Title
Assessment of the Magnitude and Asymmetry of Micro-Implant-Assisted Rapid Maxillary Expansion

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Assessment of the Magnitude and Asymmetry of Micro-Implant-Assisted Rapid Maxillary Expansion

A thesis submitted in partial satisfaction of the

requirements for the degree Master of Science

in Oral Biology

by

Islam Mohamed Hassan Elkenawy

2020

ABSTRACT OF THE THESIS

Assessment of the Magnitude and Asymmetry of Micro-Implant-Assisted Rapid Maxillary Expansion

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Islam Mohamed Hassan Elkenawy

Master of Science in Oral Biology

University of California, Los Angeles, 2020

Professor Won Moon, Co-Chair

Professor Sanjay Mallya, Co-Chair

Micro-implant assisted rapid palatal expander such as the Maxillary Skeletal Expander (MSE) have been utilized to achieve skeletal expansion as an alternative to surgically assisted expansion with some success. Previous studies show significant effects on the mid-face, including a degree of asymmetry. The aim of this study is to quantify the magnitude, parallelism, and asymmetry of expansion in non-growing patients and to explore possible factors that can predict the pattern of asymmetry of expansion.

We examined orthodontic non-growing patients (n=31) with an average age of 20.4 years old, with Cone Beam Computed Tomography (CBCT) images taken before and right after expansion using MSE. Those images were superimposed, and expansion was analyzed utilizing the Mid-Sagittal Plane (MSP) as a reference plane. Average magnitude of total expansion was 5

mm at the Anterior Nasal Spine (ANS), and 4.77 mm at the Posterior Nasal Spine (PNS) which showed statistical significance using a paired t-test with $p<0.01$. Expansion was parallel in the antero-posterior dimension where expansion at the PNS was 95% of that at the ANS. The sample was evaluated for asymmetry and divided into two groups; symmetric (n=15) and asymmetric (n=16), with 16 out of 31 patients exhibiting statistically significant asymmetry. The asymmetric group showed statistical significance asymmetry at $p<0.05$ when comparing expansion at both sides.

In order to validate any possible predicting factors, correlation of the asymmetry of expansion and multiple measurements of predicting factors was performed to both compare the direction of asymmetry, as well as the total magnitude of asymmetry.

MSE achieved highly parallel expansion in the sagittal plane in non-growing patients with an average magnitude of 5 mm at the ANS. However, transverse asymmetry of expansion was noted in 51% of the patients where one side expanded more than the other by at least 1.1 mm.

Lack of correlation was noted between the magnitude of asymmetry and both the initial asymmetry of the mid-face, as well as the difference in density values bilaterally. However, the direction of asymmetry of expansion at ANS was moderately associated with the initial asymmetry of the frontozygomatic suture.

The thesis of Islam Mohamed Hassan Elkenawy is approved.

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INTRODUCTION

Transverse maxillary deficiency (TMD) is a common malocclusion that is diagnosed when the maxilla is narrow in relation to the mandible.[1] Patients with TMD often present with unilateral or bilateral posterior crossbite, anterior crowding, and lengthened buccal corridors upon smiling.[2] Adequate transverse maxillary dimension is critical for stable, well-balanced and proper functional occlusion. Traditionally, rapid palatal expander (RPE) is the appliance of choice to treat patients diagnosed with TMD to increase transverse maxillary dimension, which is usually used to perform expansion during childhood or adolescence before the midpalatal suture has fused.[3,4] The midpalatal suture becomes more interdigitated and denser with age, and is said to be fully fused by the age of 15-19.[5] Once the midpalatal suture is interdigitated, RPE appliances become less effective in achieving basal skeletal expansion and the force they apply may lead to dentoalveolar tipping.[6] Studies have shown and confirmed that all circummaxillary sutures (frontonasal, zygomaticomaxillary, intermaxillary, midpalatal, frontozygomatic) are affected by RPE appliances .[7-9]

Recently, bone-borne expanders utilizing Temporary Anchorage Devices (TADs) such as Maxillary Skeletal Expander (MSE) (Fig. 1) are being used to reduce the drawbacks of dentoalveolar tipping caused by RPE, particularly when the midpalatal suture has fused.[10-12] It is hypothesized that through the use of TADs, sutures which have fully interdigitated can still be split open yielding true skeletal mid-face expansion.[13] According to Cantarella et al., expansion using MSE demonstrates great parallelism, as the PNS (Posterior Nasal Spine) has been measured to expand up to 90% of the amount of expansion at the ANS (Anterior Nasal Spine).[7] This parallelism differs from that of traditional RPE appliance which splits the midpalatal suture in a triangular shape with the greatest expansion occurring anteriorly and the least amount of opening posteriorly at the apex of the nasal cavity.[3] Although MSE has shown to lead to more symmetric expansion in the anterior-posterior dimension[7], only few studies have quantified the amount of expansion as well as the degree of parallelism, and none have focused on non-growing patients exclusively. [14]

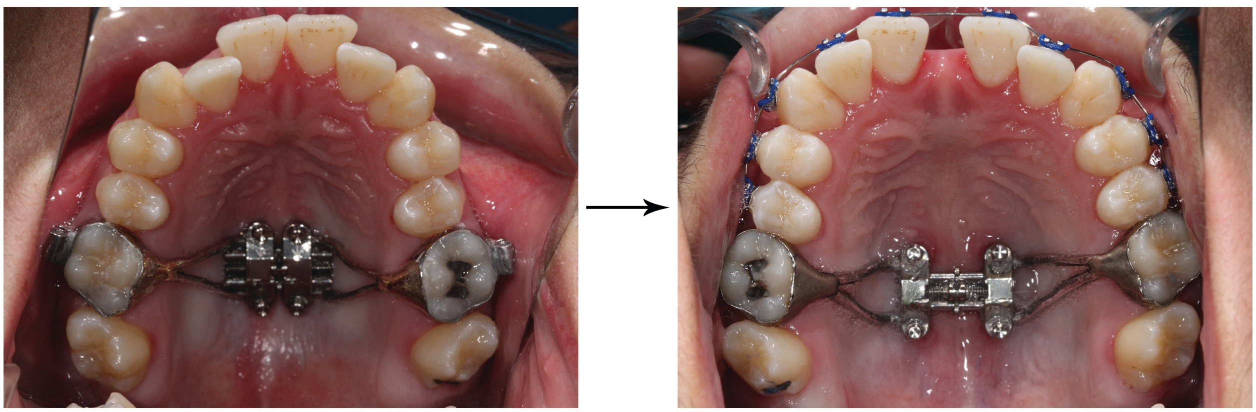

Figure 1: Occlusal view before and after expansion using MSE, with a clinically visible anterior diastema.

Current literature studying the skeletal effects induced by traditional RPE has not addressed the variation in the symmetry of expansion in the transverse dimension. However, with the increased use of MSE to successfully expand adults whose sutures have likely fused[15], clinically significant asymmetry of expansion has also been documented.[7] In addition, surgically assisted rapid palatal expansion (SARPE) was also shown to exhibit significant asymmetry in the transverse direction as recently documented.[16]

These new discoveries have raised a number of questions and hypotheses about different factors that could be attributed to this asymmetric expansion, such as the difference in density of the circummaxillary sutures and the surrounding bones, presence or absence of crossbite, and difference in the morphology of bones on each side. Even though in one study suture density ratio has been proposed as a possible predictor for the amount of orthopedic expansion[17], the nature of this asymmetry is yet to be adequately studied and documented, as its clinical significance remains poorly elucidated. Correlation between any of the aforementioned factors and the amount of expansion on both sides of the midpalatal suture are not documented in the literature. Since all of these factors could potentially vary on one side compared to the other, studying their correlation with the amount and pattern of expansion can be used to discover predicting variables that help indicate the expansion pattern and symmetry prior to starting treatment.

Facial asymmetry is a common manifestation and is associated with differences between the right and left sides of the face.[18] The clinical evaluation of facial asymmetry in the transverse plane may reveal skeletal anomalies, or may be due to the overlying soft tissures.[18,19] The use of Cone Beam Computed Tomography (CBCT) provides clinicians with exceptional detailed images, that have not been explored in previous studies which utilized traditional two-dimensional imaging.[3] While initial asymmetry of the mid-face can play a significant effect on the symmetry of the expansion induced by MSE, another important factor is difference in resistance to expansion between the right and left sides of the suture. The greatest area of lateral resistance to expansion is the zygomatic buttress bone and the pterygomaxillary junction, which is the area of focus when performing SARPE. Surgeons release the zygomatic buttress and the pterygomaxillary junction in order to reduce or eliminate the greatest resisting structures and allow for expansion to occur.[20,21] Therefore, the buttress bone morphology could be a predicting factor that affects the transverse symmetry of expansion due to differential resistance between the right and left structures.

Bone density may also play a factor in this asymmetry, as a denser bone will offer more resistance against expansion treatment. No previous studies have compared the difference in density between two sides of the zygomaticomaxillary complex of patients undergoing expansion.

Another factor to consider is the pattern of dental crossbite, as it may also show an associated with the resultant pattern of expansion. Since the expander being studied is of skeletal nature and is being used to treat TMD, and not dental crossbite, patients presenting different patterns of crossbites were included in this sample. The use of 3D multi-planar software allows for more robust analysis of the nature of the pattern of expansion, in addition to helping clinicians make an accurate diagnosis and to subsequently treat facial skeletal asymmetry.[18,22] Clinically, facial asymmetry may span from hardly measurable to substantially noticeable differences. The magnitude at which acceptable asymmetry becomes abnormal is not easily classified.[18] Thus, as clinicians it is important to assess initial asymmetry and devise treatment plans that will create an achievable balance for the patient.

OBJECTIVES AND SPECIFIC AIMS

Maxillary skeletal expander can be utilized to achieve skeletal expansion in non-growing patients, but the amount and symmetry of this expansion has not been explored sufficiently. While initial reports indicated possible asymmetry of expansion, it has not been studied exclusively on non-growing patients where the amount of asymmetry can be localized to the expansion with no confounding variables. We hypothesize that MSE can successfully achieve skeletal expansion in non-growing patients, but there is a variation in the symmetry of expansion, particularly in the transverse plane. We also hypothesize that the extent of the symmetry of expansion is correlated to one or more predicting variables. In order to test our hypotheses, we proposed the following specific aims:

Aim 1: Assess the magnitude, parallelism, and transverse asymmetry of expansion induced by MSE using Cone Beam CT (CBCT) imaging through:

a) Evaluating the amount of total expansion achieved and its parallelism in non-growing patients
b) Quantifying the frequency, and amount of asymmetry between the contra-lateral sides.

