Volume and shape changes of mandibular condyles in growing patients treated with fixed Class II appliances using CBCT

By

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Abstract

Objective: Evaluate the changes in the mandibular condyle volume and shape in growing Class II malocclusion patients, following the use of fixed functional Class II appliances (Herbst and Crossbow) compared to a control group that did not have any inter-arch Class II appliances. A validated semi-automatic condylar segmentation technique of the pre- and posttreatment 3D CBCT images were used to help understand which appliance might cause more changes.

Methods: Fifty-one growing adolescent patients were randomly allocated to one of the three groups (Herbst appliance, Crossbow appliance, and Control group). A total of 102 CBCT images were taken pre- and posttreatment (average interval was 11.7 months). The pre- and posttreatment CBCT images were segmented using a newly developed and validated semi-automatic condylar segmentation technique. The mandibular condyle volume was assessed using Avizo software. The quantitative assessment of the condyle shape was done using Visualization Toolkit software, and the quantitative assessment of the mean distance differences of the condyle surfaces was done using Iterative Closest Point technique.

Results: A statistically significant increase in condylar volume was observed in all three groups (Herbst, Crossbow and Control) and no significant differences in the magnitude of condylar volumes between the Herbst and Crossbow groups were found. There were no statistically significant changes in the mean distance differences of the condyles shape in all three groups. The three groups (Herbst, Crossbow and Control) expressed different patterns of shape changes with no clear pattern associated with the treatment groups (Herbst and Crossbow).

Conclusion: The use of fixed Class II functional appliances (Herbst and Crossbow) in Class II growing patients is not associated with any statistically significant changes in mean condyle volume and shape. All three groups in this study showed similar increases in condylar volume and no clear patterns of condylar shape changes, suggesting that any changes seen in the condyle volume and shape might be part of overall normal condylar growth.

PREFACE

This thesis is an original work by Ibtisam Al Riyami.

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Chapter 1: Introduction

1.1 Statement of the problem

In orthodontics, skeletal Class II patients are those who present with a mismatch between the maxillary and the mandibular jaw with the majority of them tending to have a smaller and posteriorly positioned mandible (1) and according to the angle classification, the Class II malocclusion is where the lower first molar is distal to upper first molar (1). The skeletal Class II discrepancy treatment can vary depending on severity of the malocclusion and maturation stage (1). In mild to moderate cases it can either be accepted and treated by dental camouflage such as extraction of premolar teeth (1),(2),(3) or improved by using functional appliances (4),(5),(6),(7). In severe cases, it can be corrected surgically once the growth is completed (1),(3). Growing patients who present with mild to moderate skeletal Class II can possibly be treated using functional Class II appliances in an attempt to improve their skeletal and dental discrepancy. The functional Class II appliance is an appliance that aims to posture a patient's mandible to a more forward position and transmits the created pressure from stretching the muscles and soft tissues to the dental and skeletal structures to try to improve the skeletal and dental relationship in growing Class II patients (1). Several types of functional appliances, both removable and fixed, have been developed and used in orthodontic treatment (1). The main difference between removable and fixed appliances is that with removable appliances the clinician relies mainly on patient compliance, whereas with fixed appliances the patient compliance is not a concern since the appliance is permanently attached to the patient. There are different types of fixed Class II appliances available in the market today. Herbst is an example of a fixed Class II appliance that continuously holds the mandible forward by the use of a rigid metal rod which prevent the patient from repositioning the mandibular condyle back in the temporomandibular joint (4). On the other hand, the Crossbow appliance is an example of a fixed Class II appliance that uses coil springs to to push the mandible forward (8). The patient is able to overcome the coil spring force to relocate the mandible posteriorly with the teeth in occlusion (8). The Herbst appliance is expected to induce more changes in TMJ morphology compared to Crossbow appliance, as the Herbst appliance continuously hold the mandible in a forward position. While Crossbow appliance allows full range of movement of the condyle including positioning the condyle in the centre of the glenoid fossa.

Bone remodeling in response to loading conditions is dependent on force direction, force magnitude and force duration (1). The magnitude and direction of force being applied to the condyle is unknown for both appliances. However, the continuous nature of altered condyle position with the Herbst appliance suggests that the more bone remodeling with shape and volume change would result from the Herbst.

The mandibular condyle plays an important role as a growth site of the mandible and, in conjunction with the glenoid fossa, it helps to define the anterior-posterior position of the mandible (1). Functional appliances have been used to enhance the growth of the condyle and facilitate temporomandibular joint (TMJ) remodeling to maximize the overall growth of the mandibular length (1). Advancement of the mandible with functional appliances can produce biomechanical forces at the condyle, which, in turn, may prompt tension of the posterior fibres of the disc in the direction of the mandibular advancement which may increase cellular density and cell to cell interaction (9). This process can lead to stimulation and maturation of the chondrogenic cells which might increase endochondral ossification in the condyle, suggesting possible remodeling of the condyle in response to stimuli (10). With the increase in use of functional appliances, their impact on mandibular condyles is of interest. The majority of previous studies were done investigating either Herbst or twin block appliances since they have been on the market for a longer period (11),(12). Despite this, there is still significant controversy in regard to the impact of functional appliances on mandibular condyle growth/remodeling and the exact mechanism for any noticeable remodeling (11),(12). Some studies suggested that remodeling in the glenoid fossa causes anterior displacement of the condyle while other studies suggested that it causes increased growth on posterior aspect of the condyle with compensatory resorption on the anterior aspect of the condyle (13),(14),(15). The majority of those studies were done using 2-Dimensional (2D) images to study 3-Dimensional (3D) structures. One of the main disadvantages of using the 2D images is the superimposition of surrounding structures particularly in the TMJ area (16), making it difficult to accurately investigate the structure which is may explain why conflicting data is found in the literature.

The development of Cone Beam Computed Tomography (CBCT) has provided clinicians and researchers with a method to generate 3D reproductions of dentofacial structures. This is done with less radiation exposure compared to conventional Computed Tomography (CT) (17). CBCT reconstructions allow for 3D visualization of osseous structures which provides clinicians and researchers the opportunity to investigate complex structures that were difficult to visualize using traditional 2D imaging modalities due to the superimposition (18). Furthermore, the use of CBCT images allows clinicians to distinguish the region of interest within the 3D reconstruction and process the data to convert the region of interest to a 3D model (19). This process is known as image segmentation, and it permits better visualization of the investigated structure and allows clinicians to obtain quantitative measures such as volumes and distances (19). Different segmentation techniques have been developed and used to segment different structures. Segmentation can be completed with manual, semi-automated and fully automated techniques (19). Manual segmentation technique is the gold standard segmentation technique in which the operator manually outlines the frame and borders of the area of interest in each CBCT slice (19). Despite the high accuracy of the technique, the main drawback that it is tedious and time-consuming, and the inter-rater reliability of the technique relies on operator's knowledge and experience (19). The automatic segmentation technique is a promising method in reducing an operator's time to segment structures from CBCT images; however, this technique is less accurate and the use of this technique on the mandibular condyle has not been studied nor validated (20). Semi-automatic segmentation technique is a method where the operator uses an automatic segmentation followed by manual check of each CBCT slice to ensure adequate selection of a particular craniofacial structure (21). This technique reduces researcher selection bias associated with manual segmentation while enhancing efficiency by reducing the time taken to delineate an anatomical structure (19),(21),(22),(23),(24). The use of this technique in mandibular condyles has been validated by Kim and others (21). They reported that the use of semi-automatic segmentation is highly accurate and reliable in mandibular condyle volume assessment (21).

It is critical to understand the potential effect of using fixed functional appliances that advances the mandible on condyle shape and volume. Understanding the effects of such external forces on condyle shape and volume would provide valuable information about the sustainability of such treatments. This information is beneficial for clinical orthodontic practice as it will give insight into to effect of those appliances on the short- and long-term growth of the mandible.

1.2 Research objective

The overall objective of this research study is to determine if there are changes in the condylar volume and shape in growing patients treated with Herbst and Crossbow fixed Class II functional appliances compared to those without any inter-arch Class II mechanics, evaluated using the 3D CBCT imaging method.

1.3 Research hypothesis

Growing Class II patients treated with the Herbst appliance will show more volumetric and shape changes in mandibular condyles compared to patients treated with the Crossbow appliance given that the mandible is in a fixed forward position with the Herbst appliance, whereas with the Crossbow appliance patients may overcome the coil spring force and reposition the condyle posteriorly in the glenoid fossa.

1.4 Research questions

Primary:

1. Are there differences in in condylar volume in growing patients treated with two types of fixed Class II correctors (Crossbow and Herbst) and those treated without any inter-arch mechanics?
2. Are there differences in condylar shape change in growing patient treated with two types of fixed Class II (Crossbow and Herbst) and those treated without any inter-arch mechanics?

Secondary:

1. Are there differences in between left and right condylar volume change treated with fixed Class II appliances?
2. Are there differences in condylar shape change between left and right condylar treated with fixed Class II appliances?

Chapter 2: Literature Review

2.1 Introduction

Orthodontic treatment aims to achieve stable Class I dental occlusion (where “mesial buccal cusp of the maxillary first molar aligns with the buccal groove of the mandibular first molar” (1)) along with harmonious facial esthetics. The Class II malocclusion is estimated to occur in one third of the American population (24) and presents as a discrepancy between the upper and lower jaws where the lower jaw is usually underdeveloped. The treatment of patients with Class II malocclusion depends on the cause, severity, growth potential, and the patient’s desires and expectations for treatment outcome (25). Functional orthopedic appliances can be used to improve the Class II malocclusion discrepancy in growing patients. Numerous studies have been published to assess and understand the method and effect of using functional appliances in the correction. Despite the long history of some of the functional appliances, the effect of such appliances on the mandibular condyle, which is considered a growth site of the mandible, is still not fully established since the majority of studies were done using 2D imaging modalities (e.g., 2D cephalometric image). Such methods come with limitations in terms of accurately identifying the landmarks, especially in the TMJ area due to the superimposition of the surrounding structures, and lack of 3D analysis such as shape and volume.

The introduction of CBCT imaging into dentistry and orthodontics has been instrumental in providing the clinician with better 3D diagnosis and treatment planning tools (1),(26). Several studies have explored the use of CBCT in TMJ (27),(28). These studies reported that CBCT is better than the conventional radiographic method such as a panoramic image in assessing the TMJ osseous structures and abnormalities (29). It was also reported that CBCT helps to clarify the morphological aspect of the mandibular condyle including shape, volume, location, and symmetry of the condyles which is impossible to analyze using 2D images (30).

This chapter aims to review literature that describes the effect of using fixed Class II corrector appliances on the TMJ using 3D imaging modalities. Although there are a number of fixed functional Class II appliances used in clinical practice, this review will focus primarily on the use of the Herbst and Crossbow appliances and their role in correcting the Class II malocclusion as they will be the focus of this thesis.

2.2 Review of TMJ structure and effect of mechanical loading

The TMJ connects the mandible, lower jaw, to the rest of the skull. Understanding the anatomy and the role of the TMJ in growth is critical to better understand and predict the effect of using different appliances that aim to stimulate the growth of mandible and lower facial structures.

The TMJ consists of the mandibular condyle that articulates relative to the glenoid fossa and articular eminence of the temporal bone (Figure 2.1). The articular disc is normally interposed between the condyle and the articular eminence to prevent direct bone-on-bone contact and minimize functional loading of the condyle (31),(32),(33). The biconcave articular disc is a fibrocartilaginous tissue made mostly of type I collagen (34). The articular disc divides the TMJ into upper and lower compartments and plays an important role in TMJ function and jaw movement (35). The upper compartment allows sliding movement of the mandible, while the lower compartment permits rotational movement (36). The internal surfaces of the joint cavity are filled with a synovial fluid which is secreted by the specialized endothelial cells (36). The synovial fluid serves as lubricant between articular surfaces during function to minimise the friction. Moreover, the synovial fluid is considered the main source of metabolic nutrition for the joint (37). The articular disc and the body articulating surfaces are enclosed by the articular capsule which has ligament, tendon, soft tissue, and muscles augmented to it to provide stability of the joint during function (38).

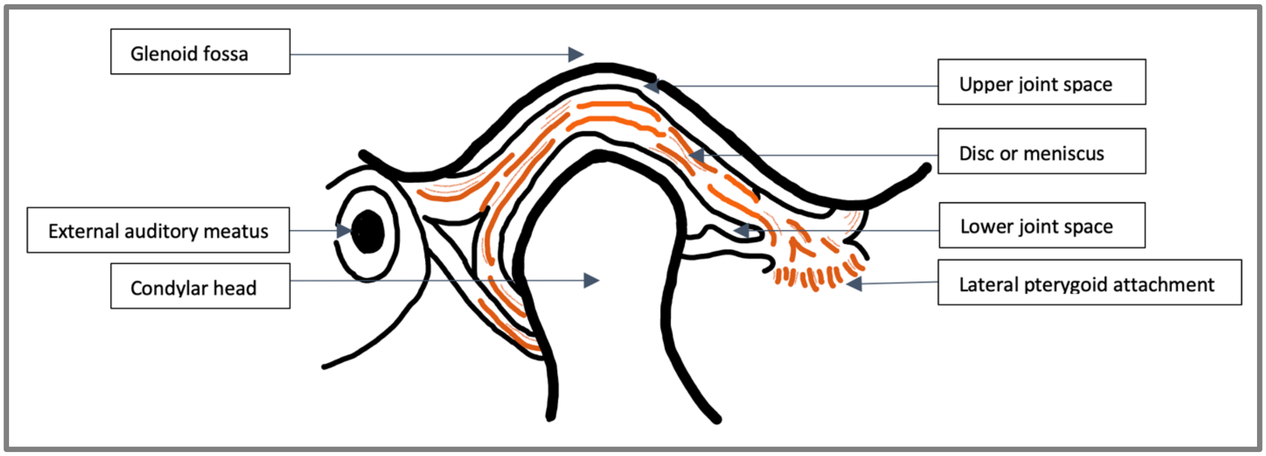


Figure 2.1 TMJ anatomy

The human masticatory system permits the movement of the mandible by allowing the movement of mandibular condyle in the TMJ through contractions of the masticatory muscles (39). During both normal functions such as chewing and abnormal function such as bruxism, the joint is exposed to mechanical load. There are three types of mechanical loading modalities the TMJ experiences: compression, tension, and shear (39). A systematic review which investigated the effect of mechanical load on the metabolic activity of the TMJ joint concluded that the mechanical loading of the TMJ plays an important role in stimulating the mandibular growth and homeostasis of TMJ cartilage by promoting stimulation and maturation of the chondrocyte cells within the condylar cartilage and increase amount of collagen type I and II (40),(41). However, sustained or excessive loading can adversely affect the joint and lead to breakdown of the cartilage and reduce the stiffness of the fibrocartilaginous network (40),(41). This allows the proteoglycan water gel to accumulate and escape to the joint space causing softening of the articular surface. This process is known as chondromalacia (36) and it can initially be reversed by unloading the joint such as wearing a mouth guard or splint to prevent excessive loading of the TMJ. However, irreversible changes can occur to the articular tissues if the load continues causing irregularities on the surface and sticking of the articular surfaces which can change condylar movement mechanics (42). Another consideration with loading the TMJ is the hypoxia-reperfusion theory, where excess load can exceed the intra-articular pressure of the TMJ, supressing the peripheral arteriolar pressure and potentially resulting in hypoxia. During hypoxia, local cells at the TMJ undergo a shift in metabolism leading to production of free radicals which are released into the synovial joint (43). The free radicals, such as superoxide anion and hydroxyl radicals, are highly active molecules and can cause changes in intracellular and extracellular matrix as well as activation of extracellular matrix such as DNA damage, extracellular matrix turnover, and lipid oxidation (44). The free radicals at the TMJ joint can result in reduction of synovial fluid viscosity, reduction of lubrication of the articular surface, activate cartilage degrading enzyme such as matrix metalloproteinase and breakdown the collagen proteoglycan at the joint (44). When that occurs, the protective layer can be lost resulting in friction of the joint which can lead to disc displacement (45).

