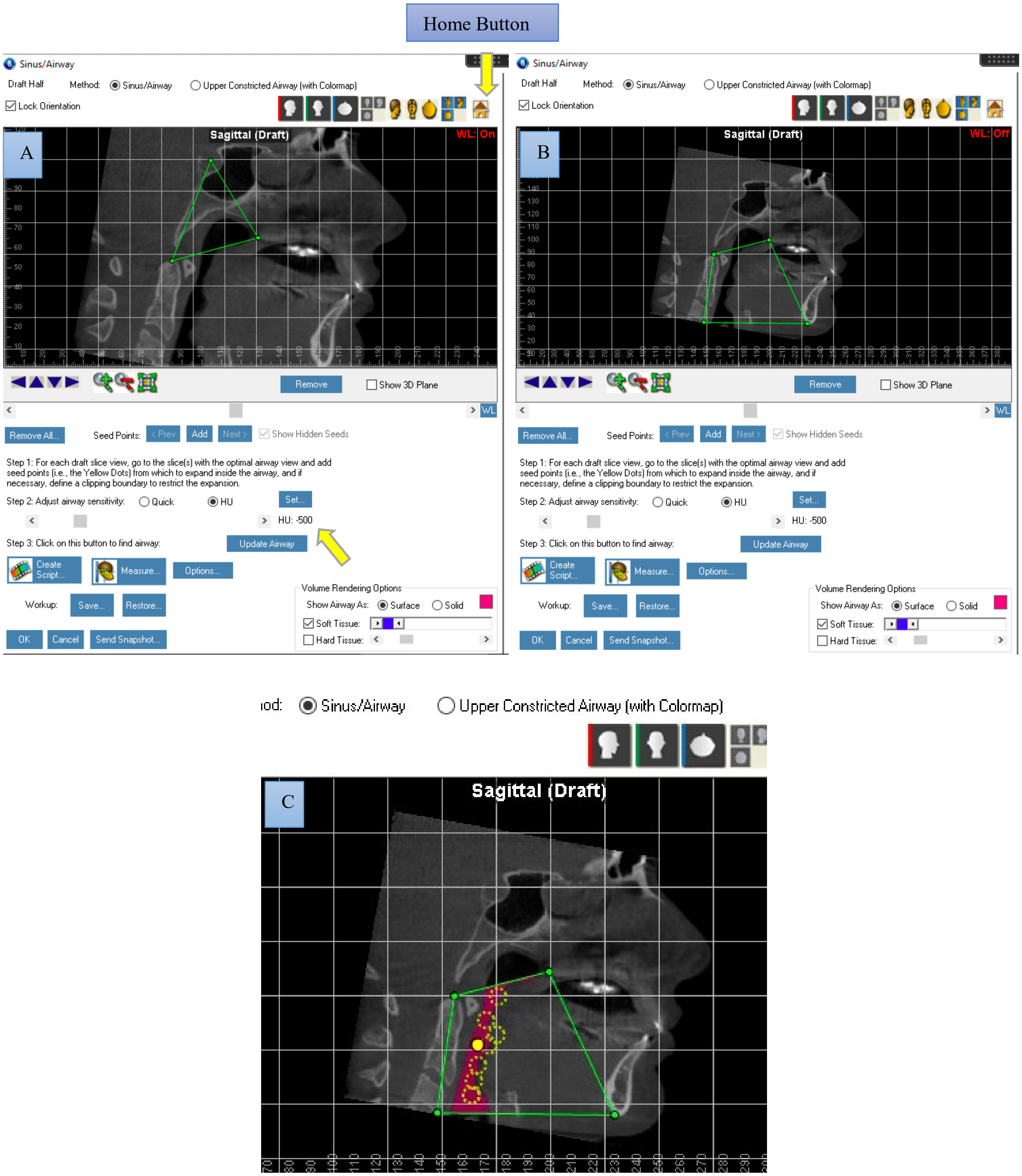


Figure 3.3 CBCT images of the nasopharynx and oropharynx and their boundaries: (A) Nasopharynx boundaries, (B) Oropharynx boundaries. (C) Seed points (yellow) used to fill the airway spaces. Yellow arrows (A) showing the “Home” button and the HU value.

A

B

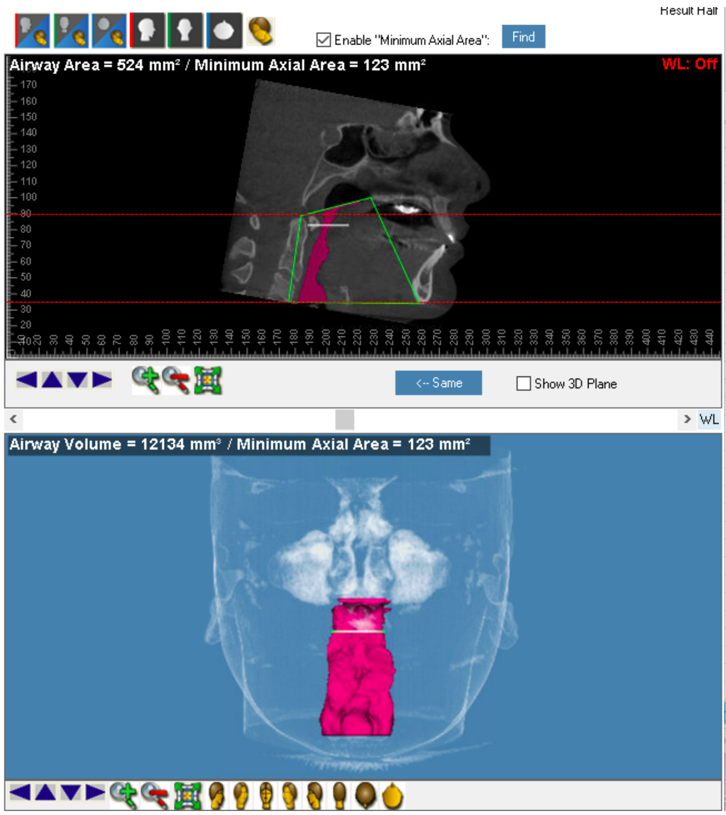


Figure 3.4 (A) Oropharynx minimal cross-sectional area (Grey line), (B) Oropharynx airway volume and minimal cross-sectional area (MCA).

3.1.6. Peak Nasal Inspiratory Flow (PNIF)

PNIF was measured at two time points: T_0 and T_1 using an In-Check medical device (Figure 3.5). Each measurement was taken three times and an average was taken to ensure accurate readings. Proper instructions were given to patients before each measurement was taken. Patients were asked to inhale through the nasal mask of the device. They were then asked to stand and exhale the entire air volume in their lungs. Finally, they were asked to inhale with maximum force through the nasal mask of the In-Check medical device. Same procedure was done for each individual nostril. Patients were instructed to place a cotton roll in one nostril to block the nostril and PNIF of the other nostril was recorded. The following measurements were taken for each patient: PNIF with both nostrils (PNIFBN), PNIF with left nostril blocked (PNIFLB), and PNIF with right nostril blocked (PNIFRB).

Figure 3.5 Peak nasal inspiratory flow (PNIF), In-Check medical device

3.1.7. Nasal Obstruction Symptom Evaluation (NOSE) questionnaire

Items of the subjective NOSE questionnaire are presented in Figure 3.6. The questionnaire is given to each patient at T_0 and T_1. There are a total of five questions in each questionnaire. Each question can be rated from 0-4, where zero indicates no problem with breathing and 4 indicates severe problem. Patients were instructed on how to complete the questionnaires. The final rates were then multiplied by 5 to reach a grade ranging from 0-100[94]. A classification system for severity of subjective nasal obstruction was developed by Lipan and Sam in 2013 and was used to analyze the NOSE questionnaire data (Table 3.1, Appendix 2) [94]. According to their classification system, NOSE questionnaire between 5-25 is considered as mild, 30-50 is considered as moderate, 55-75 is considered as severe, and 80-100 is considered as extreme[94].

Nasal Obstruction Symptom Evaluation (NOSE) Instrument

To the patient: Please help us to better understand the impact of nasal obstruction on your quality of life by completing the following survey. Thank you!

Over the past month, how much of a problem were the following conditions for you? (Please circle the most correct response.)

	Not a problem	*Very mild problem*	*Moderate problem*	*Fairly bad problem*	*Severe problem*
Nasal congestion or stuffiness	0	1	2	3	4
Nasal blockage or obstruction	0	1	2	3	4
Trouble breathing through my nose	0	1	2	3	4
Trouble sleeping	0	1	2	3	4
Unable to get enough air through my nose during exercise or exertion	0	1	2	3	4

Modified from the The NOSE Scale© 2003, the American Academy of Otolaryngology-Head and Neck Surgery Foundation

Figure 3.6 Nasal Obstruction Symptom Evaluation (NOSE) questionnaire

3.2. Statistical Analysis

The statistical analysis was carried out using IBM SPSS version 27 for Mac (IBM Corp., Armonk, N.Y., USA) and the significance level was set at $\alpha = 0.05$. Seven hypotheses were tested for upper airway changes and are summarized in Table 3.2, Appendix 2.

3.2.1. Intra-examiner reliability and measurement error

Intra-examiner reliability was calculated using Intra-class Correlation Coefficient (ICC) to determine agreements between CBCT measurements on patients outside of the study. Five external patients who were not part of this study and had large field of view CBCT were selected at random from the University of Alberta patient pool, and the reliability of nasopharynx volume (NPV), oropharynx volume (OPV), and oropharynx minimal cross-sectional area (OPMCA) were assessed. All measurements were repeated three times with one week apart.

The results were evaluated according to Portney and Watkin's ICC guidelines[95] (Table 3.3). The method is considered "good" for any ICC between 0.75 and 0.90, and is excellent for any ICC above 0.90[95]. Any value less than 0.75 is considered “inadequate” and would require better landmark identification and calibration[95].

Table 3.3. Intra-class Correlation Coefficient (ICC) guidelines according to Portney and Watkin to assess for method reliability[95].

ICC>0.90	Excellent Agreement
0.75>ICC>0.89	Good Agreement
0.51>ICC>0.74	Moderate Agreement
ICC<0.50	Poor Agreement

In addition to ICC, measurement errors were also calculated to assess accuracy of the measurements.

3.2.2. Response and factor variables

For upper airway analysis, the response variables are as follows: NPV (mm^3), OPV (mm^3), OPMCA (mm^2), peak nasal inspiratory flow with both nostrils (PNIFBN) (L/min), peak nasal inspiratory flow with left nostril blocked (PNIFLB) (L/min), peak nasal inspiratory flow with right nostril blocked (PNIFRB) (L/min), and nasal obstruction symptom evaluation (NOSE) questionnaire (NQ). There are two factor variables: 1) appliance, with two levels: Dresden expander and Moon expander. Appliance is considered a between-subject factor; and 2) time (PrePost), with two levels: T_0 and T_1. Time is considered a within-subject factor.

3.2.3. One-way repeated measure mixed ANOVA test

Six separate one-way repeated measure mixed ANOVA tests were conducted to assess whether there are any differences in the NPV, OPV, OPMCA, PNIFBN, PNIFRB, PNIFLB, from T_0 to T_1, between the Dresden and the Moon appliances. Bonferroni correction was done to adjust the p-values to reduce the type I error. All p-values were multiplied by 6 (total number of tests) and any adjusted p-value above 1 was given a value of 1.00. The two conditions for conducting a one-way repeated measure mixed ANOVA are having at least one dependent variable and one within subject factor with two or more levels. Both conditions are met in this analysis.

Assumptions testing for one-way repeated measure mixed ANOVA test are summarized in Table 3.5, Appendix 2.

3.2.4. Mann-Whitney U test (Nonparametric test) for NOSE questionnaire

For NOSE questionnaires, a nonparametric test (Mean-Whitney U test) was conducted to evaluate if there are differences in NOSE questionnaire answers in patients treated with either Moon or Dresden expander. Since nonparametric test was done, median hypothesis was tested.

3.2.5. Paired sample t-test

Paired sample t-tests were also conducted to test for significant changes on upper airway after maxillary expansion within each treatment group.

3.3. Results

3.3.1. Reliability results

Table 3.3, Appendix 2 summarizes ICC for upper airway changes. At the end of the process, the ICC results were excellent as the ICC was above 0.90 for all data.

Results for measurement errors are shown in Table 3.4, Appendix 2. Small mean measurement errors of 224.67 mm^3 (3.44 %), 255.73 mm^3 (1.50 %), and 0.00 mm^3 (0%) were found for NPV, OPV, and OPMCA respectively. 224.67 mm^3 for NPV approximates 4.5 drops of water and 255.73 mm^3 for OPV approximates 5 drops of water.

3.3.2. Descriptive statistics

According to the descriptive statistics table (Table 3.7, Appendix 2), the airway volume for NPV (mm^3), OPV (mm^3) and the oropharynx minimal cross-sectional area (OPMCA, mm^2) have increased from T_0 to T_1 for both treatment groups. The peak nasal inspiratory flow for both nostrils (PNIFBN, L/min) have remained unchanged from T_0 to T_1 for Dresden expander group and increased for the Moon expander group. The PNIF with left nostril blocked (PNIFLB) has slightly decreased at T_1 for Dresden group and increased for the Moon expander group. The PNIF with right nostril blocked (PNIFRB) have increased at T_1 for Dresden group and slightly decreased for the Moon expander group. Raw data for PNIF results are demonstrated in Table 3.6, Appendix 2.

According to the descriptive statistics table for NOSE questionnaire (Table 3.8, Appendix 2), the results indicate that for the Dresden appliance, the “median” of NQ before starting treatment was 20 and remained the same (20) after maxillary expansion. For the Moon expander group, the "median" of NQ before starting treatment was 10 and it changed to 15 after maxillary expansion.

3.3.3. Results of repeated measure mixed ANOVA test: within and between-subject effects

Results of within-subject effects and between-subject effects are summarized in Table 3.11 and Table 3.12 of the Appendix 2, respectively. All adjusted p-values are more than 0.05 for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB. Therefore, results suggest that for all research questions regarding upper airway changes, there is not enough convincing evidence to reject the null hypothesis. In other words, there are no differences in the NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, from T_0 to T_1, between the Dresden and the Moon appliances. In terms of interactions between PrePost*Appliance, p-values for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB were more than 0.05 and therefore statistically not significant.

3.3.4. Result of Mean-Whitney U test for NOSE questionnaire

For NOSE questionnaire, a nonparametric test was conducted to check whether there is any difference in the median of NOSE questionnaire answers in patients treated with either Moon or Dresden expander group. Results are summarized in Table 3.13, Appendix 2. To answer the research questions, the difference between the two time points were taken (T_1 -T_0). Results showed that the adjusted fisher exact sig. was 1.00 ($p>0.05$) and therefore, there is no convincing evidence against the null hypothesis. In other words, there is no difference in the median NOSE questionnaire answers in patients treated with either Moon or Dresden expander.

The NOSE questionnaire results were also analyzed using Table 3.1 (Appendix 2), which is a classification system developed by Lipan and Sam in 2013 to analyze severity of nasal obstruction using NQ data[94]. According to this table, the severity of nasal obstruction in patients in both the Dresden and the Moon appliance group is considered as "mild" both before and after treatment.

3.3.5. Results for paired sample t-tests

In addition to one-way repeated measure mixed ANOVA tests, paired sample t-tests were also conducted to test for significant changes on upper airway before and after maxillary expansion (T_1-T_0) within each treatment group, and results are demonstrated in Table 3.14 and 3.15

(Appendix 2). Results showed no statistically significant changes ($P>0.05$) in NPV, OPV, OPMCA, PNIFBN, PNIFLB, and PNIRB within each treatment group from T_0 to T_1.

Chapter 4 - Skeletal and Dental Changes

4.1. Methods

The inclusion and exclusion criteria, subject demographics, full description of appliance insertion protocols are explained in detail in chapter 3 (section 3.1).

4.1.1. Landmark identification for analysis of skeletal and dental changes from CBCT scans

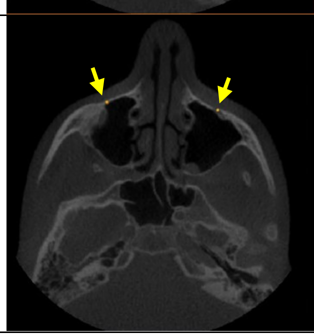
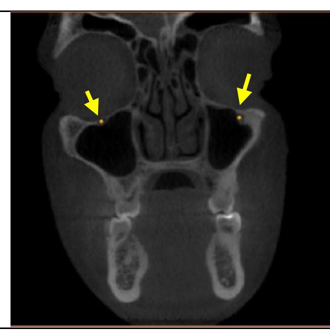
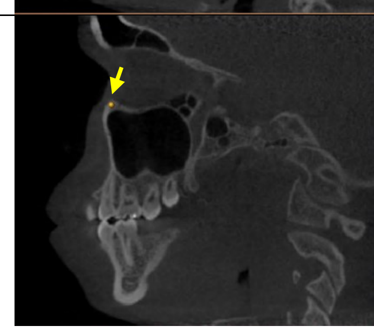
The raw CBCT data (DICOM images) were transferred to Avizo software 8.0 (Visualization Sciences Group, Burlington, MA, USA). ISO surface was used for evaluation of the data in exposure of 500-1000. Spherical marker was used in a 0.5 mm diameter to identify each landmark. A total of twenty skeletal and dental landmarks were chosen. Landmark definitions and their acronyms are summarized in Table 4.1 and Table 4.2. Out of the twenty landmarks, eight landmarks were used as a 3D anatomical reference for superimposition. The eight landmarks used for superimposition are as follows: for the mid-sagittal plane (transverse, X-axis), the mid-point of the right and left foramen spinosum (mid-spinosum), the mid-point of the nasopalatine foramen (mid-NPF), and foramen magnum were used. For the palatal plane (vertical, Z-axis): right and left greater palatine foramen and mid-NPF were used. For the frontal plan (antero-posterior, Y-axis): right and left infraorbital foramen and mid-NPF were used. Landmark derived superimposition technique was adapted from previously published studies by Lagravere et al and DeCesare et al [97, 98].

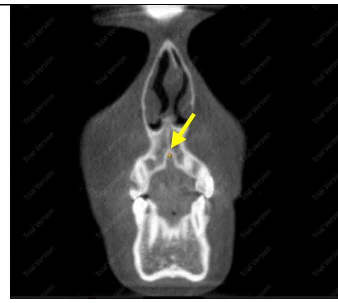
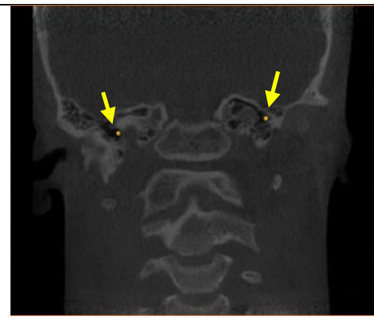
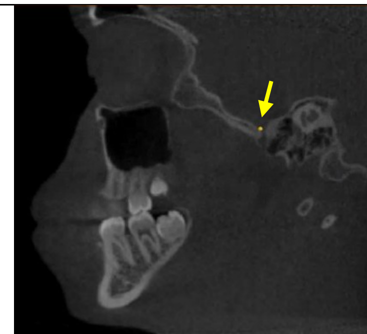
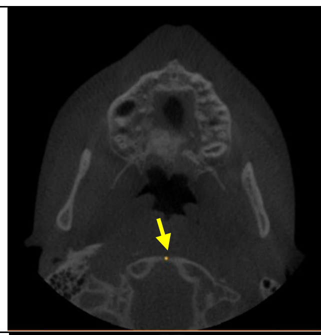
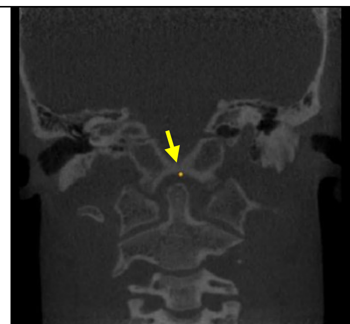
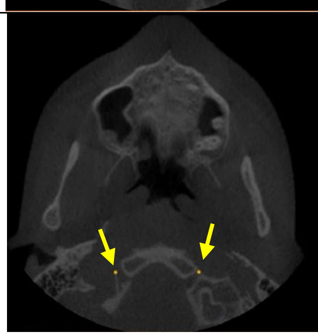
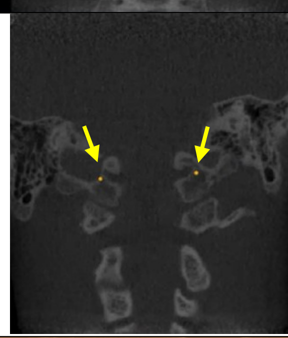
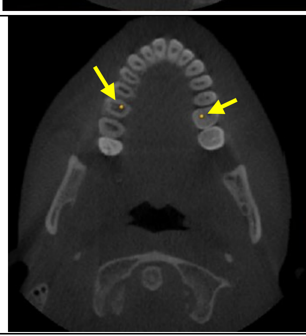
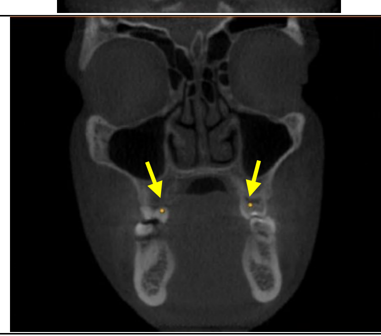
Out of the twenty landmarks, twelve landmarks were used for this analysis and were located using X, Y, and Z coordinates: R and L hypoglossal canal, pulp chamber of tooth # 1.6, mesio-buccal root apex of tooth # 1.6, buccal alveolar bone of tooth # 1.6, pulp chamber of tooth # 2.6, mesio-buccal root apex of tooth # 2.6, buccal alveolar bone of tooth # 2.6, pulp chamber of tooth # 1.4, 2.4, 3.6, and 4.6. Once data collection was completed in Avizo software, the data were exported as an Excel 2021 spreadsheet. Analysis and measurements of the skeletal and dental changes were done by one calibrated and trained examiner. Each measurement was done three times, and an average of the three values was taken. Step-by-step of landmark identification in AVIZO software is demonstrated in section 4.1.2 of the Appendix 3 (Figures 4.2-4.8). The protocol used for analysis of Skeletal and Dental changes is similar to the ones previously described and established in the literature[67, 73, 99, 100].