Aim 2: Evaluate for association between the extent of asymmetry of expansion, and any of the following possible predicting variables:

c) Initial asymmetry of the mid-face.
d) Density value difference of the zygomatic, maxillary, and palatine bones.
e) Pattern of dental crossbite.

MATERIALS AND METHODS

Study Design

The study included 31 subjects who have undergone expansion using MSE (BioMaterials Korea, Inc.) with a mean age of 20.4 ± 3.2 years (range 17-27 years) and of diverse ethnic backgrounds. Crossbite presentation of patients included: twelve with bilateral posterior crossbite, six patients with unilateral right crossbite, five patients with unilateral left crossbite and seven patients with maxillary transverse deficiency without posterior dental crossbite. All patients were treated at the same institution. MSE treatment was initiated and completed prior to bonding of brackets or other orthodontic appliances, and CBCT images were obtained before, and right after expansion was complete.

Inclusion Criteria

The inclusion criteria were the following: (1) diagnosis of transverse maxillary deficiency based on a recently published adaptation of Andrews' analysis of six elements [23], (2) no craniofacial abnormalities, (3) no previous orthodontic treatment, (4) adequate clinical radiographic records, and (5) non-growing patients with Cervical Vertebral Maturation Stage (CVMS) V.

Bone-borne MSE appliance was chosen instead of a traditional tooth-borne expander, based on the following characteristics: patient maturity (presence of secondary sexual features, such as facial hair, change in pitch of voice, onset of menstruation cycle, CVMS greater than IV, dolichofacial vertical biotype (determined with MP-SN and FMA angles on lateral cephalometric analysis) and history of nasal airway obstruction. Based on previous studies, it is preferred to treat dolichofacial patients with MSE rather than with a tooth-borne maxillary expander because bone-borne appliances are believed to lead to lesser dentoalveolar tipping and less posterior mandibular rotation.[12,20,24]

Expander Design and Activation Rates

The same MSE design (Fig. 1) was used for all patients. The MSE contains a central jackscrew unit, positioned at the posterior palate with four micro-implants size 1.8 x 11mm, and attaches to the molars with connecting arms and molar bands. The activation protocol was set at four turns (0.56 mm) per day for all patients until a diastema appears. The rate was then switched to two turns per day. Expansion was complete when the maxillary arch width was equal to the mandibular width. Average duration of expansion was 25 ± 10 days. After proper maxillary expansion was achieved, the MSE remains in place for 3-6 months to allow for adequate retention.

3D Analysis

CBCT scans were taken prior to expansion and within 3 weeks following completion of maxillary expansion on all patients. The post-expansion scans were always taken prior to bonding of brackets or any orthodontic appliance other than MSE, these two factors ensured that the sutures remained patent prior to bone formation to allow for accurate measurements.

All CBCT scans were taken by a NewTom 5G scanner in an 18 × 16 field of view with a 14-bit gray scale and with a voxel size of 0.3 mm. Scan times were 18 s (3.6 s emission time), with 110 kV, and utilized an automatic exposure control that adjusted the milliampere based upon the patient's anatomic density. Five hundred thirty-eight axial slices with 609 × 609 resolution and a slice thickness and increment of 0.3 mm and pixel spacing of 0.3 mm were obtained. The Fusion module by OnDemand 3D (Cybermed Inc., Korea) was used to superimpose the post-expansion CBCT on the pre-expansion CBCT using the anterior cranial base as a stable reference on non-growing patients, as proposed by Cevidanes et al.[25] This is a fully automated tool by the software that relies on grayscale values and multiple iterations of best fit, to circumvent errors related to the operator. This method was verified for accuracy by Weissheimer et al.[17,25]

The Mid-Sagittal Plane (MSP) was utilized as the plane of reference for all measurements to assess the amount of expansion, as it was found to be the most accurate plane to quantify lateral maxillary expansion based on a recent publication.[26] MSP is a plane passing through the Nasion (N), Anterior Nasal Spine (ANS) and Posterior Nasal Spine (PNS), generated on the pre-expansion CBCT (Figs. 2 & 3). It is created based on the pre-expansion CBCT image and remains a fixed reference to measure post-expansion changes with the pre and post-expansion CBCT scans superimposed. The axial palatal plane (APP) is perpendicular to the MSP and passes through the ANS and PNS (Figs. 2, 3). Lateral measurements were made on axial sections that were created at the level of this plane.

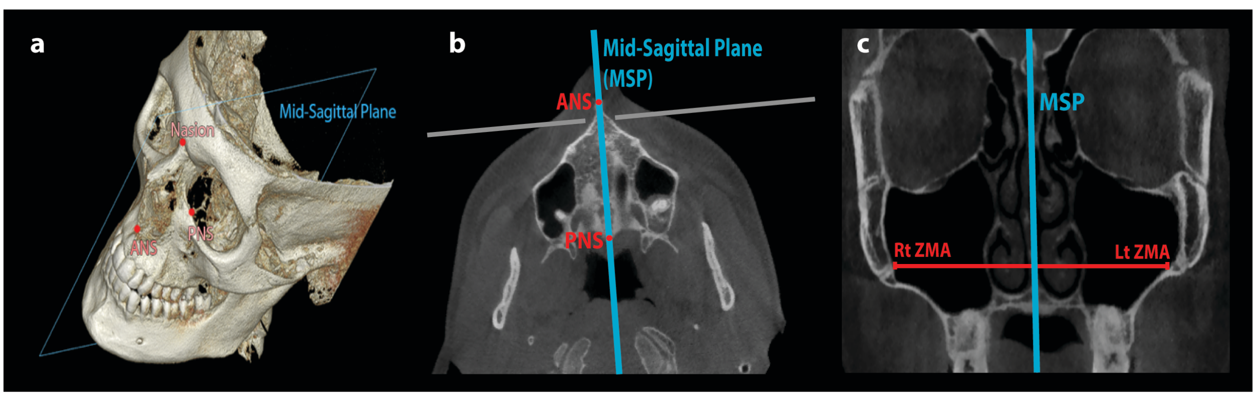

*Figure 2: **(a)** CBCT image showing Mid-Sagittal Plane (MSP) on an initial CBCT using OnDemand (Cybermed, Korea). ANS, PNS and Nasion can be viewed as separate skeletal landmarks on the MSP. **(b)** Axial slice at pre-expansion with vertical line passing through ANS and PNS. **(c)** Coronal view of pre-expansion CBCT displaying measurements from the MSP to both the right and left ZMA. Right and left ZMA landmarks indicated in red at the most medial-superior location of the zygomatic-maxillary suture.*

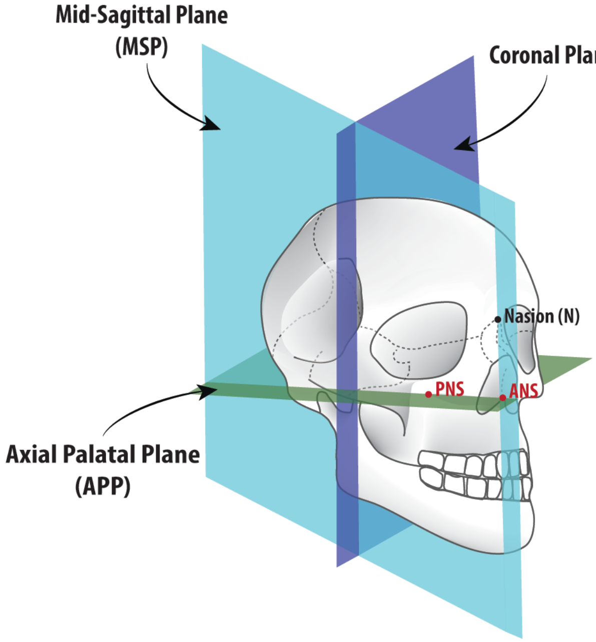

Figure 3: Illustration of the two main reference planes: mid-sagittal plane (MSP) and axial palatal plane (APP) and coronal plane added for orientation. Planes are identified in the pre-expansions CBCT and become the reference lines to measure the displacement of skeletal landmarks in the post-expansion CBCT. Note that the MSP passes through the ANS, PNS and Nasion on the pre-expansion CBCT. The APP also passes through the ANS and PNS in the pre-expansion CBCT.

Measurements at the Mid-Sagittal Plane (MSP)

To accurately quantify the extent of skeletal expansion, the method proposed by Cantarella et al[7] will be used with slight modifications. In the present study, the MSP has been used to study the split of the midpalatal suture. Lateral displacement was measured from the right or left sides to MSP for skeletal landmarks, including: Anterior Nasal Spine (ANS), Posterior Nasal Spine (PNS), Zygomaticomaxillary point (ZMA). The MSE splits the midpalatal suture, in which the previously singular ANS and PNS skeletal landmarks will be divided into their respective right (Rt) and left (Lt) landmarks in each patient following skeletal expansion (Fig. 4).

In the pre-expansion CBCT, the MSP passes through the ANS and PNS, then in the post-expansion CBCT linear measurements were made from the right and left sides of the ANS and PNS skeletal landmarks to the MSP in the axial cuts at the level of the APP. The post-expansion Rt and Lt distances of each landmark represent the lateral expansion of each side. Zygomaticomaxillary point (ZMA), represents the most medial aspect of the zygomaticomaxillary suture when viewed in the Coronal Zygomatic Section (CZS) (Fig. 2C).

CZS is a section that passes through the lowest point of the zygomaticomaxillary sutures and the uppermost point of the frontozygomatic sutures.[27] Similarly, in pre and post-expansion CBCT images, the distance from the right and left Zygomaticomaxillary Suture was measured to the mid-sagittal plane at the level of the axial palatal plane. The sum of displacement of right and left sides represented the total amount of expansion while the difference represented the transverse asymmetry.

