Clinical Oral Investigations (2021) 25:1775–1785
https://doi.org/10.1007/s00784-020-03480-5

ORIGINAL ARTICLE

Evaluation of mandibular changes after rapid maxillary expansion: a CBCT study in youngsters with unilateral posterior crossbite using a surface-to-surface matching technique

Rosalia Maria Leonardi [1] · Khaled Aboulazm [2] · Antonino Lo Giudice [1] · Vincenzo Ronsivalle [1] · Vincenzo D'Antò [3] · Manuel Lagravère [4] · Gaetano Isola [1]

Received: 8 May 2020 / Accepted: 27 July 2020 / Published online: 2 August 2020

Abstract

Objectives The purpose of this study was to evaluate mandibular asymmetry in youngsters with posterior unilateral crossbite (PUXB), through cone-beam computed tomography and reverse engineering technique, before and after rapid maxillary expansion (RME) treatment.

Materials and methods Forty cone-beam computed tomography (CBCT) images were obtained from all patients at two time points, namely T0 acquired before the placement of a Hyrax expander and T1 after appliance removal. The CBCT scans were segmented and volume rendered into a surface there-dimensional (3D) mesh model. Thereafter, mandibular models were digitally registered by using a "best-fit" algorithm. Surface and volumetric changes, between T0 and T1, were compared by using Student's *t* tests.

Results A slight increase of 0.45 cm^3 of the total mandibular volume was found at T1 when compared with T0 ($p < 0.001$). The mandibular hemi-volume on the crossbite side (CB) was slightly smaller than the non-crossbite side both at T0 and T1. However, the mean differences of hemi-volume from the CB (crossbite) and non-CB side between T0 and T1 show a decrease of 0.26 cm^3 ($p < 0.001$). Findings for the surface-to-surface deviation analysis demonstrated a fine percentage of matching at T0 which slightly improved at T1 ($p < 0.001$).

Conclusions Youngsters affected by PUXB showed a very slight and not statistically significant volumetric and morphological asymmetry between CB side and non-CB side at T0. However, the change in mean differences of 0.26 cm cannot be considered clinically relevant.

Clinical relevance Mandibles in young PUXB patients exhibit only a very mild mandibular asymmetry. Although the statistically significant mean change found right after RME removal cannot be considered clinically relevant, a more consistent sample and a longer follow-up could be of interest in explaining the short-term findings.

Keywords RME · Crossbite · Facial asymmetry · CBCT · Orthodontics

✉ Rosalia Maria Leonardi
rleonard@unict.it

[1] Department of Orthodontics, School of Dentistry, Policlinico Universitario "Vittorio Emanuele", University of Catania, Catania, Italy

[2] Department of Orthodontics, School of Dentistry, Pharos University, Alexandria, Egypt

[3] Department of Neuroscience, Reproductive Science and Dentistry, University of Naples Federico II, Naples, Italy

[4] Department of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada

Introduction

Posterior crossbite is characterized by the presence of one or more upper teeth of the posterior group occluding lingually to the buccal cusps of the corresponding mandibular teeth [1, 2]. Posterior unilateral crossbite (PUXB) is the most common form of posterior crossbite, with a prevalence reported from 8.7 to 23% among malocclusions [3–5]. It can be defined as either a functional posterior crossbite or a true unilateral posterior crossbite. In youngsters with PUXB, the mild bilateral constriction of the maxillary arch creates occlusal interferences that leads to a functional shift of the mandible toward the crossbite side from the centric to intercuspidal position [6, 7]. This displacement is usually in a transverse and antero-posterior direction. The displacement is corrected at maximum aperture and normally disappears when the crossbite is corrected [8].

It has been postulated by some authors that PUXB, if left untreated, could lead to skeletal asymmetry of the mandible due to the persistence of an asymmetrical position of the condyles with respect to the glenoid fossa [8]. In fact, it is believed that this mandibular functional deviation, together with an asymmetric masticatory muscle activity may induce remodeling of mandibular bone resulting in an asymmetry being the crossbite (CB) side smaller than the non-crossbite side [9]. However, any existing relationship between PUXB and mandibular morphology is still controversial, and no definitive conclusion has been reached [10–12]. This may be due to the methods used to assess the skeletal asymmetry which were mainly based on two-dimensional (2D) radiographs [10, 11, 13–17] and to the lack of follow-up studies.

The advent of cone-beam computed tomography (CBCT) has added the third dimension and has allowed to overcome 2D radiograph limitations [18]. Accordingly, some studies have used CBCT to assess mandibular dimensions in young patients affected by PUXB [9, 19–21]. However, findings from these investigations were based exclusively on linear and/or angular 2D measurements of condyle, ramus, and mandibular body, which were carried out on 3D images or 3D models. This measurement approach, however, can underestimate the real dimension of any curved surface, the chord of a surface being measured rather than the real contour of the bone. Only one study [9] assessed mandibular asymmetry in youngster PUXB patients, using a volumetric evaluation of hemi-mandibular dimensions, while, in the same investigation, 2D surface measurements of linear distances were still carried out. These were all observation studies of untreated subjects. The only study [22] that has examined PUBX mandibular asymmetries before and after rapid maxillary expansion (RME) was still based on angular and linear cephalometric measurement. This study [22], however, was still based on angular and linear measurements between cephalometric points.

Nowadays, with progress in radiographic techniques and the use of sophisticated reverse engineering software, 3D bone structures obtained from CBCT scans can be mirrored and then superimposed or just superimposed without mirroring. The purpose is to evaluate growth/treatment changes through the Euclidean distance measurements between surfaces of the two 3D models. A 3D color map of the changes in different colors can also be viewed with some specific software.

Accordingly, the aims of this study were to evaluate and compare in youngsters the following: (1) mandibular and hemi-mandibular volumes from the CB and non-CB sides in the same patient before (T0) and after (T1) therapy with RME and (2) mandibular surface matching percentage of CBCT 3D models at T0 and at T1 (inter- and intra-time comparisons) in order to assess the effects of RME on the mandible.

Materials and methods

In order to avoid radiation exposure and in accordance with the “as-low-as-reasonably achievable” (ALARA) principle [23], this study was conducted using CBCT data set from previous published materials [24–26] of patients who required maxillary expansion as part of their comprehensive orthodontic treatment. The study followed the Helsinki Declaration on medical protocols. Ethical approval was obtained from the Institutional Review Board of Indiana University-Purdue University (IRB protocol number: 1708606623).

The sample consisted of 20 subjects (10 boys, 10 girls) with a mean age of 13.8 ± 1.1 years and C4 skeletal maturation stage determined according to the cervical vertebral maturation method (CVM), at T0. The inclusion criteria were the following: PUXB malocclusion involving at least two posterior teeth, mandibular shift with the lower midline deviation to the crossbite side 2 ≤ and ≤ 3 mm [22], availability of complete initial (T0), and final records following RME treatment (T1) including good quality CBCT scans with a large field of view (FOV), photographs, dental casts, medical history of each patient, and good general health. The exclusion criteria were presence of dento-facial deformities and/or facial asymmetry (based on clinician’s facial examination/perception and confirmed by CBCT), medical history of a previous orthodontic treatment, maxillofacial surgery, or facial trauma; TMJ disease; impacted/unerupted mandibular tooth/teeth (except the third molar); anterior crossbite; poor quality CBCT scans; or missing records.