2.3 Mandibular growth and remodeling

Understanding the stage of condyle growth can help the orthodontist evaluate the growth potential for each patient and anticipate the treatment response. A study was conducted by Buschang et al, to create sex specific data for the incremental growth of the mandibular condyle (46). A total of 113 male and 108 female subjects between the ages of 6 to 16 years old were followed annually where the condyle growth was assessed using lateral cephalometric images. They concluded that the males have a mean vertical condylar growth ranging between 2.1 and 3.1 mm/year. It was also noted that the growth decreased during childhood and increased during adolescence. The males reached a maximum of 3.1 mm/year by age of 14.5 years old. On the other hand, the females had a more constant rate of condylar growth at approximately 2.0–2.7 mm/year during childhood. In their adolescent peak they showed less condylar growth of 2.3 mm/year around the age of 12.2 years old. The females also had a rapid decrease in the growth following adolescence (46).

The TMJ condyle cartilage is a secondary cartilage capable of regional adaptive growth (1). There is still controversy in regard to mandibular growth and whether it is derived genetically or by influence of the environment (47),(48),(49). The first school of thought is that the mandibular condylar cartilage grows under genetic control which leads to forward and downward positioning of the mandible (47),(48). The second thought is that the cartilage is controlled indirectly by genetics (epigenetics) and the cartilage responds to signals from the surrounding soft tissues such as skeletal muscles (49). As the mandible moves forward and downward in response to the stimulation from the soft tissues, the mandibular condyle responds with increased growth on the posterior/superior aspect and compensatory resorption along the anterior aspect of the condyle while maintaining condyle/fossa articulation (49). Proffit suggests that interlocking of the occlusion influences the mandibular forward translation (1). The maxilla undergoes a downward and outward movement simultaneously with mandibular growth and therefore the occlusion state is maintained. The nature of TMJ growth modification is still not fully understood and not clearly explained.

The remodeling process of the TMJ can be classified as progressive or regressive (50). In progressive remodeling, proliferation of the articular tissue occurs which result in thickening of the articular tissues along with the calcification of the subchondral bone subsequently the calcified cartilage is invaded by the vascular tissues from the adjacent structures which result in resorption of the calcified tissue and lay down of new bone (50). The new bone will slowly advance in the joint space to replace the resorbed calcified cartilage tissue and, as that happens, the cartilage above the resorbed calcified tissue will continue to remodel and proliferate to maintain the integrity of the joint. On the other hand, the regressive remodeling of the bone resorption takes place where bone is removed over time by the osteoclast cells which produce a defect in the tissues and as it progress the defect gets filled with mesenchymal tissue which later differentiate to fibrous connective tissue and fibrocartilage (50). In this type of remodeling the subchondral bone resorbs away from the articular surface (50). In the mandible, endochondral ossification occurs in the condyle (51) with intramembranous ossification in the glenoid fossa (52). The effect of remodeling varies between people because of different composition and thickness of cell layers (52).

Animal studies in rats were done to evaluate the effect of growth modification appliances on condyle remodeling processes and it was reported that the stress from forward positioning of the mandible enhances maturation of the chondrocyte which increases the synthesis of type II and X collagen that contribute to endochondral ossification and condylar adaptation (51),(52). It was also suggested that treatment duration, force direction, magnitude, and loading modality (e.g., tension vs. compression) play a role in the amount of changes seen in the mandibular condyle (52). Moreover, it was found that forward positioning of the mandible also stimulates the remodeling of the glenoid process, leading to bone formation in the anterior, middle and posterior of the glenoid fossa, with highest level of bone formation in the posterior region (53).

2.4 Review of TMJ Imaging

A number of image modalities have been used to assess the TMJ, including Magnetic Resonance Imaging (MRI), Panoramic radiography, CBCT, CT and arthroscopy (54). MRI is a non-invasive 3D imaging technique and has been the gold standard for the soft tissue examination of the TMJ including disc position and configuration (55),(56),(57). MRI utilizes powerful magnets which produce a strong magnetic field that forces the body protons to align with that field and once the radiofrequency field is turned off, the protons will realign themselves and during that process a sensor can detect the energy released from each proton as they realign (57). The main limitation of this technique is the low sensitivity in detecting osseous changes in the TMJ which are commonly of interest in studying clinical treatment outcomes (58).

The use of a 2D panoramic radiograph in assessing TMJ is considered inexpensive and a relatively simple and quick technique to assess the gross TMJ osseous structures while exposing the patient to a low radiation dose compared to 3D imaging modalities (54),(59). The X-ray source and detector rotates in a semi-circle around the patient's head. The machine projects the X-ray beam to the patient and into the detector on the other side (60). This imaging modality, however, has several limitations. For instance, the semi-circular rotation of the X-ray beam, results in superimposition of different structures such as the zygomatic process from one side to the opposite side (61). This would in turn produce a distorted image (61) with acceptable reliability to evaluate the condyle while a poor reliability in assessing the temporal component (62),(63). Moreover, the image modality has low sensitivity (64) and limited visualization of the entire TMJ structure (27).

Transcranial 2D imaging technique is a non-invasive technique that is normally used to provide a sagittal view of the lateral aspect of the condyle (60). When the patient is positioned at the cephalostat (an instrument used to orient and position the patient's head to ensure reproducibility of the produced image), the X-ray beam is directed 25 degrees down and 20 degrees anterior of the TMJ of interest (60). It was reported that this technique is more accurate in detecting freedom of diseases (25-56% of the time). However, a study was done that reported the technique showed a high false negative result (44-74%) (65).

The development of the liner or complex motion tomography helped to overcome the superimposition limitation of panoramic radiograph. The sagittal tomography was considered the standard modality of choice to assess the TMJ osseous structures (66). The liner tomography is a 3D imaging technique where the X-ray tube is moved in a straight line in one direction while moving the detector in the opposite direction. The X-ray tube produces beams that hit the body structures while the patient is in the supine position. The structures that coincident with the pivot point are in focus while other structures will be blurred. It was reported that sensitivity (true positive) of tomography in detecting osseous changes ranged from 53% to 90% and the specificity (true negative) ranged from 73% to 95%(67). Moreover, it was reported that the tomography underestimates any small osseous changes that can be seen in the TMJ and therefore reduces the accuracy of the image modality (68).

The Computed Tomography (CT) imaging modality showed a superior image quality to assess the osseous structures of the TMJ when compared to linear tomography radiograph in terms of contrast and spatial resolution (69). The CT is a 3D imaging technique using an X-ray beam that rotates around a circular opening of a donut shaped structure called a gantry while the patient is positioned supine on a bed (60). CT images are detected using digital X-ray detectors situated on the other side of the object of interest which are then transmitted to a computer. The images can either be displayed individually or reconstructed to form a 3D image. It was also reported that CT has a sensitivity of 75% and a specificity of 100% for detecting any osseous changes with a positive predictive value of 100% and a negative predictive value of 78% (70). The CT imaging modality comes with some limitations including the high cost, more patient radiation exposure and limited access to the equipment (66).

The introduction of Cone Beam Computed Tomography (CBCT) imaging modality allowed the clinician to use 3D reconstructed images while reducing the patient time, cost and radiation exposure compared to CT scans (71). The CBCT technique is done by using a rotating gantry to which an X-ray source and detector are fixed. A divergent X-ray beam leaving cone shaped source to the patient is then detected by the X-ray detector (60). The CBCT has been reported to be superior to panoramic radiograph in terms of reliability, sensitivity, and specificity in detecting any osseous changes (72). CT showed a superior image quality to assess the osseous structures of the TMJ when compared to CBCT in terms of contrast and spatial resolution (69). Although the CT is a superior imaging modality for the assessment of detailed osseous changes in TMJ, the use of CBCT has increased over the years (73) and it has been recognized as a reliable imaging modality to evaluate the TMJ osseous structures, bony contours, and positional relationship between mandibular condyle and fossa (27),(74),(75),(76).

2.5 Review of CBCT

The reconstruction of a 3D CBCT image from the individual 2D X-ray projections can be broadly divided into two steps: image acquisition and image reconstruction. Image acquisition is the process of generating the X-ray beams that get released from the X-ray tube. The process starts with heating the cathode by an electrical current which then generates electrons that attracts to the anode generating heat and small amounts of electromagnetic radiation (77) as seen in the Figure 2.2. The beam that is directed towards the aperture and towards the detector is the only beam that leaves the tube. The tube current and exposure time (mAs) are directly proportional to the amount of x-ray photons leaving the tube. Therefore, changing the current will only affect the radiation dose exposure (77).

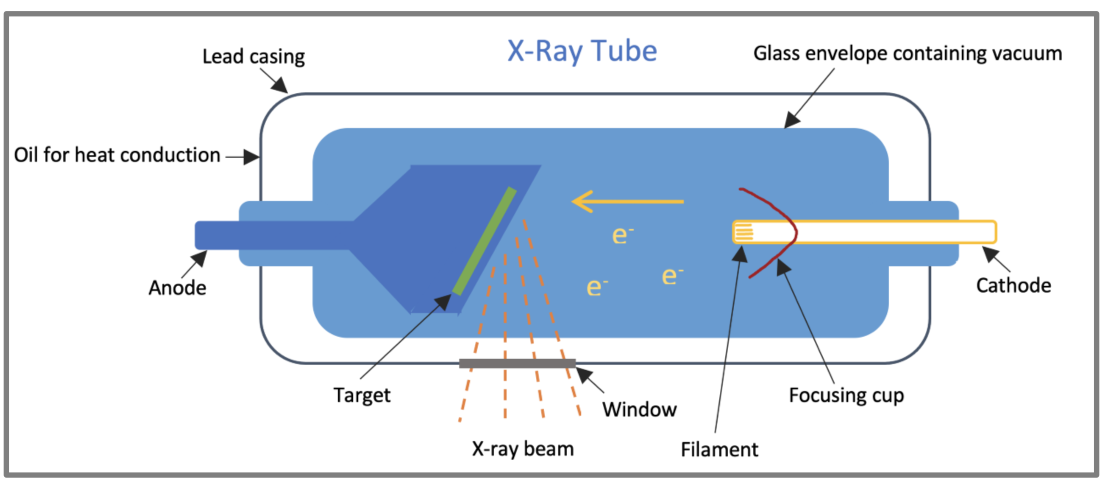


Figure 2.2 Simple schematic of X-ray tube.

Field of view can be adjusted by determining the size of the physical colimitation of the X-ray beam. As the scanner rotates between 180 to 360 degrees, for 10 and 40 seconds, hundreds of 2D images of the region of interest are produced (77). Soft tissues in the region of interest will allow the X-ray beam to pass through and appears darker while hard tissue will absorb the X-ray and prevent the beams from passing through hence appearing lighter. The source-to-object distances and object-to-detector distances differ between scanners, and this plays an important role in determining the sharpness of the images as can be seen in Figure 2.3. The un-sharpness edges of the image are referred to as Penumbra (77).

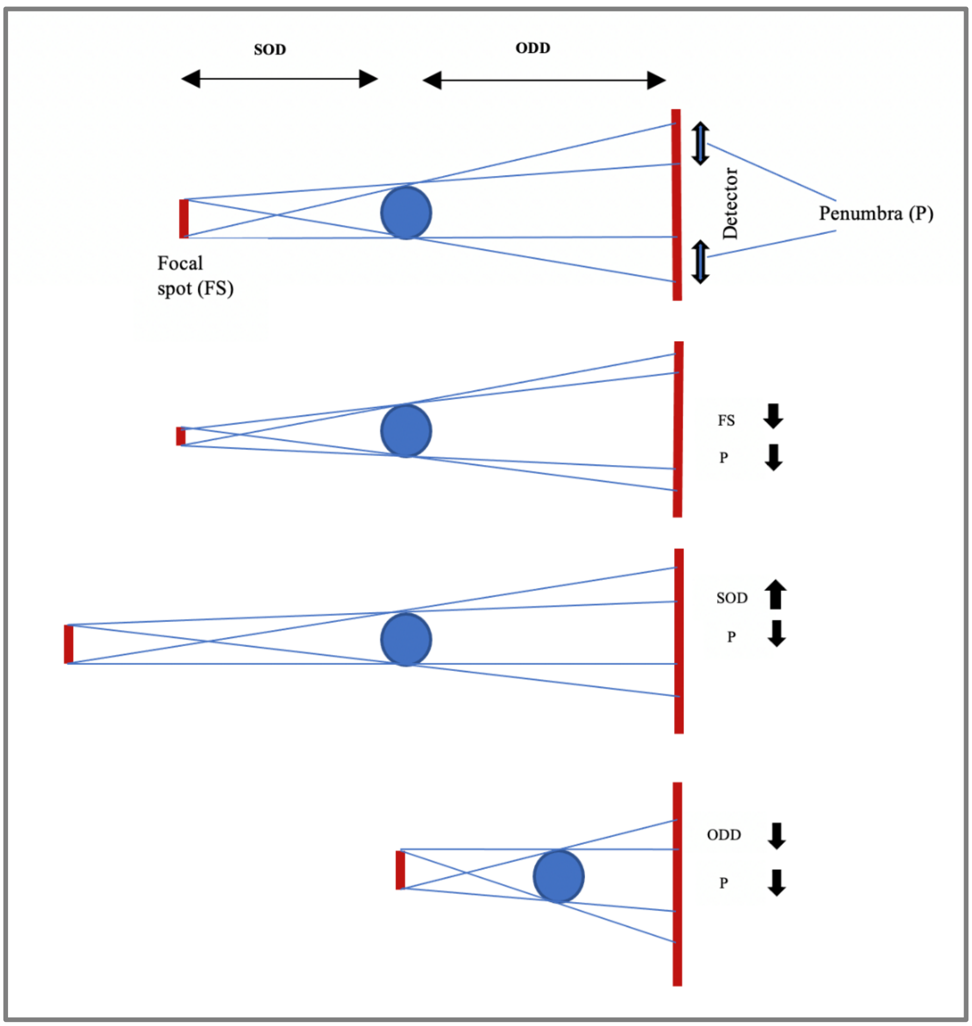


Figure 2.3 Effect of Focal Spot (FS) size. Source to Object Distance (SOD), Object to Detector Distance (ODD), penumbra (P). Small FS, larger SOD and smaller ODD all reduce the penumbra width hence increase image sharpness.