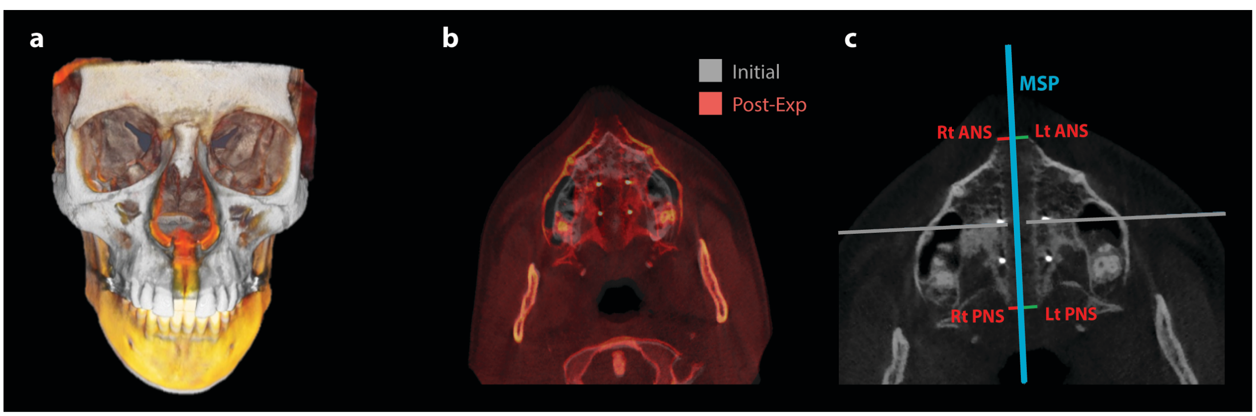

*Figure 4: **(a)** 3D superimposition of pre and post-expansion on an individual patient demonstrating changes to mid-face. **(b)** Axial view of superimposed pre and post expansion. Expansion evident at ANS and PNS landmarks. **(c)** Axial view of post-expansion CBCT showing measurement from MSP to both the right and left ANS and PNS landmarks with apparent asymmetry.*

Magnitude of Expansion and Deviation

For all patients, total expansion was measured by adding the amount of expansion on both sides of the MSP (Rt + Lt Post-expansion – Rt + Lt Pre-expansion). For all three skeletal landmarks, if the right and left halves did not expand equally, then a deviation was present, and in order to quantify the amount of said deviation, the difference of the right and left side expansion values will be calculated. A positive value reflects right-side dominant expansion, whereas a negative value represents left-side dominant expansion. The movement at the ANS was chosen to further group the subjects because changes at the ANS have a smaller standard deviation for total expansion. Additionally, another publication chose the movement of the ANS as a parameter to analyze expansion because changes at ANS reflect modifications in the anterior part of the maxilla more closely and therefore can have a larger impact on the soft tissues of the face.[7,14]

To determine the extent and incidence of transverse asymmetry of expansion, the absolute value of the difference between the right and left sides was calculated for ANS, PNS, and ZMA. Based on the standard deviation of ANS as well as clinical significance, the subjects were split into two groups (Symmetric and Asymmetric) to determine an estimated prevalence, as well as to conduct further analysis of each group.

Correlation of Possible Predicting Factors of Asymmetry

In order to detect any possible association of the direction and magnitude of asymmetry with the hypothesized predicting factors, the initial pre-expansion CBCT image of all 31 patients will be used to detect any possible difference between the right and left sides of the same patients prior to expansion.

- Initial asymmetry of the mid-face:

In order to evaluate if the pattern of expansion is either directly or inversely correlated to the initial asymmetry in both magnitude and direction, three linear measurements are used to quantify the initial asymmetry of the face. Utilizing the MSP, three bilateral landmarks were measured on the initial CBCT of each patient, measuring the distance between the MSP and the frontozygomatic sutures (FZ), the zygomaticomaxillary sutures (ZM), and the most lateral-inferior point of the alveolar bone around the first molars (Alveolar Point). All measurements were made on the Coronal Zygomatic Section (CZS) using OnDemand 3D. (Fig. 5)

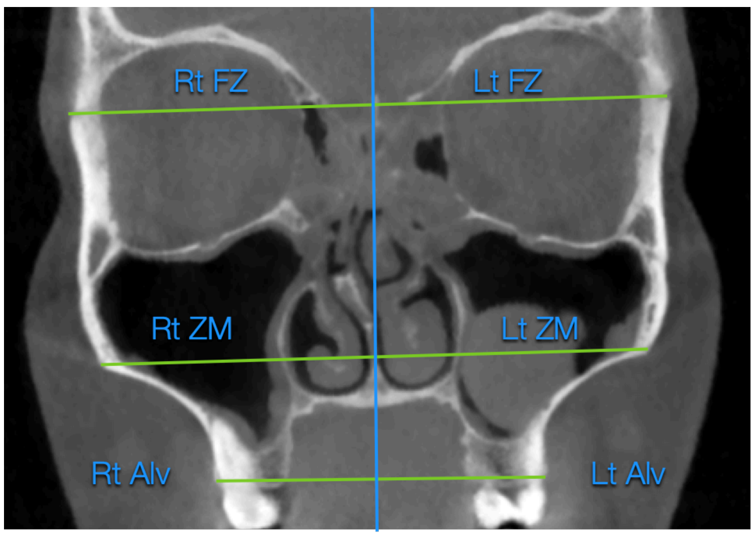

Figure 5: Coronal Zygomatic Section view showing the three landmarks used to evaluate initial asymmetry: FZ (Frontozygomatic Suture), ZM (Zygomaticomaxillary Suture), and Alv (Alveolar Point).

- Density of the zygomaticomaxillary complex:

The same Coronal Zygomatic Section will be used to assess the bone density of the zygomaticomaxillary complex. Using OnDemand 3D, three density boxes of 3 x 3 voxels dimension will be equally distributed within the cortical bone of the zygomatic bone, maxillary bone, and palatal bone on both the right and left sides (Fig. 7). To evaluate palatal bone at different levels, the coronal plane will be moved to the level of upper second premolars, then upper second molars where density of the palatal bone will be measured again using one box at each side, these two measurements will represent the palatal process of the maxilla. Finally, the coronal plane will be moved to the level of upper second molars, and palatine bone density measurements will be performed representing the actual palatine bone. The three measurements for each anatomical structure will be averaged to obtain right and left measurements as such: Zygomatic bone density (ZygD), Maxillary bone density (MaxD), Palatal bone density at first molars (P1MD), Palatal bone density at second molars (P2MD), and Palatine bone density at second premolars (P2PD).

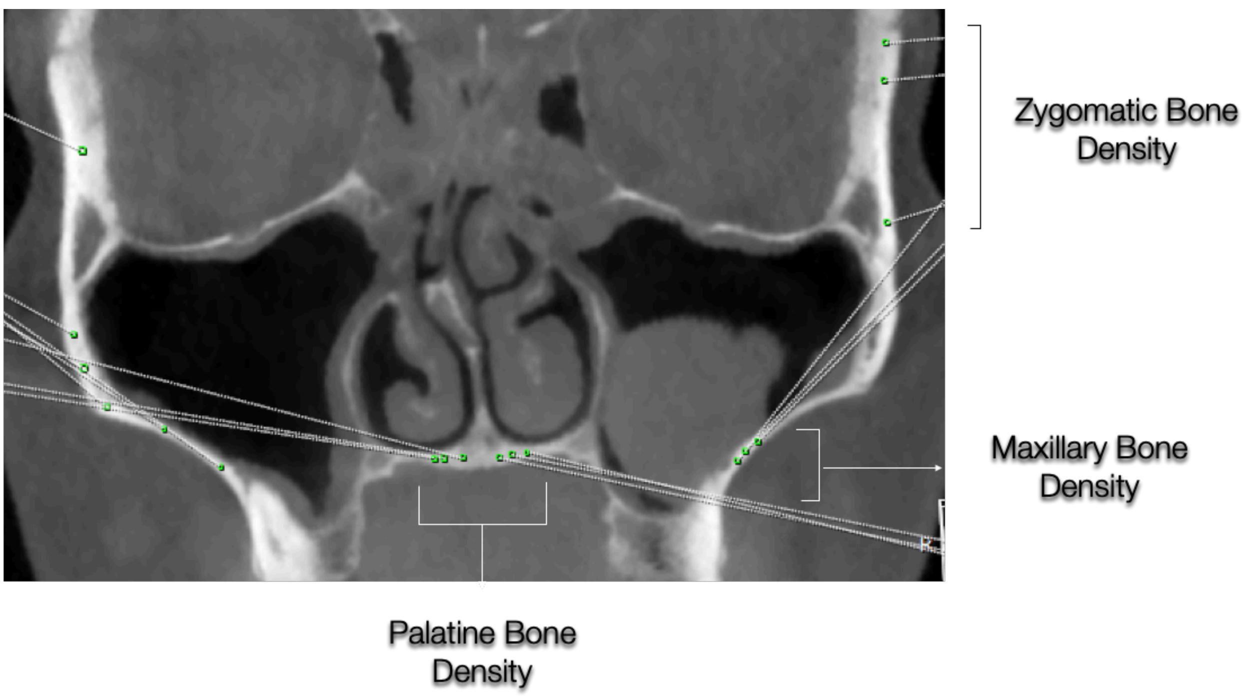

Figure 6: Density boxes (3 x 3 voxels) measuring bone density in Hounsfield Units (HU). Three boxes are used on each side of the Zygomatic, Maxillary, and Palatine bones.

Both the initial asymmetry of the mid-face, and the density of the zygomaticomaxillary complex predicting factors were quantified using the previously mentioned measurements: FZ, ZM, Alveolar Point, ZygD, MaxD, P1MD, P2MD, P2PD were calculated (Figs. 5,6).
Afterwards, the difference between right and left was calculated for each of them as and denoted as "Asymmetry" (i.e., FZ Asymmetry = [Right FZ - Left FZ], ZM Asymmetry = [Right ZM - Left ZM], etc.).

The data was then re-organized to calculate the absolute difference between the greater and lesser side denoted as "Deviation" for all measurements (i.e., FZ Deviation = [Greater FZ - Lesser FZ], MaxD Deviation = [Greater MaxD - Lesser MaxD], etc.). For purposes of correlation, not only the ANS Deviation was used, but also the ANS Asymmetry where ANS Asymmetry = [Right ANS – Left ANS] maintaining the sign where if ANS Asymmetry is positive, it indicates the right side was larger and vice versa. This was done in order to quantify the direction of the asymmetry against the direction of asymmetry of each predicting variable.

- <u>Pattern of dental crossbite:</u>

  In order to evaluate possible correlation between dental crossbite pattern and the asymmetry of expansion, patients were grouped into four possible crossbite patterns: no crossbite, bilateral crossbite, right side unilateral crossbite, or left side unilateral crossbite. Posterior dental crossbite is defined as an inadequate transversal relationship where the buccal cusps of the maxillary teeth are in contact with the central fossae of the mandibular teeth.[28,29] This was diagnosed using the study casts to denote a crossbite pattern for each patient. The four different types will be plotted against the resultant ANS Deviation to evaluate any possible correlation.