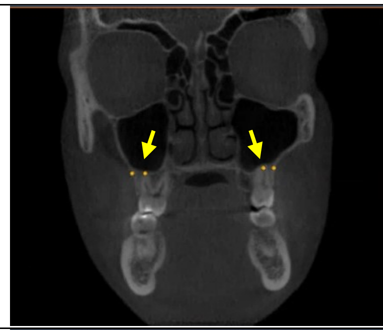
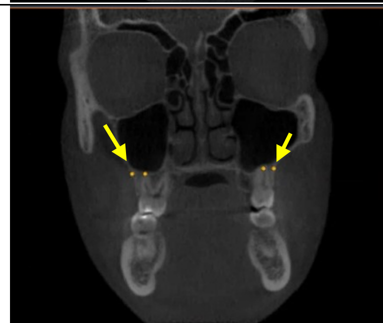
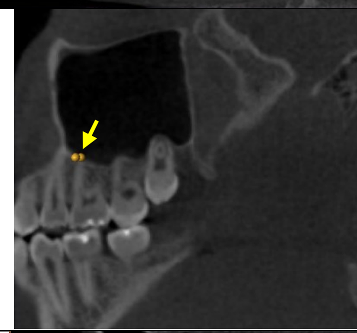
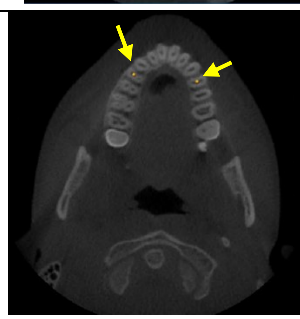
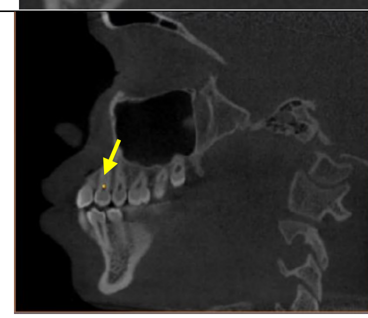
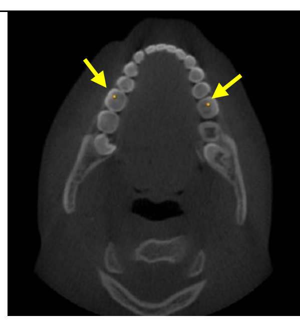
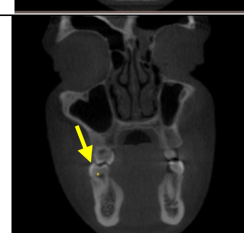
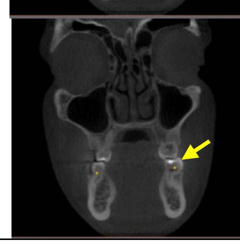
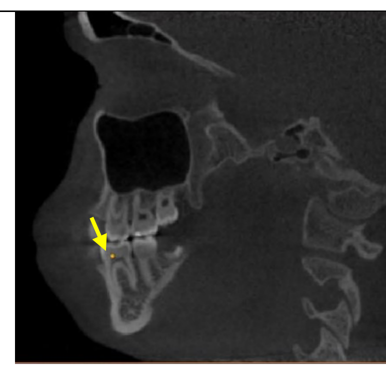
Table 4.1 Twenty Skeletal and Dental Landmarks

Acronyms	Skeletal Landmark Name	Acronym	Dental Landmark Name
RGPF	Right Greater Palatine Foramen	PC16	Pulp Chamber of tooth # 1.6
LGPF	Left Greater Palatine Foramen	MBA16	Mesio-Buccal Root Apex of tooth # 1.6
InfraOR	Right Infraorbital Foramen	ALB16	Buccal Alveolar Bone of tooth # 1.6
InfraOL	Left Infraorbital Foramen	PC26	Pulp chamber of tooth # 2.6
Mid-NPF	Mid-Nasopalatine Foramen	MBA26	Mesio-Buccal Root Apex of tooth # 2.6
FSR	Right Foramen Spinosum	ALB26	Buccal Alveolar Bone of tooth # 2.6
FSL	Left Foramen Spinosum	PC14	Pulp chamber of tooth # 1.4
FM	Foramen Magnum	PC24	Pulp chamber of tooth # 2.4
HCR	Right Hypoglossal Canal	PC36	Pulp chamber of tooth # 3.6
HCL	Left Hypoglossal Canal	PC46	Pulp chamber of tooth # 4.6

Table 4.2 Skeletal and Dental Landmark Definitions[67,73,100].

Landmark description	Axial view (XY)	Coronal View (XZ)	Sagittal view (YZ)
Greater Palatine Foramen (R and L) = As soon as a well-defined radiolucency forms in Axial view. Choose superior-center-most of the radiolucency.			
Infraorbital Foramen (R and L) = As soon as the foramen is fully formed in Axial view. Choose superior-center-most of the radiolucency.			

Mid-Nasopalatine Foramen = As soon as the radiopaque borders fully form around the foramen in Axial view. Choose the superior-most part of the radiopacity.			
Foramen spinosum (R and L) = As soon as the radiopaque borders fully form around the radiolucency in Axial view. Choose the superior-center-most.			
Foramen Magnum = As soon as the right and left bony cortices first join in Axial view.			
Hypoglossal Canal (R and L) = As soon as the top part of the canal closes, and the bony cortices join in Axial view.			
Pulp chamber of tooth # 1.6 and 2.6= Choose palatal area of the pulp chamber, as soon as the radiolucency appears in Axial view.			

Mesio-buccal root apex of tooth # 1.6 and 2.6= As soon as the mesio-buccal root disappears in Axial view.			
Buccal alveolar bone of tooth # 1.6 and 2.6= Buccal alveolar bone parallel to MB root apex (Draw an imaginary line parallel to the mesio-buccal root apex landmark chosen above).			
Pulp chamber of tooth # 1.4 and 2.4 = As soon as the furcation appears, choose the center-most area of the furcation in Axial view.		 	
Pulp chamber of tooth # 3.6 and 4.6= Choose the mesio-buccal area of the pulp chamber, as soon as the radiolucency appears in Axial view.		 	

4.2. Statistical Analysis

The statistical analysis was carried out using IBM SPSS version 27 for Mac (IBM Corp., Armonk, N.Y., USA) and the significance level was set at $\alpha = 0.05$. Three hypotheses were tested for skeletal and dental changes and are summarized in Table 4.1, Appendix 3.

4.2.1. Intra-examiner reliability and measurement error

Intra-examiner reliability was calculated using Intra-class Correlation Coefficient (ICC) to determine agreements between CBCT measurements on patients outside of the study. Five external patients who were not part of this study and had large field of view CBCT were selected at random from the University of Alberta patient pool, and the reliability of forty-one skeletal and dental landmarks were assessed for each patient (Table 4.2, Appendix 3). Results were evaluated using Portney and Watkin's ICC guidelines[95] (chapter 3-Table 3.3). Out of these forty-one landmarks, twenty landmarks were selected for this analysis, out of which eight were used for superimposition purposes and twelve were used for landmark identification of skeletal and dental changes.

In addition to ICC, measurement errors were also calculated to assess accuracy of the measurements.

4.2.2. Response and factor variables

The variables for skeletal and dental changes are the following: 1) Orthogonal distances (*mm*) in X, Y, Z directions for twelve landmarks: HCR, HCL, PC16, MBA16, ALB16, PC26, MBA26, ALB26, PC14, PC24, PC46, PC36); 2) Type of appliance; and 3) Time (PrePost).

Orthogonal distance (*mm*) is response variable, while appliance and time are factor variables. Appliance has two levels (Dresden and Moon), and time (PrePost) also has two levels (before maxillary expansion (T_0) and after maxillary expansion (T_1)). Appliance is considered a between-subject factor, whereas time is considered a within-subject factor.

4.2.3. One-way repeated measure mixed ANOVA test

Thirty-six separate one-way repeated measure mixed ANOVA tests were conducted to assess whether there are differences in the mean orthogonal distances, from T_0 to T_1, in the transverse (X), A-P (Y), and vertical (Z) directions between the Dresden and the Moon appliances for the following twelve landmarks: HCR, HCL, PC16, MBA16, ALB16, PC26, MBA26, ALB26, PC14, PC24, PC46, PC36. Bonferroni correction was done to adjust the p-values to reduce the type I error. All p-values were multiplied by 36 (total number of tests) and any adjusted p-value above 1 was given a value of 1.00.

Assumptions testing for one-way repeated measure mixed ANOVA tests are summarized in Table 4.5, Appendix 3.

4.2.4. Paired sample t-test

Paired sample t-tests were also conducted to test for significant skeletal and dental changes after maxillary expansion within each treatment group.

4.3. Results

4.3.1. Reliability results

Table 4.3, Appendix 3 summarizes ICC results. At the end of the process, the ICC results were excellent as the ICC was above 0.90 for all forty-one landmarks.

Results for measurement errors are shown in Table 4.4, Appendix 3. Small measurement errors of $\leq$0.73 mm, $\leq$ 0.87 mm, and $\leq$ 0.93 mm were found in the mid-sagittal plane, frontal plane, and palatal plane, respectively.

4.3.2. Descriptive statistics

According to the descriptive statistics table (Table 4.6, Appendix 3), the mean orthogonal distances (*mm*) for all the landmarks remained similar from T_0 to T_1, for both the Moon and the Dresden expander groups except for the following landmarks:

1. For the Moon expander group, the mean orthogonal distance changes from T_0 to T_1 are as follows: pulp chamber of tooth # 1.6 in X direction (PC16_X) (increased 1.92 mm at T_1), buccal alveolar bone of tooth # 1.6 in X direction (ALB16_X) (increased 1.08 mm at T_1), pulp chamber of tooth # 2.6 in X direction (PC26_X) (increased 2.31 mm at T_1), pulp chamber of tooth # 1.4 in X direction (PC14_X) (increased 1.07 mm at T_1), pulp chamber of tooth # 2.4 in X direction (PC24_X) (increased 1.19 mm at T_1), pulp chamber of tooth # 4.6 in Y direction

(PC46_Y) (increased 2.31 mm at T_1), and pulp chamber of tooth # 3.6 in Y direction (PC36_Y) (increased 2.16 mm at T_1).

2. For the Dresden expander group, the mean orthogonal distance changes from T_0 to T_1 are as follows: pulp chamber of tooth # 4.6 in Z direction (PC46_Z) (increased 1.40 mm at T_1), pulp chamber of tooth # 1.4 in Y direction (PC14_Y) (decreased 1.87 mm at T_1), and pulp chamber of tooth # 1.4 in Z direction (PC14_Z) (increased 1.00 mm at T_1).

4.3.3. Results of repeated measure mixed ANOVA test: within and between-subject effects

Results of within-subject effects and between-subject effects are summarized in Table 4.9 and Table 4.10 of the Appendix 3, respectively.

For within-subject effects (time), the only statistically significant p-values were for pulp chamber of tooth # 1.6 in X direction (PC16_X, p=0.04), pulp chamber of tooth # 2.6 in X direction (PC26_X, p=0.04), and pulp chamber of tooth # 2.4 in X direction (PC24_X, p=0.04).

The results obtained from between-subject effects (appliance) were not statistically significant for any of the landmarks measured. Therefore, it can be concluded that there is not enough convincing evidence to reject the first null hypothesis (Table 4.1, Appendix 3). In other words, there are no differences in the mean orthogonal distances (*mm)*, from T_0 to T_1, in the transverse (X), vertical (Z), and A-P (Y) directions between the Dresden and the Moon appliances.

In terms of interactions between PrePost*Appliance, p-values for all landmarks were not statistically significant ($p>0.05$). Therefore, there is not enough convincing evidence to reject the second null hypothesis (Table 4.1, Appendix 3). In other words, there is no interaction between appliance type and time (PrePost) on the orthogonal distances.

For PC16_X, PC26_X, PC24_X, post hoc tests with Bonferroni correction were conducted for within-subject effects (PrePost) (Table 4.11, Appendix 3). Results indicated that regardless of the type of appliance used, the mean orthogonal distances increased from T_0 to T_1 for all three landmarks. At T_1, the mean difference for orthogonal distances for PC16_X, PC26_X, and PC24_X were 1.30 (mm), 1.66 (mm), and 0.83 (mm), respectively compared to T_0.

4.3.4. Results for paired sample t-tests

Mean differences were obtained by subtracting T_1 by T_0 distances, and percentage changes were calculated (mean difference/pre-expansion mean x100) (Table 4.12, Appendix 3). Results are demonstrated in Figure 4.1 and can be summarized as follows:

1. **Transverse (X) changes relative to mid-sagittal plane:**
   - For the Moon expander group: the orthogonal distance changes were not statistically significant from T_0 to T_1, except for the following landmarks:
     - PC16_X (P=0.04), 1.92 mm expansion (buccal displacement) achieved at T_1.
     - PC26_X (p=0.04), 2.31 mm expansion achieved at T_1.
     - PC24_X (p=0.04), 1.20 mm expansion achieved at T_1.
   - For the Dresden expander group, the orthogonal distance changes were not statistically significant for any of the landmarks from T_0 to T_1 (p>0.05).

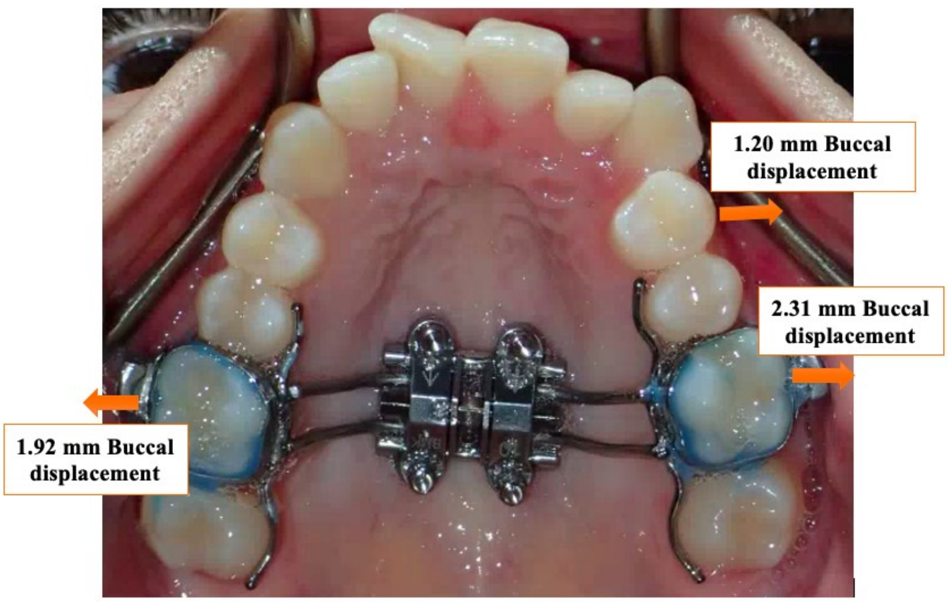


Figure 4.1 Statistically significant changes in transverse (X) direction relative to mid-sagittal plane for PC16_X, PC26_X, and PC24_X for Moon Expander group.

2. **Anteroposterior (Y) changes relative to frontal plane:**
   - No statistically significant changes (P>0.05) were found within each treatment group from T_0 to T_1.
3. **Vertical (Z) changes relative to the palatal plane:**
   - No statistically significant changes (p>0.05) were found within each treatment group from T_0 to T_1.

According to the above conclusions for the paired sample t-test, for the Moon expander group, there is enough evidence to reject the third null hypothesis (Table 4.1, Appendix 3), meaning there are statistically significant changes ($p<0.05$) on the mean orthogonal distances from T_0 to T_1 within this treatment group.

For the Dresden expander group, there is not enough evidence to reject the third null hypothesis. In other words, there are no statistically significant changes on the mean orthogonal distances from T_0 to T_1.

Chapter 5 - Discussion, Conclusions, and Future Recommendations

5.1. Discussion

This analysis is part of an ongoing retrospective secondary pilot study on a randomized clinical trial. The purpose of this study was to evaluate the effect of none-surgical maxillary expansion techniques on upper airway and skeletal and dental changes in young adults, using two different maxillary expanders: Moon and Dresden expanders. The changes in upper airway were evaluated using CBCT scans in Dolphin software, peak nasal inspiratory flow (PNIF) (objective measurement), and NOSE questionnaires (subjective measurement). The skeletal and dental changes were analyzed using various skeletal and dental landmarks in CBCT, using Avizo software.

5.1.1. Upper airway changes

For upper airway changes, results showed no statistically significant differences in the NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, and NQ from T_0 to T_1, between the Dresden and the Moon appliances.

Regarding the oropharynx volume, the results of this study supported the findings by Kavand et al[86] (11-15 years old patients) and Yi et al[29] (15-29 years old patients), as they also reported no statistically significant changes in OPV after using MARPE appliances. The definition of upper airway compartments used in Kavand et al [86] study and Yi et al[29] study is very similar to the current study, which makes the comparison between studies possible. However, it is important to emphasize that Kavand et al[86] study was conducted on adolescents, the study by Yi et al [29] had samples composed of both adults and children, while current study was done in adults (>17 years of age). The lack of any significant increase in OPV could be explained by a study conducted by Ghoneima et al[42]. They evaluated the effect of Rapid Maxillary Expansion (RME) on cranial and circummaxillary sutures in patients 13.8 ± 1.3 years of age and concluded that the forces applied when using RME primarily affects anterior sutures (such as intermaxillary, internasal, maxillonasal, frontomaxillary, and frontonasal sutures), while posterior craniofacial structures (such as zygomatic interface) are minimally affected [42]. Therefore, effect of RME is limited to structures that are directly adjacent to anterior sutures such as nasal cavity and nasopharynx [88]. The study by Ghoneima et al[42] was conducted in adolescents and future studies on effect of

MARPE appliances in adults and their effect on different cranial and intermaxillary sutures is recommended.

The results for oropharynx minimal-cross-sectional area (MCA) also support the findings by Kabalan et al[1] (11-17 years old) and Li et al[27] (22.6 +/- 4.5 years old), as they reported no changes in MCA after maxillary expansion using MARPE appliances. There is, however, inconsistent evidence in literature regarding OPV and MCA after using MARPE and RME appliances. Gianoni-Capenakas S et al [49] evaluated the effect of RME on oropharynx volume and MCA in patients 11 to 17 years of age using CBCT, and found a statistically significant increase in both (18% increase in OPV and 23% in MCA). Zhao et al[91] , however, reported no significant increase in OPV and MCA in patients 12.8 +/- 1.85 years of age. It is important to note that the study by Gianoni-Capenakas S et al [49] and Kabalan et al [1] were conducted in children (≤ 17 years of age), whereas current study and the study by Li et al [27] were done on adults (>17 years of age).

For nasopharynx volume, results obtained from current study did not support the findings by Mehta et al[85] (11-15 years old patients), Kavand et al[86] (11-15 years), Kim et al[26] (22.7 +/- 3.3 years), Li et al[27] (22.6 +/- 4.5 years), and Yi et al[29] (15-29 years), as they all reported an overall increase in NPV after using MARPE appliances by 21.8%, 20.00%, 10.5%, 14.1 %, 8.48%, respectively. Storto et al[28] also reported an increase in NPV from 16,058 (+/- 2171.98) to 21,835.55 (+/-1937.64) mm^3 after using MARPE appliance in patients composed of adults and children (average age of 17). The disagreement could be due to various reasons such as different definitions of airway compartments used in each study, different appliance designs, differences in age ranges in each study, or the small sample size used in the current study that could have contributed to some errors in experimental results. Same argument is also true in regard to OPV and MCA.

The PNIF results obtained from this analysis did not support the findings by Storto et al[28], as they reported an increase in nasal inspiratory flow (using nasal inspiratory peak flow meter), immediately after maxillary expansion using MARPE appliance, and 5 months post treatment (mean age of 17.1 years). Although to date, there is no consensus of "normal values" for PNIF[101] and there are inconsistencies between studies, having an understanding of "normal" values is crucial in evaluating the values obtained from PNIF devices. Several authors have established normative PNIF values for healthy individuals with particular ethnicities[102]. In a study by Ottoviano et al(2012) [103], they attempted to establish normative values for adult patients for PNIF and results are demonstrated in Table 4.1, Appendix 4. In another systematic review conducted by

Mo et al (2020)[101], the mean value of PNIFBN in patients with no nasal obstruction was 138.4 L/min, whereas the mean value in patients with nasal obstruction was 97.5 L/min. The PNIF results obtained from current study showed no statistically significant differences between the Moon and Dresden appliances from T_0 to T_1. Majority of patients in this analysis had lower PNIF values compared to the "normative" values in Table 4.1 (Appendix 4), which is an indication of potential nasal obstruction and could be attributed to their maxillary transverse deficiency. However, it is important to emphasize that none of the patients in this analysis were diagnosed with obstructive sleep apnea (OSA).

The Nasal Obstruction Symptom Evaluation (NOSE) scale was originally introduced in 2004 by Stewart and collogues as a subjective outcome measure of septoplasty in patients with nasal obstruction[104]. The test is validated by the American Academy of Otolaryngealology and has proved to be reliable and valid in evaluation of nasal obstruction [105]. The NOSE questionnaire from this analysis showed no statistically significant difference in the median NOSE questionnaire answers in patients treated with either Moon or Dresden expander. For the Dresden expander group, the median of NQ before starting treatment was 20 and remained the same (20) after maxillary expansion. For the Moon expander group, the median of NQ before starting treatment was 10 and it increased to 15 after maxillary expansion. It is important to note that all patients in this analysis were categorized as "mild" according to the classification system developed by Lipan and Sam in 2013 [94] (Table 3.1, Appendix 3). Results from this analysis, however, did not support the findings by Li et al[27], as they found a statistically significant reduction in NOSE questionnaire answers after endoscopically assisted surgical expansion for treatment of OSA in patients 15-61years old [106]. This could simply be due to the fact that patient in this analysis were already in the "mild" category in terms of nasal obstruction. In a study conducted by Menegat et al (2015)[107], nasal obstruction symptoms were evaluated using NOSE questionnaires (age 31 +/- 7.7 years) after surgically-assisted rapid maxillary expansion (SARME). Results showed that patients either experienced a subjective improvement or no worsening of nasal obstruction after SARME procedure[107]. Our analysis had similar results as patients in the Dresden expander group showed no significant changes after expansion, and patients in both Dresden and Moon expander groups remained as "mild" according to the classification system by Lipan and Sam [94].

5.1.2. Skeletal and dental changes

For skeletal and dental changes, results demonstrated no statistically significant differences in the mean orthogonal distances (*mm)*, from T_0 to T_1, in the transverse (X), vertical (Z), and A-P (Y) directions between the Dresden and the Moon appliances, except for pulp chamber (PC) of tooth # 1.6, 2.6 and 2.4 in transverse direction.

At the level of hypoglossal canals, there were no statistically significant changes from pre-treatment to post-treatment in both appliances. This was expected as hypoglossal canals are far from the point of force application and therefore, the effect of expansion is limited on them. This finding corresponds to the study that was conducted by Braun et al[108], where they showed that centre of rotation of maxilla during expansion using RME appliances is at the frontonasal suture[108]. With the hypoglossal canal being away from this centre of rotation, it was expected to see minimal changes on this skeletal landmark.

In terms of transverse changes relative to mid-sagittal plane, more buccal displacement (expansion) was noted by Moon expander compared to Dresden expander for the variables PC16_X (1.92 mm, 9.83%, P= 0.04), PC26_X (2.31mm, 11.49%, P= 0.04), and PC24_X (1.20 mm, 7.28%, p=0.04). Therefore, most clinically significant changes happened in dental landmarks, and not skeletal landmarks. Although the amount of expansion at the level of PC24 showed to be statistically significant, it may not be clinically significant as the value is very close to the measurement error of 0.73mm for the transverse dimension. Therefore, results should be interpreted with caution. Findings are consistent with previous studies that found more changes in dental structures compared to skeletal landmarks by either Rapid palatal expansion (RPE) or MARPE appliances[109]. Storto C.J. et al [28] evaluated skeletal and dental changes in patients with average age of 17 years and reported a statistically significant increase in midpalatal suture opening (4.7 mm at level of first premolar (P1) and 4mm at first molar (M1)), interdental distance (3.59mm at P1 and 5.34 mm at M1), tooth inclination for upper first molar (3.61mm), and alveolar bone width (3.59 mm at P1 and 3.88 at M1). The tooth inclination for upper first premolars was not statistically significant (1.83 mm of change (P=0.173)). Similar to our study (for Moon appliance group), the study by Storto et al[28] used 4 miniscrews paramedial to the mid-palatal suture. Therefore, their results are comparable to our study. However, the amount of interdental distance at the level of first molar and first premolar were higher in Storto et al[28] study compared to ours.

This could be explained by the fact that they used linear measurements for evaluation of skeletal and dental changes, whereas current analysis analyzed landmarks in different planes of space separately and the images were standardized using reference planes.

