Soft Tissue Facial Changes in Patients 7-11 years of age having Maxillary Expansion

by

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Abstract

Introduction: Maxillary transverse discrepancies are typically treated with palatal expansion treatment modalities. In addition to skeletal and dental changes with maxillary segment width enhancement, maxillary expansion may also impact the facial soft tissues, and past studies have shown varied results. The objective of this study is to evaluate the effects of maxillary expansion on facial soft tissues in children aged 7-11 years, utilizing both CBCTs and 3D facial scans.

Methods: Data was collected from 32 patients, consisting of two groups: control and treatment (Hyrax expansion via RME, 1 turn/day). The inclusion criteria were as follows: patients 7-11 years of age presenting with a maxillary transverse deficiency of at least 5mm or bilateral posterior crossbite. The exclusion criteria were as follows: patients with any previous history of craniofacial diseases or syndromes and any previous history of orthodontic therapy or maxillary expansion. Each patient in each group underwent CBCTs, 3D facial scans and hand-wrist radiographs at two time points: pre-treatment (T0, before maxillary expansion), after the completion of expansion at post-retention (T1, 12 months after). CBCTs were assessed using 3D Slicer software and 3D facial scans were assessed using OrthoInsight 3D software. The soft tissue measurements evaluated included the following: alar width, alar base width, mouth width, philtrum width, nasal tip prominence, nasolabial angle, upper lip to E-line, lower lip to E-line, upper lip height, height of vermillion of upper lip, lower lip height, height of nose, lower facial height and intercanthal width.

Results: Children aged 7-11 years who have undergone rapid maxillary expansion experience facial soft tissue changes comparable to patients who have not undergone any expansion, in regards to both CBCTs and 3D facial scans, with no statistically significant differences found between the two groups over the one-year observation period. However, when comparing the two modalities utilized in this study (CBCT imaging and 3D facial scanning), the correlation was not as optimal for specific outcome variables such as alar base width and intercanthal width, potentially due to anatomic, imaging protocols and patient related factors.

Conclusion:

The findings of this research study suggest that children between the ages of 7-11 years affected with maxillary transverse deficiency treated by rapid maxillary expansion using a Hyrax expansion device experience facial soft tissue changes similar to those of patients without any expansion, over a period of one year, in regards to both CBCTs and 3D facial scans. However, given the limitations with regard to imaging protocols and sample size, the results must be interpreted with caution.

Preface

This thesis is an original work by Nafisa Marium Molla. This research study was conducted at the Orthodontics Graduate Clinic at the University of Alberta with ethics approval from the Research Ethics Board (Pro00061538) from the University of Alberta. No part of this thesis has been previously published in any form.

Dedication

To Hussein, my love and soulmate,

For your unwavering support, love and encouragement, this work is dedicated to you.

Throughout my academic and personal journey since we met in dental school, you have been my pillar of strength, inspiring and guiding me through every opportunity and challenge.

Thank you for all your support and sacrifices, love, and inspiring me to dream big. This achievement is as much yours as it is mine and I look forward to the next steps in our journey and future together as a family (along with Mr. Cat).

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To my mother, Kumi, and my siblings Anisa and Shoon, thank you for your unconditional love and support, endless encouragement, sacrifices and belief in me. I could not be here without you all, including Taibo and Sumi.

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Chapter 1 – Introduction and Problem Statement

1.1 Introduction

Rapid maxillary expansion (RME) is a therapeutic modality utilized by orthodontists in order to increase the transverse dimension of the maxilla and correct transverse maxillary discrepancies [1-4]. It is a treatment option commonly utilized in cases presenting with posterior crossbite and maxillary crowding, and was initially introduced by E.C. Angell in 1860 [1, 2, 5, 6]. This method of expansion generally involves the use of a fixed or removable appliance in order to create expansion at an incompletely fused mid-palatal suture, and thus it is a treatment generally undertaken in the pediatric population [1-3]. It also can be utilized in adult populations, patients presenting with fused mid-palatal sutures, but in that case usually involves a combination approach with initial or concomitant surgical therapy [1-4]. Over the years, there have been different designs of appliances for maxillary expansion, ranging from removable, acrylic appliances to those that are banded or bonded, consisting of a midline screw [1, 6, 7]. In pediatric patients, RME entails activating an expansion screw in order to create mid-palatal sutural separation which thereby is expected to result in the formation of new bone [7, 8]. In addition to causing skeletal and dental changes, it has also been established that RME can influence the facial soft tissue profile of patients [1-3].

Huang et al conducted a systematic review and meta-analysis in 2018 which investigating the literature focusing on facial soft tissue changes resulting from nonsurgical RME in patient populations aged 6.7-15.6 years [2]. The authors concluded from their study that rapid maxillary expansion was shown to result in significantly increased nasal width,

mouth width, upper philtrum width, and distance from the lower lip to the E line after the retention phase [2]. Moreover, Berger et al. conducted a study in which they utilized sequential clinical extraoral photographs in order to assess soft tissue facial changes associated with surgical and rapid maxillary expansion treatment [9]. They concluded that both the surgical and non-surgical treatment groups showed statistically significant differences in nasal widths between the initial records and 1 year retention records [9]. Further adding support to the notion that rapid maxillary expansion results in both hard tissue and soft tissue changes is the cone beam computer tomography (CBCT) focused study by Torun [10]. In this study, 28 patients underwent expansion with bonded rapid maxillary expanders[10]. Each patient underwent pre-treatment and post-retention CBCT imaging [10]. The study concluded that both pre- and post-pubertal groups underwent statistically significant changes in soft tissue nasal base, philtrum width, upper lip length, columella width, columella height, and cheek projection [10].

Majority of studies on the effects of non-surgical RME have compared different types of expansion devices such as banded, bonded or modified expanders with acrylic splints [11-16]. In comparison, a fewer number of studies have compared experimental groups with a control group, which could potentially benefit us in differentiating whether the changes are due to natural growth and development or a true expression of the effects of non-surgical RME [17-20]. Different studies have also utilized different methods of assessing the outcomes – for example using lateral or antero-posterior cephalograms, CBCTs or three-dimensional stereophotogrammetry. However, to date, no studies have investigated soft tissue facial changes associated with rapid maxillary expansion utilizing

both CBCT and three-dimensional facial photographic scanning as investigating modalities [2, 10, 13]. The systematic review and meta-analysis by Huang et al indicated that studies by Torun and Pangrazio-Kulbersh et al utilized both CBCT and 3D imaging, but upon further investigation, the 3D images were renderings derived from CBCT data rather than three-dimensional facial photographic scanning [2, 10, 11]. Moreover, a research study by Abedini et al. published in 2018 was one of the few studies found focusing on maxillary skeletal expansion and the resulting effects on the soft tissues of the face as measured through the use of three-dimensional facial images (3dMD) [21]. This study, however, focused on the use of micro-implant supported maxillary skeletal expansion[21]. The study results indicated that “there are significant changes in paranasal, upper lip, and at both cheeks following expansion using (micro-implant supported expansion) [21].

As such, the current body of evidence may be benefited from a research study investigating facial soft tissue changes associated with RME utilizing CBCTs as well as 3D facial scans as investigating modalities, in addition to the inclusion of a control group for comparison, and that is the aim of this proposed research study.

1.2 Research Questions and Hypothesis

Part A

1. Are there differences in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)?
2. Are the CBCT and 3D facial scan derived facial soft tissue measurements jointly reliable at pre-treatment (T0), and post-treatment (T1)?

Part B

3. Are there differences in the mean facial soft tissue 3D facial scan measurements j jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)?
4. Are there differences in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)?
5. Are there differences in the mean change (T1-T0) of soft tissue 3D facial scan measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)?
6. Are there differences in the mean change (T1-T0) of soft tissue CBCT measurements jointly from pre-treatment (T0) to post-treatment (T1), between

patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)?

Hypotheses (Part A):

1. H_o → There is no difference in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)

   H_a→ There is a difference in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)

2. H_o → The CBCT and 3D facial scan derived facial soft tissue measurements jointly are reliable at pre-treatment (T0), and post-treatment (T1)

   H_a→ The CBCT and 3D facial scan derived facial soft tissue measurements jointly are not reliable at pre-treatment (T0), and post-treatment (T1)

Hypotheses (Part B):

3. H_o → There is no difference in the mean facial soft tissue 3D facial scan measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

   H_a→ There is a difference in the mean facial soft tissue 3D facial scan measurements jointly between patients that underwent maxillary expansion

(treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

4. H_o → There is no difference in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

   H_a→ There is a difference in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

5. H_o → There is no difference in the mean change (T1-T0) of soft tissue 3D facial scan measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)

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Chapter 2 – Soft Tissue Facial changes in Patients following Non-surgical, Rapid Maxillary Expansion: A Systematic Review

2.1 Introduction

A maxillary transverse deficiency is typically defined by a maxilla that is narrow in relation to the rest of the face [1]. It also commonly presents with a narrow palate and a posterior crossbite.[1] Maxillary transverse discrepancies are typically treated with maxillary or palatal expansion treatment modalities alongside orthodontic tooth movement [2].

There are three main types of expansion - namely rapid (RME), slow (SME) and surgically assisted maxillary expansion (SARME); the use of which varies according to the patient's age, dental and/or skeletal malocclusion as well as clinician preferences [1, 2]. The transverse is the first dentofacial dimension that stops growing, at the start of the bridging of the midpalatal suture, which is typically during early adolescence [1]. Therefore, transverse maxillary expansion prior to the adolescence stage would require less forces, whereas after adolescence it would require heavier forces or surgical intervention to open the midpalatal suture [1].

The main differences between RME and SME are the rate of activation and amount of forces applied – rapid expansion is carried out at a rate of 0.5mm per day (two quarter turns of a screw) at 10-20 pounds of pressure across the midpalatal suture, and slow expansion at a rate of less than 2mm per week at 2 pounds of pressure [1]. On the other hand, for patients that are in late adolescence or adulthood, microimplant-

supported expansion (MARPE) and surgically assisted maxillary expansion (SARME) are treatment modalities that are utilized [1, 2].

RME generally involves the use of a fixed or removable appliance in order to create expansion at an incompletely fused mid-palatal suture, and thus it is a treatment generally undertaken in the pediatric population [1-3]. In addition to causing skeletal changes and expansion at the mid-palatal suture and resulting maxillary segment width enhancement, it is important to note that studies have shown RME treatment also can influence and impact the facial soft tissues [1-4,9,10,13,18,21,22]. To date, many studies have investigated skeletal and dental changes associated with RME, as well as nasal airway changes. In comparison to such studies, a lesser number of studies have assessed the associated soft tissue changes, which is an important factor to consider, as orthodontic treatment aims to not only achieve occlusal harmony but also an esthetically pleasing soft tissue balance. In addition, some studies have reported significant short-term soft tissue changes whereas long-term changes are not deemed significant or are similar to natural growth. The objective of this systematic review was to methodically analyze the available literature investigating facial soft tissue changes that may occur after non-surgical, RME in patients with a maxillary transverse deficiency, especially considering that over the years, there have been many new advancements in technology and techniques with a shift from two dimensional to three dimensional imaging systems [2].

2.2 Materials and Methods

2.2.1 Study Protocol

This systematic review was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.[23]

2.2.2 Eligibility Criteria - Inclusion and Exclusion Criteria

A PICOS (population, intervention, comparison, outcomes, study design) question was established as inclusion criteria. The population of interest were medically and orally healthy individuals. The intervention was non-surgical, rapid maxillary expansion. The comparison involved the changes of the soft tissue profile of patients undergoing expansion with either different types of non-surgical, RME appliances or patients that did not undergo any sort of expansion. Included study types were randomized controlled trials (RCTs), clinically controlled trials (CCTs), and prospective/retrospective clinical studies (PCS/RCS). The outcome of interest was soft tissue changes in the orofacial region after rapid maxillary expansion. Subsequently, patients were excluded if they presented with craniofacial diseases or syndromes or if they had any previous orthodontic therapy. In vitro or animal studies, reviews, case reports, and commentaries were also excluded.

2.2.3 Search strategy

A literature search was done in August 2022, across the following electronic databases: Cochrane Library (Wiley), PubMed and Medline via Ovid, and Google Scholar. No time or language restrictions were applied in order to attain the maximum number of results related to maxillary expansion. A great diversity of keywords combinations were utilized during the search process. Utilized keywords were Palatal or Maxillary expander or expansion technique, Rapid or Removable or Fixed, facial, nasal lip(s), cheek, mouth, chin measure or outcome or result. A summary of the search strategy and keywords can be visualized in Appendix 2A.

2.2.4 Study Selection

The process to screen the papers was performed by two authors in an independent manner. The initial screening consisted of examining the title and abstract of generated records directly on the database search. After that step, full-text studies that appeared to meet our inclusion criteria were downloaded for further assessment. The same authors independently performed a second screening of the remaining records. The final selection of studies was made by discussion between authors under PICOS-based inclusion/exclusion criteria. Disagreements were settled through discussion and consensus, and when required, a third author's opinion. The citations were saved in a bibliographic reference manager (EndNote, X9 version; Clarivate Analytics, Philadelphia, Pa).

2.2.5 Data Extraction and Items Extracted

A standardized table (Table 1, Appendix 2B) was utilized for extracting the following data: authors, study design, year of publication, participant characteristics, description of groups, interventions, analyses, and main conclusions. Any discrepancies were resolved through re-evaluation of the study in question, and the data was compared for accuracy.

2.2.6 Risk of bias in Individual Studies and Quality of Evidence

The studies were evaluated by two reviewers (NMM and RC) utilizing the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) and the ROBINS-I tool for The Risk of Bias In Non-randomized Studies - of Interventions. [12-14] Disagreements were resolved by consensus and a third reviewer (MG) where necessary.

2.3 Results

2.3.1 Study Selection

Figure 2.1 presents the selection process of the studies via a flowchart. The search strategy in the above mentioned databases yielded a total of 987 records. After deleting duplicates, there were 763 records for screening, from which 747 were excluded. Sixteen records were selected for full-text reading, out of which four studies were excluded.

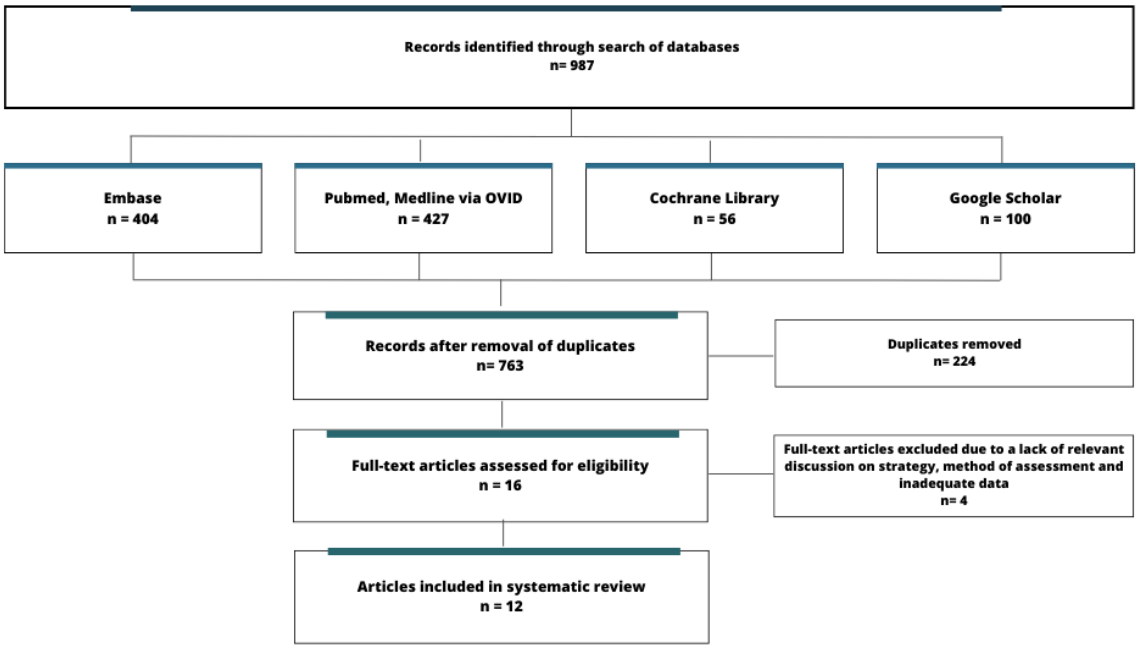


Figure 2.1 Flow diagram depicting selection of studies

2.3.2 Study characteristics

Tables 1 and 2 in Appendix 2B present the descriptive characteristics of the twelve studies included in the systematic review. The selected studies were based in five different countries including Brazil(1), Hungary(1), Italy(1), Turkey(6), and United States(3).

The sample size of the different studies ranged from 18 to 102 participants, with age ranges between 7 to 16 years. The observation timepoints for the outcome evaluations varied amongst the studies, with six out of the twelve studies evaluating at two different timepoints [10-14, 18 and the remainder at three different timepoints [15-17,19,20,27].

Evaluation times included at baseline for T0 to immediately post-expansion for T1 and ranging from 4 months to 2.84 years post expansion for T2.

Majority of the studies identified the appliance type and expansion protocol followed. The expansion protocol was not identified in two studies [13,19]. In addition, three studies stated the total number of turns of the appliance screw [11,12,18]. Five studies stated the amount of expansion done in millimeters [10,13,18,27], whereas the rest of the studies mentioned that expansion was done until the crossbite was corrected or up to 3mm overexpanded.

Three studies used CBCT images to obtain measurements [10,13,17], three studies used 3D stereogrammetry [11,12,14]. 2D images (lateral/AP radiographs) were used in three studies [15,16,20] and one study used both PA cephalograms and 3D facial images [18]. Direct caliper measurements were utilized in two out of the sixteen studies [20, 22].

2.3.3 Risk of bias assessment

Out of the twelve studies included in the review, four were identified as randomized controlled trials (RCTs) [11-13, 18], four were cohort studies [10,14-16] and the other four were controlled clinical trials (CCTs) [17,19,20,27]. For the CCTs and Cohorts, the ROBINS-I tool for The Risk of Bias In Non-randomized Studies of Interventions was utilized, and biases related to potential confounding variables, patient selection,

intervention, assessment of outcome and reporting of results were evaluated and the overall bias was reported as low/moderate/serious/critical/NI. For the RCTs, the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was utilized and potential biases in the process of randomization, or in relation to the intervention, assessment of outcome and reporting of results were identified, with the overall risk of bias reported as low/high/some concerns. Three studies were found to have a low risk of bias [13,15,18], six were considered to have moderate risk of bias. One study was considered to have serious risk of bias [27] and two as having some concerns [11,12].

2.3.4 Results on Individual Studies

The studies utilized different methods of data analysis such as linear and angular measurements via usage of landmarks. The mean linear and angular measurements are reported in Table 2.1. In studies that had no control group and consisted of two or more different types of RME devices, the two groups were considered. The measurements were compared at different timepoints including pre-RME and post-RME, pre-RME and post-retention. The most commonly measured outcomes were included in the table (Table 2.1).

Table 2.1 Results of the review on mean changes in facial soft tissues according to outcomes

Pre-RME versus Post-RME		
Outcome/measurement	*Study*	*Mean change*
Alar width	Truong et al[17]	0.65mm
	Uysal et al[20]	1.45mm*
	Santariello et al[19]	0.88mm*
	Pangrazio-Kulbersh et al[13]	Banded group: 1.34mm* Bonded group: 1.24mm*
	Johnson et al[27]	Pre-pubertal group (F): 0.5mm Pre-pubertal group (M): 0.9mm* Post-pubertal group (F): 0.9mm* Post-pubertal group (M):0.8mm*
Alar base width	Truong et al[17]	1.60mm*
Nasal tip prominence	Kilic et al[16]	0.12mm
Height of nose	Truong et al[17]	0.34mm
Lower face height	Santos et al[15]	4.86mm*
Nasolabial angle	Santos et al[15]	-3.0 degrees

*:*Significance p<0.05 within groups; (F = females, M = males)*

Articles not mentioned in the table above did not assess the outcome in their studies

Pre-RME versus Post-Retention		
Outcome/measurement	*Study*	*Mean change*
Alar width	Akan et al[11]	Hyrax group: 0.94mm* Hybrid group: 2.21mm*
	Alkhayer et al[14]	1.02mm
	Truong et al[17]	Treatment group: 2.17mm* Control group: 1.83mm*

	Altindis et al[12]	Banded group: 1.35mm* Bonded group: 1.16mm* Modified bonded group: 0.94mm*
	Baysal et al[18]	Treatment group: 1.42mm Control group: 0.43mm
	Uysal et al[20]	Treatment group: 0.25mm* Control group: 0.16mm
	Santariello et al[19]	Treatment group: 0.79mm* Control group: -0.14mm
	Johnson et al[27]	Pre-pubertal group (F): 0.5mm Pre-pubertal group (M): 1.3mm* Post-pubertal group (F): 0.5mm* Post-pubertal group (M):0.8mm
Alar base width	Alkhayer et al[14]	1.21mm
	Truong et al[17]	Treatment group: 1.95mm* Control group: 1.29mm*
	Torun[10]	Pre-pubertal group: 1.5mm Post-pubertal group: 1.1mm
Nasal tip prominence	Kilic et al[16]	0.23mm
Philtrum width	Akan et al[11]	Hyrax group: 0.46mm Hybrid group: 0.1mm
	Torun[10]	Pre-pubertal group: 0.9mm* Post-pubertal group: 0.6mm*
	Baysal et al[18]	Treatment group: 0.69mm Control group: 0.56mm
Mouth width	Akan et al[11]	Hyrax group: 1.32mm Hybrid group: 0.9mm
	Alkhayer et al[14]	2.62mm
	Altindis et al[12]	Banded group: 1.80mm* Bonded group: 2.02mm*

		Modified bonded group: 1.62mm*
	Baysal et al[18]	Treatment group: 1.86mm Control group: 1.23mm
Upper lip length	Akan et al[11]	Hyrax group: -0.02mm Hybrid group: 0.36mm
	Torun[10]	Pre-pubertal group: 0.5mm* Post-pubertal group: 1.1mm*
	Altindis et al[12]	Banded group: 0.20mm Bonded group: -0.25mm Modified bonded group: 0.31mm
	Baysal et al[18]	Treatment group: 0.23mm Control group: 0.33mm
Upper vermillion length	Akan et al[11]	Hyrax group: -0.94mm Hybrid group: 0.29mm
	Altindis et al[12]	Banded group: -0.01mm Bonded group: -0.37mm Modified bonded group: 0.36mm
Lower lip length	Akan et al[11]	Hyrax group: 1.2mm Hybrid group: 1.67mm*
	Altindis et al[12]	Banded group: 0.48mm Bonded group: 0.65mm Modified bonded group: 0.36mm
	Baysal et al[18]	Treatment group: 0.39mm Control group: -0.04
Height of nose	Truong et al[17]	Treatment group: 4.39mm* Control group: 2.87mm*
Lower face height	Akan et al[11]	Hyrax group: 1.29mm Hybrid group: 1.96mm
	Altindis et al[12]	Banded group: -0.26mm Bonded group: 0.44mm Modified bonded group: 0.56mm
	Baysal et al[18]	Treatment group: 1.14mm

		Control group: 1.26
	Santos et al[15]	1.38mm
Nasolabial angle	Akan et al[11]	Hyrax group: 1.82 degrees Hybrid group: 1.24 degrees
	Torun[10]	Pre-pubertal group: -1.6 degrees Post-pubertal group: -1.9 degrees
	Altindis et al[12]	Banded group: 0.24 degrees Bonded group: 0.10 degrees Modified bonded group: -2.35 degrees
	Uysal et al[20]	Treatment group: 2.28 degrees* Control group: 1.31 degrees*
	Santos et al[15]	0.5 degrees

*:*Significance p<0.05, within groups; (F = females, M = males)*
Articles not mentioned in the table above did not assess the outcome in their studies

2.4 Discussion

Facial esthetics is an important factor that should be carefully evaluated during orthodontic planning. RME is an orthopedic procedure for correcting maxillary discrepancies that has been described in the literature since 1860 [5,28,29]. Some studies have reported dental-skeletal alterations arising from RME [29-32]. Despite the large amount of information available in the literature, on the skeletal effects of RME, in comparison, fewer studies have evaluated the changes in the soft tissues of the face. Bearing in mind that the principles of orthodontic treatment include esthetics, function, stability and occlusion, it is essential to consider the possible consequences of this treatment on soft tissues.

Our review summarized the results from twelve studies (four RCTs, four cohorts and four CCTs). After assuring the studies fit our inclusion criteria, the first factors that added bias to the results were the follow-up and expansion time. The time of post-expansion assessment varied largely, making the comparison between studies difficult. Some studies were also not clear on expansion time, however for those which specified, there was a range from 2-6 weeks. The follow-up time could be directly related to the outcomes observed as the patients could be close to peak of growth and could either be followed for 4 months or almost 3 years. Adolescence has been defined by the World Health Organization as ages from 10 to 19 years of age and the facial peak of growth begins at around 11.96 years (lasts until approximately 14.35 years of age) for males and 9.77 years (lasts until approximately 11.5 years of age) [30]. During that time, it is known that several facial changes are expected such as nose prominence, increased downward projection of the chin, lower and upper lips may shift downward, flattening of the cheeks and a certain degree of deepening of the orbital region [33]. Hence the importance of standardizing follow-up time when performing studies that aim to look at facial changes.

There were several facial outcomes measured; alar width was the most commonly assessed as an immediate post-RME outcome. For the studies that compared their findings to post-retention measurements, the outcomes most commonly assessed were: alar width, alar base width, philtrum width, mouth width, upper vermillion width, lower lip length, lower face height, and nasolabial angle. The nasal cavity is in close contact with

the maxilla, therefore measurements that were related to the nose seemed to be more frequently included [34]. In regards to immediate post-expansion alar width assessment, only three studies reported the actual amount of maxillary expansion, which allowed us to conclude that the immediate expansion observed (alar width) corresponded to about 10-12% of the maxillary expansion in millimetres [13,20,27]. This is in agreement with previous studies that looked at immediate changes post-RME and they showed changes in the alar width of up to 2mm [9,12]. Changes mentioned are all in absolute values and not compared to controls, therefore, future studies that aim to assess soft tissue changes immediately post-RME including a control group are encouraged.