Statistical Analysis

Sample size power analysis was calculated with 80% power and an alpha value of 0.05 using G*power 3.1.9.3 software (Franz Faul, Universität Kiel, Germany), and a minimum of N=20 samples was needed.[30] Descriptive statistics, including means and standard deviations were calculated for the Aim 1 data. Shapiro-Wilk test was used to assess the normality of the data.[31]

Paired *t*-test (Wilcoxon signed-rank test) was performed to compare the pre and post-expansion measurements at the ANS, PNS and ZMA based on central limit theorem. Within the asymmetric group of patients, same t-test was utilized to compare the greater vs lesser measurements at the ANS, PNS and ZMA. To evaluate interobserver reliability, all measurements on 10 patients were repeated by three different investigators. A paired t-test was performed, and limits of agreement and an intra-class correlation coefficient (ICC; one-way random model, absolute agreement) were calculated. Statistical analyses were performed in SPSS Statistics 25 (IBM Corporation, Armonk, NY, USA). A 95% confidence level ($p < 0.05$) was considered statistically significant.

Pearson correlation coefficients (r) and their p-value were calculated for the correlation among ANS Deviation, and ANS Asymmetry with all the possible predicting variables to evaluate possible associations using Pearson's correlation test.

RESULTS

Aim I Results:

Total Magnitude of Expansion

Initial values of ANS and PNS before MSE were 0mm, as they are a singular landmark prior to expansion (Table I). MSE expansion resulted in significant increase in transverse dimension at the ANS, PNS and ZMA. The Wilcoxon signed-rank test was used, and the expansion was statistically significant with p-values <0.001 at all three landmarks (Table I). The magnitude of expansion at the ANS showed the greatest average displacement of 4.98mm compared to the PNS and ZMA (Table I). The largest range of expansion was seen at the PNS (0-13.3 mm), taking into consideration that two patients did not display any measurable expansion at the PNS; this could be due to either actual lack of split, or due to bone density thresholds not permitting proper visualization of the split. The difference in the post-expansion lateral measurements at the ANS, PNS and ZMA were significantly greater than their respective pre-expansion values (P < 0.001). Following MSE treatment in all patients, the average expansion at the ANS was 4.98 mm, with the PNS displaying 4.77 mm of average expansion. The smallest change in average expansion was observed at the ZMA, with a mean magnitude of 4 mm. (Table I, Fig. 4,7).

	Initial		Post-expansion		Treatment change		
	Mean	SD	Mean	SD	Mean	SD	P-value
Total ANS expansion	0	0	4.98	1.98	4.98	1.98	< .0001
Total PNS Expansion	0	0	4.77	2.65	4.77	2.65	< .0001
Total ZMA expansion	80.53	4.91	84.52	5.35	3.99	1.6	< .0001

Table I: Total ANS, PNS and ZMA expansion was calculated as Post-expansion - Pre-expansion for Right + Left values for each of the three landmarks. The Wilcoxon signed-rank test was used to compare pre and post-expansion.

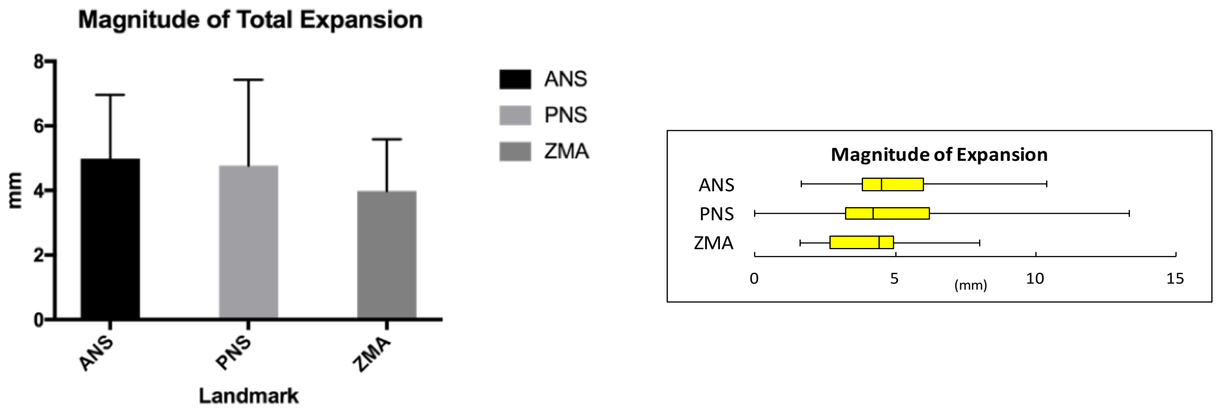

Figure 7: Plot comparing the magnitude of expansion at the three main landmarks: ANS, PNS, and ZMA. The right-side plot shows the means and standard deviations, while the left side is a box and whiskers plot showing the range and distribution.

Parallelism

To evaluate the parallelism in the sagittal dimension, the ratio of the amount of expansion at the ANS to the amount of expansion at PNS was measured. Average PNS expansion was 4.8mm and average ANS expansion was 5 mm giving a 95.7% parallel expansion in the anterior-posterior dimension.

Asymmetry

The prior singular ANS and PNS skeletal landmarks can now be visualized as having a right (Rt) and left (Lt) in each subject (Fig. 4C). The absolute value of the difference in expansion between the two sides was calculated; this value represents the magnitude of the deviation for the ANS or PNS. The SD of the ANS Deviation (Rt ANS – Lt ANS absolute, which is Greater - Lesser ANS) was 1.1 mm as seen in Table II. The subjects were then divided into 2 groups based on their ANS deviation value of 1.1 mm; this value was used to change the methodology of subgrouping. From 31 total subjects, 15 had an ANS deviation less than 1.10mm, which were placed in the symmetric group. The other 16 subjects had an ANS deviation greater than 1.10mm and were placed in the asymmetric group (Fig. 10). To validate the grouping, a t-test was calculated comparing the greater versus lesser ANS expansion across both symmetric and asymmetric groups. Within the symmetric group, the difference between the greater and lesser values was not statistically significant. In the asymmetric group, there was a statistical significance between the greater and lesser ANS measurements verifying accurate grouping. (Table III). Based on this sample size, the percentage of patients exhibiting statistically significant ANS deviation representing asymmetry at a magnitude of at least 1.1mm was 51%.

	Mean (mm)	SD (mm)
ANS Deviation |Rt -Lt|	1.37	1.10
PNS Deviation |Rt -Lt|	1.16	0.99

Table II: ANS and PNS deviation values for all patients (N = 31).

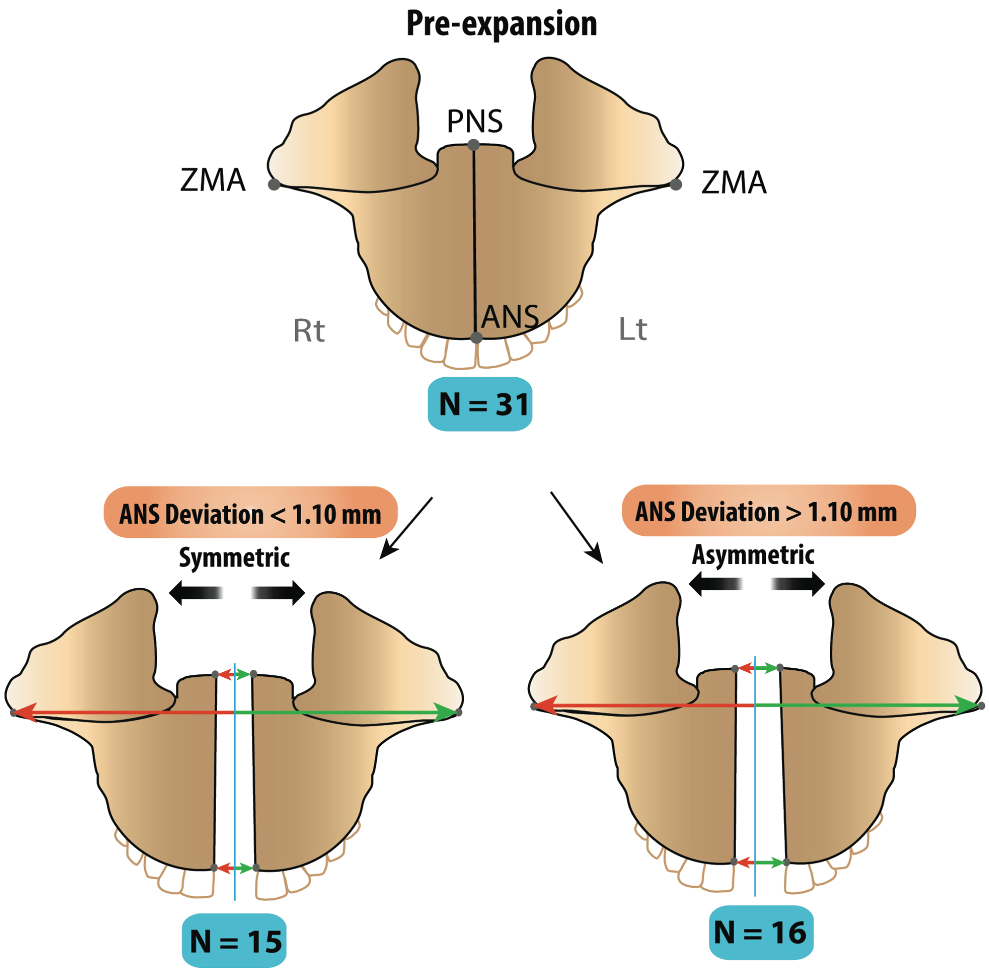

Figure 8: Illustration of pre-expansion and post-expansion symmetric and asymmetric groups after MSE treatment. The symmetric group had an ANS Deviation less than 1.1mm, while the asymmetric group had an ANS deviation more than 1.1mm. Within each group, the direction of expansion (right or left) was not considered, and instead all expansion measurements were sorted into either "Greater" or "Lesser" values for the purpose of evaluating the amount of absolute asymmetry.