Studies on children with maxillary transverse deficiency using RPE or MARPE appliances have also showed more dental changes compared to skeletal changes. Lagravere et al (2010)[73] compared a bone-borne expander (consisted of two onplants, two miniscrews, and an expansion screw) with a tooth-borne expander (with bands on upper first premolars and first molars), using CBCT in 62 patients, 11-17 years of age. The expansion screw was activated twice per day (0.5 mm daily) for the tooth-borne appliance, and one turn every other day for the bone-borne appliance. They reported more dental crown expansion compared to skeletal expansion in both treatment groups[73]. In their study, CBCT images were taken before expansion, immediately after maxillary expansion, after removing the appliance (6 months) and before full bonding (12 months). They reported a significantly more long-term (after 12 months) maxillary expansion at the premolar crowns and roots of patients with tooth-borne expansion compared to bone-borne expansion[73]. Their results also showed that patients with bone-borne and tooth-borne appliances had similar results, with most changes in transverse dimension, while the changes in antero-posterior (A-P) and vertical dimensions were negligible[73]. This finding is also consistent with the findings in our study where most changes were seen in transverse dimensions relative to the mid-sagittal plane in both Dreseden and Moon appliance groups. Similarly, in a study conducted by Luebbert et al (2016) in 41 patients, 11-17 years of age, they used the same traditional hyrax expanders in both treatment groups, but with different expansion protocols and retention times. The first group activated the appliance one turn, twice per day (0.5 mm daily activation) with retention period of 6 months after appliance insertion, whereas the second group activated the appliance two turns, twice per day (0.8 mm daily expansion) with retention period of 3 months following the last activation of the RME. CBCT images were taken at pre-treatment and post-treatment and expansion was assessed using AVIZO software. They reported a ratio of 4:1 for dental versus skeletal changes[109]. They also reported no statistically significant differences between the two treatment groups with respect to skeletal and dental changes in transverse, A-P, and vertical directions. With respect to using MARPE appliances in adults, it is recommended that future studies also focus on the rate of expansion and retention protocols in adult patients. It is also important to note that although the results of the current study are consistent with the findings from

Lagravere et al (2010)[73] and Luebbert et al (2016)[109], there are several differences between current study and theirs. First, those studies were conducted on children and adolescents (11-17 years of age) whereas our analysis focused on adult patients (>17 years of age). Secondly, sample sizes in both studies were larger than the sample size in our study. Thirdly, both studies used linear distances, while current analysis analyzed landmarks in sagittal, A-P, and transverse planes and the images were standardized using reference planes. Due to these differences, it is difficult to compare clinical results.

The Moon expander group had greater crown expansion than root expansion (for tooth # 1.6: 1.92 mm crown expansion (9.83%) versus 0.50 mm (2.03%) root expansion/ for tooth # 2.6: 2.31 mm (11.49%) crown expansion versus 0.67 mm (2.90%) root expansion). These findings were expected as the Moon expander's design involves two bands on upper first maxillary molars, while the Dresden appliance has no bands on upper teeth. Therefore, more buccal crown tipping was expected in patients with the Moon appliance as the force application on the teeth and roots were higher with this appliance. No statistically significant difference was noted between crown and root expansion for the Dresden expander group. This was expected as during expansion using Dresden expander, the pressure from cheeks on the teeth could theoretically have prevented teeth from flaring out.

Several publications have discussed the downward and forward displacement of maxilla after maxillary expansion[110 111]. The effect on mandible is commonly reported as a downward and backward movement and opening of the mandibular plane angle[111]. In this analysis, in terms of vertical (Z) changes relative to the palatal plane, no statistically significant differences were found between Moon and Dresden appliances.

For anteroposterior (Y) changes relative to palatal plane, no statistically significant differences were found between Moon and Dresden appliances. These findings are consistent with a systematic review conducted by Lagravere et al (2005)[112], where they evaluated the long term dental arch changes after using rapid maxillary expanders and reported no statistically significant anteroposterior or vertical changes associated with RME [112]. Results are also consistent with the findings from Lagravere et al (2020)[67], as they reported minimal changes in anteroposterior and vertical dimensions after using RME, which allows clinicians to focus on the main concern of transverse correction without a significant concern regarding bite opening from these applianaces[67].

5.1.3. Clinical significance

Since this study is an ongoing retrospective secondary pilot study on a randomized clinical trial, causal inferences could be made. However, it is important to note that due to the small sample size, the results of this study should be used with caution. This is a new area of research and future studies are needed with larger sample size.

According to the results of this analysis, Moon and Dresden appliances do not affect the upper airway dimension and function. Results also showed that both appliances affect the skeletal and dental structures in a similar fashion and one appliance is not better than the other. This allows orthodontists to have more options when choosing an appropriate maxillary expander appliance for adults.

The decision to use the Moon versus Dresden appliance in adults depends on operators' preferences and any dental or skeletal considerations for the patient. For example, patients with craniofacial anomalies who have multiple congenitally missing teeth, adults who previously lost their upper molars, or those with large restorations on posterior teeth may not be good candidates for Moon appliance and Dresden appliance might be preferred in those scenarios. In addition, if the clinician desires to do a full bonding while completing maxillary expansion, Dresden appliance could be the preferred option. On the other hand, Moon appliance with bands on upper first molars could be considered in situations where molar or premolar expansion is needed as part of the orthodontic treatment. According to Lagravere et al (2010), they reported a significantly more long-term maxillary expansion at the premolar crowns and roots of patients with tooth-borne expansion compared to bone-borne expansion in patients 11-17 years of age[73].

5.2. Conclusions

The following general conclusions can be made from this analysis:

<u>Upper Airway changes:</u>

1. Moon and Dresden expanders showed to have no significant effect on upper airway dimensions and function.
2. No statistically significant differences were found in the NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, and NQ from T_0 to T_1, between the Dresden and the Moon appliances.

Skeletal and dental changes:

3. Moon expander resulted in buccal displacement of pulp chamber of maxillary first molars and maxillary left first premolar. However, such changes may not be clinically significant. For example, the amount of buccal displacement obtained for PC24_X (1.20 mm) is very close to the measurement error of 0.73 mm in the mid-sagittal plane.
4. Dresden expander did not make any significant changes on the skeletal or dental landmarks after maxillary expansion.
5. No other differences were found between the two groups in transverse, vertical, and A-P directions.
6. Pulp versus apex transverse discrepancy (comparing PC16_X and MBA16_X / PC26_X and MBA26_X)
   - In the Moon expander group, greater crown expansion than root expansion was noted (for tooth # 1.6: 1.92 mm crown expansion versus 0.50 mm root expansion/ for tooth # 2.6: 2.31 mm crown expansion versus 0.70 mm root expansion).
   - No statistically significant difference was noted between crown and root expansion for the Dresden expander group.

5.3. Limitations

One of the main limitations of this study was the small, and unequal sample size in the two treatment groups. Increasing the number of patients would reduce sampling errors for the statistical analysis. Future studies are recommended with a larger sample size.

Secondly, the software used in this analysis (dolphin for upper airway dimensions analysis and Avizo for skeletal and dental changes) require substantial training. Accurate identification of 3-D landmarks requires one to constantly switch between the 3 axial planes and multiple orthogonal slices which could increase the chance of operator's errors[67]. This could potentially change once 3D monitors become more commonly accessible[67]. Patient's cooperation while taking the CBCT images was also crucial since during the time that CBCT scans were being taken, although patients were instructed to maintain maximum intercuspation with their tongue touching behind the upper central incisors and avoid any swallowing during the scanning, patients were not always cooperative and that affected two of the scans in our sample.

5.4. Methodological limitations

5.4.1. Limitations encountered during data collection in Dolphin software and troubleshooting

While taking the CBCT scans, two of the scans were taken while patients were swallowing (or moving their tongue). Therefore, the oral cavity space could be seen as part of the oropharynx area. To de-select the oral cavity space from the oropharynx, first the oropharynx area was selected in the sagittal view (Figure 5.1A). After that, in the axial view, the oropharynx was selected, and oral cavity was eliminated (Figure 5.1B). This allowed us to consistently measure the oropharynx area only and eliminate the oral cavity area (Figure 5.1C). This was done for all patients in both groups to ensure accuracy of the measurements.

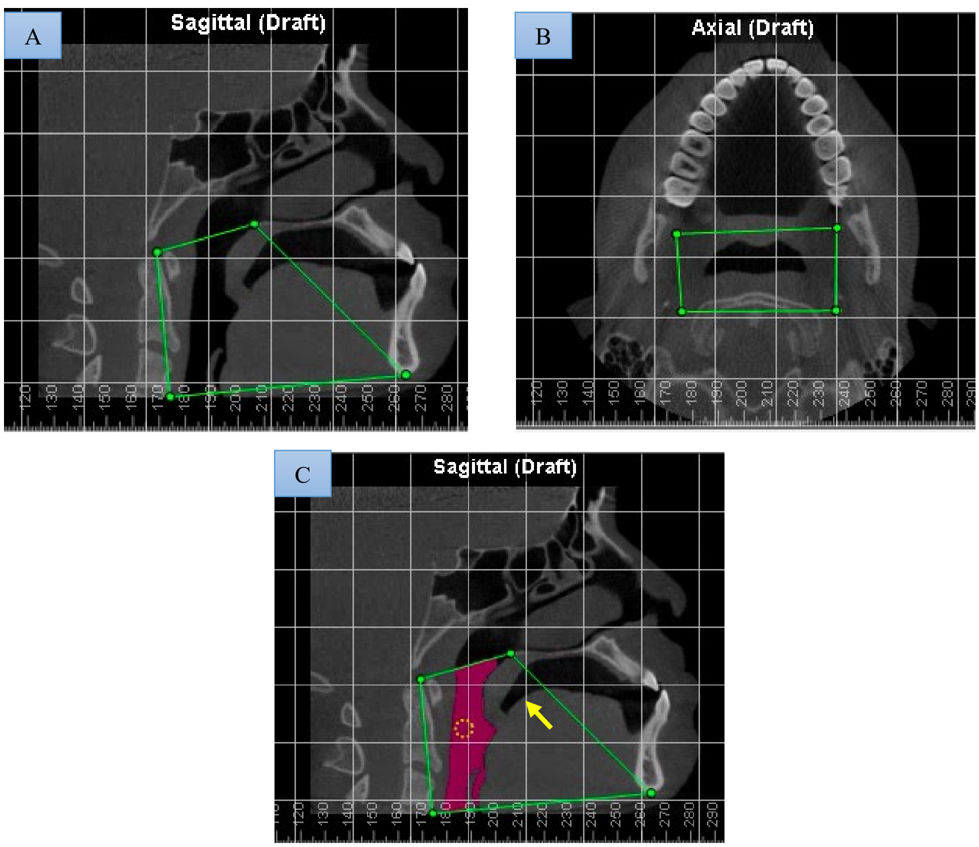


Figure 5.1 Method used to eliminate oral cavity from oropharynx measurements. A. In sagittal view, Oropharynx area was selected. B. In Axial view, Oropharynx area was selected, and oral cavity area was de-selected. C. Sagittal view demonstrating how the seed points filled the oropharynx area without filling the oral cavity space (yellow arrow).

5.4.2. Limitations encountered during data collection in Avizo software for skeletal and dental changes and troubleshooting

Two of the patients in this analysis had full coverage porcelain crowns on tooth # 3.6 and 4.6. Therefore, the place of the pulp chamber of tooth # 3.6 and 4.6 was estimated for these patients. Another patient had an implant for the space of tooth # 2.6. Therefore, tooth # 2.7 was evaluated for pulp chamber, mesio-buccal root apex, and buccal alveolar bone. The measurements for all the landmarks were done three times and all these estimates were consistent between each reading.

5.5. Future recommendations

Research agenda was already discussed in detail in chapter 2, section 2.7 and it applies to our study as well.

- There are multiple designs of MARPE available in the market with different TAD locations in the palate, which could in turn affect the amount and direction of force application. Future studies could be conducted (with a larger sample size) comparing other types of MARPE appliances, to allow clinicians make a better decision when it comes down to clinical practice.
- To date, there is limited evidence concerning the efficacy of MARPE appliances for adult patients with maxillary transverse deficiency. In a systematic review and metal analysis conducted by Kapetanovic et al (2021)[55], they evaluated the skeletal and dental changes after using MARPE appliances in late adolescents and adults (≥ 16 years of age) [55]. They included eight articles[27, 56-62], out of which seven had serious risk of bias, one had moderate risk of bias, and the GRADE quality of evidence was found to be very low[55]. Therefore, future well controlled randomized clinical trial studies are needed in this topic.
- In literature, there are only three long-term studies [26, 28, 85] that evaluated the effect of MARPE on airway and skeletal and dental changes. More long-term studies are needed to consider the effect of relapse after maxillary expansion.
- Future studies could also focus on the following topics on the effect of MARPE appliances on adult patients with maxillary transverse deficiency:
    1. Effect of tongue posture.
    2. Effect of MARPE appliances on different cranial and intermaxillary sutures
    3. Studies focusing on the rate of expansion and retention protocols in adult patients.

4. Future studies focusing on buccal and palatal bone thickness after maxillary expansion in adults using MARPE appliances.

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Appendix 1

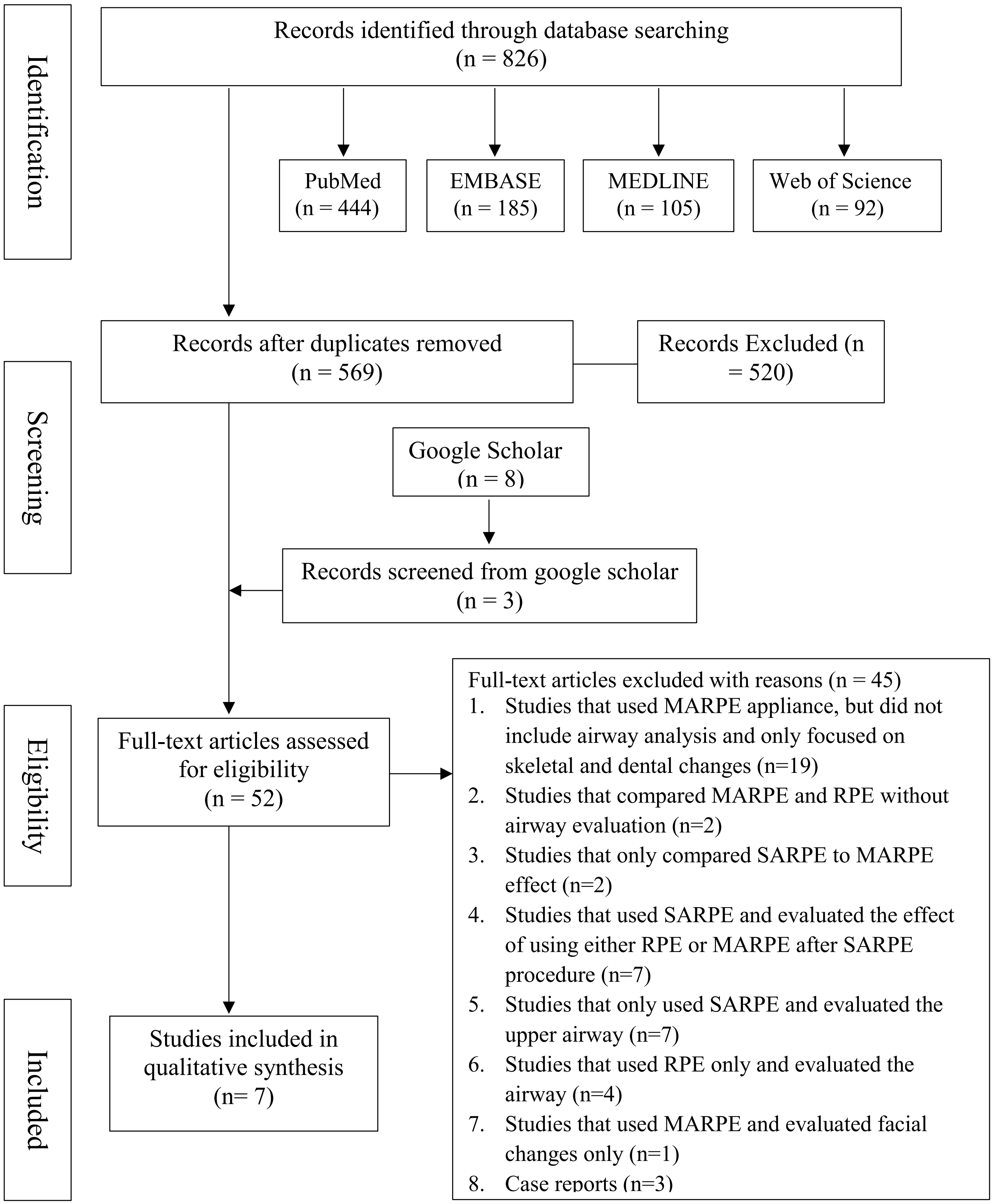


Figure A2.1 PRISMA flow diagram of literature search and selection criteria

Table A2.1 Summary of the study characteristics and main outcomes of the included articles

Author, Year, Country	Cases/ Mean age	Type of Appliance	Control	Type of airway evaluation	Type of skeletal and dental evaluation	Time points	Diagnostic test/ radiograph/ Software	Main findings
Mehta S. et al [85], 2021, USA, CA	(n = 60) 11-15 yrs	MARPE, RME	Yes, No treat-ment	Nasal cavity volume, nasal cavity area, nasopharyngeal volume, nasopharyngeal area, oropharyngeal volume, oropharyngeal area, Laryngopharyngeal area, Laryngopharyngeal volume, Total airway volume, Total airway area, Minimal Cross-sectional area (MCA)	Maxillary intermolar width, External maxillary width, Palatal width	T_1: Pre-treatment T_2: After maxillary Expansion T_3: Post-treatment (avg. 2 years and 8 months after T_1)	CBCT/ Dolphin	-No significant difference between MARPE and RPE -In short term: both MARPE and RPE significantly increased NCV, OPV, NPV, NPA, TAV, MIW, EMW, and PW -In long term: MARPE led to a significant increase in the NPV and PW compared to RPE. No significant increase in TAV in long term. -All other upper airway parameters that increase in short term, also increased in long term

								- In the control group, from T1 to T3, there was a significant increase in the NCV, NCA, NPV, OPV, TAV, and MCA.
Kavand G. et al [86], 2019, USA, CA	(n= 36) 11-15 yrs.	Tooth-borne and Bone-borne RME	No	Nasal Cavity Volume (NCV), Nasopharynx Volume (NPV), Oropharynx Volume (OPV), Right Maxillary Sinus Volume (RMSV), Left Maxillary Sinus Volume (LMSV)	Intermolar width at the first molar central fossa level, Intermolar width at the first molar palatal apex level, External maxillary width, Palatal width, Maxillary right first molar buccal inclination, Maxillary left first molar buccal inclination	T_1 and T_2 (3 months post expansion)	CBCT/Dolphin	-In Both tooth-borne and bone-borne RME, NCV and NPV increased. -More significant buccal tipping of maxillary molars noted using tooth-borne expander
Kim S-Y. et al [26], 2018,	(n = 14) 22.7 +/- 3.3 yrs	MARME	No	NCV, NPV, Total volume, Cross-	-	T_0 : Pre-treatment	CBCT/OnDemand3D software	- Cross-sectional area of airway on anterior (ANS-perp), middle

Seoul, Korea				sectional area of airway on anterior (ANS-perp), middle (choanae), and posterior (C3)		T_1: immediately after maxillary Expansion T_2: 1 year after expansion		(choanae) increased significantly after expansion -Increase in NCV, with further increase after 1 year and Increase in NPV -Increase in NCV> NPV
Li Q. et al[27], 2020, China.	(n = 22) 22.6 +/- 4.5)	MARME (type II by Dr. Moon)	No	Retropalatal Airway Volume (RPAV), Retroglossal Airway Volume (RGAV), hypopharyngeal airway volume, MCA (Nasal cross-sectional height (ANS), Nasal cross-sectional width (ANS),	Maxillary width (HP) (The width of maxilla tangent to the hard palate at its most inferior Level) - Zygomatic bone width (The distance between the foramina of the left and right zygomatic bone at the axial slice) -Temporal bone width (left and	T_1: before treatment T_2: After expansion	CBCT/ Dolphin	-Increase in NCV and dimension, and NPV and dimension. -At the PNS, enlarged nasal width contributed to increase in nasopharynx volume. -no significant changes on RPAV, RGAV, Hypopharyngeal airway volume (HPAV) and MCA -increase in maxillary width is negatively affected by thickness

				Nasal cross-sectional height (midpoint), Nasal cross-sectional width (midpoint), Nasal cross-sectional height (PNS), Nasal cross-sectional width (PNS)) , height of nasopharyngeal airway, height of retropalatal airway, height of retroglossal airway, height of hypopharyngeal airway volume,	right the inferior border of joint Tubercle) - Palate thickness (The average thickness of left and right sides 3 mm to midpalatal Suture) nasal lateral width (NLW), Nasal floor width (NFW)			of the hard palate (HP). -No clear association was found between vertical skeletal patterns and changes of upper airway after MARME due to the complex structures involved.

				Latero-lateral distance (PNS), antero-posterior distance (PNS), latero-lateral distance (uvula), antero-posterior distance (uvula), antero-lateral distance (epiglottis), antero-posterior distance (epiglottis), cross-sectional area (PNS), cross-sectional area (uvula), cross-sectional				

				area (epiglottis).				
Kabalan O. et al[1], 2015, Canada	(n = 61) 11-17 yrs	Tooth-borne and Bone-borne RME	Yes, treatment delayed for 6 months	-MCA, Nasal cavity volume/	-point where lateral and inferior walls of the nasal cavity connect in the xz dimension parallel to the apices of the roots of the upper cuspids, upper first bicuspids, upper second bicuspids, upper first molars -points where the base of each inferior nasal concha meets the lateral wall of the nasal cavity in the xz dimension parallel to the apices of the roots	T_1: before treatment T_2: 6 months after expansion completed	CBCT and Acoustic Rhinometry (AR)/ Avizo	-No significant changes in airway volume and MCA after using the two appliances - No correlation between skeletal changes and the amount of airway intake after maxillary expansion (P> 0.05) and no significant skeletal and dental expansion noted compared to the control group.

					of the upper cuspids -The most superficial points of the infra-orbital canals in the xy dimension parallel to the level of the inferior conchae			
Storto C.J. et al[28], 2019, USA, Brazil.	(n = 20) Avg. 17.1 yrs	MARPE	No	-Minimum Inspiratory Pressure (MIP), Maximum Expiratory Pressure (MEP), oral expiratory peak flow, and Nasal Inspiratory peak flow - Nasal cavity width (linear distance)	- Midpalatal suture opening - Alveolar bone width - Interdental distance (mid-fossae of R and L upper first molars and premolars) - Tooth inclination (long axis of first premolars and molars to the palatal base of the maxilla)	CBCT data: T_0: before treatment and T_1: immediately after expansion/ Airway data: $T_{0:}$ before treatment T_1: immediately after expansion	CBCT/ - analogue manometer-for respiratory muscle strength measurement (MIP and MEP) - ASSESS expiratory peak flow meter device- to measure maximum airflow - In Check Nasal device -used to evaluate nasal inspiratory peak	-Significant increase in MIP from T_0 to T_2 and MEP between T_0 and T_1 - Increase in Oral and nasal peak flow (especially in patients with initial signs of airway obstruction) - Significant enlargement of the nasal cavity, Midpalatal suture opening, interdental distance at M_1, tooth inclination for upper

						T_2: after 5 months	flow	first molar and alveolar bone width at M_1. -The tooth inclination changes for upper first premolars were not clinically significant -Strong positive correlation between airway volume and NIPF, OEPF, and MIP, which means that an increase in the airway volume had a positive effect in airflow (NIPF and OEPF) and muscular strength during MIP
Yi F. et al[29], 2020, China	(n = 19) 15-29 yrs	MARPE	No	Upper airway volume: -naso-pharyngeal volume, palate-pharyngeal	-The lateral maxillary expansions of the first premolars , second premolars first molars, second molars	T_0: before treatment and T_1: 3 months after expansion	CBCT/Dolphin	-Statistically significant increase (P< 0.005) in NPV and increase (P<0.001) in NLW, P1NLW, P2NLW,

				Volume, glosso-pharyngeum volume,oro-pharyngeal volume, total airway volume. Upper airway Area: -MCA for Oropharynx, palato-pharynx, glossopharynx -PNS plane cross section area, SP plane cross-section area, and C3pi plane cross-section area Upper Airway Length:	-Transverse skeletal expansion was evaluated with linear measurements at three different levels: nasal floor, hard palate, and hard palate below 5mm.			M1NLW and M2NLW -No significant changes found in PPV, GPV, OPV, and TAV.

				nasal lateral width (NLW), coronary-level lateral NLW at P1 region, coronary-level lateral NLW at P2 region, coronary-level lateral NLW at M1 region, coronary-level lateral NLW at M2 region.				