The appliance used was a tooth-borne hyrax expansion appliance with bands on the permanent first molars and first premolars. The appliance was activated by the parent, and the patients were checked regularly during active expansion. The regime used was a quarter turn (0.25 mm) twice a day until the palatal cusp of the upper molars was touching the buccal cusp. That is, the appliance was activated until the palatal cusps of maxillary first molars were in contact with the buccal cusps of mandibular first molars. After active expansion treatment, the appliance was kept in place passively for 6 months. During this period, no other orthodontic treatment was done on all patients.

All the CBCT images were acquired with I-CAT machine (120 kVp, 23.87 mAS, 8.9 s exposure time, large field of view (FOV), 0.3 mm voxel size) with the patient in maximum intercuspation and Frankfort horizontal plane parallel to the floor following common CBCT imaging protocols [27]. CBCT scans were performed before (T0) and after treatment (T1), immediately after appliance removal (mean interval, 6.7 months ± 0.8). The DICOM slice data were converted into 3D volumetric images using Mimics Research software (vr. 19.0.0.347, Materialize NV, Liege, Belgium) and installed on a personal computer (Lenovo IdeaPad L340 Gaming, Intel Core i7-9750H processor, 15.6 in. monitor) for further analysis of data.

The protocols used in this study for segmentation, model rendering, and deviation analysis (Fig. 1) were previously validated and clearly described [28–30].

Step 1. Generating the segmentation mask The first step was performed to develop the segmentation mask (Fig. 2a–c). The "automatic threshold" function of the Mimics Research software was set to "compact bone" and each scan was adjusted to automatically detect the voxel density values and boundaries of the mandibular bone. Afterwards, in order to improve the quality and precision of the mandible segmentation, the mask was cropped by using the "Split Mask" function and the excess parts of the segmentation mask outside the mandibular bone's boundaries were removed. Then, the inner part of the mandible was filled.

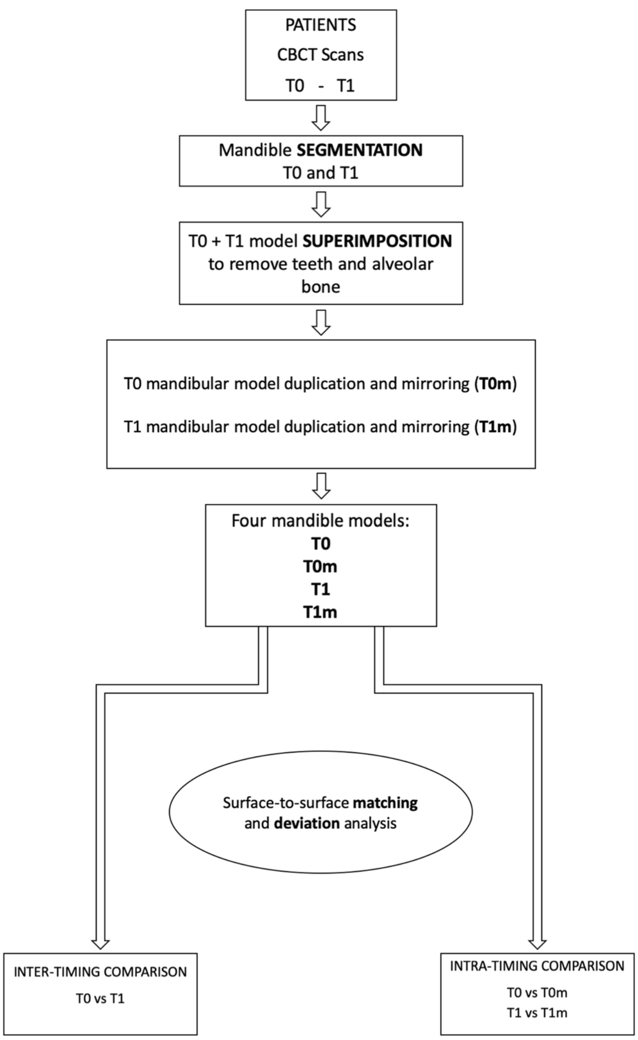

Fig. 1 Workflow of the study. T0, before treatment; T1, after rapid maxillary expansion (RME) therapy; T0m and T1m, mandibular model duplication and mirroring to obtain a specular copy of the model at T0 and T1. Surface-to-surface matching of the models for the inter- and the intra-timing comparisons

Step 2. 3D model rendering The mandibular segmentation mask was rendered into a 3D surface model (.stl) with Mimics (Fig. 2d). To improve quality and contour delineation, the mask was smoothed and finely adjusted by using the interactive "Contour Edit" function.

Step 3. 3D model rendering In order to evaluate only mandibular bone and exclude teeth and alveolar ridges from the deviation analysis, these models were imported onto 3-matic research software (vr. 11.0.0.109, Materialize NV, Liege, Belgium). To achieve this objective, the mandibles were superimposed and then the teeth and alveolar ridges were removed according to the following described procedure.

At first, a point-based superimposition was made by selecting the same four points on the surfaces of each mandible [31]. Namely, the points selected on the mandible were the apical tip of the right (point 1) and left (point 2) of mandibular lingula around the mandibular foramen and the geometric center of the right (point 3) and left (point 4) mental foramina (Fig. 3).

Once T0 and T1 mandible for each patient were superimposed, two cutting plans were drawn, as follows:

1. A plane passing through the lowest alveolar ridge of mandibular teeth (LARM) and parallel to an arbitrary mandibular occlusal plane (passing through the distobuccal cusp tips of the right and left mandibular first molars to the lower midline at most occlusal level) (Fig. 4a, b).
2. A plane tangent to the arbitrary mandibular occlusal plane and going through the most distal point of the equator of the second molar (ESM) (Fig. 4a, b).

Then teeth and alveolar ridge were cropped from superimposed mandibles (Fig. 4c, d), so at last two mandibular basal bones of each patient at T0 and T1, which were cut at the same level, were obtained.

Each mandible, for each patient, at each time (T0 and T1) was duplicated, after that, the duplicated mandibular models were mirrored by using the mandibular symphysis plane (MSP) as a reflecting plane (in order to change the image orientation from right-to-left to left-to-right). This plane passed through the mandibular symphysis, and it was drawn through the following three reliable landmarks, specifically: menton, genial tubercle, and supramental points as previously described [31–33] (Fig. 5).