One study looked at alar width immediately post-RME divided their sample in pre-pubertal and post-pubertal groups, according to their cervical maturation stage [27]. The changes were smaller in the prepubertal group (0.5mm) when compared to post-pubertal group (0.9mm) in females, however the opposite was seen in males. Two other studies that included only patients below 10 years of age also found similar values (0.65-0.88m) and the studies that looked at patients over 13 years had increased values (1.24-1.45mm). It is known that soft tissue growth in the face occurs in a similar rate, regardless of age, and some studies point at pre-pubertal individuals presenting with greater annual growth in the middle third height vs post-pubertal individuals having increased rates in chin protrusion. However, the alar width does not seem to differ in a way that would explain increased findings for post-pubertal studies included. As none of these studies had a control group, this could be the explanation in the discrepancies seen [35].

When comparing the outcomes for the post-retention phase, the changes for alar width varied from 0.5mm to 2.21mm. For the studies that had a control group, the change was smaller, from a 0.14mm decrease to a 1.83mm increase. As only three studies had a control group, it is difficult to assess how much of the normal growth could be masking the actual difference; however, even in the studies that had a control group, only two were statistically significant and they concluded that those differences were not clinically significant as the nose continues to grow throughout life and there is some soft tissue elasticity present. The same justification is valid for alar base width; however, the variation was larger for this outcome as it ranged from a decrease of 0.17mm to an increase of 2.81mm.

For the philtrum width and upper lip length, the only study that had a control group showed no clinical or statistically significant differences [18]. Amongst all included studies, the variation was from 0.1mm to 0.9mm of increase for the philtrum width and for the upper lip length from a 0.02mm decrease to a 0.5mm increase. Elongation of the upper lip that was statistically significant has been previously reported [9,36], however one of these studies also had surgical expansion and evaluation was performed via photographs and not CBCT and for the one that used CBCT, no control group was included.

Mouth width increased from 0.9mm to 2.02mm and only one study included a control group for this assessed outcome. When compared to control, there was an increase in the mouth width of 0.63mm and this was statistically but not clinically significant. Some

studies that show an increase in the mouth width that was statistically significant did not have a control group, so when we compare their absolute numbers to the ones that included a control group, it seems they are all within the same range (average of 1.67 mm).

For the lower lip length, all studies showed no difference that were statistically significant, which is in agreement with the current literature that assess long-term effects of RME. [14,17] All the studies used similar methods of expansion that typically also do not present a difference in the expansion outcome (banded vs bonded expander) therefore, in this case the soft tissue changes were expected to be similar [37]. Correspondingly, for the lower face height measurement, there was a variation from a decrease of 0.26mm to an increase of 1.96mm. Regardless of having a control group or not, none of them were statistically significant.

The nasolabial angle is the angle formed by the lower edge of the nose and the philtrum, with normal values ranging from 97 to 110 degrees [38]. This angle is a significant component in the harmony of the face and is closely related to orthodontic treatment [38]. Some authors have reported that the retraction of the upper incisors influences the increase in the nasolabial angle, consequently modifying the facial profile of patients [39]. Only one of the included studies showed a difference that was statistically significant in this angle, where the control group had a change of 1.31 degrees and treatment group presented 2.28 degrees. The overall variation was from a 1.6 degree decrease to a

maximum of 2.23 degree decrease. As there is an expected forward movement of the nose, upper lip and maxilla, the nasolabial angle does not typically change in a significant manner in most studies, and the authors of the study that found a difference that was statistically significant considered it to be clinically insignificant. However, some differences may be explained by patients' age and sex, as girls reach puberty at an earlier age than boys and could be more resistant to expansion forces [20].

2.5 Limitations

This study is limited considering the following factors that the patients were part of the growing phase, with majority of the studies not including a control group for comparison. In addition, the observational periods varied widely, from immediately after RME to almost three years. Therefore, given the above, the findings should be interpreted with caution.

2.6 Conclusion

Our findings suggest that RME results in variable soft tissue facial changes over time. However, despite some of the findings being statistically significant including those of alar width, alar base width, height of the nose and nasolabial angle, the changes may not be clinically significant overall and thereby should be construed carefully.

Chapter 3 – Methodology

3.1 Methods

In this prospective study, the data was collected from a total of 32 patients at the University of Alberta Graduate Orthodontics Clinic, consisting of two groups:

Control group: This group consisted of 16 patients between 7-11 years of age who had not undergone maxillary expansion. Due to aging, these patients may have undergone facial soft tissue changes due to natural growth.

Treatment Group: This group consisted of 16 patients between 7-11 years of age who had undergone maxillary expansion (Hyrax expander, rapid expansion, 1 turn per day) who had undergone facial soft tissue changes due to natural growth and also possibly due to expansion.

The study was conducted at the Orthodontics Graduate Clinic at the University of Alberta with ethics approval from the Research Ethics Board (Pro00061538) from the University of Alberta.

3.1.1 Inclusion and exclusion criteria

The inclusion criteria were as follows: patients 7-11 years of age presenting with a maxillary transverse deficiency of at least 5mm or bilateral posterior crossbite (wherein the maxillary transverse deficiency was calculated as the difference between the palatal

cusp tips of the maxillary first molars and the central fossae of mandibular first molars). Additionally, an overcorrection of 20% was further added in order to account for any potential relapse. The exclusion criteria were as follows: patients with any previous history of craniofacial diseases or syndromes and any previous history of orthodontic therapy or maxillary expansion.

3.1.2 Sample size calculation

The sample size was calculated based on the findings of the study by Santariello et al (2014) which examined the effect of rapid maxillary expansion on soft tissue nasal widths. [19] The study consisted of two groups (treatment and control) with demographic characteristics of subjects similar to our study.

Santariello et al (2014) reported an increase in nasal width from an average of 29.98mm (SD = 2.53) before expansion to an average of 30.77mm (SD = 2.40) post-retention, with an increase of 0.79 mm corresponding to a small effect size (Cohen's d = 0.32). [19] In the control group, there was a small decrease in nasal width measurements from an average of 29.68mm (SD = 2.62) before expansion to an average of 29.54mm (SD = 3.07) post-retention, with a decrease of 0.14 mm corresponding to a small effect size (Cohen's d = -0.05). [19] The difference between the two groups in terms of the standardized effect size was Cohen's d = 0.37.

Using G*Power software (version 3.1.9.2; Heinrich Heine University, Düsseldorf, Germany), a sample size of 184 subjects (92 subjects per group) was predicted to provide 80% statistical power at $\alpha = 0.05$ significance level. For our study, a total of 32 patients were enrolled as part of the ongoing prospective clinical trial.

3.1.3 Randomization

In order to determine grouping, Microsoft Excel was utilized to generate a random sequence for assigning study participants into the treatment and control groups. Once the inclusion criteria were satisfied, and written parental/guardian consent was obtained, each study participant was assigned to a group which was reviewed by the primary investigator as per the randomized table that had been generated.

3.1.4 Blinding

Complete blinding was not achievable as the participants of the study and the overseeing clinician were not blinded; however, those involved in assessment of the outcome, interpretation of hand-wrist radiographs for skeletal age determination and statistical analyses were blinded.

3.1.5 Experimental design

Each patient in each group underwent CBCTs, 3D facial scans, hand-wrist radiographs, and extra/intra oral photographs at two time points: pre-treatment (T0, before maxillary expansion), after the completion of expansion (T1, 12 months after T0).

CBCTs were obtained by means of the I-CAT New generation Machine (large field of view 16 x 13.3 cm with a voxel size of 0.30mm, 120 kVp, 18.54 mAS over 8.9 seconds), with patients' Frankfort horizontal planes parallel to the floor and head stabilized via strips. Patients were also instructed to avoid swallowing and maintain maximum intercuspation as well as place their tongues against the lingual surfaces of the maxillary central incisors while the images were being taken. All CBCTs were taken by a radiology technician at the University of Alberta. The files were stored in DICOM format and coded and blinded for the purposes of the study. The CBCTs were assessed using 3D Slicer software (version 4.11.20210226, Boston, MA, USA).

3D facial scans were obtained on the same day as the CBCTs by means of the Facial Insight 3D Scanner (Motion View LLC, Chattanooga, TN, USA). The facial scans were taken with the patients' Frankfort horizontal planes parallel to the floor, while maintaining a neutral facial expression. All data collected were coded and blinded for the purposes of the study.

Patients in the treatment group underwent RME using a Hyrax-type expander (10mm Forestadent, Pforzheim, Germany). The Hyrax expander consisted of metal bands cemented on the maxillary first molars using Ultra Band-lok (Orthodontic Supply Canada, Fredericton, Canada), which was soldered to a midline palatal jackscrew and metal arms that extended to maxillary deciduous first molars or first premolars. The patients were then instructed to turn the jackscrew with a handheld Hyrax key for activation of the appliance at a rate of one turn or 0.25mm per day. The patients were instructed to stop once the number of prescribed turns had been achieved and attended follow up appointments to ensure expansion was completed as prescribed. All patients underwent a minimum of 5mm of activation in total or until overcorrection of the maxillary transverse deficiency, once the palatal cusps of the maxillary molars touched the buccal cusps of the mandibular molars as per the McNamara protocol. [7,40] A 0.08” in diameter, stainless steel ligature was then tied into the jackscrew to inhibit additional movement. On average, the patients underwent 6.53mm of expansion (26.13 turns), with an overall range between 20-36 turns.

Four months following the last day of activation of the appliance, the Hyrax expander was then replaced with a standard passive transpalatal arch with bands cemented on the maxillary first molars using Band-lok, for 6 months after expansion during the stability period. The Hyrax expansion device (10mm Forestadent, Pforzheim, Germany) is showcased in Figure 3.1.

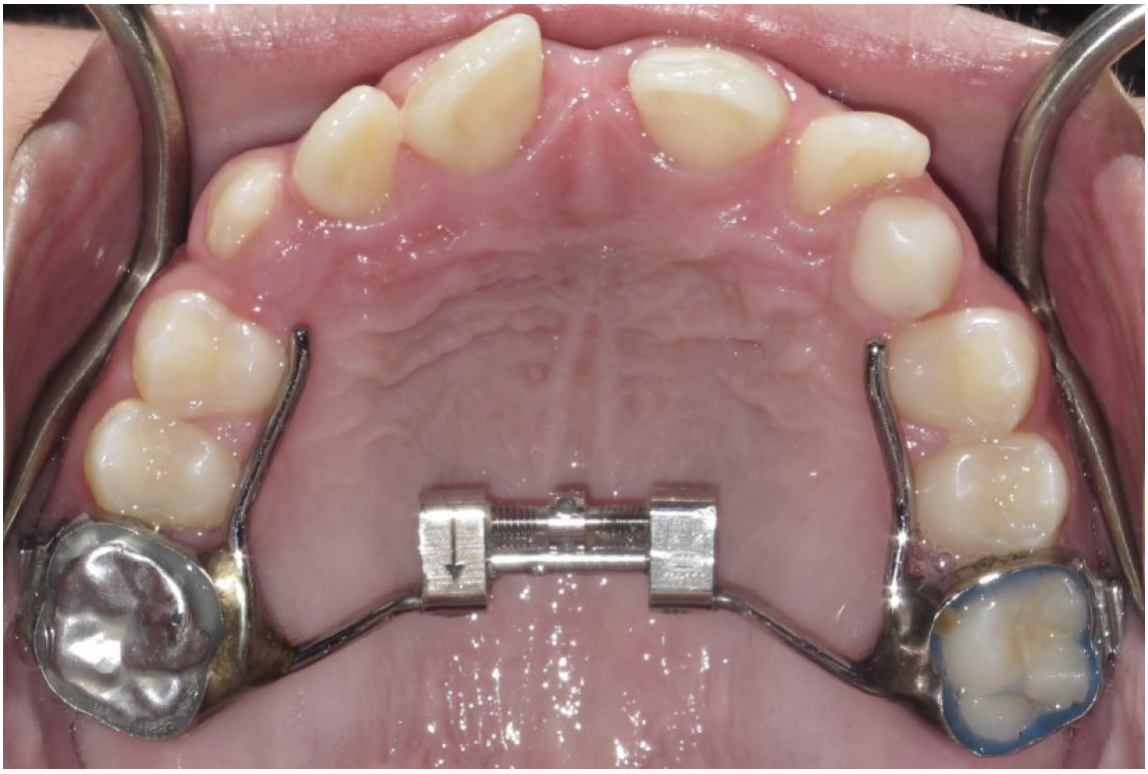


Figure 3.1 Hyrax expansion device in the maxillary arch

3.1.6 Method used for determination of skeletal maturation

Skeletal maturation was determined by analyzing hand-wrist radiographs utilizing the Fishman skeletal maturity index (SMI). Radiographic hand-wrist analysis has been utilized as an analytic tool over many years and has been validated by a number of studies as the time of craniofacial pubertal growth has been shown to correlate to certain ossification events in the hand-wrist area, especially in comparison to cervical vertebral maturation analysis [41,42]. The Fishman index involves evaluation of six anatomic hand-wrist sites on the thumb, third and fifth fingers and radius to identify four bone maturation

stages or eleven skeletal maturity indicators [43]. There are various events that occur with the progression of growth, which include the development of ossification centres, epiphyseal widening of the phalanges followed by capping and fusion of the epiphysis and diaphysis [41,43]. In studies that have correlated SMI with the percentile of residual pubertal growth, it was seen that at indices 1-2, there is about 85-100% of pubertal growth left, 65-85% growth left at indices 3-4, 25-65% growth left at indices 5-6 and so on until there is no growth remaining at a SMI of 11 [44,45]. However, these values tend to vary with sex, growth velocity rates and potentially different ethnic backgrounds [43,44,46]. At an SMI of 6, there is about 50% of growth of the maxilla and mandible [43]. Figure 3.2 demonstrates typical hand-wrist radiographs of the participants.

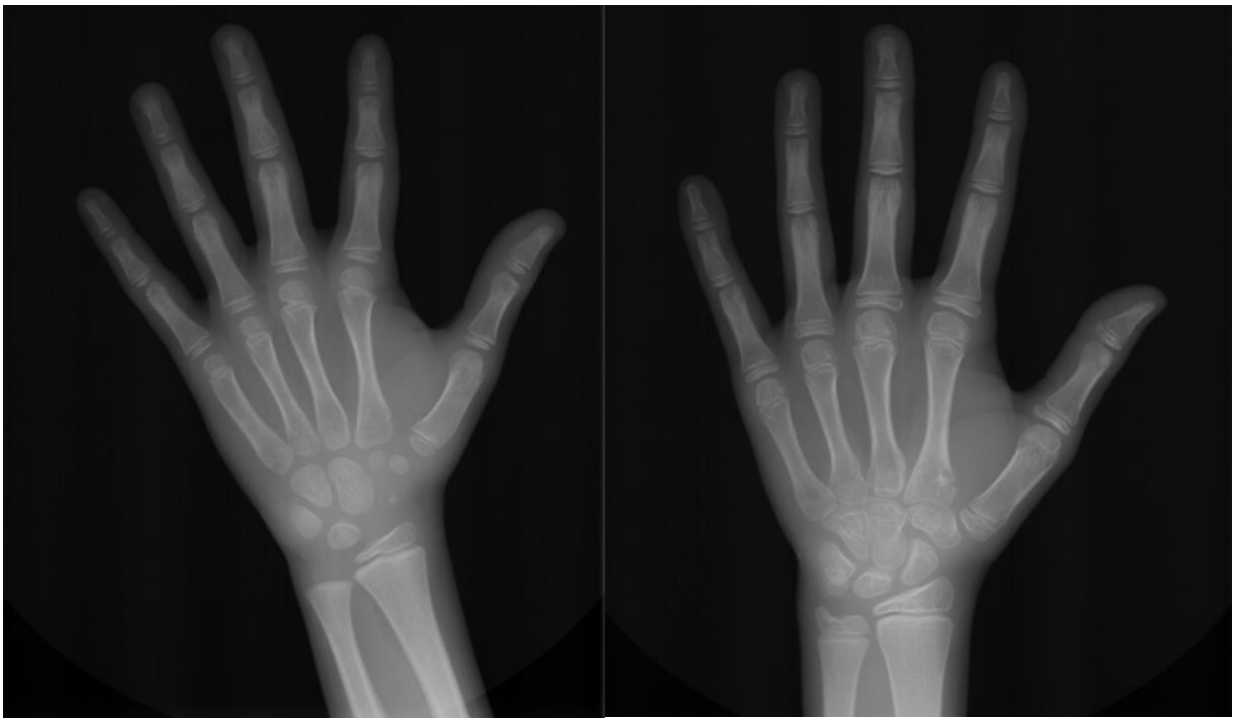


Figure 3.2 Hand-wrist radiographs of participants of the study

3.1.7 Head orientation of CBCTs and 3D facial scans prior to facial soft tissue landmarking and measurements

To ensure that all scans were measured in the same orientation, the CBCTs were re-oriented in three different planes using the 3D Slicer software (version 4.11.20210226, Boston, MA, USA). The orientation marker was set to axes and the images were then re-oriented according to the reference planes. The horizontal reference plane was established as passing through the right and left exocanthion (Figure 3.3 A), the sagittal reference plane was established as the plane perpendicular to the horizontal reference plane and passing through the soft tissue nasion and soft tissue pogonion (Figure 3.3 A), and lastly, the coronal reference plane was established as the plane perpendicular to the other two planes and passing through the soft tissue nasion (Figure 3.3 B). The overall orientation can be visualized in Figure 3.3 C. Similar to the CBCTs, the 3D facial scans were re-oriented using the same reference planes (horizontal, sagittal, coronal) utilizing the OrthoInsight 3D software (Version 7.7.5570; Motion View LLC, Chattanooga, TN, USA).

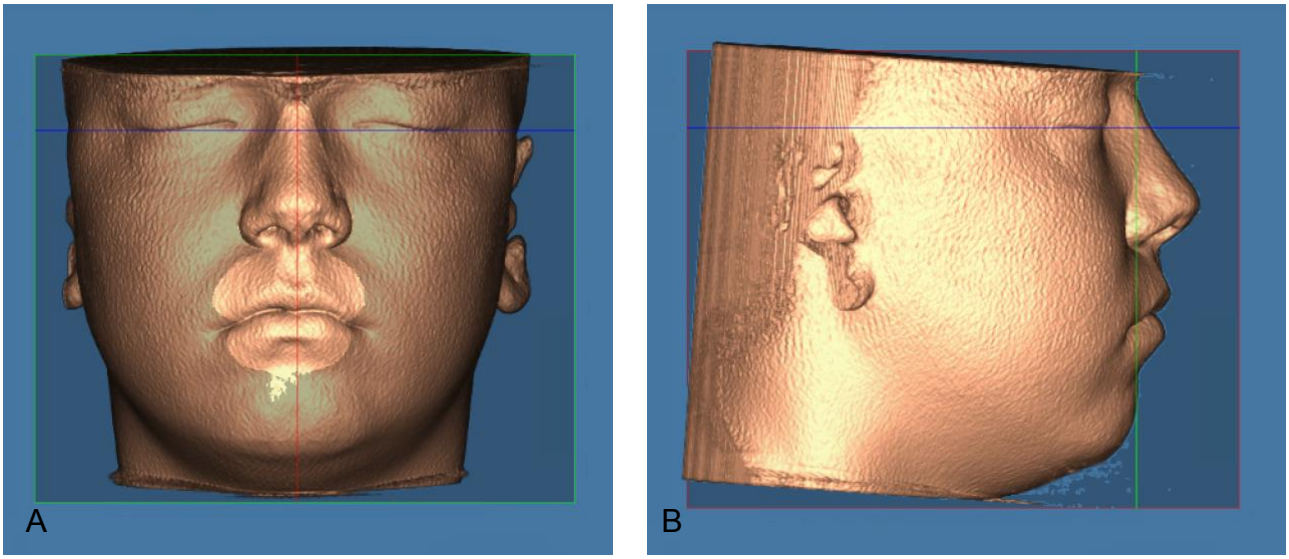
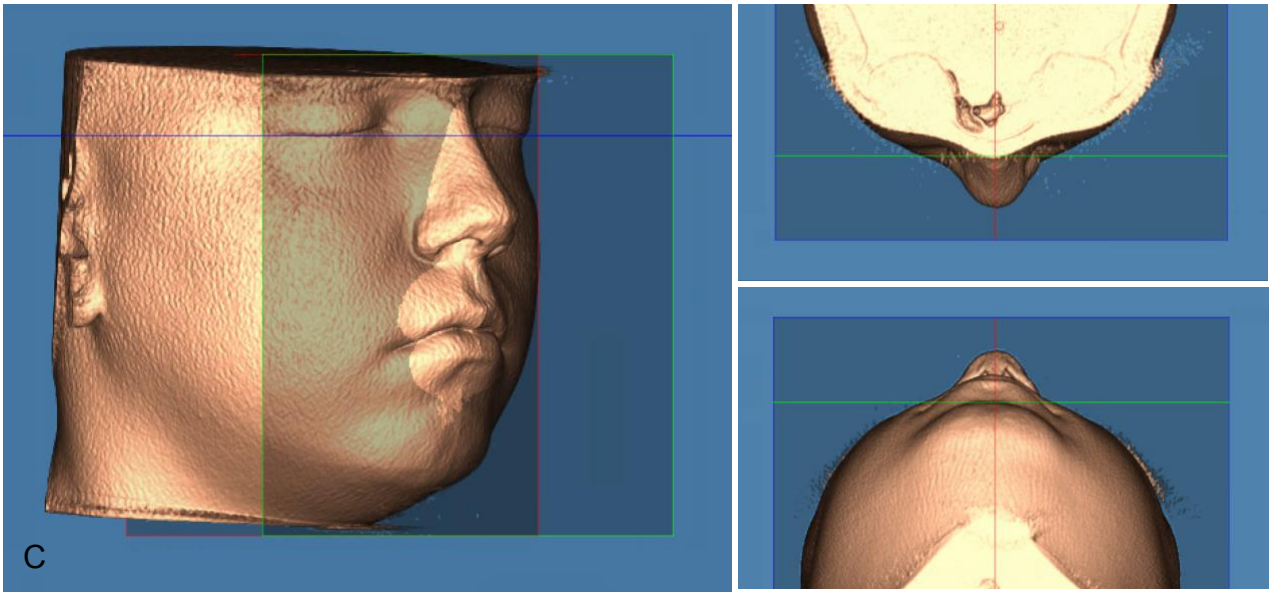


Figure 3.3 A: Horizontal and sagittal reference planes, B: Coronal reference plane and C: Horizontal, sagittal and coronal reference planes from different views (below)



3.1.8 Method used for CBCT and 3D facial scan analyses of facial soft tissues

Once the CBCTs were obtained, they were saved as DICOM files and coded for the purpose of blinding. The data was then transferred to the 3D Slicer software (version 4.11.20210226, Boston, MA, USA) for the soft tissue measurements. Soft tissue preset display was selected for viewing and a 0.5mm diameter spherical marker was utilized to identify the landmarks. The 3D facial scans were saved as OI3D files and also coded for blinding purposes. OrthoInsight 3D software (Version 7.7.5570; Motion View LLC, Chattanooga, TN, USA) was used to perform the soft tissue analysis using landmarks, linear and angular measurements. A 0.5mm diameter spherical marker was used for identification of the landmarks. Standard reference planes (coronal, sagittal and horizontal) were set up for both CBCTs and 3D facial scans prior to identification of landmarks and measurements. Manhattan distance measurements utilizing the soft tissue curvatures as well different techniques of surface registrations were attempted, however, due to time and software related limitations and challenges, only Euclidean distances were measured for this particular research study.

A total of twenty-two soft tissue landmarks were chosen and utilized. The definitions of the various landmarks are summarized in Tables 3.1 and 3.2. The landmarks can be visualized in Figure 3.4 A and Figure 3.4 B.