To further describe the extent of asymmetry, a narrowed scope looking only within the asymmetric group (n=16), magnitude of expansion at all three landmarks (ANS, PNS, and ZMA) showed statistically significant difference when comparing greater to lesser values for each patient, using a non-parametric paired t-test. The greatest deviation from greater to lesser was observed at ANS with a mean of 2.22 mm, followed by PNS (1.77 mm), and the least was at ZMA expansion (1.3 mm). (Table III)

Asymmetric Group	Treatment Change		
	Mean	SD	p-value
Greater ANS	4.08	1.22	< .0001
Lesser ANS	1.86	0.97	
ANS Deviation	2.22	0.89	
ANS Deviation %	37.4		
Greater PNS	3.81	1.44	< .0001
Lesser PNS	2.04	1.55	
PNS Deviation	1.77	1.11	
PNS Deviation %	30.3		
Greater ZMA	2.83	1.23	<.05
Lesser ZMA	1.53	0.85	
ZMA Deviation	1.3	1.18	
ZMA Deviation %	29.8		

Table III: Asymmetric group (n = 16) means and standard deviations for greater and lesser expansion (mm) at ANS, PNS and ZMA after MSE. Deviation % was also calculated. All three landmarks (ANS, PNS, and ZMA) showed statistically significant difference when comparing greater to lesser values for each patient, non-parametric paired t-test was used.

To further investigate this asymmetry difference, the methodology was altered to add Deviation % measurement. Although the values are higher at ANS and PNS, the mean deviation as a percentage of the mean of the total expansion was calculated as [$Deviation\,\% = \frac{Deviation}{Greater+Lesser} \times 100$]. Deviation % was 39% at ANS, and 30% at both ZMA and PNS.

<u>Aim II Results:</u>

Correlation

Pearson correlation coefficients were calculated to evaluate if the magnitude of asymmetry at the ANS landmark (ANS Deviation = Greater – Lesser ANS) was correlated to the magnitude of the difference between each variable regardless of direction (i.e., ZM Deviation, FZ Deviation, etc.). All eight variables representing both the magnitude of the initial asymmetry of the midface (FZ Deviation, ZM Deviation, and Alv. Deviation) as well as the deviation in the density between both sides of the various bony structures (ZygD, MaxD, P2PD, P1MD, and P2MD) were used in this analysis. P-value was also calculated for each variable to evaluate the statistical significance at $p<0.05$. All but one variable showed very little correlation ($r<0.25$), and no statistical significance ($p>0.05$). The only variable showing statistically significance correlation was P2MD (Palatal bone density at the 2nd Molar) $r=0.443$ indicating a positive correlation relationship where the bigger the difference in density of the palatine bone at the second molar level is, the bigger the magnitude of asymmetry (i.e., ANS Deviation) is. (Table IV)

Bivariate correlation with ANS Deviation (Magnitude)		
Predicting Variables	**Pearson Correlation coeffecient = r**	**p-value**
FZ Deviation	-0.020	0.9170
ZM Deviation	-0.110	0.5620
Alveolar Point Deviation	-0.138	0.4671
ZygD Deviation	0.227	0.2270
MaxD Deviation	0.101	0.5956
P2PD Deviation	0.065	0.7347
P1MD Deviation	-0.003	0.9881
P2MD Deviation	**0.443**	**0.0143***

Table IV: Correlation coefficients and their p-values for all 8 variables in relation to ANS Deviation representing initial asymmetry of the mid-face, and the density deviation of the zygomaticomaxillary complex. P2MD showed statistically significant p-value, while all other variables showed no correlation.

To further explore the lack of correlation, scatterplots of ANS Deviation against each factor's deviation were created showing a clear lack of correlation between any of the variables and the resultant expansion deviation. Although P2MD showed higher correlation with statistical significance, a clear inconsistency is evident in the scatterplot that should be taken in consideration. (Fig. 10) This shows a lack of correlation between any of the hypothesized predicting variables, and the resulting expansion at ANS (ANS Deviation) in regard to the deviation (i.e., absolute magnitude) of the initial asymmetry of the patient's mid-face, and the deviation of the densities between right and left sides. This data does not include the direction of expansion nor the right and left initial values of each variable.

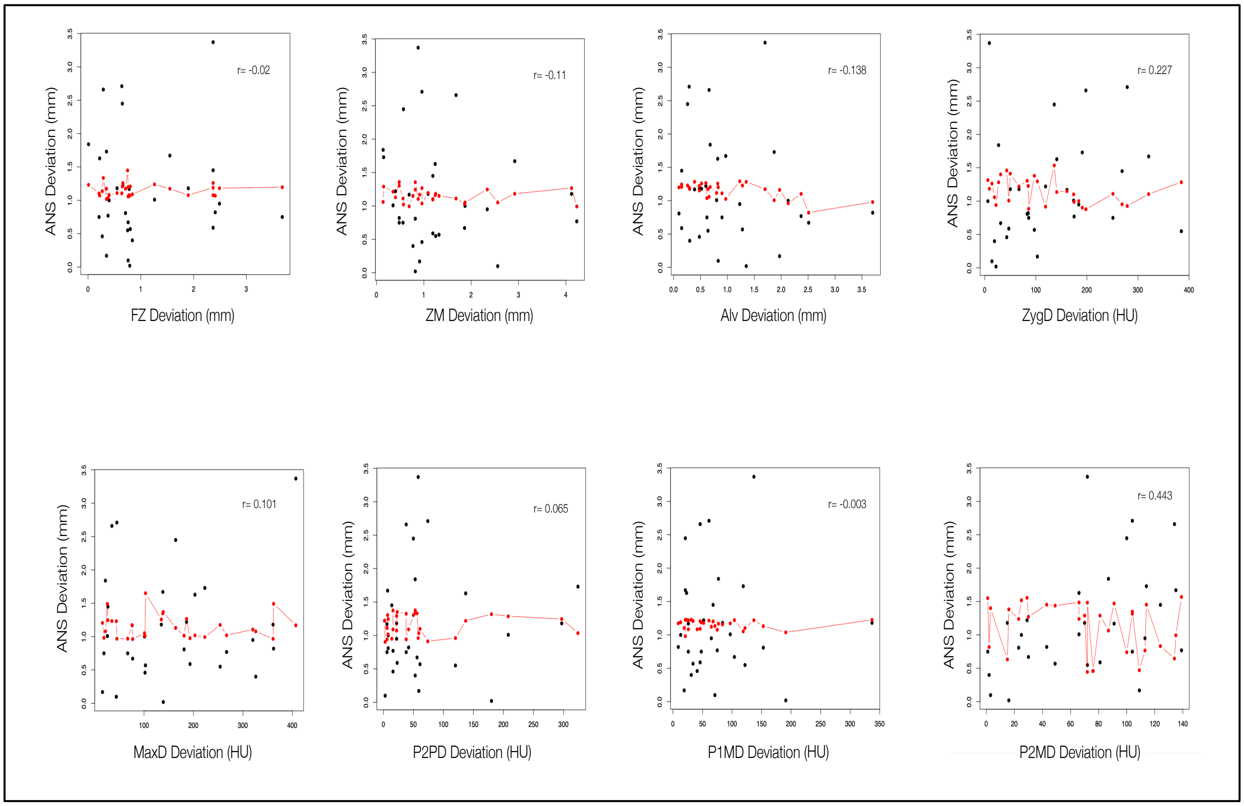

Figure 9: Scatterplots of the relationship between ANS Deviation (y-axis) and each independent variable (x-axis): FZ Deviation, ZM Deviation, Alv Deviation, ZygD Deviation, MaxD Deviation, P2PD Deviation, P1MD Deviation, and P2MD Deviation in mm or Hounsfield Units (HU) as indicated. The red line and points represent the line of best fit calculated to represent the correlation relationship.

To evaluate the possible correlation in direction (i.e., whether any of the predicting factors being larger on one side is correlated to the same side showing more or less expansion at ANS), the re-organized data was used to study the relationship between ANS Asymmetry (Right - Left ANS) and the respective asymmetry (Right - Left) of each predicting factor. (Table V)

The same correlation analysis was used to calculate Pearson correlation coefficients and their corresponding p-values for each of the eight factors against ANS Asymmetry. Table V shows generalized lack of correlation with no statistical significance with the exception of FZ asymmetry which is inversely correlated with ANS asymmetry with a Pearson's correlation coefficient of r= -0.367 and p<0.05. This indicates that when FZ Asymmetry is large (i.e., Right FZ is larger than left FZ when measured from the MSP), ANS Asymmetry was small (i.e., the right ANS displaced a shorter distance compared to the left side after expansion). Scatterplots were also created to visualize this lack of correlation in direction. (Fig. 11) Similar to the previous findings, although FZ Asymmetry is showing statistically significant correlation, there is an inconsistent region where the line of best fit is no longer linear due to the random middle region where the correlation does not appear to be consistent.

Bivariate correlation with ANS Asymmetry (Direction)		
Predicting Variables	**Pearson Correlation coeffecient = r**	**p-value**
FZ Asymmetry	**-0.367**	**0.046***
ZM Asymmetry	-0.241	0.1998
Alveolar Point Asymmetry	-0.010	0.9579
ZygD Asymmetry	-0.176	0.3522
MaxD Asymmetry	0.026	0.8933
P2PD Asymmetry	-0.254	0.1760
P1MD Asymmetry	0.169	0.3720
P2MD Asymmetry	0.183	0.3321

Table V: Correlation coefficients and their p-values for all 8 variables in relation to ANS Asymmetry representing the direction (sign included) of the initial asymmetry of the mid-face, and the density difference of the zygomaticomaxillary complex. FZ asymmetry correlation coefficient is significant at p<0.05.*

Based on these findings, none of the hypothesized factors representing the initial asymmetry of the mid-face, or the density difference of the zygomaticomaxillary complex are significantly correlated. This lack of correlation with the asymmetry is found in both the magnitude (ANS Deviation), and the direction (ANS Asymmetry) except for P2MD Deviation and FZ Asymmetry. However, those two variables have low Pearson's correlation coefficients ($-0.5<r<0.5$) that are further explained by lack of an adequate linear correlation on the scatterplots. None of the hypothesized factors appear to play in a role in the direction, or amount of the asymmetry of expansion by MSE appliance, and therefore cannot be used as predicting factors.