The second step is to reconstruct all the 2D images that reached the detector into a 3D image. Each of the 2D raw data is composed of pixels that have a different grey value according to the X-ray intensity (61). The 2D raw data undergo a preprocessing step before the 3D reconstruction, where any defect between the detector pixels and the detector such as faulty pixels or projection are corrected, to produce a clean processed data set (60). The reconstruction of the 2D image in CBCT happens by transforming the scanned object into a 3D matrix of voxels where each voxel has a voxel size in all three planes (axial, coronal and sagittal). The image reconstruction most commonly used is the filtered back-projection technique using the Feldkamp Davis Kress algorithm (60). The first step of filtered back projection is to calculate the location of each X-ray beam that passes the voxel matrix to the detector. Then invert or back project the measured X-ray beam from the detector back to the 3D matrix of voxels where attenuation coefficient of each voxel size is determined, this process is repeated for every voxel in all planes and projections (60). The final 3D matrix then undergoes a different process to improve the blurriness and enhance image sharpness (60). The final 3D image develops into one image which is known as a sinogram (60).

The detail and resolution of the CBCT image is influenced by the physical pixel size of the detectors. The smaller the detector pixel size, the better the spatial resolution. However, reducing the pixel size will also increase the image noise (77). Moreover, the voxel size (3D analog of the pixel) of the reconstructed image can affect the spatial resolution (77). The CBCT images generally use small detector pixels and smaller image voxels which give it a good spatial resolution. However, the CBCT images when compared to CT images have poorer contrast resolution and nosier images due to radiation scatter (deflected X-ray beam), smaller detector pixels, and lower tube output (77).

2.6 Review of CBCT image quality parameters

There are several parameters which impact the quality of CBCT images. Some of the parameters vary between machines and can be adjusted such us the Field of view (27). It is important to adjust the parameters for optimal visualization of a particular structure. The following parameters affect image quality: contrast resolution, special resolution, noise and artefact (27) (77). Contrast resolution is the ability to distinguish between two objects based on the differences of their radiodensity that are displayed with different grey scale (78). Contrast resolution in CBCT imaging is limited due to the use of a short object to detector distance and low tube output (i.e. kV and mAs) which results in a higher amount of scattered radiation affecting the resolution (78).

Spatial resolution describes the ability to distinguish between two structures that have different densities and are near each other. It is related to the voxel size, where the smaller the voxel size the greater the spatial resolution (79). Pixel density at the detector and fill factor also play a role in spatial resolution (77). The fill factor is the area of radiosensitive elements to the total pixel area. The smaller the detector pixel sizes, the better spatial resolution (77). However, reducing the pixel size would increase the image noise because that would result in a smaller variation of the grey value between the adjacent structures (77). Other factors that can affect spatial resolution include patient motion, focal spot size, beam geometry, scatter, and the reconstruction algorithm (79). Partial volume averaging is an important concept to understand. A voxel represents one grey value and any adjacent objects with a different density that encompassed within one voxel will produce a beam attenuation that is an average of both tissues (80). This will affect the ability to distinguish the boundaries between the two objects especially small structures, therefore reducing the spatial resolution (80).

Another parameter which affects image quality is image noise which refers to the random variation in gray value of an image with a uniform density (77). The measurement noise can be caused by random interaction of the x-ray with detector or by the detectors during the conversion and transmission (77). Finally, image quality can be affected by image artifact which refers to any random object which appears on the acquired image that does not correspond to the real object (77). The main source of artifacts in CBCT is related to X-ray scatter which refers to the deflection of X-ray beam from their original path as they contact high density materials such as the dental implant, amalgam dental material, or orthodontic appliances, leading to shading and streaks similar to beam hardening effects (81). Another source of artifact is patient motion present as a double contour which can be reduced by reducing exposure time (81). Additionally, some artifacts can be caused by the scanner itself and appear as circular dark rings in the axial plane centred around the axis of rotation (81).

2.7 Review of mandibular condyle segmentation techniques

Segmentation techniques assist orthodontists to delineate shape, volume and position of craniofacial structures from reconstructed 3D images. There are various segmentation techniques that have been developed to define the mandibular condyle accurately. Manual segmentation is a technique in which the researcher manually outlines the frame and borders of the area of interest in each CBCT slice (82). Once all the 2D slices are done and the boundaries are selected, each two adjacent points in a boundary will be sampled with the same number of points. Next, all the sampled points from the 2D slices will be stacked together following their pixel distance from the CT scanning. This technique has been extensively studied and demonstrated to have high accuracy and reliability in segmenting the condyle (82). As one might anticipate, this process is time-consuming and has variable inter-rater reliability due to evaluator bias which limits its use in regular daily clinical practice (82). It might not be easy to use this technique where clinicians tend to have a busy schedule with limited time between patients and all clinicians have different clinical experience which might impact the result and make it hard to compare the clinical results.

Another technique is known as the threshold-based segmentation technique. This technique is similar to the manual segmentation technique where the operator would use software to adjust the threshold of the gray value to sculpt and segment the area outside the area of interest instead (83). The main difference between the manual segmentation technique and the threshold-based segmentation is the segmentation area, where in manual segmentation the area of interest is segmented and in threshold-based segmentation technique the surrounding structures are segmented. Subsequently, what is left behind becomes the segment used for analysis. In other words, it eliminates the region outside the area of interest in this case is a mandibular condyle. The downside of this technique is that it relies heavily on the experience of the operator in order to delineate the boundaries of the area of interest which can affect the accuracy of the final analysis result (83).

Semi-automatic segmentation was developed in order to reduce the subjective bias from other fully manual segmentation techniques and allow the operator to use an automated process followed by a manual check to improve the precision of outlining the area of interest (19). During the segmentation, each voxel image is labelled according to their greyscale value to identify and separate the objects in 3D image. The operator selects the best grey threshold value that distinguishes the region of interest from the surrounding structure and automatically applies that grey threshold value to all the slices. Once the automatic segmentation is done, the operator then checks every single slice to ensure that the area of interest is accurately outlined. Each of those labelled voxels will be used to determine the overall condyle volume (19),(22),(23). A recent systematic review was conducted to evaluate the accuracy and reliability of the various segmentation techniques of the mandibular condyle using CBCT imaging (84). It was concluded that manual segmentation has the highest accuracy; however, the accuracy relies on operator experience. On the other hand, the semi-segmentation technique showed high reliability without adequate data on accuracy of the technique. Kim et al. later investigated the accuracy of the semi-automatic technique in evaluating the condyle volume by comparing the CBCT image and physical models of the same objects. They concluded that the semi-automatic segmentation showed strong accuracy and reliability with interclass correlation coefficient of 0.988 [0.918, 0.998] between the physical models and the segmented CBCT image and reported no statistical difference between the measurement in terms of condyle volumes (21).

2.8 Review of Fixed Class II appliances (Herbst and crossbow)

The Herbst appliance was first introduced in 1905 by Emil Herbst at the Berlin Dental congress (85). However, the appliances were not widely used until Hans Pancherz brought it back to attention in 1979 (1). The Herbst appliance consist of two tubes, two plungers, two rods and screws as seen in Figure 2.4. The appliance aims to continuously and rigidly protrude the mandible to end to end incisor position with maxilla to stimulate the growth of the mandible (1).

The crossbow appliance was introduced in 2002 by Duncan Higgin as part of phase I treatment of Class II malocclusions (8). The appliance pushes the mandible forward by the use of flexible coil spring instead of rigid rods (8). The appliance consists of maxillary expander, lower lingual and labial bow and forsus fatigue resistant device springs (3M Unitek, Monrovia, Calif) as seen in Figure 2.5 (8). The maxillary expander has bands on the first molars and rest seats on premolars. The coil spring is inserted at the headgear tube of the upper first molar and connected to the lower labial bow at canine-first premolar region that advances the mandible to correct the Class II malocclusion (Figure 2.5). The device can easily be reactivated without the use of any shims, through the reactivation of the Gurin lock in the lower bow. The lower bows are in passive contact to the mandibular teeth. The coil spring is not rigid and allows the patient to move the mandible freely to overcome the forward position of the mandible (8). The main difference between the two appliances is the type of force applied, with Herbst appliance the mandible is continuously hold in a forward position by a metal rod, while Crossbow appliance the mandible is pushed forward with the use of coil spring which patient can overcome and reposition the mandible posteriorly.

Figure 2.4 Clinical picture of Herbst appliance

Figure 2.5 Clinical picture of Crossbow Appliance

2.9 Review of current understanding of the effect of the fixed Class II appliances on the TMJ

Forward positioning of the mandible with the use of functional appliances appears to alter the stress state of tissues within the TMJ (86). Finite element analysis permits further understanding of the effect of stress in structure. Chaudhry et al, studied the effect of fixed functional appliances (Forsus appliance) on the condyle using finite element analysis and they concluded that stress levels within the condyle are doubled with the use of flexible fixed functional appliances (86). Therefore, according to the Chaudhary et al study the Crossbow appliance that uses springs to advance the mandible might induce more stress to the condyle. Another study by Shrivastava et al reported that there is accumulation of tensile stress in the posterior superior portion of the condyle and on the posterior aspect of the glenoid fossa with the forward positioning of the mandible (87). Chu et al, reported that there is a compressive force on the anterior superior of the condyle with the use of the functional appliances (88).

In 2003, a systematic review was done to evaluate the effect of Herbst appliances on the TMJ (89). They included all studies from 1966-2001, and five studies fulfilled the inclusion criteria. In four of the studies, MRIs was used and one study used linear tomography. It was concluded that due to lack of randomized control trial and quality of included studies, no conclusion on the nature of condylar and glenoid fossa and disc position could be made.

In 2015, a systemic review was published evaluating the effect of the fixed Class II appliances on the TMJ using a 3D image (11). The study included all the articles until May 2015. Fourteen articles were included in the study, where 12 used MRI, one used CT, and one article used CBCT images. None of the studies were completed using crossbow appliances. Due to the high risk of bias in gender as a confounding variable, blinding, and lack of a control group for comparison, no conclusion was drawn on the effect of the fixed Class II appliances on the TMJ (11). Another systematic review which was done in 2016 assessed the skeletal changes of the fixed functional appliances (90). Based on a weak level of evidence, they concluded no significant changes were found following the use of fixed functional appliances.

In 2016 another systematic review was published to evaluate the effect of all types of functional appliance on TMJ. They concluded that the use of mandibular advancement appliances resulted in forward displacement of the condyle, remodeling of the condyle and adaptive changes in the glenoid fossa. There were no significant adverse effects of using the appliances on the TMJ identified. However, the systematic review had multiple limitations; lack of randomized studies, lack of methodological homogeneity, small sample sizes, different treatment time, and the use of different appliance design. (91).

More recently another systematic review with a meta-analysis was done to evaluate the effect of the functional appliances on the TMJ (12). They included all the studies up to June 2019, where a total of 11 articles met the selection criteria and were included in the study. In the current systematic review, they evaluated the effect of normal growth by including studies with control groups and they determined the risk of bias of using nonrandomized studies. Most of the included studies used MRI and only one study used a CBCT image to evaluate the TMJ after the use of twin block appliances. None of the studies were done evaluating the crossbow appliance.

In regards to the skeletal and positional changes of the TMJ, they found some evidence that the treated group had increase in mandibular condyle width after 6-9 months. However, the effect was small and close to measurement error. Moreover, they found small increase in condylar dimension and volume post treatment with anterior and inferior displacement of the condyle. They also reported some displacement of glenoid fossa following the use of functional appliances.

In 2019 a study was published which assessed condyle glenoid fossa relationship after the use of Herbst appliances during different stages of craniofacial skeletal maturation using CBCT images (92). They found no statistically significant changes in the condyle-glenoid fossa relationship with the use of Herbst appliances. Cheib et al. using CBCT images reported that after the use of Herbst appliance the condyle was displaced anteriorly and inferiorly with no difference between left and right sides (93). They also noted that with each 1mm correction in overjet with the appliance there is about 0.95mm anterior displacement of the condyle (93), which suggests that the correction of the overjet with the use of Herbst appliance, was achieved by condyle glenoid fossa remodeling rather than condylar growth.

A 2020 study evaluated 3D condylar changes using mandibular 3D regional superimposition techniques in adolescent patients treated with Herbst appliances followed by multibracket treatment (94). The sample included 20 patients with Herbst appliances compared with 11 patients who were treated with Class II elastics. The CBCT images were taken before treatment, 8 weeks after Herbst removal, and after the completion orthodontic treatment. An automatic segmentation method was used, and the mandibles were then superimposed using 3D voxel based mandibular superimposition after manual selection of the landmarks. The condyle growth was determined by measuring the distance difference of the selected landmarks on the condyle in different timeline. The study reported that the two-phase treatment had additional of 0.96mm posterior and 2.27mm vertical growth in the condyle, however it was not statistically different than what is seen in the compared group.

Another 2020 study was also published which used 3D CBCT images to assess the condylar effects of Herbst appliances in 20 growing patients (6 males, 14 females; mean age ±

SD: 12.76 ± 0.89 years). There was no control group; they compared the treatment group to a model for normal growth of mandible that was done based on the population. The study used a non-validated automatic segmentation technique. The pre- and post CBCT images were superimposed using a marker-based water-shed transform technique. They concluded that 85-100% of the Herbst group showed significant increase in condyle length by outward growth at the mandibular condyle head (less than 0.5 mm) and 40-50% had 1.5-2mm increase in mandibular condyle length and very small number of cases had more than 1.5mm (95).

In conclusion, due to methodologic limitations in published studies, there is still a paucity of evidence regarding effects of fixed functional appliance treatments on condyle size and shape. For example, lack of control group comparison, lack of randomisation, use of small sample size, use of a non-validated segmentation technique, lack of an appropriate imaging modality to evaluate the bony structure of the condyle and lack of methodological homogeneity. Moreover, no studies were done to evaluate the effect of crossbow appliances in TMJ, as the majority of studies looked at Herbst and twin block appliances.

Chapter 3: Condyle volume and shape changes in growing patient treated with fixed Class II corrector appliances (Herbst and Crossbow) using a semi-automatic mandibular condyle segmentation technique

3.1 Introduction

Angle Class II malocclusion is the most common orthodontic malocclusion occurring in 33% of the North American population (24). There are many types of functional Class II treatment appliances available in the market today. Such appliances aim to improve the anteroposterior relationship between maxilla and mandible by stimulating an orthopedic effect to enhance the overall growth of the mandible and improve the Class II malocclusion through a combination of skeletal and dental effect (1). Functional appliances can be removable or fixed (i.e., permanently attached to the patient).

A Herbst appliance is a type of fixed functional Class II appliance that has been in the market since 1930 (1). The Herbst appliance, as shown in Figure 3.1, functions by holding the mandible forward and maintaining that position until class I occlusion is achieved by multiple factors including remodeling and soft tissue readjustment (1). A Crossbow appliance, as shown in Figure 3.2, is a newer fixed Class II corrector appliance that has been gaining popularity (8). The main difference between Herbst and Crossbow is the type of arm that is used to advance the mandible. With a Herbst appliance, a fixed and rigid metal rod is used to maintain the mandible in a forward while in a Crossbow appliance a coil spring is used to push the mandible forward (8). Therefore, Herbst appliance rigidly and continuously hold the mandible forward, while the Crossbow appliance exerts a spring force on the mandible to push the condyle towards a more anterior position and patient can reposition the mandible posteriorly.

