Maturational Staging of the Midpalatal and Zygomaticomaxillary Sutures: A Morphological Study Using CBCT

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Objective: The aim of this study was to observe the patency of the midpalatal (MPS) and zygomaticomaxillary (ZMS) sutures relative to age, gender, cervical vertebrae maturation stage (CVMS), palatal and zygomatic dimensions and malocclusion.

Method: The sample comprised of 278 subjects selected from one private orthodontic office. The necessary information from their records was reviewed and documented. Their pre-treatment cone-beam computed tomography (CBCT) images were obtained for orthodontic diagnosis and treatment planning purposes. These images were exported to the Invivo 5 program (Anatomage, San Jose, California), in which orthogonal and oblique sections were obtained from the MPS and ZMS for morphologic evaluation. The five MPS (A, B, C as open; D, E as closed) and five ZMS (A, B as open; C, D, E as closed) morphological maturational stages of patency were classified based on previous studies (Angelieri et al 2015, 2017) by a single examiner. Cohen's kappa was applied for intraexaminer agreements, and their values were 0.95 and 0.83 for the MPS and ZMS, respectively.

Result: The patency of the MPS and ZMS are significantly associated with age, gender, CVMS and Angle Class I and Class II malocclusions. The MPS patency is associated with the palatal depth/length (P_d/P_l) ratio, while the ZMS patency is not. Statistically, Class III malocclusion was found to significantly related to the ZMS patency, but not at the MPS.

Conclusion: There is a strong association of an open MPS when ZMS is open. In Class I and II malocclusions in which maxillary expansion is indicated, the MPS is normally open in CVMS I and II. In Class I or mild Class III malocclusions in which maxillary expansion and a facemask is considered, the MPS and ZMS should be evaluated at CVMS II or earlier. Deeper and shorter palates are associated with open MPS.

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Preface

I would like to express my most sincere gratitude to Dr. Timothy Snyder and the members of his practice at LOA Orthodontics. They made sure all the hardware and software were in place to allow this project to be possible. With their help, I was able to obtain a large amount of data that would not otherwise have been available from the dental school. I would also like to convey my appreciation to Dr. Joseph FA Petrone and Dr. Nilesh Shah for their support and guidance through the construction and organization of the study.

1.0 Background

The orthodontic specialty studies the direction of growth at different sutures in the skull to determine how the face grows and why it grows the way it does (Bjork and Skieller 1972). The maturation of the circummaxillary sutures and mandibular growth have been assessed in relation to the overall growth of an individual based on chronological age, hand-wrist skeletal maturation index (SMI), cervical vertebrae maturation stages (CVMS), peak height velocity and bone density, to name a few (Tanner 1962; Fishman 1982; Baccetti et al 2006; Leichter et al 1981). Of particular interest, the midpalatal (MPS) and the zygomaticomaxillary (ZMS) sutures have clinical significance to orthodontics.

Maxillary constriction in the transverse dimension is clinically encountered in association with posterior crossbite (dental and/or skeletal), deficient maxillary arch perimeter, Class I, II, or III malocclusions, mouth breathing, and oral habits (tongue/finger). The concept of expanding the maxilla at the MPS was first introduced by Angell in 1860 and was later made popular by Haas based on his study on rapid maxillary expansion (RME) (Haas 1961). In the past, treatment timing for maxillary transverse deficiency by conventional RME has been limited to growing patients as best evaluated based on their chronological age and skeletal maturity.

In individuals who present with midface hypoplasia, prominent mandibular growth, or a combination of midface hypoplasia with prominent mandibular growth in relation to the maxilla, intervention has been recommend prior to puberty. The treatment timing and the remaining effects of orthopedic modification in an individual as a result of when intervention commences have also been evaluated based upon chronological age, dental age, and skeletal age (Ngan and Moon 2015; Lee et al 2010; Baccetti et al 2014). The treatment of Class III skeletal form varies from RME, chin cup, protraction facemask or a combination of these modalities (Ngan and Moon 2015). All of these approaches involve either a direct or indirect effect on the MPS and ZMS (Ngan and Moon 2015; Ghoneima et al 2011; Cleall et al 1965).

Autopsy studies of the MPS and the ZMS have shown these structures to be unfused in second- or third-decade adults (Cohen 1993; Knaup et al 2004; Korbmacher et al 2007). The level of maturation at the circummaxillary sutures impacts the degree to which orthopedic modification has an effect on the maxilla. Both the MPS and ZMS have been studied through cone beam computed tomography (CBCT) imaging by Angelieri et al to classify the morphological maturity on an individual basis. From these studies, a morphological classification of five maturational stages has been devised for the MPS and ZMS (Angelieri et al 2013; Angelieri et al 2017). The correlation of individualized characteristics, such as gender, malocclusion and skeletal maturity in as they relate to the developmental stages at each suture could provide further insight towards appropriate treatment timing.

1.1 The Midpalatal Suture

1.1.1 History of RME

The earliest written reference for rapid expansion of the maxillary arch was by Angell in 1860 (Angell 1860). He used a jackscrew across the roof of the mouth of a 14-year old girl while anchoring against the bicuspids and turned the jackscrew twice a day (Angell 1860). This method raised significant doubt due to the lack of additional evidence at that time. Clinicians in the orthodontic and rhinology fields made further attempts with varying success up to the late 1920s, but this method fell out of popularity until Haas conducted a histologic study in pigs and then clinically in a select group of patients from his private practice. Haas was able to demonstrate separation between the palatal shelves, new bone formation and the response of maxillary incisors and mandibular teeth to RME, as well as the orthopedic changes that were seen in serial lateral and posteroanterior cephalograms. Based on these findings, RME could be used to treat maxillary constrictions, Class III and pseudo-Class III malocclusions (Haas 1961). With respect to Class II malocclusions, McNamara et al demonstrated 81% of Class II patients and 69% of end-to-end patients in the mixed dentition showed a positive change in the molar relationship. This study also observed a 2 mm or greater change in 49% and 23% of Class II and end-to-end patients. McNamara et al's study using RME has been shown to improve the molar relationship when patients are treated in the mixed dentition followed by a transpalatal arch retention protocol. This phenomenon of sagittal relationship improvement as a result of treatment in the transverse dimension is significant in Class II malocclusion correction (McNamara et al 2010).

1.1.2 Visualization of the MPS

While conventional radiography with occlusal film was the predominant technique for assessing the MPS, Wehrbein's radiological-histological study demonstrated that the visualization of the MPS highly depends on the X-ray path along the oronasal suture. Results of high false positive for sutural fusion with occlusal films in Wehrbein's study suggested that this technique poorly visualizes a 3-dimensional structure with a 2-dimensional image (Wehrbein and Yildizhan 2001). CBCT is used in orthodontics for the detection of supernumerary, ectopic and impacted teeth as well as root resorption (Eslami et al 2017). Although CBCT radiation exposure doses may be higher than that experienced in plane film use, a single CBCT scan can replace all conventional orthodontic radiographs: occlusal film, lateral cephalograms, posteroanterior cephalograms, and panoramic radiographs (Signorelli et al 2016). When possible, by limiting the field of view setting and shielding radiation-sensitive organs, the exposure dose could be lowered (Signorelli et al 2016). CBCT allows for 3-dimensional inspection of hard tissue anatomical structures, the images of which are usually overlapped by another hard and/or soft tissue structures in two-dimensional plane films. In this study, CBCT scans are used to visualize the MPS and ZMS directly without superimposed structures.

1.1.3 Negative Effects of RME

Historically, the dental and skeletal changes that occurred with RME were not always clear. Before the 1960s, it was accepted that orthodontic expansion of the maxilla led to only dentoalveolar changes by buccally tipping the posterior teeth. Although Cleall's study was conducted in rhesus monkeys, he found that all expanded animals demonstrated a widened, flattened palate, which was likely due to the palatal processes, teeth and the alveolar processes rotating outward. Based on that observation, posterior teeth would appear to have been tipped laterally with little reaction in the alveolar bone. From cephalometric radiographs and occlusal films, Cleall argued that a 10-15 degrees change in buccal inclination of teeth was unlikely to have occurred in two weeks' time (Cleall 1965). Whether an expander is tooth-borne or tooth-tissue borne for conventional RME or surgically assisted RME (SARME/SARPE), or bone-borne with microimplant assisted rapid palatal expansion (MARPE) (Garib et al 2006), the RME force application at the anchored teeth have been shown to demonstrate some level of unwanted buccal tipping (Garib et al 2006; Sendyk et al 2018; Nguyen 2017). Other computed tomography and clinical studies related to both conventional and surgical RME have also found occurrences of significant bone dehiscence, fenestration, decreased buccal bone plate thickness, reduction in alveolar bone crest level, root resorption, gingival recession, alveolar bending and chronic occlusal balancing interferences (Garib et al 2006; Langford 1982; Sendyk et al 2018; Morris et al 2017; Alpern and Yurosko 1987). More specific complications that have been reported in association with SARPE include hemorrhage, injury to the maxillary nerve branches, alar base flaring, sinus infection, extrusion of teeth, devitalization of teeth and altered pulpal blood flow (Suri and Taneja 2008).

1.1.4 Palatal growth

There are three postnatal developmental periods of the MPS. During the infantile period, the suture is broad and Y shaped in cross-section and the vomerine bone is situated in the V-shaped groove created by the two halves of the maxilla. In the juvenile period, the suture develops a wavier morphology. In the adolescent period, the suture adopts a tortuous character with increased interdigitation (Melsen 1975).

The general growth pattern of the maxillary hard palate of the boney maxilla is bone resorption on the nasal side and apposition on the oral side (Bjork and Skieller 1972). The growth in length of the hard palate continues into adulthood (Melsen 1967). In a human autopsy study, Melsen found the nasal surface of the hard palate had continued resorption until 14 to 15 years of age (Melsen 1975). The apposition of the oral surface continued to 13 to 14 years of age. The transverse palatine suture continues to change from birth to 14 years, during which there is a change from overlapping part of the maxilla to interdigitation, and shortening of the suture. Between the two parts of the palatine bone, the connective tissue sheet becomes narrower after 13 to 14 years. The growth in the length of the hard palate up to puberty in the transverse suture is due to both growth in the suture and apposition on the posterior margin of the palatine bone. Melsen found no marked differentiation between the amount of activity along the anterior and posterior bony borders of the transverse palatine suture (Melsen 1975).

In the sutures of 18-year olds, even when the MPS had heavy interdigitation, the connective tissue demonstrated stratification of three distinct layers. The lower aspect of the suture had fibers, originating from the periosteum, extend into the central layer, parallel with the two bone surfaces of the suture. Uninterrupted Sharpey’s fibers could also be followed across the suture (Melsen 1975).

1.1.5 MPS Biochemical Composition and Obliteration Variability

The biochemical composition of the sutures is mainly consisted of fibronectin, osteonectin, type I, III and type V collagen. At different locations across the same suture there are varied rates of bone formation, proliferation, and calcification (Cohen 1993). Histologically, facial sutures react to compression by bone resorption along the sutural margins, and tension across the suture leads to an increased rate of bone deposition. The sutures normalize histologically when forces cease (Wegeman et al 1988).

Sutures are located at the borders of bones separated by connective tissue. The sides of the bones progress from straight to increased interdigitation over time by means of increased distribution of osteoblasts at the tip of each interdigitation. In a young suture, the collagen fibers are found to be evenly distributed throughout the suture. With age, fibroblasts reduce in number and collagen fibers become irregularly spaced. (Cohen 1993).

Vascular, hormonal, genetic, mechanical and local factors all have been studied as attributes to suture closure. Even though human facial growth ceases by age 20 years, studies on the circummaxillary sutures have demonstrated that the MPS and ZMS begins to close between 30-35 years and 70-72 years, respectively (Cohen 1993).

Occlusal films were the most frequently utilized technique to assess the suture morphology prior to the advent of CBCT or other types of 3-dimensional imaging. Wehrbein and Yildizhan's radiological-histolgical study using autopsy specimen of young adults from 18 to 38-years old reiterates that conventional radiographs merely offer a depiction of a 3-dimensional structure in a 2-dimensional image. The vomer and the external nose overlap the midpalatal suture and may prevent true determination of the morphology based on a radiological interpretation dependent upon the X-ray path through the course of the oronasal suture. Their study revealed that in the young adult sample, there was a fifty percent false positive of sutural obliteration based on the occlusal radiographs when histologically no obliteration was found, which makes this simple technique an inadequate basis for making treatment decisions. Based on this study, an indiscernible MPS does not equate to a histologically closed suture. This study cautions against the use of 'fusion' in occlusal films that are used for sutural status assessment (Wehrbein and Yildizhan 2001).

