Mandibular Ramus Heights in Patients with Unilateral Posterior Crossbite

A Thesis Submitted to the Faculty of the University of Minnesota
by:

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Abstract

Introduction: Unilateral posterior crossbite, if left untreated, may lead to mandibular and facial asymmetry.

Aim: To assess differences in mandibular ramus height in patients with unilateral posterior crossbites before and after correction with orthodontic appliances.

Materials and Methods: Ramus heights were measured as the linear distance between the most anterior point of the condyle and gonion inferius on pre-treatment (T1) and post-treatment (T2) cone-beam computed tomography scans of 59 adolescent patients (mean age at T1 = 12.4, age range 8 - 16 years) who underwent rapid maxillary expansion followed by comprehensive orthodontic treatment with fixed appliances. Paired and two-sample t-tests were used to determine if the change in ramus height from T1 to T2 was associated with the crossbite side.

Results: The difference between ramus heights of the crossbite and non-crossbite sides at T1 was not significant ($P = 0.86$). On both the crossbite and non-crossbite sides, the change in ramus height from T1 to T2 was significant ($P < 0.0001$). However, the difference between crossbite and non-crossbite side change from T1 to T2 was not significant ($P = 0.39$). There was no difference between males and females for any variable tested.

Conclusions: Unilateral posterior crossbite in adolescents was not associated with shorter ramus height on the side of the crossbite. Hence, crossbite correction did not lead to more symmetrical ramus heights. Despite the lack of long-term controlled studies, early treatment of unilateral posterior crossbite may allow for more symmetrical mandibular growth.

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List of Abbreviations

CBCT – Cone-Beam Computed Tomography

FFA – Full-Fixed Appliances

MARPE – Miniscrew-Assisted Rapid Palatal Expansion

RME – Rapid Maxillary Expansion

SARME – Surgically-Assisted Rapid Maxillary Expansion

UPC – Unilateral Posterior Crossbite

Introduction

An assessment of facial symmetry should be part of every orthodontic patient's initial evaluation. In addition to attaining an ideal occlusion, optimizing facial balance is an important goal of orthodontic treatment (1). However, choosing the appropriate treatment modality to correct a facial asymmetry can be difficult given that the etiology of facial asymmetry may be multifactiorial. In addition to general growth patterns, genetics, and environmental factors, some malocclusions have been found to cause facial asymmetry if left untreated (2, 3, 4). One such malocclusion is the unilateral posterior crossbite (UPC) (5). Therefore, the American Association of Orthodontists states that patients with posterior crossbite may benefit from early diagnosis and treatment (6).

Untreated UPC may lead to progressive asymmetry of the mandible as patients continue to grow throughout adolescence. Specifically, differences in crossbite- and non-crossbite-side ramus heights and condyle-fossa relationships have been found. However, some of the findings are controversial. Some studies on patients with UPC, utilizing 2D radiographs, have shown that vertical measures of the mandible including ramus height, condylar height, and total ramus height can be significantly lower on the side of the crossbite (7, 8). More recently, in a study on adults with UPC using 3D cone-beam computed tomography (CBCT), regions of mandibular asymmetry were shown to exist especially at the condyle, the mandibular angle, the alveolus, and the mandibular ramus (9). In contrast, other studies suggest that there is *not* a significant difference in mandibular symmetry in patients with UPC when compared to controls (4, 5). Varying radiograph (2D versus 3D) and evaluation type (line, point, volumetric) hinder the consistency of results and present holes in the topic of interest. Additionally, the degree to which this possible skeletal asymmetry translates to detectable soft tissue facial asymmetry is an area that still needs further exploration.

In a growing patient, the most common orthodontic approach to correct a UPC is the use of rapid maxillary expansion (RME). RME is a treatment modality with a long history in orthodontics (10). Numerous indications for the use of RME have been reported in the literature – anteroposterior discrepancies, cleft lip and palate patients who present with collapsed maxillary segments, gaining arch length, and most pertinently, for patients "who have lateral discrepancies that result in either unilateral or bilateral posterior crossbites" (10). UPC can be of dental, skeletal, or combined dental and skeletal origin. Skeletally, the discrepancy can be due to a narrow maxilla or a wide mandible (with pathology and syndromes being exceptions to this generalization), and dentally, the UPC can be due to ectopic eruption of maxillary or mandibular teeth. A rapid maxillary expander is a tooth-born appliance that works by applying force that exceeds the limits of orthodontic tooth movement to posterior teeth, which then acts as an orthopedic force to open the maxillofacial sutures (10). The open midpalatal suture then fills with bone. The transverse expansion that is achieved by RME allows for both a skeletal and a dental correction of a UPC.

With the introduction of CBCT in orthodontic clinical practice, it is now possible to visualize the whole maxillary-mandibular complex in relation to the cranial base without any overlapping structures or magnification. 2D radiographs, which have historically been used to evaluate craniofacial anatomy, present with shortcomings due to inherent magnification and distortion. In this study, differences in mandibular ramus height is assessed on CBCT images in patients with unilateral posterior crossbites before and after correction with orthodontic appliance.

Review of the Literature

Etiology of Unilateral Posterior Crossbite and Facial Asymmetry

Lingual posterior crossbite is a malocclusion defined as a transverse arch discrepancy in which the palatal cusps of one or more of the maxillary posterior teeth do not occlude in the central fossae of the opposing mandibular teeth. The maxillary posterior teeth are lingually positioned relative to the mandibular teeth, and this can either occur unilaterally or bilaterally. Lingual posterior crossbite is the most common deviation from the normal transverse relationship, and it occurs in 9% of the US population according to National Health and Nutrition Examination Survey data (NHANES III) (2, 11). Other studies report the prevalence in children to be between 8.7% and 23.3% (5).

The development of a posterior crossbite is variable and multifactorial. The apparent malocclusion may be dental in origin, skeletal (narrow maxilla or wide mandible), or combined dental and skeletal. It is important for the orthodontist to evaluate the underlying skeletal relationship to distinguish which is at fault, as this can have clinical treatment implications. A purely dental crossbite would present as maxillary teeth positioned lingual to their normal position while the individual has adequate palatal width. A skeletal crossbite would present with inadequate palatal width or excess mandibular width. There can also be relationships where both problems are present (11). If there is a skeletal component to the crossbite, this would be a reason for early intervention, the objective being to provide skeletal correction while a child is still growing (12).