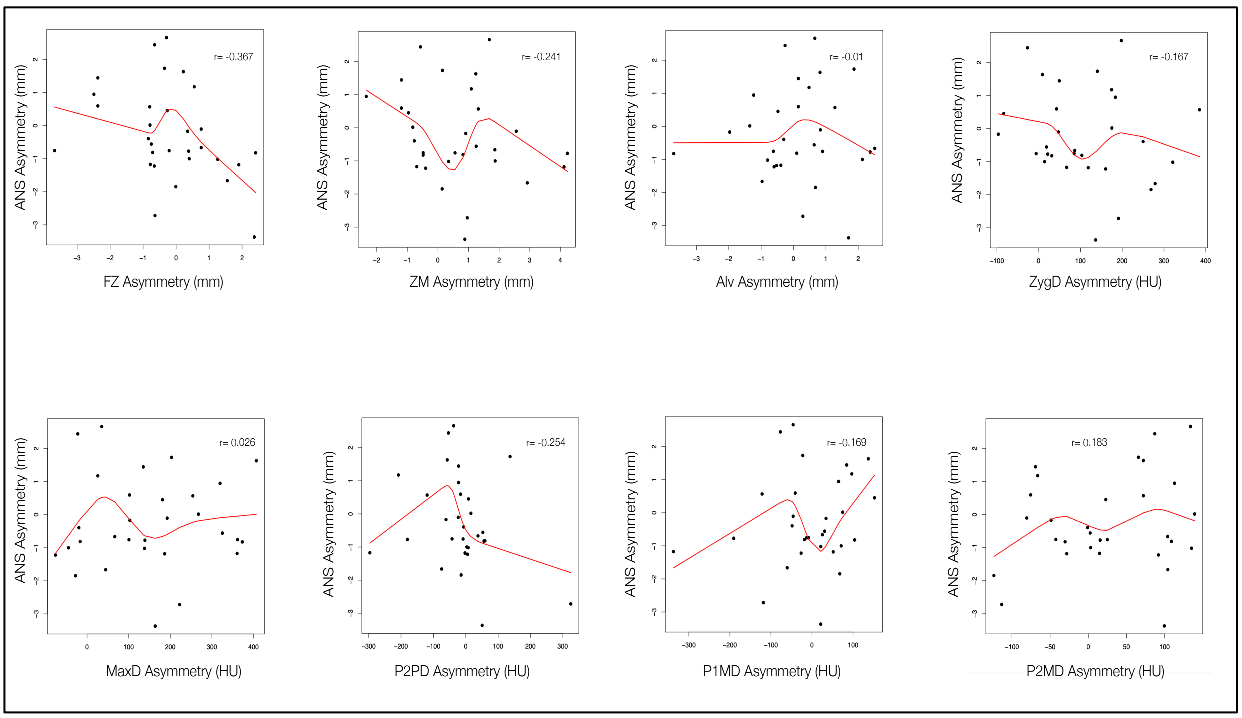

Figure 10: Scatterplots of the relationship between ANS Asymmetry (y-axis) and each independent variable (x-axis): FZ Asymmetry, ZM Asymmetry, Alv Asymmetry, ZygD Asymmetry, MaxD Asymmetry, P2PD Asymmetry, P1MD Asymmetry, and P2MD Asymmetry in mm or Hounsfield Units (HU) as indicated. The red line represents the line of best fit calculated to represent the correlation relationship.

Due to the nominal nature of the pattern of crossbite, a scatterplot was created plotting the four different types (1 - No crossbite, 2 - Unilateral right-side crossbite, 3 - Unilateral left-side crossbite, and 4 - Bilateral crossbite) on the x-axis against ANS Asymmetry on the y-axis.

(Fig. 12) The scatterplot shows all 31 patients' crossbite pattern against the ANS Asymmetry (Right - Left ANS), where all points above the x-axis indicate patients who demonstrated more expansion on the right side, and all points below the x-axis represent patients with more expansion on the left side. All but one patient presenting with a unilateral right-side crossbite (Type 2) exhibited more expansion on the right side compared to the non-crossbite side. Similarly, all but one patient presenting with a unilateral left-side crossbite (Type 3) exhibited more expansion on the left side compared to the non-crossbite side, indicating a possible relationship. Types 1 and 4 (i.e., no crossbite, and bilateral crossbite, respectively) showed an almost random distribution of ANS Asymmetry. Due to the limited number of patients of each type this association cannot be statistically validated.

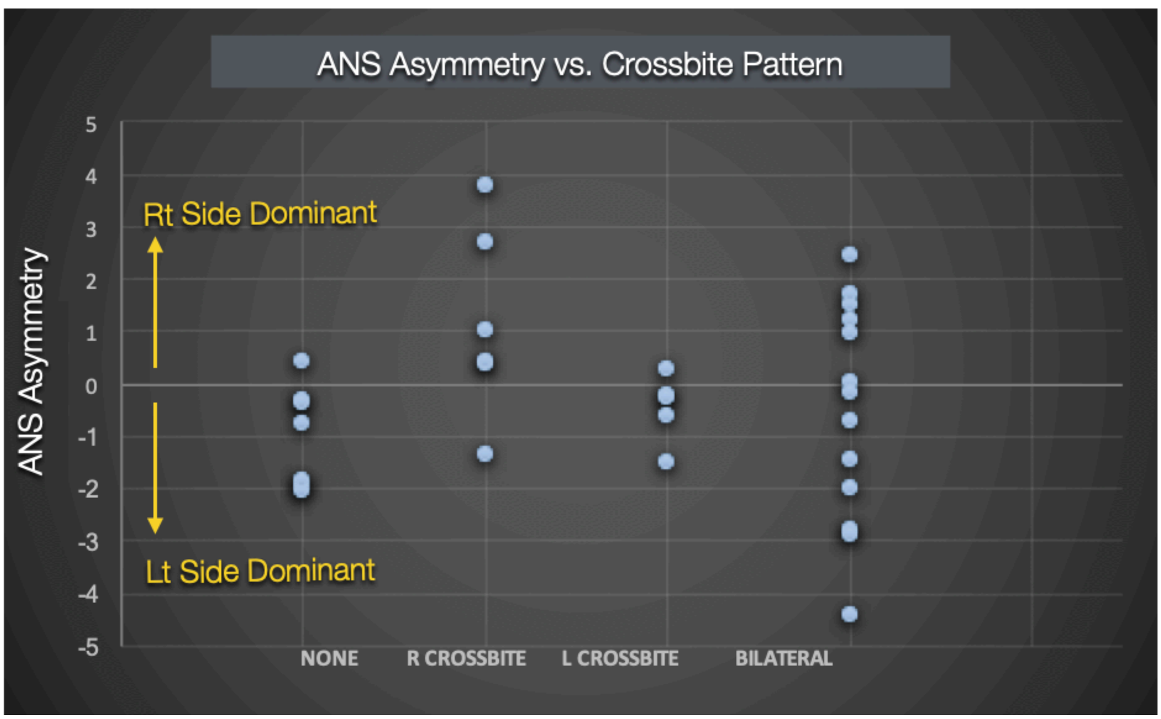

Figure 11: Correlation between presentation of posterior crossbite pattern in all 31 patients and ANS Asymmetry. A positive value for ANS Asymmetry represents Rt-side dominant expansion, whereas a negative ANS deviation value represents Lt-side dominant expansion.

DISCUSSION

Although there are numerous ways to quantify the amount of expansion, the advantage of having easily-replicated, and previously used landmarks made ANS, PNS, and ZMA the best candidates to evaluate the extent of skeletal expansion due to the ease of identification on a CBCT, and how close they are to the midpalatal suture. Using all three landmarks allows for a more accurate evaluation of expansion anteriorly, posteriorly, as well as at a higher and more lateral location in the skull.[7,25]

Although previous articles have evaluated the success of TAD-assisted expanders and their magnitudes, little is known about their effects on non-growing patients where the midpalatal suture has inter-digitated. In 47 adult patients, Handelman et al were able to use a Haas appliance to increase maxillary arch width with no evidence of suture split or true skeletal expansion.[32] However, the use of TADs is hypothesized to be able to achieve skeletal expansion in adults, therefore the Cervical Vertebral Maturation Staging (CVMS) index was used to select only non-growing patients with CVMS stage V across all samples as a validated index.[33,34] While CVMS is a validated index to evaluate growth, a more specific analysis of the midpalatal suture would give a more accurate analysis of the ability to split the suture at different stages of maturity, and the pipe proposed by Grunnheid et al should be used in future studies where the midpalatal suture maturity index is controlled.[35]

The results in this study support previous findings described by Cantarella et al in the pilot study conducted on 15 patients of different maturation stages. Despite the increased number of samples and the limitation to only non-growing patients, the difference in total expansion exhibited in this study compared to Cantarella's is minimal. Across the 31 non-growing patients, the average amount of expansion was 5 mm at ANS and 4.8 mm at PNS, while the previous pilot studies showed 4.8 mm at ANS and 4.3 mm at PNS.[7] This validation of results in non-growing patients indicates a high success rate of adequate expansion in adults, however, a larger sample size with a smaller range is required for higher accuracy. Although the previous articles focused primarily on ANS and PNS, our study opted to add ZMA to evaluate a point that is further away from the midpalatal suture and is expected to show a smaller amount of expansion due to the rotational nature of expansion, ZMA being closer to the center of rotation. This also validates the rotational theory regarding expansion as previously studied.[27].

When analyzing the sagittal parallelism, the ratio between expansion at PNS in relation to expansion at ANS was found to be 95.7%, which is higher than the previously reported 90% indicating that the expansion achieved was highly parallel in the sagittal plane, despite the likely inter-digitation of the sutures.