Figure 3.1 Clinical photo of Herbst appliance

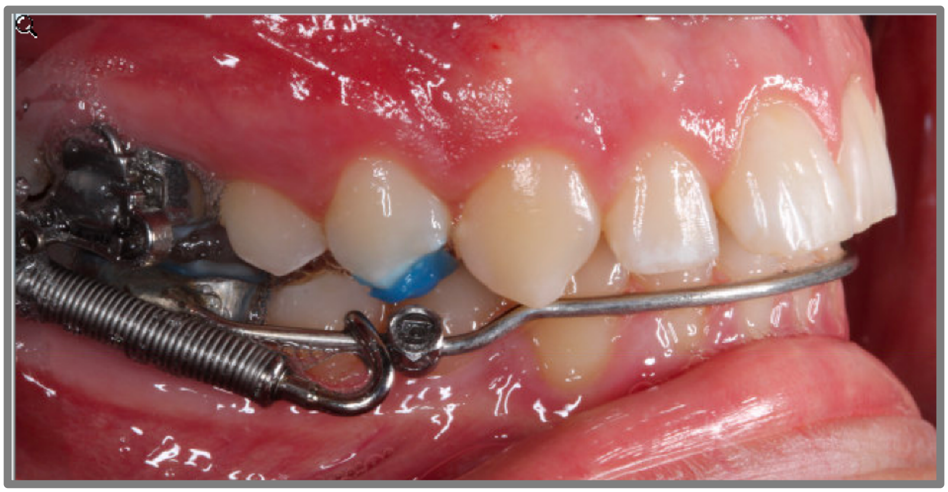


Figure 3.2 Clinical photo of Crossbow appliance

Several studies have looked into the short- and long-term dentofacial effects of fixed Class II corrector appliances. Most of the published literature focuses on the positional changes of the condyle within the TMJ using either 2D or 3D imaging modalities such as 2D cephalometric or 3D MRI (11). The majority of studies have looked at the Herbst appliance as it is the oldest fixed functional appliance to-date and there is a lack of studies looking at newer appliances such as Crossbow.

The TMJ is a complex structure consisting of a mandibular condyle that articulates with the glenoid fossa and articular eminence of the temporal, articular disc, temporomandibular ligaments and joint capsule (35). The mandibular condyle under certain loading conditions can undergo adaptive growth and/or remodeling (9). The literature regarding the impact of fixed functional appliances on components of the TMJ is variable. There are some studies which suggest some remodeling of all or parts of the TMJ while others reported no changes (96),(97),(98),(14). Therefore, there is no consensus on what the overall effect might be on the glenoid fossa, condyle, condylar position, and disc position (96),(97),(98),(14). The use of different imaging modalities to evaluate the TMJ along with the use of different Class II corrector appliances can explain the difficulty in comparing the studies which results in continued lack in published literature particularly in assessing the morphological changes that could occur from the use of fixed functional appliances in correcting Class II malocclusions (12).

CBCT is a keystone imaging modality used in modern dentistry (99). It offers a better image quality compared to the 2D images (99). In addition, this imaging modality has a relatively low radiation dose compared to conventional CT (100). The CBCT produces a 3D reconstructed image of mineralized craniofacial structures which enables orthodontists to better understand and visualize patient's craniofacial skeleton and dentition (101),(18). Moreover, CBCT image segmentation techniques allow clinicians and researchers to further assess the shape, volume and position of craniofacial structures.

There are several techniques that have been developed and studied to segment the condyle. Broadly, these segmentation techniques fall into categories of manual, threshold-based technique and semi-automatic segmentation techniques. Manual segmentation technique involves manual selection and tracing of the area of interest in every single CBCT slice (82). Although the technique showed high accuracy and intra-rater reliability in segmenting the condyle, it is time-consuming compared to other segmentation techniques and is subject to examiner bias (82). The threshold-based technique is less time consuming when it is compared to manual segmentation technique however, it still relies on operator's experience to eliminate and segment the area outside the area of interest so that what is left is used in the analysis (83).

The semi-automatic segmentation technique is a combined technique using both automatic and manual technique. Defining the area of interest is done using an automated technique to select the adequate grey value threshold to outline the area of interest from surrounding structures and then a manual inspection and refinement of each slice is done to ensure accurate selection of the structure outline. Several studies evaluated the validity of the semi-automatic segmentation technique in segmenting the mandibular condyle and determine condyle volume. Some validated the technique by comparing it to manual segmentation results (19),(22), More recently it was validated against a physical model from a cadaver's skull (21). Both of these validation methods showed that this technique is valid, highly accurate and reliable in segmenting the mandibular condyle.

The use of the semi-automatic segmentation technique to segment a 3D CBCT image permits an accurate and reliable 3D assessment and analysis of the condyle such as condyle volume, shape, and position. The 3D assessment of the condyle can help the clinician to further assess and evaluate the effects of the functional Class II appliances to better understand the possible remodeling process of the condyle and the short- and long-term effect of using such appliances.

Therefore, this study aims to utilize CBCT imaging as a source for data to analyze the condylar volume and shape changes associated with the use of Herbst and Crossbow fixed functional Class II appliances.

3.2 Material and methods

3.2.1 Study sample

The data for this retrospective research project was collected from a randomized clinical trial that was approved by the University of Alberta, Research Ethics Office (Pro00045191). The study sample was comprised of growing Class II patients who were treated orthodontically at the University of Alberta, Orthodontics Graduate Clinic at the Kaye Edmonton Clinic. Table 3.1 summarizes the inclusion and exclusion criteria used in the study. Treatment was performed by a single clinician. True blinding during clinical treatment was not possible as the study was performed by a single clinician who could easily differentiate between the appliances used in this study. To ensure equal group sampling, a block randomization method was done by a third-party statistician. The assignments were concealed in a numbered sealed envelope to ensure randomization was correctly done.

Table 3.1 A summary of inclusion and exclusion criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Cl II malocclusion end to end and above	Syndromes
ANB ≥ 4°	Craniofacial anomalies
Late mixed or early permanent dentition	Gingival recession below CEJ
At least first molar and first premolars erupted in upper	TMJ pathology
Age range 10-14 girls and 11-16 boys	≥ 6 mm crowding
OJ ≥ 1mm	Congenitally missing permanent teeth (not including the third molars)
OB ≥ 1mm	No history of trauma to TMJ

The sample consisted of 51 healthy growing adolescent patients that were randomly assigned to one of three different groups: treatment with Herbst appliance; treatment with Crossbow appliance; control group with no class II mechanics during the considered time period. Table 3.2 is a summary of the sample patients including age and treatment time for all three groups. Records were previously collected including full Field of CBCT images at different time intervals: Pretreatment (T1) and posttreatment (T2) after 12 months. The 12 months period was chosen to allow full completion of the Class II correction and to and to minimize patient exposure to radiation in short interval. The control group patients were initially treated with full fixed appliances without any inter-arch mechanics to allow for normal growth expression so that the control group can be compared with the intervention groups (Herbst and Crossbow). After obtaining the T2 CBCT images, forsus springs (3M Unitek, Monrovia, Calif) connected to the archwires were used to correct the antero-posterior arch discrepancy in the control group. The activation of the Herbst and Crossbow appliances in the treatment groups were done bilaterally along with placement of orthodontic brackets (3M Victory Series Active Self-Ligating .022 slots brackets) and segmental archwire on maxillary central and lateral incisors on the same day of fixed Class II appliance placement.

Table 3.2 Summary of patients included in the study

Treatment group	Sample size (Gender)	Pretreatment age (Mean)	Posttreatment age (Years) (Mean)	Treatment time (months) (Mean)
Herbst	6 (M)/ 11(F)	12.4	13.3	11.9
Crossbow	12 (M)/ 5 (F)	11.9	12.9	11.4
Control	11 (M)/ 6 (F)	13.1	14.1	11.9

The CBCT Images were taken in large field of view using an i-CAT machine (i-CAT, Imaging Sciences International, Hatfield, Pa) at 120kVp, 7mAs, 8.9 seconds, 13cm x 16cm FOV, and 0.3mm voxel size. The Images were then converted to Digital Imagining and Communications in Medicine (DICOM) format and analyzed using the Avizo software (standard edition version 9.1, Mercury Computer System Inc, Chelmsford, Mass). Condyles of all the 102 CBCT scans were segmented using a validated semi-automated technique (21).

3.2.2 Semi-automatic segmentation of CBCT image using Avizo software

Avizo software was used for the semi-automatic segmentation process. Once the DICOM file was loaded into Avizo software, the researcher established the Isosurface of the scanned CBCT image. Before starting the segmentation process, the greyscale value of the CBCT slice was adjusted to enhance the difference between the condyle surface and the surrounding structures relying on the density difference between the two adjacent structures. This step permitted better visualization of the condyle bone and the surrounding structures. The magic wand tool was adjusted until the outline of the region of interest was clearly highlighted to allow the semi-automatic segmentation to take a place without addition of surrounding structures. Once the appropriate threshold was selected, the next step was to inspect each slice in an axial plane. In case of the addition of any surrounding structures beyond the region of interest due to lack of contrast in the gray value between the region of interest and the surrounding structures, the operator manually adjusted the threshold range to increase the contract in gray area or add a limiting line to remove any structures outside the region of interest as shown in Figure 3.3. Once all the slices were segmented and inspected, a new surface model was generated from the segmented images and all the smoothing algorithms were turned off to avoid any process that could affect the measurements.

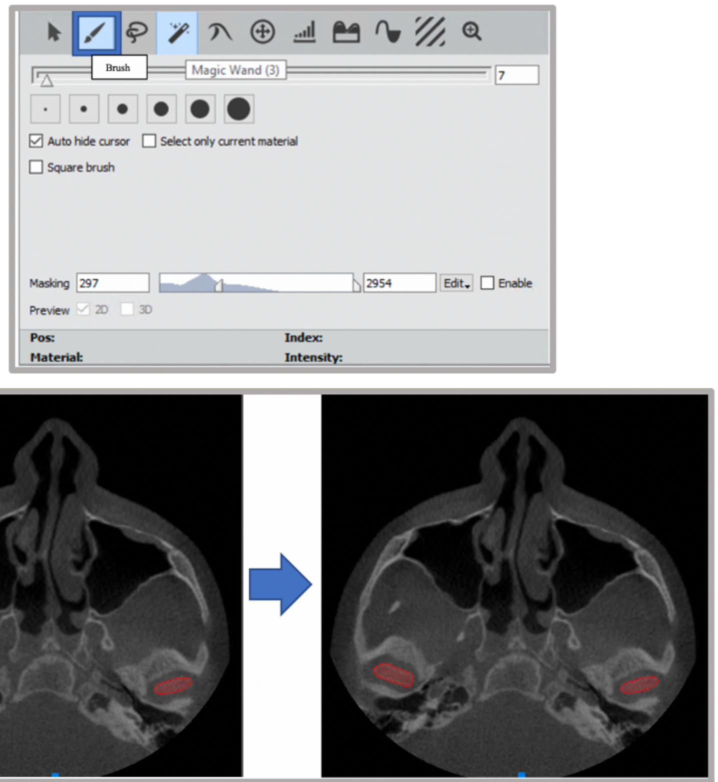


Figure 3.3 Manual adjustment with brush to remove the structures outside the region of interest

3.2.3 Region of interest determination in CBCT

Table 3.3 summarizes the landmarks used to determine condyle volume. Once the segmentation was completed the operator used the established Isosurface of the CBCT image to construct the Frankfort Horizontal (FH) plane. The FH plane was constructed using the following landmarks: both left and right infraorbitale and left or right Porion point that corresponds with the assessed condyle as seen in Figure 3.4. The condyle volume region was then determined by moving the constructed FH plane inferiorly to the sigmoid notch so that any structures above that line were to be analyzed for condyle volume (Figure 3.5). To remove any structures anterior to the sigmoid point a vertical plane perpendicular to the FH plane at sigmoid notch was added, so that any structures above and posterior to two planes were used in determining the condyle volume (Figure 3.6). Once the segmentation was complete, the landmarks and the boundaries of the region of interest were determined; the volume was calculated in mm^3.

Table 3.3 Definition of landmarks

landmark	description	Definition
Porion	Po	Upper and outermost point on bony external auditory meatus.
Orbitale	Or	Most inferior point in orbital margin.
Sigmoid	SN	Curved depression on the upper border of the lower jaw between the coronoid process and the condyloid process.

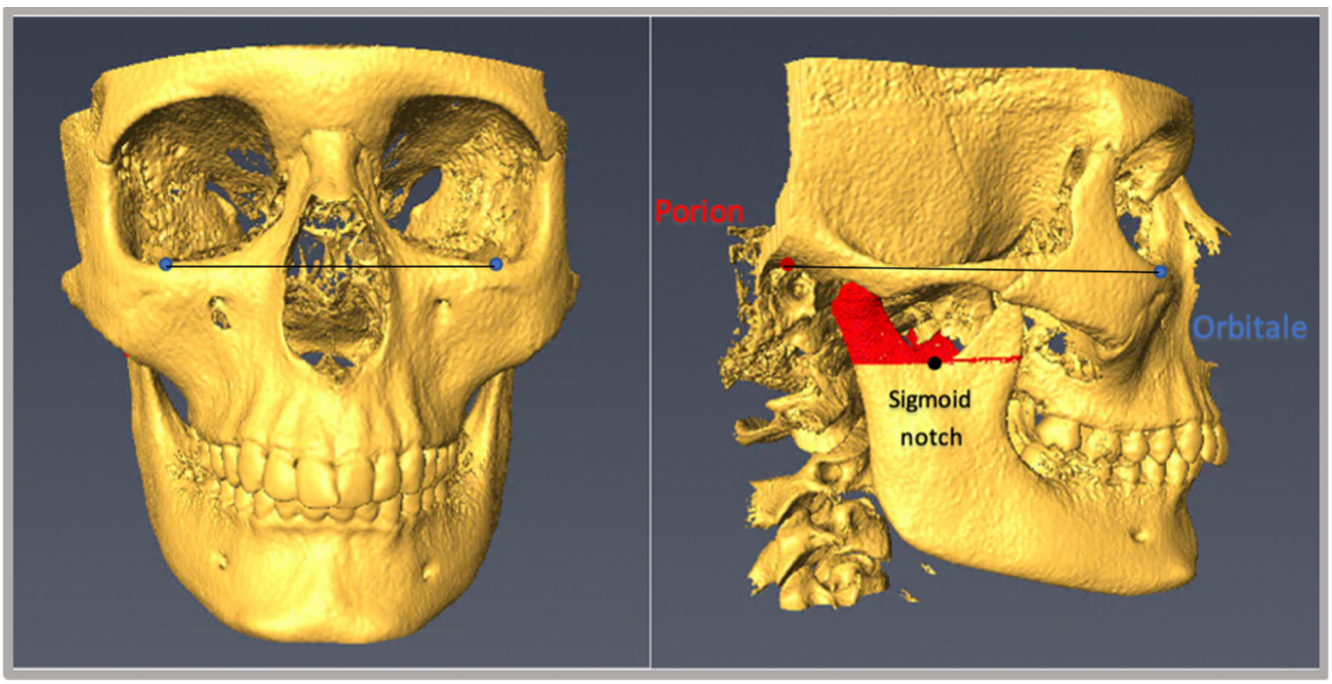


Figure 3.4 Manual adjustment with brush to remove the structures outside the region of interest

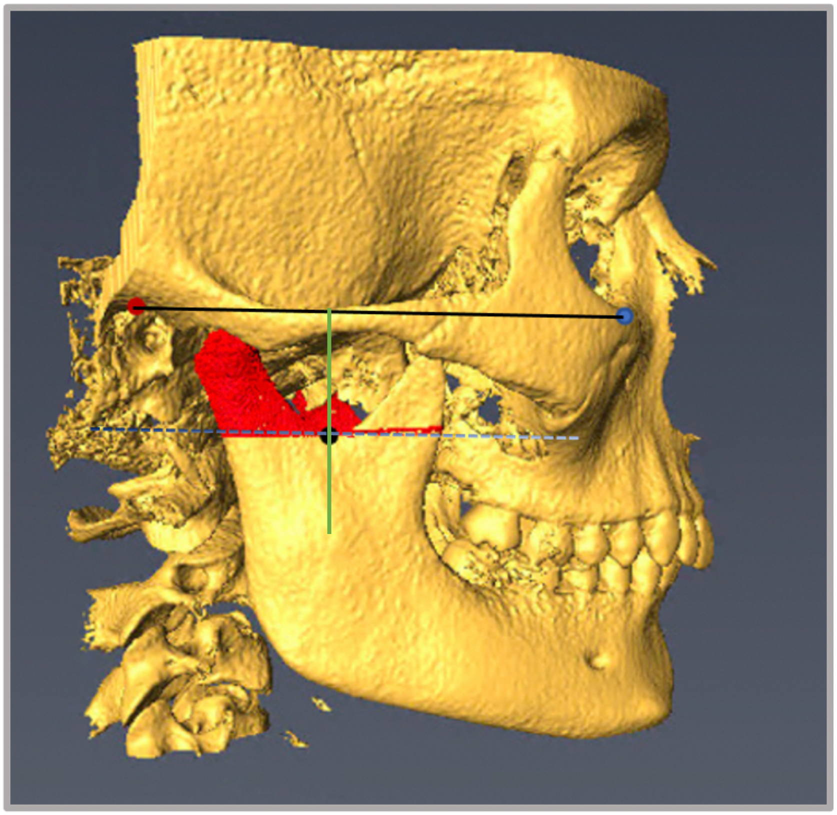


Figure 3.5 Translation of Frankfurt plane inferiorly to the sigmoid notch (dotted blue), vertical plane perpendicular to FH plane (green) at sigmoid notch.