Thus, for every patient, four 3D models of the mandible were available, namely: T0 before RME therapy, T0m the same mandible mirrored, T1 after RME therapy, and T1m the same mandible mirrored. These models were used respectively for the intra-timing comparison (T0 versus T0m and T1

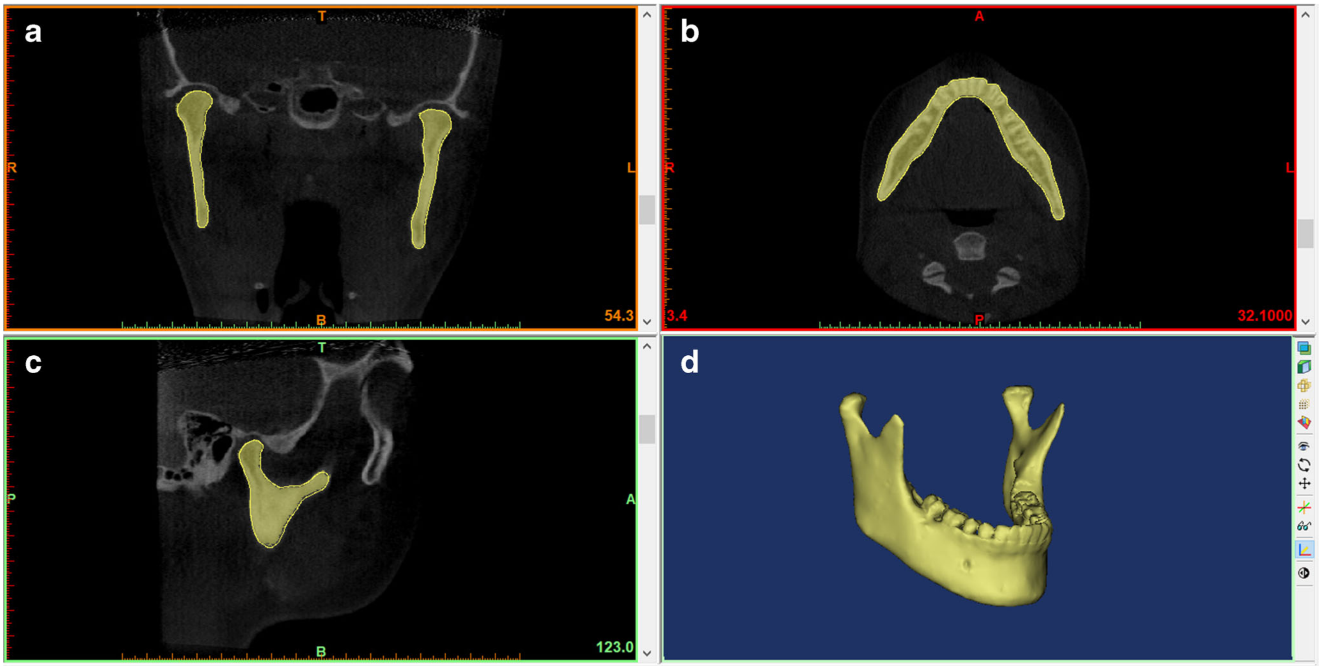

Fig. 2 Generation of the segmentation mask of the mandible by using the automatic threshold function of mimics and outline of the mandible boundaries. **a** Coronal view; **b** axial view; **c** sagittal view. **d** Rendering of the 3D mandible model

versus T1m), and for the inter-timing comparison (T0 versus T1), in order to establish the degree of matching before therapy and compare it thereafter, to evaluate any change before and after maxillary expansion (Fig. 1).

Step 4. Final registration, surface-based These four models were imported in the Geomagic Control X software (3D Systems, version 2018.1.1, 3D Systems, USA), in order to carry out the surface deviation analysis, which served to: (a) evaluate changes on mandibular surface morphology determined by RME therapy, and where it has occurred, by superimposing the mandible of each patient at T0 (before) to T1 (after RME therapy) for the inter-timing comparison (Fig. 6); (b) compare each mandible at T0 and T1 (intra-timing comparison), by matching each other T0 versus T0m and T1 versus T1m, in order to assess any difference in mandibular surface morphology before and after RME (Fig. 7).

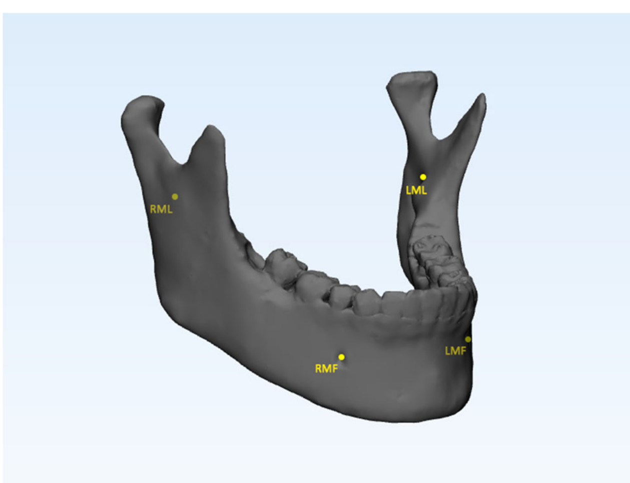

Fig. 3 Landmarking four points on 3D mandibular model superimposition. RML, right mandibular lingual; LML, left mandibular lingual; RMF, right mandibular foramen; LMF, left mandibular foramen

Step 5. 3D Deviation analysis After superimposition, surface-based deviation analysis was carried out using the specific function in the Geomagic Control X software, which automatically calculates the average linear differences between the two STL files (Euclidean distance), i.e., the two superimposed 3D mandibular models, based on data from all points of the surface shells of the two models. These values were measured across 100% of the surface points and represented on a color map of the mandibular model which showed deviation in different colors. To better evaluate and locate any skeletal mandibular asymmetry, the three ranges of tolerance (A, B, and C) were set respectively to 0.4, 0.6, or 0.8 mm. When the distance values were greater than the positive limits of the ranges of tolerance, they were represented in red while values smaller than the negative limits were represented in blue. Instead, all the values included in the tolerance range were represented in green.

Step 6. Matching percentage calculation Once the deviation analysis was carried out, the percentages (%) of all the distance values within the tolerance ranges were calculated for the three ranges of tolerance. These values represented the degree of matching and symmetry between the pairs of