Table 3.1 Twenty-two soft tissue landmarks with definitions

Soft Tissue Landmark		Definition
Alare	Al*	Most lateral point on each alar contour
Alare base	Ab*	Point where the nasal alar intersects the face on the inferior margin of the nose
Pronasale	Prn	Most anterior midpoint of the apex of the nose
Subnasale	Sn	Midpoint between columella nasi and philtrum of upper lip
Labiale superius	Ls	Midpoint of the vermillion of the upper lip
Upper lip anterior Point	Ulap	Point at the most anterior point of the upper lip
Lower lip anterior Point	Llap	Point at the most anterior point of the lower lip
Stomion	Stm	Midpoint of the horizontal labial fissure
Chelion	Ch*	Point at each labial commissure
Columella	Col	Point of inferior margin of the nasal septum linking the nasal tip to the nasal base
Crista philtri	Cph*	Point of crossing of the vermillion of the upper lip and elevated margin of the philtrum
Soft tissue nasion	Na	Intersecting point between soft tissue profile and the sella-nasion line
Soft tissue menton	Me	Most inferior midpoint on soft tissue contour of the chin
Soft tissue pogonion	Pg	Most anterior midpoint on soft tissue contour of the chin
Endocanthion	En*	Point at the inner commissure of the fissure of the eye
Exocanthion	Ex*	Point at the outer commissure of the fissure of the eye

* indicates bilateral landmarks (right, left)

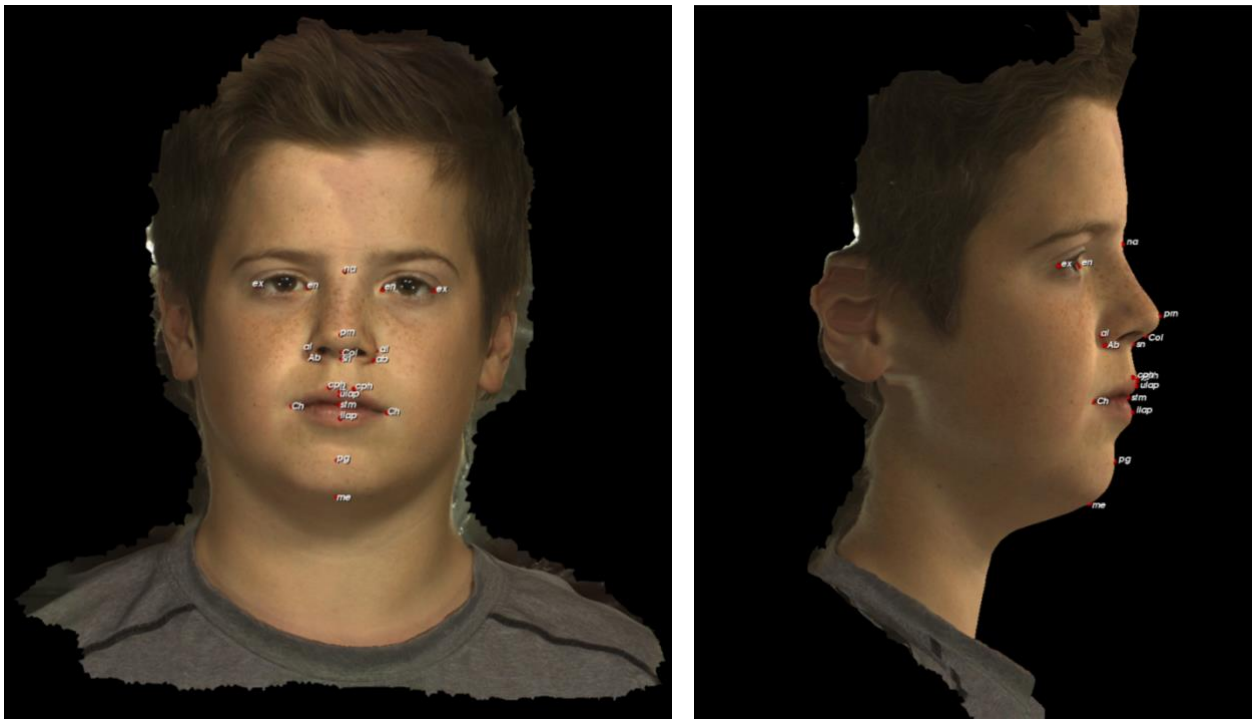


Figure 3.4 A: Landmark identification (frontal view) and B: Landmark identification (lateral view)

When analyzing the CBCT and 3D facial scan data, fourteen soft tissue measurements (thirteen linear measurements and one angular measurement) were utilized, as presented in Table 3.2. The landmarks can be visualized in Figure 3.4 A and Figure 3.4 B., and the measurements can be visualized in Figure 3.5 A and 3.5 B.

Table 3.2 Thirteen linear measurements and one angular measurement with definitions

Linear and Angular Measurements		Definition
Alar Base Width	ABW	Most lateral point of the base of insertion of each nostril
Alar Width	AW	Most lateral point to the contour of each nostril
Mouth Width	MW	Right labial commissure to left labial commissure
Philtrum Width	PW	Right to left christa philtri at the vermillion border of the upper lip
Height of Nose	HofN	Soft tissue nasion to subnasale
Nasolabial Angle	NL	Angle between soft tissue nasion, subnasale and labrale superioris
Height of Upper Lip	HofUL	Subnasale to stomion
Height of Vermillion of Upper Lip	HofVUL	Labiale superius to stomion
Height of Lower Lip	HofLL	Stomion to soft tissue menton
Lower Facial Height	LFH	Subnasale to soft tissue menton
Upper Lip to E-line	ULtoE	Upper lip to E-line (pronasale to soft tissue pogonion)
Lower Lip to E-line	LLtoE	Lower lip to E-line (pronasale to soft tissue pogonion)
Nasal tip prominence	NTP	Ala to pronasale
Intercanthal Width	ICW	Right to left endocanthion

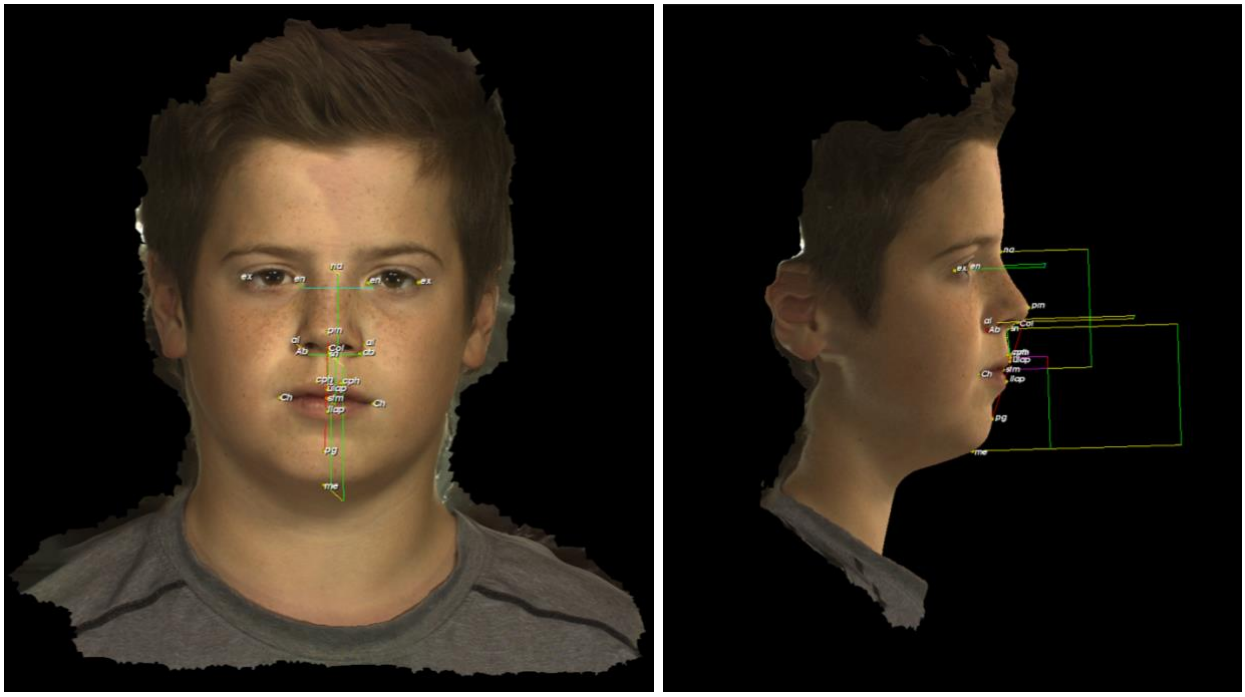


Figure 3.5 A: Measurement identification (frontal view) and B: Measurement identification (lateral view)

The literature focusing on this topic has shown most consistently that the above measurements and components have generally shown the greatest potential changes with RME.

3.1.9 Statistical Methods

The statistical analysis was performed using the Statistical Package for Social Science (IBM SPSS, version 28.0, SPSS Inc., Chicago, IL, USA). The significance level was set at $p < 0.05$. with the significance level set at $\alpha = 0.05$.

Intra-rater and Inter-rater reliability were conducted using the intraclass correlation coefficient. The reliability trials were performed on ten CBCT scans and ten 3D facial scans utilizing 5 landmarks and three linear measurements at three timepoints, seven days apart. Inter-rater reliability was performed between the author and GSK (orthodontic resident with training using CBCTs and 3D facial scans).

The results of the reliability analysis were assessed as per the Portney and Watkin's ICC guidelines [47] as shown in Table 3.2. ICC ranging between 0.75 to 0.90 is considered "good", and above 0.90 is considered "excellent". [47] Values below 0.5 are considered "inadequate" and necessitate better identification of landmarks and standardization. [47]

Table 3.3 Intra-class Correlation Coefficient (ICC) guidelines (Portney and Watkin) for assessment of reliability

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

Additionally, in order to assess the accuracy of the measurements, measurement errors were also calculated.

Intra-rater and inter-rater reliability was conducted for determination of skeletal maturity utilizing hand-wrist radiographs and Fishman's skeletal maturity index. Ten randomly chosen hand-wrist radiographs were evaluated at three timepoints, seven days apart, and the reliability analysis using intraclass correlation coefficient was performed.

For the statistical analyses, the following variables were identified:

14 Dependent/outcome variables (continuous) for 3D face scans and CBCTs (28 total):

- 13 linear distance measurements (measured in millimeters): ABW: alar base width; AW: alar width; MW: mouth width; PW: philtrum width; HofN: height of nose; HofUL: height of upper lip; HofVUL: height of vermillion of upper lip; HofLL: height of lower lip; LFH: lower facial height; UliptoE: upper lip to E line; LliptoE: lower lip to E line; NTP: nasal tip prominence; ICW: intercanthal width
- 1 angular measurement (measured in degrees): NL angle: nasolabial angle

Independent/predictor variables for 3D face scans and CBCTs:

- Treatment (between-subjects factor with two levels – treatment group and control group)
- Time (within-subjects factor with two levels – T0 and T1)

The following research questions and sets of multivariate hypotheses were evaluated:

Part A

1. Are there differences in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)?

2. Are the CBCT and 3D facial scan derived facial soft tissue measurements jointly reliable at pre-treatment (T0), and post-treatment (T1)?

Part B

3. Are there differences in the mean facial soft tissue 3D facial scan measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)?
4. Are there differences in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)?
5. Are there differences in the mean change (T1-T0) of soft tissue 3D facial scan measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)?
6. Are there differences in the mean change (T1-T0) of soft tissue CBCT measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)?

Hypotheses (Part A):

1. H_o → There is no difference in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)

   H_a→ There is a difference in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)

2. H_o → The CBCT and 3D facial scan derived facial soft tissue measurements jointly are reliable at pre-treatment (T0), and post-treatment (T1)

   H_a→ The CBCT and 3D facial scan derived facial soft tissue measurements jointly are not reliable at pre-treatment (T0), and post-treatment (T1)

Hypotheses (Part B):

3. H_o → There is no difference in the mean facial soft tissue 3D facial scan measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

   H_a→ There is a difference in the mean facial soft tissue 3D facial scan measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

4. H_o → There is no difference in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

   H_a→ There is a difference in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)

5. H_o → There is no difference in the mean change (T1-T0) of soft tissue 3D facial scan measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)

   H_a→ There is a difference in the mean change (T1-T0) of soft tissue 3D facial scan measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)

6. H_o → There is no difference in the mean change (T1-T0) of soft tissue CBCT measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)

H_a→ There is a difference in the mean change (T1-T0) of soft tissue CBCT measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)

For Part A, question 1, the difference (in millimeters) between CBCT and 3D facial scan derived facial soft tissue measurements were first calculated (CBCT-3D facial scan). For Part B, questions 5 and 6, the changes (in millimeters) were first calculated using the formula (T1-T0).

Main analyses were performed using multivariate analysis of variance (MANOVA). The data was sampled independently where each observation of one group must not influence the other group. The normality of the outcome variables was assessed with scatterplots and Q-Q plots, potential outliers were assessed with Mahalanobis distances with *p*-values, as well as performing tests of normality. Homogeneity of variance was assessed by Box's test of equality of covariance matrices.

Chapter 4 – Results

4.1 Recruitment and participant flow

The participants were admitted to the study beginning from August 2016 onwards and the cutoff for inclusion in data analyses was October 2022. There were initially thirty-two patients included in the study with 16 patients in the control group and 16 patients in the treatment group. However, one study participant in the treatment group did not have data available for the initial timepoint due to a corrupt file that could not be recovered. Another study participant in the control group did not complete the trial and dropped out due to a move to a different province.

Figure 4.1 below shows a summary of the flow of study participants. For the statistical analysis, the final sample entailed 30 participants (15 patients in the control group and 15 in the treatment group).

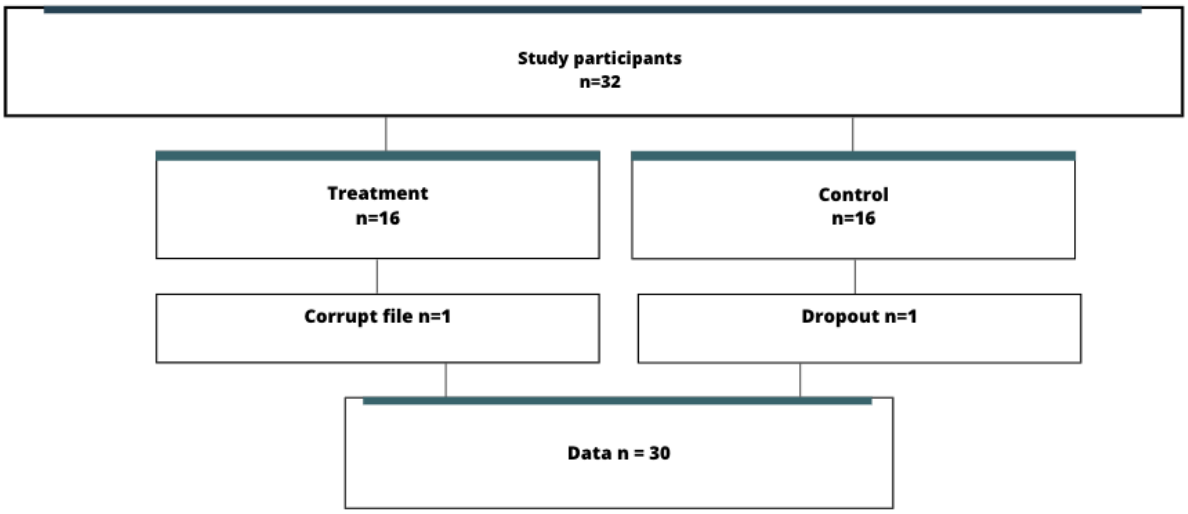


Figure 4.1 Summary of study participant flow

4.2 Baseline data

Baseline characteristics for the participants of the study are shown below in Table 4.1. Comparison between the groups was performed using inferential statistical analyses. The chronologic age and SMI(Fishman) was compared between groups using independent samples t-test and the gender composition was compared using the chi-squared test of independence. The t test was utilized due to the presence of a dependent quantitative variable and independent categorical variable and the chi-square test was utilized due to the presence of 2 categorical variables.

As per the results of the tests mentioned above, no statistically significant differences were found between the treatment and control groups in regards to the demographic characteristics of the sample participants: chronologic age ($p = 0.94$), gender ($p = 0.06$) and SMI ($p = 0.99$).

Characteristics	Control Group (n = 15)	Treatment Group (n = 15)	Comparison between groups
	M ± SD or Frequency (%) (95% CI)	M ± SD or Frequency (%) (95% CI)	
Chronologic Age (years)	9.72 ± 1.23 (9.04, 10.40]	9.76 ± 1.42 (8.98, 10.55)	t(28)=0.08, p = 0.94
Gender Females Males	 7 (46.7%) 8 (53.3%)	 12 (80.0%) 3 (20.0%)	$\chi^2(1)=3.59$, p = 0.06
SMI	2.93 ± 0.88 (2.44, 3.42)	2.93 ± 0.96 (2.40, 3.47)	t(28)=0.00 p = 0.99

Notes: M = mean, SD = standard deviation; CI = confidence interval

Table 4.1 Mean values of baseline demographic characteristics between groups

4.3 Reliability, Intraclass correlation coefficients

According to the Portney and Watkin's ICC guidelines, the author demonstrated "excellent" agreement for landmark measurements and assessment of skeletal maturation for both intra-rater and inter-rater (between the author and SKG) reliability conducted using the intraclass correlation coefficient. Tables 1 and 2, Appendix 4A demonstrate the reliability for the landmark measurements and Fishman's skeletal maturity index, respectively.

Table 3, Appendix 4A demonstrates the intraclass correlation coefficients between CBCT and 3D facial scan. Table 4, Appendix 4A demonstrates the measurement errors in millimeters, calculated as an average value of within-subject standard deviations.

4.4 Statistical analysis

Part A:

In order to address research question 1 as identified in Chapter 3, multivariate analysis of variance (MANOVA) was conducted.

For the multivariate analysis, the following assumptions were tested:

The data was sampled independently where each observation of one group must not influence the other group. Linearity assumption was evaluated and met by visual

inspection of scatterplots, where the CBCT-3D differences at T0 and T1 were assessed. (Figures 1 and 2, Appendix 4B).

Univariate normality assumption was examined using Q-Q plots for the outcome variables (Figures 3 and 4, Appendix 4B). The variables appear to follow the diagonal lines fairly closely in the Q-Q plots (Figures 3 and 4, Appendix 4B). Boxplots (Figures 5 and 6, Appendix 4B) were also assessed, demonstrating fairly symmetrical boxes with relatively similar sized whiskers, although CBCT-3D difference in MW (T0), HofN (T0), NL (T0) appear to be left skewed with longer whiskers at the bottom. Outliers were noted in ABW (T0 and T1), AW (T0), MW (T1), HofVUL (T1), HofLL (T0), ICW (T0). In addition, Kolmogorov–Smirnov test of normality was performed (Table 1, Appendix 4B). Two measurements (HofN at T0 and T1) demonstrated significant *p*-values, thereby indicating that those values may not follow normal distribution. Overall, although the groups are of equal size (n=15 for treatment group, n=15 for control group), they are overall small in regards to the sample size, and thereby a limitation in our study. Homogeneity of variance-covariance was assessed and met by Box's test of equality of covariance matrices (Table 2, Appendix 4B).

For multivariate normality assessment, Mahalanobis distances were calculated for the soft tissue measurements and converted to *p*-values using chi-squared distribution. The data was assessed for multivariate outliers, and all *p*-values were > 0.001, suggesting that there were no multivariate outliers (Table 3 Appendix 4B). However, when univariate

outliers were assessed via boxplots mentioned above (Figures 5 and 6, Appendix 4B), there were univariate outliers present in ABW (T0 and T1), AW (T0), MW (T1), HofVUL (T1), HofLL (T0), ICW (T0). The presence of outliers could potentially be explained by the inherent characteristics of the datasets as well as how the data was collected. More specifically, the outliers may have resulted from a combination of the subjective nature of landmark placements in the CBCT and 3D facial scan landmark placements and subsequent measurements, patient positioning errors, patients not having a related lip posture or neutral facial expression during the CBCT or 3D facial scan image capture, as well as potential errors in orientation of the images.

In order to address research question 2 as identified in Chapter 3, reliability testing was conducted using intraclass correlation coefficients. In addition, *p*-values and 95% confidence intervals were also assessed, as further described later in this Chapter.

Part B:

In order to address research questions 3 and 4 identified in Chapter 3, multivariate analysis of variance (MANOVA) was conducted.

For the multivariate analysis, the following assumptions were tested:

The data was sampled independently where each observation of one group must not influence the other group. Linearity assumption was evaluated and met by visual

inspection of scatterplots, where the mean change in the outcome variables was assessed. (Figures 1 and 2, Appendix 4C).

Univariate normality assumption was examined using Q-Q plots for the outcome variables (Figures 3 and 4, Appendix 4C). The variables appear to follow the diagonal lines fairly closely in the Q-Q plots (Figures 3 and 4, Appendix 4C). Boxplots (Figures 5 and 6, Appendix 4C) were also assessed, demonstrating fairly symmetrical boxes with relatively similar sized whiskers. Outliers were noted in ABW (3D facial scan and CBCT), AW (3D facial scan), NL angle (3D facial scan and CBCT), ICW (3D facial scan and CBCT). NL angle appear to be negatively skewed with outliers on the lower end. In addition, Kolmogorov–Smirnov test of normality was performed (Table 1, Appendix 4C). NL angle (3D facial scan and CBCT) and LliptoE (3D facial scan) demonstrated significant p-values, thereby indicating that those values may not follow normal distribution. Overall, although the groups are of equal size (n=15 for treatment group, n=15 for control group), they are overall small in regards to the sample size, and thereby a limitation in our study. Homogeneity of variance-covariance was assessed and met by Box's test of equality of covariance matrices (Table 2, Appendix 4C).

For multivariate normality assessment, Mahalanobis distances were calculated for the soft tissue measurements and converted to *p* values using chi-squared distribution. The data was assessed for multivariate outliers, and all *p* values were > 0.001, suggesting that there were no multivariate outliers (Table 3, Appendix 4C). However, when univariate

outliers were assessed via boxplots mentioned above (Figures 5 and 6, Appendix 4C), there were univariate outliers present in ABW (3D facial scan and CBCT), AW (3D facial scan), NL angle (3D facial scan and CBCT), ICW (3D facial scan and CBCT). The presence of outliers could potentially be explained given the subjective nature of the landmark placements and subsequent measurements, patient positioning errors, patients not having a relaxed lip posture or neutral facial expression, as well as potential errors in orientation of the images.

In order to address research questions 5 and 6 identified in Chapter 3, multivariate analysis of variance (MANOVA) was conducted.

For the multivariate analysis, the following assumptions were tested:

The data was sampled independently where each observation of one group must not influence the other group. Linearity assumption was evaluated and met by visual inspection of scatterplots, where the mean change in the outcome variables was assessed. (Figures 1 and 2, Appendix 4D).

Univariate normality assumption was examined using Q-Q plots for the outcome variables (Figures 3 and 4, Appendix 4D). The variables appear to follow the diagonal lines fairly closely in the Q-Q plots (Figures 3 and 4, Appendix 4D). Boxplots (Figures 5 and 6, Appendix 4D) were also assessed, demonstrating fairly symmetrical boxes with relatively similar sized whiskers, although NL change (3D face scan and CBCT) appear to be right

skewed with longer whiskers at the top. Outliers were noted in HofUL change (3D face scan), LliptoE change (3D face scan), MW change (CBCT), HofVUL change (CBCT), HofLL change (CBCT), and LliptoE change (3D face scan and CBCT), all of which appear to be right skewed with longer whiskers at the top. In addition, Kolmogorov–Smirnov test of normality was performed (Table 1, Appendix 4D). One 3D facial scan measurement (ICW) and two CBCT measurements (MW and HofVUL) demonstrated significant p-values, thereby indicating that those values may not follow normal distribution. Overall, although the groups are of equal size (n=15 for treatment group, n=15 for control group), they are overall small in regards to the sample size, and thereby a limitation in our study. Homogeneity of variance-covariance was assessed and met by Box's test of equality of covariance matrices (Table 2, Appendix 4D).

For multivariate normality assessment, Mahalanobis distances were calculated for the soft tissue measurements and converted to *p* values using chi-squared distribution. The data was assessed for multivariate outliers, and all *p* values were > 0.001, suggesting that there were no multivariate outliers (Table 3, Appendix 4D). However, when univariate outliers were assessed via boxplots mentioned above (Figures 5 and 6, Appendix 4D), there were univariate outliers present in HofUL change (3D face scan), LliptoE change (3D face scan), MW change (CBCT), HofVUL change (CBCT), HofLL change (CBCT), and LliptoE change (3D face scan and CBCT). The presence of outliers could potentially be explained given the subjective nature of the landmark placements and subsequent measurements, patient positioning errors, minor differences in imaging protocols, patients

not having a relaxed lip posture or neutral facial expression, as well as potential errors in orientation of the images.

4.5 Descriptive statistics

The mean difference between CBCT and 3D facial scan (CBCT-3D facial scan), was calculated for each outcome variable separately for T0 and T1. Mean and 95% CI are described in Table 4.2 and Table 4.3 below.

	Mean	Standard Deviation	Minimum	Maximum	95.0% Lower CL for Mean	95.0% Upper CL for Mean
ABW T0	-1.24	1.13	-4.38	1.72	-1.67	-0.82
AW T0	-0.79	1.00	-3.36	1.51	-1.17	-0.42
MW T0	-0.34	1.10	-3.11	1.27	-0.75	0.07
PW T0	-0.19	0.59	-1.20	0.90	-0.41	0.03
HofN T0	-0.75	0.91	-2.94	0.53	-1.09	-0.41
NL angle T0	-0.51	1.34	-3.25	2.08	-1.01	-0.01
HofUL T0	-0.76	0.82	-2.34	0.75	-1.07	-0.46
HofVUL T0	-0.01	0.56	-1.49	0.93	-0.22	0.20
HofLL T0	-0.99	1.17	-3.87	2.19	-1.43	-0.55
LFH T0	-0.88	1.11	-2.89	1.05	-1.30	-0.47
UliptoE T0	0.02	0.37	-0.69	0.87	-0.12	0.16
LliptoE T0	0.01	0.40	-0.64	0.70	-0.14	0.16
NTP T0	-0.15	0.86	-1.91	1.45	-0.47	0.17
ICW T0	-1.38	0.80	-2.98	0.79	-1.68	-1.08

Table 4.2 Descriptive statistics including mean, SD, Min, Max and 95% CI for 14 outcome variables at T0

	Mean	Standard Deviation	Minimum	Maximum	95.0% Lower CL for Mean	95.0% Upper CL for Mean
ABW T1	-1.08	0.99	-4.55	0.86	-1.45	-0.71
AW T1	-0.63	0.84	-2.04	1.17	-0.95	-0.32
MW T1	-0.51	1.05	-2.34	2.14	-0.90	-0.12
PW T1	-0.18	0.57	-1.09	1.17	-0.39	0.03
HofN T1	-0.61	0.89	-2.54	0.96	-0.95	-0.28
NL angle T1	-0.32	1.27	-3.99	1.85	-0.80	0.15
HofUL T1	-0.76	0.77	-2.19	0.72	-1.05	-0.47
HofVUL T1	0.08	0.49	-1.24	1.05	-0.11	0.26
HofLL T1	-0.92	1.07	-3.15	1.07	-1.32	-0.52
LFH T1	-0.94	1.20	-2.62	1.74	-1.38	-0.49
UliptoE T1	-0.04	0.28	-0.64	0.45	-0.14	0.07
LliptoE T1	0.09	0.26	-0.32	0.61	-0.01	0.18
NTP T1	-0.15	0.77	-1.51	1.35	-0.44	0.14
ICW T1	-1.21	0.85	-2.64	1.27	-1.53	-0.89

Table 4.3 Descriptive statistics including mean, SD, Min, Max and 95% CI for 14 outcome variables at T1

At T0, pertaining to Table 4.2 above, the mean values indicating the difference between CBCT and 3D facial scan measurements ranged from 0.01mm-1.38mmm and similarly, at T1, pertaining to Table 4.3 above, the mean values ranged from 0.08mm-1.21mm. Through these descriptive statistical analyses, it was also determined that there were potential concerns for the measurements ABW at T0 and T1 as well as ICW at T0 and T1.