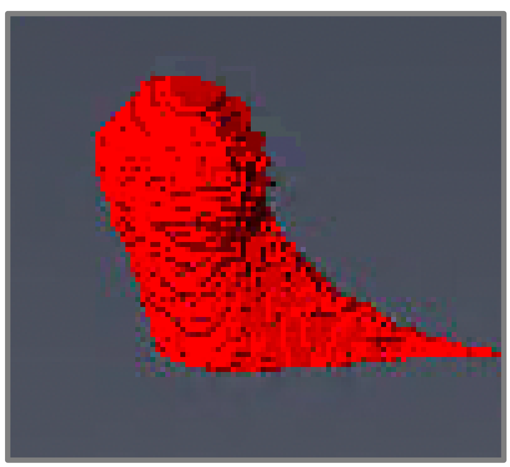


Figure 3.6 Segmented condyle after selecting the region of interest

3.2.4 Shape analysis of the segmented condyle

To analyze the condyle shape, all of the segmented CBCT DICOM files were converted to Standard Tessellation Language (STL) files. In order to compare the pre- and posttreatment segmented condyles, the STL file for each segmented condyle, was oriented in a common standard space. The Iterative Closest Point (ICP) technique was used to align and analyze the shape of the Condyles (102). ICP is a technique that takes an input of 2D or 3D points and produces a linear transformation matrix to align one set of points to the other. The transformation matrix consists of a rotation and a translation, which reduces the error and minimizes the difference between the two sets of 3D points contained in the meshes. The transformation matrix is produced by taking a point on the first mesh and matching it with the closest point to the other mesh in an iterative fashion. This process is repeated until there is no change in the data association and the error is small. The Python programming language and Visualization Toolkit (VTK) is an open-source software which was used to implement the algorithms and display the condyles. For the current project condylar volumes pre (orange) and post (green) treatment were compared as shown in Figure 3.7. Figure 3.8 shows the pre- and post-condyles that have been aligned using the ICP process.

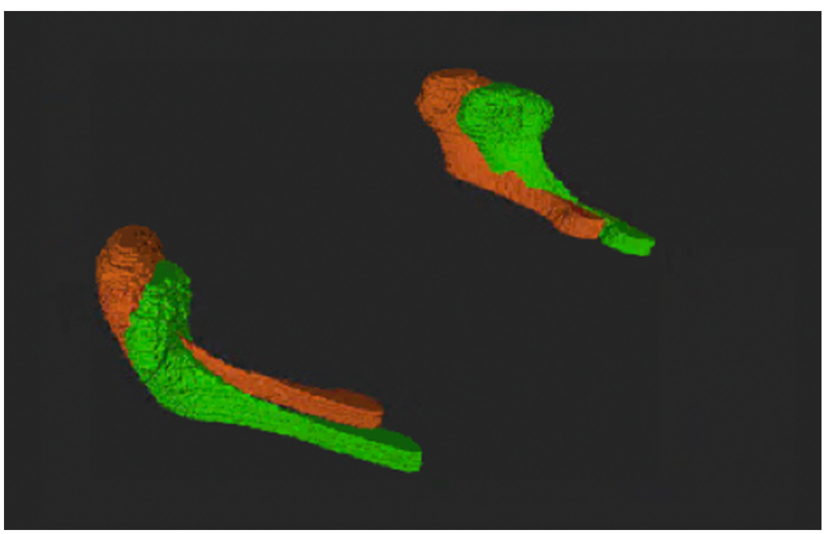


Figure 3.7 pre and post condyles aligned and displayed in VTK software

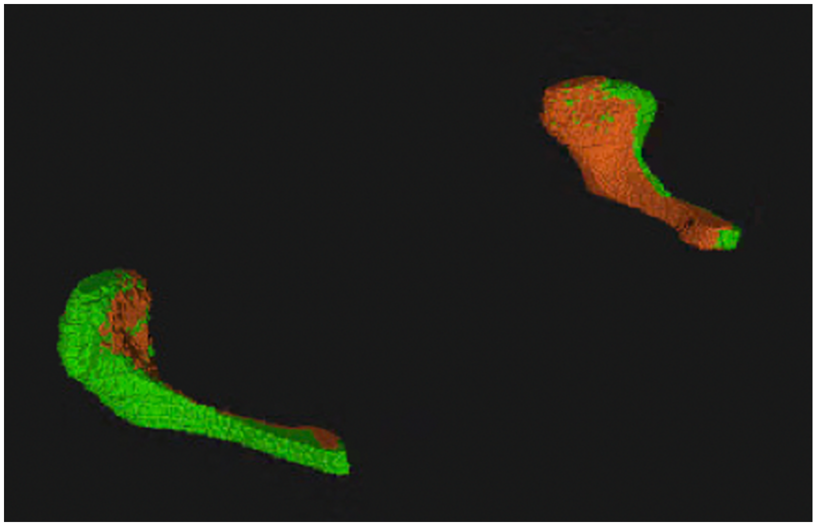


Figure 3.8 pre and post condyles after ICP computation

In order to quantify the difference between the aligned pre- and posttreatment condyles, the Mean Absolute Distance (MAD) was calculated by taking the average distance of all the closest points between the two meshes. The lower this value, the more closely aligned the two meshes are. VTK was used to calculate the difference between the meshes and display the data. The condyle was colour mapped to match the mean distance scale. The mean distance difference was calculated in mm, where the blue colour represents a small distance difference between the two mesh points and the closer to red, the larger the mean distance value (Figure 3.9). Each superimposed condyle was assessed individually in all views (frontal, lateral, medial, superior and inferior) after clipping the inferior and anterior border to the Sigmoid notch, as seen in Figure 3.10. The condyle surface displacement was categorized as mild (blue, < 0.5mm), moderate (purple, 0.5-1mm) and severe (green 1-1.5mm). Each condyle was divided into condyle head and neck as seen in Figure 3.11. The descriptive analysis was repeated three times by the same researcher two weeks apart from each other.

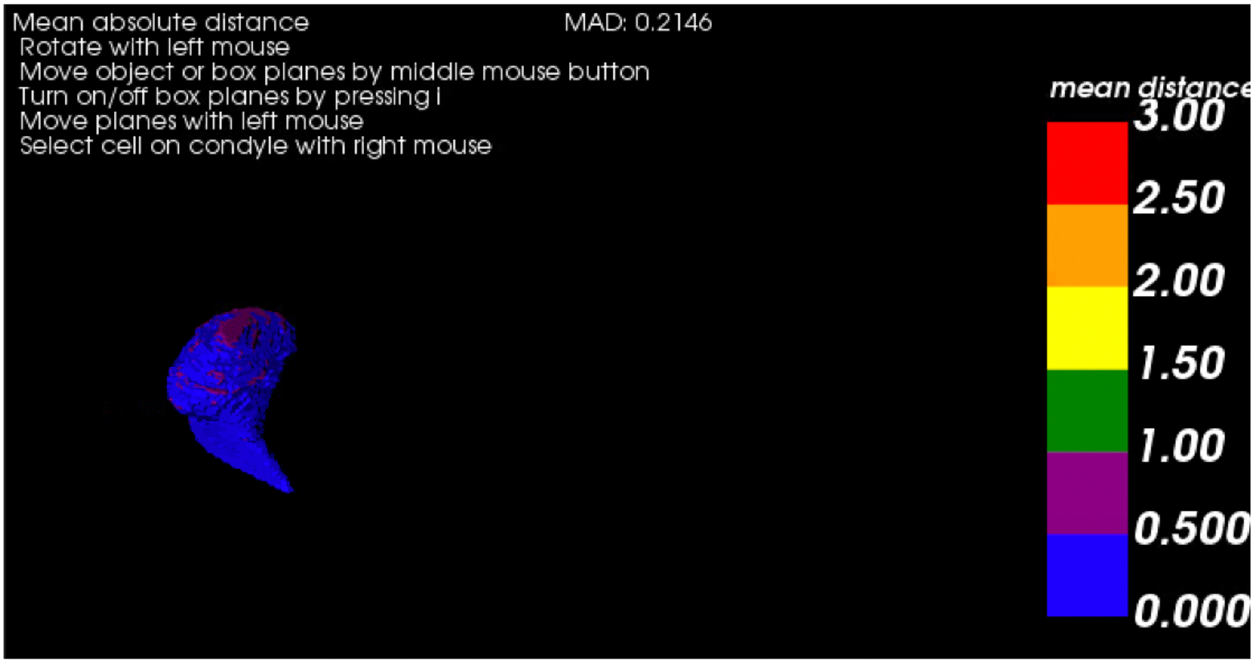


Figure 3.9 Right condyles after using the clipping plane to clip the anterior and inferior border to sigmoid notch. The scale on the right displays the mean distance difference (mm).

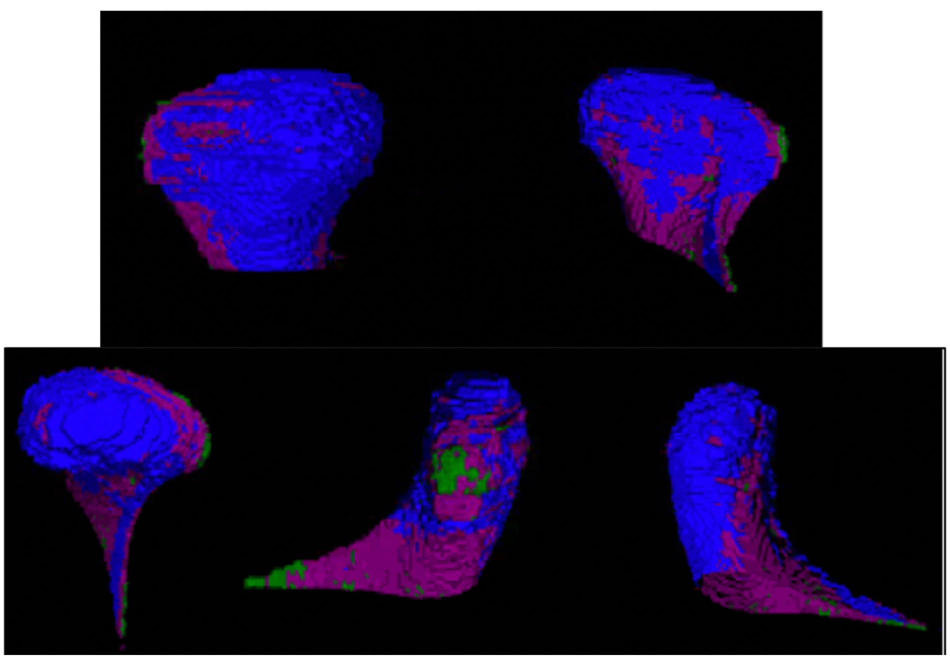


Figure 3.10 An example of assessing the left condyle in posterior view (top left), anterior view (top right), superior view (bottom left), left view (bottom middle) and right view (bottom right)

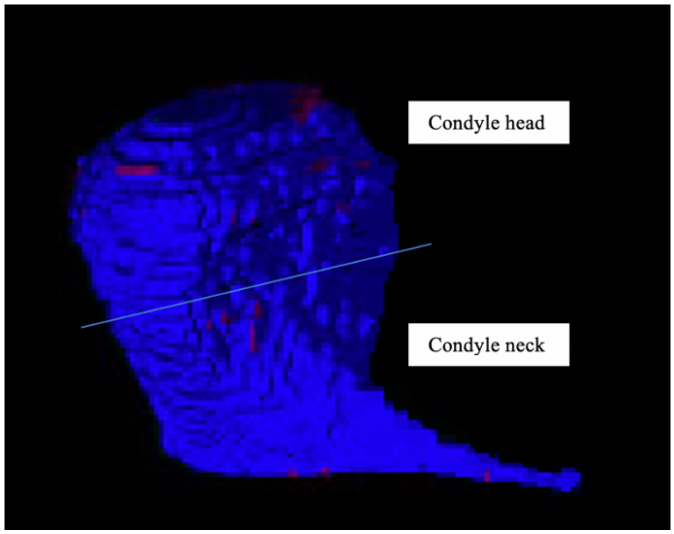


Figure 3.11 Mandibular condyle anatomy

3.3 Statistical analysis

All the statistical analyses were performed using IBM SPSS Statistics software (version 26.0 for Mac). A significance level of α=0.05 was chosen for all statistical analysis.

3.3.1 Inter-rater reliability test

Ten patients were randomly selected from the pool of 51 patients who were part of the fixed Class II corrector study to determine the reliability of the segmentation method used in this project. The patient, condyle side and time were randomized. The measurements were repeated blindly three times by the same researcher. Each set of measurements was done one week apart from each other. Statistical analysis was performed using IBM SPSS Statistics software (version 27.0 for Mac, IBM Corp., Armonk, NY). A significant level of α=0.05 was chosen for all statistical analyses.

The Intraclass Correlation Coefficient (ICC) was used to assess the intra-rater reliability. A two-way mixed model was chosen since the patients/condyles were chosen randomly while the rater remained fixed. The ICC value was Interpreted using the guidelines described by Koo and Li (103)

• ICC > 0.90: Excellent agreement

• ICC > 0.75: Good agreement

• ICC > 0.51 and < 0.74: Moderate agreement

• ICC < 0.50: Poor agreement

3.3.2 Condylar volume statistical analysis

A three-way repeated ANOVA was determined as the statistical analysis of choice to evaluate the change in mean condylar volume between the three groups: Herbst, Crossbow, and Control group.