Persson and Thilander examined histologically the MPS closure in human autopsy specimens from 15 to 35 years of age. The result from this study indicate that the intermaxillary suture interdigitates earlier in the posterior part than the anterior, and on oral rather than the nasal aspects of the suture. Sutural closure varies greatly not only between individuals of the same age group, but also in different parts of the same suture within the same individual. While the palatal suture may start the obliteration process during adolescence, it is not until the third decade of life that significant amount of closure is found. This study indicated that the earliest obliteration was found to begin in the posterior part of the intermaxillary suture in a 15-year old girl, and a 27-year old woman was the oldest person that did not demonstrate sutural fusion in their sample. Even though there is an increase of areas with bony bridges going from the middle of the third decade, some of those were slender bony spicules. The highest areas of obliteration were found in the posterior part of the intermaxillary suture. Even though there is a greater activity in the sutural closure of the palate between 20 to 25 years of age, the obliteration index was still below 5% in older age individuals (>26 years). Perrson and Thilander (1977) described the Obliteration Index to quantify the obliterated suture length versus the total suture length when the MPS is observed in axial sections that were hemalum-eosin stained. The bony bridges present in the suture are measured and summed to compare to the total suture length seen in that section, multiplied by 100, to arrive at the Obliteration Index (Persson and Thilander 1977).

Based on Persson and Thilander and Knaup et al, emphasis is placed on the percentage of the suture found to be obliterated rather than the presence or absence of obliteration alone. Theoretically, based on these findings, conventional RME should be successful in most individuals even in the second or third decades of life; however clinical experience shows that conventional RME is often difficult to perform in older subjects (Persson and Thilander 1977, Knaup et al 2004).

In another human-palate specimen study of individuals aged 14-71, it also revealed that the degree of obliteration is generally low and that interdigitation in the horizonal plane is independent of age. However, bone density was an age-dependent factor, such as increased bone volume in the middle-aged group (Korbmacher et al 2007).

1.1.6 Histological Presentation of RME post-expansion

When forces are applied at the sutures, the immediate response consists of traumatic tears, minor fractures of bony interdigitations, exudate, fibroblast deaths, collagen fiber disruption and acute inflammation. Bone formation is observed as quick at 3 to 4 days at the edges of the suture; fibroblasts can be seen remodeling. Within about 2 to 3 weeks, bone remodeling at the suture is seen and continues until normal morphology is restored (Wegemans et al 1988).

Caprioglio et al reported the cellular changes following 7 and 30 days after RME based on two 8-year olds. At 7 days after RME, there was evidence of blood clot from the mechanical trauma, newly formed bone trabeculae aligned parallel to each other. At 30 days post-RME, portions of the bone margins were lined by osteoblasts producing osteoid matrix. Although there is an increased number of newly formed bone trabeculae, the bone character was still immature with poorly organized collagen (Caprioglio et al 2017).

Even though previous studies have shown well established mineralization at the MPS at three months after expansion (Ekstrom et al 1977, Mohan et al 2016), the individual variability in bone remodeling capacity and the amount of expansion, the healing period and mineralization to re-establish normal sutural morphology may continue for more than three months (Caprioglio et al 2017).

In an animal study where maxillary expansion in rhesus monkeys was performed, different periods of expansion, retention and post-retention protocols were applied. In the monkey that was evaluated two weeks after expansion, histological section showed the bony defect was filled with disorganized fibrous connective tissue, irregularly positioned bone spicules and a mild chronic inflammatory response; the cellular reactions showed reparatory and osteoclastic activity. Expansion followed by a 3-month retention period had similar MPS morphology to the control, but adjacent bone trabeculae were very cellular and irregular; both osteoclastic and osteoblastic activities were seen. For the monkey that had not only 3 months of retention but also a 3-month post-retention period, there was evidence of cells that had formed more rapidly, but the MPS appears to be histologically normal and more consolidated (Cleall et al 1965).

RME produces an increased width at the MPS in the transverse dimension. However, RME also impacts the cranial and circummaxillary sutures. Ghoneima et al's study using CT scans found significant width increase in the internasal, maxillonasal, frontomaxillary, and frontonasal sutures as well as the intermaxillary suture. Less pronounced changes were found with RME at frontozyomatic, zygomaticomaxillary, zygomaticotemporal and pterygomaxillary sutures. The anterior sutures are affected more by resultant RME forces than the posterior sutures (Ghoniema et al 2011).

1.2 The Zygomaticomaxillary Suture

1.2.1 Biochemical Composition of the ZMS

The composition of the ZMS is similar to other facial sutures. Biochemically, the suture mainly consists of osteonectin, fibronectin, and type I, type III and type V collagen. Unlike the tensional forces applied for maxillary expansion, forces that is applied across the ZMS is a combination of compression and tension due to the complicated orientation of the suture and the direction of force application in relation to the suture (Wegemans et al 1988). When maxillary protraction was applied to rhesus monkeys, Nanda found the pattern of bone apposition and resorption on a particular suture depended on the direction of the force applied. Circummaxillary sutures have complex interdigitation; sutures such as the ZMS had areas of resorption and apposition around each of its boney projections (Nanda 1978). Similar to maxillary expansion, there is an initial traumatic response at the ZMS characterized by a connective tissue repair stage; new bone is laid down at the edges of the suture in areas of tension and bone resorption in areas of compression. Bone remodeling continues to reestablish the original morphology (Wegemans et al 1988).

Most of the facial structures remain patent into adulthood due to the mechanical strain that is applied through mastication. Many of the circummaxillary sutures such as the frontomaxillary, nasomaxillary, and the zygomaticomaxillary sutures do not begin to fuse until the sixth or seventh decade (Cohen 1993). In a study conducted in rats, an age-related decrease in systemic and local osteogenesis activity was revealed which potentially explains the physiologic limitations related to age when extraoral forces are applied in an attempt to protract the maxilla (Yin et al 2015).

1.2.2 Extraoral Force Effects at the ZMS

In response to extraoral forces on the maxilla, of the Macaca irus, Kambara observed there was sutural opening of the circummaxillary sutures, new bone deposition with more active osteoblastic activity and highly stretched fiber bundles. The study also noted that the ZMS is the longest of all the circummaxillary sutures. In addition, the transverse palatine suture showed a large separation with marked new bone deposition with fiber bundles that were extremely stretched in the anterior-posterior direction as a result of the applied protracting extraoral force (Kambara 1977). Nanda also observed that the midfacial bones can be displaced anteriorly with maxillary protraction. Since the articulations of different midfacial bones are of varied lengths and orientation in relation to the line of force, these bones displace in more than one direction, which is likely due to the moments of force produced at the sutures (Nanda 1978).

The ZMS has a significant role in Class III skeletal malocclusion treatments since it is affected by both RME and maxillary protraction treatments (Ghoneima et al 2011, Nanda 1978). Historically, Class III treatment has evolved from using the bandeau and an expansion arch to chin-cup and using elastics with a maxillary lingual arch, to finally maxillary expansion with a reverse-pull headgear (Ngan and Moon 2015). The limit of anterior movement of the maxilla with RME and facemask is 2 to 4 mm (Ngan and Moon 2015). An expansion-constriction protocol used with RME and facemask was found to be more effective than a protocol utilizing expansion alone (Wilmes et al 2014). Bone-anchored maxillary protraction has also been proposed as a method to not only have better vertical control, but has also been demonstrated to produce 2 to 3 mm more sagittal change than RME with facemask (Cevidanes et al 2010).

1.2.3 Visualizing the ZMS

The ZMS suture follows a convoluted path that is not in direct visualization of X-ray paths of conventional radiography techniques used in orthodontics (Angelieri et al 2017). While the CVMS method and hand-wrist films have been used to indicate overall skeletal maturity, those were not used as direct assessment methods of the ZMS (Baccetti et al 2005, Fishman 1982). Some studies have been able to examine the ZMS directly through the use of 3-dimensional imaging and lower dose radiation CBCT machines when compared to medical CTs. Kajan et al's CBCT study assessed the ZMS in axial sections to determine whether the suture was open or closed based on the presence of a radiolucent line in the slices viewed. An association was found between the open or closed status of the ZMS to the mean MPS opening depth (Kajan et al 2018). The ZMS was considered open when visualized as a radiolucent line in upper axial slices. The opening depth of the MPS is the length of the radiolucent line present between the two halves of the maxilla at the MPS in the coronal view (Kajan et al 2018).

Conventional radiography involving lateral cephalograms or posteroanterior cephalograms displays a 2-dimensional image with many anatomical structures overlapping the ZMS. As previously mentioned, CBCT scans are used in this study to visualize the complicated path of the ZMS, which due to overlapping structures would not have been able to be assessed with conventional orthodontic radiographs. A recent CBCT study defined the maturation of the ZMS morphologically, which has not been previously described and validated until Angelieri et al's classification method of five maturational stages (A-E) (Angelieri et al 2017). Stage A is seen as a uniform radiopaque line with nearly no interdigitation. Stage B will begin to show scalloped features in the radiopaque line. Stage C is indicated as two parallel radiopaque, scalloped lines that are separated by a small radiolucent distance. Stage D indicates fusion in the infrazygomatic portion of the ZMS. In stage E, complete fusion with increased adjacent bone density is seen. The current investigation will utilize these five stages proposed by Angelieri et al to assess the subjects under study. In Angelieri et al.'s study sample of 5 to 58-year olds, the ZMS was found to be unfused up to 10 years of age, adolescents were found to be within the range of all five stages, and most subjects older than 15 years demonstrated fusion of the suture (Angelieri et al 2017).

The morphological maturational stages of the ZMS were also applied to a group of Class III patients that received either RME with facemask or bone-anchored maxillary protraction (BAMP) to evaluate the influence of the different maturational stages on maxillary protraction. The amount of maxillary protraction is inversely associated with the ZMS maturational stages. Stages A and B produced greater treatment response. Stage C was associated with a decrease in response to maxillary protraction. The two treatment protocols both found greater maxillary protraction at stages earlier than stage C or later. However, depending on the treatment goals, RME with facemask produced greater downward movement than BAMP and BAMP produced greater forward displacement than RME with facemask (Angelieri et al 2017).

1.3 Orthopedic treatment timing

The chronological timing of pubertal growth spurt varies between individuals. The physiologic maturity of an individual is important when considering treatment goals and treatment planning.

Pediatricians have relied on using the hand-wrist films as a way to indicate the skeletal maturity of an individual. In the past, orthodontics has used the hand-wrist films to do the same. Research in pediatrics have found the cervical vertebrae maturation level had a significant correlation with the skeletal maturity from hand-wrist analysis. When looking at the comparison of cervical bone and hand-wrist development in relation to chronological age, there is a stronger correlation between the cervical and hand-wrist skeletal age than between the cervical skeletal age and chronological age (Litsas and Ari-Demirkaya 2010). The CVMS method is preferable over the hand-wrist analysis to reduce radiation exposure in orthodontics since the lateral cephalogram is part of the standard records obtained for routine diagnosis and treatment planning (Baccetti et al 2002, Litsas and Ari-Demirkaya 2010). More specifically, Jang et al. evaluated correlation between bone age, by using the hand wrist method (Fishman 1982) and CVMS (Hassel and Farman 1995), and the midpalatal suture maturation. This study found that before stage 6 of the hand wrist method no fusion was observed in the MPS (stages D and E) (Jang et al 2016). Cangialosi's study found no difference between utilizing hand-wrist skeletal maturation index and Baccetti's CVMS

(Cangialosi 2018). The study also corroborated Jang et al's findings, which indicated hand wrist stages 1 through 6 correlated with CVMS I to II (Jang et al 2016; Cangialosi 2018).

In a study that looked at using the mandibular canine and second molar to identify the pubertal growth spurt indicated that dental maturation should not be used to determine treatment timing (Perinetti et al 2013). However, in the study conducted by Coutinho et al, the found the mandibular canine calcification stages could be used as one of the indicators to determine the status of an individual's pubertal growth spurt. The onset of puberty has initiated when the mandibular canine is at the calcification stage of having a funnel shaped apex in which the root length is equal to or greater than the crown height. When the canine root lengthens and the canal walls are parallel with partially open apex it correlates with the presence of the adductor sesamoid, the capping of the third middle and the fifth proximal phalanges, which indicates peak height velocity. Based on Coutinho et al's finding, the early stages of the pubertal growth spurt is between these two canine calcification stages (Coutinho et al 1993).