Table A2.2 Summary of the most common upper airway portions that were discussed in included studies

Nasal Cavity Volume (NCV)	1. Mehta et al[85] reported an increase in NCV by 14.4 % in MARPE and 11.5 % for RPE group 2. Kavand et al[86] reported an increase in NCV by 16.1% in MARPE and 12.5% in RPE group 3. Kim et al[26] Reported an increase in NCV by 9.99%, 5.5%, and 15.4% from T_0 to T_1, T_1 to T_2, and T_0 to T_2, respectively 4. Li et al[27] reported an increase in NCV by 16.2 % with MARPE appliance 5. Kabalan et al[1] reported no significant changes to NCV after using RPE or MARPE.
Nasopharynx Volume (NPV)	1. Mehta et al[85] reported an increase in NPV by 21.8% in MARPE and 24.1% RPE group 2. Kavand et al[86] reported an increase in NPV by 20.0% in MARPE and 21.8% in RPE group 3. Kim et al[26] reported an increase in NPV by 6.4%, 4.1%, and 10.5% from T_0 to T_1, T_1 to T_2, and T_0 to T_2, respectively 4. Li et al[27] reported an increase in NPV by 14.1% with MARPE appliance 5. Storto et al[28] reported an increase in NPV from 16,058 (+/- 6 2171.98) to 21,835.55 (+/- 6 1937.64) mm^3. 6. Yi et al[29] reported an increase in NPV by 8.48% with MARPE appliance
Oropharynx Volume (OPV)	1. Mehta et al[85] reported an increase in OPV by 19.2 % in MARPE and 26.4 % in RPE group 2. Kavand et al [86]and Yi et al[29] reported no changes in OPV
Total Airway Volume (TAV)	1. Mehta et al[85] reported an increased in TAV in short term (20.5 % in MARPE and 25.5% in RPE group). However, no significant increase on TAV noted in the long term. 2. Kim et al[26] reported an increase in TAV from T_0 to T_2 (2652.6 mm^3 increase) 3. Yi et al[29] reported no changes in TAV
Minimal Cross-sectional Area (MCA)	1. Mehta et al[85] reported an increase in MCA (20.3% for MARPE and 21.7% for RPE group) 2. 'Kabalan et al[1] and Li et al[27] reported no changes in MCA of the nasal cavity after maxillary expansion

Table A2.3 Summary of the most common skeletal and dental landmarks that were discussed in included studies

<table>
<tr><td>Maxillary Intermolar Width (MIW)</td><td>1. Mehta et al[85] reported
• Increase in MIW (10.7% for MARPE and 14.3% for RPE)
• At T_2, the amount of MIW was greater in RPE (14.3%) compared to MARPE (10.7%). However, in long term for MIW, there was no significant difference between MARPE (12.4%), RPE (9.9%) and control groups (8.6%).
2. Kavand et al[86] reported a statistically significant increase in MIW (10.3% for RME and 7.3 % for MARPE at level of central fossae)</td></tr>
<tr><td>External Maxillary Width (EMW)</td><td>1. Mehta et al[85] reported an increase in EMW (2.8% for MARPE, 3.3% for RPE).
2. Kavand et al [86] reported a statistically significant increase in EMW (3.5 % for RME and 2.7% for MARPE)</td></tr>
<tr><td>Palatal Width (PW)</td><td>1. Mehta et al[85] reported:
• An increase in PW (10.4% for MARPE, 6.4% for RPE) in short term (immediately after expansion (T_2))
• In short term, no significant difference was noted between the MARPE and RPE groups. However, in long term, MARPE resulted in a more significant increase in PW (9.3% for MARPE Vs. 4.8% for RPE) compared to RPE
2. Kavand et al[86] reported a statistically significant increase in PW (6.5% for RME and 10.1% for MARPE)</td></tr>
<tr><td>Midpalatal suture opening</td><td>1. Storto reported an increase in Midpalatal suture opening (4.7 mm at level of first premolars(PM_1) and 4mm at first molars (M_1))
2. Yi et al[29] reported an increase in Midplatal suture opening (change from pre-expansion to post expansion was 2.19 mm at PM1, 1.45 mm at PM2, 1.25 at M1, 0.93 at M2)</td></tr>
<tr><td>Nasal Lateral Width (NLW)</td><td>1. Li et al[27] reported an increase in NLW (6.9%)
2. Yi et al reported an increase in NLW (6.61%)</td></tr>
<tr><td>Nasal Floor Width (NFW)</td><td>1. Li et al[27] reported an increase in NFW (\2.3 mm, 7.5%),
2. Yi et al[29] reported an increase in NFW (1.97 mm at P1, 2.11 at P2, 1.77 at M1, and 1.45 at M2)</td></tr>
<tr><td>Tooth inclination and buccal cusp changes</td><td>1. Storto et al[28] reported a statistically significant increase in tooth inclination for upper first molar (3.61mm), and alveolar bone width (3.59 mm at PM_1 and 3.88 at M_1).
2. Yi et al[29] reported that the increase in the buccal cusp changes were 3.14 mm at PM1, 3.61 at PM2, 3.92 at M1, and 3.61 at M2.</td></tr>
</table>

Table A2.4 PICO statement and eligibility criteria

Domain	Inclusion criteria	Exclusion criteria
Population	• Patients with maxillary transverse deficiency (unilateral or bilateral posterior crossbite) requiring maxillary expansion • No age limitation	• Patients with syndromes (ex. Cleft lip and palate) • Patients with any systemic disease • Patients who had existing maxillary expansion
Intervention	Orthodontic maxillary expansion using any design of MARPE appliances that evaluated upper airway dimensions and function (which may or may not have included skeletal and dental changes)	• Any other appliance or procedure used for maxillary expansion other than MARPE (Ex. Surgical expansion, tooth borne RPE, ect) • Studies comparing SARPE with MARPE • Studies that only compared different designs of MARPE and did not focus on upper airway dimensions
Comparison	Conventional rapid maxillary expansion design (RME) or no comparators	-
Outcome	1) Short- and long-term influences on upper airway dimensions (shape, size, volume, function) after using MARPE appliances 2) Short- and long-term skeletal and dental changes after using MARPE appliances	-
Study Design	• Randomized Controlled Trial studies (RCT) (prospective and retrospective) • Only papers that used CBCT diagnostic imaging were selected • Studies with and without a control group were chosen • Only studies with English language (or translated to English) were considered	• Any study other than RCTs such as reviews, systematic reviews and metal analysis, book chapters, case reports, personal opinions, letters, conference abstracts were excluded • RCTs that used diagnostic imaging other than CBCT

PubMed search:

(((((((((((Skeletal changes) OR (Dental changes)) OR (Nasal cavity functional changes)) OR (Dentofacial)) OR (Upper Airway resistance)) OR (Nasal cavity volume)) OR (Nasal shape)) OR (Nasal dimension)) AND (((((((CBCT) OR (Cone Beam Computer Tomography)) OR (Polysomnography)) OR (PSG)) OR (nasal peak airflow)) OR (Peak Nasal Inspiratory Flow)) OR (PNIF))) AND ((((((((((((((((((Non-surgical Maxillary Expan*) OR (Adult Maxillary Expan*)) OR (Miniscrew-Assisted Rapid Palatal Expan*)) OR (TAD*)) OR (Temporary Anchorage Devices)) OR (Moon)) OR (BARME)) OR (Bone-Anchored Rapid Maxillary Expan*)) OR (B-RME)) OR (Bone-borne Rapid Maxillary Expan*)) OR (Midfacial Skeletal Expan*)) OR (MSE)) OR (C-Expander)) OR (Dresden Expander)) OR (SARPE)) OR (Surgically Assisted Rapid palatal Expan*)) OR (Bone Anchored Expan*)) OR (MARPE))) OR (SARME)) OR (Surgically Assisted Rapid Maxillary Expan*)

Appendix 2

Table A3.1Severity Classification System (adapted from Lipan and Sam, 2013)[94]

Severity class	NOSE survey score range
Mild	5-25
Moderate	30-50
Severe	55-75
Extreme	80-100

Abbreviation: NOSE: Nasal Obstruction Symptom Evaluation.

Table A3.2 Hypothesis testing for upper airway changes

1. H_0: There are no differences in the **nasopharynx volume**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **nasopharynx volume**, from T_0 to T_1, of at least one of the appliances is different from the other.
2. H_0: There are no differences in the **oropharynx volume**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **oropharynx volume**, from T_0 to T_1, of at least one of the appliances is different from the other.
3. H_0: There are no differences in the **oropharynx MCA**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **oropharynx MCA**, from T_0 to T_1, of at least one of the appliances is different from the other.
4. H_0: There are no differences in the **PNIFBN, PNIFLB, PNIFRB**, from T_0 to T_1, between the Dresden and the Moon appliances. H_a: The **PNIFBN, PNIFLB, PNIFRB**, from T_0 to T_1, of at least one of the appliances is different from the other.
5. H_0: There is no interaction between appliance type and time (PrePost) on upper airway (NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB). H_a: There is an interaction between appliance type and time (PrePost) on upper airway (NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB).
6. H_0: There is no difference in the median NOSE questionnaire answers in patients treated with either Moon or Dresden expander. H_a: There is a difference in the median NOSE questionnaire answers in patients treated with either Moon or Dresden expander.
7. H_0: Within each treatment group, there are no statistically significant changes on upper airway for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, from T_0 to T_1. H_a: Within each treatment group, there are statistically significant changes on upper airway for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, from T_0 to T_1.

Table A3.3 Intra-examiner reliability (Intra-class Correlation Coefficient (ICC)) using single measures from three repeated measurements (five external patients)

Upper Airway Compartment	Intraclass Correlation *(Single Measures)*	*95% confidence Interval* Lower Bound	*95% confidence Interval* Upper bound
NPV (mm^3)	0.99	0.95	1.00
OPV (mm^3)	1.00	0.98	1.00
OPMCA (mm^2)	1.00	1.00	1.00

Table A3.4 Measurement error from three repeated measurements (five external patients)

Upper Airway Compartment	Mean ± SD	Min	Max	Percentage (%) mean
NPV (mm^3)	224.67 ± 131.94	75.33	400.00	3.44 %
OPV (mm^3)	255.73 ± 291.33	0.00	595.33	1.50 %
OPMCA (mm^2)	0.00	0.00	0.00	0.00 %

Table A3.5 Assumption testing for one-way repeated measure mixed ANOVA

Three model assumptions of ANOVA were investigated. The three model assumptions are normal distribution and the independent sampling (for the within and between-subject factors), sphericity assumption (for the within subject factors), and checking for any significant outliers. Normality assumption was assessed using Shapiro-Wilk test and results showed that assumption of normality is met ($P > 0.05$) for all the airway measurements, except for PNIFLB at T_0 ($P < 0.05$) (Table 3.9, Appendix 2). However, since the ANOVA test is robust against normality [96], it can be concluded that overall, assumption of normality is met for this analysis. In addition, visual assessment of the box plots indicates that there are only a few outliers and therefore, bootstrapping or log transformation are not indicated in this analysis (Figure. 3.3, Appendix 2). The independent sampling assumption was also met since the data for each variable was collected from a different patient and the selection of one patient was not dependent on the other. Sphericity assumption is tested when the within subject factors have three or more levels. However, for this analysis, all the within subject factors have only two levels and therefore, sphericity assumption is assumed to be met. There were no outliers, as assessed by examination of studentized residuals for values +/- 3. Levene's test resulted in p-values more than 0.05 at T_0 and T_1 for all upper airway measurements (Table 3.10, Appendix 2). Therefore, to test for equal variances, the ratio between the largest and the smallest standard deviation (SD) was taken instead. For the following airway measurements, the ratio between the largest and the smallest SD was more than 2 and the equal variance assumption was not met: PNIFBN_pre, PNIFRB_pre, PNIFLB_post, PNIFRB_post. For the remaining airway measurements, the ratio was less than 2 and therefore, there is evidence that the equal variance between the samples is met.

Table A3.6 Raw data for PNIFBN, PNIFLB, PNIFRB

Pt#	Appliance	gender	Age	PNIFBN_pre L/min	PNIFLB_pre L/min	PNIFRB_pre L/min	PNIFBN_post L/min	PNIFLB_post L/min	PNIFRB_post L/min
1	Moon	Male	18.80	50.00	20.00	26.67	53.33	36.67	40.00
2	Moon	Female	33.50	93.33	90.00	76.67	146.67	110.00	83.33
3	Moon	Female	29.70	153.33	140.00	143.33	75.00	53.33	48.33
4	Moon	Male	17.10	40.00	23.33	40.00	53.33	50.00	56.67
5	Moon	Male	17.50	26.67	20.00	30.00	40.00	26.67	30.00
6	Moon	Female	21.30	50.00	43.33	35.00	93.33	53.33	70.00
7	Moon	Female	33.10	46.67	40.00	3.33	63.33	56.67	50.00
8	Moon	Female	22.90	20.00	23.33	30.00	40.00	30.00	-
9	Dresden	Male	27.90	73.33	60.00	50.00	63.33	31.67	23.33
10	Dresden	Female	17.10	75.00	41.67	48.33	100.00	33.33	46.67
11	Dresden	Male	18.10	65.00	49.33	42.67	56.67	43.33	40.00
12	Dresden	Female	19.10	70.00	43.33	56.67	70.00	50.00	51.67
13	Dresden	Female	25.70	50.00	40.00	6.67	43.33	23.33	45.00

Table A3.7 Descriptive Statistics Chart for Upper Airway Changes

Upper Airway Measurements	Appliance	Mean	Standard Deviation	N	Upper Airway Measurements	Appliance	Mean	Standard Deviation	N
	Dresden	5518.20	601.93	5		Dresden	66.67	10.07	5
NPV_Pre	Moon	6297.08	1763.84	8	PNIFBN_Pre	Moon	60.00	43.61	8
	Total	5997.51	1446.08	13		Total	62.56	33.98	13
	Dresden	5871.73	1659.84	5		Dresden	66.67	21.08	5
NPV_Post	Moon	6486.79	1733.76	8	PNIFBN_Post	Moon	70.63	35.55	8
	Total	6250.23	1663.97	13		Total	69.10	29.82	13
	Dresden	16375.00	6180.45	5		Dresden	46.87	8.14	5
OPV_Pre	Moon	14668.71	6589.63	8	PNIFLB_Pre	Moon	50.00	43.21	8
	Total	15324.97	6229.72	13		Total	48.80	33.37	13
	Dresden	17005.93	7892.55	5		Dresden	36.33	10.44	5
OPV_Post	Moon	17094.71	6814.44	8	PNIFLB_Post	Moon	52.08	26.06	8
	Total	17060.56	6917.67	13		Total	46.03	22.27	13
	Dresden	210.53	125.67	5		Dresden	40.87	19.76	5
OPMCA_Pre	Moon	189.75	90.12	8	PNIFRB_Pre	Moon	48.13	43.49	8
	Total	197.74	100.57	13		Total	45.33	35.31	13
	Dresden	223.00	122.11	5		Dresden	41.33	10.89	5
OPMCA_Post	Moon	258.00	108.57	8	PNIFRB_Post	Moon	47.29	25.35	8
	Total	244.54	110.27	13		Total	45.00	20.58	13

Table A3.8 Descriptive statistics for NOSE questionnaire

Time	Appliance	Median
	Dresden	20.00
T_0	Moon	10.00
	Dresden	20.00
T_1	Moon	15.00

Table A3.9 Test of Normality: Shapiro-Wilk test

Upper airway	Statistics	df	Sig.	Adjusted Bonferroni p-value [1]
Studentized Residual for NPV_Pre	0.98	13	0.97	1.00
Studentized Residual for NPV_Post	0.95	13	0.60	1.00
Studentized Residual for OPV_Pre	0.94	13	0.50	1.00
Studentized Residual for OPV_Post	0.94	13	0.42	1.00
Studentized Residual for OPMCA_Pre	0.92	13	0.24	1.00
Studentized Residual for OPMCA_Post	0.97	13	0.86	1.00
Studentized Residual for PNIFBN_pre	0.83	13	0.02	0.10
Studentized Residual for PNIFBN_Post	0.87	13	0.05	0.28
Studentized Residual for PNIFLB_Pre	0.80	13	0.01	0.06*
Studentized Residual for PNIFLB_Post	0.84	13	0.02	0.12
Studentized Residual for PNIFRB_Pre	0.87	13	0.05	0.30
Studentized Residual for PNIFRB_Post	0.95	13	0.58	1.00

1. Adjusted Bonferroni p-value= p-value*6
2. *Significant adjusted p-value

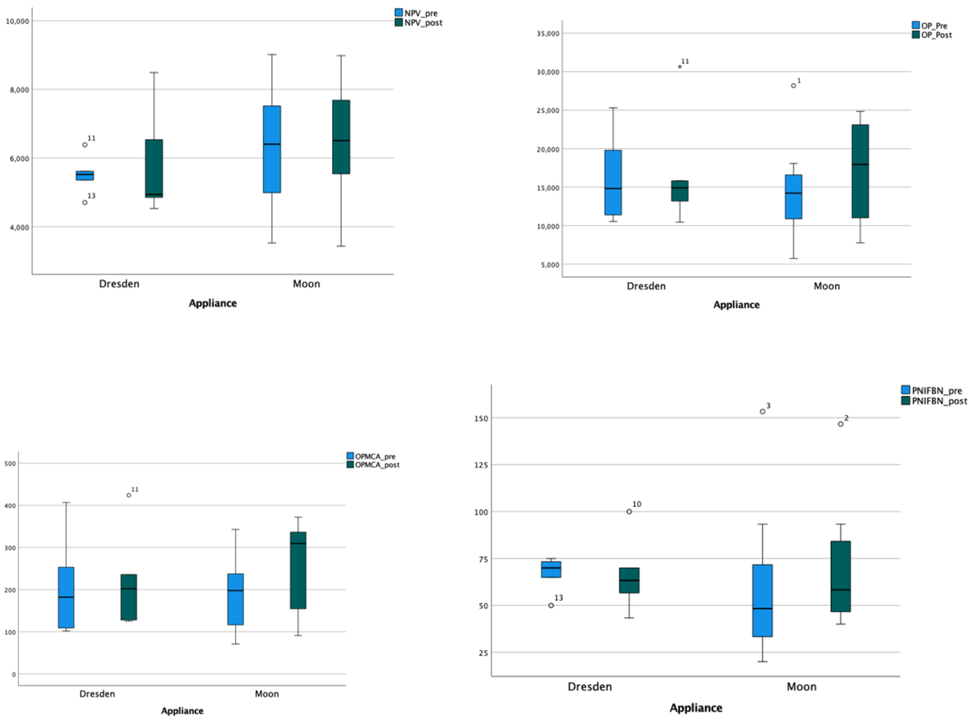


Figure A3.1 Box plot of NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB, and NQ for the Dresden and Moon expanders, at T_0 and T_1.

Table A3.10 Levene's test of Equality of Error Variances

Upper airway measurements	Sig. *(Based on Mean)*	Adjusted Bonferroni p-value[1]
NPV_Pre	0.08	0.45
NPV_Post	0.92	1.00
OPV_Pre	0.81	1.00
OPV_Post	0.77	1.00
OPMCA_Pre	0.44	1.00
OPMCA_Post	0.81	1.00
PNIFBN_Pre	0.08	0.48
PNIFBN_Post	0.34	1.00
PNIFLB_Pre	0.05	0.28
PNIFLB_Post	0.39	1.00
PNIFRB_Pre	0.23	1.00
PNIFRB_Post	0.22	1.00

1. Adjusted Bonferroni p-value= p-value*6

Table A3.11 Tests of within-subject effects for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB

Upper Airway Measurements		df	Mean square	F	Sig	Adjusted Bonferroni p-value[1]
	PrePost	1	454017.71	0.45	0.51	1.00
NPV	PrePost*Appliance	1	41290.20	0.04	0.84	1.00
	Error (PrePost)	11	999403.29	-	-	-
	PrePost	1	14376679.30	0.86	0.37	1.00
OPV	PrePost*Appliance	1	4957329.78	0.30	0.60	1.00
	Error (PrePost)	11	16768442.80	-	-	-
	PrePost	1	10023.35	1.90	0.20	1.00
OPMCA	PrePost*Appliance	1	4787.35	0.91	0.36	1.00
	Error (PrePost)	11	5287.02	-	-	-
	PrePost	1	173.67	0.32	0.58	1.00
PNIFBN	PrePost*Appliance	1	173.68	0.32	0.58	1.00
	Error (PrePost)	11	538.11	-	-	-
	PrePost	1	109.86	0.24	0.63	1.00
PNIFLB	PrePost*Appliance	1	244.89	0.54	0.48	1.00
	Error (PrePost)	11	454.90	-	-	-
	PrePost	1	0.21	0.00	0.99	1.00
PNIFRB	PrePost*Appliance	1	2.60	0.00	0.95	1.00
	Error (PrePost)	11	728.94	-	-	-

1. Adjusted Bonferroni p-value= p-value*6

Table A3.12 Tests of between-Subject effects (Appliance) for NPV, OPV, OPMCA, PNIFBN, PNIFLB, PNIFRB

Upper Airway Compartment	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
NPV	Appliance	1	2989343.65	0.74	0.41	1.00
	Error	11	4026860.32	-	-	-
OPV	Appliance	1	4025169.50	0.05	0.82	1.00
	Error	11	76956971.70	-	-	-
OPMCA	Appliance	1	310.94	0.02	0.90	1.00
	Error	11	18548.05	-	-	-
PNIFBN	Appliance	1	11.29	0.01	0.94	1.00
	Error	11	1674.48	-	-	-
PNIFLB	Appliance	1	548.59	0.45	0.52	1.00
	Error	11	1228.90	-	-	-
PNIFRB	Appliance	1	268.75	0.25	0.63	1.00
	Error	11	1068.97	-	-	-

1. Adjusted Bonferroni p-value= p-value*6

Table A3.13 Mean-Whitney U test (nonparametric) for NOSE questionnaire

T1-T0	Median	Fisher Exact Sig (Independent sample Median test)	Adjusted Bonferroni p-value[1]
Diff_NQ	0.00	0.59	1.00

1. Adjusted Bonferroni p-value= p-value*6

Table A3.14 Paired sample t-test: Upper airway changes for Moon Expander group

	T_0 Mean (SD)	T_1 Mean (SD)	Mean Change (T_1-T_0) (SD)	%Change (T_1-T_0)	p-value	Adjusted Bonferroni p-value
NPV, mm^3	6297.08 (1763.84)	6486.79 (1733.76)	189.71 (1468.96)	3.01%	0.73	1.00
OPV, mm^3	14668.71 (6589.63)	17094.71 (6814.44)	2426.00 (4489.03)	16.54%	0.17	1.00
OPMCA, mm^2	189.75 (90.12)	258.00 (108.57)	68.25 (90.58)	35.97%	0.07	0.42
PNIFBN, L/min	59.99 (43.61)	70.63 (35.55)	10.63 (39.64)	17.71%	0.47	1.00
PNIFLB, L/min	49.99 (43.21)	52.08 (26.06)	2.08 (36.51)	4.17%	0.88	1.00
PNIFRB, L/min	48.13 (43.49)	47.29 (25.35)	-0.83 (44.44)	1.73%*	0.96	1.00

1. * 1.73% reduction in PNIFRB from pre-treatment to post-treatment

Table A3.15 Paired sample t-test: Upper airway changes for Dresden Expander group

	T_0 Mean (SD)	T_1 Mean (SD)	Mean Change (T_1-T_0) (SD)	%Change (T_1-T_0)	p-value	Adjusted Bonferroni p-value
NPV, mm^3	5518.20 (601.93)	5871.73 (1659.83)	353.53 (1311.68)	6.41%	0.58	1.00
OPV, mm^3	16375.00 (6180.45)	17005.93 (7892.55)	630.93 (7547.29)	3.85%	0.86	1.00
OPMCA, mm^2	210.53 (125.67)	223.00 (122.107)	12.47 (121.33)	5.92%	0.83	1.00
PNIFBN, L/min	66.67 (10.07)	66.67 (21.08)	-0.002 (14.48)	0.00%	1.00	1.00
PNIFLB, L/min	46.87 (8.14)	36.33 (10.44)	-10.53 (13.00)	22.48% *	0.14	0.84
PNIFRB, L/min	40.87 (19.76)	41.33 (10.89)	0.47 (23.53)	1.14%	0.97	1.00

1. *22.48 % reduction in PNIFLB from pre-treatment to post-treatment

Appendix 3

Table A4.1 Hypothesis testing for skeletal and dental changes

1. H_0: There are no differences in the mean orthogonal distances (*mm*), from T_0 to T_1, in the transverse (X), vertical (Z), and A-P (Y) directions between the Dresden and the Moon appliances. H_a: The mean orthogonal distances, from T_0 to T_1, in the transverse, vertical, and A-P directions of at least one of the appliances is different from the others.
2. H_0: There is no interaction between appliance type and time (PrePost) on the mean orthogonal distances. H_a: There is an interaction between appliance type and time on the mean orthogonal distances.
3. H_0: Within each treatment group, there are no statistically significant changes on the mean orthogonal distances from T_0 to T_1. H_a: Within each treatment group, there are statistically significant changes on the mean orthogonal distances from T_0 to T_1.