The following variables were identified in this study:

- Three factors' variables (discrete):
    - Two Within subject factor:
        - Condylar side with two levels: Left and Right
        - Time with two levels: Pre-treatment (T1) and Post-treatment (T2).
    - One Between subject factor:
        - Treatment types with three levels: Control, Herbst and Crossbow
- One response variable (continuous):
    - Volume (mm^3)

Prior to applying the three-way repeated mixed ANOVA, the model assumptions were tested for normality and linearity to confirm that the data can be analyzed using the three-way repeated ANOVA. The normality was assessed using boxplots and linearity was assessed using scatter plots. To simplify the visualization of the boxplots (Appendix, Figures A1.1 and A1.2) it was divided into two: mean difference of right condylar volume (R T2-T1) and mean difference of left condyle volume (L T2-T1). The visual assessment of the box plots revealed potential left skewedness in the value of mean difference in condylar volume of left and right sides of the control group, while the Herbst showed potential right skewness in both right and left side. However, Crossbow revealed potential left skewness in the mean difference of the right side with two outliers and in the left side potential right skewness with one outlier. Therefore, normal assumption was not met. There were a number of outliers that were taken care of by using examination strategy where statistics were run with and without the outliers; no change in the result was found. Hence the decision was made to report the result including the outlier. Linear relationships were present in all four graphs; therefore, linearity assumption was met (Appendix, Figure A1.3). Given that there were only two levels for the within subject factors, the sphericity assumption did not apply.

Three-way repeated ANOVA evaluated the following null hypothesis:

$H_0$1: The mean condylar volumetric changes pre- and posttreatment are independent of left and right condyle side.

H_a1: The mean condylar volume changes pre- and posttreatment are not independent of left and right condyle side.

$H_0$2: The mean condylar volume changes pre- and posttreatment are independent of treatment type.

H_a2: The mean condylar volume changes pre- and posttreatment are not independent of treatment type.

$H_0$3: The mean condylar volume changes pre- and posttreatment are independent of condyle side and treatment type.

H_a3: The mean condylar volume changes pre- and posttreatment are not independent of condyle side, and treatment type.

3.3.3 Condylar shape statistical analysis

A two-way mixed ANOVA was determined as the statistical analysis of choice to evaluate the change in mean distance difference of the pre- and posttreatment condyle between the three groups: Herbst, Crossbow, and Control group.

The following variables were identified in this study:

- Two factors' variables (discrete):
    - One Within subject factor*:*
        - Condylar side with two levels: Left and Right
    - One Between subject factor:

- Treatment types with three levels: Control, Herbst and Crossbow

- One response variable (continuous):
  - Mean Distance difference (mm).

In order to apply two-way mixed ANOVA, the model assumptions of normal distribution, equal variance, homogeneity of covariance and sphericity were investigated. To assess the distribution the sample data, a box plot was constructed (Appendix, Figure A1.4). A visual assessment of the data demonstrated an overall right positive skewness with no outliers. That said, while the assumption of normality is violated, the equal sample size per group are rebuts against departure from normality. The assumption of equal variance was evaluated using Levene's test and indicated no strong evidence against equal variances (p-value< 0.001). The homogeneity of covariances was assessed by Box's test of equality of covariances matrices and was not met. Given that there were only two levels for the within subject factors, the sphericity assumption did not apply

The Two way-mixed ANOVA evaluated the following hypothesis:

$H_0$1: There is no difference in the mean distance difference among the three different treatment types.
H_a1: The mean distance difference of at least one treatment type differs from the other treatment types.

$H_0$2: There is no interaction between condyle side and treatment type on the mean distance difference.
H_a2: There is an interaction between condyle side and treatment type on the mean distance difference.

3.4 Results

3.4.1 intra-rater reliability

The ICC single measures value of the condylar volume and shape was 0.998 95% CI [0.995,1.000] and 0.989 95% CI [0.951,0.998] respectively, showing an excellent agreement between the measurements. Table 3.4 summarizes the results of the intra-rater ICC consistency of the condyle volume and shape, respectively. Figure 3.12 and Figure 3.13 present the plot of the mean condylar volume and shape.

Table 3.4 Intra-examiner ICC values for mean condylar volume and shape

		95% Confident Interval		
	ICC	Lower bound	Upper bound	P-value
Condyle volume	0.998	0.995	1.000	< 0.001
Condyle shape	0.989	0.951	0.998	< 0.001

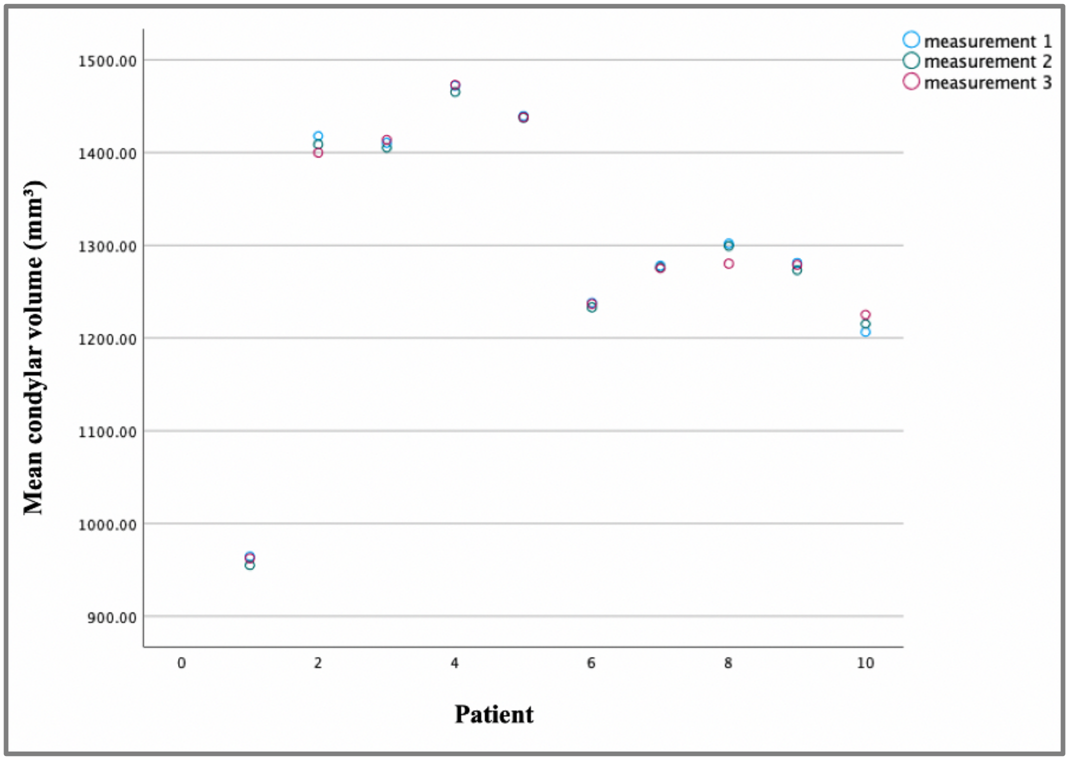


Figure 3.12 Plot of mean condylar volume

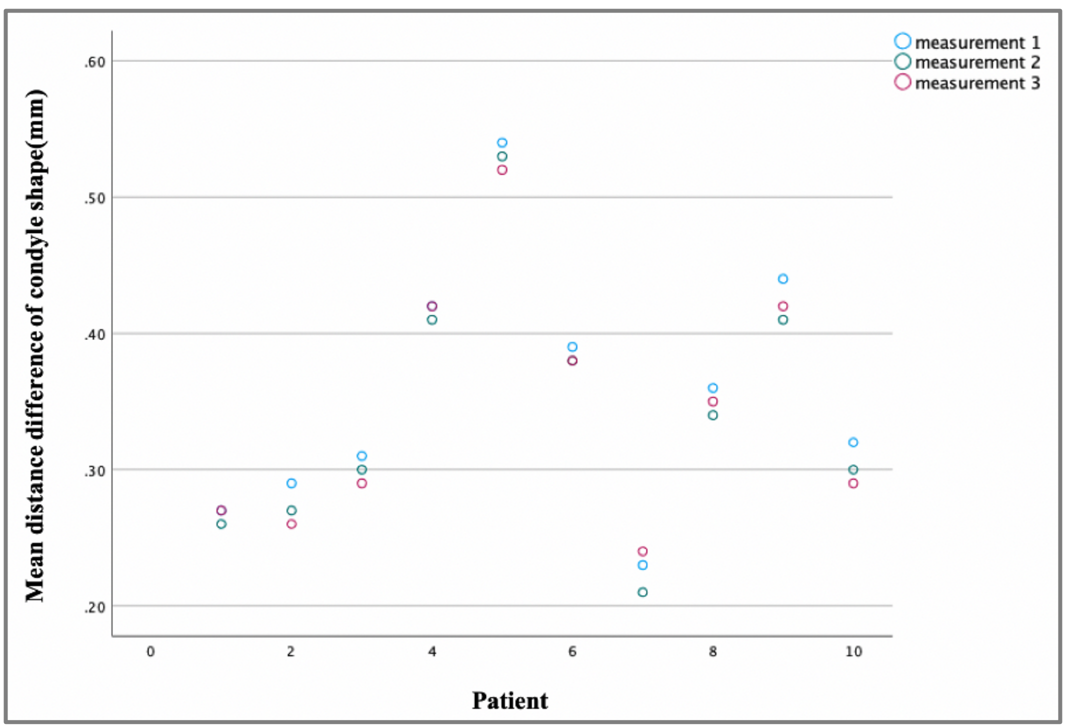


Figure 3.13 plot of mean distance difference of condyle shape

3.4.2 Pre-treatment group comparison

One way ANOVA was used to test the interaction between the age and treatment groups at baseline. There were no significant differences in patient age between the three groups (control, Herbst and Crossbow) pretreatment, $F(2,49) = 0.830$, $p=0.442$. The mean age pretreatment was 12.8 ± 1.18 years. Pearson Chi square test was used to test the interaction between the gender and treatment groups at baseline. There was weak evidence to accept the null hypothesis $F(1, 50) = 3.767$, $p=0.058$. Therefore, the age was equal between the groups prior to the start of treatment but there is possible difference in sex distribution among the groups.

3.4.3 Condylar volume

A full summary of the descriptive statistics exhibiting mean condylar volume with 95% confidence intervals for all variables can be seen in the appendix (Table A1.1). At T1 the Crossbow group started with higher right and left mean condylar volume compared to the Control and the Herbst groups. Furthermore, the left condylar side for crossbow appliance showed higher mean condylar volume compared to the right side, the mean condylar volume was 1507.52 ± 255.46 mm^3. At T2, similar pattern was found where the mean condylar volume for Crossbow group was higher compared the other two groups and the left condyle side was slightly higher with mean condylar volume of 1554 ± 245.25 mm^3.

Table 3.5 represent the results of the overall three-way repeated mixed ANOVA F-test. The data showed convincing evidence against the null hypothesis in terms of change in mean condylar volume pre- and posttreatment regardless of condyle side and treatment $F(1, 50) = 62.092$, $p<0.001$. Pairwise comparisons employing Bonferroni correction was used to determine the mean difference in condylar volume between pre- and posttreatment (Appendix, Table A1.2), which showed the mean difference in condylar volume of 65.51 mm^3 [48.81,82.21] from pre to post treatment. Table 3.6 summarizes the increase in mean condylar volume for all the three groups.

Table 3.5 Three-way repeated mixed ANOVA test result (p-value)

	df	Mean	F	P-value
Time	1	226861.96	62.09	<0.001
Time* Treatment	2	5358.90	1.47	0.240
Condyle Side	1	14303.92	0.675	0.415
Condyle side * Treatment	2	20532.34	0.969	0.387
Time* Condyle side	1	11.2	0.12	0.915
Time* condyle side* Treatment	2	4.038	0.004	0.996

Table 3.6 Mean increases in condylar volume from T1 to T2 of different treatment group

Treatment	Mean increase (mm^3)	Mean precentage increase
Crossbow	45.46	3%
Herbst	72.18	5.95%
Control	78.93	5.65%
Total	65.15	4.77%

The result of the overall test also revealed that the data is consistent with the null hypothesis, supporting that the mean condylar volume changes before and after the treatment are independent of treatment $F(2, 49) = 1.376$, $p>0.05$ ($p=0.240$) and condyle side $F(2, 50) = 0.915$, $p>0.05$ ($p=0.387$).

3.4.4 Condylar shape

Table 3.7 represents the results of the overall two-way mixed ANOVA F-test. The results revealed that the data is consistent with the null hypothesis, supporting that the mean distance difference of right and left condyles are independent of treatment type F (2, 50) = 1.22, p>0.05 (p=0.305). Profile plot and Pairwise comparisons employing Bonferroni correction was used to further assess the interaction (Appendix, Table A1.3 and Figure A1.5). Additionally, the result data showed no statistical significance in mean distance difference among the different treatment groups F (2, 50) = 1.47, p=0.238 and the mean condyle surface displacement of Crossbow group was about 0.066 mm [-0.045,0.177] higher than Herbst group (Table 3.8). Table 3.8 summarizes the mean MAD (mm) of right and left condyles in all three groups.