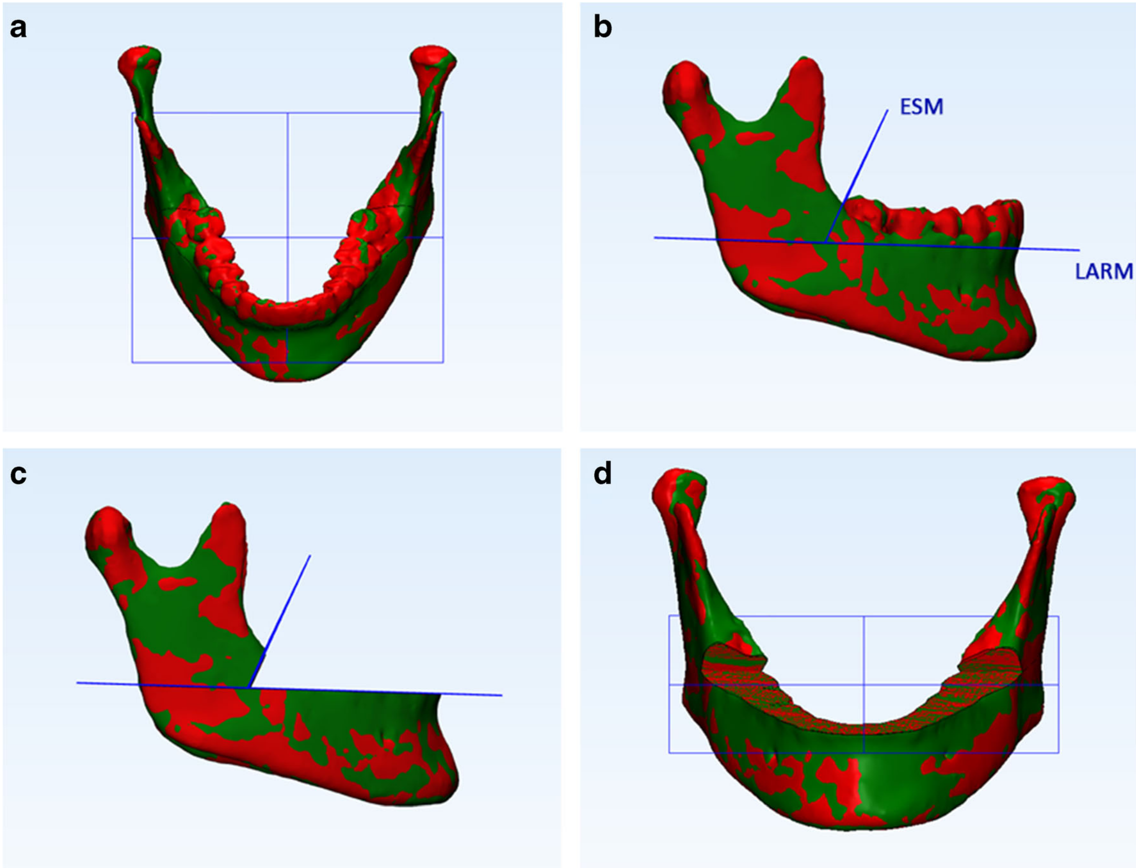

Fig. 4 3D mandibular models of each patients are superimposed in order to remove alveolar processes and teeth. LARM, a plane passing through the lowest alveolar ridge of the mandibular teeth; ESM, a plane perpendicular to LARM and passing distally through the equator of the second mandibular molar

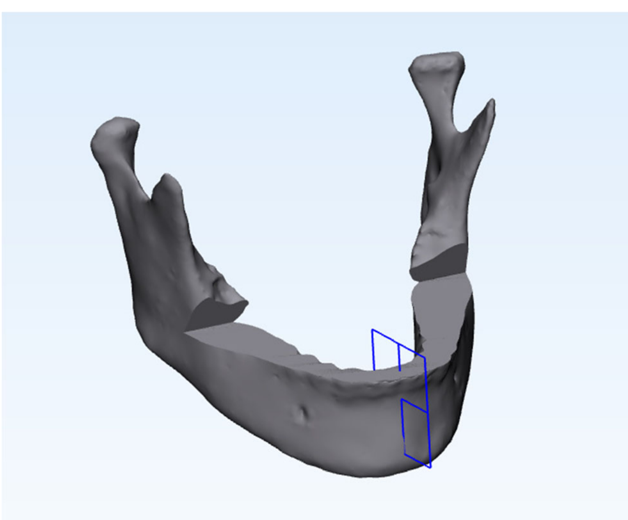

Fig. 5 Construction of the MSP plane passing through Me, Gt, and B points and splitting the mandible in two halves in order to evaluate the hemi-volumes. Me (mention), the most inferior midpoint on the mandibular symphysis; Gt (genial tubercle), the center of the four GTs of the mandible; B (supramental), the most concave midpoint on the mandibular symphysis

mandibular 3D models. The higher was the value, the better was the symmetry.

Total volume and hemi-mandibular were also calculated. To obtain the hemi-mandibular volumes, the 3D mandibular models were separated into two sides as previously described [9]. Briefly, the same plane used in step 2 as reference for the mirroring of the mandible (Fig. 5) was used as cutting plane to separate the mandibular 3D model and to obtain the hemi-volume measurements.

We considered two main outcomes of the study: the mean difference of hemi-volume at the beginning of treatment (T0), crossbite side versus non-crossbite side, and the percentage of matching at 0.6 mm of tolerance level.

All the digital measurements were performed by a single examiner, with 25 years of orthodontic research experience on CT scans of cranio-facial bones (R.L.). The examiner processed only three CBCT scans each day to avoid fatigue. The CBCT images were randomly examined. Twenty CBCT exams were randomly selected, and the entire work-flow including segmentation and relative mask generation was repeated twice by the same operator 6 weeks apart for the intra-observer and random error calculation.

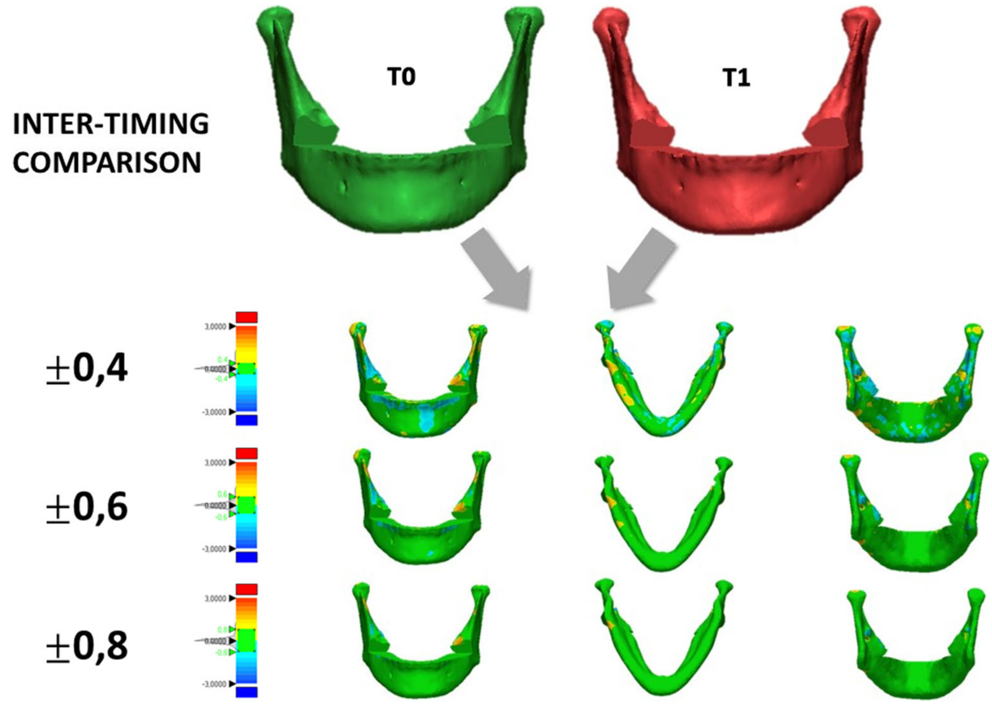

Fig. 6 Inter-timing comparison. Superimposed mandible (T0–T1) and representation of linear distances between the surfaces of the two mandibles on color maps. The green of the color scale bar, on the right represents the range of tolerance. **a** Color map set to a range of tolerance of ± 0.4 mm; **b** color map set to a range of tolerance of ± 0.6 mm; **c** color map set to a range of tolerance of ± 8 mm