The most frequent cause of a posterior crossbite is a reduction in the maxillary dental arch width (13, 14), but a large mandible rather than a transversely deficient maxilla has also been implicated (5, 12). Maxillary constriction has been associated with unfavorable environmental and social factors that influence the development of the maxilla such as finger-sucking habits, perioral muscle functions, poor positioning of the tongue, and nutrition habits (7, 10, 13, 14, 15). Arch form is affected by an alteration in the balance between cheek and tongue pressures. With thumb-sucking for example, the tongue is lowered which decreases the pressure of the tongue on the lingual side of the maxillary posterior teeth. At the same time, the musculature in the cheeks will be amplified as the buccinator contracts during sucking (11). Additional causes of a posterior crossbite are congenital cleft lip and/or palate, genetic syndromes, early loss or prolonged retention of deciduous teeth, adenoid hypertrophy and obstruction of the upper airway (11, 12).

The development of facial asymmetry is related to many etiologic factors. Contributing factors reported in the literature include genetic or congenital malformations, environmental factors such as trauma or habits, functional deviations, and condylar hyperplasia (16). Craniofacial asymmetry can also occur as a pseudo-asymmetry, termed *displacement asymmetry*, which involves mandibular displacement without a true morphologic shape change in the related structures (17).

The question of what came first, UPC or related skeletal asymmetry, is reminiscent of the chicken or the egg dilemma. Is the dental crossbite a consequence of asymmetric mandibular growth or is the dental crossbite the cause of the mandibular asymmetry? It is difficult to know with certainty because it appears that both exist in nature. Obwegeser described mandibular asymmetries as anomalies in growth patterns, and he characterized them as either hemimandibular elongation or hemimandibular hyperplasia (18). Hemimandibular elongation can occur as elongation of either the condyle or ramus in the vertical plane or the mandibular body in the horizontal plane. Hemimandibular hyperplasia means that one half of the entire mandible is enlarged. With hemimandibular elongation, a UPC will be present on the opposite side of the elongation (19). These mandibular asymmetries can also be described as a skeletal crossbite, which is characterized by an asymmetric mandible that shows joint space symmetry and no shift between centric relation and maximal intercuspal position. Centric relation (CR), as defined by *The Glossary of Prosthodontic Terms*, is a "maxillomandibular relationship, independent of tooth contact, in which the condyles articulate in the anterior-superior position against the posterior slopes of the articular eminences" (10). Maximal intercuspal position (MIP) is "the complete intercuspation of the opposing teeth independent of condylar position" (10). If the occlusion is not stable when the condyles are seated in CR, then a shift will occur to a more stable, interdigitated maximal intercuspal position. In a functional crossbite, the mandible is symmetric but is shifted and positioned asymmetrically in maximal intercuspation to achieve a more stable occlusion (8).

Conversely, numerous studies have found no significant difference in maxillary or mandibular skeletal symmetry in UPC adults compared to controls (4, 5). Asymmetric muscular activity is well studied, and despite uncertainty about permanent skeletal change with UPC, differences in muscle activity on the crossbite and non-crossbite sides can asymmetrically position the mandible (20).

Growth Consequences

An untreated UPC appears to influence and have lasting effects on dentofacial growth and development. In a growing person, a recurrent mandibular displacement can change the modeling process of the mandible, and such permanent growth change can be considered an adaptation to the displacement to preserve normal function (17). An untreated UPC has been associated with right-to-left-side differences in the condyle-fossa relationship, asymmetric contraction of the masticatory muscles, altered chewing pattern and bite force, occlusion and dental changes, and asymmetric functioning of the temporomandibular joint, all of which may cause differential development of the right and left sides of the mandible over time (2, 7, 21, 22). Kutin and Hawes found that in untreated crossbites, the permanent dentition erupted into the same crossbite relationship as in the deciduous molars (23). One study used panoramic radiographs to examine the effect of UPC on mandibular measurements (condylar height, ramus height, and condyle plus ramus height), and found significantly lower vertical parameters on the side of the UPC (7). A study by Santos Pinto *et al*. showed similar results, finding that positional asymmetry produced mandibular skeletal asymmetry in their study sample, in particular causing a shorter ramus on the side of the UPC (8).

Functional Shift

Unilateral posterior crossbites can feature a functional component of a mandibular lateral shift towards the crossbite side (22). This *functional shift* results from a premature occlusal contact while closing that guides the mandible into the maximal intercuspal position (5). Santos Pinto *et al*. found that there is an antero-posterior component to the shift as well, with the molars on the non-crossbite side positioned more anteriorly than the contralateral side (8). Alternatively, it has been proposed that there is a neuromuscular guidance of the mandible directly into an intercuspal position, arguing that a displaced mandible is not forced laterally due to interfering occlusion alone (13).

With the laterally shifted mandible, a bilaterally asymmetric condylar position within the temporomandibular joints occurs. The crossbite-side condyle is forced posterior-superiorly and the non-crossbite-site condyle is forced anterior-inferiorly within the glenoid fossa (4, 5). This shift causes alterations in the activity of the jaw musculature and may lead to skeletal changes over time (24). One study showed that as a consequence of an untreated UPC, there was displacement of the ipsilateral condyle toward the crossbite side and an increased growth of the contralateral condyle (2). Numerous studies have evaluated the condyle and glenoid fossa relationship in individuals with UPC, but more recently Muraglie *et al*. looked at the glenoid fossa in *adults* with UPC compared to controls using surface-to-surface matching on CBCT images. They found significant right- and left-side differences (greater than 11%) in the articular eminence and lateral-posterior wall of the glenoid fossa in UPC patients compared to controls (25). As expected from these findings, it has also been found that the mandibular ramus height on the crossbite side remained relatively shorter during growth (17, 26). Hesse *et al*. found that eliminating the lateral shift through expansion of the maxilla resulted in a more symmetric seating of the condyle within the TMJ (4). Additionally, functional shifts are rarely detected in adults with UPC, indicating that boney and soft tissue adaptive changes likely occur over time, leading to skeletal asymmetry (14).