Reviewing both Tables 4.2 and 4.3, first taking ABW data into perspective, it was noted that the mean ABW difference at T0 was -1.24mm and the mean ABW difference at T1 was -1.08mm. Similarly, for the ICW data, it was noted that the mean ICW difference at T0 was -1.38mm and the mean ICW difference at T1 was -1.21mm. Clearly, for both of these outcome variables, there was a difference between what was found using CBCT imaging and what was found using 3D facial scans. This was further confirmed through

MANOVA statistical analysis, the results of which are presented later in Tables 4.8 and 4.9 of this chapter. It can be seen in tables 4.8 and 4.9 that that the ABW and ICW measurements are the most different between the two imaging modalities and this finding is further elaborated upon in the discussion section in Chapter 5.

The percentage change was also calculated using the formula (T1-T0)/T0*100%. Average percentages and 95% CI are described in Table 4.4 and 4.5 below.

			Mean	Standard Deviation	Minimum	Maximum	95.0% Lower CL for Mean	95.0% Upper CL for Mean
GROUP	Control	ABW % change	3.66	2.50	-0.60	8.78	2.27	5.04
		AW % change	1.73	2.81	-3.55	6.42	0.17	3.29
		MW % change	3.12	2.88	-0.85	8.16	1.53	4.71
		PW % change	10.60	9.86	-5.51	31.82	5.14	16.06
		HofN % change	2.56	2.55	-1.11	8.18	1.15	3.98
		NLangle % change	-0.46	1.50	-2.80	2.05	-1.29	0.37
		HofUL % change	3.87	3.56	-2.01	8.79	1.90	5.84
		HofVUL % change	13.94	11.76	-1.67	36.48	7.43	20.46
		HofLL % change	5.21	2.02	1.23	7.89	4.09	6.33
		LFH % change	3.26	1.67	0.21	6.07	2.33	4.18
		UliptoE % change	42.96	66.44	-46.94	197.10	6.17	79.76
		LliptoE % change	-8.83	63.66	-177.89	74.42	-44.08	26.42
		NTP % change	5.87	4.02	-2.76	10.17	3.64	8.10
		ICW % change	1.52	1.57	-0.52	4.33	0.65	2.39
	Treatment	ABW % change	4.02	4.06	-0.35	11.16	1.77	6.27
		AW % change	2.62	3.22	-0.90	7.57	0.83	4.40
		MW % change	3.80	2.92	-1.23	9.27	2.18	5.42
		PW % change	10.35	8.95	-4.16	25.62	5.39	15.30
		HofN % change	1.61	3.06	-2.81	6.67	-0.08	3.30
		NLangle % change	-1.65	1.88	-3.26	2.91	-2.69	-0.61
		HofUL % change	5.86	6.83	-4.64	25.01	2.07	9.64
		HofVUL % change	8.23	10.89	-10.57	29.37	2.20	14.26
		HofLL % change	3.26	3.26	-2.38	11.99	1.46	5.07
		LFH % change	2.34	1.66	-0.31	5.05	1.42	3.26
		UliptoE % change	-47.54	149.98	-553.85	61.83	-130.60	35.51
		LliptoE % change	-46.09	116.58	-456.67	36.41	-110.65	18.47
		NTP % change	4.71	3.07	0.29	9.48	3.01	6.41
		ICW % change	1.18	0.92	-0.20	3.23	0.68	1.69

Table 4.4 Descriptive statistics for percentage change in 3D facial scan measurements by study groups

			Mean	Standard Deviation	Minimum	Maximum	95.0% Lower CL for Mean	95.0% Upper CL for Mean
GROUP	Control	ABW % change	4.92	3.00	-1.18	10.34	3.26	6.59
		AW % change	2.56	2.32	0.16	8.20	1.28	3.85
		MW % change	2.59	3.52	-3.75	7.56	0.64	4.54
		PW % change	11.23	10.08	-3.27	28.16	5.65	16.82
		HofN % change	3.20	2.95	-1.18	10.65	1.56	4.83
		NLangle % change	-0.15	2.07	-3.36	4.73	-1.30	0.99
		HofUL % change	3.54	4.18	-3.42	9.03	1.23	5.86
		HofVUL % change	13.85	12.43	-0.62	41.64	6.96	20.73
		HofLL % change	5.12	2.85	1.14	12.77	3.55	6.70
		LFH % change	3.09	2.10	-0.29	7.82	1.93	4.25
		UliptoE % change	80.67	159.71	-60.39	582.35	-7.77	169.12
		LliptoE % change	-3.99	67.59	-178.57	93.00	-41.43	33.44
		NTP % change	5.93	4.32	-1.49	15.30	3.54	8.33
		ICW % change	2.65	2.14	-0.99	6.17	1.47	3.84
	Treatment	ABW % change	4.08	3.27	0.22	9.91	2.27	5.89
		AW % change	2.84	3.08	-2.31	8.42	1.14	4.55
		MW % change	3.74	3.70	0.31	13.41	1.70	5.79
		PW % change	9.70	7.18	-0.58	20.70	5.72	13.68
		HofN % change	1.72	2.86	-2.79	6.11	0.14	3.30
		NLangle % change	-1.61	1.93	-3.33	2.59	-2.68	-0.54
		HofUL % change	6.58	6.36	-6.55	21.87	3.06	10.10
		HofVUL % change	9.53	11.97	-9.41	37.38	2.90	16.16
		HofLL % change	3.96	4.49	-2.50	16.37	1.47	6.44
		LFH % change	2.48	1.80	-0.08	5.97	1.48	3.48
		UliptoE % change	-72.12	255.22	-975.00	56.59	-213.45	69.21
		LliptoE % change	-34.95	98.17	-379.07	34.10	-89.32	19.41
		NTP % change	4.66	3.52	-1.01	11.27	2.71	6.62
		ICW % change	1.33	1.29	-1.18	3.04	0.62	2.05

Table 4.5 Descriptive statistics for percentage change in CBCT measurements by study groups

Another interesting observation from Tables 4.4 and 4.5 above is that some of the outcome variables showed slightly higher percentage changes for the control group as opposed to the treatment group, whereas the opposite may be expected considering the effects of RME. For example, looking at the CBCT percentage changes shown in Table 4.5, it can be seen that the ABW (alar base width) mean percentage change was 4.92% in the control group whereas it was slightly lower in the treatment group at 4.08%.

However, it is important to note that the mean percentage difference between the two groups was only 0.84%, which is very minimal. Lastly, it is important to note that when analyzing the data pertaining to 3D facial scan measurements in Table 4.4 and the data pertaining to CBCT measurements in Table 4.5, there are aberrations noted in the mean percentage changes shown for Upper Lip to E plane and Lower Lip to E plane. In Table 4.4, it can be seen that for the 3D facial scanning modality, in the treatment group, the mean percentage change for the U lip to E line was -47.54% with a standard deviation of 149.98%, a minimum of -553.85%, and a maximum of -456.67%. The mean percentage change seen for the L lip to E line in the same group was -46.09%, with a standard deviation of 116.58%, a minimum of -456.67% and a maximum of 36.41%. The mean percentage changes, standard deviation, minima and maxima seen for the corresponding control group, as well as for the treatment and control groups for the CBCT imaging modality, were correspondingly aberrant as opposed to the other outcome variable related data, and this is seen in both Tables 4.4 and 4.5. This is further elaborated upon in the discussion section of Chapter 5.

The mean changes in each of the 13 linear distances and 1 angular measurement were calculated between two time points: post-treatment (T1) and pre-treatment (T0). The results are summarized in Table 4.6 and Table 4.7 below.

Measurement	Control Group (n = 15)			
	3D Facial Scan		CBCT	
	M ± SD	[Min, Max] (95% CI)	M ± SD	[Min, Max] (95% CI)
Alar Base Width (ABW)	1.12 ± 0.76	[-0.16, 2.57] (0.70, 1.54)	1.41 ± 0.78	[-0.29, 2.58] (0.98, 1.85)
Alar Width (AW)	0.55 ± 0.94	[-1.22, 2.41] (0.03, 1.07)	0.81 ± 0.72	[0.05, 2.55] (0.41, 1.20)
Mouth Width (MW)	1.26 ± 1.14	[-0.34, 3.22] (0.63, 1.90)	1.01 ± 1.39	[-1.57, 3.22] (0.24, 1.78)
Philtrum Width (PW)	0.91 ± 0.77	[-0.56, 2.17] (0.48, 1.34)	0.95 ± 0.81	[-0.33, 2.27] (0.50, 1.40)
Height of Nose (HofN)	1.06 ± 1.03	[-0.46, 3.17] (0.49, 1.63)	1.29 ± 1.14	[-0.46, 3.97] (0.66, 1.92)
Nasolabial Angle (NL)	-0.60 ± 1.76	[-3.56, 2.43] (-1.57, 0.37)	-0.27 ± 2.24	[-4.30, 4.20] (-1.51, 0.97)
Height of Upper Lip (HofUL)	0.83 ± 0.76	[-0.37, 2.01] (0.40, 1.25)	0.73 ± 0.85	[-0.65, 1.82] (0.26, 1.20)
Height of Vermillion of Upper Lip (HofVUL)	0.92 ± 0.70	[-0.08, 2.32] (0.54, 1.31)	0.97 ± 1.02	[-0.03, 3.31] (0.41, 1.54)
Height of Lower Lip (HofLL)	2.21 ± 0.87	[0.62, 3.61] (1.73, 2.69)	2.11 ± 1.22	[0.55, 5.54] (1.44, 2.78)
Lower Facial Height (LFH)	2.12 ± 1.13	[0.11, 4.17] (1.50, 2.75)	1.94 ± 1.37	[-0.21, 5.15] (1.18, 2.70)
Upper Lip to E-line (ULtoE)	0.19 ± 0.79	[-1.16, 1.36] (-0.25, 0.63)	0.15 ± 1.01	[-1.38, 1.98] (-0.40, 0.71)
Lower Lip to E-line (LLtoE)	0.15 ± 0.97	[-1.69, 2.09] (-0.39, 0.69)	0.32 ± 1.18	[-2.00, 2.39] (-0.33, 0.97)
Nasal tip prominence (NTP)	1.47 ± 0.96	[-0.65, 2.53] (0.94, 2.00)	1.47 ± 0.99	[-0.34, 3.54] (0.93, 2.02)
Intercanthal Width (ICW)	0.50 ± 0.52	[-0.17, 1.40] (0.21, 0.79)	0.82 ± 0.66	[-0.29, 1.81] (0.45, 1.18)

Notes: M = mean, SD = standard deviation

Table 4.6 Changes in facial soft tissue measurements in the control group, n = 15

Measurement	Treatment Group (n = 15)			
	3D Facial Scan		CBCT	
	M ± SD	[Min, Max] (95% CI)	M ± SD	[Min, Max] (95% CI)
Alar Base Width (ABW)	1.21 ± 1.22	[-0.12, 3.36] (0.53, 1.88)	1.24 ± 0.99	[0.07, 3.14] (0.69, 1.79)
Alar Width (AW)	0.87 ± 1.06	[-0.29, 2.57] (0.29, 1.46)	0.93 ± 1.02	[-0.84, 2.83] (0.36, 1.49)
Mouth Width (MW)	1.60 ± 1.16	[-0.55, 3.45] (0.95, 2.24)	1.51 ± 1.37	[0.14, 4.92] (0.75, 2.27)
Philtrum Width (PW)	0.96 ± 0.83	[-0.42, 2.65] (0.50, 1.42)	0.95 ± 0.70	[-0.05, 2.32] (0.56, 1.33)
Height of Nose (HofN)	0.68 ± 1.33	[-1.28, 2.57] (-0.06, 1.42)	0.73 ± 1.25	[-1.34, 2.69] (0.03, 1.42)
Nasolabial Angle (NL)	-1.93 ± 2.19	[-3.87, 3.34] (-3.14, -0.71)	-1.89 ± 2.26	[-3.90, 3.10] (-3.14, -0.64)
Height of Upper Lip (HofUL)	1.16 ± 1.23	[-1.04, 4.19] (0.48, 1.84)	1.26 ± 1.16	[-1.41, 3.68] (0.62, 1.90)
Height of Vermillion of Upper Lip (HofVUL)	0.52 ± 0.64	[-0.72, 1.68] (0.17, 0.88)	0.66 ± 0.74	[-0.84, 1.97] (0.25, 1.07)
Height of Lower Lip (HofLL)	1.35 ± 1.31	[-1.23, 4.55] (0.63, 2.08)	1.59 ± 1.73	[-1.29, 6.03] (0.63, 2.54)
Lower Facial Height (LFH)	1.50 ± 1.03	[-0.21, 3.21] (0.93, 2.08)	1.58 ± 1.17	[-0.05, 3.94] (0.93, 2.23)
Upper Lip to E-line (ULtoE)	-0.23 ± 0.80	[-1.85, 1.03] (-0.67, 0.21)	-0.30 ± 0.71	[-1.81, 0.67] (-0.69, 0.09)
Lower Lip to E-line (LLtoE)	-0.28 ± 0.90	[-1.64, 0.89] (-0.78, 0.22)	-0.30 ± 0.89	[-1.90, 0.89] (-0.80, 0.19)
Nasal tip prominence (NTP)	1.20 ± 0.75	[0.09, 2.38] (0.78, 1.61)	1.21 ± 0.89	[-0.27, 2.83] (0.71, 1.70)
Intercanthal Width (ICW)	0.40 ± 0.33	[-0.06, 1.15] (0.22, 0.58)	0.43 ± 0.41	[-0.36, 0.98] (0.21, 0.66)

Notes: M = mean, SD = standard deviation

Table 4.7 Changes in facial soft tissue measurements in the treatment group, n = 15

Table 4.6 presents descriptive analysis summarizing the change in measurements over time for each of the fourteen measurements separately by the two modalities. Negative values indicate decrease in outcomes and positive are increases. Majority of the changes have positive mean values suggesting that the values have increases in post-measurements compared to pre-treatment measurements. When evaluating the data in Tables 4.6 and 4.7 above, the mean values presented are nearly 1mm on average for the

linear measurements, and the mean changes in soft tissue facial measurements for 3D facial scans are fairly similar to those measurements for CBCT imaging, which suggests that both imaging tools can capture the mean changes over time in a fairly similar manner. Looking at the confidence intervals associated with the mean changes in soft tissue measurements presented in Table 4.6, it can be seen that the majority of confidence intervals with the exception of nasolabial angle, upper lip to E line, and lower lip to E line, do not include zero and thus suggest that these mean changes in soft tissue measurements may be interpreted as statistically significant at the p=0.05 level. The outcome variables with confidence intervals that include zero, specifically, nasolabial angle, upper lip to E line, and lower lip to E line, indicate that no significant change in measurements took place from the initial to the final time point. The minimum and maximum values provide a range of changes (negative being decreases and positive being increases).

Table 4.7 is similar to Table 4.6, but for patients in the treatment group. The values are similar between Tables 4.6 and 4.7, suggesting that changes occurred in a similar way in both control and treatment groups. The average increase is also about 1mm in the treatment group for the linear measurements. There is, however, one noticeable difference in the treatment group. Nasolabial angle values have decreased significantly (both boundaries of the confidence interval are negative), while in the control group, nasolabial angle had no significant change.

The variability of data can be assessed using standard deviation and ranges (minimum/maximum values) and is similar between 3D facial scan and CBCT measurements and between the control and treatment groups. In the treatment group, it ranges from 1.9mm decrease to 6.03mm increase and from 2.0mm decrease to 5.5mm increase in the control group for the linear measurements. In addition, the outcome variables for both control and treatment groups for 3D facial scans appear to have a similar range of mean changes for linear measurements (from 1.85mm decrease to 4.19mm increase). Similarly, for CBCTs, the mean changes (from 2.00mm decrease to 6.03mm increase) also demonstrate limited variability.

4.6 Results pertaining to Part A research questions

Part A question 1:

1. Are there differences in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and post-treatment (T1)?

MANOVA model results

	Model 1	**Model 2**
DV	Difference between CBCT and 3D facial scan at T0	Difference between CBCT and 3D facial scan at T1
	$F_{(14,16)} = 15.30$, $p < 0.001$	$F_{(14,16)} = 13.31$, $p < 0.001$

Note: DV = dependent variable; Wilk's Lambda statistics is reported

The *p*-values in the table above indicate that there are statistically significant differences in the mean facial soft tissue measurements jointly between CBCTs and 3D facial scans at pre-treatment (T0), and similarly at post-treatment (T1).

Part A question 2:

2. Are the CBCT and 3D facial scan derived facial soft tissue measurements jointly reliable at pre-treatment (T0), and post-treatment (T1)?

Table 4.8 and Table 4.9 below provides statistics pertaining to research question 2, including the mean difference between CBCT and 3D facial scan (CBCT-3D facial scan), for each of the fourteen outcome variables, the p-values, intraclass correlation coefficients and 95% confidence intervals.

Dependent Variable	Mean difference	Sig. (p- value)	95% Confidence Interval Lower Bound	Upper Bound	Intraclass Correlation[b]	95% Confidence Interval Lower Bound	Upper Bound
ABW T0	-1.245	<0.001	-1.667	-0.823	0.865[a]	0.266	0.958
AW T0	-0.791	<0.001	-1.165	-0.417	0.878[a]	0.562	0.954
MW T0	-0.342	0.100	-0.754	0.069	0.952[a]	0.764	0.984
PW T0	-0.193	0.082	-0.413	0.026	0.952[a]	0.776	0.983
HofN T0	-0.748	<0.001	-1.089	-0.408	0.829[a]	0.329	0.940
NL angle T0	-0.510	0.046	-1.009	-0.010	0.957[a]	0.912	0.979
HofUL T0	-0.762	<0.001	-1.066	-0.457	0.843[a]	-0.022	0.960
HofVUL T0	-0.012	0.908	-0.223	0.199	0.970[a]	0.859	0.989
HofLL T0	-0.988	<0.001	-1.425	-0.550	0.992[a]	0.983	0.996
LFH T0	-0.883	<0.001	-1.296	-0.469	0.960[a]	0.917	0.981
UliptoE T0	0.020	0.766	-0.118	0.159	0.985[a]	0.968	0.993
LliptoE T0	0.012	0.866	-0.136	0.160	0.951[a]	0.900	0.976
NTP T0	-0.155	0.331	-0.475	0.165	0.935[a]	0.865	0.969
ICW T0	-1.384	<0.001	-1.685	-1.083	0.989[a]	0.977	0.995

Two-way mixed effects model where people effects are random and measures effects are fixed.
a. The estimator is the same, whether the interaction effect is present or not.
b. Type A intraclass correlation coefficients using an absolute agreement definition.
Note: Significant mean difference values, p-values and 95% CI <0.7 are highlighted in blue

Table 4.8 Mean difference between CBCT and 3D facial scan (CBCT-3D facial scan), p-values, intraclass correlation coefficients and 95% confidence intervals at T0

Dependent Variable	B (Mean difference)	Sig. (p- value)	95% Confidence Interval Lower Bound	Upper Bound	Intraclass Correlation[b]	95% Confidence Interval Lower Bound	Upper Bound
ABW T1	-1.083	<0.001	-1.454	-0.712	0.898[a]	0.364	0.969
AW T1	-0.634	<0.001	-0.949	-0.319	0.924[a]	0.717	0.972
MW T1	-0.511	0.012	-0.902	-0.120	0.955[a]	0.767	0.985
PW T1	-0.181	0.093	-0.393	0.032	0.950[a]	0.828	0.981
HofN T1	-0.614	<0.001	-0.948	-0.280	0.850[a]	0.332	0.949
NL angle T1	-0.323	0.175	-0.799	0.152	0.974[a]	0.947	0.988
HofUL T1	-0.759	<0.001	-1.048	-0.470	0.875[a]	0.089	0.966
HofVUL T1	0.079	0.389	-0.105	0.263	0.967[a]	0.854	0.988
HofLL T1	-0.920	<0.001	-1.318	-0.522	0.996[a]	0.991	0.998
LFH T1	-0.935	<0.001	-1.382	-0.488	0.956[a]	0.893	0.980
UliptoE T1	-0.037	0.473	-0.139	0.066	0.987[a]	0.974	0.994
LliptoE T1	0.086	0.080	-0.011	0.183	0.959[a]	0.916	0.980
NTP T1	-0.150	0.292	-0.437	0.136	0.938[a]	0.873	0.970
ICW T1	-1.209	<0.001	-1.527	-0.891	0.995[a]	0.989	0.997

Two-way mixed effects model where people effects are random and measures effects are fixed.
a. The estimator is the same, whether the interaction effect is present or not.
b. Type A intraclass correlation coefficients using an absolute agreement definition.
Note: Significant mean difference values, p-values and 95% CI <0.7 are highlighted in blue

Table 4.9 Mean difference between CBCT and 3D facial scan (CBCT-3D facial scan), p-values, intraclass correlation coefficients and 95% confidence intervals at T1

In Tables 4.8 and 4.9 above, the mean values at T0 and T1 were below 1mm with the exception of alar base width and intercanthal width. 8 out of the 14 outcome variables at both T0 and T1 show a statistically significant difference in the mean facial soft tissue measurements between CBCTs and 3D facial scans.

4.7 Results pertaining to Part B research questions

Part B question 3 and 4:

3. Are there differences in the mean facial soft tissue 3D facial scan measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)?

4. Are there differences in the mean facial soft tissue CBCT measurements jointly between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group) at pre-treatment (T0)?

MANOVA model results

	Model 1 Difference between treatment and control groups at T0 utilizing 3D facial scan	**Model 2** Difference between treatment and control groups at T0 utilizing CBCT	**Model 2A** Difference between treatment and control groups at T0 utilizing CBCT (ABW and ICW only)
Group	$F_{(14,15)} = 1.51$, $p = 0.220$	$F_{(14,15)} = 2.08$, $p = 0.086$	$F_{(2,27)} = 1.54$, $p = 0.232$

Note: DV = dependent variable; Wilk's Lambda statistics is reported

As per the results above, the *p*-values indicate that there is no statistically significant difference between treatment and control groups at T0 utilizing 3D facial scans and CBCTs. When considering the difference between treatment and control groups at T0 utilizing CBCT for the outcome variables of ABW and ICW only, there was also no statistically significant difference between the two groups, and these findings are further discussed in Chapter 5.

Part B question 5 and 6:

5. Are there differences in the mean change (T1-T0) of soft tissue 3D facial scan measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)?

6. Are there differences in the mean change (T1-T0) of soft tissue CBCT measurements jointly from pre-treatment (T0) to post-treatment (T1), between patients that underwent maxillary expansion (treatment group) and patients that did not undergo maxillary expansion (control group)?

MANOVA model results

	Model 1 Difference between treatment and control groups from T0 to T1 utilizing 3D facial scan soft tissue measurements	**Model 2** Difference between treatment and control groups from T0 to T1 utilizing CBCT soft tissue measurements	**Model 2A** Difference between treatment and control groups from T0 to T1 utilizing CBCT (ABW and ICW only)
Group	$F_{(14,15)} = 1.14$, $p = 0.400$	$F_{(14,15)} = 1.76$, $p = 0.143$	$F_{(2,27)} = 1.76$, $p = 0.192$

Note: DV = dependent variable; Wilk's Lambda statistics is reported

As per the results above, the *p*-values indicate that there is no difference between treatment and control groups from T0 to T1 utilizing 3D facial scan soft tissue measurements and CBCT measurements alike. Similarly, when the difference between treatment and control groups from T0 to T1 utilizing CBCTs with respect to ABW and ICW only were assessed, there was no statistically significant difference noted.

Chapter 5: Discussion, Limitations and Conclusions

5.1 Discussion

Our study was intended to explore the effects of maxillary expansion on facial soft tissues in children aged 7-11 years with maxillary constriction, utilizing both CBCTs and 3D facial scans. At the time of this study, there were no other known studies assessing the effects of maxillary expansion on facial soft tissues utilizing both modalities (CBCTs and 3D facial scans). In addition, there were a limited number of existing studies that included a control group, which would be beneficial in identifying any potential effect on the facial soft tissues from natural growth; thereby, this was an important factor to consider in this study [2,10,13,15,16,36].

Focusing first on the recruited treatment and control groups included in the study, it was found through inferential statistical analysis that when comparing key characteristics between the two groups at baseline including parameters such as chronological age, gender and Fishman's SMI, no statistically significant differences were found between the two groups. This was further confirmed through MANOVA statistical analysis, the results of which are presented in Section 4.7 of Chapter 4 (results pertaining to part B Research Questions 3 and 4). MANOVA analysis revealed that there was no difference between groups at baseline (T0). There was no evidence against H_o ($p = 0.22$), indicating that there is no difference in treatment and control groups at T0 utilizing 3D facial scans, weak evidence ($p = 0.086$) supporting no difference in treatment and control groups at T0 utilizing CBCTs. When considering the difference between treatment and control groups at T0 utilizing CBCT for the outcome variables of ABW

and ICW only, there was no evidence against H_o ($p = 0.232$), indicating that there is no difference. These findings indicate that the two groups, each consisting of 15 patients, were well balanced and contributed to the strength of the results and validity of this case control study.

Furthermore, in comparison with other recent and applicable research studies focusing on the soft tissue effects of RME therapy on young patients, this study included a control group whereas the majority of those studies did not include a control group as a method of standardization and as a point of comparison with the treatment group [2,10,13,15,16,36]. As per the systematic review conducted by Huang et al in 2018, only 5 of the 15 included studies in the review noted the presence of a control group [2]. The authors of this systematic review and meta analysis noted that one of the key limitations of the current body of existing literature focusing on this particular orthodontic subject is the lack of use of control groups and the overall moderate quality of evidence that is currently available [2]. Therefore, one of the positive attributes of the present study is the inclusion of the control group as a mode of reference, comparison, and as a contribution to the validity of the results of the study.