Table 3.7 Two-way repeated mixed ANOVA test result (p-value)

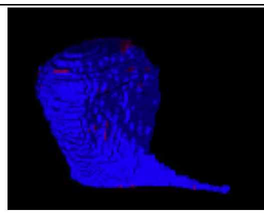
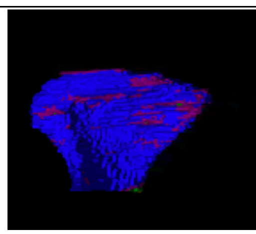
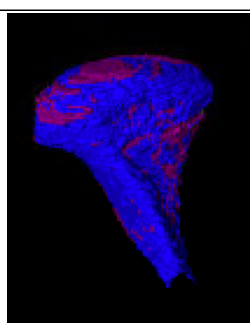
	df	Mean square	F	p-value
Condyle side	1	0.000	0.021	0.885
Treatment	2	0.052	1.477	0.238
Treatment*condyle side	2	0.011	1.216	0.305

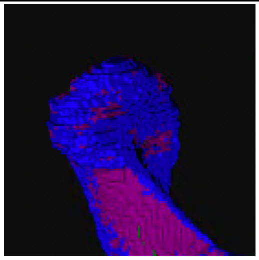
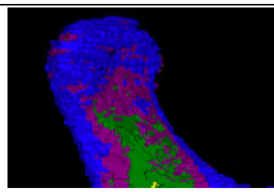
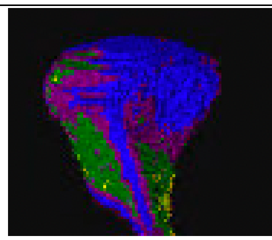
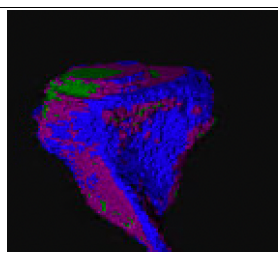
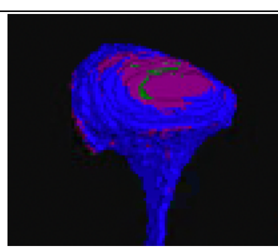
Table 3.8 Mean of MAD (mm) of left and Right condyles with 95% Confident interval (CI)

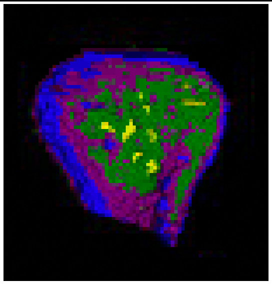
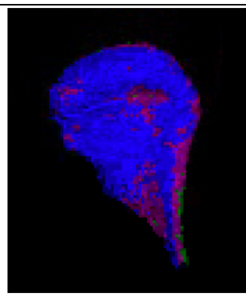
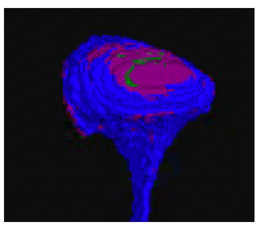
Treatment	Right condyle mean (mm) 95%CI	Left condyle mean (mm) 95%CI
Crossbow	0.445 [0.363,0.525]	0.409 [0.341, 0.478]
Hebst	0.357 [0.283,0.429]	0.365 [0.308,0.421]
Control	0.444 [0.354,0.409]	0.409 [0.341,0.547]

Table 3.9 summarizes the area of shape changes in all three groups. The three groups (Herbst, Crossbow and Control) expressed different patterns of shape changes with no clear pattern was associated with the treatment groups (Herbst and Crossbow). The Crossbow group had 8 cases that showed moderate (0.5-1mm) displacement of the condyle surface posttreatment in the medial and lateral aspect of the condyle head and neck, 2 cases had moderate displacement in lateral of condyle head and neck plus superior of the condyle head, 2 had moderate changes in superior of the condyle head and the rest showed mild to moderate changes in different areas of condyle. Only 4 of the cases showed some area of severe (1-1.5mm) displacement in different areas of condyle head and neck. In the Herbst group, 3 cases showed moderate displacement in lateral aspect of the condyle neck, 3 cases showed moderate displacement of the condyle in the medial and lateral aspect of the condyle head and neck and 1 case showed moderate displacement in medial and lateral of condyle head and neck plus the superior of condyle head. The rest of the cases showed mild to moderate changes in different areas of the condyle. Only 2 cases in the Herbst group showed some area of severe displacement in different parts of condyle. The control group had 2 cases of moderate changes in lateral of condyle neck, 4 cases showed moderate displacement in lateral of condyle head and neck, 4 cases showed moderate displacement in medial and lateral of condyle head and neck and 2 cases had moderate changes in superior of the condyle head along the medial and lateral of the condyle head and neck. The rest showed mild to moderate changes in different areas of the condyle. Only 5 cases in the control group showed some area of severe condyle displacement in different areas of the condyle.

Table 3.9 Summary of area of condylar shape change in all three groups (Crossbow, Herbst and control)

Type of change	Sample image	Crossbow group (Total of 17)		Herbst Group (Total of 17)		Control Group (Total of 17)	
		Right condyle	Left condyle	Right condyle	Left condyle	Right condyle	Left condyle
No Change		2	2	2	2		
Scatters				4	4	1	1
Medial of condyle neck and head		1	1			1	1

Lateral of condyle neck		1	1	2	3	2	2
Lateral of condyle neck and head				1		4	3
Medial and lateral of condyle neck and head		8	8	3	3	4	3
Medial and lateral of condyle head and neck + superior of the condyle head		2	1	1	1	1	2
Superior head		2	2	3	2	2	2

Entire condyle head & body			1				1
Medial and lateral neck+ superior head	 	1	1	1	2	2	2

3.5 Discussion

The effectiveness of fixed Class II functional appliances in correcting the Class II malocclusion has been extensively studied particularly in an attempt to understand the effect of those appliances in remodeling potential of the TMJ. The majority of those studies assessed the condyle positional change following the use of the Herbst and Twinblock appliances and no studies were done assessing the condylar positional changes following the use of the Crossbow appliances. Two studies investigated the condyle shape following the use of Herbst appliances, and both studies used a non-validated automatic segmentation technique (94),(94) and no study investigated the condyle volume following the use of the Herbst and Crossbow appliances. The development of the 3D image using CBCT enabled researchers to better visualize and analyze the TMJ while reducing the image distortion from the superimposition and exposing the patient to a low radiation dose compared to CT image (28),(27). Segmentation techniques permit clinicians and researchers to construct a 3D model of the condyle to study the volume and shape.

The semi-automatic segmentation technique permits the use of automatic segmentation to minimize operators' error in segmentation, followed by a manual check to ensure high degree of accuracy. Previous studies reported high accuracy and reproducibility in segmenting the mandibular condyles (19),(22),(21),(83),(23). In the present study the reliability of the previously validated semi-automatic segmentation technique in assessing condyle volume and shape showed excellent intra-rater reliability as assessed by ICC values of 0.998 95% CI [0.995,1.000] and 0.989 95% [0.951,0.998], respectively.

Assessing and measuring the condyle volume and shape accurately relies on precisely identifying landmarks and the outline of the region of interest. The FH plane that was used in this study is a horizontal plane extending from infraorbital to the porion bony landmarks. These particular craniofacial structures develop early in life and are stable by age 7 (1), however these landmarks are subject to identification error and bias. Studies have indicated that porion point is more prone to error than infraorbital point particularly in 2D lateral cephalometric images (16). That could be due to the close proximity and superimposition of the surrounding structures at porion point compared to infraorbital. Nevertheless, using CBCT the porion is reasonably easier to identify compared to 2D cephalometric. Kim et al. reported a difference of 25.49± 6.92 mm^3 in condylar volume when they purposely translated the FH plane 0.3mm (approximately the size of one voxel) from where it should be to assess the sensitivity of the analysis (21). Furthermore, they reported that the 1.5mm vertical displacement of the porion landmark resulted in a mean condylar volume difference of 13.86 ±9.92 mm^3. They also reported that 1 degree of clockwise and counter clockwise rotation of the FH plane resulted in a mean condylar difference of 12.67±3.08 mm^3 and 13.86±9.92 mm^3, respectively. The results from their study suggest that the semi-automatic segmentation technique is a very reliable technique, and any identification error of the landmark is unlikely to constitute a clinically significant difference in measurement of condylar volume.

The present study demonstrated that using fixed Class II appliances (Herbst, Crossbow) had no statistically significant effect on the mean condylar volume posttreatment. The results also revealed that there is mean increase of 4.77% in mean condylar volume posttreatment in all three groups (control, Herbst and Crossbow) regardless of condyle side (left and right). This indicates that remodeling and/or growth of mandibular condyles and its volume increase reflect possible normal growth rather than an orthodontic treatment effect. This result was surprising since the Herbst appliance is designed to prevent the condyle from seating in the glenoid fossa and produce continuous displacement force on the condyle which theoretically would be expected to induce more condylar remodeling response than the Crossbow. However, our result showed that the Herbst group had a non-significant increase of 2.95% in condylar volume compared to the Crossbow group. Our findings were similar to the Arici et al. study in which they used CT images to evaluate the TMJ response following the use of the Forsus appliance (Forsus nitinol flat-spring, 3M Unitek Corp, Monrovia, Calif) which is considered a flexible fixed functional Class II appliance because of the flexibility of the spring. In their study, 3 transverse CT slices of the condyle were aligned using points on the medial and lateral surfaces, once the condyles were aligned, the differences in condyle volume pre-and posttreatment were measured. The name of the program used and the selected landmarks were not reported in the study. The study reported that both the control and treatment group had an increase in condylar volume and the increase was not statistically significant between groups and there was no statistical difference between left and right condyles (104). The result from the present study also showed no statistically significant difference in mean condylar volume between left and right condyle posttreatment. Our result corresponds to the Nota et al. study where 3D CBCT was used to assess the condylar changes in growing patients (ages 11-26). They reported increase in mean condylar volume and no statistically significant change in condylar volume between left and right (105).

Regarding the condyle shape, the result from this study showed no statistically significant differences in average condylar surface displacement among the three groups. This suggests that the force applied by the fixed Class II appliances did not result in any significant change in the condyle shape. Previous studies have reported that the mandibular condyle increases size and the shape changes from round to oval during childhood (0-17 years of age) (106). A recent study by Fan et al. used 3D CBCT images to analyse the effect of Herbst appliances in the mandible by superimposing the 3D images from the pre-treatment and 8 weeks after removal of the Herbst (95). They used marker-based watershed transform which is a region-growing approach, where corresponding points were automatically applied across the entire mandibular surface and then a colour map plotted the differences between corresponding points of the mandible to visualize the changes between the timelines. Their results suggested that the greatest morphological changes were seen in the mandibular condyle followed by dento-alveolar bone and chin (95). They reported that 85-100% of the Herbst group showed 0.5mm significant increase in condyle head height by outward growth at the superior of condyle head and 50% of the study sample showed 1.5 mm change in condyle length. Moreover, a small number of cases in the Herbst group had more than 1.5 mm change in condyle height. However, there was no comparison group and therefore they could not separate change due to growth from change due to treatment. Another study was done by Wei et al. using 3D CBCT images to evaluate the condylar changes in 20 adolescent patients with Class II division 1 malocclusions treated with Herbst appliances followed by orthodontic treatment and they matched it to 11 patients with Class II malocclusion treated with Class II elastics (94). Their time points include pre-treatment and 8 weeks post removal of appliance. They used an automatic segmentation technique with 3D mandibular regional voxel-based superimposition techniques to reconstruct the mandible and measure the amount and region of condylar change. They reported that the Herbst appliances resulted in 1 to 1.9 mm growth at the posterior region of the condyle head and 2.7- 3mm at the superior of the condyle over period of 7.79±1.82 months (94). However, in their study there was no randomization done, unequal sample sizes, different disruption of sex in the groups and different treatment times which might have overestimated the reported condylar growth following the use of Herbst appliances.

While a limited number of studies in the literature reported the change in condyle volume and shape with fixed Class II appliances, several studies looked into the positional change of the condyle glenoid fossa following the use of the appliances. Some studies using 3D CBCT images reported no statistically significant change in condyle glenoid fossa relationship after a period of 8-12 months of using Herbst appliances (93),(92). However, one study reported forward displacement of the condyle after the use of Herbst appliances (107). Unfortunately, due to study limitations such as small sample size, lack of randomization and methodical variation, no consensus can be drawn. The positional changes of the condyle without seeing any remodeling changes in the condyle can possibly be due to one of the following reasons: remodeling of the glenoid fossa which could displace the condyle, changes in the articular disc from the displacement force, or temporary or permanent tolerance of the muscles attaching the TMJ structures to the cranial base to stretch further without firing pain, or habitual behaviors can be sustained following the use of the mandibular advancement appliance. This suggests that further studies evaluating the changes in the glenoid fossa and positional changes of the condyle following the use of fixed Class II appliances can help clarify the impact of such appliances on the TMJ.

Measurement errors in condylar segmentation technique can possibly affect the mean differences observed in condylar volume and shape. However, it was reported by Kim et al. that the result of the semi-automatic segmentation technique used in their study had a measurement error of 4.836 ±11.89 mm^3 comparing it to physical model, applying this to current study, it would result in a 0.32% change in overall condyle volume from pre- to posttreatment. Similar to Kim et al study, the present study demonstrated excellent intra-rater reliability; therefore, measurement error was anticipated to have minimal impact on the overall condyle volume measurements. Moreover, sex has been shown to influence condylar growth (46). Males typically have more condylar growth than females especially during adolescent years (46). Females tend to reach their peak approximately two years earlier than boys (12.2 years and 14.3 years for females and males, respectively) (46). A study was done by Saccucci et al. to investigate the condylar growth in different groups age, gender and malocclusion and they found that male tend to have statistically bigger condylar volume and surface compared to female (108). Therefore, gender is critical to account for understanding condylar growth and interpreting the result. In the present study the Herbst group had 50% more females compared to Control and Crossbow groups where they had more males than females, hence the result has to be explained with some caution. Another factor that would be nice to consider in future studies is patient facial type. The study by Pancherz et al. have suggested that hyperdivergent facial profile patients are likely to have more condylar growth than other types of facial profiles (109). It is, therefore, important to account for such variables in any interpretation.

3.6 Clinical significance

The use of fixed Class II fixed appliances (Herbst and Crossbow) did not result in any additional remodeling and changes in condyle volume and shape. Suggesting that an increase in mandibular condyle volume and the changes in condyle shape following the use of such appliances is likely part of the normal growth, not due to the force load applied to the joint during Class II fixed functional appliance treatment Despite no additional changes in condyle shape or volume, it is still possible that there might be positional change of the condyle and/or remodeling of the glenoid fossa and sigmoid notch.

3.7 Conclusion

Fixed Class II appliances (Herbst and Crossbow) are not associated with any statistically significant change in mean condyle volume in Class II occlusion in growing patients. All the three groups in this study showed comparable increase in condylar volume, suggesting it might be part of overall normal condylar growth. Additionally, there was no statistically significant change in condylar shape and no clear pattern of shape changes associated with the treatment group (Herbst and Crossbow). However, about 50% of the shape changes were in the medial and lateral of condylar neck and head in all three groups. Finally, there was no side differential growth (right versus left) of subanalysis of the results. Nevertheless, further research might be required to assess if the main impact of such appliances comes from the positional change of the condyle or remodeling of the glenoid fossa rather than volumetric or shape change.

Chapter 4: Final Discussion

4.1 General Discussion

About quarter of patients who seek orthodontic treatment present with angle Class II malocclusion (24). Several treatment options have been offered to patients including surgical, camouflage treatment and functional orthopedic appliances (100). Functional appliances have been proposed to enhance the mandibular growth to maximize the anterior posterior correction of Class II malocclusion. Condylar remodeling in response to altered joint loading associated with forward posturing of the mandible has been suggested as a potential mechanism for increasing mandibular length (12),(110). Furthermore, change in joint loading may result in and adaptive condyle shape change.

The present study aimed to use 3D images from CBCT to segment the mandibular condyle using a validated semi-automatic segmentation technique to examine the mandibular condyle volume and shape in growing with Class II malocclusion patients treated with fixed Class II corrector appliances (Herbst and Crossbow). The semi-automatic segmentation technique used in this study was previously shown to have excellent accuracy and reproducibility in segmenting the mandibular condyle (21), (19). The intra-observer reliability of the segmentation method also showed an excellent reliability (ICC= 0.998) in the present study.

The results from this study showed a statistically significant increase in posttreatment condylar volume in all three groups (Control, Crossbow and Herbst), with overall mean increase estimated to be 65.51 mm^3 [48.81,82.21] and 4.77%. However, there was no statistical difference in mean condylar volume and the increase in volume in all three groups is likely due to normal growth. Individual patients demonstrated altered condyle shape, with the majority of shape change being in the medial and lateral aspects of the condyle head and neck in all three groups. However, there was no consistent difference in pattern of shape change observed between groups.

The present study did not quantify magnitude, direction of duration of joint loading. It can however be assumed that if the appliances do alter joint loading, there is limited adaptive osseous condylar remodeling in response to joint loading.