It has been shown that on the side of UPC, muscle tension is reduced due to lower mechanical load compared to the non-crossbite side, which has slight hypertrophy of masticatory muscles as a compensation for the increased mechanical load (27). The displaced mandible elicits a change in pattern and intensity of functional forces applied to both the mandible itself as well as the temporomandibular joints (5). An abnormal chewing pattern, termed *reverse-sequencing*, is associated with UPC (28). One study found that elimination of UPC normalized the chewing cycle duration, which was previously longer compared to controls, but the reverse-sequencing chewing pattern remained (29).

Growing children with UPC demonstrate a variety of patterns of behavior in response to their malocclusion. The variety of adaptations and habits may explain the diversity of findings regarding amount and degree of skeletal asymmetry observed among subjects (8).

<u>Treatment of Unilateral Posterior Crossbite</u>

There is robust support in the literature that correction of UPC should be addressed early (4, 5, 6, 14). UPC tends to develop early in the mixed dentition stage and has a low rate

(0-20%) of spontaneous correction (5, 14). Studies have found that, if a crossbite remains untreated, malocclusion and dental asymmetries tend to worsen and can begin to impact the skeletal structures of the mandible and maxilla, including the temporomandibular joints (5, 30). Treatment should consist of early expansion of the maxillary arch, and could be accompanied by selective exercises (28). In a study by Nerder *et al.* investigating condylar and midline changes in children with UPC, the UPC was corrected with a reflex-releasing splint and expansion plate. The authors found that a differentiated growth pattern in the TMJs during the treatment period had eliminated the prior asymmetry (13).

Rapid Maxillary Expansion

There are a number of treatment modalities available to correct UPCs. Methods of treatment for UPC vary with age, growth, and severity of the transverse discrepancy. For growing individuals with a mild transverse discrepancy, auxiliary appliances such as a transpalatal arch, a removable expansion plate, or cross-elastics, for example, can be used to address the crossbite. For more severe transverse discrepancies in growing individuals, the most common method is to expand the maxilla by utilizing a rapid maxillary expansion device (14). Maxillary expansion has a long history in orthodontics and is a widely accepted treatment modality in both the late mixed dentition and permanent dentition for space and transverse deficiencies, for posterior crossbite, as well as facilitating correction of Angle Class II and Class III malocclusions (10, 31). A limiting factor for traditional rapid palatal expansion is the ossification of the craniofacial sutures. Knowing the exact moment and degree of ossification when a patient presents would be ideal, however, indicators such as chronologic age have been shown to be unreliable in "determining the developmental status of the suture during growth" (31). Methods have been proposed for staging midpalatal suture maturation, most recently using CBCT, to help guide the decision on whether to utilize RME in patients (31). Bishara and Staley suggest that the optimal age for expansion is before 13 – 15 years old, while Angelieri *et al*. suggests that before age 10, maxillary expansion with skeletal effects is more easily obtained than in later circumpubertal ages (11-18 years) (10, 31). It is possible to claim that the older the patient is, the greater the likelihood that the suture has become ossified (32).

RME has been shown to separate the midpalatal suture, after which new bone gets deposited in the areas of expansion (31, 33, 34). Traditional banded rapid maxillary expanders are tooth-born appliances, consisting of fitted metal bands which are bonded to the permanent first molars and the first permanent premolars and that are soldered to a jack-screw body which sits in the palatal vault. With every turn of the screw, force is exerted onto the supporting teeth. Rapid force applied on the posterior teeth transfers to the suture allowing for the suture to open with minimal dental movement (11). When the midpalatal suture is opened, a few phenomena are expected. The suture will open along its axis in the anteroposterior direction, the maxillary central incisor crowns will converge while the roots diverge, the alveolar processes will move laterally, the maxilla will move anterior and inferior, and an inferior and backward rotation of the mandible will occur in response to the change in maxillary position (34). In order to compensate for an inevitable degree of relapse, it is recommended to over-expand the maxillary arch in order to account for the loss of width in the subsequent period (34). Spillane and McNamara reported that 2.4 years into the retention period of patients treated with RME, arch width averaged 72 - 91% of the post-expansion width, suggesting that 9 – 28% relapse occurred post-treatment (35).

As mentioned previously, adults with a severe transverse discrepancy who have completed facial growth will have fused craniofacial sutures, and therefore require surgical treatments such as surgically-assisted rapid maxillary expansion (SARME) or a two-piece LeFort osteotomy, in conjunction with orthodontic treatment (36). More recently, miniscrew-assisted rapid palatal expansion (MARPE) have been introduced as a non-surgical treatment option in adults (32).

Cone Beam Computed Tomography

Accurate diagnosis of facial and dental asymmetry is critical for appropriate treatment in orthodontic practice. Historically, facial symmetry was largely evaluated and measured through panoramic, submentovertex, or postero-anterior cephalometric radiographs (3, 8, 37, 38). While they are still valuable tools today, these imaging modalities suffer from shortcomings in that they are two-dimensional projections of a three-dimensional structure. That causes possible distortion of the image, magnification errors, and difficulty distinguishing structures due to overlap.

Three-dimensional imaging has been an evolving and vital component of diagnostics in medicine for years. Computer tomography (CT) is one example of medical-grade imaging that evaluates an area of interest in the body. CT is different from conventional radiography in that it uses a motorized x-ray source that rotates around the patient, and the x-rays are detected on a digital detector opposite the source (39). Traditional medical CT uses a fan-shaped x-ray beam in a helical progression. Each time the x-ray source completes a full rotation, a two-dimensional image slice is created, and this process continues until the desired area of interest is scanned. The slices are then “stitched” together by a software program to form a three-dimensional volume image (39).

In dentistry, despite the wealth of knowledge that can be gained from conventional CT, its application has been limited due to cost, access, and radiation dose concerns (40). With the advent of cone-beam computed tomography (CBCT), visualizing the maxillofacial region in 3D has been made a more viable option for diagnosis and treatment planning (7, 41). CBCT uses a divergent cone-shaped x-ray source and rotates around a rotation fulcrum. Orthogonal planar images are secondarily reconstructed by a software program from the collected projection data (Figure 1) (40).