Moreover, within the study itself, descriptive statistical analyses were conducted in order to analyze data and produce useful results and connections. As per Tables 4.2 and 4.3 in Chapter 4, taking both the CBCT and the 3D facial scan data for each outcome variable at T0 and also at T1, the mean difference between the two modalities was calculated (CBCT-3D facial scan), and the means and 95% confidence intervals were

presented in the aforementioned tables. The intention of this statistical analysis and the fabrication of these two tables was to confirm similarities and identify major potential differences between measurements that were found using the CBCT imaging modality as compared with the 3D facial scanning modality. Ideally, the difference between the two measurements determined by the two different imaging modalities for one particular outcome variable at either T0 or T1 should be zero or as close to zero as possible. It has been identified that absolute differences between these two values greater than 1 millimetre are considered pertinent with respect to the accuracy of directly comparing the measurements obtained from each modality [48-53]. This statement is widely supported by the literature that has focused on comparing, registering, and superimposing imagery obtained through 3D facial scanning and CBCT imaging with respect to the investigation of craniofacial soft tissues and soft tissue measurements [48-53]. In the Kyung-Yen Nahm et al study focusing on the accurate registration of CBCT scans and 3D facial scans, the authors found that on average, the soft tissue surface discrepancy between the two modalities should be approximately 0.60 mm [52].

The authors also found that discrepancies between imagery obtained through the two modalities can be the result of CBCT data inaccuracy, alterations in facial expressivity, changes in spatial soft tissues, and alterations in the positioning of patients [52]. Furthermore, other studies also focusing on this topic have shown that the level of registration or superimposition accuracy between CBCT imaging and 3D facial scanning is between 0.3 mm and 1.5 mm on average, taking the composite of what has been seen in these other studies [48-53]. A landmark study by Aljawad et al comparing the

two different imaging modalities with respect to soft tissue measurements and analyses used three separate methods to integrate the CBCT and 3D facial scanning images for each patient [48]. The authors found and concluded that for all three methods, the soft tissue surface differences on average were less than 1mm [48]. In the study by Toma et al, it was found that most of the twenty-one facial landmarks that were identified were within 1mm and considered acceptable, with a range from 0.39 to 1.49mm [51]. With the aforementioned in mind, the author of this study found it prudent that, based on the current body of evidence available, variations in measurements between the two imaging modalities for outcome variables less than 1mm are clinically acceptable with respect to accuracy and validity of comparison [48-53].

As per Tables 4.8 and 4.9 in the results section of Chapter 4 pertaining to the difference between the two modalities, all the mean values at T0 and T1 alike were below 1mm with the exception of alar base width and intercanthal width. The difference in absolute values between the two imaging modalities in relation to the two variables of ABW and ICW are greater than one, and thereby raise the question whether they are comparable and interchangeable for these two outcome variables in particular. A question into this conundrum leads to the potential that the resulting data that was collected through these two different modalities in this study has limitations or potential deficits. It may have well contributed to the outcome of finding either or both statistically and clinically insignificant final results and raises the limitation of the applicability of these study results to clinical orthodontic and dental practices. Some potential explanations can be suggested as to why the absolute value differences for mean ABW and mean ICW are

above the value of one. First, it was noted by the author that with the collected CBCT imaging data, the patients eyes were normally closed whereas in the 3D facial scanning imaging data, the patients eyes were normally open. As the state of the eyes being open or closed may affect the ICW (intercanthal width) measurement, this finding and potential limitation in the data could help explain the aforementioned anomaly in the descriptive statistics. An example of this is illustrated in Figures 5.1 A and B below, wherein in the 3D facial scan, the patient's eyes are open but in the CBCT image of the same patient at the same observation timepoint, the eyes are closed.

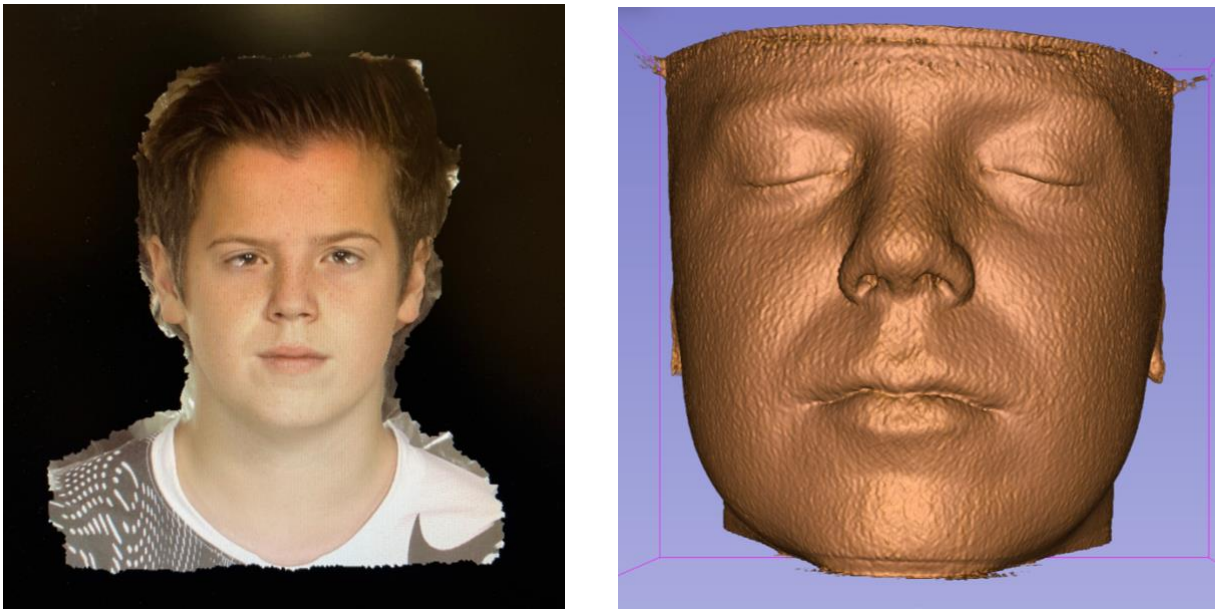


Figure 5.1 A: 3D facial scan (OrthoInsight 3D) and B: CBCT (3D slicer)

Moreover, in regards to the ABW (alar base width) measurements for both modalities, the placement of measuring landmarks was more subjective as opposed to the placement of measuring landmarks for other outcome variables. The presence of

patient positioning errors, patients not having a relaxed lip posture of neutral facial expression, and potential errors in image orientations could have further contributed to the aforementioned limitations. Through an investigation of other relevant and current studies focusing on soft tissue measurements using both CBCT imaging and 3D facial scanning, it can be seen that such discrepancies in soft tissue measurements between the two imaging modalities are widely present and the reasons provided for these discrepancies are similar to what was previously mentioned earlier in the discussion [48-53]. In addition, it should also be kept in mind that CBCT images have a poorer soft-tissue contrast in comparison to 3D facial scan images and that there may be an intrinsic error of 1 voxel when obtaining soft tissue data from CBCTs, as was also noted in the Nahm et al study [52]. In order to overcome measurement errors due to patient movement during image-taking or distorted anatomical data, fusion of the two modalities may be utilized, as described in the Jayaratne et al study [54].

The above discussion sheds more light with respect to what was found in response to research question 2 pertaining to the reliability of the CBCT and 3D facial scan derived facial soft tissue measurements. To further elaborate on the findings, it was found that intra and inter-rater reliability for CBCT and 3D facial scanning was optimal but the correlation between the two different imaging modalities was not as optimal as under ideal circumstances. As per the data presented in Table 1 in Appendix 4A, (Intra-rater and inter-rater reliability of measurements), it can be seen that for intra-rater reliability, for both 3D facial scans and CBCTs, the ICC values showed excellent agreement. For inter-rater reliability, the single measurements for ICC for both imaging modalities

showed excellent agreement; the 95% confidence intervals indicate that the inter-rater reliability ranged between good agreement at the lower end of the confidence intervals to excellent agreement at the upper bounds of the confidence intervals. Now taking Table 3 in Appendix 4A into context, the intraclass correlation coefficients between the two modalities, CBCT imaging and 3D facial scanning, can be visualized. In Table 3 in Appendix 4A, the author presents the correlation between the two imaging modalities utilizing three main outcome variables: alar width, mouth width, and nasal tip prominence. It can be seen that the ICC single measurements range from a low of 0.65 to a high of 0.98, which indicates a range of moderate agreement to excellent agreement as per the Portney and Watkin guidelines [55].

The confidence intervals for these ICC values, however, present a different perspective. For example, it can be seen that for the outcome variable of mouth width, the confidence interval for the ICC measurement ranges from 0.06 to 0.90. An interpretation of this confidence interval may be a point of concern as such a large range from a lower bound to an upper bound brings the correlation between CBCT imaging and 3D facial scanning into question. This phenomenon can perhaps be explained when considering that during CBCT imaging, the patients are instructed to bite in maximum intercuspation and place their tongues against the lingual surfaces of the maxillary central incisors as per the imaging protocols, and during 3D facial scanning, this was not the case. Given the younger age of the patients, some patients may have inadvertently not maintained a neutral facial expression when biting down in maximum intercuspation, and thereby affected the mouth width measurements in particular. An example of this is illustrated in

Figures 5.2 A and B below, wherein in the 3D facial scan, the patient has maintained a neutral facial expression but in the CBCT image of the same patient at the same observation timepoint, the facial expression is no longer neutral when in maximum intercuspation.

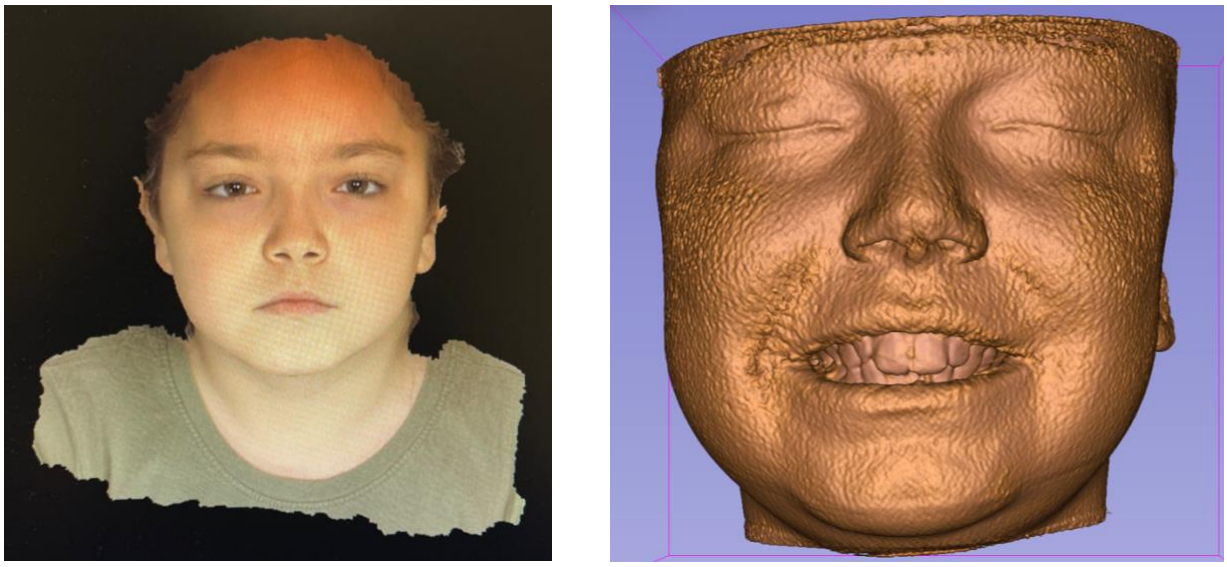


Figure 5.2 A: 3D facial scan (OrthoInsight 3D) and B: CBCT (3D slicer)

In comparison to previous studies, it was noted that soft tissue landmarks are less precise on the right and left lateral regions of the face [51,56]. The lower correlation seen have also been explained by the variability in subcutaneous soft tissues and the bony curvature of the facial structure on the lateral regions of the face [51,56]. In another study by Ayoub et al, in which stereophotogrammetry was compared with 3D CT scans taken separately, the errors were within ±1.5mm, and more so in the areas of the eyelids and cheeks, attributed to surface shape variances [53].

An additional key aspect of the study was calculating and investigating the percentage changes that were seen for each outcome variable from T0 to T1 for each of the two imaging modalities, CBCTs and 3D facial scans, as reported in Tables 4.4 and 4.5 of Chapter 4. This was completed for both the treatment group and the control group that were included within this study.

Reviewing the statistical data that was determined through analytical methods, it can be said that when comparing the percentage change for one particular outcome variable for both treatment and control groups, the percentage changes were fairly similar in value. For example, looking at ABW (alar base width) a commonly utilized soft tissue outcome variable investigated in comparable research studies, it can be seen that for the 3D facial scanning modality, the mean percentage change for the treatment group was 4.02% and this was quite similar to the mean percentage change of 3.66% for the control group. This finding is quite comparable to that found in the study by Truong et al from 2021 which showed that the treatment group underwent a total change in ABW of 1.95 mm ±1.8 mm while the control group underwent a total change in ABW of 1.29 mm ±1.4 mm [17]. These changes were not statistically significant, and due to the arithmetic closes of the differences seen in the treatment and control groups, the authors declared that the effect of RME on this soft tissue outcome variable, among many others, was not clinically significant [17]. Truong et al found similar results for a wide range of other soft tissue measurements including alar width, nasal length, nasal height, nasion-ANS height, and ANS-PNS height, to name a few [17]. Moreover, while also using alar base

width as a prime example, the study by Torun et al from 2017 further supports the discussion above [10]. Torun et al studied the effects of rapid palatal expansion on the craniofacial soft tissues of both pre and post-pubertal patients, and for both groups found statistically and clinically insignificant changes in alar base width measurements among others including nasal base width, philtrum width, upper lip length, nostril width, nostril height, columella width, nasolabial angle, and cheek projection [10]. Interestingly, Torun et al found that from the beginning of RPE therapy to 6 months post retention, the difference in alar base width over time was only 0.5 mm for the postpubertal group and 1 mm for the prepubertal group [10].

To further support the above claim, the outcome of mouth width as analyzed In Table 4.5 of Chapter 4, presented a mean percentage change of 2.59% in the control group and 3.74% in the treatment group. The difference between these two values indicates that the treatment group only experienced a comparable mean increase of 1.15% in mouth width as opposed to those patients included in the control group. The question that arises is whether this difference is clinically significant. That very question has been posed by many authors who have conducted similar research studies, and the overwhelming conclusion that has been seen by many authors is that the soft tissue differences noted between patients treated with RME therapy as opposed to those not treated with RME therapy are clinically insignificant although they may or may not be statistically significant [2,12,16,17,19,20,57]. The study by Baysal et al can shed more light on this perspective. In the study, which looked at craniofacial soft tissue changes after RPE utilizing 3D facial scanning, the authors completed a MANOVA statistical

analysis and found overwhelmingly statistically and clinically non significant differences between the RME treatment group and control group [18]. For mouth width specifically as an example, the difference between treatment and control at the end timepoint was a minimal 0.629mm, considered as non-significant [18].

As described in the results section in Chapter 4, there was a large range between the minimum and maximum values as well as standard deviations for certain outcome variables. The question may arise to the reader as to why this is so, and why the data presents in such an aberrant manner. The author suggests that the explanation for this lies in the fact that occasionally during data collection it was noted that the initial values for upper lip or lower lip to E line were quite small at T0, and these same values were quite larger at T1. A change of this manner that may be considered small in absolute measurement units such as in millimeters may appear excessively large in percentage terms.

For example, a patient in the control group who presented with 0.69mm distance from upper lip to E-line at T0 and 2.05mm at T1 utilizing 3D facial scans, demonstrates an increase of 197.1%. Similarly, for the lower lip to E-line, a patient in the control group presenting with -1.73mm at T0 and 0.36mm at T1 demonstrates a change of -177.9%. When evaluating the control group utilizing CBCTs, a patient who presented with 0.34mm distance from upper lip to E-line at T0 and 2.32mm at T1, demonstrates an increase of 582.4%. In the treatment group, utilizing CBCTs, a patient who presented with 0.12mm distance from upper lip to E-line at T0 and -1.05mm at T1, demonstrates a

change of -975%. These examples thus help explain the very large standard deviations and wide intervals seen between minima and maxima in Tables 4.4 and 4.5 of Chapter 4.

Furthermore, an analysis of the data presented in Tables 4.6 and 4.7 of Chapter 4 reveals more as to what can be deduced from the data collected in this research project and as to what may be the facial soft tissue changes attributed to RME therapy in growing children. Both Tables 4.6 and 4.7 present the mean changes in facial soft tissue measurements from the initial to the final time point (T0 to T1), and data is presented for both treatment and control groups as well as for both imaging modalities used in this study. When evaluating both Tables 4.6 and 4.7, all the measurements demonstrated positive changes over time, except nasolabial angle in both treatment and control groups, position of upper and lower lip to E line in the treatment group which demonstrated decreases in the angle and an overall retruded position of the upper and lower lip, which are similar to findings in other previously conducted studies. [2,10,15] This decrease in values may potentially be explained by the lip being stretched with expansion and thereby decreasing in thickness, as also reported by Kim et al. [36]

When taking Table 4.6 into perspective, which focuses on the mean changes in soft tissue measurements in the control group, the descriptive analysis shows that all the mean soft tissue facial changes have positive mean values with the exception of nasolabial angle, which suggests that the measurements have decreased from the initial to the final time point. This correlates to what was also seen in the study by

Santos et al, where the authors found a change of -3.0 degrees in the nasolabial angle from the initial to immediately post-expansion, which regressed to 0.5 degrees at the final time point of post-retention at 6 months [15]. The study by Torun et al corroborates this finding as it pertains to the nasolabial angle, as the authors found a net decrease of nasolabial angle of -1.6 degrees and -1.9 degrees in the pre-pubertal and post-pubertal groups, respectively, at 6 months retention [10]. However, it must be noted that other studies, including those by Altinidis et al, Akan et al, and Uysal et al, found net positive changes in the nasolabial angle over the course of the study, with an overall variation from 0.24 to 2.28 degrees increase [11,12,20]. However, only one of these three studies had a control group and statistically significant results which were considered as clinically insignificant [20]. This could potentially be explained by the variability in the patient ages, as all of these studies had average ages ranging from 12.4-13.4 years, in comparison to the patients included in this study (7-11 years of age), the design of expansion devices utilized (banded or bonded or acrylic splint RME), as well as other patient-related factors [10-12,15,20].

With respect to the soft tissue measurements of upper lip and lower lip to E line, a study by Halıcıoğlu et al found that both immediately after expansion with two different types of expanders, there was approximately 1mm decrease which was statistically significant, and after the retention period of 6.42 months on average, it regressed to that of pre-expansion values and was thereby not statistically significant [58]. Similarly, the systematic review by Huang et al found, that from pre expansion to post retention evaluating two relevant studies, the effect estimate mean difference was -0.11 mm for

the upper lip to E line measurement and 0.42 mm for the lower lip to E line measurement and thereby non-significant, similar to this present study [2]. Therefore, the authors concluded that RME likely did not cause clinically important changes in the relationships of the upper and lower lips to the E line, any changes that may have been caused acutely by RME post-expansion quickly and significantly relapsed following retention, and this relapse was likely due to maxillary and mandibular movement and rotation [2]. This is similar to the findings of our study and explains why there were minimal changes in those outcome variables over a one-year retention period.

Similarly, by reviewing the data presented in Table 4.7 of Chapter 4, which focuses on the treatment group, it can be seen that the majority of confidence intervals with the exception of nasolabial angle, upper lip to E line, and lower lip to E line, do not include zero and thus suggest that these mean changes in soft tissue measurements can be interpreted as statistically significant, as aforementioned for the control group. With this in mind, as was previously discussed and seen in other studies, statistical significance does not necessarily correlate to clinical significance [2,12,16,17,19,20,57]. The mean values of soft tissue measurement change for both the treatment group and control group, that are statistically significant, are nearly 1 mm, and this can be interpreted as not being clinically significant. Furthermore, by comparing the mean changes in facial soft tissue measurements for the treatment group as opposed to the control group, it can be seen that for those changes that were greater in the treatment group as opposed to the control group, the differences are minimal and generally less than 1 mm, further adding to the suggestion that the changes produces by RME therapy on facial soft

tissues is clinically insignificant. Another important observation to note is that some mean changes in facial soft tissue measurements for the treatment group were slightly lower in value than those of the control group. For example, considering the outcome variable of height of the nose, it can be seen that for the control group there was an increase of 1.06 ±1.03 mm as per the 3D facial scanning data. For the treatment group, there was a lower increase of 0.68 ±1.33 mm. At first glance, this would suggest that the control group underwent a greater increase in height of the nose from the initial to the final time point as opposed to the treatment group. However, it is again critical to note that both values are very similar with a mean difference of only 0.38mm which is clinically insignificant. In comparison to this finding, the study by Truong et al found that, for the height of the nose, the treatment group underwent an increase only 0.34mm immediately post-expansion which then increased to 4.39 mm over a time period of 2.84 years, whereas the control group underwent an increase of a lesser 2.87 mm over 2.25 years, with a difference of 1.52 mm between the groups that was found to be statistically non-significant between the two groups [17].Truong et al concluded in this study that in the long term, any gains seen in the treatment group as opposed to the control group were clinically similar and the authors supported the idea that rapid maxillary expansion did not produce differences in soft tissue measurements between treated and untreated patients [17].

When considering the lower facial third, previous studies have indicated that the mandible rotates downwards and backwards with RME, and similarly, this pattern is also seen with growth and development [1,15,30]. This may lead to a subsequent

increase in the lower facial height or lower lip height as well as soft tissue related changes in the nose and lips and in this present study, there were no significant differences between the treatment and control groups, when considering both modalities. These findings are supported the results of the review by Huang et al, in which the mean lower facial height changed by 0.42mm and the mean lower lip height changed by 0.48mm from pre-expansion to post-retention, and were statistically not significant [2].

In comparison to previous studies, certain outcome measurements, for example alar width, alar base width, nasal height and nasolabial angle demonstrated statistically significant but clinically insignificant changes in the treatment group over a shorter period of time (immediately post-expansion), which regressed to being similar to the control group and therefore statistically insignificant when observed over a longer period of retention time [17, 20]. In addition, it was seen that studies with no control groups for comparison typically demonstrated a higher number of statistically significant changes in various soft tissue measurements such as alar width, philtrum width, mouth width and lower face height [10-13,15,57]. However, having a control group is very important for comparison as growth is a significant factor that needs to be accounted for and evaluated, especially in a younger population.

MANOVA analysis conducted to address questions 5 and 6 demonstrated no evidence against H_o ($p = 0.400$), indicating that there is no difference between treatment and control groups from T0 to T1 utilizing 3D facial scan soft tissue measurements and no

evidence against H_o ($p = 0.143$), indicating that there is no difference between treatment and control groups from T0 to T1 utilizing CBCT soft tissue measurements. When the difference between treatment and control groups from T0 to T1 utilizing CBCTs with respect to ABW and ICW only were assessed, there was no evidence against H_o ($p = 0.192$), indicating no statistically significant difference. The findings above suggest that the patients treated with RME experience facial soft tissue changes similar to those of patients without any expansion over a period of one year, in regards to both CBCTs and 3D facial scans. The findings of our study, in contrast with other studies that demonstrated statistically significant changes, either immediately post-expansion or post-retention, indicate that perhaps those changes were largely due to natural growth and development, and not necessarily due to RME treatment, especially in studies without any control group for comparison [2,14,16]. This is further supported by studies that showed that non-significant changes overall, or studies that demonstrated that the significant changes at post-expansion regressed to a mean of normal growth over a longer observation period [12,13,15,17,58].

In addition, in regards to the findings of this study not yielding statistically significant results in regards to soft tissue facial changes over time between the treatment and control groups, it may be inferenced that the findings are thereby also not clinically relevant as the overall changes in facial soft tissues are likely too small to have any implications on orthodontic treatment planning as well as patient perceptions, especially when compared to children undergoing natural growth and development. This is further supported by comparison to studies that demonstrated statistically significant yet

clinically non-significant changes after RME, where the authors mentioned that the differences were not significant enough to impact the entire face and patients' perceptions [18, 20].

5.2 Limitations

Certain considerations for this study include that although both CBCT and 3D facial scan records were taken on the same day for study participants, the protocols, particularly in regards to patient positioning were somewhat different, thereby potentially affecting facial expressions inadvertently. Outcome variables such as the height of the upper lip for example that could have been potentially affected by changes in facial expressions, and these study participants may have been excluded; had it not been for the limited sample size.

Additionally, when obtaining the soft tissue volume rendering utilizing the 3D slicer software for the CBCT images, it should be taken into consideration that there may still be potential for inaccuracy errors when comparing semi-automatic algorithms versus manual algorithms, although studies have shown that the proportions are fairly equivalent between the two methods, yet varied between different types of software utilized [59, 60].

As per the sample size determination calculations, a much larger sample size of 184 study participants (92 patients in each group) was suggested by the calculations, and this thereby can be perceived to be a limitation of this study. However, with this in mind, it must be stated that given the limited age range (7-11 years) and specific inclusion criteria of this study, recruiting such a large sample size would be challenging in the context of this study. In comparison to other past similar studies that have evaluated the effects of RME as per the systematic review by Huang et al, the sample sizes for majority of the included studies (8 out of 15) had sample sizes ranging from 14 to less than 30, 4 studies had sample sizes ranging from 30 to 36, and 3 studies had sample sizes ranging from 42 to 102 participants [2], and overall included a larger age range of 7-16 years. From a clinical perspective, it may be challenging to obtain such a large sample size from one institution and clinical trial, and perhaps collaboration with other institutions or private practices may be considered in order to meet the needs of the sample size calculation. It is also important to note that the prospective clinical trial is still ongoing at this time.

Although weak evidence was noted in that there was no statistically significant difference between the genders of sample participants in the treatment and control groups at baseline, there were 7 females in the control group compared to 12 in the treatment group and 8 males in the control group compared to only 3 in the treatment group. Gender may influence the amount of difference in the outcome measurements as it has been known that females tend to reach puberty approximately two years sooner than males on average [1]. It may be noteworthy to see whether or not gender

may affect the rate and amount of changes expected in the facial soft tissues with expansion versus natural growth. In a study by Johnson et al, it was found that gender did not have any significant effects on soft tissue changes, however, the patients were 13.5 years on average, and the retention period was 5.7 months on average [57]. Given the time limitations and prospective nature of this research, this could not be addressed as part of this study as a more equal distribution of genders in the treatment and control groups would be required, as well as a larger sample size for appropriate statistical analyses.