As previously observed in two separate studies, transverse asymmetry following MSE expansion was present both in the skeletal structure, as well as in the soft tissue of the face.[7,14] Asymmetries of the face both prior to treatment, and after treatment are well researched, and with the advent of CBCT imaging, it has become significantly more accurate and reproducible. Previously, Lateral cephalograms provided restricted information, as structures on the right and left sides are overlapped, while panoramic radiographs revealed skeletal as well as dental structures of the maxilla and mandible in order to assess the right and left sides, allowing potential asymmetries to be examined. However, these imaging modalities present with shortcomings, such as image magnification and overlapping structures which obstruct evaluation of facial asymmetry.[19]

When analyzing transverse asymmetries due to expansion, the variation between symmetric and asymmetric patients can skew the data towards one way or another when averaged. Another potential bias is that within the asymmetric group, some expand to the right while some to the left, this creates the possibility of false numbers and identification of asymmetry due to the averaging out of all samples. Therefore, subgrouping was performed using the standard deviation of ANS deviation as a threshold. When calculating ANS deviation, the absolute value of Greater - Lesser ANS was used to negate any bias resulting from whether each suture expanded more to the right or to the left. When analyzing the entire sample of 31 patients, ANS mean deviation was 1.37 ± 1.10 mm, while PNS deviation was 1.16 ± 1 mm. This measurement indicates the amount by which one side of the ANS expanded more than the other, and these results support previous studies. (Table II) However, after the subgrouping was done as shown in Figure 5, only 15 patients were deemed symmetric based on having an ANS deviation of less than 1.1 mm, while the remaining 16 were considered asymmetric, giving a percentage of asymmetry of about 50%. Within each group, the right and left denominations were erased and replaced by “Greater” and “Lesser” giving two values for each landmark, irrelevant of its location. T-tests were used to validate the subgrouping where in the symmetric group, there was no statistical significance between greater and lesser values for ANS, PNS, or ZMA, while in the asymmetric group, p value was less than 0.01.

Within the asymmetric group of 16 patients, the values of asymmetry increased significantly when compared to total size comparisons. The amount of asymmetry was highest at ANS, followed by PNS then ZMA. However, to accurately compare the three, we calculated the Deviation % relative to the magnitude of total expansion for each landmark, and the percentages were almost equal indicating that when there is significant asymmetry, it is equal across all three landmarks. This finding eliminates the idea that asymmetry occurs only at the dentoalveolar portion and indicates that it is a true mid-facial expansion asymmetry. The magnitude of asymmetry at ANS of 2.22 mm is almost double of what was previously discovered when assessing the sample as a whole, including truly symmetrically expanded patients. While in this study, among the total population (n=31), the average magnitude of asymmetry was 1.37 mm, and the range extended from 0.04 mm to 4.4 mm of ANS deviation from one side to the other. As such, clinical significance can vary greatly depending on the actual magnitude of asymmetrical expansion.

While asymmetry of expansion was not assessed frequently in the literature, another study looking at asymmetry in patients undergoing surgically assisted bone-borne expansion(i.e., SARPE) showed asymmetry of more than 3 mm in at least 55% of the patients, this indicates a similar frequency of asymmetry, but a greater magnitude than what is exhibited using MSE. This difference in magnitude could be attributed to the larger magnitude of total asymmetry usually performed using the surgical technique, a study comparing percentages could be conducted for a more accurate comparison, rather than linear measurements.

All previous studies regarding asymmetry of expansion have not attempted to evaluate any possible predicting factors that could equip clinicians with the ability to predict which side would expand more compared to the other, or whether there will be any asymmetry at all. Correlation analysis was performed on both the re-organized sample of Greater - Lesser (ANS Deviation), as well as Right - Left (ANS Asymmetry) in order to evaluate whether our hypothesized predicting factors play a role in either the direction, or amount of resultant asymmetry.

Initial asymmetry of the mid-face was included as a possible predicting factor as previous literature shows that while many human body parts undergo development with bilateral symmetry, asymmetry occurs frequently due to both biologic factors during development, as well as environmental disturbances. Perfect bilateral symmetry is rarely found.[36] The face often presents with a mild degree of asymmetry, with an underlying skeletal asymmetry of the mid-face, this is due to the fact that the mid-face as well as the lower face develop from both the medial and lateral nasal, the maxillary process, and the mandibular processes, and despite being intrinsically coordinated, failure of development, or change in growth velocity might lead to varying degrees of asymmetry. [19,37,38] This inherent asymmetry was assumed to play a role in the direction, and magnitude of the resulting asymmetry of expansion, and therefore was used as a possible predicting factor. The results show complete lack of correlation when it comes to ANS Deviation with FZ, ZM, and Alv Deviation. This indicates that the magnitude of the initial asymmetry does not affect the magnitude of asymmetry resulting from MSE expansion. Interestingly, when evaluating the direction of asymmetry instead of the magnitude, ANS Asymmetry was significantly inversely correlated with FZ Asymmetry. This shows that when the frontozygomatic suture is closer to the MSP on one side (i.e., FZ is smaller), the same side tends to expand more than the contralateral side. This could be attributed to the fact that the center of rotation of MSE expansion is close to the FZ point[27], and the rotational movement might be the reason expansion is enhanced on the side where the rotational fulcrum is closer to the suture. However, further studies exploring the exact rotational movement in 3D to also include the FZ level in the vertical dimension, as well as the initial asymmetry of the entire skull in 3D is required to validate this assumption. Another reason this correlation may not be very clinically relevant is that the scatterplot shows high inconsistency, especially when the magnitude of FZ deviation is low (-1 to 1 mm), and the correlation coefficient r is not bigger than 0.5.

Hounsfield Units (HU) are used in the medical field as a quantitative scale for describing radiodensity; HU can be accurately displayed on a medical CT allowing for easy measurements of tissue density, which has been used to great extent in the dental field for assessment of bone density prior to implant placement.[39] However, with Cone Beam Computed Tomography (CBCT), we are unable to show the actual HU as the degree of x-ray attenuation is shown by gray scale (voxel value) as opposed to medical CT where HU reflect the attenuation coefficients per voxel to reflect the true tissue density.[40] A major challenge in utilizing CBCT scans to measure density using grayscale values is the fact that they are not calibrated, the grayscale values are in fact arbitrary. One study showed the tissue density (based on grayscale value) on two CBCT scans, even on the same patient, cannot be compared directly.[41] Recent studies have shown that grayscale values obtained from CBCT can be correlated to HU values from CT, utilizing liner attenuation coefficients as an intermediate step to extrapolate the actual HU values, indicating that they can be used to determine density in lower radiation CBCT's routinely used in dental practice. Grayscale is still less accurate due to higher noise levels, more scattered radiation, and beam hardening artifacts. [42,43] Despite the pitfalls of measuring density on CBCT scans, 3D imaging software with built-in linear coefficient could be used to compare the density of structures on different patients in the same sample. However, accuracy of density comparison is further improved when comparing multiple structures within the same CBCT scan of the same patient, since no calibration is required, and the coefficient multiplier will be equal across the entire scan.[35]

The zygomatic, maxillary, and palatine bone densities were selected as possible predicting factors as they play a main role in the resistance to expansion as previously discussed. When measuring the palatal bone in the coronal section, the section was moved to evaluate it at different levels where the measurements at the level of the second premolar and the first molar (i.e., P1MD and P2PD) represent the palatal process of the maxilla, while the palatal bone measurements at the second molar (i.e., P2MD) represents the actual palatine bone. The results showed no correlation between ANS Deviation and deviation in any of the factors as it relates to magnitude, except for P2MD Deviation which is the difference in palatine bone density at the level of the second molars. P2MD Deviation was positively correlated with ANS Deviation as seen in Table IV. This only indicates that as the difference in density between both sides increases, the magnitude of asymmetry of expansion is likely to increase. However, density measurements showed complete lack of correlation with ANS Asymmetry. (Table V) The evidence of mild correlation (r=0.4) at the level of second molars only can be attributed to P2MD being the most posterior point of the palatine bone evaluated, and it represents the actual palatine bone as opposed to the palatal process of the maxilla, and therefore it may play a bigger role in the resistance to asymmetry. However, since ANS Asymmetry was not correlated to P2MD Asymmetry, this inconsistency in findings alludes to the fact that this predicting variable will not be reliable enough to be used by clinicians, and further investigation is required.

The pattern of crossbite was also correlated with the pattern of asymmetry as shown in Figure 12, the results indicate a possible positive relationship where more expansion is likely to occur on the same side as the side of the crossbite in cases of unilateral crossbites, however, a larger sample of patients with unilateral crossbite is needed to validate such relationship. This association could be explained by the lack of function on the crossbite side leading to weaker bite force[44] and decreased muscle activity[45] which could decrease the resistance against expansion on the crossbite side. However, the non-crossbite group exhibited more asymmetry on the left side, which can be attributed to the smaller number of samples. The bilateral crossbite group showed an almost equal distribution of right and left dominant asymmetry subtypes, which does not go against the aforementioned hypothesis.

Due to the lack of strong correlation, the hypothesized predicting factors were not found to be reliable in predicting the direction, or magnitude of asymmetry. However, these findings can bring clinicians closer to finding an answer by eliminating some of the factors, as well as aiding future research.

Limitations:

The limitations of the first aim of our study include the need for subgrouping which reduces the sample size. Although the size remains within the required number based on power analysis, the clinical impact is weakened due to the subgrouping necessary to perform accurate analysis regarding the asymmetry of expansion. The subgrouping is also done based only on one landmark only (ANS), and that may weaken our results. Another limitation is that expansion is only evaluated using three anatomical landmarks, and while they are validated in previous studies, a more accurate analysis can be conducted using 3D mesh analysis utilizing the entire skull, and not only a few select landmarks. The main limitations of the second aim are that correlation studies require a larger sample size for high clinical relevance, and this study was done on only selected possible factors relying on certain landmarks which may narrow the scope of the analysis. While one variable alone may not be correlated, a multiple regression model should be created with a much larger sample size.

CONCLUSIONS

Micro-implant-assisted rapid palatal expanders such as the Maxillary Skeletal Expander (MSE) can be used to achieve skeletal expansion in non-growing patients with an average magnitude of 5 mm anteriorly, and 4.7 mm posteriorly. This expansion was greater anteriorly (ANS) and decreases as the measurements move posteriorly (PNS) or superiorly (ZMA), validating the center of rotation being near the frontozygomatic suture. The nature of expansion was highly parallel (95%) in the anteroposterior direction, however, it was not always symmetric in the transverse plane, with 51% of the patients exhibiting transverse asymmetry of at least 1.1 mm. The asymmetry was found to be equally distributed such that the percentage of asymmetry to the total expansion is almost equal at ANS, PNS, and ZMA.

When exploring possible factors that can influence the magnitude and direction of this transverse asymmetry, he magnitude of initial asymmetry of the mid-face does not appear to influence the magnitude of asymmetry of expansion using MSE. However, there is a mild association in the direction of initial asymmetry relating to the frontozygomatic suture; as the frontozygomatic suture is closer to the Mid-Sagittal Plane on one side, the same side tends to expand more than the contralateral side when MSE is utilized. When assessing the difference in density values between the bilateral sides of the zygomaticomaxillary complex, it showed no influence on the magnitude or direction of the asymmetry of expansion. The pattern of dental crossbite showed a favorable association in unilateral crossbite patients, where the crossbite side tends to expand more than the non-crossbite side.