With 3D images, dental practitioners can utilize imaging software to evaluate maxillofacial structures for diagnosis and treatment planning. CBCT images can be produced with submillimeter isotropic voxel resolution, enabling precise measurements due to the accurate spatial resolution (40, 42). Unlike 2D images, 3D measurements are made between points on a volume and are therefore not subject to projection distortion (43). 3D landmark identification can be done in three planes of space using the multiplanar reconstruction images, which allows for unique (compared to 2D imaging) identification from multiple views (44). Ludlow *et al*. found that measurement accuracy for well-defined points in 2D images had average errors less than 1.2%, while 3D measurement techniques had average errors of less than 0.6% (43). In the same study, head position was evaluated, as it has been found to affect accuracy of measurements in 2D images. It was found that in contrast to accuracy of measurements taken on cephalometric and panoramic images, measurements on CBCT volumes were uninfluenced by skull orientation (43, 44).

CBCT is a superior modality to evaluate craniofacial morphology, particularly vertical variables, compared to digital 2D images like panoramic and submentovertex radiographs (47, 50). De Moraes *et al*. found that CBCTs had almost perfect measurement agreement (kappa = 0.92) with human skull physical measurements, while digital 2D measurement had poor agreement (kappa = 0.07) (51). Additionally, postero-anterior cephalometric radiographs have previously been used to evaluate facial asymmetry, but also have inherent distortion, magnification, and positional sensitivity. A study by Cook *et al*. compared two postero-anterior cephalometric radiographs and found that a 5° rotation of the head holder resulted in a complete reversal of an apparent asymmetry in a given subject (47). CBCT volumes can be manipulated by computer programs to normalize head position so that skull orientation during image acquisition is not a concern when using this imaging modality. The present study oriented all subject images to Frankfort-horizonal prior to taking measurements.

In studies exploring mandibular asymmetry with CBCT, volumetric differences, mirror-image analysis, measurements to a midsagittal plane, and other point-to-point, plane-to-plane, and tangent line measurements have been utilized. Points *condylion* and *gonion inferius* have been previously identified and utilized in the literature for measuring *total ramus height* and were therefore chosen as the measurement to evaluate ramus height in this study (45).

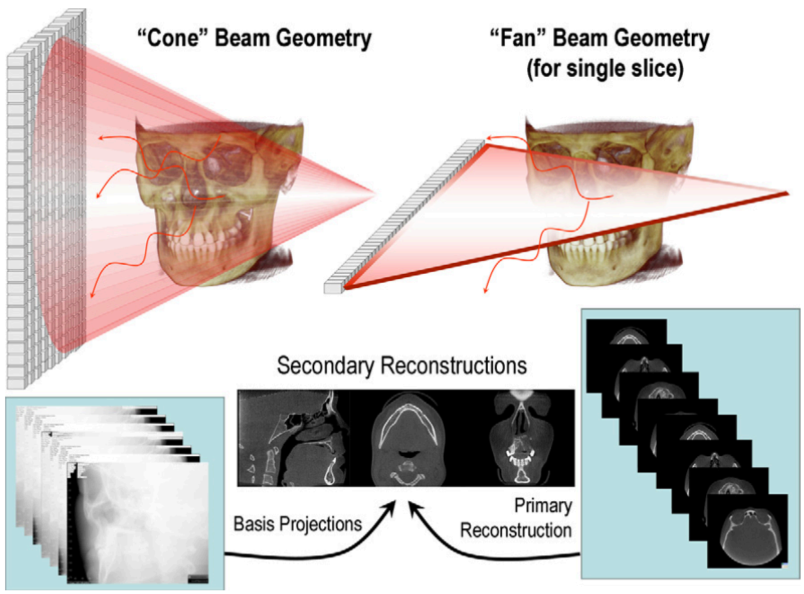

Figure 1. Cone-beam CT (left) and conventional CT (right) x-ray beam projection geometry and resultant image production (From Scarfe & Farman, 2008).

Aims and Hypotheses

The general aim of this study was to assess mandibular ramus height in subjects with UPC before and after correction with rapid maxillary expansion (RME) and full-fixed appliances (FFA) using CBCT data. More specifically the aims where to:

- determine if there is a side difference in mandibular ramus height, i.e. shorter ramus height on the crossbite side, in patients with UPC pre-treatment and,
- if a difference is present, determine if it is corrected with orthodontic intervention with RME and FFA

The following hypotheses were tested:

1. Subjects with UPC have associated mandibular asymmetry expressed as a side difference in mandibular ramus height.
2. Subjects with UPC treated with RME and FFA see improvement in asymmetry after treatment.

Materials and Methods

Subjects and Treatment Protocol

The study protocol of this retrospective cohort study, which included the use of existing CBCT data, was approved by the Institutional Review Board at the University of Minnesota (study number: 00008651). A total of 59 subjects were included in the study based on the following inclusion criteria:

- They were treated at the University of Minnesota School of Dentistry Orthodontic Clinic with RME and FFA as part of their comprehensive orthodontic treatment
- They presented with a UPC
- They showed no signs or symptoms of temporomandibular dysfunction.

Subjects were excluded if:

- They presented with a cleft lip/palate or other developmental craniofacial anomalies,
- They had surgical correction of their malocclusion as part of their orthodontic treatment plan
- They did not have complete data at start or end of treatment.

Subjects' electronic health records were utilized to collect information including sex, expander type, and age in years at the beginning and at the end of treatment.

RME appliances included Hyrax and Quad-Helix appliances, but the vast majority of subjects (98%, 58/59 subjects) were treated with a Hyrax appliance. Hyrax appliance designs varied from four-banded (bands on maxillary 1st permanent molars and 1st premolars) to two-banded (bands on maxillary 1st permanent molars only with extension arms to the 1st premolars). Each subject was prescribed a different amount of expansion depending on their initial transverse deficiency, but activation of the expander was monitored by the clinician until the desired correction was reached. At that point, the subjects were either held in retention until the start of phase II or transitioned directly into FFA. Retaining maxillary width was handled multiple ways. For example, some patients had phase I, were held with the expander for a few weeks, then were given Hawley removable retainers for retention until the start of phase II. Others had RME then once adequate expansion was achieved, they were constructed and a TPA was placed. The TPA was then utilized for either a few months or for the whole length of treatment. After expansion and maxillary width retention, comprehensive orthodontic treatment was then completed and retention prescribed.