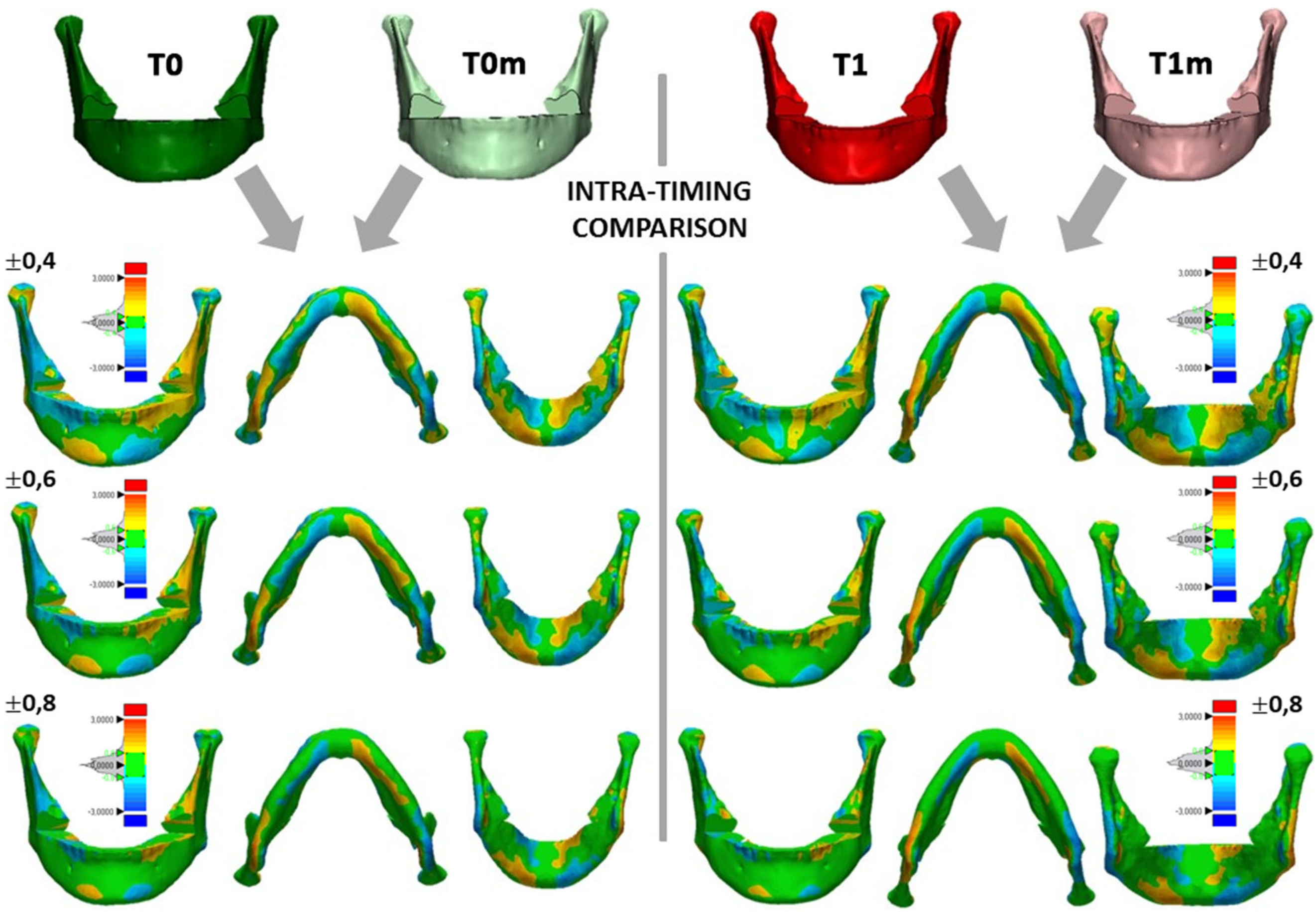

Fig. 7 Intra-timing comparison. Superimposed mandible (T0–T0m and T1–T1m) and representation of linear distances between the surfaces of the two mandibles on color maps. The green of the color scale bar, on the right represents the range of tolerance. **a** Color map set to a range of tolerance of ± 0.4 mm; **b** color map set to a range of tolerance of ± 0.6 mm; **c** color map set to a range of tolerance of ± 8 mm

Statistical analysis

All the measurements were recorded on Microsoft Excel spreadsheet (Microsoft, Redmond, WA, USA) and analyzed using SPSS version 24 Statistics software (IBM Corporation, 1 New Orchard Road, Armonk, New York, USA) with p-values of less than 0.05 considered statistically significant. A preliminary power analysis was performed using pre-treatment and post-treatment data, the analysis suggested that 16 patients were required to detect a mean change of 1.17 cm^3 of the volumetric differences between CB and non-CB side at T0 to T1, with 80% power, a confidence level of 95% and a beta error level of 20%. However, according to the inclusion criteria, we were able to include 20 subjects which increased the robustness of the data. The Kolmogorov–Smirnov test was used to test the normality of the data. Since data were normally distributed, parametric tests were used to evaluate potentially significant differences between the measurements taken at T0 and T1.

The Student's paired t test was used to assess the inter-timing difference of mandibular total volumes (T0–T1), the inter-timing difference (T0–T1) of intra-timing volumetric difference between the CB and non-CB sides at T0 and T1, and the inter-timing difference of matching percentage between the original and mirrored mandibular shells at T0 and T1, at three different levels of tolerance (i.e., 0.4, 0.6, and 0.8 mm). Independent Student's t test was also performed to assess differences between the hemi-mandibular volumes at T0 and T1.

Multiple regression analysis was performed to investigate the effect of predictor variables (age and gender) on the main outcomes investigated, i.e., the mean difference of total mandibular volume between T0 and T1 and the inter-timing mean difference of the CB/non-CB volumetric differences recorded at T0 and T1.

To assess the intra-observer reliability of the mandibular volumetric measurements (volumetric differences between T0 and T1), the intra-class correlation coefficient was used (ICC). The magnitude of the random error was assessed using the Dahlberg formula [34].

Results

All volumetric measurements were highly reliable with correlation values of 0.958 for inter-timing total volume differences and 0.881 for inter-timing difference of intra-timing volumetric difference between the CB and non-CB sides. The random error was 0.003 and 0.019 cm^3 for the same outcomes. Means, standard deviations, and comparisons of mandibular volumetric and matching measurements between T0 and T1 are given in Tables 1 and 2.

The mandibular volume was smaller at T0 (mean value, 47.90 ± 6.57 cm^3) than T1 (mean value, 48.35 ± 6.65 cm^3) with a difference of 0.45 cm^3 that was statistically significant ($p \leq 0.001$) (Table 1).

The CB side was found to be smaller than the non-CB sides, with a mean difference of 1.29 cm^3 at T0 and 1.03 cm^3 at T1; however, these differences were not statistically significant ($p > 0.05$) (Table 1).

Comparing the CB and non-CB side hemi-volume differences recorded at T0 and T1 (intra-timing difference) shows a mean difference of 0.26 cm^3, which was statistically significant ($p < 0.001$) (Table 1).

Table 2 shows results of the surface-to-surface deviation analysis for the inter-timing (Fig. 6) and intra-timing (Fig. 7) comparisons at the three different tolerance levels both for the intra- and inter-timing comparisons.

Matching percentages between the mandibular models before (T0) and after RME (T1) at the three levels of tolerance selected for this study showed a nearly fair agreement at a tolerance level of 0.8 mm being the matching percentage of 96.70% between T0 and T1. While a small higher mismatch (87.75%) was recorded for a range of tolerance of 0.4 mm (Fig. 6).