Another consideration may be that bearing in mind that the Canadian population in general is fairly diverse, and no background data was available in regards to the ethnic backgrounds of the study participants, it may be interesting to see if that may potentially affect the amount of change in facial soft tissues at different timepoints in the growth cycle. Different ethnic populations generally show different growth patterns, such as Asian populations generally displaying maxillary deficiencies associated with skeletal Class III malocclusions and Caucasian populations generally displaying mandibular deficiencies associated with skeletal Class II malocclusions [1].

Another potential limitation of the study is in the number of time points assessed (pre-expansion versus post-retention at a one-year time period). Ideally, if possible, a future study may benefit from examining measurements at several timepoints, including pre-expansion, immediately post-expansion, post-expansion at 6 months retention, and successive post-retention measurements. By having several measurements at various

timepoints, a more comprehensive and detailed analysis of soft tissue changes post-expansion could be completed. However, considering the amount of radiation and the ALARA (as low as reasonably achievable) principle as outlined by the Centers for Disease Control and Prevention, this may pose a potential challenge, and perhaps 3D facial scans could be utilized instead to minimize the risks of radiation [61]. In addition, as noted previously, CBCT imaging may include more potential for patient positioning errors as well as field of view considerations.

Moreover, given the current technology available, it may also be notable to compare different modalities of assessing the soft tissue facial changes – for example linear measurements derived from landmarks versus superimposition of images or surface registrations which may potentially yield more accurate results. Given the time limitations of this study and the specific software programs needed, this could not be assessed as part of this study, although a comparison between CBCT scans and 3D facial scans was assessed. In addition, Manhattan distances may be assessed instead of Euclidean distances due to the high dimensionality of facial soft tissues. Euclidean distance is defined as the shortest distance between two points whereas Manhattan distance is measured along axes at right angles [62]. The above considerations may be important factors to consider in future studies.

5.3 Conclusions

The results of this study pertain to populations of children aged 7-11 years affected by maxillary transverse deficiencies without any other pertinent medical conditions. A casual inference may thereby be drawn for other similar populations, that maxillary expansion does not cause any significant facial soft tissue changes in comparison to those expected with natural growth and development.

The currently available body of literature focusing on the soft tissue effects of rapid maxillary expansion (RME) consists of evidence of a moderate quality, as many studies did not include control groups and had widely varying observational periods, to name but a few limitations.

It can be concluded that the correlation between the two different imaging modalities utilized in this study (CBCT imaging and 3D facial scanning) was not as optimal for specific outcome variables such as alar base width and intercanthal width, potentially due to anatomic, imaging protocols and patient related factors.

The results of this study suggest that children aged 7-11 years affected with maxillary transverse deficiency treated by rapid maxillary expansion using a Hyrax expansion device experience facial soft tissue changes similar to those of patients without any

expansion over a period of one year, in regards to both CBCTs and 3D facial scans. However, given the limitations in regards to imaging protocols, analysis and sample size as mentioned above, the results are to be interpreted with caution.

This research study was the first of its kind to utilize both CBCTs and 3D facial scans in relation to RME and its potential facial soft tissue effects. Further similar research studies are encouraged and would bring considerable value to this area of investigation.

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Appendix 2A

Embase	1 Palatal Expansion Technique/718 2 (((palatal or Maxilla*) adj3 Expansion*) or ((Rapid or removable or fixed*) adj3 (Maxillary Expander* or palatal expander*)) or (HYRAX adj3 (expander* or expansion*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] / 2723 3 face/ or cheek/ or chin/ or mouth/ or lip/ or nasolabial fold/ or nose/ 130407 4 ((facial or face or nasal or nose* or lip or lips or cheek* or mouth* or chin or chins or Nasolabial) adj3 (change* or effect* or outcome* or result* or measure* or assess* or impact*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] / 56593 5 1 or 2 /2723 6 3 or 4 /177222 7 5 and 6 /404	404
Pubmed, Medline Via OVID	1 Palatal Expansion Technique/3003 2 (((palatal or Maxilla*) adj3 Expansion*) or ((Rapid or removable or fixed*) adj3 (Maxillary Expander* or palatal expander*)) or (HYRAX adj3 (expander* or expansion*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] / 3583 3 face/ or cheek/ or chin/ or mouth/ or lip/ or nasolabial fold/ or nose/ 106928 4 ((facial or face or nasal or nose* or lip or lips or cheek* or mouth* or chin or chins or Nasolabial) adj3 (change* or effect* or outcome* or result* or measure* or assess* or impact*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] / 42737 5 1 or 2 /3683 6 3 or 4 /141247 7 5 and 6 /527	427
Cochrane Library	(("palatal expansion" OR "maxillary expansion" OR "rapid palatal expansion" OR "rapid maxillary expansion") AND ("facial" OR "face" OR "cheek" OR "nose" OR "mouth" OR "chin" OR "nasal" OR "lip" OR "nasolabial fold"))	56
Google Scholar	With all of the words: Rapid Palatal Expansion With at least one of the words: facial or face or soft tissues Where my words occur: anywhere in the article Chosen by relevance (first 10 pages)	100
In Total		987

224 duplicates were automatically removed with excel, 763 left

Appendix 2B

Table 1 Descriptive characteristics of studies included in the systematic review

No.	Author Year	Design	Journal	Groups	Sample Size	Males/ Females	Average Age (year)	Appliance	Type of Expansion	Expansion Protocol	# turns	Expansion Duration	Retention Duration	Method of Measurement	Timepoints
1 [11]	Akan 2021	RCT	Orthod Craniofac Res	Bonded RME Tooth-bone-borne RME	16 16	9M/7F 6M/10F	13.4±1.3 13.05±1.24	Hyrax Hybrid Hyrax	RME RME	2 turns/day for the first week then 1/day (until the palatal tubercles of the upper molars came into contact with the buccal tubercles of the lower molars)	25.25 ± 4.42 24.88 ± 3.40	_	3 months	3D Stereophotogrammetry	T0 (pre-RME), T2 (4 months after T0)
2 [14]	Alkhayer 2021	Cohort (prospective)	Int. J. Environ. Res. Public Health	Bonded RME	25	12M/13F	11.6 (8.1-14.4)	Hyrax	RME	2 turns/day (0.5mm) until palatal cusp of the upper molars was touching the buccal cusp of the lower molars	_	2-3 weeks	6 months	3D facial images	T0 (pre-RME) T2 (6 month retention)
3 [17]	Truong 2021	Retrospective case control	Angle Orthod	Treatment Control	35 28	17M/18F 12M/16F	9.39±1.4 8.81±1.6	Full-coverage Bonded RME	RME	2 turns/day (0.2mm/turn) until adequate expansion reached	_	_	_	CBCT	T0 (pre-RME) T1 (immediate post-RME for TG only) T2 (2.84 years post-RME for 25 patients of TG, 2.25 years post-RME for Control)
4 [10]	Torun 2017	Cohort (restrospective)	J Orofac Orthop	Treatment group only divided into 2 groups – pre vs post-pubertal	14 14	10M/18F	13.91±1.8	Hyrax screw	RME	2 turns/day (0.5mm/day) 9–10 mm	_	3-4 weeks	6 months	CBCT	T0 (pre-RME) T2 (at 6-month retention)
5 [12]	Altindis 2016	RCT	Angle Orthod	Banded RME Acrylic Splint RME Modified Acrylic Splint RME	14 14 14	6M/8F 7M/7F 5M/9F	12.7±0.6 12.4±0.8 12.5±0.8	Hyrax screw	RME	1 turn/day (0.2mm/turn) until buccal segments overcorrected	29.8±4.2 29.0±4.0 31.6±5.9	_	3 months	3D facial images	T0 (pre-RME) T2 (3 month retention)
6 [18]	Baysal 2016	RCT	Angle Orthod	Treatment Control	17 17	9M/8F 9M/8F	13.4±1.4 12.8±1.3	Bonded acrylic splint expander	RME	2 quarter turns/day for the first week, then quarter turn/day until the palatal cusps of the maxillary molar contacted the buccal cusps of the mandibular molar 6.25±2.9mm	25±11.6	0.7±0.4 month	_	PA cephalograms 3D facial images	T0 (pre-RME) T2 (immediate post-retention/observation 6.1±0.6 months)
7 [20]	Uysal 2015	CCT	Eur J General Med	Treatment Control	20 16	8M/12F 6M/10F	13.4±0.99 13.25±1.18	Acrylic bonded RME appliance	RME	1 quarter turn/day 8mm on average	_	1.1 months	6 months	Lateral and AP radiographs	T0 (pre-RME) T1 (post-RME for TG only) T2 (at 7-month retention)
8 [19]	Santariello 2014	CCT	Minerva Stomatologica	Treatment Control	61 41	35M/26F 15M/26F	10.5±1.8 10.7±2.2	Hyrax	RME	_	_	3-4 weeks	~6 months	Caliper measurements	T0 (pre-RME) T1 (after completion of active expansion for TG only) T2 (at 6 months after expansion)
9 [13]	Pangrazio-Kulbersh 2012	RCT	Angle Orthod	Banded RME Bonded RME	13 10	7M/6F 5M/5F	12.6±1.8 13.5±2.1	Hyrax	RME	_ 6-10mm	_	4-6 weeks	6 months	CBCT	T0 (pre-RME) T1 (immediately after appliance removal)
10 [15]	Santos 2012	Cohort	EurJ Orthod	Bonded RME	20	10M/10F	9.3±0.83	Modified acrylic Hyrax (with occlusal splint)	RME	2 turns/day (0.5mm/day) starting one week after insertion until the maxillary lingual cusps of upper first molars contacted facial cusps of mandibular lower first molars	_	3-4 weeks	6 months	Lateral cephalograms	T0 (pre-RME), T1 (post-RME) T2 (post-retention at 6 months)
11 [27]	Johnson 2010	CCT	Angle Orthod	Treatment pre-pubertal Treatment post-puberal	31 48	12M/19F 17M/31F	13.5 (10-16)	Hyrax	RME	1 turn/day (0.2mm/turn) for 7mm on average	_	35 days	5.7 months	Direct caliper measurements	T0 (pre-RME) T1 (post-RME) T2 (post-retention at ~5.7 months)
12 [16]	Kilic 2008	Cohort	EurJ Orthod	Bonded RME	18	3M/15F	13.50±1.07	Rigid acrylic bonded appliance	RME	2 quarter turns/day until crossbites eliminated and 3mm overexpanded	_	0.82±0.14 months	5.95±0.35 months	Lateral cephalograms	T0 (pre-RME) T1 (post-RME at 0.82±0.14 months) T2 (post-retention at 5.95±0.35 months)

Table 2 Summary of results of studies included in the systematic review

No.	Author Year	Landmarks	Conclusion
1 [11]	Akan 2021	12 linear measurements, 6 proportional measurements, 9 angular measurements	Both the hyrax and hybrid hyrax expanders affected soft tissue profile with an increased lower face height and anterior face height, upper lip length increased more in the hybrid group (0.36 mm) compared to the hyrax group (0.10 mm).
2 [14]	Alkhayer 2021	18 landmarks, 4 linear, 3 angular measurements	RME using a Hyrax expansion device resulted in significant changes in the nasal region as well as upper lip area after 6 months of retention.
3 [17]	Truong 2021	10 landmarks, 8 linear measurements	Significant increases in the nasal soft tissues were seen immediately after expansion, however, over a period of time, it reverted to the mean of typical growth. Long term, pyriform width and height was affected by RME.
4 [10]	Torun 2017	9 linear measurements, 1 angular	Although significant soft tissue facial changes were seen after RME, the differences between pre and post-pubertal groups were not significant.
5 [12]	Altindis 2016	15 landmarks, 9 linear and 6 angular measurements	All three groups showed no significant differences in regards to soft tissue facial changes after RME. More protrusion of the upper lip was noted in the modified acrylic splint RME group.
6 [18]	Baysal 2016	21 landmarks, 28 linear measurements	The treatment group showed an increase in the alar base, with other soft tissue changes being similar between the groups. Skeletal and soft tissue changes were found to be weakly associated.
7 [20]	Uysal 2015	4 linear measurements (GAC, Nasal cavity width, sagittal and vertical distances) and 2 angular measurements (SNA, NL)	Overall, soft tissue facial changes were not significantly different between the treatment and control groups. Greater alar cartilage width and SNA° reverted to their original values, the width of the nasal cavity and nasolabial angle increased, and the tip of the nose moved slightly down and to the frontward
8 [19]	Santariello 2014	2 linear measurements (AB and GAC)	There was an increase of ~1mm in the greater alar cartilage width in the pre-pubertal group which was not clinically significant, with the alar base width increase being less so and of no statistical significance.
9 [13]	Pangrazio-Kulbersh 2012	14 linear measurements, 3 angular measurements and 2 volumetric	Both groups of appliances showed similar expansion of the maxilla although the banded group demonstrated more tipping dentally as well as alveolar bending. There was skeletal widening of the nasal cavity with subsequent soft tissue changes and an increase in airway volume.
10 [15]	Santos 2012	10 linear measurements and 2 angular measurements according to Holdaway, Steiner, Ricketts, Legan and Burstone, McNamara and Vertical analyses	Although the post-expansion measurements were significantly different than the pre-expansion and post-retention measurements. When pre-expansion and post-retention were compared, it was noted that RME did not cause any statistically significant changes in the soft tissue facial profiles. RME with an occlusal splint also did not cause significant changes at the post-retention phase and may thereby be useful in combatting potential adverse vertical effects of RME such as an increased anterior face height.
11 [27]	Johnson 2010	2 linear measurements	Both the pre and post-pubertal groups showed no differences between the groups with no significant changes on the widths of the nasal apical base and the greater alar cartilage
12 [16]	Kilic 2008	10 linear measurements, 2 angular measurements (Holdaway analysis)	In the post-expansion phase, significant changes were noted in regards to a decrease in the facial soft tissue angle, whereas there was an increase in the skeletal convexity of the profile and H angle. In the post-retention phase, there was a slight and insignificant increase in the facial soft tissue angle and a decrease in the H angle, with a significant decrease in the skeletal profile convexity. Therefore, RME may affect Holdaway facial soft tissue measures.

Appendix 4A

Table 1. Intra-rater and inter-rater reliability of measurements

Landmark measurement	ICC (single measurement)	95% CI for ICC	
		Lower bound	Upper bound
Intra-rater reliability			
3D Facial Scan			
Alar width	0.98	0.97	0.99
Mouth width	0.99	0.98	1.00
Nasal tip prominence	0.98	0.96	0.99
CBCT			
Alar width	0.97	0.94	0.99
Mouth width	0.99	0.98	1.00
Nasal tip prominence	0.98	0.95	0.99
Inter-rater reliability			
3D Facial Scan			
Alar width	0.97	0.83	0.99
Mouth width	0.97	0.87	0.99
Nasal tip prominence	0.97	0.93	0.99
CBCT			
Alar width	0.94	0.87	0.97
Mouth width	0.99	0.97	0.99
Nasal tip prominence	0.94	0.85	0.97

Note: ICC = intraclass correlation coefficient; CI = confidence interval

Table 2. Intra-rater and inter-rater reliability of SMI

Index	ICC (single measurement)	95% CI for ICC	
		Lower bound	Upper bound
Intra-rater reliability			
SMI	0.92	0.85	0.97
Inter-rater reliability			
SMI	0.92	0.84	0.96

Note: ICC = intraclass correlation coefficient; CI = confidence interval

SMI = skeletal maturity indicator (Fishman)

Table 3. Intraclass correlation coefficients between CBCT and 3D facial scan

Landmark measurement	ICC (single measurement)	95% CI for ICC	
		Lower bound	Upper bound
Reliability between CBCT and 3D facial scan			
Alar width	0.78	0.34	0.94
Mouth width	0.65	0.06	0.90
Nasal tip prominence	0.98	0.92	0.99

Note: ICC = intraclass correlation coefficient; CI = confidence interval

Table 4. Measurement error (mm)

Landmark measurement	Measurement error	
	3D Facial Scan	CBCT
Alar width	0.29	0.42
Mouth width	0.33	0.50
Nasal tip prominence	0.35	0.41

Appendix 4B

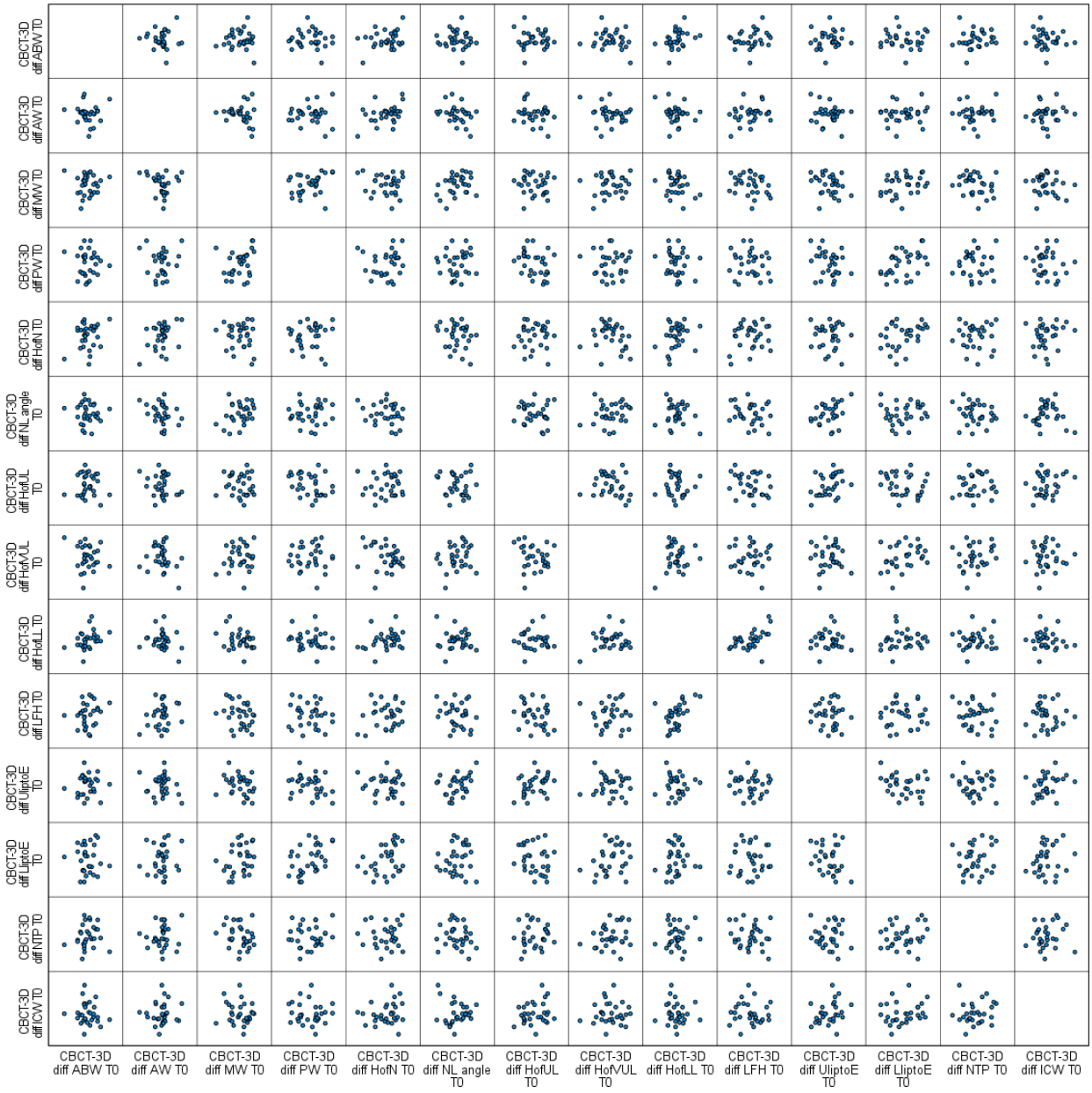

Fig 1. Scatterplot matrix of fourteen dependent variables (CBCT-3D difference at T0)

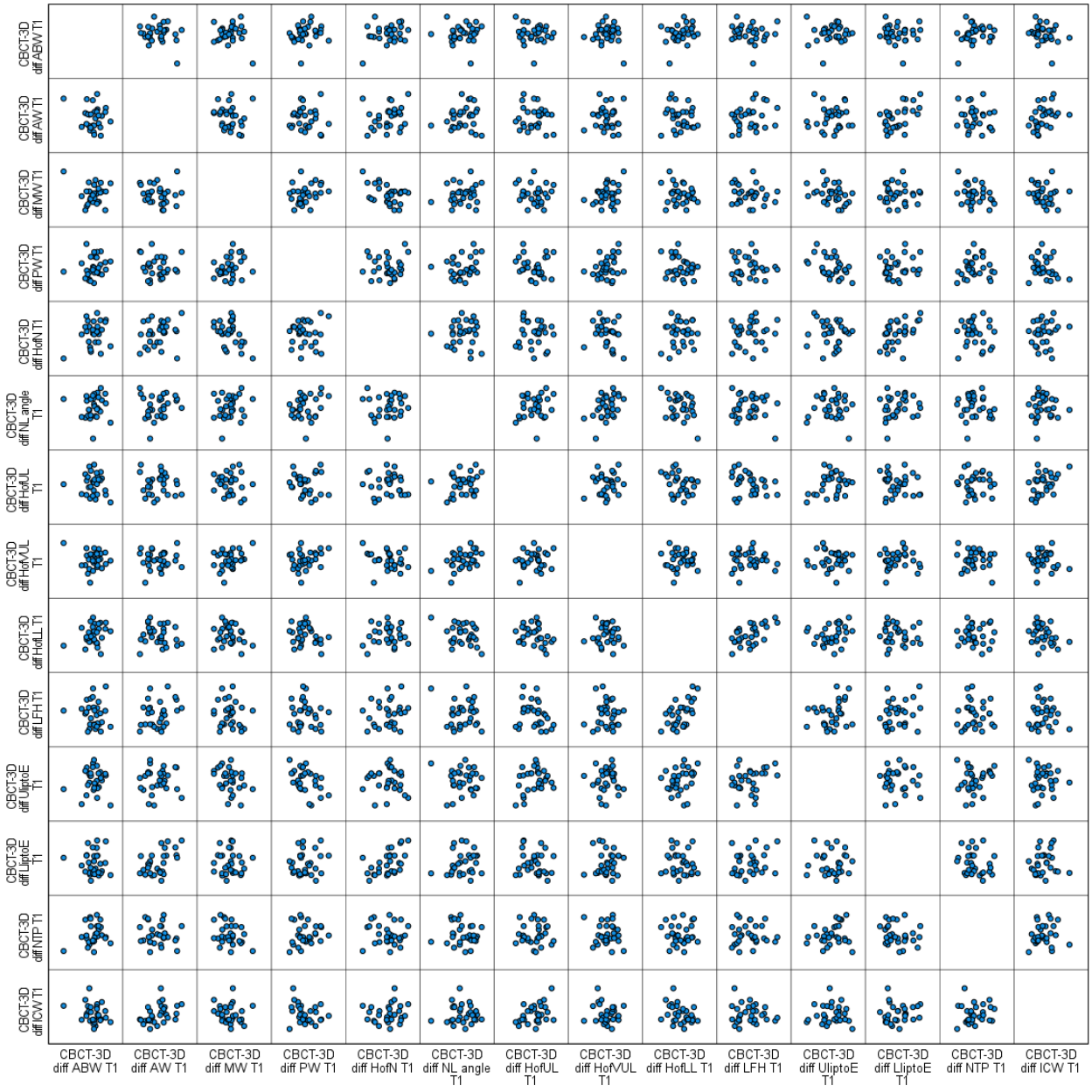

Fig 2. Scatterplot matrix of fourteen dependent variables (CBCT-3D difference at T1)

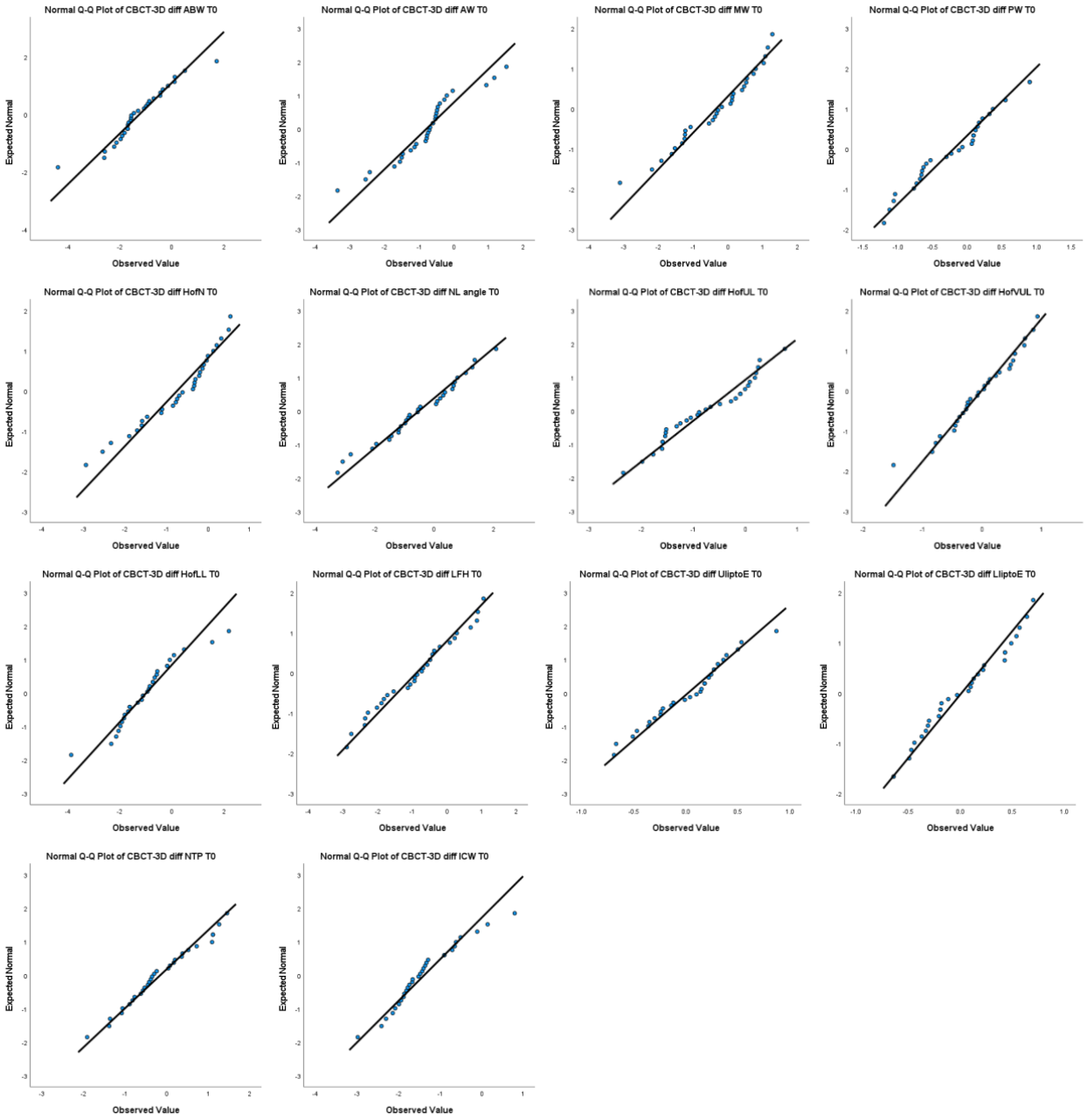

Fig 3. Q-Q plots of CBCT-3D difference of 14 dependent variables (at T0)