A description of the study sample is provided in Tables 1 and 2. The distribution of the 59 subjects into the subcategories of sex and crossbite side are shown in Table 1. Mean values, standard deviations, and ranges of the population continuous variables collected are shown in Table 2. Time between T1 and T2 had a wide range between subjects. The reason for this is varying lengths of active and retentive treatment. Different scenarios include: phase I with a retention period then phase II, phase I that transitioned directly into a phase II, single phase treatment, or phase I with retention followed by two rounds of FFA.

Table 1. Descriptive statistics of categorical population variables.

Variable	Category	Occurrence
Sex	Male	18
	Female	41
Crossbite Side	Right	27
	Left	32

Table 2. Descriptive statistics of continuous population variables.

	Mean +/- SD	Range
Age at T1	12.4 +/- 1.9	8 - 16
Age at T2	16.0 +/- 1.8	12.9 – 20.9
Time between T1 and T2 (years)	3.1 +/- 1.3	1.3 – 10

Image Acquisition

Pre- and post-treatment CBCT images were acquired with an i-CAT Next Generation CBCT unit (Imaging Sciences International, Hatfield, PA). All scans were acquired at 18.54 mAs and 120 kV, utilizing a pulsed scan time of 8.9 seconds for a full field of view (17 x 23 cm) scan with a 0.30 mm^3 voxel size. Subjects were instructed to bite in maximal intercuspal position with their heads centered along the midsagittal plane during image acquisition. CBCT volumes were manipulated in Dolphin Imaging (version 11.95, Dolphin Imaging and Management Solutions, Chatsworth, CA).

Data Collection

All measurements were made using Dolphin Imaging software by the same investigator to ensure consistency. The CBCT volume was oriented from both the frontal and lateral translucent views. First, in the frontal view, the CBCT volume was tipped in a superior or inferior manner along the mid-sagittal plane until the inferior border of the orbital rims were on the same axial plane. Next, in the lateral view, the volume was manipulated until superimposition was achieved of the inferior border of the orbital rim and the zygomatic process of the maxilla. The right-side lateral view was then used to orient the volume to Frankfort Horizontal. Frankfort Horizontal is a plane that tangents the upper rims of the external auditory meatus (porion) and the inferior borders of the orbital rims (orbitale), and it was adopted as the best representation of the natural skull orientation (11). This orientation was achieved by placing the crosshairs at porion and tipping the volume clockwise or counterclockwise until the inferior borders of the orbital rims (orbitale) were on the horizontal reference plane created from the crosshairs (Figure 2).

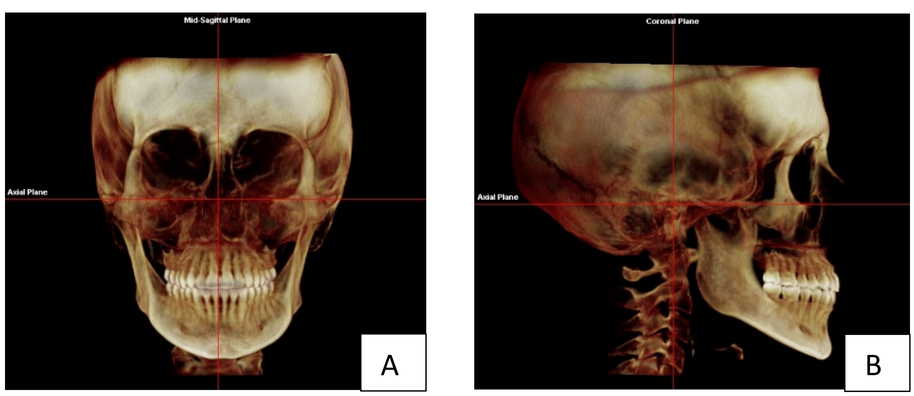

Figure 2. Orientation of a 3D volume reconstruction in Dolphin Imaging. A) Translucent frontal view used to orient inferior orbital rims. B) Right lateral translucent view used to superimpose inferior orbital rims and the zygomatic process, then orient the volume to Frankfurt Horizontal.

After orientation of all subjects' volumes and prior to data collection, ramus height was measured on ten randomly chosen subjects within the data set. After a 4-week washout period, measurements were repeated to evaluate intra-rater reliability.

Craniofacial landmarks referenced in this study are defined in Table 3. Figures 3 & 4 show the 3D image reconstruction used to identify/locate landmarks *condylion* and *gonion inferius*, the landmarks used to measure ramus height in this study. To establish the condylion landmark, a point was identified on the most superior aspect of the condyle in the coronal view. Then the point was adjusted to the most superior aspect on the sagittal and axial views. For the gonion inferius, a point was identified on the most inferior and anterior point on the angle of the mandible. Then the point was adjusted to the most inferior and anterior aspect on the sagittal and axial views. The CBCT software then calculated the linear distance between these two points to establish the ramus height.

Table 3 Landmark definitions for orientation and symmetry assessment.

Landmark	Definition
Orbitale	The lowest point on the inferior margin of the orbit
Porion	The midpoint of the upper contour of the external auditory canal
Condylion	The most superior point of the condyle
Gonion Inferius	The most inferior and anterior point of the angle of the mandible, as indicated by when the buccal and lingual cortical plates met in the axial slice