Results of the intra-timing comparison (T0 versus T0m and T1 versus T1m) showed a slight degree of mismatching of mandibular shells both at T0 and T1, in agreement with the differences between the mandibular hemi-volumes (CB versus non-CB sides). However, matching percentage values set at the three levels of tolerance were slightly higher at T1, reaching an 86.66% of matching for the tolerance range of ± 0.8 mm level (Fig. 7).

Additionally, the three-dimensional color maps provided by the surface-to-surface analysis both for the inter-timing (Fig. 6) and intra-timing (Fig. 7) highlighted that the mandibular areas expressing greater mismatches was localized at the condyle and at the ramus.

Significant correlation was found between the main two variables, i.e., the inter-timing mean difference of total mandibular volume between T0 and T1 and the inter-timing mean difference of the CB/non-CB volumetric differences recorded at T0 and T1 (intra-timing difference) and potential predictor variables such as age and gender, according to the linear regression models performed. The R-squared value, which reflects the percentage of variability in each dependent variable attributed to the changes of the predictor (age and/or gender), was significant only for gender and not for age (Table 3).

Discussion

Previous evidences [35–40] suggested an asymmetrical muscle activity of masticatory muscles and differences in condyle position within the fossa between the CB side and non-CB side in PUXB patients. Accordingly, it was speculated that the asymmetrical muscle activity is transferred to the mandibular

Table 1 Comparison of mandibular volumetric measurements before rapid maxillary expansion (T0) and after rapid maxillary expansion (T1)

Study group	Total	Mean total volume (cm^3)	SD	Mean difference (cm^3)	Significance*	Mean hemi-volume (cm^3)		SD	Mean difference (cm^3)	Significance**	Significance***
T0	20	47.9	6.57	0.45	$p < 0.001$	CB side	23.30	3.29	1.29	NS	$p < 0.001$
						Non-CB side	24.59	3.27			
T1	20	48.35	6.65			CB side	23.65	3.36	1.03	NS	
						Non-CB side	24.68	3.31			

Cb, crossbite; *non-CB*, non-crossbite; *SD*, standard deviation; *NS*, not significant

**p* value set at 0.05 and based on paired Student's *t* test (inter-timing comparison); ***p* value set at 0.05 and based on independent Student's *t* test (inter-timing comparison); ****p* value set at 0.05 and based on paired Student's *t* test, for inter-timing comparison of CB/non-CB volumetric differences before and after RME

bone. Some other investigations suggested that with the mandible being "rotated" posteriorly on the crossbite side when compared with the cranial floor [41], the condyles on the crossbite side were positioned relatively more superiorly and posteriorly in the glenoid fossa than those on the non-crossbite side. This displacement of the mandible seemed to be compensated through an increased growth of the contralateral condyle and a reduced growth of the ipsilateral condyle [41]. However, there is a lack of evidence to prove that either facial, muscle asymmetries, or mandibular rotation have repercussions at a skeletal level.

Measuring asymmetric growth patterns in individual bones such as the mandible, however, remains challenging, if landmark 2D superimposition is used [42]. In fact, changes to the location of landmarks on the mandible can be due to either remodeling or positional displacement. Asymmetric translation of the mandible and changes to the glenoid fossa and cranial base can all contribute to positional or "platform" asymmetry of the mandible, thus confounding the measurement of actual asymmetry [43]. Therefore, true measurement of mandibular asymmetry over time necessitates identifying a reliable reference [43]. Thus, studies with a 3D evaluation of mandibular basal bone have been encouraged to elicit a reasonable evidence [12]. In fact, the deformities in mandibular asymmetry occur in all three planes of space and studies with a 3D approach are best suited to study growth and remodeling patterns in these conditions.

To overcome this issue, new methods have been proposed on CBCT-derived models; among these are the surface-based and the voxel-based superimpositions [44, 45]. The combined used of CBCT with superimposition technique could be helpful in demonstrating if youngster patients with PUXB should be orthodontically treated to avoid asymmetric growth of the mandible [46], beside the main goal of RME therapy, that is the correction of maxillary transversal deficiency.

In this respect, two recent researches carried out on CBCT scans demonstrated a slight mandibular asymmetry in adults [31] and children [22] with PUXB, and also a mandibular positional asymmetry [22].

Accordingly, in order to enrich the background with further evidence, this study aimed to evaluate mandibular shape using 3D mandibular models from CBCT and a surface-based superimposition technique, in youngsters with PUXB, before and after treatment with RME, in order to unveil if these

Table 2 Matching percentage between T0 (before rapid maxillary expansion) and T1 (after rapid maxillary expansion) mandibular shells and between original and mirrored mandibular shells at T0 and T1

	Total	% Matching[a] (mean)	SD	Significance*	% Matching[b] (mean)	SD	Significance*	% Matching[c] (mean)	SD	Significance*
T0/T1	40	87.57	2.63	–	92.82	2.17	–	96.70	1.54	–
Original/mirrored (T0)	40	70.62	4.02	$p < 0.001$	77.67	3.79	$p < 0.001$	83.50	3.53	$p < 0.001$
Original/mirrored (T1)	40	74.00	3.50		79.81	3.06		86.66	2.66	

SD, standard deviation; *RME*, rapid maxillary expansion

**p* value set at 0.05 and based on paired Student's *t* test (inter-timing comparison)

[a] Range of tolerance set to 0.2 mm

[b] Range of tolerance set to 0.40 mm

[c] Range of tolerance set to 0.6 mm

Table 3 Multiple linear regression model using age and gender as independent variable (predictor) and the mean differences of total volume and the mean difference of the hemi-volume difference (CB side/non-CB side) between T1 and T2 as dependent variables

	Dependent variables	Predictor variables	*R*	*R*-squared	Coefficients		*t*	Significance	95% coefficient interval (B)	
					Beta	Standard error			Lower limit	Upper limit
Study group	Total volume difference (T0–T1) (inter-timing comparison)	Age	0.946	0.896	− 0.056	0.015	− 0.675	0.509	− 0.041	0.021
		Gender			− 0.965	0.033	− 11.538	0.000	− 0.447	− 0.309
	CB/non-Cb volume differences (T0–T1) (inter-timing comparison)	Age	0.940	0.884	0.070	0.014	0.793	0.439	− 0.019	0.041
		Gender			− 0.913	0.032	− 10.353	0.000	− 0.394	− 0.260

patients show a mandibular asymmetry before therapy and weather if it is present, they could benefit from RME treatment. We excluded from the study subjects with dento-facial deformities and/or facial asymmetry in order to avoid biases from these confounding factors.

The present findings demonstrated that youngster with PUXB present a very slight mandibular asymmetry before treatment, being hemi-mandibular volume at the CB side smaller than non-CB side. Following RME therapy, there was a small increase of hemi-mandibular volume on the CB side compared with the non-CB side, slightly attenuating the very mild volumetric asymmetry. According to the linear regression analysis, this increment was even lower in females probably because of the less residual potential growth compared with males [47].

Also, inter-timing (T0 versus T1) superimposition of mirrored mandibular models and deviation analysis showed a small increment of the degree of matching after RME (T1) which reflected a slight improvement of very mild mandibular asymmetry. These data were statistically significant at all the range of tolerance set in the present investigation. All in all, findings from the present study demonstrated (both volumetric and deviation analyses) that there is a very slight and clinically negligible mandibular asymmetry before therapy that very modestly improves after RME therapy.