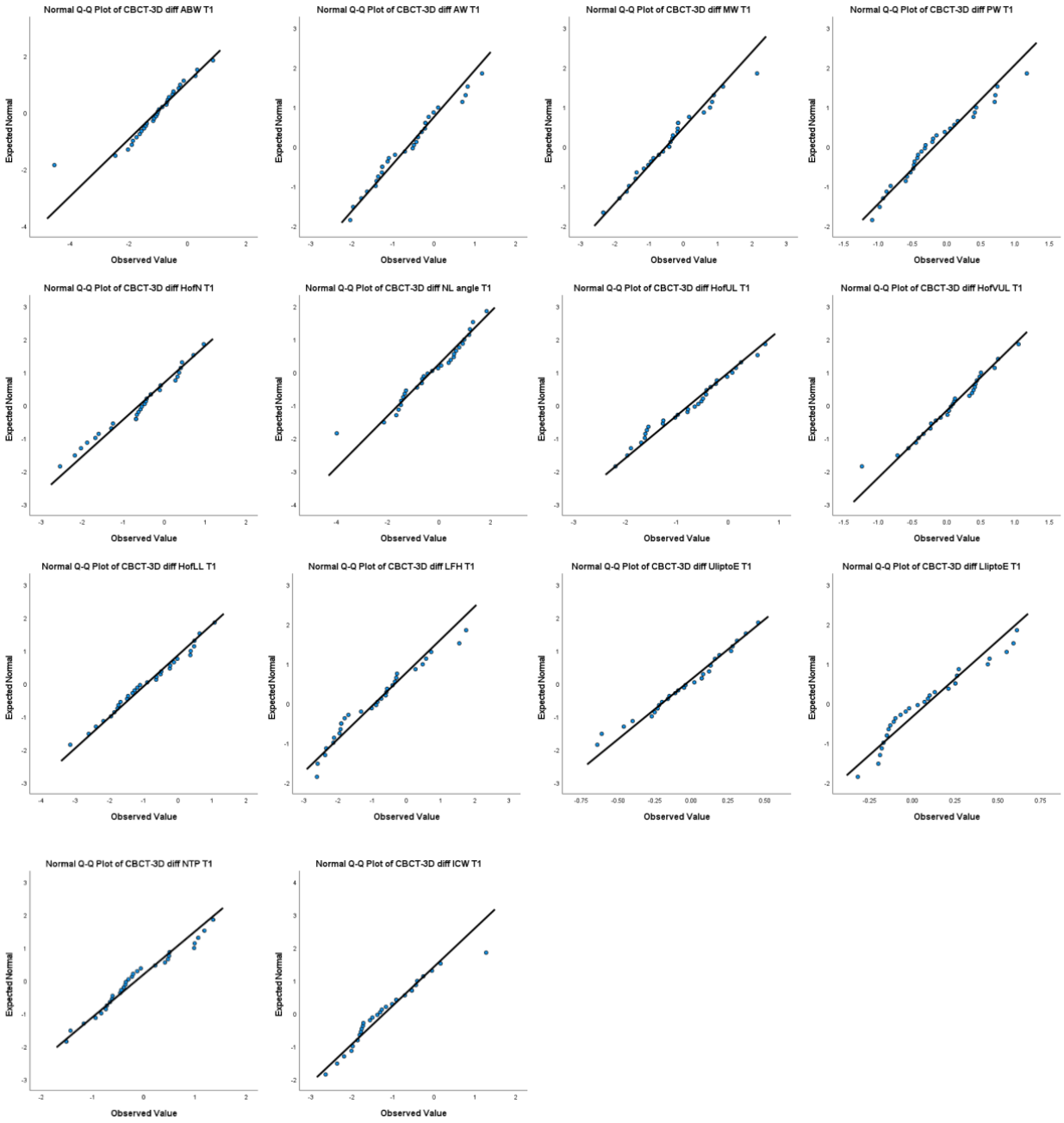

Fig 4. Q-Q plots of CBCT-3D difference of fourteen dependent variables (at T1)

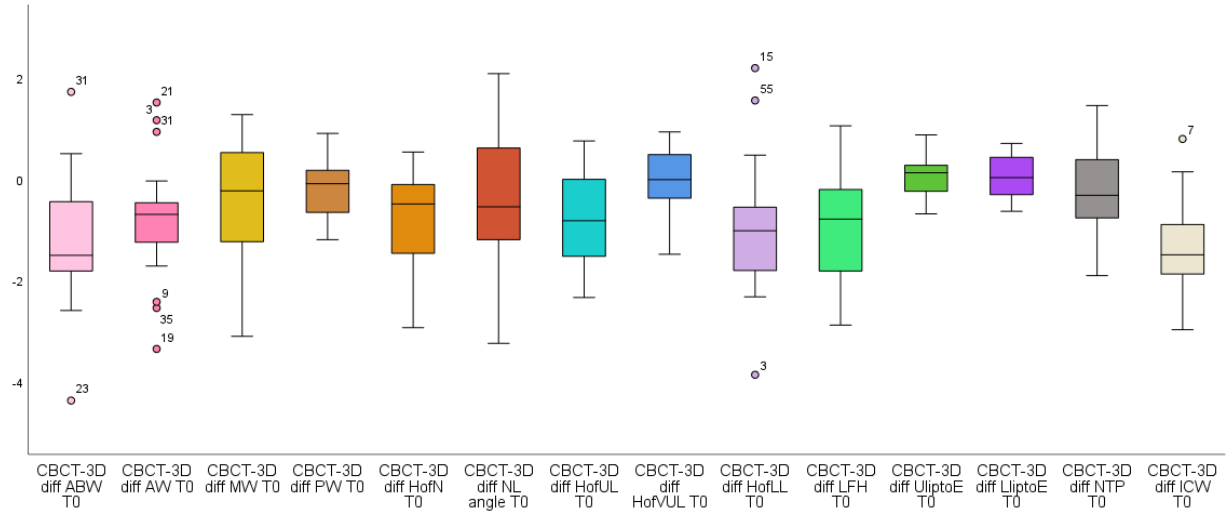

Fig 5. Boxplots of mean change of fourteen dependent variables (CBCT-3D difference at time T0)

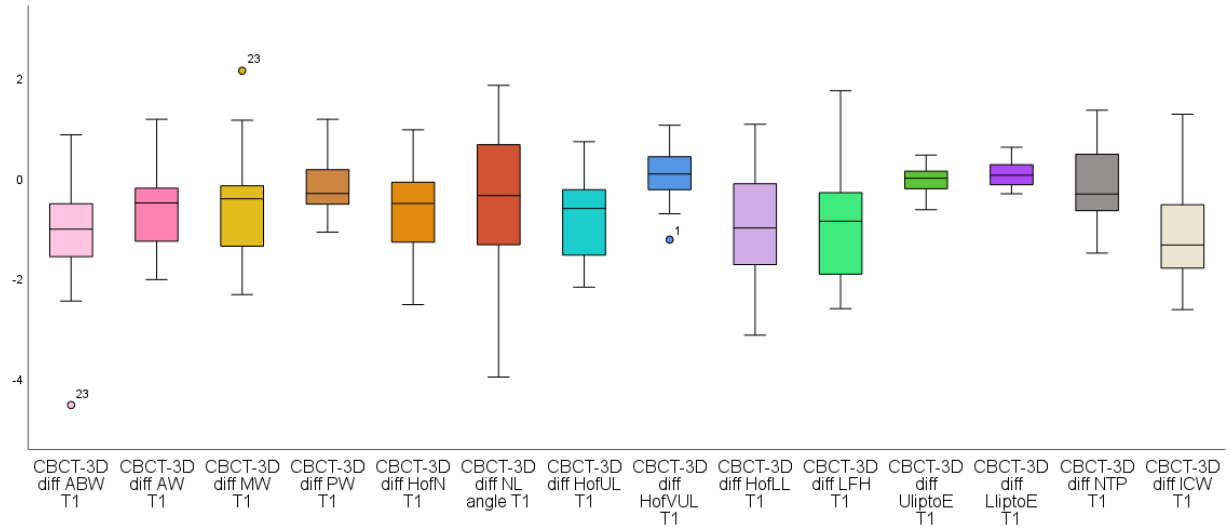

Fig 6. Boxplots of mean change of fourteen dependent variables (CBCT-3D difference at time T1)

Measurement	Kolmogorov-Smirnov test for normality	
	T0	T1
ABW	p = .20	p = .20
AW	p = .06	p = .20
MW	p = .20	p = .17
PW	p = .16	p = .20
HofN	p = .046*	p = .034*
NL	p = .20	p = .20
HofUL	p = .20	p = .20
HofVUL	p = .20	p = .20
HofLL	p = .20	p = .20
LFH	p = .20	p = .15
UliptoE	p = .20	p = .20
LliptoE	p = .20	p = .20
NTP	p = .20	p = .20
ICW	p = .07	p = .20

Note: * significant p-values

Table 1. Kolmogorov–Smirnov test for normality

	T0	T1
Box's M	296.486	305.502
F	1.247	1.285
df1	105	105
df2	2442.470	2442.470
Sig.	.048	.029

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

Table 2. Box’s Test of Equality of Covariance Matrices

CBCT-3D difference at time T0		CBCT-3D difference at time T1	
Mahalanobis distance	**p-value**	**Mahalanobis distance**	**p-value**
13.80	0.54	17.92	0.79
20.29	0.88	9.03	0.17
13.15	0.49	12.02	0.40
18.46	0.81	16.63	0.72
9.77	0.22	10.22	0.25
7.67	0.09	8.16	0.12
15.88	0.68	18.87	0.83
16.74	0.73	20.55	0.89
10.79	0.30	7.75	0.10
17.78	0.78	15.57	0.66
17.36	0.76	13.88	0.54
16.70	0.73	20.57	0.89
13.89	0.54	15.97	0.68
16.00	0.69	17.23	0.76
14.95	0.62	11.41	0.35
16.89	0.74	12.20	0.41
11.15	0.33	11.40	0.35
10.05	0.24	11.25	0.33
14.50	0.59	15.18	0.63
10.45	0.27	16.64	0.72
6.51	0.05	9.99	0.24
12.90	0.47	12.82	0.46
13.19	0.49	12.89	0.47

Table 3. Mahalanobis distance and *p*-values

Appendix 4C

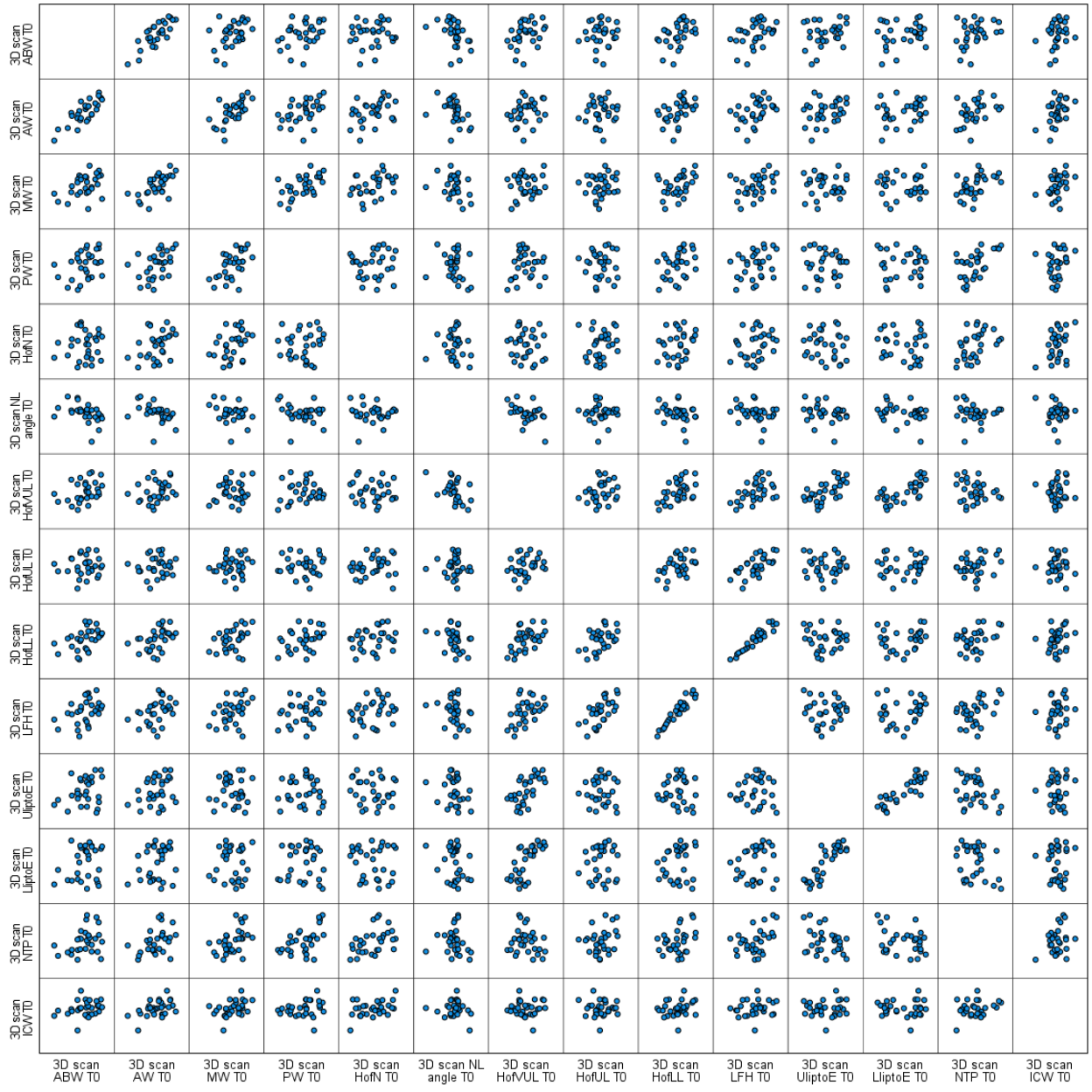

Fig 1. Scatterplot matrix of fourteen dependent variables (3D at time T0)

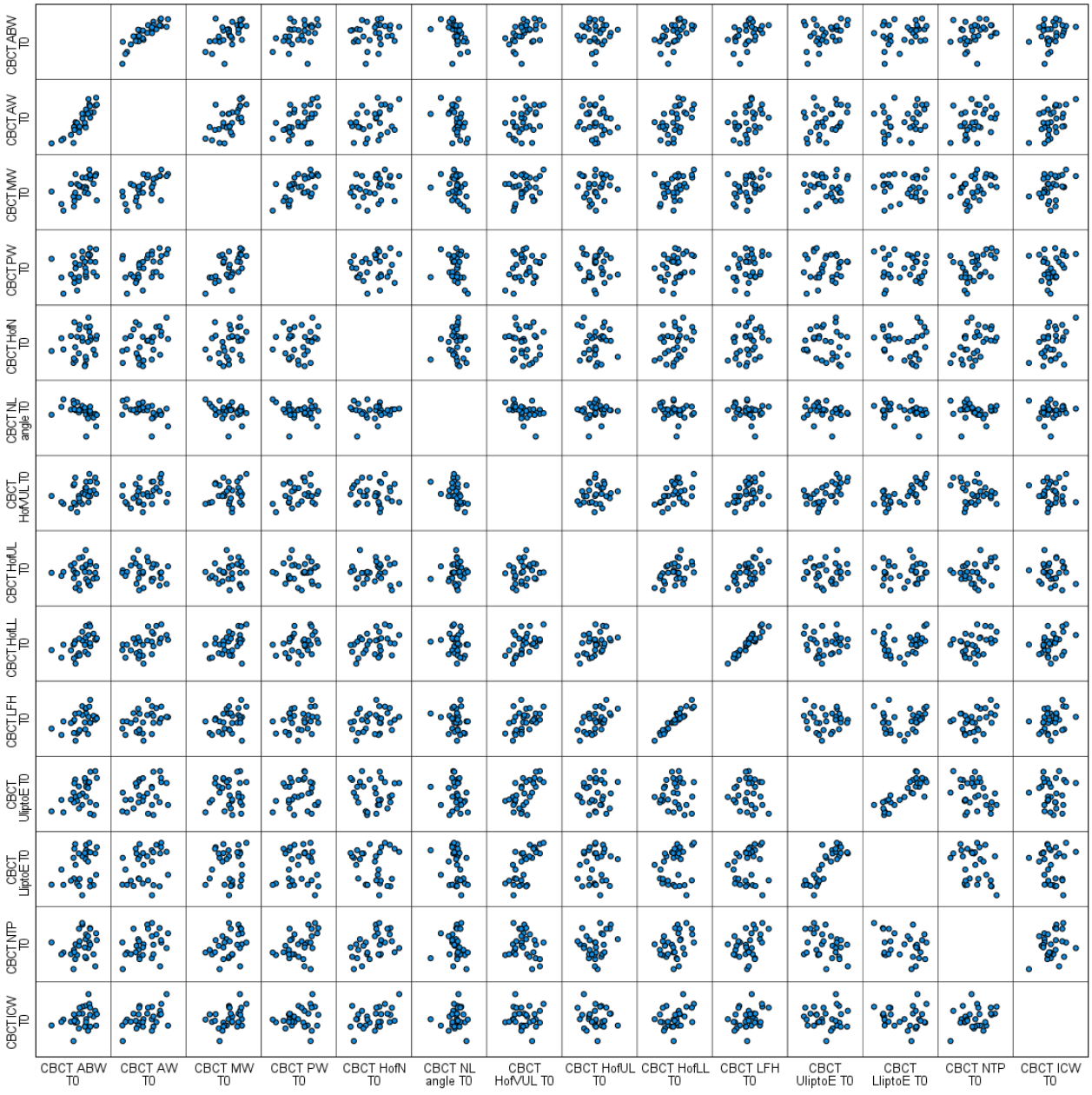

Fig 2. Scatterplot matrix of fourteen dependent variables (CBCT at time T0)

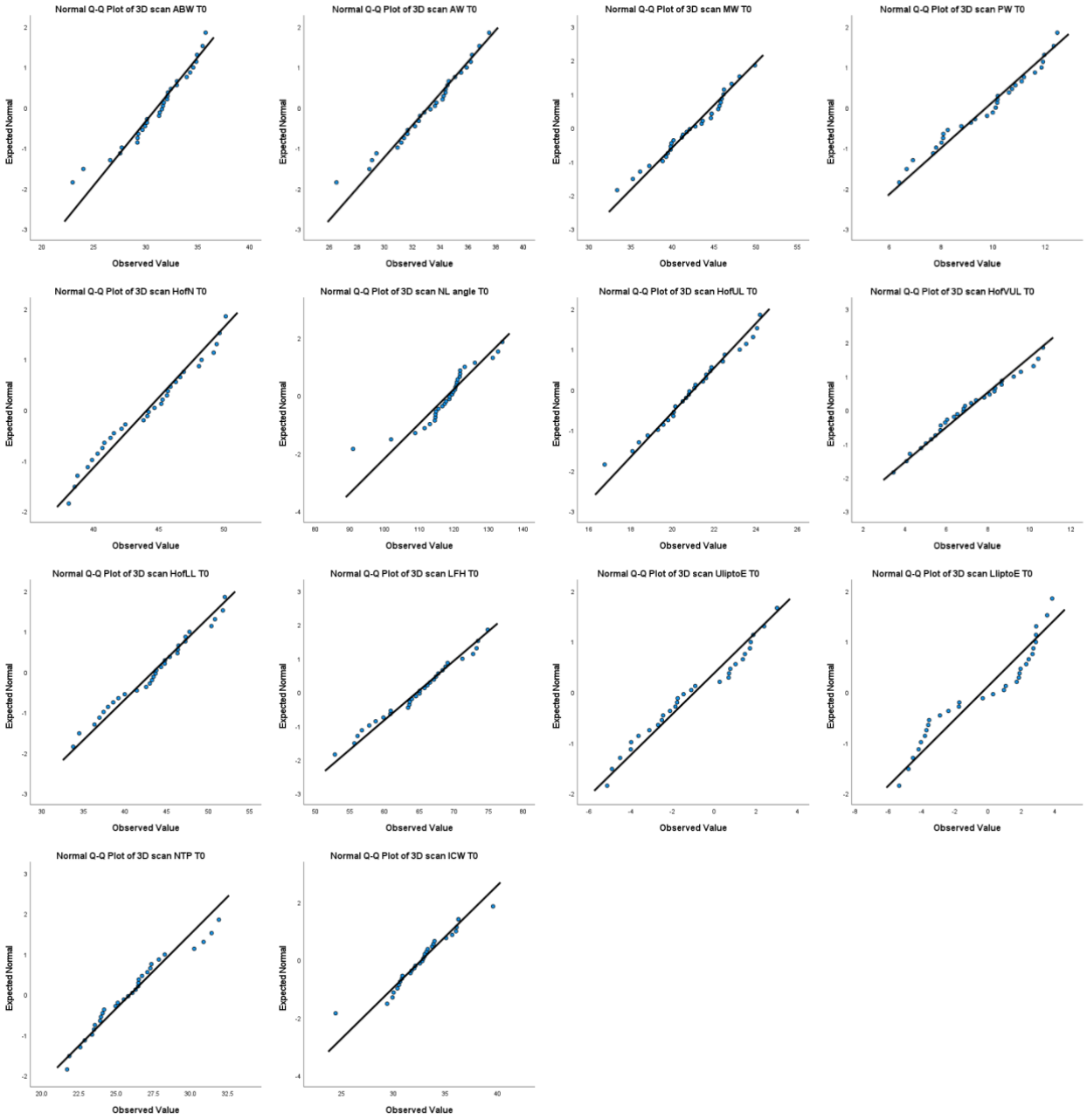

Fig 3. Q-Q plots of fourteen dependent variables (3D facial scan at time T0)

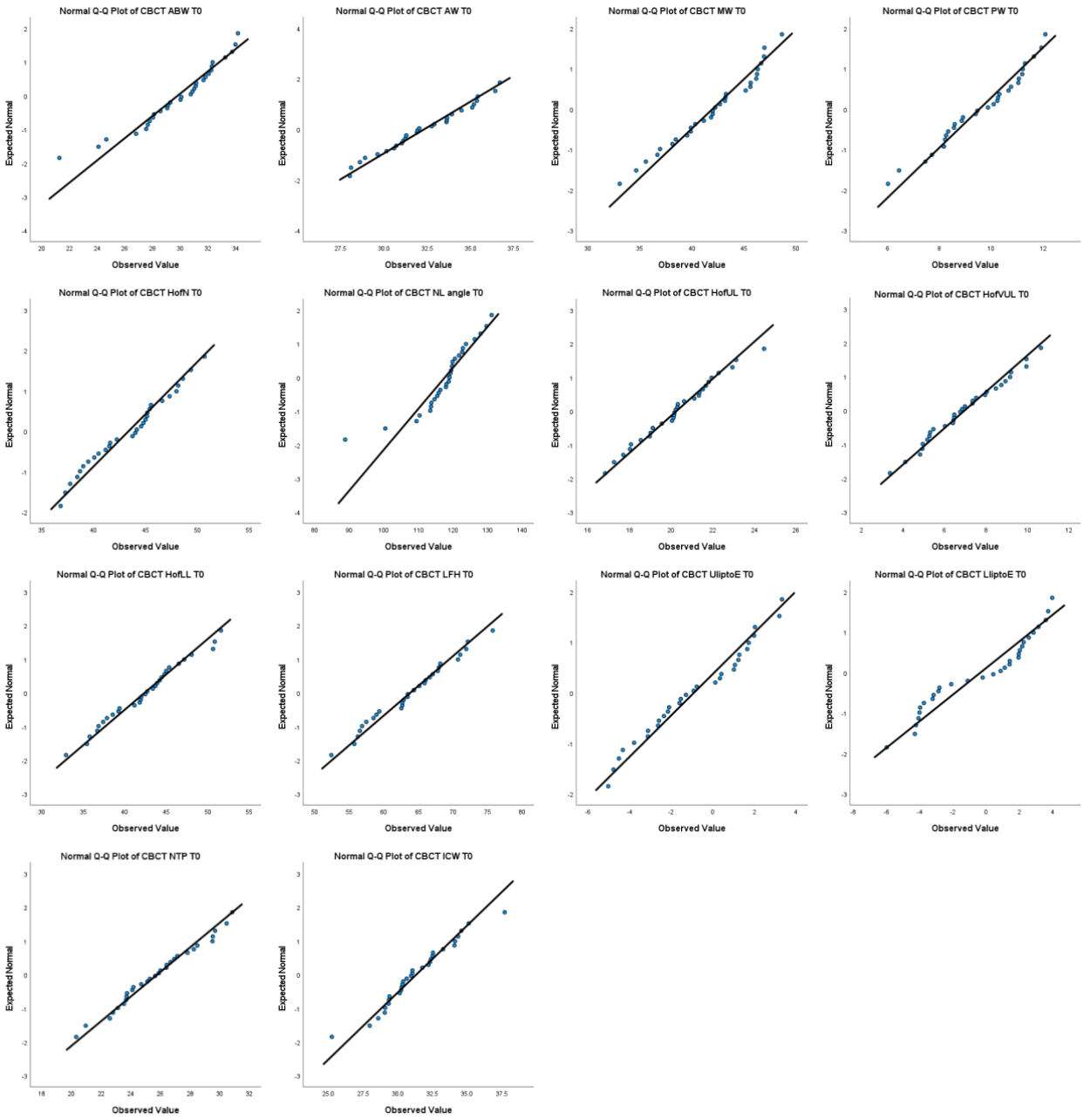

Fig 4. Q-Q plots of fourteen dependent variables (CBCT at time T0)