In a more recent study, Angelieri et al examined the association between CVMS specifically correlating to the stages of maturation of the MPS (Angelieri et al 2015). The study found prepubertal stages at CVMS I and II are reliable indicators for MPS maturational stages A and B, CVMS III for stage C, CVMS V for stages D and E. CBCT was recommended for individualized assessment of the MPS for post-pubertal patients since the suture has been found to be open in 16 to 20-year olds and adults >30 years (Angelieri et al 2015; Angelieri et al 2017; Ladewig et al 2018).

Bone density differences in relation to age and gender had been studied in orthopedics. The general findings in Leichter et al's study in 20 to 80 years old subjects indicated the average bone density for males is higher than for females. Males' density did not change across the different age groups whereas females' density began to decrease at age 50 (Leichter et al 1981). However, female cortical index was found to be greater than males between 30 and 50 years on the basis of muscle strength, body size or weight (Leichter et al 1981; Kelly et al 1990).

In a study conducted in dizygotic twins of differing within-pair gender indicated that the gender difference of osteoporotic fracture occurrences is not due to a sex difference in peak adult bone density at the lumbar spine or femoral neck. The adult bone mineral density difference is more likely due to postmenopausal bone loss and/or sex differences in the rate of bone loss that occurs with aging rather than gender (Kelly et al 1990).

Adolescence is marked by peak height velocity in stature and the development of secondary sexual characteristics. Growth of the maxilla and the mandible accelerate to reach maximum velocity a few months after peak height velocity in stature (Tanner 1962). The mandible has been observed to continue to grow slightly after maxillary growth ceases (Tanner 1962). In correlation with the CVMS, this would mean CVMS II is the optimal stage for growth modification as neither the maxilla nor the mandible has reached its peak growth (Tanner 1962; Baccetti et al 2002). De Clerck and Proffit summarized the general consensus of growth modification of the maxilla and mandible: in both jaws, skeletal changes are easier before adolescence with transverse expansion and extra-oral force. During adolescence, more force is required to achieve clinical goals, and either partial or complete surgical assistance is required after adolescence (De Clerck and Proffit 2015).

Baccetti et al's examined treatment timing for RME in relation to cervical maturation. The study evaluated posteroanterior cephalograms based on skeletal and dental landmarks. The result showed more significant transverse craniofacial changes when RME is performed prior to peak skeletal growth velocity whereas more dentoalveolar changes is seen in subjects that were treated after the peak skeletal maturation (Baccetti et al 2001).

Surgical procedures to facilitate the correction of maxillary transverse deficiency in skeletally mature individuals involve either the LeFort osteotomy or the surgically assisted rapid palatal expansion (SARPE). Chronological age has been considered as an indicator for delineating between the choice of conventional RME or SARPE. However, past literature reports inconsistencies of recommended age for surgical treatment. Some recommend surgical assistance in patients over 16 years, and others recommend the limit of 25 years of age (Epker and Wolford 1980; Timms and Vero 1981). Some have suggested gender should be considered in treatment decision of conventional or surgical assistance. Females up to 18 and males up to 21 years old and that women over 20 and men over 25 years were set as age limits for conventional or surgically assisted expansion, respectively (Alpern and Yurosko 1987).

Orthognathic surgery for the treatment of mandibular prognathism, with or without maxillary surgery, generally is recommended at the end of adolescence to be able to assess the malocclusion to its fullest extent (Baccetti et al 2004). The methods of evaluating timing have been based on CVMS, hand-wrist skeletal maturation index, growth stature and menarche status in females (Baccetti et al 2002; Fishman 1982; Tanner 1962).

Recent advances in technology has led to the use of computed tomography (CT) and its properties to individualize the assessment of the MPS without superimposition of anatomical structures as seen in conventional radiography. A study that used Hounsfield Units, which is a property of CT that quantifies mineral density based on grayscale differences, found strong correlation between MPS density increase and intermolar angle increase (Acar et al 2014). Other studies have used bone density measured from a CBCT and obtained results that indicate increased bone density with cervical vertebrae maturation and morphological maturation (Abo Samra et al 2018, Angelieri et al 2013). Another quantitative study that measured the percentage of the MPS opening depth in the anterior, middle, and posterior MPS. The percentage of the MPS opening depth decreases after 20-years old (Kajan et al 2018).

Previous studies have looked at the orthopedic impact of maxillary protraction based on chronological age, dental age, hand-wrist by Tanner-Whitehouse 2 system, and the cervical vertebrae maturation (CVM) method (Kapust et al 1998; Lee et al 2010; Suda et al 2000; Baccetti et al 2004). Kapust et al.'s examination of treatment response relative to age in 4 to 13-year olds showed that facemask with expansion therapy can be beneficial for older children but it is the most effective in younger children of ages 4 to 7 years (Kapust et al 1998). Lee et al's study looked at treatment effect difference between the primary and mixed dentitions to determine the lower limits of when maxillary protraction therapy without RME could begin to induce skeletal changes. Based on dental age, Lee et al. found facemask therapy without RME could be delayed until early mixed dentition since treatment that began in the primary dentition demonstrated a higher relapse tendency even though a more effective treatment response was seen (Lee et al 2010). By using the Tanner-Whitehouse 2 system approach to determine bone age, Suda et al was able to conclude that younger bone age correlated with increased maxillary protraction, but this method appeared to be more useful in male than female subjects (Suda et al 2000). Baccetti et al's studies have found indicators of success or failure of Class III malocclusion orthopedic treatment in patients that began treatment at CVMS I (Baccetti et al 2004). The three indicators that have an 83% probability of predicting success or failure of early orthopedic treatment followed by a phase with fixed appliances include: the length of the mandibular ramus, angulation of the cranial base, and inclination of the mandibular plane to the cranial base (Baccetti et al 2004). The CVMS method indicates stage II as the ideal stage for functional orthopedic treatment of the jaws (Baccetti et al 2002).

This study utilizes the five morphological maturational stages proposed and validated (as ground truth) by Angelieri et al (Angelieri et al 2013). This method has been used to classify individuals to predict RME success or failure. Various studies have used these five stages to examine pre-adolescents, adolescents, post-adolescents, young adults (≤ 25 years) and adults up to 66 years (Angelieri et al 2013; Tonello et al 2017; Ladewig et al 2018; Jimenez-Valdivia et al 2019; Angelieri et al 2017). Although chronological age is a poor indicator for skeletal maturity, higher percentage of pre-adolescents and adolescents were reported in stages A, B, and C (Angelieri et al 2013; Tonello et al 2017). However, when this method was used to examine adults, there were individuals found to be in stages B and C (Angelieri et al 2017). Stage A indicates a relatively straight radiopaque line eat the midline. In stage B, the suture appears as a scalloped high-density line. In stage C, the midline would show two scalloped, parallel radiopaque lines that are in close proximity and separated by small low-density spaces. In stage D, the suture appears the same as in stage C, but the same characteristic can only be visualized in the maxillary portion of the palate, not in the palatine bone. In stage E, the suture cannot be identified in the maxillary and palatine bone (Angelieri et al 2013).

2.0 Purpose of the Present Study

The aim of this study was to observe the maturational stages of the midpalatal and zygomaticomaxillary sutures in relation to an individual's age, gender, cervical vertebrae maturation stages, palatal depth and length ratio (P_d/P_l), zygomatic width, and malocclusion to determine how these factors are associated with sutural patency. The secondary aim of this study is to determine how the findings of this study may be utilized for individualized orthodontic clinical diagnosis and treatment planning based on whether these sutures are open or closed.

3.0 Materials and Methods

All cone beam CT images used in this study were de-identified and collected from a private orthodontic practice in Lancaster, Pennsylvania. All subjects selected were patients that had appointments in the practice between June 2019 to August 2019. Available scans based on these patients were accessed and the scans were dated between 2011 to 2019. Baseline diagnostic CBCT images studied were initially acquired for clinical purposes in 375 subjects. However, a resultant collection of 298 scans was analyzed because some subjects had multiple CBCT scans. A single CBCT scan from subjects with serial scans was selected by using an online random number generator tool (https://www.random.org). The remaining scans of those subjects were excluded to prevent introduction of confounding variables and to maintain the independence of each subject's scan. Subjects with ages ranging from 7 to 75 years were examined for ten measures. The medical history for subjects were reviewed, and all subjects were found to be healthy with no craniofacial anomalies, sutural synostosis or metabolic conditions that may link to abnormal bone metabolism. All scans were reviewed by a single examiner (E.C.). This descriptive cross-sectional study received institutional review board approval from the University of Pittsburgh.

For each subject, ten measures were collected: age, gender, malocclusion type, CVMS, MPS maturational stage, right and left side ZMS maturational stage, palatal length (ANS-PNS), palatal thickness at the level of the incisive foramen, and right and left zygomatic widths (in millimeters). Final data analysis reflects subjects that had complete data sets. Subjects whose data was incomplete were included in analyses that did not require the missing data (i.e. If a subject had all ten measures recorded except CVMS, the overall CVMS evaluation this particular subject would be excluded, but all other nine measures would be evaluated.).

CBCT scan images were obtained with i-CAT cone-beam 3-dimensional imaging system (Imaging Sciences International, Hatfield, PA). Each subject was positioned upright with the Frankfort horizontal plane (superior aspect of the external auditory canal to infraorbital rim line) parallel to the ground during the scanning process. For all scans, the field of view was 120mm by 220mm or 160mm by 160mm, and the scan time ranged from 4.8 to 14.7 seconds with a resolution of 0.25 to 0.4mm. Slice thickness for all scans were set at 0.5mm per slice. All images viewed for analysis were displayed on high-definition computer monitors. Image analysis was performed using Invivo5 (Anatomage, San Jose, CA). No changes were made of these images in contrast or brightness.

3.1 Midpalatal suture maturational stages, palatal depth, and palatal length

The following steps were implemented for determining and analyzing the maturational stages of the MPS, palatal depth, and palatal length by using Invivo5.

1. Head orientation. Natural head position in all 3 planes of space was verified or reoriented to correct for roll, pitch and/or yaw during image acquisition. The position indicator was positioned at the subject's midsagittal plane in both the coronal and axial views. In the sagittal view, the patient's head as adjusted so that the anteroposterior long axis of the palate was horizontal. To ensure the best view for visualization of the midpalatal suture and the measurement of the palatal depth and palatal length, the sagittal slice chosen was one with the most inclusive view of the incisive foramen by analyzing the slices medio-laterally (See Figure 2).
    a. Purple indicates the level at which the coronal section is viewed.

b. Green indicates the level at which the sagittal section is viewed.

c. Orange indicates the level at which the axial section is viewed.

2. Standardization of the axial cross-sectional slice used for sutural assessment. On the midsagittal section in the sagittal plane, the software's horizontal orange line was placed parallel to and centered to the palate in the superioinferior direction. This was used to classify the maturational stage of the MPS in the axial cross-sectional slices. For thicker palates, slices above and below the most central axial slices were viewed to determine MPS stage. If a palate's anterior and posterior portion cannot be visualized in the same axial slice, the subject is considered to have a curved palate (Figure 1.). For these subjects, the sagittal view is rotated clockwise to center the posterior palate for MPS visualization in the axial view.

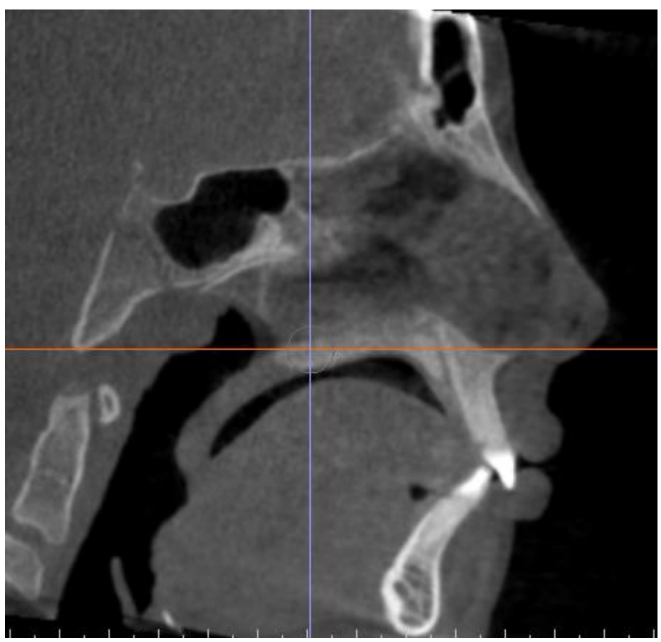

Figure 1. Example of cruved palate

3. Standardization of the sagittal cross-sectional slice used for the measurement of the palatal depth and length.

   a. The palatal depth is measured perpendicular to the horizontal line along the palate from the most inferior-palatal of the incisive foramen to the nasal surface of the maxillary bone at that level.
   b. The palatal length is measured along the horizontal line along the palate from anterior nasal spine (ANS) to posterior nasal spine (PNS).