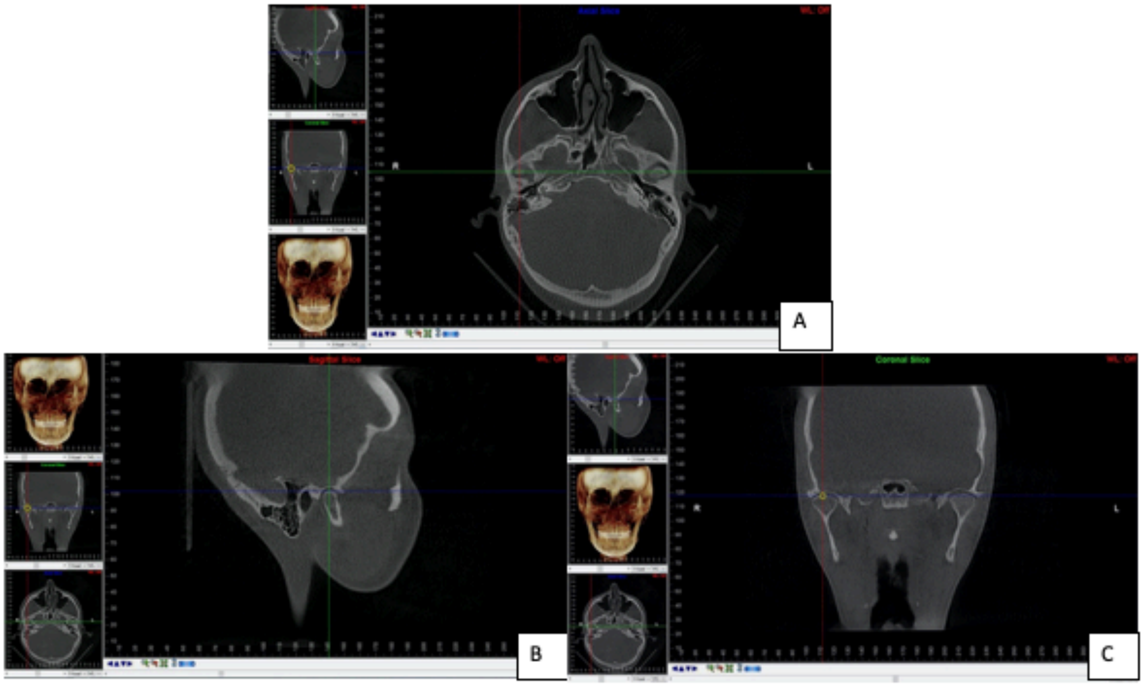

Figure 3. Condylion was identified in three planes of space – (A) axial, (B) sagittal, and (C) coronal slices. The coronal slice is where the measurement was taken.

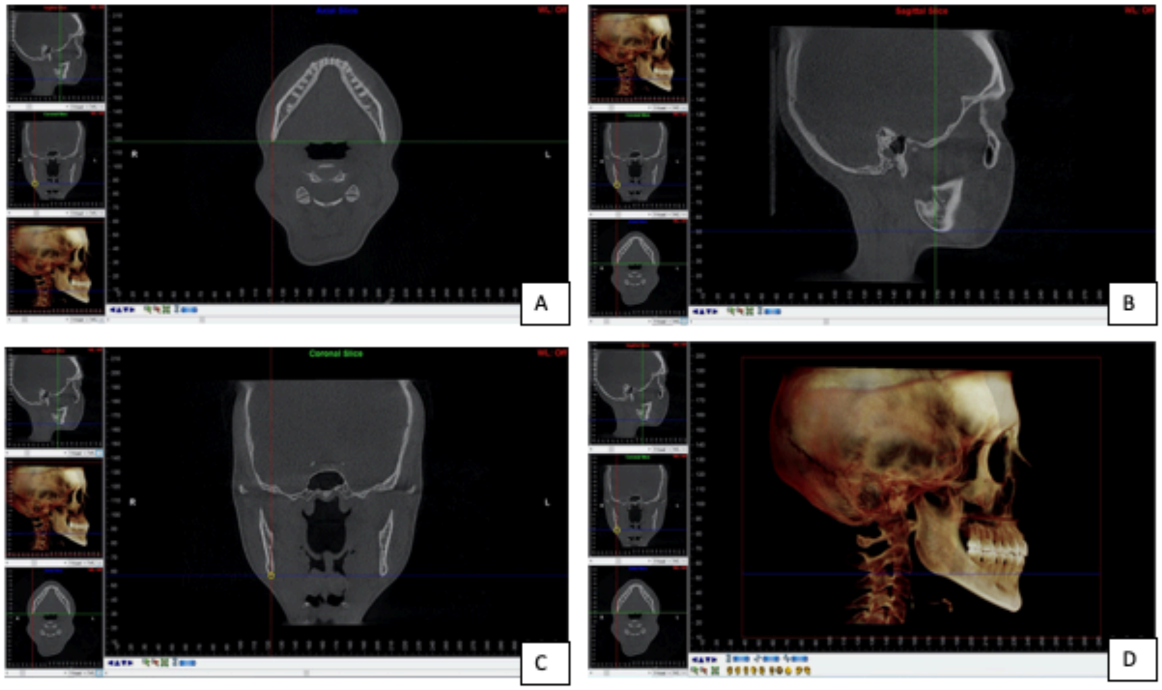

Figure 4. Gonion inferius was identified in three planes of space and confirmed on the translucent volume. (A) axial, (B) sagittal, (C) coronal slices, and (D) translucent lateral view. The coronal slice is where the measurement was taken.

To measure bilateral ramus height before (T1) and after (T2) orthodontic intervention in the study sample, the distance from condylion to gonion inferius was measured in millimeters in the coronal plane. This measurement was taken systematically, always measuring the subject-right then subject-left sides. Measurements for each CBCT were always taken at the same session but total data collection occurred over numerous sessions.

Statistical Analysis

Intra-rater reliability was assessed using intraclass correlation coefficients and Bland-Altman plots (46). Ten right side measurements and ten left side measurements were plotted against their difference from the mean. It is expected that 95% of differences are less than two standard deviations (also defined as 1.96 times the standard deviation of the difference between the measurements) if they follow a normal distribution.

Descriptive statistics for the sample population were calculated. Paired and two-sample t-tests were used to test differences between the right and left side, crossbite and non-crossbite side change, and different groups at T1 and T2 time points for statistical significance. Subgroup analyses by gender were conducted to evaluate gender differences. Analyses were performed using SAS 9.4 (SAS Institute, Cary NC). P values less than 0.05 were considered statistically significant.

Results

The intraclass correlation coefficient (ICC) for the right side was 0.86 and for the left side was 0.74, indicating excellent and good intra-rater reliability, respectively.

Bland-Altman comparison of linear measurements of the *right side* assessed at two different time points yielded a mean difference of 0.09 mm with limits of agreement of -4.51 and 4.69 mm at 95% confidence interval (Figure 5). Bland-Altman comparison of the *left side* assessed at two different time points yielded a mean difference of 0.05 mm with limits of agreement of -4.80 and 4.90 mm at 95% confidence interval (Figure 6). Data points represent the differences between the original measurements and the repeated measurements against the mean.