Overall, MSE expansion showed successful highly parallel expansion in non-growing patients with varying degrees of transverse asymmetry, and only a few predicting factors showed potential correlation at predicting the pattern of asymmetry.

Recommendations for future studies:

- Evaluating initial asymmetry and difference in bone morphology using 3D morphometric analysis.
- Follow-up study with larger sample size including a multiple regression model to simultaneously analyze the effect of all predicting factors.
- Measuring the bite force and/or muscle strength in unilateral crossbite patients and correlating with the asymmetry to validate current findings.
- Conducting more in-depth analysis on how the frontozygomatic suture relates to asymmetry in all three dimensions.

Clinical relevance:

Due to the increased use of bone-borne maxillary expanders, it is critical to understand all facets of the effects induced by such expander. Clinicians must consider the potential asymmetry of expansion when using bone-borne expanders during the course of treatment. Although no predicting factor showed clear-cut correlation with the pattern of asymmetry, our findings bring clinicians and researchers closer to an answer; helping future research proceed in the right direction.

REFERENCES

1. Betts NJ, Vanarsdall RL, Barber HD, Higgins-Barber K, Fonseca RJ. Diagnosis and treatment of transverse maxillary deficiency. *Int J Adult Orthodon Orthognath Surg.* 1995;10(2):75-96.
2. Ramires T, Maia RA, Barone JR. Nasal cavity changes and the respiratory standard after maxillary expansion. *Braz J Otorhinolaryngol.* 2008;74(5):763-769.
3. HAAS AJ. THE TREATMENT OF MAXILLARY DEFICIENCY BY OPENING THE MIDPALATAL SUTURE. *Angle Orthod.* 1965;35:200-217.
4. Wertz R, Dreskin M. Midpalatal suture opening: a normative study. *Am J Orthod.* 1977;71(4):367-381.
5. Persson M, Thilander B. Palatal suture closure in man from 15 to 35 years of age. *Am J Orthod.* 1977;72(1):42-52.
6. Gurel HG, Memili B, Erkan M, Sukurica Y. Long-term effects of rapid maxillary expansion followed by fixed appliances. *Angle Orthod.* 2010;80(1):5-9.
7. Cantarella D, Dominguez-Mompell R, Mallya SM, et al. Changes in the midpalatal and pterygopalatine sutures induced by micro-implant-supported skeletal expander, analyzed with a novel 3D method based on CBCT imaging. *Prog Orthod.* 2017;18(1):34.
8. Ghoneima A, Abdel-Fattah E, Hartsfield J, El-Bedwehi A, Kamel A, Kula K. Effects of rapid maxillary expansion on the cranial and circummaxillary sutures. *Am J Orthod Dentofacial Orthop.* 2011;140(4):510-519.

9. Woller JL, Kim KB, Behrents RG, Buschang PH. An assessment of the maxilla after rapid maxillary expansion using cone beam computed tomography in growing children. *Dental Press J Orthod.* 2014;19(1):26-35.

10. Tausche E, Hansen L, Schneider M, Harzer W. [Bone-supported rapid maxillary expansion with an implant-borne Hyrax screw: the Dresden Distractor]. *Orthod Fr.* 2008;79(2):127-135.

11. Suzuki H, Moon W, Previdente LH, Suzuki SS, Garcez AS, Consolaro A. Miniscrew-assisted rapid palatal expander (MARPE): the quest for pure orthopedic movement. *Dental Press J Orthod.* 2016;21(4):17-23.

12. Lin L, Ahn HW, Kim SJ, Moon SC, Kim SH, Nelson G. Tooth-borne vs bone-borne rapid maxillary expanders in late adolescence. *Angle Orthod.* 2015;85(2):253-262.

13. Cantarella D, Dominguez-Mompell R, Moschik C, et al. Zygomaticomaxillary modifications in the horizontal plane induced by micro-implant-supported skeletal expander, analyzed with CBCT images. *Prog Orthod.* 2018;19(1):41.

14. Abedini S, Elkenawy I, Kim E, Moon W. Three-dimensional soft tissue analysis of the face following micro-implant-supported maxillary skeletal expansion. *Prog Orthod.* 2018;19(1):46.

15. Spillane LM, McNamara JA, Jr. Maxillary adaptation to expansion in the mixed dentition. *Semin Orthod.* 1995;1(3):176-187.

16. Huizinga MP, Meulstee JW, Dijkstra PU, Schepers RH, Jansma J. Bone-borne surgically assisted rapid maxillary expansion: A retrospective three-dimensional evaluation of the asymmetry in expansion. *J Craniomaxillofac Surg.* 2018;46(8):1329-1335.

17. Weissheimer A, Menezes LM, Koerich L, Pham J, Cevidanes LH. Fast three-dimensional superimposition of cone beam computed tomography for orthopaedics and orthognathic surgery evaluation. *Int J Oral Maxillofac Surg.* 2015;44(9):1188-1196.

18. Anison J. J RL, Ragavendra B. Understanding Asymmetry - A Review. *Biomed Pharmacol J.* 2015;October Spl Edition.

19. Thiesen G, Gribel BF, Freitas MP. Facial asymmetry: a current review. *Dental Press J Orthod.* 2015;20(6):110-125.

20. MacGinnis M, Chu H, Youssef G, Wu KW, Machado AW, Moon W. The effects of micro-implant assisted rapid palatal expansion (MARPE) on the nasomaxillary complex--a finite element method (FEM) analysis. *Prog Orthod.* 2014;15:52.

21. Suri L, Taneja P. Surgically assisted rapid palatal expansion: a literature review. *Am J Orthod Dentofacial Orthop.* 2008;133(2):290-302.

22. Netherway DJ, Abbott AH, Gulamhuseinwala N, et al. Three-dimensional computed tomography cephalometry of plagiocephaly: asymmetry and shape analysis. *Cleft Palate Craniofac J.* 2006;43(2):201-210.

23. Andrews LF. The 6-elements orthodontic philosophy: Treatment goals, classification, and rules for treating. *Am J Orthod Dentofacial Orthop.* 2015;148(6):883-887.

24. Krüsi M, Eliades T, Papageorgiou SN. Are there benefits from using bone-borne maxillary expansion instead of tooth-borne maxillary expansion? A systematic review with meta-analysis. *Prog Orthod.* 2019;20(1):9.

25. Cevidanes LH, Bailey LJ, Tucker GR, Jr., et al. Superimposition of 3D cone-beam CT models of orthognathic surgery patients. *Dentomaxillofac Radiol.* 2005;34(6):369-375.

26. An S, Lee JY, Chung CJ, Kim KH. Comparison of different midsagittal plane configurations for evaluating craniofacial asymmetry by expert preference. *Am J Orthod Dentofacial Orthop.* 2017;152(6):788-797.

27. Cantarella D, Dominguez-Mompell R, Moschik C, et al. Midfacial changes in the coronal plane induced by microimplant-supported skeletal expander, studied with cone-beam computed tomography images. *Am J Orthod Dentofacial Orthop.* 2018;154(3):337-345.

28. Agostino P, Ugolini A, Signori A, Silvestrini-Biavati A, Harrison JE, Riley P. Orthodontic treatment for posterior crossbites. *Cochrane Database Syst Rev.* 2014(8):CD000979.

29. Almeida RR, Almeida MR, Oltramari-Navarro PV, Conti AC, Navarro ReL, Marques HV. Posterior crossbite--treatment and stability. *J Appl Oral Sci.* 2012;20(2):286-294.

30. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods.* 2007;39(2):175-191.

31. Shapiro SS, Wilk MB. An Analysis of Variance Test for Normality (Complete Samples). *Biometrika.* 1965;52(3/4):591-611.

32. Handelman CS, Wang L, BeGole EA, Haas AJ. Nonsurgical rapid maxillary expansion in adults: report on 47 cases using the Haas expander. *Angle Orthod.* 2000;70(2):129-144.

33. Franchi L, Baccetti T, McNamara JA, Jr. Mandibular growth as related to cervical vertebral maturation and body height. *Am J Orthod Dentofacial Orthop.* 2000;118(3):335-340.

34. Baccetti T, Franchi L, McNamara JA, Jr. An improved version of the cervical vertebral maturation (CVM) method for the assessment of mandibular growth. *Angle Orthod.* 2002;72(4):316-323.

35. Grunheid T, Larson CE, Larson BE. Midpalatal suture density ratio: A novel predictor of skeletal response to rapid maxillary expansion. *Am J Orthod Dentofacial Orthop.* 2017;151(2):267-276.

36. Lindauer SJ. Asymmetries: diagnosis and treatment. *Semin Orthod.* 1998;4(3):133.

37. Haraguchi S, Iguchi Y, Takada K. Asymmetry of the face in orthodontic patients. *Angle Orthod.* 2008;78(3):421-426.

38. Cheong YW, Lo LJ. Facial asymmetry: etiology, evaluation, and management. *Chang Gung Med J.* 2011;34(4):341-351.

39. Norton MR, Gamble C. Bone classification: an objective scale of bone density using the computerized tomography scan. *Clin Oral Implants Res.* 2001;12(1):79-84.

40. Valiyaparambil JV, Yamany I, Ortiz D, et al. Bone quality evaluation: comparison of cone beam computed tomography and subjective surgical assessment. *Int J Oral Maxillofac Implants.* 2012;27(5):1271-1277.

41. Katsumata A, Hirukawa A, Okumura S, et al. Relationship between density variability and imaging volume size in cone-beam computerized tomographic scanning of the maxillofacial region: an in vitro study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;107(3):420-425.

42. Razi T, Niknami M, Alavi Ghazani F. Relationship between Hounsfield Unit in CT Scan and Gray Scale in CBCT. *J Dent Res Dent Clin Dent Prospects.* 2014;8(2):107-110.

43. Mah P, Reeves TE, McDavid WD. Deriving Hounsfield units using grey levels in cone beam computed tomography. *Dentomaxillofac Radiol.* 2010;39(6):323-335.

44. Sonnesen L, Bakke M, Solow B. Bite force in pre-orthodontic children with unilateral crossbite. *Eur J Orthod.* 2001;23(6):741-749.

45. Alarcon JA, Martin C, Palma JC. Effect of unilateral posterior crossbite on the electromyographic activity of human masticatory muscles. *Am J Orthod Dentofacial Orthop.* 2000;118(3):328-334.