Weaknesses in the study are identified which were inherent to the sample and to the surface-to-surface matching technique. In fact, it was not possible to identify the exact onset time of the crossbite (whether it started in the primary dentition, early mixed dentition, or late mixed dentition). Accordingly, the onset of mandibular shift could not be identified, and this could affect the skeletal growth. Furthermore, a PUXB control group was not included in the present study. The reason behind this is that the current study considered most importantly the ethical issues in regard to obtaining 3D scans of untreated PUXB patients. This limited the inclusion of an age-matched control sample.

Last but not least, the short observational period in the current investigation could account for the relatively small clinical not significant skeletal mandibular changes. However, previous studies on functional appliance have shown greater skeletal changes with even shorter observational periods (6 months) [48].

As far as the surface-to-surface technique is concerned, some bias cannot be excluded due to the technique itself. In fact, it could be argued that there is an overestimation of differences obtained from the comparison between smaller surfaces, for example, the condyle since the larger surface (body and ramus) could guide the superimposition, leaving the smaller surfaces (condyle) to appear more dissimilar. Last but not least, the matching percentage was referred to the whole hemi-mandible, making it impossible to evaluate exactly which mandibular functional unit contributed to the slight mismatching recorded in our study. It would seem from the color map that there were some regional differences. Further studies are required to clarify this association. In conclusion, based on the current findings and very recent previous literature [21, 22, 31], it must be underlined that the crossbite does not result in significant skeletal mandibular asymmetry from a clinical standpoint. Instead, its importance is solely statistical. Thus, the decision to treat PUXB early should not be made to prevent possible mandibular skeletal asymmetry in youngsters [21]. In fact, the decision, to an early treatment of PUXB, should be based exclusively, on the fact that this malocclusion is not self-correcting but, rather, dependent on loosening maxillary sutures and maxillary buttress, which are most easily obtained during early ages [21].

Conclusions

Youngsters affected by unilateral posterior crossbite showed the following:

- A slightly smaller mandibular base volume on the crossbite side, which increases marginally 6 months after rapid palatal expansion.

- Surface-to-surface matching technique illustrates through the matching percentage how differences between the two hemi-mandibles in crossbite patients decrease after rapid palatal expansion.

Funding information This work has been performed with funds of the Department of General Surgery and Surgical-Medical Specialties, University of Catania, Catania, Italy.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the Institutional Review Board of Indiana University-Purdue University (IRB protocol number: 1708606623).

Informed consent Informed consent was obtained from all individual participants included in the study

References

1. Bjoerk A, Krebs A, Solow B (1964) A method for epidemiological registration of malocclusion. Acta Odontol Scand 22:27–41
2. Iodice G, Danzi G, Cimino R, Paduano S, Michelotti A (2016) Association between posterior crossbite, skeletal, and muscle asymmetry: a systematic review. Eur J Orthod 38:638–651. https://doi.org/10.1093/ejo/cjw003
3. Kutin G, Hawes RR (1969) Posterior cross-bites in the deciduous and mixed dentitions. Am J Orthod 56:491–504
4. Egermark-Eriksson I, Carlsson GE, Magnusson T, Thilander B (1990) A longitudinal study on malocclusion in relation to signs and symptoms of cranio-mandibular disorders in children and adolescents. Eur J Orthod 12:399–407
5. Zhu JF, Crevoisier R, King DL, Henry R, Mills CM (1996) Posterior crossbites in children. Compend Contin Educ Dent 17: 1051–1054 1056, 1058
6. Schroder U, Schroder I (1984) Early treatment of unilateral posterior crossbite in children with bilaterally contracted maxillae. Eur J Orthod 6:65–69
7. Baka ZM, Akin M, Ucar FI, Ileri Z (2015) Cone-beam computed tomography evaluation of dentoskeletal changes after asymmetric rapid maxillary expansion. Am J Orthod Dentofac Orthop 147:61–71. https://doi.org/10.1016/j.ajodo.2014.09.014
8. Rilo B, da Silva JL, Mora MJ, Cadarso-Suarez C, Santana U (2008) Midline shift and lateral guidance angle in adults with unilateral posterior crossbite. Am J Orthod Dentofac Orthop 133:804–808. https://doi.org/10.1016/j.ajodo.2006.05.046
9. Veli I, Uysal T, Ozer T, Ucar FI, Eruz M (2011) Mandibular asymmetry in unilateral and bilateral posterior crossbite patients using cone-beam computed tomography. Angle Orthod 81:966–974. https://doi.org/10.2319/022011-122.1
10. Langberg BJ, Arai K, Miner RM (2005) Transverse skeletal and dental asymmetry in adults with unilateral lingual posterior crossbite. Am J Orthod Dentofac Orthop 127:6–15; discussion 15–6. https://doi.org/10.1016/j.ajodo.2003.10.044
11. O'Byrn BL, Sadowsky C, Schneider B, BeGole EA (1995) An evaluation of mandibular asymmetry in adults with unilateral posterior crossbite. Am J Orthod Dentofac Orthop 107:394–400
12. Talapaneni AK, Nuvvula S (2012) The association between posterior unilateral crossbite and craniomandibular asymmetry: a systematic review. J Orthod 39:279–291. https://doi.org/10.1179/1465312512z.00000000041
13. Ferro F, Spinella P, Lama N (2011) Transverse maxillary arch form and mandibular asymmetry in patients with posterior unilateral crossbite. Am J Orthod Dentofac Orthop 140:828–838. https://doi.org/10.1016/j.ajodo.2011.08.003
14. Kilic N, Kiki A, Oktay H (2008) Condylar asymmetry in unilateral posterior crossbite patients. Am J Orthod Dentofac Orthop 133: 382–387. https://doi.org/10.1016/j.ajodo.2006.04.041
15. Uysal T, Sisman Y, Kurt G, Ramoglu SI (2009) Condylar and ramal vertical asymmetry in unilateral and bilateral posterior crossbite patients and a normal occlusion sample. Am J Orthod Dentofac Orthop 136:37–43. https://doi.org/10.1016/j.ajodo.2007.06.019
16. Lam PH, Sadowsky C, Omerza F (1999) Mandibular asymmetry and condylar position in children with unilateral posterior crossbite. Am J Orthod Dentofac Orthop 115:569–575
17. Pinto AS, Buschang PH, Throckmorton GS, Chen P (2001) Morphological and positional asymmetries of young children with functional unilateral posterior crossbite. Am J Orthod Dentofac Orthop 120:513–520. https://doi.org/10.1067/mod.2001.118627a
18. Spampinato C, Pino C, Giordano D, Leonardi R (2012) Automatic 3D segmentation of mandible for assessment of facial asymmetry
19. Halicioglu K, Celikoglu M, Yavuz I, Sekerci AE, Buyuk SK (2014) An evaluation of condylar and ramal vertical asymmetry in adolescents with unilateral and bilateral posterior crossbite using cone beam computed tomography (CBCT). Aust Orthod J 30:11–18
20. Illipronti-Filho E, Fantini SM, Chilvarquer I (2015) Evaluation of mandibular condyles in children with unilateral posterior crossbite. Braz Oral Res 29:49. https://doi.org/10.1590/1807-3107BOR-2015.vol29.0049
21. Cardinal L, Martins I, Gribel BF, Dominguez GC (2019) Is there an asymmetry of the condylar and coronoid processes of the mandible in individuals with unilateral crossbite? Angle Orthod 89:464–469. https://doi.org/10.2319/052518-398.1
22. Evangelista K, de Oliveira CFP, de Almeida BL, Avelino MAG, Cevidanes LHS, de Oliveira Ruellas AC, Valladares-Neto J, Silva MAG (2020) Three-dimensional assessment of craniofacial asymmetry in children with transverse maxillary deficiency after rapid maxillary expansion: a prospective study. Orthod Craniofac Res. https://doi.org/10.1111/ocr.12370
23. Jaju PP, Jaju SP (2015) Cone-beam computed tomography: time to move from ALARA to ALADA. Imaging Sci Dent 45:263–265. https://doi.org/10.5624/isd.2015.45.4.263
24. Kavand G, Lagravere M, Kula K, Stewart K, Ghoneima A (2019) Retrospective CBCT analysis of airway volume changes after bone-borne vs tooth-borne rapid maxillary expansion. Angle Orthod 89: 566–574. https://doi.org/10.2319/070818-507.1
25. Pham V, Lagravere MO (2017) Alveolar bone level changes in maxillary expansion treatments assessed through CBCT. Int Orthod 15:103–113. https://doi.org/10.1016/j.ortho.2016.12.002
26. Digregorio MV, Fastuca R, Zecca PA, Caprioglio A, Lagravere MO (2019) Buccal bone plate thickness after rapid maxillary expansion in mixed and permanent dentitions. Am J Orthod Dentofac Orthop 155:198–206. https://doi.org/10.1016/j.ajodo.2018.03.020
27. Forst D, Nijjar S, Flores-Mir C, Carey J, Secanell M, Lagravere M (2014) Comparison of in vivo 3D cone-beam computed tomography tooth volume measurement protocols. Progr Orthod 15. https://doi.org/10.1186/s40510-014-0069-2
28. Leonardi R (2019) Cone-beam computed tomography and three-dimensional orthodontics. Where we are and future perspectives. J Orthod 46:45–48. https://doi.org/10.1177/1465312519840029
29. Leonardi R, Muraglie S, Bennici O, Cavallini C, Spampinato C (2019) Three-dimensional analysis of mandibular functional units in adult patients with unilateral posterior crossbite: a cone beam study with the use of mirroring and surface-to-surface matching