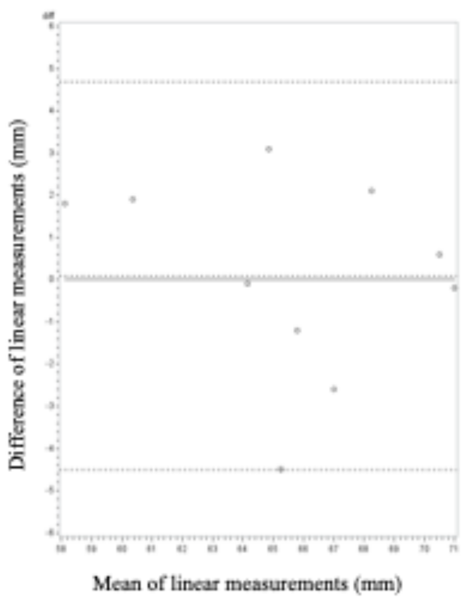

Figure 5. Bland-Altman plot for the *right side*. All the differences lie between the defined limits, indicating good agreement.

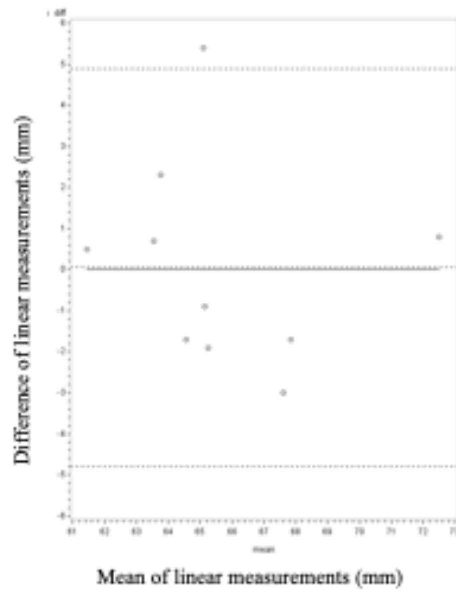

Figure 6. Bland-Altman plot for the *left side*. 9 out of 10 of the differences lie between the defined limits, indicating good agreement.

Mean total ramus height measurements on the crossbite and non-crossbite sides at T1 and T2 with standard deviation (SD) are shown in Table 4.

Table 4. Total ramus height measurements.

Overall (N = 59)	**Mean Total Ramus Height (mm)**	
	T1 (SD)	T2 (SD)
Crossbite Side	60.5 (5.3)	64.6 (4.6)
Non-Crossbite Side	60.5 (5.1)	64.4 (4)

Comparison between ramus height on the crossbite and non-crossbite sides at the start of treatment and the change in ramus height on the crossbite and non-crossbite sides are shown in Table 5. The results of paired t-test showed that the difference between ramus heights of crossbite and non-crossbite side at T1 was not significant (p=0.86). Additionally, on the crossbite side, the change in ramus height from T1 to T2 was significant (p<.0001). On the non-crossbite side, the change from T1 to T2 was also significant (p<.0001). Two-sample t-test found that the difference between crossbite and non-crossbite side change from T1 to T2 was not significant (p = 0.39).

Table 5. Paired and two-sample t-test comparisons of ramus height between groups.

	P Values		
	Overall	Female	Male
Crossbite side vs. non crossbite side at T1	0.86	0.65	0.45
Change from T1 to T2 on crossbite side	<.0001	<.0001	<.0001
Change from T1 to T2 on none crossbite side	<.0001	<.0001	<.0001
Crossbite side change vs. non crossbite side change	0.39	0.14	0.87

The mean change in ramus height, for overall, female, and male, in relation to the crossbite side is shown in Table 6. P values for all comparisons of the change in right- and left-side ramus height to the crossbite side were greater than 0.05, showing no statistically significant change. Overall, and for neither males nor females, two-sample t-tests showed that the change from T1 to T2 on the right side was not associated with the crossbite side. The change from T1 to T2 on the left side was also not associated with the crossbite side.

Table 6. Overall, female, and male changes from T1 to T2 on the right side and on the left side in relation to the crossbite side.

	Crossbite Side	N	Mean **Right-side change +/- SD**	Mean **Left-side change +/- SD**
Overall	Left	32	4.0 +/- 3.8	3.5 +/- 3.2
	Right	27	4.6 +/- 2.7	3.8 +/- 2.5
	P = 0.44			P = 0.78
Female	Left	23	2.7 +/- 2.3	2.6 +/- 2.2
	Right	18	4.1 +/- 2.7	3.4 +/- 2.6
	P = 0.08			P = 0.31
Male	Left	9	7.2 +/- 5.1	5.9 +/- 4.2
	Right	9	5.6 +/- 2.4	4.4 +/- 2.3
	P = 0.40			P = 0.37

Discussion

Unilateral posterior crossbite can present in young age and persist throughout adulthood if left untreated. It has been suggested that untreated UPC can lead to the development of skeletal asymmetry (4, 8, 47). The present study utilized CBCT volumes to examine mandibular ramus heights in adolescents and late-teenagers who presented with a UPC and were treated with RME and FFA. It was determined that crossbite-side and non-crossbite-side ramus heights, defined as the length from condylion to gonion inferius, were not significantly different at the start of treatment and they were also not significantly different at the end of treatment. The change in ramus height over the course of treatment, however, was significant. The age range of subjects in this study, 8 – 16 years old, includes a time of expected, significant normal growth for adolescents, so the difference from T1 to T2 is caused mainly by that growth. Gender was the only other variable evaluated in this study. There was no male-female difference found, which is consistent with available literature (3).

A retrospective study design was chosen, without a control arm, so that subjects were not exposed to ionizing radiation for study purposes only. In addition, the amount of expansion to correct the crossbite was not standardized, which may be a limitation of the present study. Ideally, all subjects would have had the same amount of expansion. However, this would not have been clinically or ethically feasible. The treatment protocol with RME and FFA, however, was standardized. Fifty-nine subjects were included in this study, and while that is a large cohort, a larger study population would have increased the power of the analysis. The landmarks used for measuring ramus height presented difficulties as well. Condylion and gonion inferius have been identified and utilized as landmarks in previous studies (45). A benefit of 3D landmark identification is the lack of superimposed structures, making it easier to visualize certain regions, especially the angle of the mandible which is typically overlapped in lateral and postero-anterior cephalograms (44). However, reproducibly locating any point on a rounded surface can be challenging. Schlicher *et al*. studied landmark identification in CBCT scans and found that landmarks on curves had more errors than those with clear anatomic delineations (48). Specifically, when considering gonion, the vertical dimension was the most inconsistent measurement with a discrepancy of 1.37 mm (left) and 1.78 mm (right), which the authors contributed to lack of clarity in the definition and/or anatomy of the landmark (48). In the present study, the limits of agreement in the Bland-Altman comparison of linear measurements were -4.51 and 4.69 mm for the right side and -4.8 and 4.9 mm for the left side, representing nearly 10 mm of variability around the mean. Despite landmark identification reliability falling within a 95% confidence interval, this large range and low measurement accuracy could be a potential cause for not detecting a ramus height asymmetry.