4.2 Study Limitations

The use of a randomised controlled trial study along with a validated method are considered strengths of this study. However, the shape analysis used in this study had limitations. The quantitative assessment of the mandibular condyle shape measured the mean average of the linear distance difference between the pre- and posttreatment condyles outline without assessing the direction or location of this displacement. Regional shape change may be masked by shape change in opposite directions. For example, regressive remodeling on the anterior surface with appositional remodeling on the posterior surface of the condyle would not be identified due to the averaging effect.

The current study did not evaluate the possible changes in the mandibular condyle position in relation to the glenoid fossa, and whether any changes/remodeling occurred in the glenoid fossa following the use of fixed Class II appliances. Another limitation of the study is the use of the Avizo program to segment the condyle as this program is still considered a time-consuming program as it took one hour to segment two condyles. With the development of new software, faster software might be less time consuming and more user friendly.

4.3 Future recommendations

Based on the findings in this study, the following recommendations for future studies are suggested:

- Further evaluation of condyle shape using a 3D regional registration and superimposition to assess a possible change in condyle shape that might not be detected with the used method in the current study.
- Evaluate the changes in mandibular condyle position in relation to the glenoid fossa following the use of fixed functional appliances (Herbst and Crossbow).

- Evaluate the possible changes/remodeling of the glenoid fossa following the use of fixed functional appliances (Herbst and Crossbow).

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Appendix

Table A1.1 Descriptive statistics exhibiting mean condylar volume with 95% confidence intervals and standard deviation for all variables.

Time and condyle side	Control (mm ³)	Crossbow (mm ³)	Herbst (mm ³)
T1 Right condyle	1391.22 [1203.15,1579.29]	1455.66[1304.19,1607.13]	1221.24[1091.69,1350.79]
T1 Left condyle	1401.83[1242.98,1560.67]	1507.52[1376.17,1638.68]	1206.74[1088.88,1324.59]
T2 Right condyle	1469.88[1286.08,1653.69]	1500.11[1349.15,1651.08]	1293.28[1155.83,1430.72]
T2 Left condyle	1480.97[1300.39,1661.54]	1554[1427.90,1680.10]	1279.05[1158.87,1399.22]

Table A1.2 Mean condylar volume difference and 95 % confidence interval between pre- and posttreatment using Pairwise comparisons with Bonferroni correction.

Time	Mean Difference (mm ³)	Sig.	95% confident interval for difference	
			Lower bound	Upper bound
T2-T1	65.15	<0.001	48.81	82.21

Table A1.3 Mean distance difference and 95% confident interval between time and treatment using Pairwise comparisons with Bonferroni correction.

Treatment	Mean difference (mm)	P-value	95%confident interval
Control - Herbst	0.066	0.424	[-0.043, 0.176]
Herbst - Crossbow	-0.066	0.439	[-0.177,0.045]
Crossbow -Control	0.000	1.000	[-0.111,0.111]

Figure A1.1 Box plot of mean difference of Right condyle volume

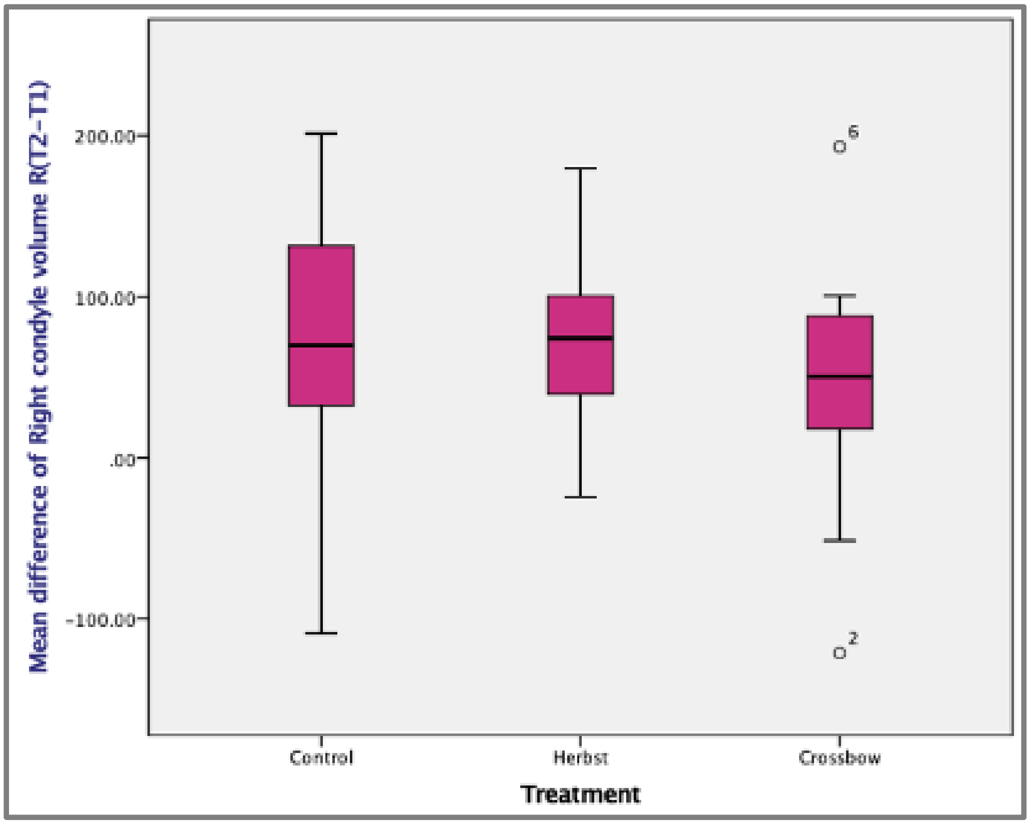

Figure A1.2 Box plot of mean difference of Left condyle volume

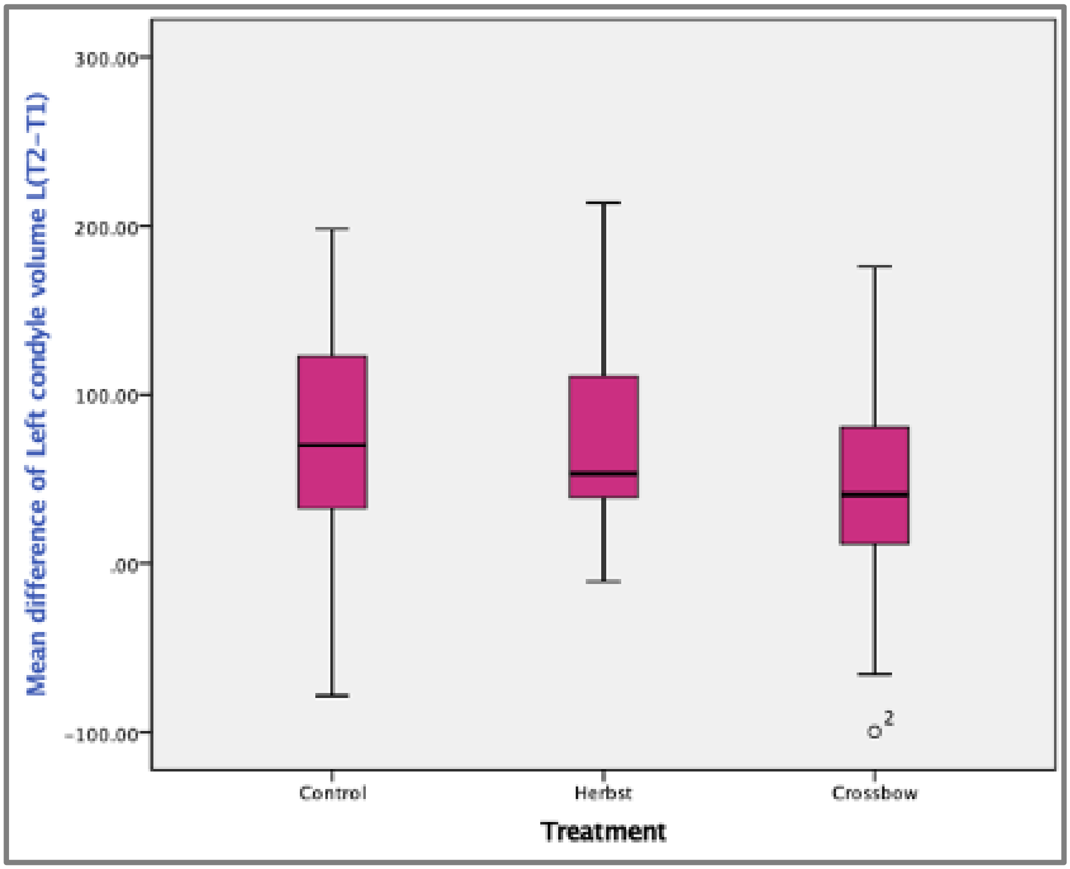

Figure A1.3 Scatter plot of the raw data

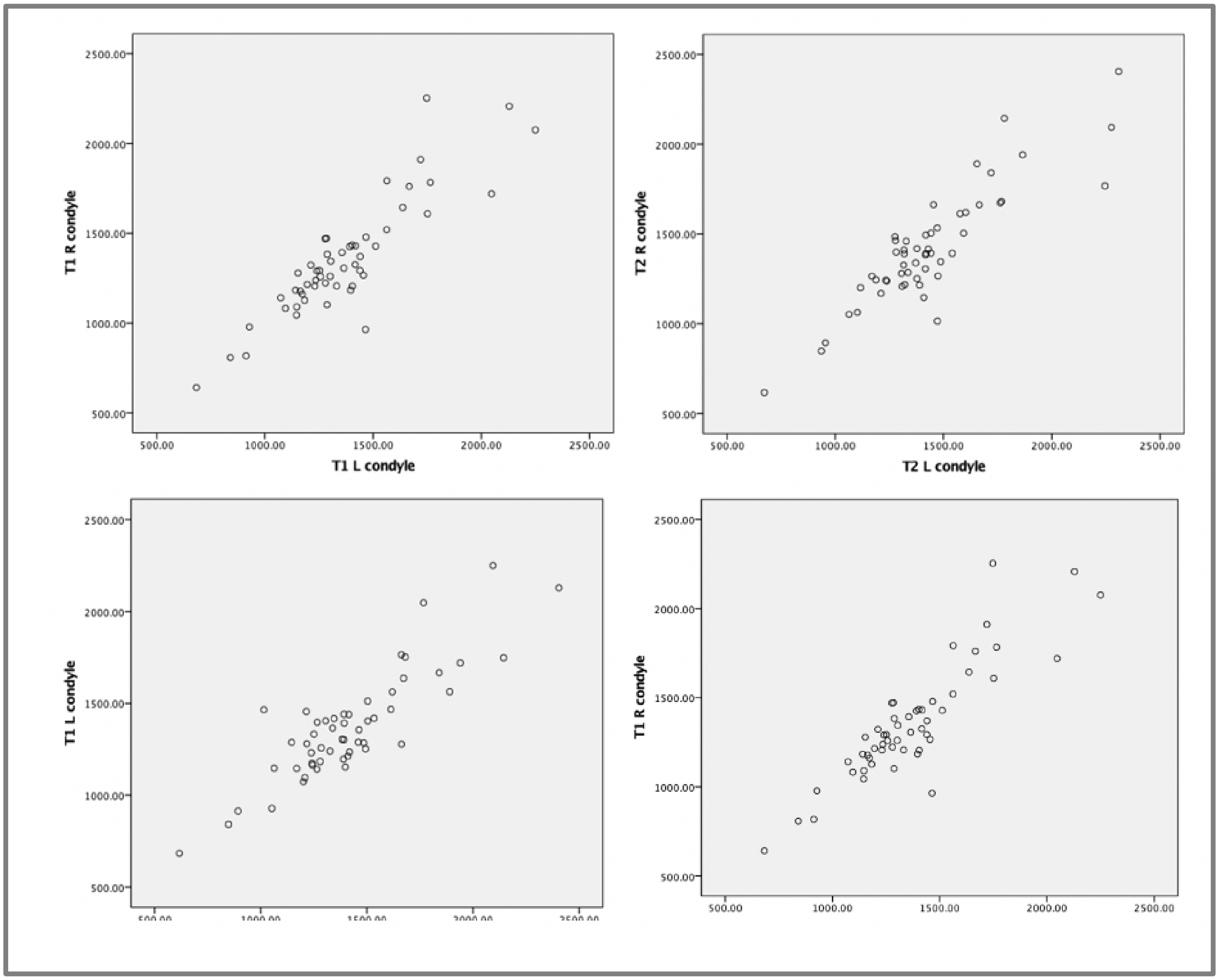

Figure A1.4 Box plot of mean distance difference of condyle shape

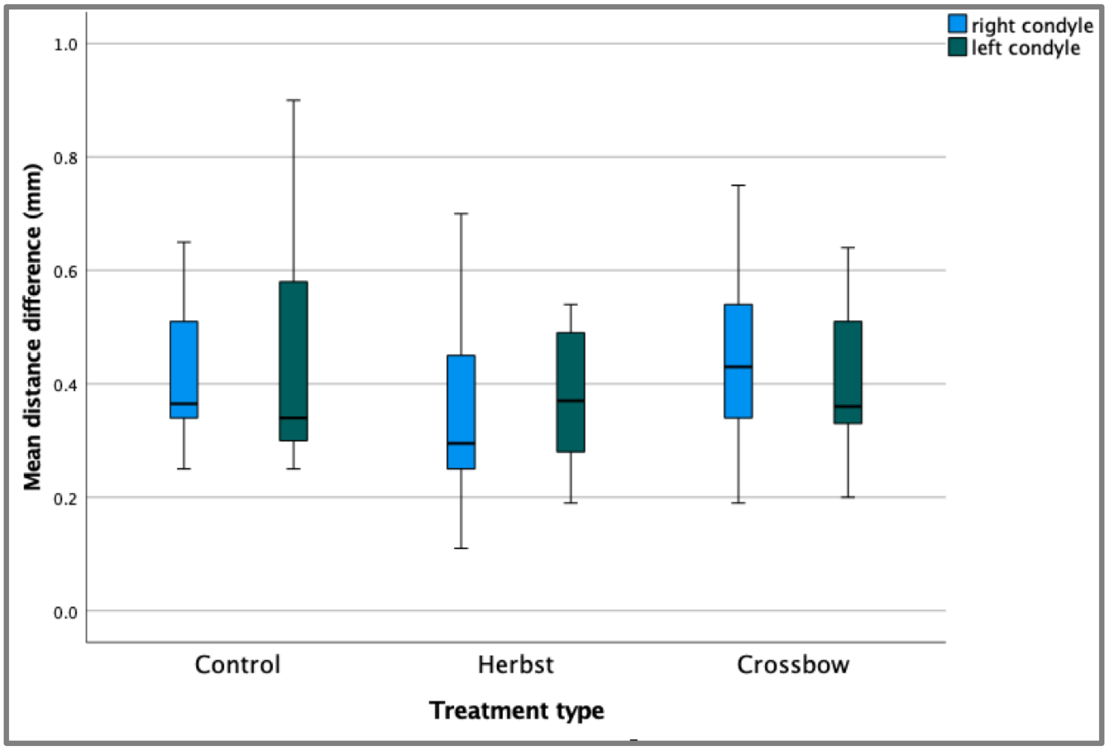

Figure A1.5 Profile plot for interaction between condyle side and treatment of condyle shape