4. Visualization and classification of the skeletal maturation stage of the MPS were carried out based on the previously described method of Angelieri et al (Angelieri 2013). Each scan was analyzed and suture categorized into five different maturation stages. A, B, and C stages were considered to have open midpalatal sutures, and D and E were considered to have closed midpalatal sutures.
5. Definition of the maturational stages of the midpalatal suture. Radiological morphology of the MPS were classified and referenced Angelieri et al (Angelieri et al 2013). See Appendix A, Figure 17, for a schematic depicting stages A through E.

Stage A. The midpalatal suture is almost a straight-high density sutural line with little or no interdigitation.

Stage B. The midpalatal suture has an irregular shape and appears as a scalloped high-density line. At this stage, there may be some small areas where two parallel, scalloped, high-density lines approximate each other yet are separated by small low-density spaces that can be seen.

Stage C. The mid palatal suture appears as two parallel, scalloped, high-density lines that approximate each other, separated by small low-density spaces in the maxillary and palatine bones from between the incisive foramen and posterior to the palatino-maxillary suture. The suture can be visualized as either a straight or an irregular pattern.

Stage D. The midpalatal suture demonstrates fusion in the palatine bone that progress from the posterior to anterior in which the palatal suture cannot be visualized. There is also increased parasutural bone density in the palatine bone compared to the maxillary parasutural bone. Fusion has not occurred yet at the maxillary midpalatal suture and two high-density lines separated by small low-density spaces can be seen.

Stage E. The midpalatal suture fusion has occurred in the maxilla. The actual suture is not visible in at least a portion of the maxilla. The bone density is the same as other regions of the palate.

Previous validation of the MPS maturational classification method for individualized assessment before RME was considered “ground truth” based on Angelieri et al 2013 (Angelieri et al 2013; Kohli et al 2017). Ground truth is the classification of each imaging examination that is made as accurate and reproducible as possible (Kohli et al 2017). Since the MPS staging cannot be verified by the gold standard of histologic examination, ground truth is used for the consensus and reproducibility of the radiographic interpretation (Angelieri et al 2013).

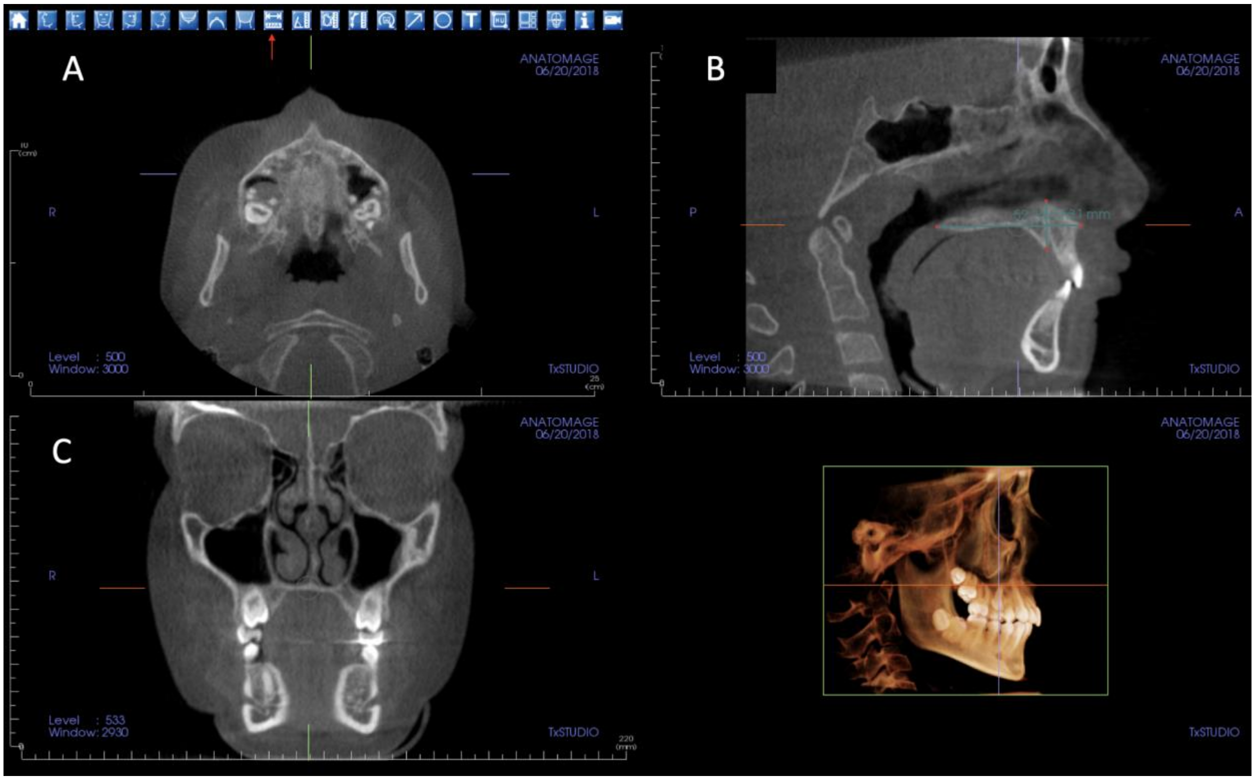

Figure 2. Standardization of head position in the A. axial; B, sagittal, and C, coronal planes to allow consistent assessments fo the midpalatal suture. B. the sagittal view, the orange line indicates the position of the axial plane view that is positioned throughed the center of the superioinferior dimension of the hard palate. Note that in B, measurement of the palatal length (along the orange horizontal line) and palatal depth (perpendicular to the orange horizontal line). Note also in A, the red arrow is the measurement tool used from Invivo5.

3.2 Zygomaticomaxillary suture maturational stages and zygomatic width

The following steps were used for determining and analyzing the maturational stages of the ZMS by using Invivo5 (Angelieri et al 2017). Due to the convoluted path of the ZMS, additional steps were included in the protocol to be able to read cross-sectional images through the long axis of the suture.

1. Head orientation: Adjustment and verification for all 3 planes were conducted in the same manner as the viewing for MPS stages.
2. In the sagittal view, the horizontal cursor (orange line) was placed at the tip of the nose parallel to the palatal plane. This view determines the axial view which is displayed as part of the ZMS obliquely bilaterally. The anteroposterior (purple line) was then positioned transversely through the ZMS bilaterally. This allows visualization of the ZMSs in the coronal view.
    a. The zygomatic widths are measured at this coronal slice from the nasal surface to the most lateral aspect of the zygomatic bone, parallel to the horizontal orange line, at the centermost aspect of the ZMS superoinferiorly (Fig. 2).

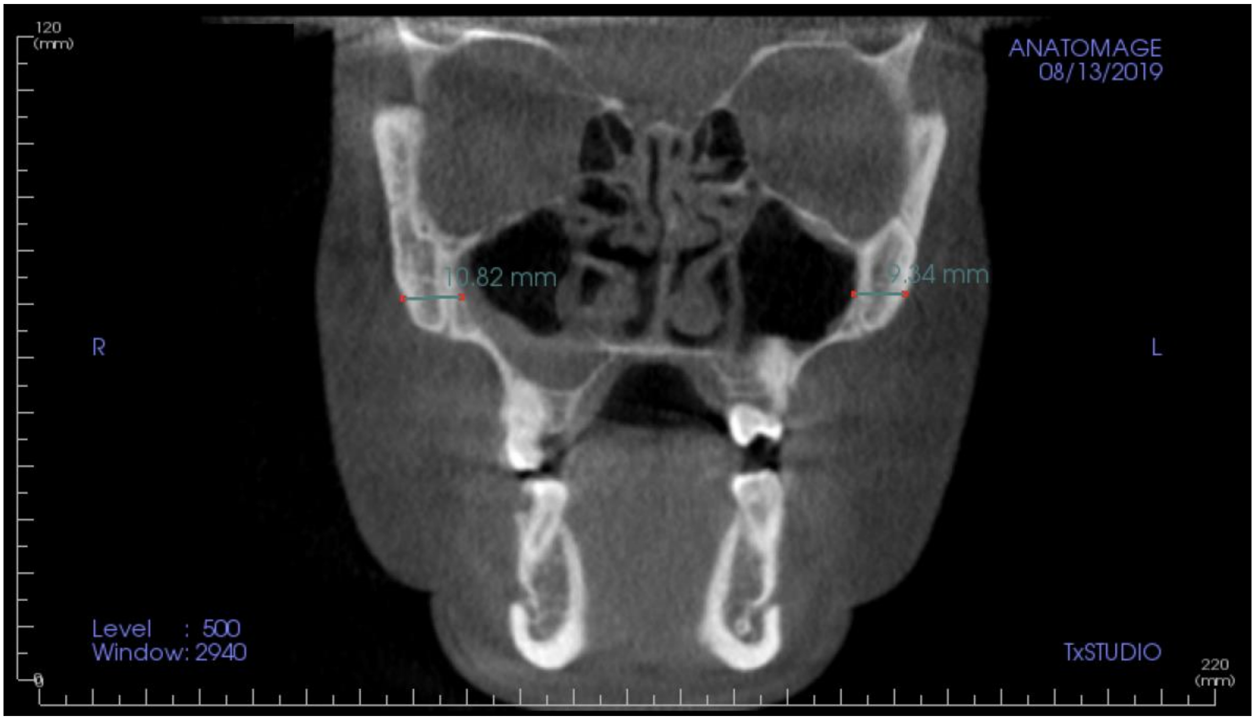

Figure 3. Measurement of the right and left zygomatic widths.

3. Visualization and classification of the skeletal maturation stage of the ZMS were carried out based on the described method of Angelieri et al 2017. Each scan was analyzed according to five different maturation stages. A and B stages were considered with open ZMS, and C, D and E were considered without open ZMS.
    a. Infraorbital, infrazygomatic, Right and left, overall
4. Definition of the maturational stages of the zygomaticomaxillary suture. Radiological morphology of the ZMS were classified according to Angelieri et al (Angelieri et al 2017).

Stage A. The ZMS is almost a straight-high density sutural line with little or no interdigitation and parasutural bone density is decreased.

Stage B. The ZMS has an irregular shape and appears as a scalloped high-density line with some interdigitation. Some areas can also be seen as a thicker, or thinner, scalloped high-density lines close to each other and are separated by small low-density spaces. The parasutural bone density is decreased as well at this stage.

Stage C. The ZMS appears as two thin, parallel, scalloped, high-density lines that are close to each other and separated by small low-density spaces in the zygomatic and maxillary bones. The parasutural bone density remains decreased.

Stage D. The ZMS has some fusion beginning in the inferior part of the suture and the parasutural bone density is increased.

Stage E. The ZMS is not visible in many areas along the suture due to multiple sites of fusion along the suture. The density of the parasutural bone is increased.

As previously stated for the MPS classification method, in the study based on Angelieri et al 2017, the method for evaluating the ZMS maturational stages is also considered ground truth (Kohli 2017).

3.3 CVMS and malocclusion classification

All CVM stages were determined according to the five stages as recorded by Baccetti et al 2002. CBCT scans that did not provide adequate visualization of the cervical vertebrae for determining the CVM stage due to the field of view limits were excluded.

Malocclusion classification records, according to Angle's malocclusion classification (Angle 1899), were based on the diagnosis of three orthodontists with at least five years of clinical experience.

3.4 Statistical Analysis

Cohen's kappa was calculated to evaluate intra-rater agreement (McHugh 2012). The agreement was defined according to the binary classification of the MPS and ZMS outcome variable.

The MPS outcome variable was codified as 0 (A, B, and C) for open suture and 1 (D and E) for closed suture. The ZMS outcome variable was codified as 0 (A and B) for open suture and 1 (C, D, and E) for closed suture (Angelieri et al 2013, 2017).

The significance of the association for comparing open or closed midpalatal and zygomaticomaxillary sutures to malocclusion and CVMS were evaluated by means of the chi-square test. Fisher's exact test was used when subgroup comparisons had smaller samples (See Appendix A, Table 15).

After conducting a Shapiro-Wilks test of normality, it was determined that subject age and the P_d/P_l ratio did not follow a normal distribution. Thus, a nonparametric test, the rank sum test, was used to analyze this outcome with respect to age and the palatal depth/palatal length (P_d/P_l) ratio. Therefore, the rank sum test was used instead of the two-sample t test. Two sample t test was used to analyze the outcome of MPS and ZMS with respect to palatal depth/palatal length ratio. A paired t test was used to analyze whether there was any difference between the right and left zygomatic widths.