Previous studies using 2D radiography have been contradictory regarding the presence or absence of mandibular asymmetry in adolescents with UPC. In a study by Santos Pinto *et al*., submentovertex radiographs taken on subjects with UPC before and after treatment were examined (8). The authors found that the mandible on the non-crossbite side was larger than the crossbite side prior to treatment, as determined by measurements such as distance from condylion to the symphyseal point and distance from condylion to the central incisors (8). Kilic *et al.* showed that in adolescents with UPC, the condyle height, ramus height, and condyle-plus-ramus height, measured on panoramic radiographs, were significantly smaller on the crossbite side than on the non-crossbite side (26). In contrast, Uysal *et al*. and O'Byrn *et al*. did not find any pre-treatment mandibular asymmetries in subjects with UPC on panoramic and submentovertex images (3, 37). The findings of the present study were in agreement with the latter studies, and found no statistically significant differences in pre-treatment crossbite and non-crossbite side ramus heights. It must be noted, however, that the previously mentioned studies used 2D radiographs, which are inherently subject to magnification and distortion errors. In addition, the previous studies used inconsistent landmarks which makes it challenging to directly compare the findings in the present study with those from the earlier 2D studies. CBCT images are uniquely suited to assess asymmetry as craniofacial structures can be studied more clearly, without overlap and distortion. The present study utilized measurements from CBCT images, which have been shown by many studies to have better accuracy (9, 43, 49, 50).

Few previous studies utilized CBCT to evaluate mandibular symmetry in subjects with UPC in different age groups. A study by Veli *et al*. examined *adolescent subjects* (mean age 13.5 +/- 2.03 years) with UPC, bilateral posterior crossbite, and a control group. Fourteen parameters were measured and side comparisons were done. The authors found that subjects with UPC did not have statistically significant differences in side comparisons (2). Another study by Halicioglu *et al.* examined *adolescent subjects* (mean age 14 years in all study groups) with UPC, bilateral posterior crossbite, and a control group. Condylar, ramal, and condylar-plus-ramal heights were measured. It was found that all three groups were similar on the right and left sides (52). A study by Leonardi *et al*. used 3D mirroring and surface-to-surface techniques to analyze mandibular symmetry in *adult subjects with UPC* (mean age 27.5 years). Using a computer software program, the mandible was isolated, mirrored and segmented. With the superimposed mandible units, differences in volume could be quantified. Compared to age- and sex-matched controls, mild regional mandibular asymmetry was present in adults with UPC, especially at the condyle, the mandibular angle, the alveolus, and the mandibular ramus (9). Analyzing the results of these studies together seems to imply that although mandibular asymmetry may not be present in adolescence, it likely develops as individuals grow into adulthood.

Mandibular remodeling occurs over the course of time, throughout childhood, adolescence, and adulthood (2, 7, 21, 22). If a UPC is left untreated, it might not present as mandibular asymmetry at 12 years old, but the continued lateral displacement of the mandible in an individual with UPC initiates an adaptive process in the masticatory system, resulting in atrophy of the jaw muscles on the crossbite side as well as bilateral differences in protein compositions and expression (54). In addition to a decrease in size of the muscles and a reduction in the cross-sectional area of the individual fibers, the fiber-type composition shifts towards a higher percentage of fast-type fibers (21). This muscular change in addition to the remodeling that occurs at the temporomandibular joint (both at the condyle and the glenoid fossa) may lead to mandibular asymmetry in adulthood. Other components of the mandible that may be influenced by an untreated

UPC include areas of muscle insertions, and that may be expressed as differences in the degree of mineralization, bone density, muscle attachment morphology and/or volumetric differences. In the present study, no ramus height asymmetry was present over the course of the average treatment time of 3.1 ± 1.3 years. The first hypothesis tested in this study – subjects with UPC have associated mandibular asymmetry expressed as side difference in mandibular ramus height – is rejected. The second hypothesis - subjects with UPC treated with RME and FFA see improvement in asymmetry after treatment – became moot with rejection of the first hypothesis and is, therefore, neither accepted nor rejected.

At the conclusion of treatment, the subjects examined in the present study had no crossbite or associated asymmetry. Petren *et al*. found that the stability of UPC correction with expansion was stable at 3 years posttreatment. In that study, subjects with UPC were compared with controls, and active RME treatment was ceased when normal transverse relationships were achieved (no overcorrection was carried out). The changes in the treated groups at 3-year follow-up were similar and comparable to those in the control group (53). The present study reinforces the suggestion that RME is an orthodontic treatment modality that alleviates UPC in adolescents. The present study evaluated one measure of mandibular symmetry, ramus height, and did not find significant differences in UPC subjects before and after treatment. Additional components, including other measures of mandibular asymmetry – glenoid fossa remodeling, muscular insertion areas, volumetric differences, for example – have the chance of presenting in untreated UPC patients. That being said, this study is not robust enough to warrant changes in the recommendation of the American Association of Orthodontists to treat UPC early (6).

In the current study, there was no negative control arm to see if subjects who were left untreated would have developed asymmetries in the future. Future studies could include retrospective untreated UPC controls to see if untreated UPCs manifest as asymmetries in adulthood. The many avenues which untreated UPC may influence mandibular symmetry need to be studied further such as changes in muscle insertion areas (density, degree of mineralization, size) and continued volumetric work with 3D data. If significant differences in symmetry are found, additional studies could investigate if the asymmetry is clinically significant in facial profile and function.

Conclusions

- In this study, UPC in adolescents was not associated with shorter ramus height on the side of the crossbite
- After treatment with RME and FFA, no ramus height asymmetry was present

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