Table A4.2 Abbreviation table: Forty-one Skeletal and Dental landmarks used for Intra-rater reliability

Skeletal/Dental Landmark	Abbreviations	Skeletal/Dental Landmark	Abbreviations
Right Greater palatine Foramen	RGPF	Mesio-Buccal root Apex of 26	MBA26
Left Greater Palatine Foramen	LGPF	Buccal Alveolar bone of 26	ALB26
Right Infraorbital Foramen	InfraOR	Pulp Chamber of 14	PC14
Left Infraorbital Foramen	InfraOL	Buccal Root Apex of 14 (as soon as the buccal root disappears)	BA14
Mid- Nasopalatine Foramen	NPF	Buccal Alveolar Bone of 14 (next to mesial root apex)	ALB14
Right Mental Foramen (largest part, beginning of the canal, as soon as the radiolucent part appears on the mesial)	MeR	Pulp Chamber of 24	PC24
Left Mental Foramen	MeL	Buccal Root Apex of 24	BA24
Crista Galli (as soon as the radiolucency appears in the middle of the radiopacity)	CG	Buccal Alveolar Bone of 24	ALB24

Skeletal/Dental Landmark	Abbreviations	Skeletal/Dental Landmark	Abbreviations
Right Foramen Ovale	FOR	Pulp chamber of 13 (as soon as the radiolucency of the pulp chamber starts to form)	PC13
Left Foramen Ovale	FOL	Root Apex of 13 (as soon as the radiolucent area of the pulp chamber disappears)	A13
Right Foramen Spinosum	FSR	Buccal Alveolar bone of 13 (next to mesial root apex)	ALB13
Left Foramen Spinosum	FSL	Pulp chamber of 23	PC23
Foramen Magnum	FM	Root Apex of 23	A23
Right Hypoglossal Canal	HCR	Buccal Alveolar bone of 23	ALB23
Left Hypoglossal Canal	HCL	Pulp Chamber of 46	PC46
Right External Auditory Meatus -as soon as the radiolucent area reaches the external border	EOMR	Mesio-Buccal Root Apex of 46	MBA46
Left External Auditory Meatus	EOML	Buccal Alveolar Bone of 46 (next to Mesial root Apex)	ALB46
Pulp Chamber of 16	PC16	Pulp Chamber of 36	PC36
Mesio-Buccal Root Apex of 16	MBA16	Mesio-Buccal Root Apex of 36	MBA36
Buccal Alveolar bone of 16	ALB16	Buccal Alveolar Bone of 36	ALB36
Pulp chamber of 26	PC26		

Table A4.3 Intra-examiner reliability (Intra-class Correlation Coefficient (ICC)) using single measures from three repeated measurements for X,Y,and Z coordinates for 41 skeletal and dental landmarks (five external patients)

Landmark	Intraclass Correlation *(Single Measures)*	*95% confidence Interval* Lower Bound	*95% confidence Interval* Upper bound	Landmark	Intraclass Correlation *(Single Measures)*	*95% confidence Interval* Lower Bound	*95% confidence Interval* Upper bound
RGPF	1.00	1.00	1.00	MBA26	1.00	1.00	1.00
LGPF	1.00	1.00	1.00	ALB26	1.00	1.00	1.00
InfraOR	1.00	1.00	1.00	PC14	1.00	1.00	1.00
InfraOL	1.00	1.00	1.00	BA14	1.00	1.00	1.00
NPF	1.00	1.00	1.00	ALB14	1.00	1.00	1.00
MeR	1.00	1.00	1.00	PC24	1.00	1.00	1.00
MeL	1.00	1.00	1.00	BA24	1.00	1.00	1.00
CG	1.00	1.00	1.00	ALB24	1.00	1.00	1.00
FOR	1.00	1.00	1.00	PC13	1.00	1.00	1.00
FOL	1.00	1.00	1.00	A13	1.00	1.00	1.00
FSR	1.00	1.00	1.00	ALB13	1.00	1.00	1.00
FSL	1.00	1.00	1.00	PC23	1.00	1.00	1.00
FM	1.00	1.00	1.00	A23	1.00	1.00	1.00
HCR	1.00	1.00	1.00	ALB23	1.00	1.00	1.00
HCL	1.00	1.00	1.00	PC46	1.00	1.00	1.00
EOMR	1.00	1.00	1.00	MBA46	1.00	1.00	1.00
EOML	1.00	1.00	1.00	ALB46	1.00	1.00	1.00

Landmark	Intraclass Correlation *(Single Measures)*	*95% confidence Interval* Lower Bound	*95% confidence Interval* Upper bound	Landmark	Intraclass Correlation *(Single Measures)*	*95% confidence Interval* Lower Bound	*95% confidence Interval* Upper bound
PC16	1.00	1.00	1.00	PC36	1.00	1.00	1.00
MBA16	1.00	1.00	1.00	MBA36	1.00	1.00	1.00
ALB16	1.00	1.00	1.00	ALB36	1.00	1.00	1.00
PC26	1.00	1.00	1.00				

Table A4.4 Measurement errors (mm) from three repeated measurements for X,Y,and Z coordinates for 41 skeletal and dental landmarks (five external patients)

	Transverse (X)			Antero-posterior (Y)			Vertical (Z)		
Landmarks	Mean ±SD (mm)	Min (mm)	Max (mm)	Mean ±SD (mm)	Min (mm)	Max (mm)	Mean ±SD (mm)	Min (mm)	Max (mm)
RGPF	0.47 ± 0.45	0.00	1.00	0.80 ±0.30	0.67	1.33	0.45 ± 0.36	0.20	1.07
LGPF	0.40 ± 0.55	0.00	1.00	0.87 ± 0.56	0.00	1.33	0.52 ± 0.39	0.20	1.07
InfraOR	0.67 ± 0.62	0.00	1.67	0.67 ± 0.47	0.00	1.33	0.10 ± 0.13	0.00	0.27
InfraOL	0.53 ± 0.67	0.00	1.67	0.40 ± 0.37	0.00	0.67	0.19 ± 0.18	0.00	0.40
NPF	0.27 ± 0.44	0.00	1.00	0.53 ± 0.56	0.00	1.33	0.25 ± 0.17	0.00	0.47
MeR	0.13 ± 0.18	0.00	0.33	0.40 ± 0.37	0.00	0.67	0.10 ± 0.13	0.00	0.27
MeL	0.09 ± 0.15	0.00	0.33	0.00 ± 0.00	0.00	0.00	0.15 ± 0.14	0.00	0.27
CG	0.20 ± 0.18	0.00	0.33	0.40 ± 60	0.00	1.33	0.25 ± 0.19	0.00	0.53
FOR	0.07 ± 0.15	0.00	0.33	0.37 ± 0.24	0.00	0.67	0.20 ± 0.12	0.00	0.27

	Transverse (X)			Antero-posterior (Y)			Vertical (Z)		
FOL	0.19 ± 0.13	0.00	0.33	0.52 ± 21	0.27	0.73	0.16 ± 0.15	0.00	0.27
FSR	0.20 ± 0.30	0.00	0.67	0.40 ± 0.37	0.00	0.93	0.93 ± 0.13	0.00	0.27
FSL	0.39 ± 0.16	0.23	0.67	0.35 ± 0.25	0.07	0.67	0.15± 0.14	0.00	0.27
FM	0.73 ± 0.28	0.33	1.00	0.35 ± 0.21	0.13	0.67	0.00 ± 0.00	0.00	0.00
HCR	0.27 ± 0.28	0.00	0.67	0.76 ± 0.32	0.00	0.80	0.21 ± 0.22	0.00	0.53
HCL	0.19 ± 0.29	0.00	0.67	0.45 ± 0.19	0.20	0.67	0.11 ± 0.15	0.00	0.27
EOMR	0.27 ± 0.28	0.00	0.67	0.69 ± 0.41	0.33	1.40	0.23 ± 0.27	0.00	0.67
EOML	0.55 ± 0.40	0.20	1.23	0.85 ± 0.71	0.13	1.80	0.27 ± 0.19	0.00	0.53
PC16	0.67 ± 0.41	0.00	1.00	0.80 ± 0.30	0.67	1.33	0.12 ± 0.12	0.00	0.27
MBA16	0.54 ± 0.40	0.00	1.05	0.67± 0.47	0.00	1.33	0.77 ± 0.50	0. 27	1.33
ALB16	0.73 ± 0.28	0.33	1.00	0.80± 0.30	0.67	1.33	0.77 ± 0.50	0.27	1.33
PC26	0.20 ± 0.45	0.00	1.00	0.13 ± 0.30	0.00	0.67	0.13 ± 0.19	0.00	0.40
MBA26	0.36 ± 0.30	0.00	0.83	0.40 ± 0.37	0.00	0.67	0.23 ± 0.25	0.00	0.60
ALB26	0.48 ± 0.35	0.07	1.00	0.40 ± 0.37	0.00	0.67	0.23 ± 0.25	0.00	0.60
PC14	0.33 ± 0.47	0.00	1.00	0.27 ± 0.37	0.00	0.67	0.47 ± 00.59	0.00	1.33
BA14	0.40 ± 0.28	0.00	0.67	0.27 ± 0.37	0.00	0.67	0.33 ± 0.36	0.00	0.80
ALB14	0.40 ± 0.44	0.00	1.00	0.53 ± 0.30	0.00	0.67	0.33 ± 0.36	0.00	0.80
PC24	0.60 ± 0.55	0.00	1.00	0.00 ± 0.00	0.00	0.00	0.16 ± 0.15	0.00	0.27
BA24	0.54 ± 0.52	0.00	1.05	0.27 ± 0.37	0.00	0.67	0.51 ± 0.42	0.00	1.02
ALB24	0.39 ± 0.44	0.00	1.00	0.40 ± 0.37	0.00	0.67	0.63 ± 0.63	0.00	1.60
PC13	0.20 ± 0.30	0.00	0.67	0.13 ± 0.30	0.00	0.67	0.31 ± 0.13	0.20	0.53

	Transverse (X)			Antero-posterior (Y)			Vertical (Z)		
A13	0.20 ± 0.30	0.00	0.67	0.40 ± 0.37	0.00	0.67	0.36 ± 0.16	0.20	0.53
ALB13	0.40 ± 0.37	0.00	0.67	0.40 ± 0.37	0.00	0.67	0.52 ± 0.30	0.27	1.01
PC23	0.40 ± 0.44	0.00	1.00	0.27 ±0.37	0.00	0.67	0.47 ± 45	0.45	1.07
A23	0.73 ± 0.64	0.00	1.67	0.53 ± 0.30	0.00	0.67	1.16 ± 0.62	0.27	1.87
ALB23	0.47 ± 0.51	0.00	1.00	0.53 ± 0.30	0.00	0.67	1.16 ± 0.62	0.27	1.87
PC46	0.67 ± 0.33	0.33	1.00	0.27 ± 0.37	0.00	0.67	0.11 ± 0.15	0.00	0.27
MBA46	0.33 ± 0.33	0.00	0.67	0.40 ± 0.37	0.00	0.67	0.29 ± 0.06	0.27	0.40
ALB46	0.53 ± 0.38	0.00	1.00	0.40 ± 0.37	0.00	0.67	0.29 ± 0.06	0.27	0.40
PC36	0.37 ± 0.29	0.00	0.67	0.53 ± 0.30	0.00	0.67	0.11 ± 0.15	0.00	0.27
MBA36	0.29 ± 0.24	0.00	0.67	0.40 ± 0.37	0.00	0.67	0.24 ± 0.15	0.00	0.40
ALB36	0.27 ± 0.24	0.00	0.60	0.40 ± 0.37	0.00	0.67	0.24 ± 0.15	0.00	0.40

Table A4.5 Assumption testing for one-way repeated measure mixed ANOVA

Three model assumptions of ANOVA were investigated. The three model assumptions are normal distribution and the independent sampling, sphericity assumption, and checking for any significant outliers.

To assess the normality assumption, Shapiro-Wilk test of normality was conducted, and the results showed that assumption of normality is met ($P > 0.05$) for all the data (Table 4.7, Appendix 3). In addition, visual assessment of the box plots indicates that there are only a few outliers and therefore, bootstrapping or log transformation are not indicated in this analysis (Figure. 4.1, Appendix 3).

The independent sampling assumption is also met since the data for each variable was collected from a different patient and the selection of one patient was not dependent on the other. Sphericity assumption is tested when the within subject factors have three or more levels. However, for this analysis, the within subject factors have only two levels and therefore, sphericity assumption is assumed to be met. There were no outliers, as assessed by examination of studentized residuals for values +/- 3.

Levene's test resulted in p-values more than 0.05 at T_0 and T_1 for all landmarks (Table 4.8, Appendix 3). Therefore, the largest standard deviation was divided by the smallest standard deviation (SD_{large} / SD_{small}) to test the equal variances. For the following landmarks, the ratio between the largest and the smallest standard deviation (SD) was less than 2 and therefore, there is evidence that the equal variance assumption is met: HCR_Y (T_0 and T_1), HCR_Z (T_0 and T_1) , HCL_X (T_0 and T_1), HCL_Y (T_0 and T_1), HCL_Z_Pre, PC16_X (T_0 and T_1), PC16_Y (T_0 and T_1), PC16_Z_Pre, MBA16_X (T_0 and T_1), MBA16_Y_Pre, MBA16_Z_Pre, ALB16_X (T_0 and T_1), ALB16_Y_Pre, ALB16_Z_Pre, PC26_X (T_0 and T_1), PC26_Y (T_0 and T_1), PC26_Z_Post, MBA26_X (T_0 and T_1), MBA26_Y (T_0 and T_1), MBA26_Z_Pre, ALB26_X (T_0 and T_1), ALB26_Y (T_0 and T_1), ALB26_Z_Pre, PC14_X_Post, PC14_Y_Post, PC14_Z_Pre, PC24_Y (T_0 and T_1), PC24_Z_Post, PC46_X_Post, PC46_Z (T_0 and T_1), PC36_X (T_0 and T_1), PC36_Z_Post. For the remaining landmarks, SD_{large} / SD_{small} was more than 2 and therefore, the equal variance between the samples is not met for these landmarks.

Table A4.6 Descriptive statistics chart for Skeletal and Dental Changes

Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N	Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N
	Dresden	22.65	3.11	5		Dresden	24.05	1.70	5
HCR_X_Pre	Moon	18.80	1.11	8	MBA26_X_Pre	Moon	23.06	2.30	8
	Total	20.28	2.78	13		Total	23.44	2.07	13
	Dresden	21.95	3.35	5		Dresden	24.53	1.66	5
HCR_X_Post	Moon	18.90	0.83	8	MBA26_X_Post	Moon	23.73	2.42	8
	Total	20.07	2.56	13		Total	24.04	2.12	13
	Dresden	78.75	2.06	5		Dresden	18.11	3.77	5
HCR_Y_Pre	Moon	79.14	4.02	8	MBA26_Y_Pre	Moon	15.28	3.58	8
	Total	78.99	3.30	13		Total	16.37	3.78	13
	Dresden	78.43	2.04	5		Dresden	18.04	4.05	5
HCR_Y_Post	Moon	78.90	3.73	8	MBA26_Y_Post	Moon	15.70	3.70	8
	Total	78.71	3.09	13		Total	16.60	3.86	13
	Dresden	15.29	3.88	5		Dresden	4.44	1.85	5
HCR_Z_Pre	Moon	13.29	3.33	8	MBA26_Z_Pre	Moon	4.08	3.70	8
	Total	14.06	3.54	13		Total	4.22	3.03	13
	Dresden	15.02	5.19	5		Dresden	4.14	1.25	5
HCR_Z_Post	Moon	13.79	3.51	8	MBA26_Z_Post	Moon	3.76	3.14	8
	Total	14.26	4.07	13		Total	3.91	2.52	13
	Dresden	19.44	0.89	5		Dresden	28.54	2.49	5
HCL_X_Pre	Moon	18.62	1.58	8	ALB26_X_Pre	Moon	26.57	2.24	8
	Total	18.94	1.38	13		Total	27.32	2.45	13
	Dresden	19.85	1.35	5		Dresden	28.80	2.42	5
HCL_X_Post	Moon	18.48	1.67	8	ALB26_X_Post	Moon	27.51	2.67	8
	Total	19.01	1.65	13		Total	28.01	2.56	13
	Dresden	78.80	3.35	5		Dresden	17.70	4.06	5
HCL_Y_Pre	Moon	79.64	4.05	8	ALB26_Y_Pre	Moon	15.00	3.53	8
	Total	79.31	3.67	13		Total	16.04	3.83	13
	Dresden	78.86	3.13	5		Dresden	17.49	4.07	5
HCL_Y_Post	Moon	79.20	3.74	8	ALB26_Y_Post	Moon	15.43	3.68	8
	Total	79.07	3.38	13		Total	16.22	3.81	13

Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N	Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N
	Dresden	15.66	2.82	5		Dresden	4.49	1.97	5
HCL_Z_Pre	Moon	13.45	4.48	8	ALB26_Z_Pre	Moon	4.09	3.73	8
	Total	14.30	3.95	13		Total	4.24	3.08	13
	Dresden	14.94	3.45	5		Dresden	4.04	1.19	5
HCL_Z_Post	Moon	13.71	4.22	8	ALB26_Z_Post	Moon	3.76	3.19	8
	Total	14.18	3.84	13		Total	3.87	2.53	13
	Dresden	19.63	1.03	5		Dresden	17.33	2.42	5
PC16_X_Pre	Moon	19.49	2.01	8	PC14_X_Pre	Moon	16.24	0.93	8
	Total	19.54	1.65	13		Total	16.66	1.66	13
	Dresden	20.31	1.94	5		Dresden	16.84	1.83	5
PC16_X_Post	Moon	21.41	2.41	8	PC14_X_Post	Moon	17.31	1.01	8
	Total	20.99	2.22	13		Total	17.13	1.33	13
	Dresden	21.26	3.00	5		Dresden	8.94	4.23	5
PC16_Y_Pre	Moon	21.44	2.59	8	PC14_Y_Pre	Moon	7.40	2.01	8
	Total	21.37	2.63	13		Total	7.99	2.99	13
	Dresden	20.59	3.14	5		Dresden	7.07	1.45	5
PC16_Y_Post	Moon	22.13	2.89	8	PC14_Y_Post	Moon	8.17	2.17	8
	Total	21.54	2.96	13		Total	7.75	1.94	13
	Dresden	16.29	2.04	5		Dresden	8.77	1.82	4
PC16_Z_Pre	Moon	15.38	3.41	8	PC14_Z_Pre	Moon	8.71	3.00	8
	Total	15.73	2.89	13		Total	11.49	10.26	13
	Dresden	16.90	1.27	5		Dresden	9.77	1.71	5
PC16_Z_Post	Moon	15.04	3.86	8	PC14_Z_Post	Moon	8.32	3.16	8
	Total	15.76	3.18	13		Total	8.64	2.71	13
	Dresden	23.12	1.51	5		Dresden	17.08	3.70	5
MBA16_X_Pre	Moon	24.50	1.81	8	PC24_X_Pre	Moon	16.45	1.63	8
	Total	23.97	1.77	13		Total	16.69	2.49	13
	Dresden	23.70	1.71	5		Dresden	17.54	3.25	5
MBA16_X_Post	Moon	24.99	2.16	8	PC24_X_Post	Moon	17.65	1.42	8
	Total	24.50	2.03	13		Total	17.61	2.17	13

Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N	Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N
	Dresden	16.44	4.07	5		Dresden	7.43	3.14	5
MBA16_Y_Pre	Moon	16.48	2.28	8	PC24_Y_Pre	Moon	7.50	2.84	8
	Total	16.46	2.93	13		Total	7.48	2.83	13
	Dresden	16.28	4.33	5		Dresden	7.35	3.57	5
MBA16_Y_Post	Moon	16.60	1.77	8	PC24_Y_Post	Moon	8.11	3.22	8
	Total	16.48	2.85	13		Total	7.82	3.23	13
	Dresden	2.49	1.73	5		Dresden	8.87	1.59	5
MBA16_Z_Pre	Moon	2.96	3.57	8	PC24_Z_Pre	Moon	9.23	3.79	8
	Total	2.77	2.92	13		Total	9.09	3.04	13
	Dresden	3.20	1.26	5		Dresden	9.29	2.02	5
MBA16_Z_Post	Moon	3.32	3.49	8	PC24_Z_Post	Moon	8.69	3.41	8
	Total	3.27	2.77	13		Total	8.92	2.87	13
	Dresden	27.49	1.81	5		Dresden	21.54	1.25	5
ALB16_X_Pre	Moon	28.25	1.23	8	PC46_X_Pre	Moon	22.24	2.80	8
	Total	27.96	1.46	13		Total	21.95	2.23	13
	Dresden	27.45	1.87	5		Dresden	21.25	1.48	5
ALB16_X_Post	Moon	29.33	1.55	8	PC46_X_Post	Moon	22.61	2.83	8
	Total	28.61	1.86	13		Total	22.04	2.38	13
	Dresden	16.74	4.08	5		Dresden	20.38	2.35	5
ALB16_Y_Pre	Moon	16.69	2.45	8	PC46_Y_Pre	Moon	20.78	5.36	8
	Total	16.71	3.00	13		Total	20.62	4.21	13
	Dresden	16.42	4.39	5		Dresden	20.64	2.85	5
ALB16_Y_Post	Moon	16.96	1.84	8	PC46_Y_Post	Moon	23.10	6.55	8
	Total	16.76	2.91	13		Total	22.07	5.29	13
	Dresden	2.42	1.77	5		Dresden	23.00	2.25	5
ALB16_Z_Pre	Moon	2.93	3.60	8	PC46_Z_Pre	Moon	22.36	2.88	8
	Total	2.74	2.94	13		Total	22.62	2.54	13
	Dresden	3.22	1.32	5		Dresden	24.40	2.03	5
ALB16_Z_Post	Moon	3.42	3.48	8	PC46_Z_Post	Moon	22.63	2.88	8
	Total	3.34	2.77	13		Total	23.37	2.62	13

Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N	Skeletal/Dental Landmark	Appliance	Mean	Standard Deviation	N
	Dresden	19.41	3.50	5		Dresden	20.03	3.65	5
PC26_X_Pre	Moon	20.12	2.65	8	PC36_X_Pre	Moon	21.41	3.01	8
	Total	19.85	2.88	13		Total	20.83	3.21	13
	Dresden	20.41	3.23	5		Dresden	20.67	3.56	5
PC26_X_Post	Moon	22.43	3.14	8	PC36_X_Post	Moon	21.27	3.05	8
	Total	21.65	3.20	13		Total	21.02	3.13	13
	Dresden	22.48	3.73	5		Dresden	19.70	2.01	5
PC26_Y_Pre	Moon	20.81	4.09	8	PC36_Y_Pre	Moon	21.06	5.64	8
	Total	21.46	3.89	13		Total	20.50	4.39	13
	Dresden	22.10	3.98	5		Dresden	20.49	2.25	5
PC26_Y_Post	Moon	21.27	4.60	8	PC36_Y_Post	Moon	23.22	6.37	8
	Total	21.59	4.22	13		Total	22.08	5.10	13
	Dresden	17.38	1.46	5		Dresden	23.34	0.56	5
PC26_Z_Pre	Moon	16.14	4.52	8	PC36_Z_Pre	Moon	23.39	3.81	8
	Total	16.61	3.61	13		Total	23.37	2.83	13
	Dresden	17.09	1.13	5		Dresden	24.32	2.04	5
PC26_Z_Post	Moon	15.26	4.29	8	PC36_Z_Post	Moon	23.59	3.90	8
	Total	15.96	3.46	13		Total	23.90	3.16	13

Table A4.7 Test of Normality: Shapiro-Wilk test

	Appliance	Statistics	df	Sig	Adjusted Bonferroni p-value
Studentized Residual for	Dresden	0.93	5	0.62	1.00
HCR_X_Pre	Moon	0.93	8	0.48	1.00
Studentized Residual for	Dresden	0.91	5	0.45	1.00
HCR_X_Post	Moon	0.84	8	0.08	1.00
Studentized Residual for	Dresden	0.90	5	0.43	1.00
HCR_Y_Pre	Moon	0.97	8	0.87	1.00
Studentized Residual for	Dresden	0.98	5	0.93	1.00
HCR_Y_Post	Moon	0.97	8	0.86	1.00
Studentized Residual for	Dresden	0.87	5	0.25	1.00
HCR_Z_Pre	Moon	0.93	8	0.53	1.00
	Dresden	0.90	5	0.39	1.00

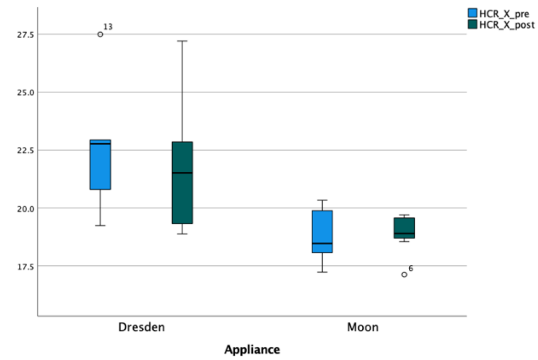
	Appliance	Statistics	df	Sig	Adjusted Bonferroni p-value
Studentized Residual for HCR_Z_Post	Moon	0.93	8	0.53	1.00
Studentized Residual for	Dresden	0.95	5	0.74	1.00
HCL_X_Pre	Moon	0.88	8	0.17	1.00
Studentized Residual for	Dresden	0.90	5	0.40	1.00
HCL_X_Post	Moon	0.88	8	0.20	1.00
Studentized Residual for	Dresden	0.94	5	0.68	1.00
HCL_Y_Pre	Moon	0.88	8	0.18	1.00
Studentized Residual for	Dresden	0.85	5	0.19	1.00
HCL_Y_Post	Moon	0.85	8	0.09	1.00
Studentized Residual for	Dresden	0.96	5	0.83	1.00
HCL_Z_Pre	Moon	0.84	8	0.07	1.00
Studentized Residual for	Dresden	0.91	5	0.45	1.00
HCL_Z_Post	Moon	0.88	8	0.17	1.00
Studentized Residual for	Dresden	0.96	5	0.83	1.00
PC16_X_Pre	Moon	0.93	8	0.56	1.00
Studentized Residual for	Dresden	0.72	5	0.01	0.36
PC16_X_Post	Moon	0.94	8	0.65	1.00
Studentized Residual for	Dresden	0.92	5	0.52	1.00
PC16_Y_Pre	Moon	0.94	8	0.63	1.00
Studentized Residual for	Dresden	0.98	5	0.94	1.00
PC16_Y_Post	Moon	0.92	8	0.41	1.00
Studentized Residual for	Dresden	0.94	5	0.66	1.00
PC16_Z_Pre	Moon	0.91	8	0.33	1.00
Studentized Residual for	Dresden	0.99	5	0.97	1.00
PC16_Z_Post	Moon	0.94	8	0.60	1.00
Studentized Residual for	Dresden	0.90	5	0.42	1.00
MBA16_X_Pre	Moon	0.92	8	0.45	1.00
Studentized Residual for	Dresden	0.90	5	0.39	1.00
MBA16_X_Post	Moon	0.89	8	0.21	1.00
Studentized Residual for	Dresden	0.97	5	0.88	1.00
MBA16_Y_Pre	Moon	0.93	8	0.50	1.00
Studentized Residual for	Dresden	0.97	5	0.88	1.00
MBA16_Y_Post	Moon	0.94	8	0.63	1.00
Studentized Residual for	Dresden	0.98	5	0.93	1.00
MBA16_Z_Pre	Moon	0.82	8	0.05	1.00
Studentized Residual for	Dresden	0.86	5	0.22	1.00
MBA16_Z_Post	Moon	0.83	8	0.06	1.00
Studentized Residual for	Dresden	0.75	5	0.03	1.00
ALB16_X_Pre	Moon	0.96	8	0.80	1.00
Studentized Residual for	Dresden	0.80	5	0.08	1.00
ALB16_X_Post	Moon	0.90	8	0.31	1.00
Studentized Residual for	Dresden	0.98	5	0.93	1.00
ALB16_Y_Pre	Moon	0.93	8	0.50	1.00
Studentized Residual for	Dresden	0.96	5	0.83	1.00
ALB16_Y_Post	Moon	0.97	8	0.93	1.00
Studentized Residual for	Dresden	0.96	5	0.79	1.00
ALB16_Z_Pre	Moon	0.82	8	0.04	1.00

	Appliance	Statistics	df	Sig	Adjusted Bonferroni p-value
Studentized Residual for	Dresden	0.79	5	0.06	1.00
ALB16_Z_Post	Moon	0.80	8	0.03	1.00
Studentized Residual for	Dresden	0.96	5	0.84	1.00
PC26_X_Pre	Moon	0.91	8	0.38	1.00
Studentized Residual for	Dresden	0.85	5	0.19	1.00
PC26_X_Post	Moon	0.79	8	0.02	0.72
Studentized Residual for	Dresden	0.85	5	0.19	1.00
PC26_Y_Pre	Moon	0.97	8	0.89	1.00
Studentized Residual for	Dresden	0.94	5	0.64	1.00
PC26_Y_Post	Moon	0.92	8	0.42	1.00
Studentized Residual for	Dresden	0.92	5	0.51	1.00
PC26_Z_Pre	Moon	0.95	8	0.69	1.00
Studentized Residual for	Dresden	0.99	5	0.97	1.00
PC26_Z_Post	Moon	0.94	8	0.56	1.00
Studentized Residual for	Dresden	0.84	5	0.17	1.00
MBA26_X_Pre	Moon	0.97	8	0.93	1.00
Studentized Residual for	Dresden	0.92	5	0.56	1.00
MBA26_X_Post	Moon	0.98	8	0.95	1.00
Studentized Residual for	Dresden	0.97	5	0.90	1.00
MBA26_Y_Pre	Moon	0.95	8	0.74	1.00
Studentized Residual for	Dresden	0.91	5	0.48	1.00
MBA26_Y_Post	Moon	0.94	8	0.58	1.00
Studentized Residual for	Dresden	0.86	5	0.23	1.00
MBA26_Z_Pre	Moon	0.93	8	0.55	1.00
Studentized Residual for	Dresden	0.97	5	0.88	1.00
MBA26_Z_Post	Moon	0.93	8	0.54	1.00
Studentized Residual for	Dresden	0.85	5	0.18	1.00
ALB26_X_Pre	Moon	0.92	8	0.40	1.00
Studentized Residual for	Dresden	0.94	5	0.64	1.00
ALB26_X_Post	Moon	0.89	8	0.25	1.00
Studentized Residual for	Dresden	0.96	5	0.83	1.00
ALB26_Y_Pre	Moon	0.96	8	0.78	1.00
Studentized Residual for	Dresden	0.91	5	0.46	1.00
ALB26_Y_Post	Moon	0.95	8	0.73	1.00
Studentized Residual for	Dresden	0.91	5	0.44	1.00
ALB26_Z_Pre	Moon	0.93	8	0.56	1.00
Studentized Residual for	Dresden	0.96	5	0.82	1.00
ALB26_Z_Post	Moon	0.92	8	0.45	1.00
Studentized Residual for	Dresden	0.87	5	0.27	1.00
PC14_X_Pre	Moon	0.98	8	0.94	1.00
Studentized Residual for	Dresden	0.98	5	0.93	1.00
PC14_X_Post	Moon	0.81	8	0.04	1.00
Studentized Residual for	Dresden	0.80	5	0.09	1.00
PC14_Y_Pre	Moon	0.93	8	0.53	1.00
Studentized Residual for	Dresden	0.79	5	0.07	1.00
PC14_Y_Post	Moon	0.94	8	0.61	1.00
Studentized Residual for	Dresden	0.91	4	0.46	1.00
PC14_Z_Pre	Moon	0.95	8	0.67	1.00

	Appliance	Statistics	df	Sig	Adjusted Bonferroni p-value
Studentized Residual for	Dresden	0.93	4	0.60	1.00
PC14_Z_Post	Moon	0.96	8	0.85	1.00
Studentized Residual for	Dresden	0.95	5	0.76	1.00
PC24_X_Pre	Moon	0.90	8	0.32	1.00
Studentized Residual for	Dresden	0.92	5	0.55	1.00
PC24_X_Post	Moon	0.97	8	0.91	1.00
Studentized Residual for	Dresden	0.89	5	0.35	1.00
PC24_Y_Pre	Moon	0.96	8	0.85	1.00
Studentized Residual for	Dresden	0.91	5	0.45	1.00
PC24_Y_Post	Moon	0.95	8	0.73	1.00
Studentized Residual for	Dresden	0.88	5	0.31	1.00
PC24_Z_Pre	Moon	0.97	8	0.88	1.00
Studentized Residual for	Dresden	0.72	5	0.02	0.72
PC24_Z_Post	Moon	0.96	8	0.77	1.00
Studentized Residual for	Dresden	0.99	5	0.97	1.00
PC46_X_Pre	Moon	0.94	8	0.64	1.00
Studentized Residual for	Dresden	0.94	5	0.66	1.00
PC46_X_Post	Moon	0.88	8	0.22	1.00
Studentized Residual for	Dresden	0.84	5	0.17	1.00
PC46_Y_Pre	Moon	0.84	8	0.09	1.00
Studentized Residual for	Dresden	0.95	5	0.71	1.00
PC46_Y_Post	Moon	0.87	8	0.17	1.00
Studentized Residual for	Dresden	0.86	5	0.23	1.00
PC46_Z_Pre	Moon	0.97	8	0.87	1.00
Studentized Residual for	Dresden	0.84	5	0.17	1.00
PC46_Z_Post	Moon	0.96	8	0.85	1.00
Studentized Residual for	Dresden	0.93	5	0.58	1.00
PC36_X_Pre	Moon	0.90	8	0.31	1.00
Studentized Residual for	Dresden	0.96	5	0.81	1.00
PC36_X_Post	Moon	0.96	8	0.85	1.00
Studentized Residual for	Dresden	0.87	5	0.26	1.00
PC36_Y_Pre	Moon	0.80	8	0.04	1.00
Studentized Residual for	Dresden	1.00	5	1.00	1.00
PC36_Y_Post	Moon	0.89	8	0.27	1.00
Studentized Residual for	Dresden	0.94	5	0.65	1.00
PC36_Z_Pre	Moon	0.90	8	0.32	1.00
Studentized Residual for	Dresden	0.89	5	0.38	1.00
PC36_Z_Post	Moon	0.92	8	0.44	1.00

1.Adjusted Bonferroni p-value= p-value*36

2.*Significant Adjusted p-value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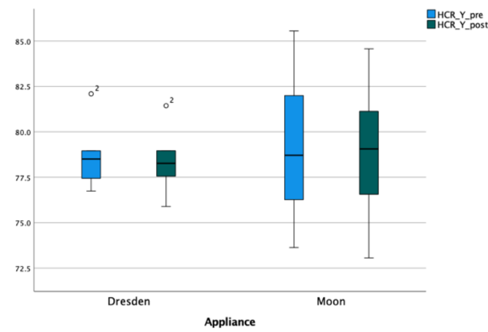
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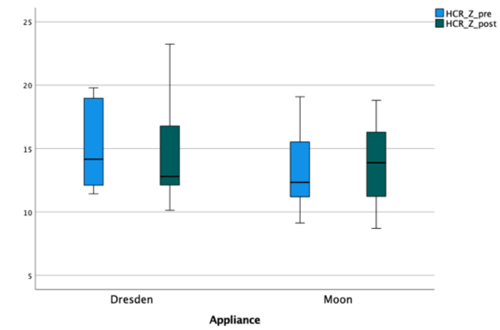
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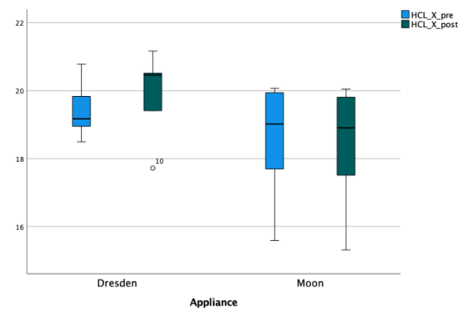
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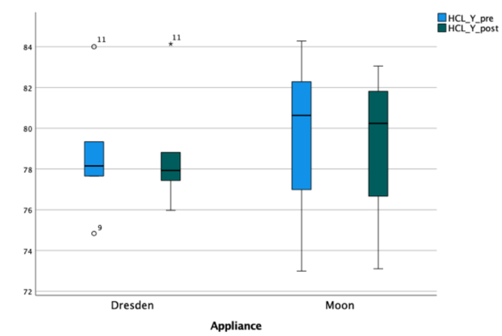
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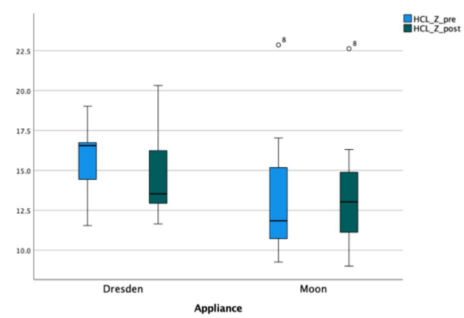
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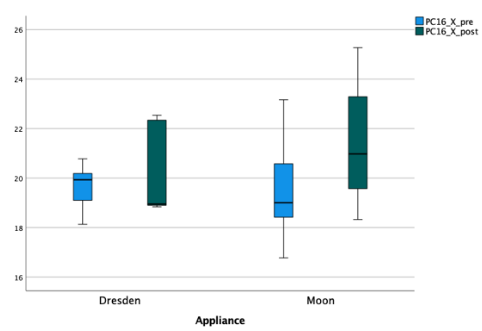
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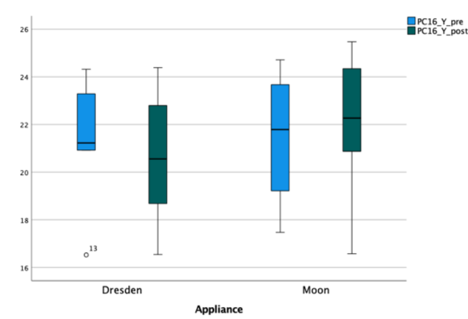
Moon
Appliance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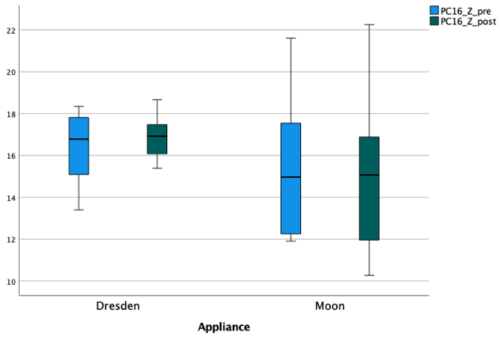
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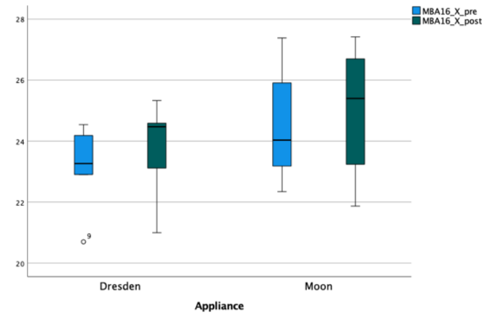
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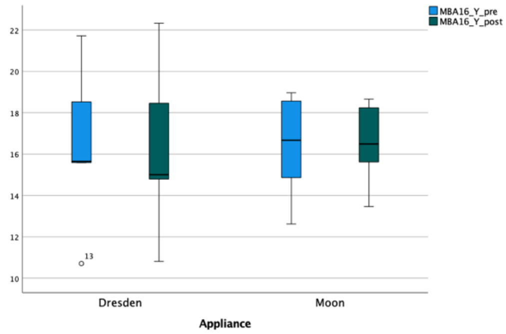
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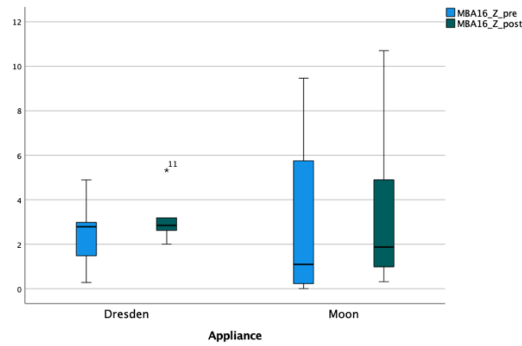
Dresden
Moon
Appliance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0
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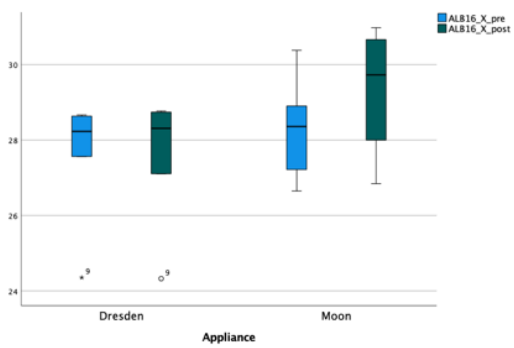
Dresden
Moon
Appliance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Dresden
Moon
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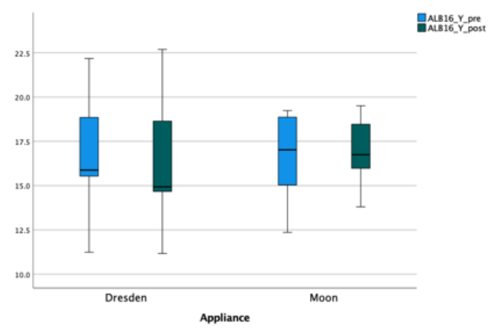
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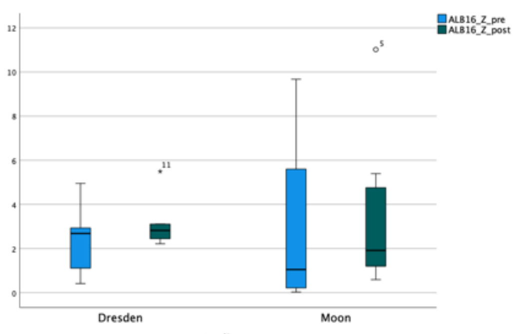
Dresden
Moon
Appliance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Moon
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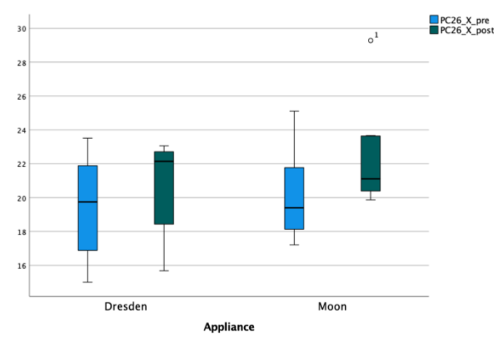
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Moon
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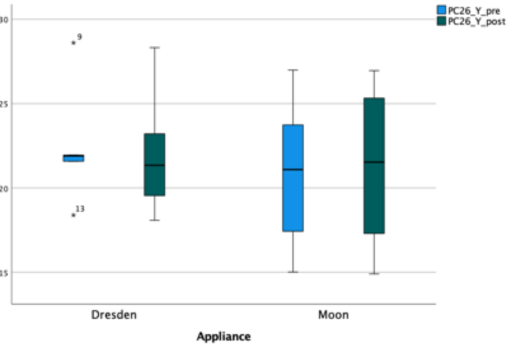
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PC26_Y_post
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Moon
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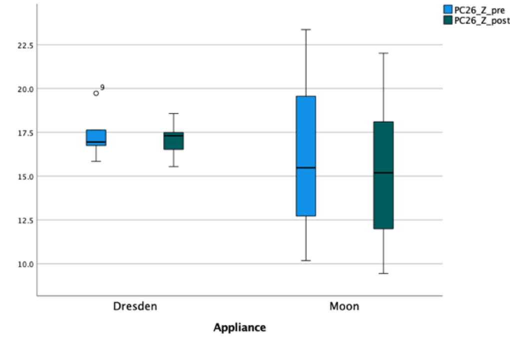
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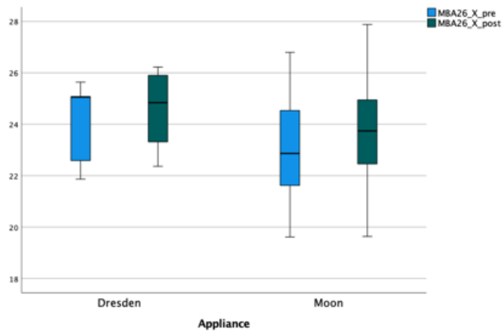
Dresden
Moon
Appliance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Dresden
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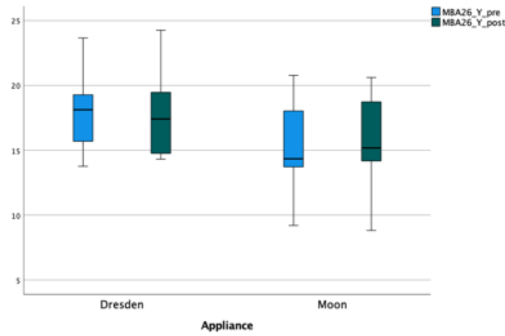
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Moon
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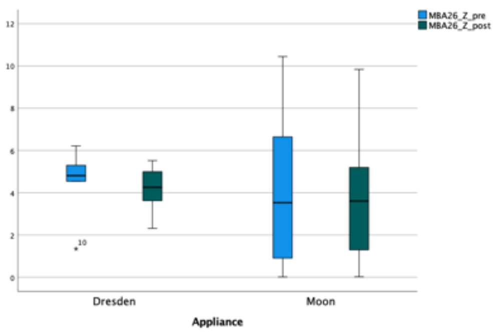
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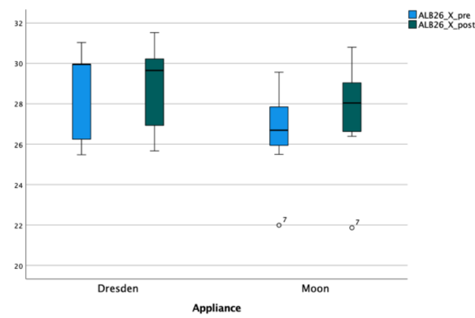
Appliance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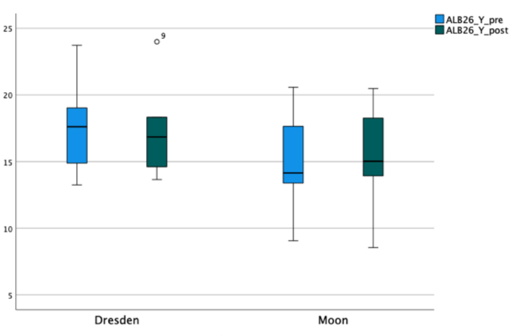
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ALB26_Y_post
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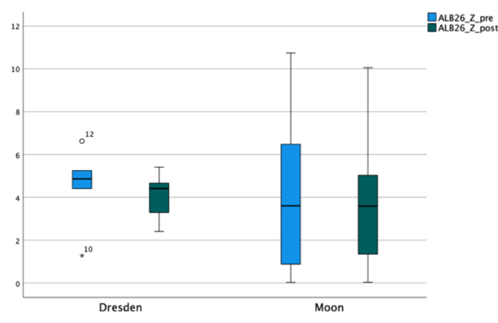
Dresden
Moon
Appliance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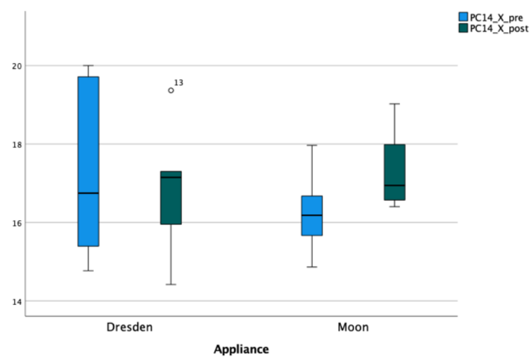
Dresden
Moon
Appliance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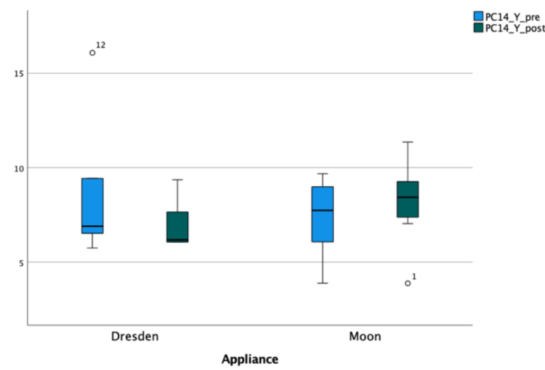
Dresden
Moon
Appliance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PC14_Y_post
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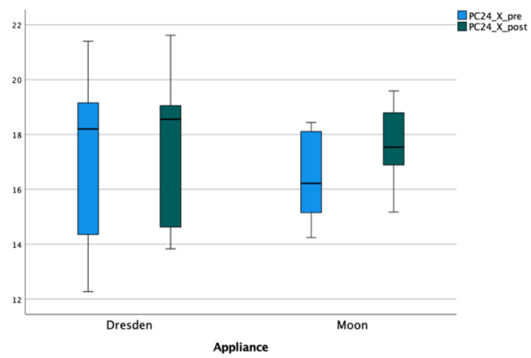
Dresden
Moon
Appliance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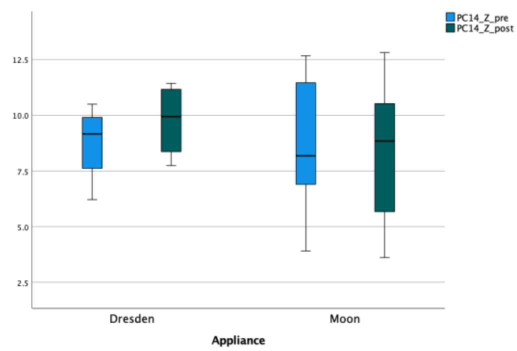
Moon
Appliance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PC14_Z_post
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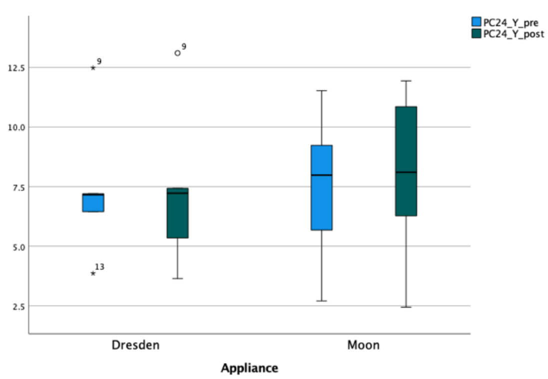
7.5
5.0
2.5
Dresden
Moon
Appliance