The statistical significance level α was set at 0.05 for all tests.

The statistical software used was StataSE (version 14.2; StataCorp LLC, College Station, Texas, USA).

4.0 Results

The intra-rater reproducibility values indicated good repeatability with Cohen's kappa coefficient for the MPS and ZMS maturation at 0.95 and 0.83, respectively (McHugh 2012).

All the data that was collected in this study was analyzed for normality using Shapiro-Wilk test. Data that was normally distributed was analyzed using parametric test such as chi-square and paired-t test. Data that was not normally distributed was analyzed using the rank sum test. (See Appendix A, Table 15).

The opening or closure of the MPS and ZMS in relation to gender of the sample observed is shown in Table 1. The distribution of gender in relation to age is seen in Table 2 and Table 3 for the MPS and ZMS, respectively. Figure 4 and figure 5 shows the distribution of age at each maturational stage for the MPS and ZMS, respectively.

From this sample, the youngest observed closed MPS is 11 years old and the oldest observed open MPS is 75 years old. Based on this sample, the youngest observed closed ZMS is 7 years old and the oldest observed open ZMS is 65 years old.

There is a statistically significant difference in the mean age of those with open MPS and those with closed MPS ($P<0.01$) based on the rank sum test. The mean age for open MPS and closed MPS were 13.5 and 27.6 years old, respectively; and the median age for open MPS and closed MPS were 11 and 21 years old, respectively. Similarly, there is a statistically significant difference in the mean age of those with open ZMS and those with closed ZMS when evaluated with the rank sum test ($P<0.01$). The mean age for open ZMS and closed ZMS were 10.5 and 10.1 years old, respectively; and the median age for open ZMS and closed ZMS were 10 and 14 years old, respectively. A test of normality with Shapiro-Wilk test was carried out for both of these tests.

When the MPS patency was compared to the P_d/P_l ratio, a statistically significant difference was found between the mean P_d/P_l ratio of open MPS and closed MPS ($P<0.01$). The mean P_d/P_l ratio for open and closed MPS were 0.31 and 0.34, respectively. However, a statistically significant difference was not found between the mean P_d/P_l ratio of open ZMS and closed ZMS ($P=0.11$). A test of normality with Shapiro-Wilk test was carried out for both of these tests as well.

The right zygomatic width compared to the left zygomatic width in a paired t-test demonstrated there is no difference between the right and left mean zygomatic widths ($P = 0.4$).

Table 1. MPS and ZMS distribution by gender

	MPS		ZMS	
	Open (A/B/C)	Closed (D/E)	Open (A/B)	Closed (C/D/E)
Male	112	24	49	86
Female	111	51	45	114
Total	223	75	94	200
	298		294	

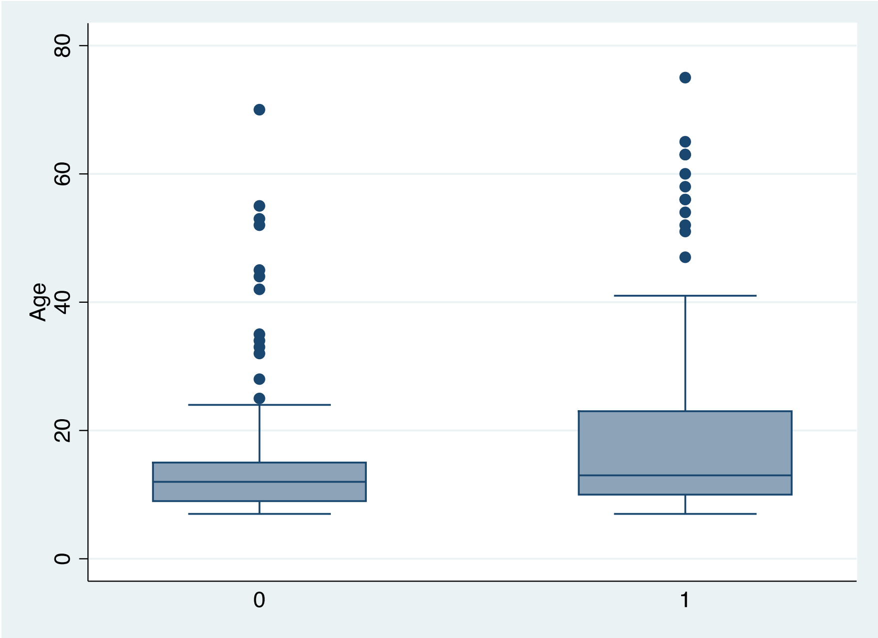

Figure 4. Age vs. Gender distribution. 0=male, 1=female

Table 2. MPS distribution by age

MPS	6-10 y		11-15 y		16-20 y		21-25 y		26-30 y		>30 y	
F (female) /M (male)	F	M	F	M	F	M	F	M	F	M	F	M
Open (A/B/C)	43	54	48	39	2	11	6	3	5	1	8	3
Closed (D/E)	0	0	14	12	8	3	4	2	8	0	16	8
Total	43	54	62	51	10	14	10	5	13	1	24	11
	97		113		24		15		14		35	

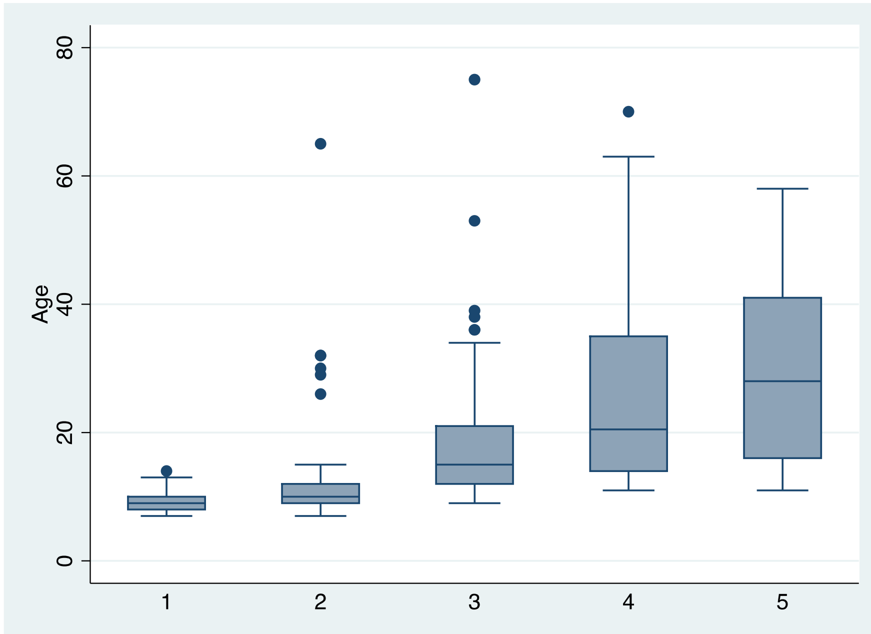

Figure 5. Age distribution vs MPS stages. Stage A=1, Stage B=2, Stage C=3, Stage 4=D, Stage 5=E

Table 3. ZMS distribution by age

ZMS	6-10 y		11-15 y		16-20 y		21-25 y		26-30 y		>30 y	
F (female) /M (male)	F	M	F	M	F	M	F	M	F	M	F	M
Open (A/B)	27	36	15	12	0	0	0	0	0	0	1	0
Closed (C/D/E)	14	17	44	37	10	14	10	5	13	1	24	11
Total	41	53	59	49	10	14	10	5	13	1	25	11
	94		108		24		15		14		36	

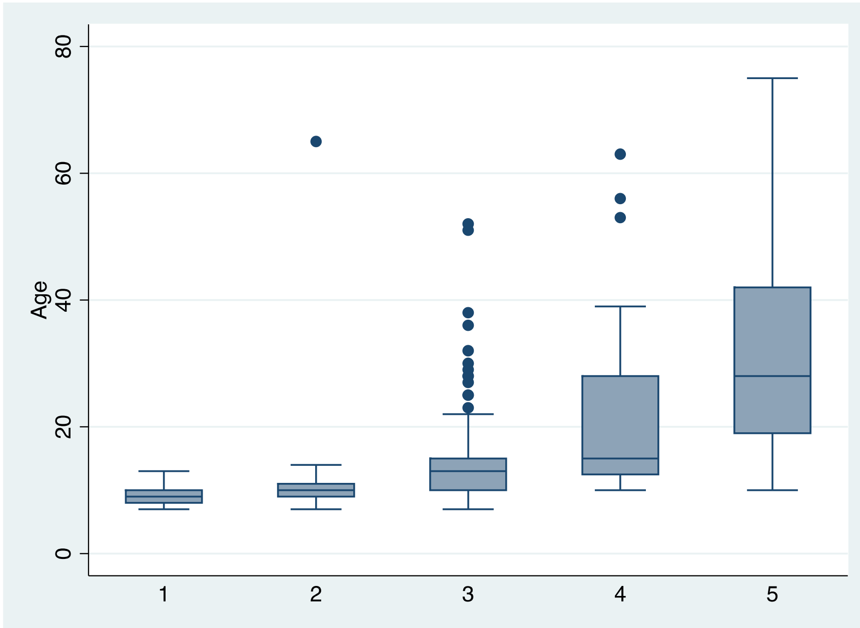

Figure 6. Age distribution vs. ZMS stages. Stage A=1, Stage B=2, Stage C=3, Stage D=4, Stage E=5

Table 4. MPS vs. ZMS: open or closed

	MPS Open (A/B/C)	MPS Closed (D/E)	Total
ZMS Open (A/B)	94	1	95
ZMS Closed (C/D/E)	125	74	199
Total	219	75	294

From this subject pool, the MPS is found to be open 99% of the time and closed 1% of the time when the ZMS is open. The MPS is found to be open 63% of the time and closed 37% of the time when the ZMS is closed (Table 4). Based on the Chi-square test, there is a statistically significant association between the opening and closure of MPS and the opening and closure of ZMS ($P<0.01$).

4.1.1 MPS opening or closure compared to CVMS in males

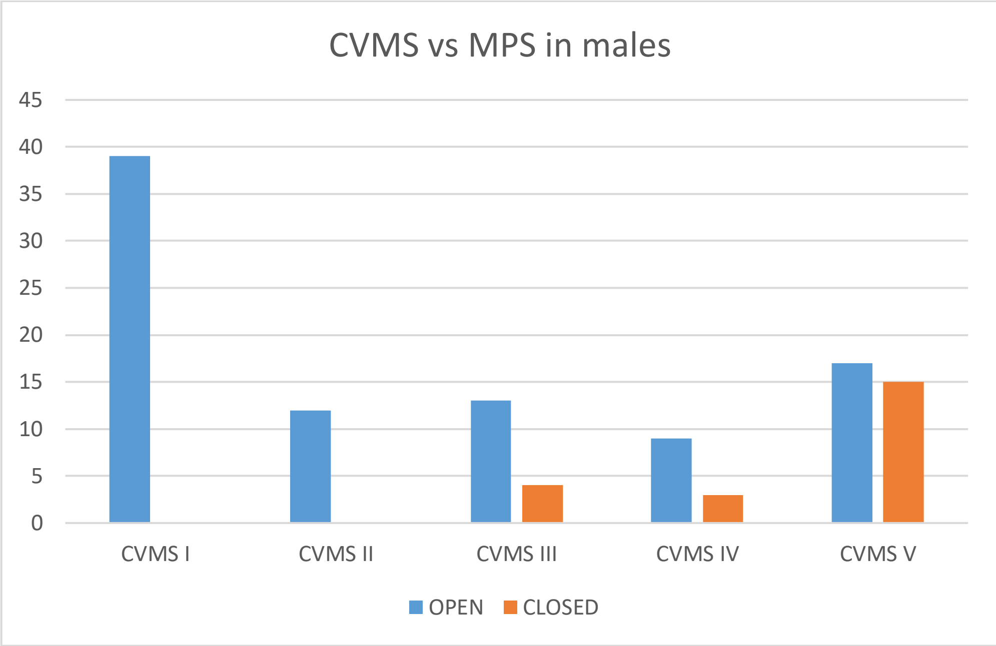

Figure 7. Bar graph demonstrating the relationship of open or closed MPS based on CVMS stages for all male subjects. y-axis = n

Table 5. CVMS in relation to MPS for all male subjects

	OPEN	CLOSED	Total
CVMS I	39	0	39
CVMS II	12	0	12
CVMS III	13	4	18
CVMS IV	9	3	12
CVMS V	17	15	32
Total	90	23	113

The comparison in males between the MPS patency to CVMS demonstrated that at CVMS I and II, the MPS is open 100% of the time. In this sample, the MPS was open 72% of the time at CVMS III and 75% of the time at CVMS IV. CVMS V shows males of having 53% open and 47% closed. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of MPS and CVM stages in males ($P<0.01$).