techniques. Angle Orthod 89:590–596. https://doi.org/10.2319/081718-607.1

30. Leonardi R, Muraglie S, Crimi S, Pirroni M, Musumeci G, Perrotta R (2018) Morphology of palatally displaced canines and adjacent teeth, a 3-D evaluation from cone-beam computed tomographic images. BMC Oral Health 18:156. https://doi.org/10.1186/s12903-018-0617-0
31. Leonardi R, Muraglie S, Lo Giudice A, Aboulazm KS, Nucera R (2020) Evaluation of mandibular symmetry and morphology in adult patients with unilateral posterior crossbite: a CBCT study using a surface-to-surface matching technique. Eur J Orthod. https://doi.org/10.1093/ejo/cjz106
32. Lee SY, Choi DS, Jang I, Song GS, Cha BK (2017) The genial tubercle: A prospective novel landmark for the diagnosis of mandibular asymmetry. Korean J Orthod 47:50–58. https://doi.org/10.4041/kjod.2017.47.1.50
33. Neiva MB, Soares AC, Lisboa Cde O, Vilella Ode V, Motta AT (2015) Evaluation of cephalometric landmark identification on CBCT multiplanar and 3D reconstructions. Angle Orthod 85:11–17. https://doi.org/10.2319/120413-891.1
34. G. D (1940) Statistical methods for medical and biological students. Interscience Publications, New York
35. Alarcon JA, Martin C, Palma JC (2000) Effect of unilateral posterior crossbite on the electromyographic activity of human masticatory muscles. Am J Orthod Dentofac Orthop 118:328–334. https://doi.org/10.1067/mod.2000.103252
36. Bresin A, Kiliaridis S, Strid KG (1999) Effect of masticatory function on the internal bone structure in the mandible of the growing rat. Eur J Oral Sci 107:35–44
37. Kiliaridis S, Mahboubi PH, Raadsheer MC, Katsaros C (2007) Ultrasonographic thickness of the masseter muscle in growing individuals with unilateral crossbite. Angle Orthod 77:607–611. https://doi.org/10.2319/101105-360
38. Rodrigues L, Traina AA, Nakamai LF, Luz JG (2009) Effects of the unilateral removal and dissection of the masseter muscle on the facial growth of young rats. Braz Oral Res 23:89–95
39. Sarnat BG (1988) Craniofacial change and non-change after experimental surgery in young and adult animals. Angle Orthod 58:321–342. https://doi.org/10.1043/0003-3219(1988)058<0321:CCANAE>2.0.CO;2
40. Tsanidis N, Antonarakis GS, Kiliaridis S (2016) Functional changes after early treatment of unilateral posterior cross-bite associated with mandibular shift: a systematic review. J Oral Rehabil 43:59–68. https://doi.org/10.1111/joor.12335
41. Nerder PH, Bakke M, Solow B (1999) The functional shift of the mandible in unilateral posterior crossbite and the adaptation of the temporomandibular joints: a pilot study. Eur J Orthod 21:155–166
42. Bazina M, Cevidanes L, Ruellas A, Valiathan M, Quereshy F, Syed A, Wu R, Palomo JM (2018) Precision and reliability of Dolphin 3-dimensional voxel-based superimposition. Am J Orthod Dentofac Orthop 153:599–606. https://doi.org/10.1016/j.ajodo.2017.07.025
43. Solem RC, Ruellas A, Ricks-Oddie JL, Kelly K, Oberoi S, Lee J, Miller A, Cevidanes L (2016) Congenital and acquired mandibular asymmetry: mapping growth and remodeling in 3 dimensions. Am J Orthod Dentofac Orthop 150:238–251. https://doi.org/10.1016/j.ajodo.2016.02.015
44. Almukhtar A, Ju X, Khambay B, McDonald J, Ayoub A (2014) Comparison of the accuracy of voxel based registration and surface based registration for 3D assessment of surgical change following orthognathic surgery. PLoS One 9:e93402. https://doi.org/10.1371/journal.pone.0093402
45. Muraglie S, Musumeci G, Loreto C, Leonardi RM (2019) Role of ADAMTS4 and ADAMTS5 during early orthodontic tooth movement. J Biol Regul Homeost Agents 33:649–655
46. Bishara SE, Burkey PS, Kharouf JG (1994) Dental and facial asymmetries: a review. Angle Orthod 64:89–98. https://doi.org/10.1043/0003-3219(1994)064<0089:DAFAAR>2.0.CO;2
47. Patcas R, Wiedemeier DB, Markic G, Beit P, Keller H (2017) Evidence of secular trend in mandibular pubertal growth. Eur J Orthod 39:680–685. https://doi.org/10.1093/ejo/cjx027
48. Hagg U, Du X, Rabie AB (2002) Initial and late treatment effects of headgear-Herbst appliance with mandibular step-by-step advancement. Am J Orthod Dentofac Orthop 122:477–485. https://doi.org/10.1067/mod.2002.128218