PC24_Y_pre
PC24_Y_post
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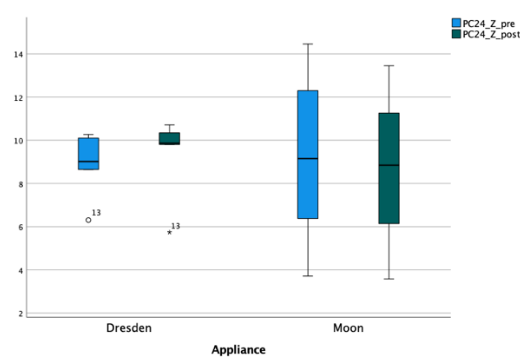
7.5
5.0
2.5
9
9
13
Dresden
Moon
Appliance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PC24_Z_post
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Dresden
Moon
Appliance

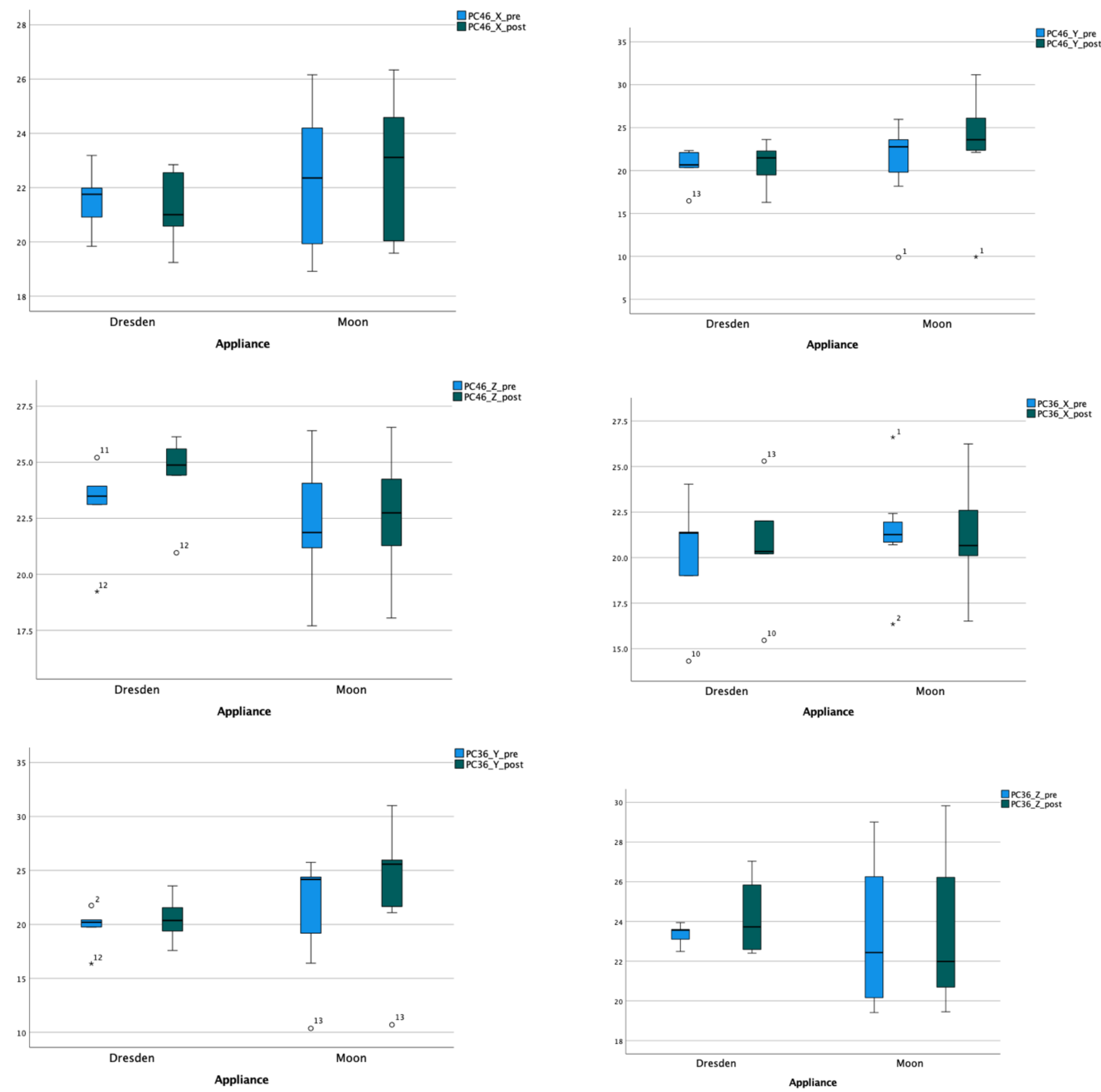

Figure A4.1 Box plot of HCR, HCL, PC16, MBA16, ALB16, PC26, MBA26, ALB26, PC14, PC24, PC46, PC36 for the Dresden and Moon expanders in X, Y, Z directions at T_0 and T_1.

Table A4.8 Levene's test of Equality of Error Variances

Skeletal/Dental landmark	Sig. *(Based on Mean)*	Adjusted Bonferroni p-value[1]	Skeletal/Dental landmark	Sig.*(Based on Mean)*	Adjusted Bonferroni p-value
HCR_X_Pre	0.14	1.00	MBA26_X_Pre	0.75	1.00
HCR_X_Post	0.02	0.76	MBA26_X_Post	0.60	1.00
HCR_Y_Pre	0.20	1.00	MBA26_Y_Pre	0.96	1.00
HCR_Y_Post	0.32	1.00	MBA26_Y_Post	0.83	1.00
HCR_Z_Pre	0.48	1.00	MBA26_Z_Pre	0.08	1.00
HCR_Z_Post	0.31	1.00	MBA26_Z_Post	0.16	1.00
HCL_X_Pre	0.20	1.00	ALB26_X_Pre	0.40	1.00
HCL_X_Post	0.52	1.00	ALB26_X_Post	0.87	1.00
HCL_Y_Pre	0.60	1.00	ALB26_Y_Pre	0.86	1.00
HCL_Y_Post	0.55	1.00	ALB26_Y_Post	0.88	1.00
HCL_Z_Pre	0.44	1.00	ALB26_Z_Pre	0.10	1.00
HCL_Z_Post	0.89	1.00	ALB26_Z_Post	0.19	1.00
PC16_X_Pre	0.30	1.00	PC14_X_Pre	0.01	0.36
PC16_X_Post	0.74	1.00	PC14_X_Post	0.26	1.00
PC16_Y_Pre	0.94	1.00	PC14_Y_Pre	0.17	1.00
PC16_Y_Post	0.86	1.00	PC14_Y_Post	0.63	1.00
PC16_Z_Pre	0.23	1.00	PC14_Z_Pre	0.19	1.00
PC16_Z_Post	0.05	1.00	PC14_Z_Post	0.24	1.00
MBA16_X_Pre	0.51	1.00	PC24_X_Pre	0.02	0.72
MBA16_X_Post	0.42	1.00	PC24_X_Post	0.02	0.72
MBA16_Y_Pre	0.27	1.00	PC24_Y_Pre	0.94	1.00
MBA16_Y_Post	0.06	1.00	PC24_Y_Post	0.92	1.00
MBA16_Z_Pre	0.04	1.00	PC24_Z_Pre	0.08	1.00
MBA16_Z_Post	0.10	1.00	PC24_Z_Post	0.25	1.00
ALB16_X_Pre	0.57	1.00	PC46_X_Pre	0.07	1.00
ALB16_X_Post	0.85	1.00	PC46_X_Post	0.10	1.00
ALB16_Y_Pre	0.30	1.00	PC46_Y_Pre	0.20	1.00
ALB16_Y_Post	0.05	1.00	PC46_Y_Post	0.39	1.00
ALB16_Z_Pre	0.06	1.00	PC46_Z_Pre	0.53	1.00

Skeletal/Dental landmark	Sig. *(Based on Mean)*	Adjusted Bonferroni p-value[1]	Skeletal/Dental landmark	Sig.*(Based on Mean)*	Adjusted Bonferroni p-value
ALB16_Z_Pre	0.13	1.00	PC46_Z_Post	0.48	1.00
PC26_X_Pre	0.44	1.00	PC36_X_Pre	0.51	1.00
PC26_X_Post	0.72	1.00	PC36_X_POst	0.87	0.86
PC26_Y_Pre	0.59	1.00	PC36_Y_Pre	0.07	1.00
PC26_Y_Post	0.48	1.00	PC36_Y_Post	0.18	1.00
PC26_Z_Pre	0.01	0.40	PC36_Z_Pre	0.06	1.00
PC26_Z_Post	0.00	0.14	PC36_Z_Post	0.07	1.00

1.Adjusted Bonferroni p-value= p-value*36

2.*Significant Adjusted p-value

Table A4.9 Tests of within-subject effects for Skeletal and Dental changes

Skeletal/Dental landmark	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
HCR_X	PrePost	1	0.56	1.55	0.24	1.00
	PrePost*Appliance	1	0.96	2.67	0.13	1.00
	Error (PrePost)	11	0.36	-	-	-
HCR_Y	PrePost	1	0.50	2.63	0.13	1.00
	PrePost*Appliance	1	0.01	0.05	0.83	1.00
	Error (PrePost)	11	0.19	-	-	-
HCR_Z	PrePost	1	0.08	0.04	0.85	1.00
	PrePost*Appliance	1	0.93	0.50	0.50	1.00
	Error (PrePost)	11	1.87	-	-	-
HCL_X	PrePost	1	0.11	0.72	0.41	1.00
	PrePost*Appliance	1	0.47	3.16	0.10	1.00
	Error (PrePost)	11	0.15	-	-	-
HCL_Y	PrePost	1	0.22	0.63	0.44	1.00
	PrePost*Appliance	1	0.38	1.11	0.32	1.00
	Error (PrePost)	11	0.34	-	-	-

Skeletal/Dental landmark	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
HCL_Z	PrePost	1	0.33	0.30	0.59	1.00
	PrePost*Appliance	1	1.50	1.37	0.27	1.00
	Error (PrePost)	11	1.09	-	-	-
PC16_X	PrePost	1	10.44	19.84	<0.001	**0.04***
	PrePost*Appliance	1	2.32	4.40	0.06	1.00
	Error (PrePost)	11	0.53	-	-	-
PC16_Y	PrePost	1	0.00	0.00	0.98	1.00
	PrePost*Appliance	1	2.80	2.24	0.16	1.00
	Error (PrePost)	11	1.25	-	-	-
PC16_Z	PrePost	1	0.12	0.29	0.60	1.00
	PrePost*Appliance	1	1.40	3.23	0.10	1.00
	Error (PrePost)	11	0.43	-	-	-
MBA16_X	PrePost	1	1.79	4.50	0.06	1.00
	PrePost*Appliance	1	0.01	0.03	0.87	1.00
	Error (PrePost)	11	0.40	-	-	-
MBA16_Y	PrePost	1	0.00	0.00	0.96	1.00
	PrePost*Appliance	1	0.13	0.22	0.65	1.00
	Error (PrePost)	11	0.56	-	-	-
MBA16_Z	PrePost	1	1.79	3.69	0.08	1.00
	PrePost*Appliance	1	0.19	0.39	0.55	1.00
	Error (PrePost)	11	0.48	-	-	-
ALB16_X	PrePost	1	1.66	8.16	0.02	0.72
	PrePost*Appliance	1	1.92	9.44	0.01	0.36
	Error (PrePost)	11	0.20	-	-	-
ALB16_Y	PrePost	1	0.00	0.00	0.96	1.00
	PrePost*Appliance	1	0.54	0.75	0.41	1.00
	Error (PrePost)	11	0.72	-	-	-
ALB16_Z	PrePost	1	2.55	5.59	0.04	1.00
	PrePost*Appliance	1	0.14	0.31	0.59	1.00
	Error (PrePost)	11	0.46	-	-	-

Skeletal/Dental landmark	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
PC26_X	PrePost	1	16.85	29.02	<0.001	**0.04***
	PrePost*Appliance	1	2.65	4.57	0.06	1.00
	Error (PrePost)	11	0.58	-	-	-
PC26_Y	PrePost	1	0.01	0.00	0.95	1.00
	PrePost*Appliance	1	1.08	0.52	0.49	1.00
	Error (PrePost)	11	2.09	-	-	-
PC26_Z	PrePost	1	2.10	4.77	0.05	1.00
	PrePost*Appliance	1	0.53	1.20	0.30	1.00
	Error (PrePost)	11	0.44	-	-	-
MBA26_X	PrePost	1	2.05	9.99	0.01	0.36
	PrePost*Appliance	1	0.05	0.26	0.62	1.00
	Error (PrePost)	11	0.21	-	-	-
MBA26_Y	PrePost	1	0.20	0.18	0.68	1.00
	PrePost*Appliance	1	0.37	0.32	0.58	1.00
	Error (PrePost)	11	1.15	-	-	-
MBA26_Z	PrePost	1	0.59	1.00	0.34	1.00
	PrePost*Appliance	1	0.00	0.00	0.98	1.00
	Error (PrePost)	11	0.59	-	-	-
ALB26_X	PrePost	1	2.26	15.23	0.002	0.072
	PrePost*Appliance	1	0.71	4.81	0.05	1.00
	Error (PrePost)	11	0.15	-	-	-
ALB26_Y	PrePost	1	0.07	0.08	0.78	1.00
	PrePost*Appliance	1	0.65	0.70	0.42	1.00
	Error (PrePost)	11	0.93	-	-	-
ALB26_Z	PrePost	1	0.94	1.37	0.27	1.00
	PrePost*Appliance	1	0.02	0.03	0.87	1.00
	Error (PrePost)	11	0.68	-	-	-
PC14_X	PrePost	1	0.52	1.03	0.33	1.00
	PrePost*Appliance	1	3.73	7.36	0.02	0.72

Skeletal/Dental landmark	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
	Error (PrePost)	11	0.51	-	-	-
PC14_Y	PrePost	1	1.85	0.50	0.50	1.00
	PrePost*Appliance	1	10.81	2.90	0.12	1.00
	Error (PrePost)	11	3.72	-	-	-
PC14_Z	PrePost	1	0.50	0.47	0.51	1.00
	PrePost*Appliance	1	2.61	2.49	0.15	1.00
	Error (PrePost)	11	1.05	-	-	-
PC24_X	PrePost	1	4.23	20.67	<0.001	**0.04***
	PrePost*Appliance	1	0.83	4.06	0.07	1.00
	Error (PrePost)	11	0.21	-	-	-
PC24_Y	PrePost	1	0.42	0.21	0.65	1.00
	PrePost*Appliance	1	0.73	0.37	0.56	1.00
	Error (PrePost)	11	1.98	-	-	-
PC24_Z	PrePost	1	0.02	0.03	0.86	1.00
	PrePost*Appliance	1	1.42	2.33	0.16	1.00
	Error (PrePost)	11	0.61	-	-	-
PC46_X	PrePost	1	0.01	0.04	0.86	1.00
	PrePost*Appliance	1	0.64	2.28	0.16	1.00
	Error (PrePost)	11	0.28	-	-	-
PC46_Y	PrePost	1	9.62	3.68	0.08	0.79
	PrePost*Appliance	1	6.18	2.36	0.16	1.00
	Error (PrePost)	11	2.62	-	-	-
PC46_Z	PrePost	1	4.10	7.57	0.02	0.72
	PrePost*Appliance	1	1.85	3.42	0.09	1.00
	Error (PrePost)	11	0.54	-	-	-
PC36_X	PrePost	1	0.36	0.96	0.35	1.00
	PrePost*Appliance	1	0.89	2.34	0.16	1.00
	Error (PrePost)	11	0.38	-	-	-
PC36_Y	PrePost	1	12.70	4.81	0.05	1.00
	PrePost*Appliance	1	2.71	1.03	0.34	1.00

Skeletal/Dental landmark	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
	Error (PrePost)	11	2.64	-	-	-
PC36_Z	PrePost	1	2.03	2.42	0.15	1.00
	PrePost*Appliance	1	0.88	1.05	0.33	1.00
	Error (PrePost)	11	0.84	-	-	-

1. Adjusted Bonferroni p-value= p-value*36
2. *Significant Adjusted p-value

Table A4.10 Tests of between-subject effects for Skeletal and Dental changes

Skeletal/Dental Landmarks	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
HCR_X	Appliance	1	73.37	8.68	0.01	0.36
	Error	11	8.45	-	-	-
HCR_Y	Appliance	1	1.15	0.05	0.82	1.00
	Error	11	22.00	-	-	-
HCR_Z	Appliance	1	16.00	0.57	0.47	1.00
	Error	11	28.28	-	-	-
HCL_X	Appliance	1	7.46	1.79	0.21	1.00
	Error	11	4.16	-	-	-
HCL_Y	Appliance	1	2.14	0.08	0.78	1.00
	Error	11	26.59	-	-	-
HCL_Z	Appliance	1	18.14	0.60	0.46	1.00
	Error	11	30.18	-	-	-
PC16_X	Appliance	1	1.43	0.19	0.67	1.00
	Error	11	7.48	-	-	-
PC16_Y	Appliance	1	4.56	0.30	0.59	1.00
	Error	11	15.17	-	-	-
PC16_Z	Appliance	1	11.76	0.64	0.44	1.00
	Error	11	18.50	-	-	-