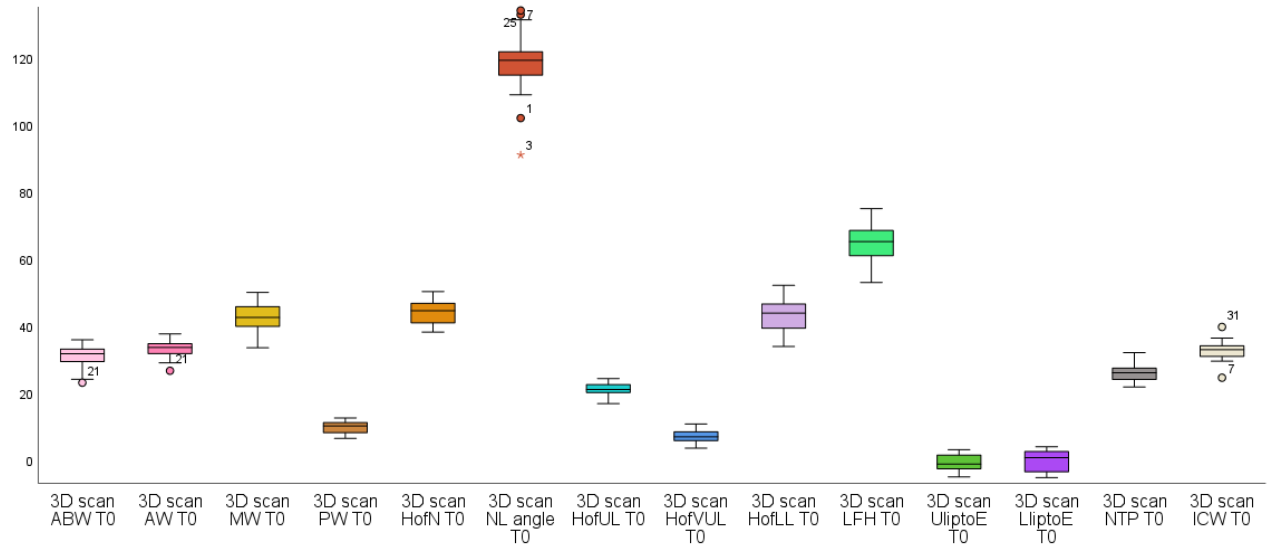

Fig 5. Boxplots of fourteen dependent variables (3D facial scan at time T0)

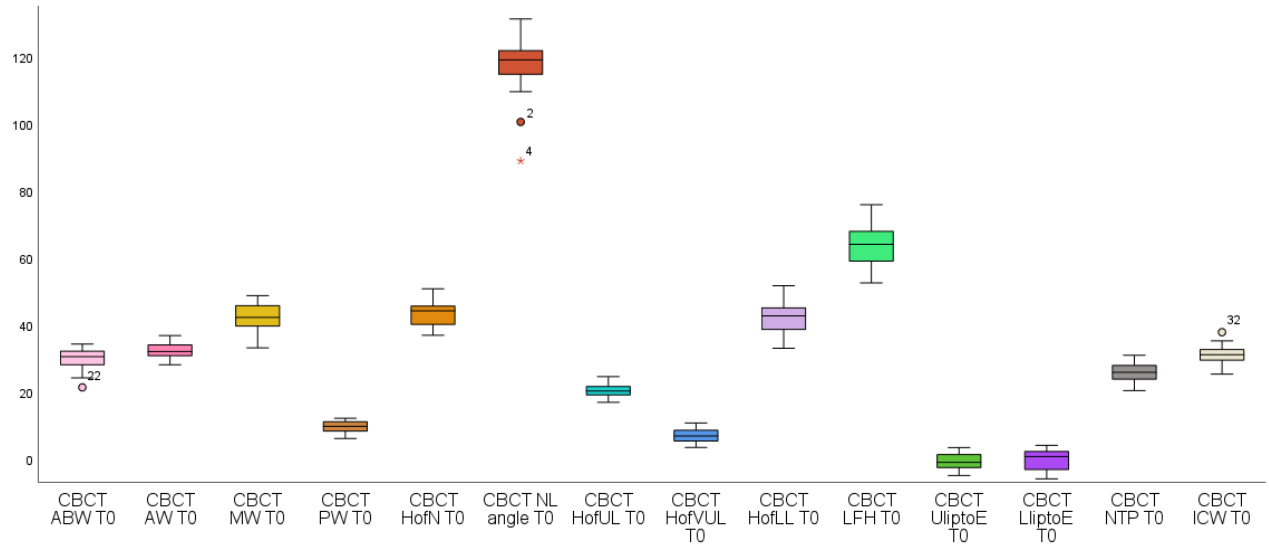

Fig 6. Boxplots of fourteen dependent variables (CBCT at time T0)

Measurement	Kolmogorov-Smirnov test for normality	
	3D facial scan at T0	CBCT at T0
ABW	p = .20	p = .20
AW	p = .20	p = .20
MW	p = .20	p = .20
PW	p = .20	p = .20
HofN	p = .20	p = .20
NL	p = .04*	p = .03*
HofUL	p = .20	p = .20
HofVUL	p = .20	p = .20
HofLL	p = .20	p = .20
LFH	p = .20	p = .20
UliptoE	p = .12	p = .20
LliptoE	p = .01*	p = .05
NTP	p = .20	p = .20
ICW	p = .20	p = .20

Note: * significant p-values

Table 1. Kolmogorov–Smirnov test for normality

	3D facial scan at T0	CBCT at time T0
Box's M	379.955	375.553
F	1.598	1.579
df1	105	105
df2	2442.470	2442.470
Sig.	<.001	<.001

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

Table 2. Box's Test of Equality of Covariance Matrices

3D facial scan at time T0		CBCT at time T0	
Mahalanobis distance	**p-value**	**Mahalanobis distance**	**p-value**
16.46	0.71	16.07	0.69
18.06	0.80	21.58	0.91
13.31	0.50	15.50	0.65
20.26	0.88	19.71	0.86
11.40	0.35	16.58	0.72
14.40	0.58	16.76	0.73
12.06	0.40	12.31	0.42
14.39	0.58	15.00	0.62
10.57	0.28	10.12	0.25
13.35	0.50	10.96	0.31
18.94	0.83	20.76	0.89
13.34	0.50	13.32	0.50
13.09	0.48	12.04	0.40
11.34	0.34	10.04	0.24
11.99	0.39	15.23	0.64
17.49	0.77	20.40	0.88
13.92	0.54	13.34	0.50
12.31	0.42	10.78	0.30
12.41	0.43	12.66	0.45
12.03	0.40	11.11	0.32
18.78	0.83	14.51	0.59
8.66	0.15	7.17	0.07
7.78	0.10	10.17	0.25

Table 3. Mahalanobis distance and *p*-values

Appendix 4D

Fig 1. Scatterplot matrix of fourteen dependent variables (3D facial scan)

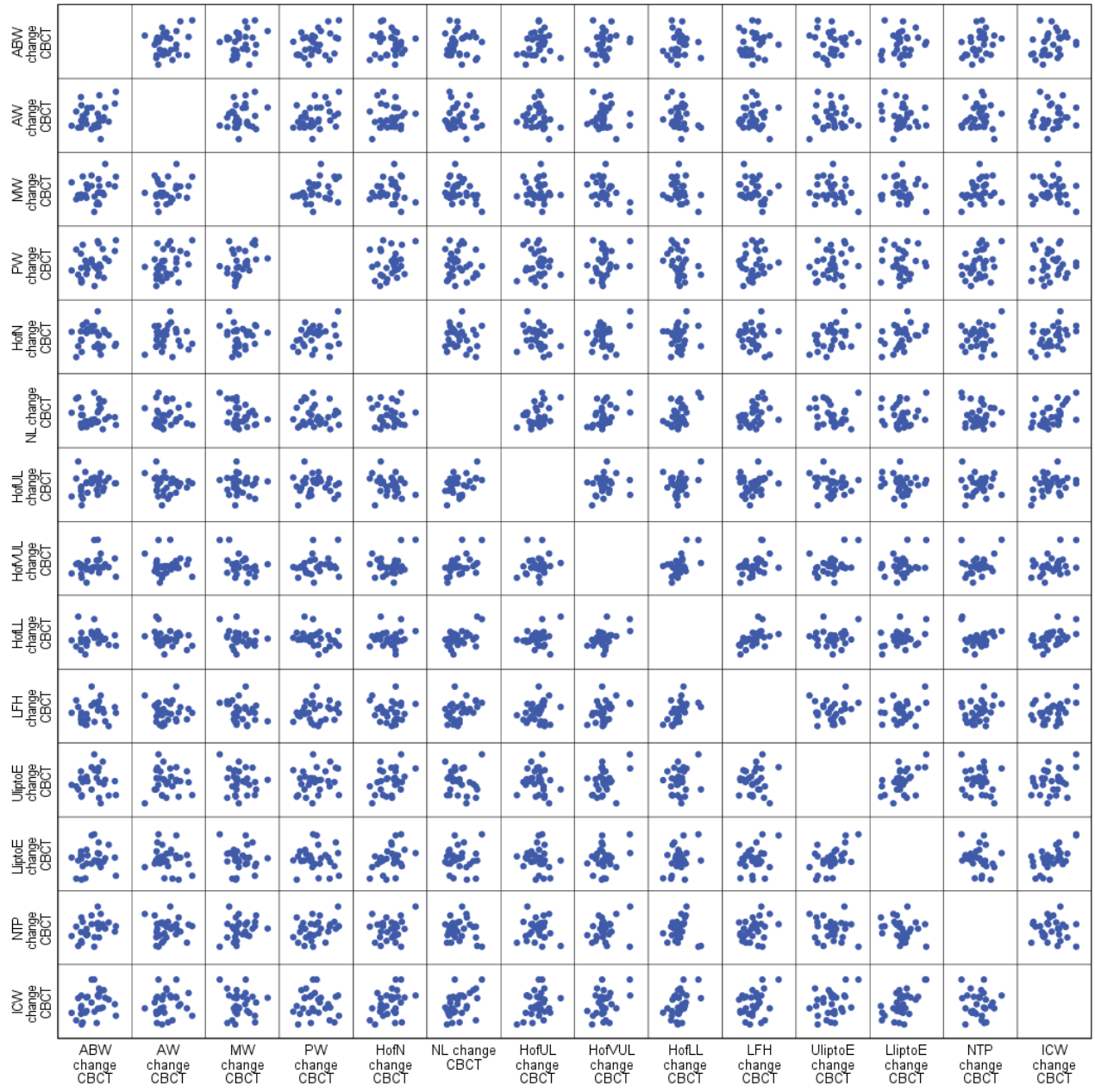

Fig 2. Scatterplot matrix of fourteen dependent variables (CBCT)

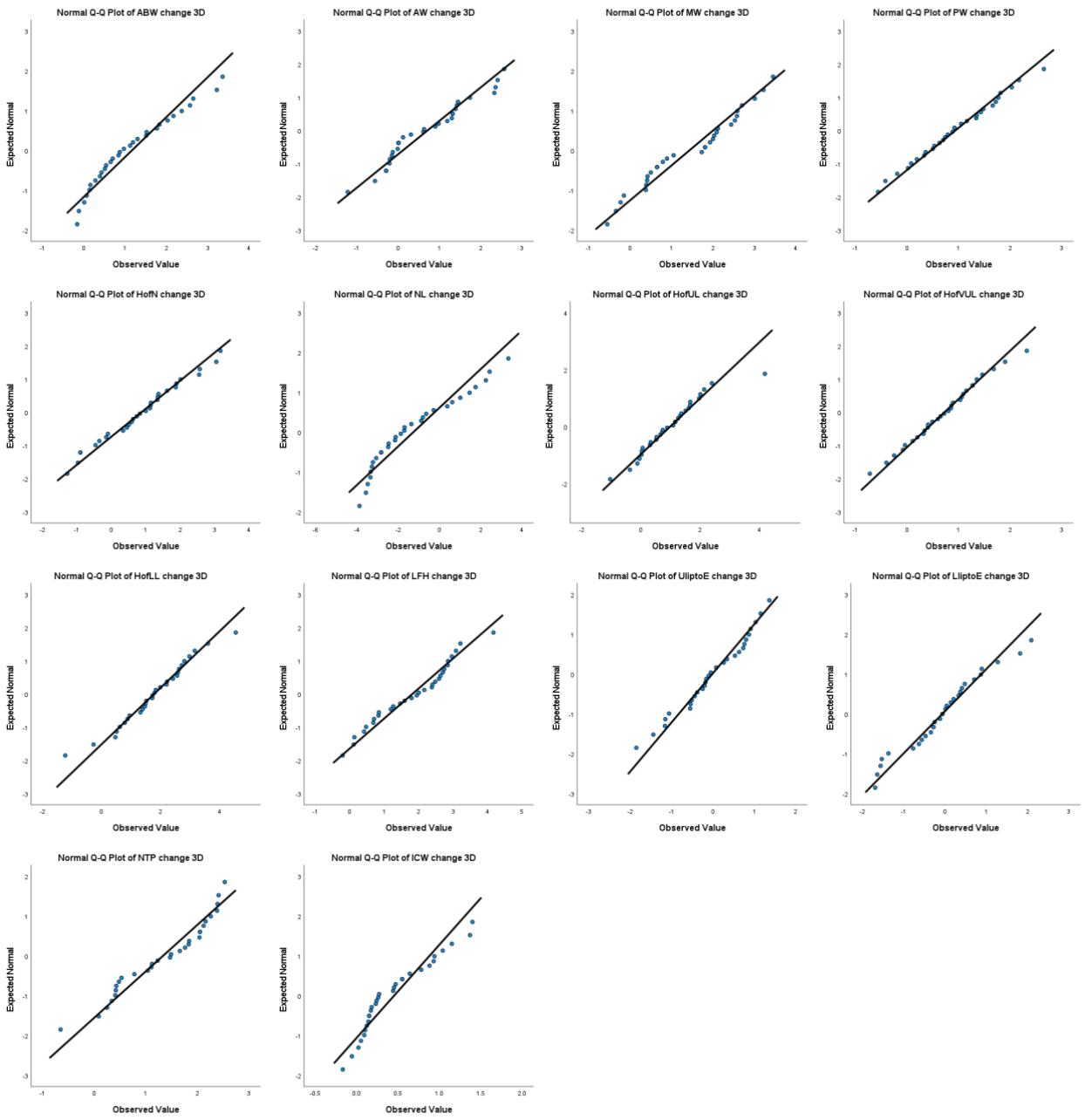

Fig 3. Q-Q plots of mean change of fourteen dependent variables (3D facial scan)

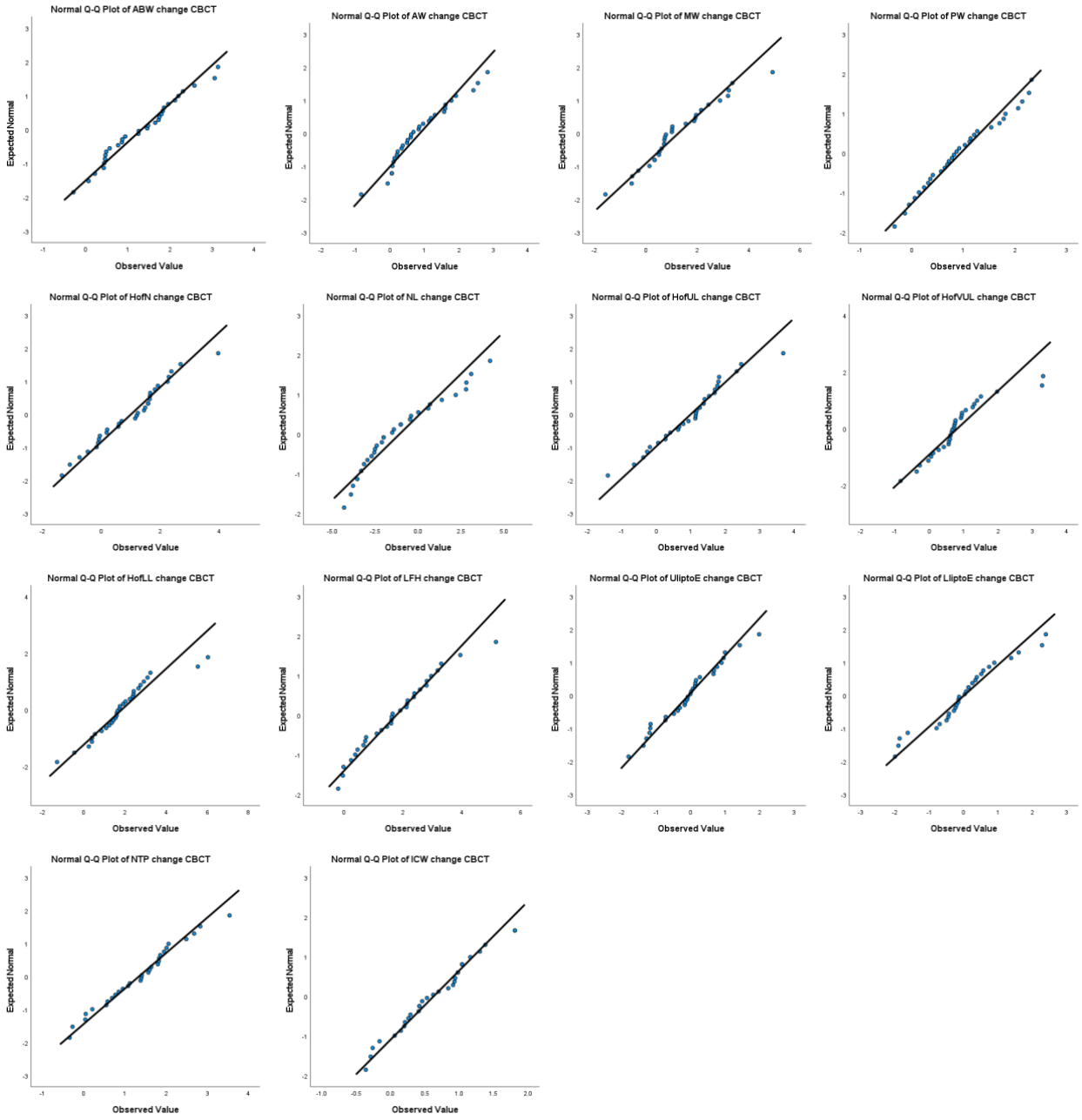

Fig 4. Q-Q plots of mean change of fourteen dependent variables (CBCT)

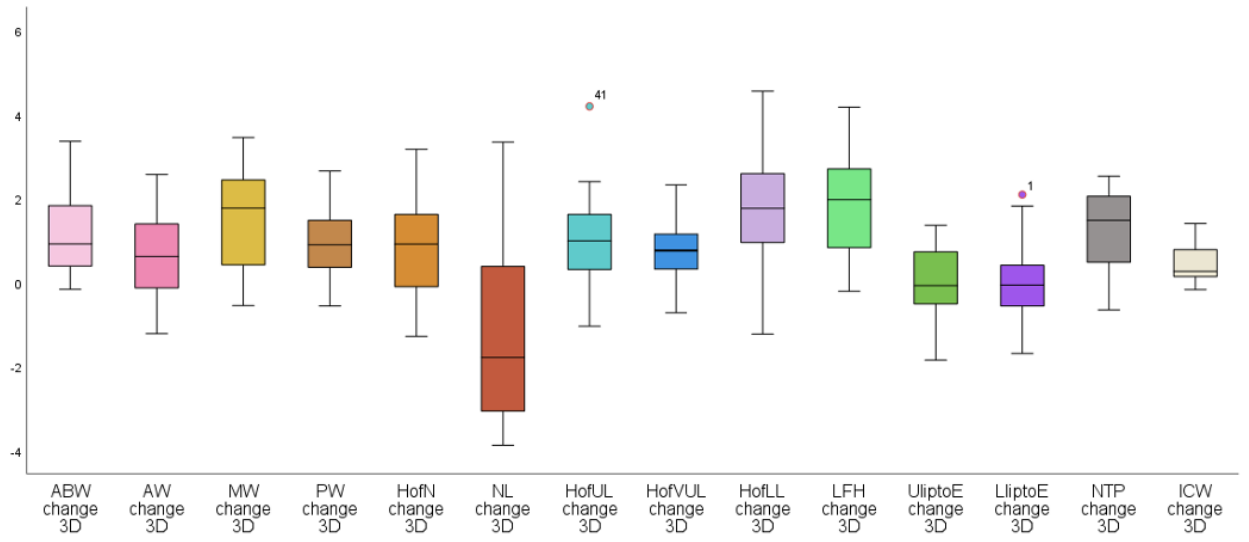

Fig 5. Boxplots of mean change over time of fourteen dependent variables (3D facial scan)

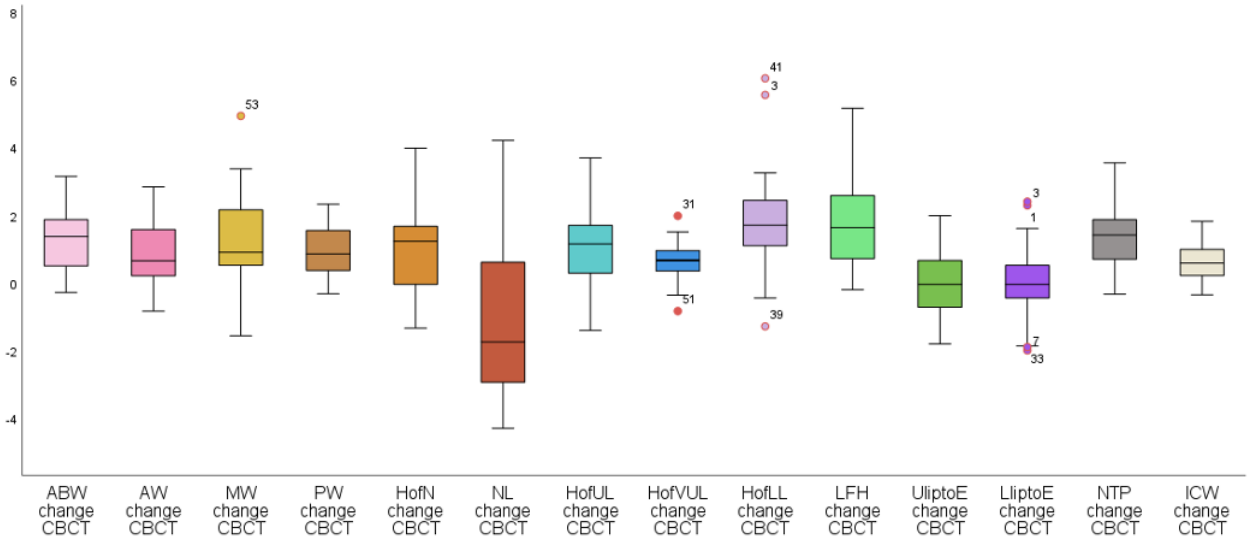

Fig 6. Boxplots of mean change over time of fourteen dependent variables (CBCT)

Measurement	Kolmogorov–Smirnov test for normality	
	3D Facial Scan	CBCT
ABW	p = .20	p = .20
AW	p = .05	p = .20
MW	p = .16	p = .03*
PW	p = .20	p = .20
HofN	p = .20	p = .20
NL	p = .09	p = .08
HofUL	p = .20	p = .20
HofVUL	p = .20	p = .02*
HofLL	p = .20	p = .20
LFH	p = .20	p = .20
UliptoE	p = .20	p = .20
LliptoE	p = .20	p = .20
NTP	p = .20	p = .20
ICW	p < .01*	p = .20

Note: *significant p-values

Table 1. Kolmogorov–Smirnov test for normality

	3D facial scan	CBCT
Box's M	350.069	349.328
F	1.472	1.469
df1	105	105
df2	2442.470	2442.470
Sig.	.002	.002

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

Table 2. Box’s Test of Equality of Covariance Matrices

3D facial scan		CBCT	
Mahalanobis distance	**p-value**	**Mahalanobis distance**	**p-value**
17.93	0.79	19.53	0.85
15.77	0.67	17.06	0.75
10.43	0.27	13.07	0.48
14.80	0.61	14.31	0.57
16.36	0.71	17.82	0.79
6.16	0.04	14.52	0.59
13.11	0.48	10.58	0.28
10.44	0.27	14.86	0.61
15.52	0.66	15.07	0.63
13.57	0.52	12.20	0.41
15.82	0.68	13.79	0.53
8.09	0.12	10.30	0.26
10.35	0.26	10.40	0.27
18.70	0.82	12.37	0.42
12.52	0.44	21.27	0.91
17.63	0.78	20.06	0.87
19.28	0.85	17.75	0.78
19.12	0.84	15.93	0.68
8.00	0.11	8.85	0.16
16.16	0.70	16.69	0.73
22.08	0.92	20.44	0.88
10.87	0.30	7.08	0.07
9.82	0.22	5.86	0.03

Table 3. Mahalanobis distance and *p*-values