4.1.2 MPS opening or closure compared to CVMS in females

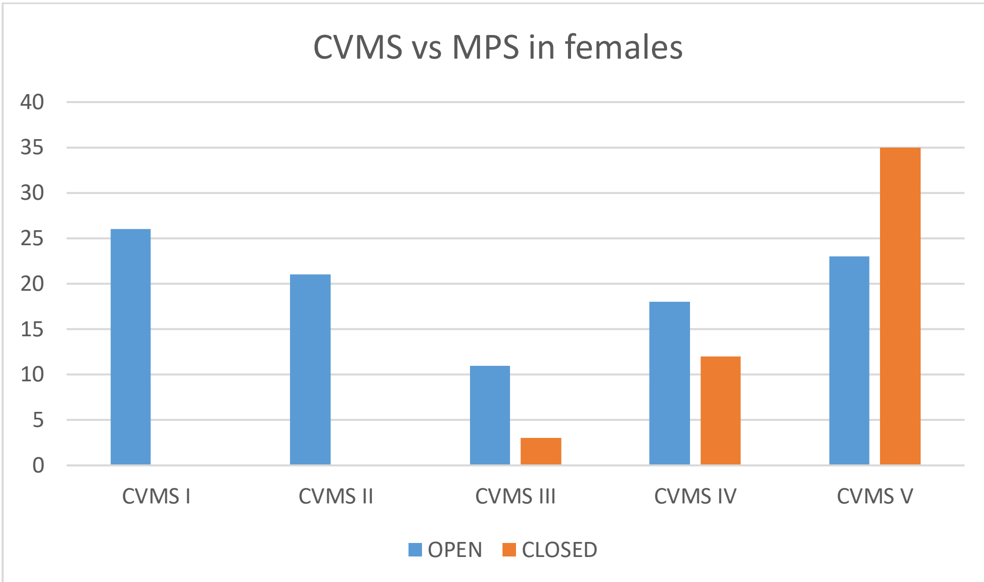

Figure 8. Bar graph demonstrating the relationship of open or closed MPS based on CVMS stages for all female subjects. y-axis= n

Table 6. CVMS in relation to MPS for all female subjects

	OPEN	CLOSED	Total
CVMS I	26	0	26
CVMS II	21	0	21
CVMS III	11	3	14
CVMS IV	18	12	30
CVMS V	23	35	58
Total	99	50	149

The comparison between females in the MPS opening or closure to CVMS demonstrated that at CVMS I and II, the MPS is open 100% of the time. At CVMS III and IV, the percentage drops to open MPS is 79% and 60%, and close is 21% and 40%, respectively. CVMS V shows females of having 40% open and 60% closed. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of MPS and CVM stages in females ($P<0.01$).

4.1.3 ZMS opening or closure compared to CVMS in males

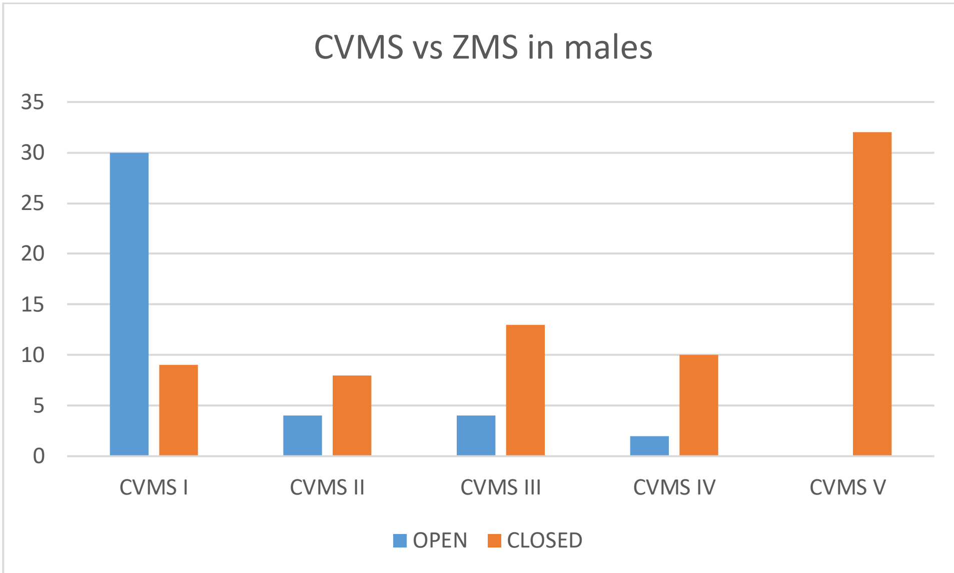

Figure 9. Bar graph demonstrating the relationship of open or closed ZMS based on CVMS stages for all male subjects. y-axis= n

Table 7. CVMS in relation to ZMS for all male subjects

	OPEN	CLOSED	Total
CVMS I	30	9	39
CVMS II	4	8	12
CVMS III	4	13	17
CVMS IV	2	10	12
CVMS V	0	32	32
Total	40	72	112

As seen in Figure 9 and Table 7, the ZMS in males in this sample at CVMS I is found to be open 77% and closed 23% of the time. The percentage of open ZMS drops dramatically to 33%, 24%, and 17%, and closed 67%, 76%, and 83% at CVMS II, III, and IV, respectively. At CVMS V, all male subjects had closed ZMS. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of ZMS and CVM stages in males ($P<0.01$).

4.1.4 ZMS opening or closure compared to CVMS in females

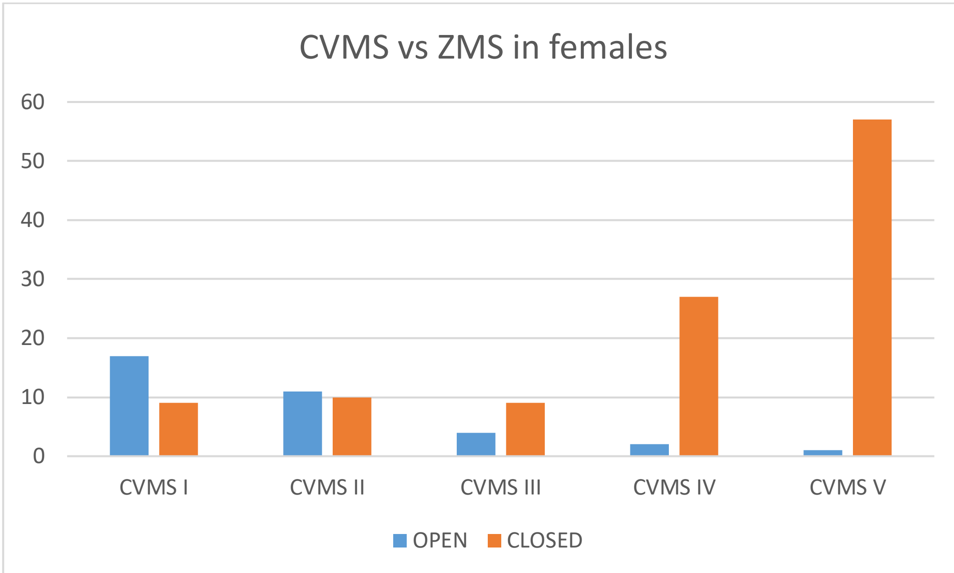

Figure 10. Bar graph demonstrating the relationship of open or closed ZMS based on CVMS stages for all female subjects. y-axis= n

Table 8. CVMS in relation to ZMS for all female subjects

	OPEN	CLOSED	Total
CVMS I	17	9	26
CVMS II	11	10	21
CVMS III	4	9	13
CVMS IV	2	27	29
CVMS V	1	57	58
Total	35	112	147

At CVMS I and II, the percentage for open and closed ZMS in females were 65% and 52% open and 35% and 48% closed, respectively. Starting at CVMS III and IV, a greater decrease in the percentage of open ZMS, 31% and 7%, and greater increase in closed, 69% and 93%, respectively. At CVMS V, females were found to have closed ZMS 98% of the time. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of ZMS and CVM stages in females ($P<0.01$).

4.1.5 MPS opening or closure compared to CVMS in Class I malocclusions

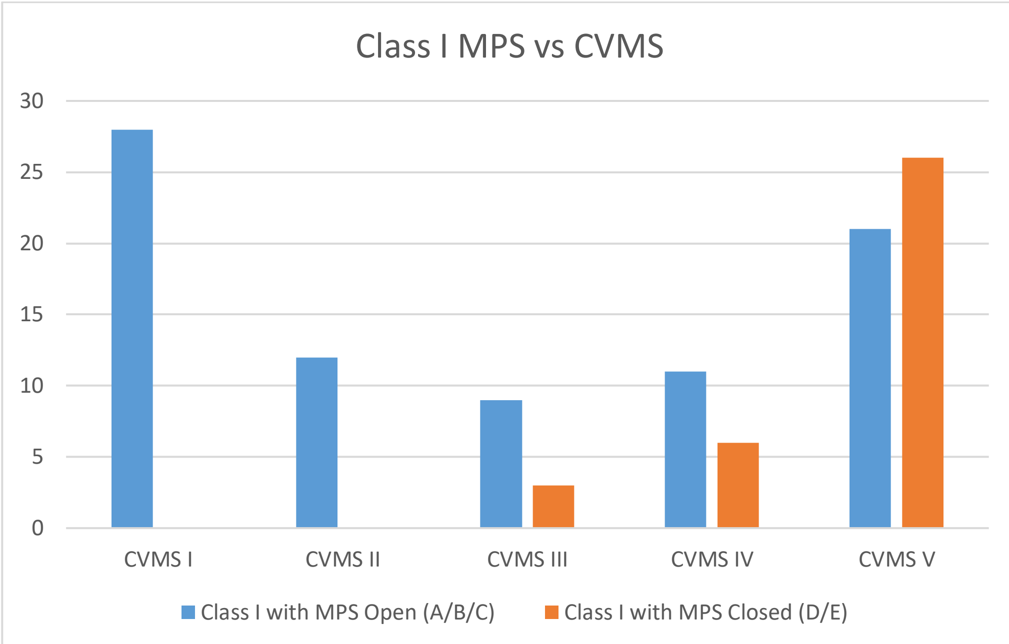

Figure 11. MPS vs CVMS stages for subjects with Class I malocclusion. y-axis = n

Table 9. MPS vs CVMS for Class I malocclusions

	Class I with MPS Open (A/B/C)	Class I with MPS Closed (D/E)	Total
CVMS I	28	0	28
CVMS II	12	0	12
CVMS III	9	3	12
CVMS IV	11	6	17
CVMS V	21	26	47
Total	81	35	116

Subjects that have class I malocclusion are found to have open MPS 100% of the time at CVMS I and II. At CVMS III and IV, the percentage of opening decreases to 75% and 65% and the percentage of closure increased to 25% and 35%, respectively. At CVMS V, 45% are open and 55% are closed. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of the MPS and CVM stages for those with class I malocclusion ($P<0.01$).

4.1.6 MPS opening or closure compared to CVMS in Class II malocclusions

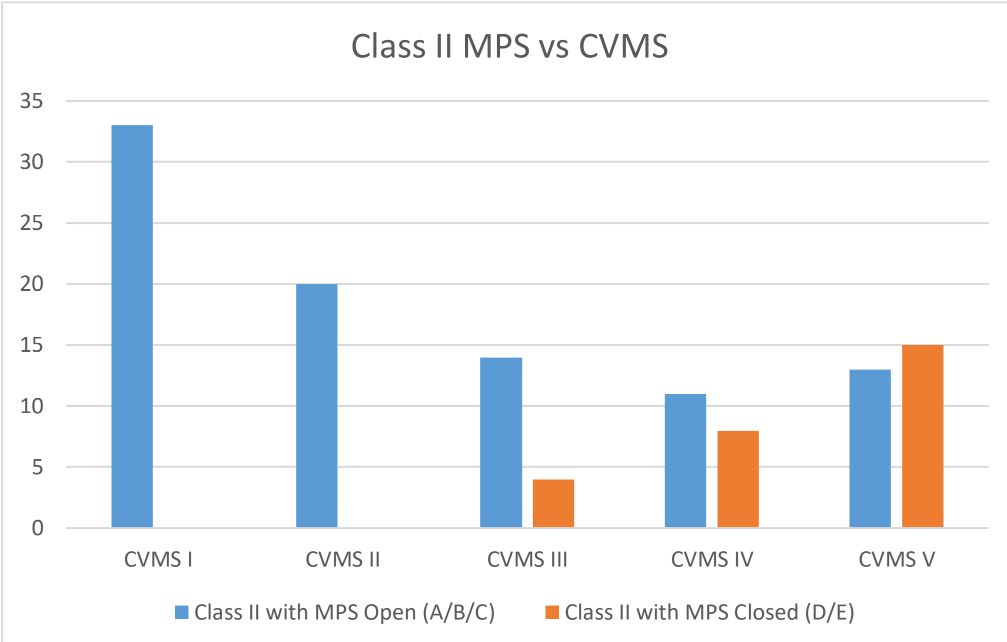

Figure 12. MPS vs CVMS stages for subjects with Class II malocclusion. y-axis = n

Table 10. MPS vs CVMS for Class II malocclusions

	Class II with MPS Open (A/B/C)	Class II with MPS Closed (D/E)	Total
CVMS I	33	0	33
CVMS II	20	0	20
CVMS III	14	4	18
CVMS IV	11	8	19
CVMS V	13	15	28
Total	91	27	118

Subjects that have class II malocclusion are found to have open MPS 100% of the time at CVMS I and II. At CVMS III and IV, the percentage of opening decreases to 78% and 58% and the percentage of closure increased to 22% and 42%, respectively. At CVMS V, 46% are open and 54% are closed. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of the MPS and CVM stages for those with class II malocclusion (P<0.01).