Skeletal/Dental Landmarks	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
MBA16_X	Appliance	1	10.98	1.68	0.22	1.00
	Error	11	6.54	-	-	-
MBA16_Y	Appliance	1	0.20	0.01	0.92	1.00
	Error	11	17.58	-	-	-
MBA16_Z	Appliance	1	0.53	0.03	0.86	1.00
	Error	11	17.07	-	-	-
ALB16_X	Appliance	1	10.68	2.25	0.16	1.00
	Error	11	4.74	-	-	-
ALB16_Y	Appliance	1	0.37	0.02	0.89	1.00
	Error	11	18.29	-	-	-
ALB16_Z	Appliance	1	0.78	0.05	0.84	1.00
	Error	11	17.26	-	-	-
PC26_X	Appliance	1	11.49	0.63	0.45	1.00
	Error	11	18.35	-	-	-
PC26_Y	Appliance	1	9.59	0.29	0.60	1.00
	Error	11	32.83	-	-	-
PC26_Z	Appliance	1	14.55	0.57	0.47	1.00
	Error	11	25.50	-	-	-
MBA26_X	Appliance	1	4.95	0.55	0.47	1.00
	Error	11	8.93	-	-	-
MBA26_Y	Appliance	1	41.20	1.53	0.24	1.00
	Error	11	26.88	-	-	-
MBA26_Z	Appliance	1	0.86	0.05	0.82	1.00
	Error	11	16.21	-	-	-
ALB26_X	Appliance	1	16.35	1.36	0.27	1.00
	Error	11	11.99	-	-	-
ALB26_Y	Appliance	1	34.73	1.26	0.29	1.00
	Error	11	27.67	-	-	-
ALB26_Z	Appliance	1	0.71	0.04	0.84	1.00
	Error	11	16.59	-	-	-

Skeletal/Dental Landmarks	Source	df	Mean square	F	Sig.	Adjusted Bonferroni p-value[1]
PC14_X	Appliance	1	0.60	0.15	0.71	1.00
	Error	11	4.04	-	-	-
PC14_Y	Appliance	1	0.29	0.03	0.86	1.00
	Error	11	9.10	-	-	-
PC14_Z	Appliance	1	3.02	0.21	0.65	1.00
	Error	10	14.10	-	-	-
PC24_X	Appliance	1	0.40	0.04	0.86	1.00
	Error	11	11.59	-	-	-
PC24_Y	Appliance	1	1.05	0.06	0.81	1.00
	Error	11	17.97	-	-	-
PC24_Z	Appliance	1	0.09	0.01	0.95	1.00
	Error	11	18.31	-	-	-
PC46_X	Appliance	1	6.25	0.58	0.46	1.00
	Error	11	10.75	-	-	-
PC46_Y	Appliance	1	11.92	0.26	0.62	1.00
	Error	11	45.83	-	-	-
PC46_Z	Appliance	1	8.47	0.65	0.44	1.00
	Error	11	13.08	-	-	-
PC36_X	Appliance	1	5.71	0.27	0.61	1.00
	Error	11	21.05	-	-	-
PC36_Y	Appliance	1	24.41	0.55	0.48	1.00
	Error	11	44.43	-	-	-
PC36_Z	Appliance	1	0.69	0.04	0.85	1.00
	Error	11	18.78	-	-	-

1. Adjusted Bonferroni p-value= p-value*36
2. *Significant Adjusted p-value

Table A4.11 Within Group Pairwise Comparison for PC16_X, PC26_X, and PC24_X based on estimated marginal means

Measure	PrePost (I)	PrePost (J)	Mean Difference (I-J)	Std. Error	Sig.	Adjusted Bonferroni p-value[1]	95% confidence Interval: Lower Bound	95% confidence Interval: Upper Bound
PC16_X	2	1	1.30	0.29	<0.001	0.04	0.66	1.95
PC26_X	2	1	1.66	0.31	<0.001	0.04	0.98	2.33
PC24_X	2	1	0.83	0.18	<0.001	0.04	0.43	1.23

1. Adjusted Bonferroni p-value= p-value*36

Table A4.12 Paired sample t-test demonstrating changes in X, Y, Z directions (T1-T0) for Moon and Dresden appliances

Skeletal/ Dental Landmark	Appliance	Mean Difference (T_1-T_0)	Standard Deviation	Direction of Movement	% Change	P-Value	Adjusted Bonferroni p-value
HCR_X	Dresden	-0.70	0.71	Left	3.13%	0.09	1.00
	Moon	0.09	0.92	Right	0.50%	0.78	1.00
HCR_Y	Dresden	-0.32	0.42	Front	0.41%	0.16	1.00
	Moon	-0.25	0.71	Front	0.31%	0.36	1.00
HCR_Z	Dresden	-0.28	2.23	Downward	1.82%	0.79	1.00
	Moon	0.50	1.75	Upward	3.75%	0.45	1.00
HCL_X	Dresden	0.41	0.75	Left	2.10%	0.29	1.00
	Moon	-0.15	0.39	Right	0.78%	0.33	1.00
HCL_Y	Dresden	0.06	0.64	Back	0.08%	0.84	1.00
	Moon	-0.44	0.92	Front	0.55%	0.22	1.00
HCL_Z	Dresden	-0.73	1.71	Downward	4.64%	0.40	1.00
	Moon	0.26	1.33	Upward	1.95%	0.59	1.00
PC16_X	Dresden	0.69	1.35	Right	3.51%	0.32	1.00
	Moon	**1.92***	0.79	Right	**9.83%***	**<0.001***	**0.04***
PC16_Y	Dresden	-0.66	0.94	Front	3.11%	0.19	1.00
	Moon	0.69	1.85	Back	3.20%	0.33	1.00
PC16_Z	Dresden	0.62	0.90	Downward	3.80%	0.20	1.00

Skeletal/ Dental Landmark	Appliance	Mean Difference (T_1-T_0)	Standard Deviation	Direction of Movement	% Change	P-Value	Adjusted Bonferroni p-value
	Moon	-0.34	0.95	Upward	2.19%	0.35	1.00
MBA16_X	Dresden	0.58	0.85	Right	2.51%	0.20	1.00
	Moon	0.50	0.92	Right	2.03%	0.17	1.00
MBA16_Y	Dresden	-0.16	0.58	Front	0.97%	0.57	1.00
	Moon	0.13	1.25	Back	77.10%	0.78	1.00
MBA16_Z	Dresden	0.71	0.73	Upward	28.68%	0.09	1.00
	Moon	0.36	1.10	Upward	12.32%	0.38	1.00
ALB16_X	Dresden	-0.04	0.24	Left	0.14%	0.74	1.00
	Moon	1.08	0.78	Right	3.81%	0.01	0.36
ALB16_Y	Dresden	-0.31	0.61	Front	1.88%	0.31	1.00
	Moon	0.28	1.44	Back	1.67%	0.60	1.00
ALB16_Z	Dresden	0.80	0.76	Downward	32.85%	0.08	1.00
	Moon	0.49	1.05	Downward	16.75%	0.23	1.00
PC26_X	Dresden	1.00	1.32	Left	5.14%	0.17	1.00
	Moon	**2.31***	0.91	Left	**11.49%***	**<0.001***	**0.04***
PC26_Y	Dresden	-0.38	1.17	Front	1.70%	0.51	1.00
	Moon	0.46	2.40	Back	2.19%	0.61	1.00
PC26_Z	Dresden	-0.29	0.96	Upward	1.68%	0.53	1.00
	Moon	-0.88	0.93	Upward	5.44%	0.03	1.00
MBA26_X	Dresden	0.49	0.41	Left	2.02%	0.06	1.00
	Moon	0.67	0.74	Left	2.90%	0.04	1.00
MBA26_Y	Dresden	-0.06	0.71	Front	0.35%	0.85	1.00
	Moon	0.43	1.82	Back	2.80%	0.53	1.00
MBA26_Z	Dresden	-0.30	1.20	Downward	6.75%	0.61	1.00
	Moon	-0.32	1.02	Downward	7.82%	0.41	1.00
ALB26_X	Dresden	0.27	0.37	Left	0.93%	0.19	1.00
	Moon	0.95	0.62	Left	3.56%	0.004	0.144
ALB26_Y	Dresden	-0.21	0.54	Front	1.21%	0.42	1.00
	Moon	0.43	1.66	Back	2.89%	0.48	1.00
ALB26_Z	Dresden	-0.45	1.33	Upward	9.98%	0.49	1.00

Skeletal/ Dental Landmark	Appliance	Mean Difference (T_1-T_0)	Standard Deviation	Direction of Movement	% Change	P-Value	Adjusted Bonferroni p-value
	Moon	-0.33	0.69	Upward	8.14%	0.41	1.00
PC14_X	Dresden	-0.49	1.31	Left	2.81%	0.45	1.00
	Moon	1.07	0.79	Right	6.58%	0.01	0.36
PC14_Y	Dresden	-1.87	3.69	Front	20.96%	0.32	1.00
	Moon	0.78	1.98	Back	10.50%	0.30	1.00
PC14_Z	Dresden	1.00	0.76	Downward	11.46%	0.43	1.00
	Moon	-0.39	1.66	Upward	4.52%	0.52	1.00
PC24_X	Dresden	0.46	0.64	Left	2.71%	0.18	1.00
	Moon	**1.20***	0.64	Left	**7.28%***	**<0.001***	**0.04***
PC24_Y	Dresden	-0.08	1.04	Front	1.12%	0.87	1.00
	Moon	0.61	2.37	Back	8.07%	0.49	1.00
PC24_Z	Dresden	0.43	0.86	Downward	4.79%	0.33	1.00
	Moon	-0.54	1.22	Upward	5.82%	0.26	1.00
PC46_X	Dresden	-0.29	0.66	Left	1.34%	0.38	1.00
	Moon	0.37	0.80	Right	1.67%	0.26	1.00
PC46_Y	Dresden	0.26	1.01	Back	1.25%	0.60	1.00
	Moon	2.31	2.84	Back	11.13%	0.07	1.00
PC46_Z	Dresden	1.40	0.73	Downward	6.09%	0.01	0.36
	Moon	0.28	1.21	Downward	1.23%	0.57	1.00
PC36_X	Dresden	0.64	0.98	Left	3.20%	0.22	1.00
	Moon	-0.14	0.79	Right	0.66%	0.65	1.00
PC36_Y	Dresden	0.79	1.87	Back	4.03%	0.40	1.00
	Moon	2.16	2.54	Back	10.24%	0.07	1.00
PC36_Z	Dresden	0.98	1.79	Downward	4.19%	0.29	1.00
	Moon	0.20	0.82	Downward	0.86%	0.54	1.00

1. *Significant Adjusted p-value

4.1.2A. ***Step by step of landmark identification in the Avizo software:***

1. Open DICOM data in Avizo software and select the "Project" tab.

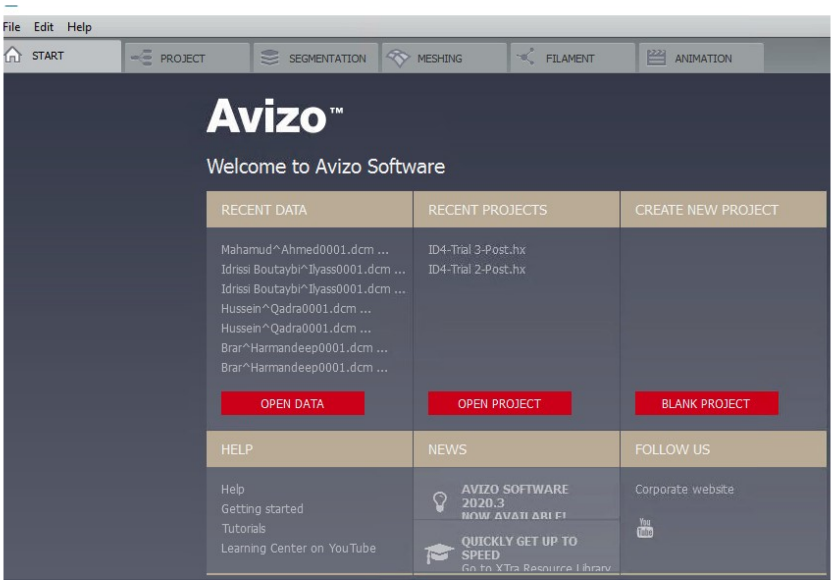

Figure A4.2 Avizo software

2. Right click on patient's chart number, click on "display", "Isosurface", and "create". This allows us to choose the threshold (between 500-1000). Do the same thing one more time and choose "ortho slice" this time and click on "create". This allows us to go through different CBCT slices in different planes.

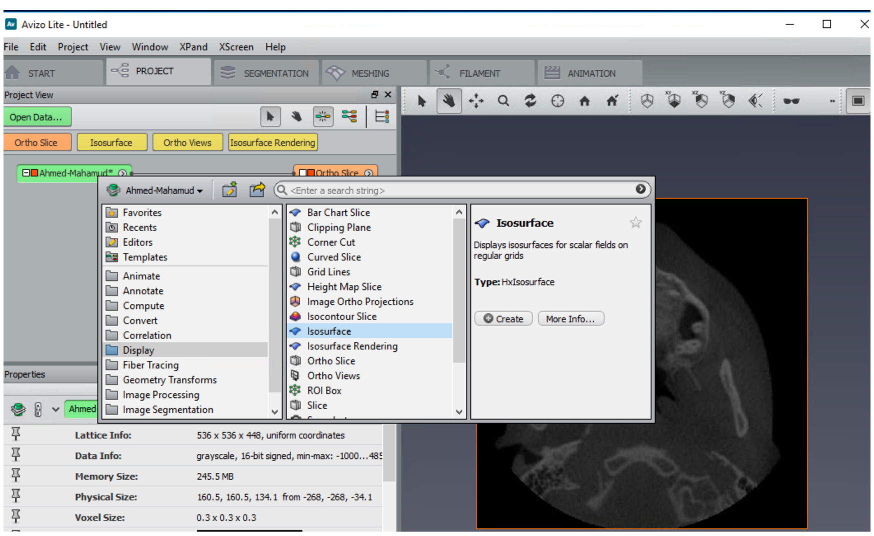

Figure A4.3 Isosurface icon allows changing of the threshold.

3. Threshold is set between 500-1000.

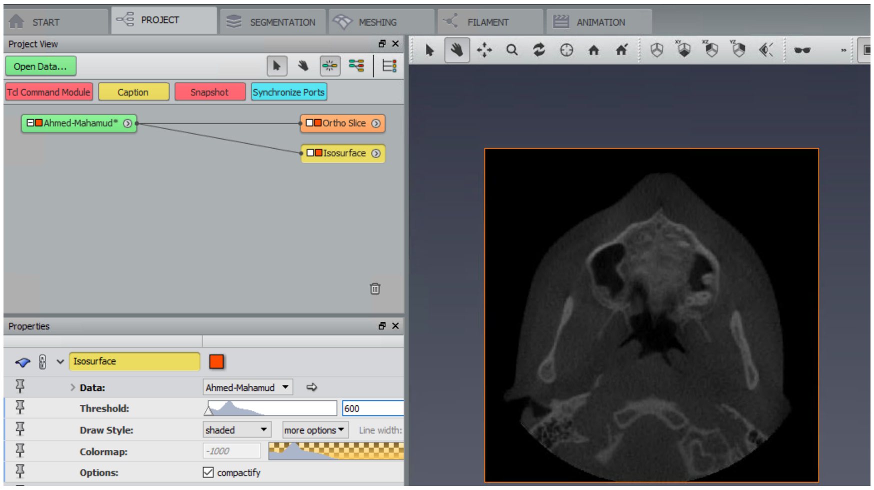

Figure A4.4 Threshold set between 500-1000.

4. To select the spherical marker, click on "project" on top right-hand side, then click on "create object", "points and lines", "landmarks", and "create". Spherical marker was set at 0.5 mm for this analysis.

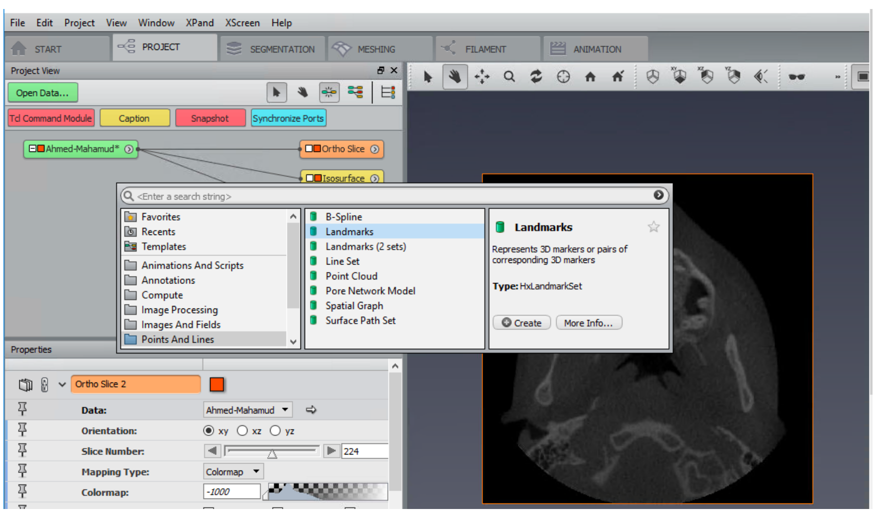

Figure A4.5 To select the spherical marker, click on "project" on top right-hand side, then "create object", "points and lines", "landmarks", and "create."

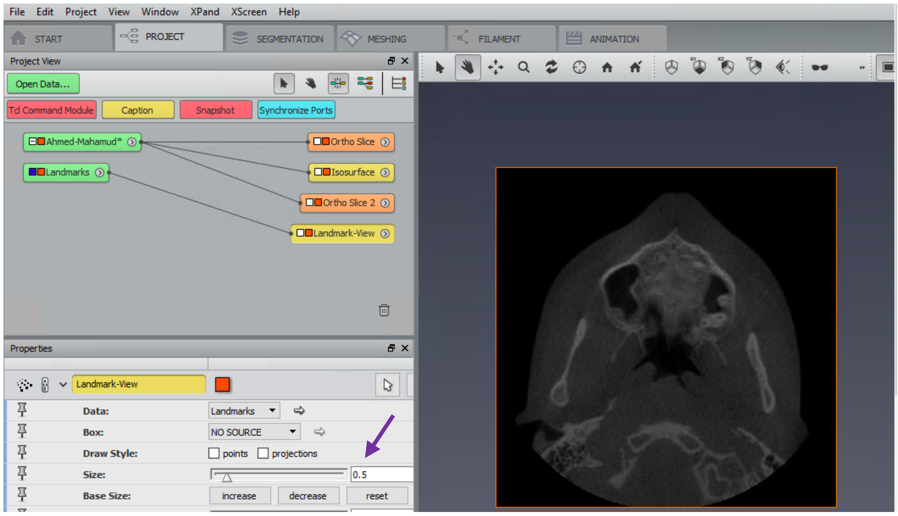

Figure A4.6 Spherical marker was set at 0.5 mm (purple arrow).

5. To save the landmarks into excel 2021, click on “landmarks”, choose “file” on Left hand -side, “save data as”, and then save. That will create a file for the patient. Then open an excel sheet, click on “file”, open and choose “all files”, “delimited” (tab and space), and click on “finish”. This will give the x, y, z coordinates in the order they were selected in the Avizo software.

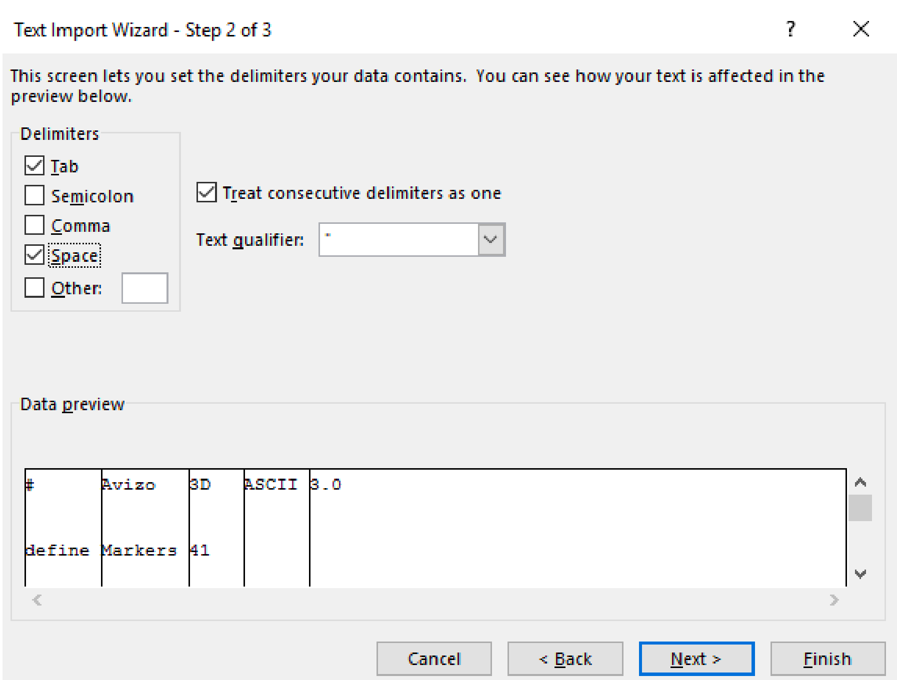

Figure A4.7 Save the selected landmarks by selecting “delimiters” and clicking on “tab” and “space” options.

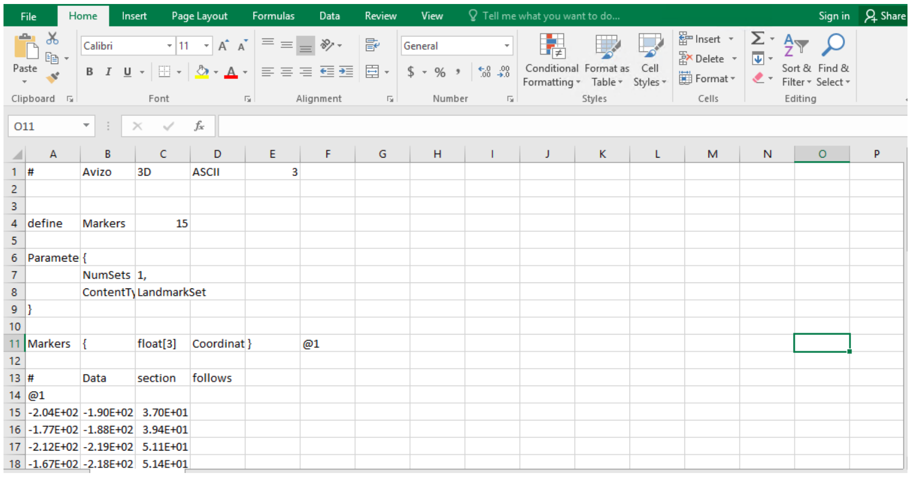

Figure A4.8 Saving the landmarks in Excel 2021.

Appendix 4

Table A5.1 Normative values for PNIFBN, PNIFLB, PNIFRB in males and females[1]

	Males (n=52)		Females (n=45)	
Variable	Mean	SD	Mean	SD
Age	42.80	15.65	42.16	16.77
Height (cm)	177.20	8.51	164.30	7.38
PNIFRB (L/min)	111.80	42.92	86.74	29.89
PNIFLB(L/min)	107.80	35.61	87.44	31.07
PNIFBN(L/min)	158.10	44.77	126.70	36.09

1. Table retrieved from MO et al, 2012[103]

***numbers might be slightly different depending on the study