4.1.7 MPS opening or closure compared to CVMS in Class III malocclusions

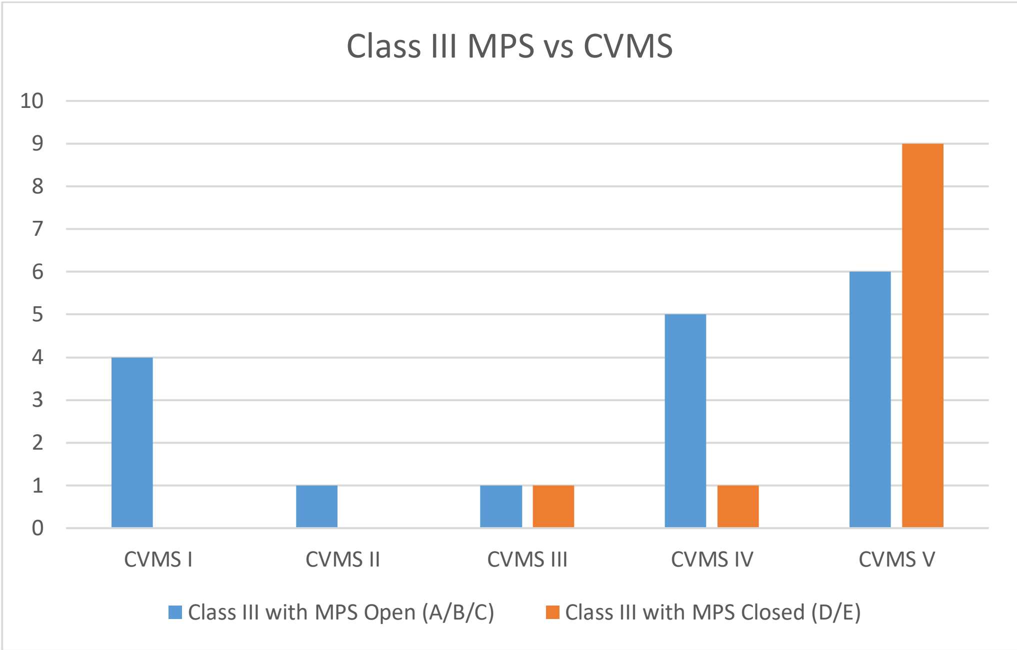

Figure 13. MPS vs CVMS stages for subjects with Class III malocclusion. y-axis = n

Table 11. MPS vs CVMS for Class III malocclusions

	Class III with MPS Open (A/B/C)	Class III with MPS Closed (D/E)	Total
CVMS I	4	0	4
CVMS II	1	0	1
CVMS III	1	1	2
CVMS IV	5	1	6
CVMS V	6	9	15
Total	17	11	28

Subjects that have class III malocclusion are found to have open MPS 100% of the time at CVMS I and II. At CVMS III the percentage of open and closed are each at 50%. CVMS IV demonstrates 83% as open and 17% as closed. At CVMS V, 40% are open and 60% are closed. Based on the Fisher's exact test, there is no statistically significant association between the opening and closure of the MPS and CVM stages for those with class III malocclusion (P=0.09).

4.1.8 ZMS opening or closure compared to CVMS in Class I malocclusions

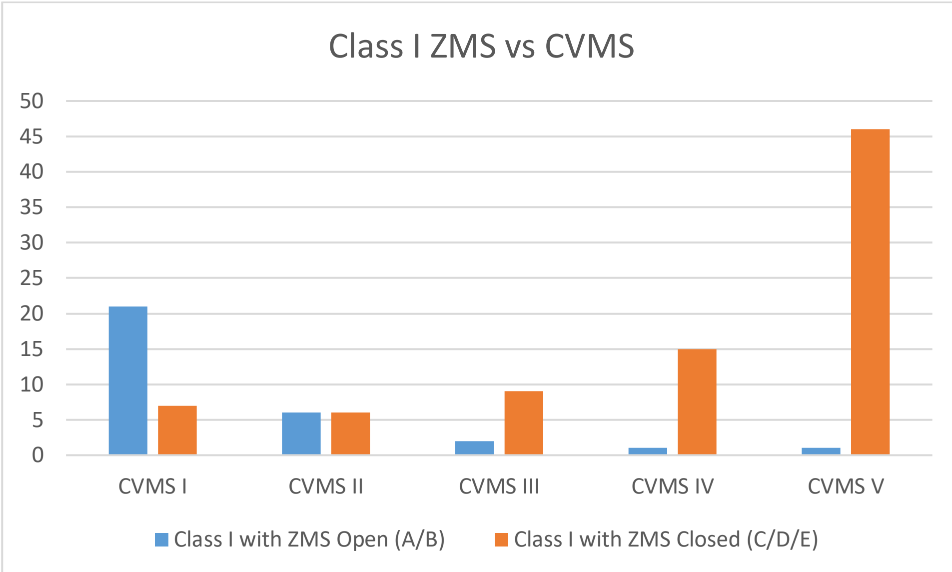

Figure 14. ZMS vs CVMS stages for subjects with Class I malocclusion. y-axis = n

Table 12. ZMS vs CVMS for Class I malocclusions

	Class I with ZMS Open (A/B)	Class I with ZMS Closed (C/D/E)	Total
CVMS I	21	7	28
CVMS II	6	6	12
CVMS III	2	9	11
CVMS IV	1	15	16
CVMS V	1	46	47
Total	31	83	114

Subjects with class I malocclusion are found to have open ZMS 75% and closed 25% at CVMS I. At CVMS II and III, the percentage for open ZMS decreased to 50% and 18%, and closed to 50% and 82%, respectively. At CVMS IV and V, the percentage for open ZMS greatly reduced to 6% and 2%, and closed ZMS at 94% and 98%, respectively. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of the ZMS and CVM stages for those with class I malocclusion (P<0.01).

4.1.9 ZMS opening or closure compared to CVMS in Class II malocclusions

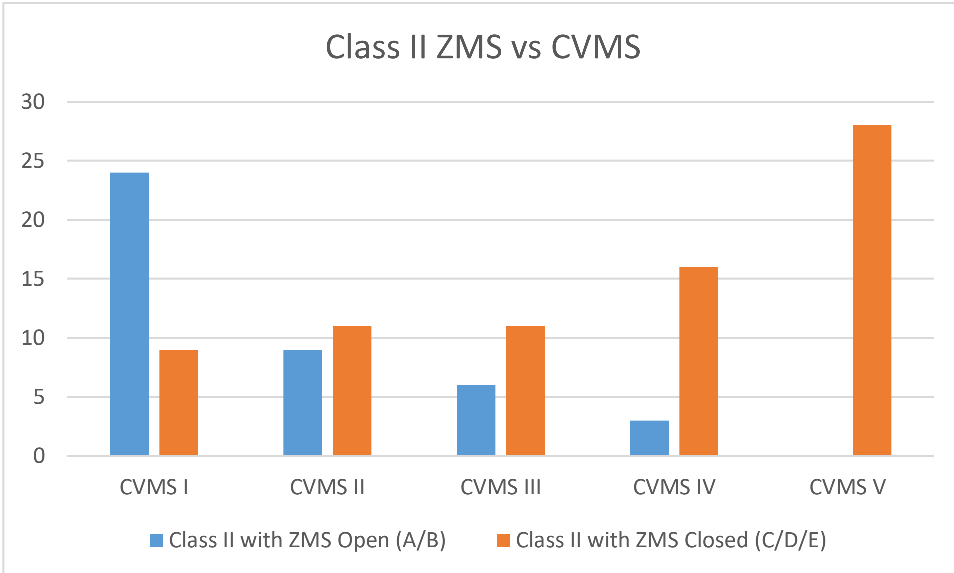

Figure 15. ZMS vs CVMS stages for subjects with Class II malocclusion. y-axis = n

Table 13. ZMS vs CVMS for Class II malocclusions

	Class II with ZMS Open (A/B)	Class II with ZMS Closed (C/D/E)	Total
CVMS I	24	9	33
CVMS II	9	11	20
CVMS III	6	11	17
CVMS IV	3	16	19
CVMS V	0	28	28
Total	42	75	117

At CVMS I, subjects with class II malocclusion have ZMS open percentage of 73% and 27% closed. CVMS II, III, and IV shows a dramatic decrease in open percentage at 45%, 35%, 16%, and increase in closed ZMS percentage at 55%, 65%, and 84%, respectively. Class II malocclusion individuals demonstrates 100% closed ZMS at CVMS V. Based on the Chi-square test, there is a statistically significant association between the opening and closure of the ZMS and CVM stages for those with class II malocclusion ($P<0.01$).

4.1.10 ZMS opening or closure compared to CVMS in Class III malocclusion

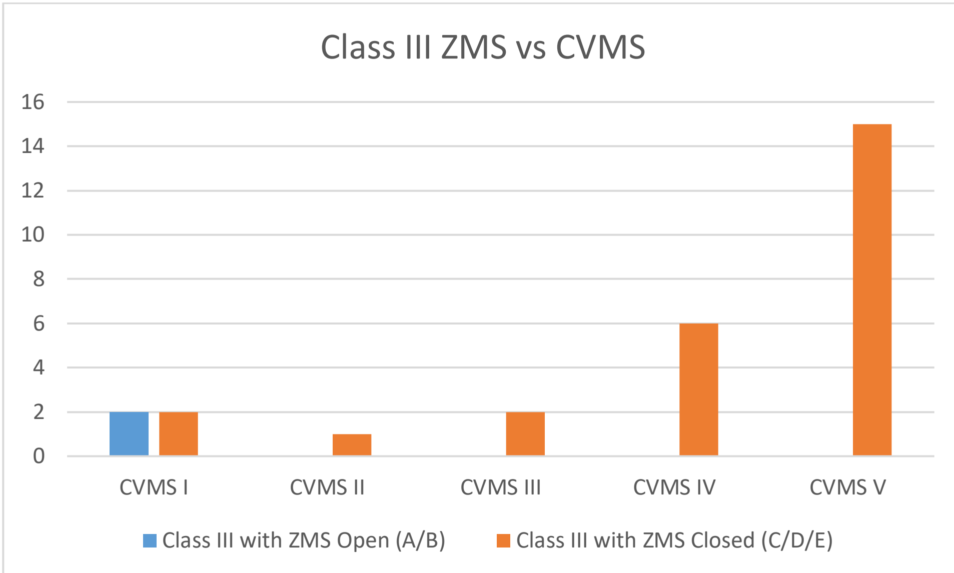

Figure 16. ZMS vs CVMS stages for subjects with Class III malocclusion. y-axis = n

Table 14. ZMS vs CVMS for Class III malocclusions

	Class III with ZMS Open (A/B)	Class III with ZMS Closed (C/D/E)	Total
CVMS I	2	2	4
CVMS II	0	1	1
CVMS III	0	2	2
CVMS IV	0	6	6
CVMS V	0	15	15
Total	2	26	28

In the subjects observed, those with class III malocclusion at CVMS I show 50% with open ZMS and 50% closed. CVMS II, III, IV, and V all demonstrate 100% ZMS closure. Based on the Fisher's exact test, there is a statistically significant association between the opening and closure of the ZMS and CVM stages for those with class III malocclusion (P=0.05).

5.0 Discussion

The MPS has been studied to examine the maturation level by a variety of methods. Some are quantitative, semi-quantitative, and qualitative (Isfeld et al 2017). Histologic studies have tried to quantify the MPS maturation by means of the obliteration index and the interdigitation index in different planes (Persson and Thilander 1977). However, studies as such utilized micro-CTs that would provide excess radiation dose and long scanning time, which would be impractical in routine clinical practice (Korbmacher et al 2007). Other semi-quantitative studies have tried to be as minimally invasive as possible by using ultrasonography for real-time chairside evaluation to obtain a bone fill score. While this has the advantage to image early bone formation, especially post-expansion, the disadvantage is ultrasound's inability to penetrate cortical bone. In addition, while ultrasound may be low cost and non-invasive, most orthodontists are not trained to routinely use this type of imaging method (Sumer et al 2012).

In this study, the youngest observed closed MPS is 11 years old and the oldest observed open MPS is 75 years old. In this study sample, the youngest observed closed ZMS is 7 years and the oldest observed open ZMS is 65 years old. This is consistent with previous studies that demonstrated variation in sutural interdigitation and fusion, not only within an individual, but also across a wide age range (Persson and Thilander 1977, Cohen 1993). In addition, Figure 5 and Figure 6 demonstrates chronological age is not as a good of an indicator for sutural patency and morphological maturational stages, a finding that corroborates previous studies (Angelieri et al 2017; Ladewig et al 2018).

Current studies indicate CBCT in general has high accuracy in measuring periodontal defects and buccal alveolar bone height measurements (Misch and Sarment 2006, Wood et al

2013). In a study that examined the accuracy of CBCT use for measuring periodontal defects, Misch and Sarment indicated (scans at medium resolution of 0.4mm, 20 second) there is no statistical differences in the linear measurements for all defects between bone sounding, radiographs, and CBCT (Misch and Sarment 2006). Spatial resolution is the minimum distance required to distinguish between two objects on the CBCT. This property is important especially in detecting and making small measurements, such as buccal bone thickness. Bone thinner than 1mm may appear as if it does not exist based on the spatial resolution (Molen 2010). Unfortunately, decreased voxel size to gain more detail in the scanned image requires longer scanning time and more exposure to radiation. The ALARA principle should be used depending on each individual's requirements for diagnosis and treatment planning (Signorelli et al 2016).

The general bone thickness and the relative cortical to cancellous bone proportion in the zygomatic and maxillary bone may be important. Depending on the general thickness of these bones, especially in individuals with thinner or narrower measurements, the radiographic morphology could be interpreted as the bone being denser and more mature. This study noticed similar observation as in Angelieri et al that thinner palates tend to show the MPS as fused, classified as E (Angelieri et al 2013). The benefit of increased image resolution with CBCT, which accompanies the risk of increased radiation exposure, in terms of clinical diagnosis and treatment planning for a particular individual is undetermined and potentially debatable.

The findings for P_d/P_l ratio relative to the patency of the MPS was statistically significant in this study. The mean P_d/P_l ratio for open MPS was 0.31 and closed MPS was 0.31 and 0.34. This could imply deeper and shorter palates are more likely to be patent and shallower and longer palates are more likely to be closed. The association of the MPS patency based on the mean P_d/P_l ratio should be interpreted with caution since the dimension of a palate could be deep and long, shallow and short given the same ratio, or vice versa. See Figure 18 in Appedix A the observed variation in the midsagittal morphology of the hard palate. Angelieri et al's finding of stage E MPS with thinner palates supports with the relationship that we found between the mean P_d/P_l ratio and MPS patency. Shin et al's study looked at predictors for MPS expansion using with skeletally anchored maxillary expanders (mini-implant assisted rapid palatal expansion, or MARPE) in young adults. Although the study was conducted using skeletal anchorage, they found there was a negative correlation between the palatal length and the MPS opening ratio. This study inferred longer palates will have more delayed anterior expansion as well since palatal fusion starts from the posterior region (Shin et al 2019, Persson and Thilander 1977). In our study, the palatal depth measurement was taken at the level of the incisive foramen. According to Persson and Thilander, the palate begins to fuse from the posterior to the anterior direction (Persson and Thilander 1977). Based on that, future studies with depth measurements in the posterior third of the palate may be able to better elucidate on whether the P_d/P_l ratio is relevant to the success or failure of RME in relation to an individual's skeletal maturity. Future study may involve studying different palatal depths while controlling for age, gender and palatal length as well. If a relationship, or a threshold, is determined between the P_d/P_l ratio and MPS, a potential benefit is the ability evaluate this indicator on a routine lateral cephalogram rather than a CBCT.

In the comparison of the MPS patency relative to CVMS for both genders, CVMS I and II was observed to have patency 100% of the time and a decline in that percentage was seen starting at CVMS III. According to our sample, males (53% open, 47% closed) were more likely to have MPS patent than females (40% open, 60% closed) at CVMS V. When the MPS patency and CVM stages were compared in males, our sample indicated the level of patency begins to decrease at CVMS III. Our sample demonstrated the MPS was open 72% of the time at CVMS III and 75%

of the time at CVMS IV. CVMS IV subjects are skeletally more mature than CVMS III and would expect to generally trend with lower proportions of MPS patency. Since this is a cross sectional study, the finding of slightly higher percentage of MPS patency at CVMS IV compared to CVMS III could be specific to this timepoint and the study sample population.

The relationship between Class I and Class II malocclusion subjects and the patency of MPS as compared to CVM stages appears to have the similar trends. For these patients, at CVMS I and II indicates the MPS is patent 100% of the time, drops to about 75% at CVMS III, and close to 50% at CVMS V. This implies that conventional RME could be successful at least 75% of the time if patient presents with CVMS III or less. This finding corroborates with Angelieri et al's finding that CVMS III correlates with MPS stage C, which indicates a suture that is soon to close, but still is considered patent (Angelieri et al 2015). Furthermore, our findings also imply if an individual with Class I or Class II malocclusion that is at CVMS V, the probability of a patent MPS is about 45% (Class I is at 45%, Class II is at 46%). Previous studies have indicated difficulty in achieving RME in skeletally matured patients, but it is possible to achieve (Suzuki et al 2018; Carlson et al 2016). More recent studies have shown adults that were treated with skeletally anchored maxillary expanders and successful expansions were achieved, some with or without reducing sutural resistance with the assistance of corticopunctures along the MPS (Suzuki et al 2016; Suzuki et al 2018; Carlson et al 2016).

The trend between males' and females' proportions in terms of relating the ZMS to the CVMS appears to be similar with a dramatic drop in patent ZMS beginning at CVMS II. Although CVMS I is considered skeletally immature, it did not correlate with a patent ZMS all the time as MPS did.

In subjects with Class I and Class II malocclusions, the ZMS patency as compared to CVMS indicates at CVMS I, the suture is patent at least 70% of the time. The probability of a patent ZMS drops dramatically to 45-50% starting at CVMS II; the likelihood drops to 18-35%, 6-16%, 0-2% for CVMS III, IV, and V, respectively.

Class III malocclusion subjects' patency of the MPS and ZMS as compared to CVM stages did not have statistically significant association at the MPS, but Class III malocclusion was statistically significantly associated with the patency of the ZMS. The lack of association at the MPS could be due to our low sample size that led to the inability to detect a difference. However, the finding of statistical significance at the ZMS should also be interpreted with caution due to our low sample size as well. Based on the data available in our sample, it could be interpreted that if individuals with Class III malocclusions, or Class I malocclusions that are tending towards Class III, who were to be considered for RME and extraoral protraction treatments, the effect of the treatment would be more predictable if it was initiated at CVMS I and no later than CVMS II.

In this study sample, we found that when the ZMS is open, the MPS is patent 99% of the time, and when the ZMS is closed, the MPS is patent 63% of the time. The ZMS had previously been studied to be the major resistance to forces produced by RME and extraoral protraction (Tanne and Sakuda 1991). As the longest circummaxillary suture with the most tortuous path, the ZMS is also unique in its oblique orientation and shape (Kambara 1977; Sholts and Wärmländer 2012). The shape of the ZMS could be angled, curved, or straight (Sholts and Wärmländer 2012). In addition to considering the patency of the ZMS and various skeletal maturity indicators, perhaps the shape of the ZMS should be evaluated as well. The shape of the ZMS could potentially impact not only the different directions of maxillary displacement, but also the success and failure of treatment with either RME or reverse pull headgear. Further CBCT and histological studies would be required to verify whether successful RME is achieved in the presence of a closed ZMS. However, studies such as those with adult subjects receiving treatment with MARPE could shed light to that question as expansion is achieved with a likely closed ZMS. Based on the present study, the ZMS has a negative relationship with increasing age and CVMS (i.e. the ZMS is more likely to be closed with older and skeletally mature individuals) (See Table 3 and Table 7). Even though our sample indicates the ZMS is closed in a greater proportion at later CVM stages, studies in young adults, with average age of about 14.5 years old (hand-wrist skeletal maturation index 10 or 11), have shown some skeletal changes with facemask treatment (Yavuz et al 2009, Halicioglu et al 2014). While there is more dentoalveolar changes, in non-severe skeletal Class III malocclusions, face mask treatment with or without RME could still produce mild skeletal changes in young adults (Yavuz et al 2009, Halicioglu et al 2014). Reports have also shown stimulated bone activity in a 16-year-old female at the ZMS when single photon emission computerized tomography (SPECT) was used (Yavuz et al 2006).

In the past, orthodontists used the CVMS to evaluate the skeletal maturity of their patients, it may be important to consider whether all of the CVM stages are achieved in adults (Perinetti et al 2020). Although it was not found in high proportions, the study found 16% of the adults they examined maintained a pubertal CVM stage four. Thus, treatment timing should not solely rely on CVM stages (Perinetti et al 2020; Baccetti et al 2005).

Our measurement of the right and left zygomatic widths based on CBCT coronal sections demonstrated no statistical difference between the mean zygomatic widths on either side within an individual. From our observation, some subjects appear to have significant differences between the two sides, which could potentially impact the effect and symmetry of maxillary protraction mechanics. Perhaps it would have been more appropriate to measure the actual ZMS length and the widths at the infraorbital and infrazygomatic level of the suture. Future studies could look at that measure and shape of the ZMS in relation to the extent of maxillary protraction achieved. Perhaps future studies could examine individuals with narrower zygomatic widths for ZMS maturity relative to chronological and skeletal age compared with individuals that have wider zygomatic widths. It is possible the ZMS could appear to be denser with narrower zygomatic widths, similar to more mature MPS stages that was observed with thinner palates. Based on this speculation, the overall contact surface area between the adjoining bones at the ZMS would theoretically be greater in individuals with wider zygomatic widths. The clinical significance and relationship of these characteristics relative to the extent of skeletal changes achieved with protraction forces is undetermined. See Figure 19 in Appendix A for examples of zygomatic width differences within individuals.

In addition, a secular trend in the age at menarche has changed in the last five to seven decades. Studies in Portugal, Israel, Mexico, Korea, China and Saudi Arabia have all indicated a trend towards earlier onset of menarche (Queiroga et al 2020; Flash-Luzzatti et al 2014; Marvan et al 2016; Oh et al 2012; Meng et al 2017; Rafique and AlSheikh 2019). Furthermore, urbanized life, increase in body mass index, and caloric intake are all negatively associated with the menarcheal age (Meng et al 2017; Oh et al 2012; Rafique and AlSheikh 2019). How these factors have changed, and may continue to change, and the impact they have when considering the skeletal maturity of orthodontic patients should be noted.

The MPS opens in a "V" shaped pattern in both the transverse and vertical dimensions, with more anterior expansion and some to near the orbits as the maxillary bone is connected superiorly to the orbits (De Clerck and Proffit 2015). Histological studies indicate the MPS closes from posterior to anterior (Persson and Thilander 1977). A recent study proposed a new type of expander that allowed differential maxillary expansion as a way to treat maxillary transverse discrepancies that are greater in the intercanine width than the intermolar width. It was able to effect greater skeletal and dental changes in the anterior region than a conventional expander (Alves et al 2020). Perhaps it may be logical to use a similar maxillary expander with differential opening (Alves et al 2020) to expand and contract anteriorly first, regardless of arch form (choose to expand anterior maxilla if V shaped arch needs to coordinate with U shaped mandibular arch, or contract anterior to where desirable), to act as a wedging effect in order to achieve posterior expansion in skeletally mature individuals.

Perhaps some emphasis on psychosocial impact of malocclusion should be considered. Based on surveys, adolescents were found to believe that orthodontic treatment could not only motivate them to look after their teeth better in the future, but also it would have a positive impact on self-confidence, be more socially accepted by friends and peers and make a good first impression for job interviews (Twigge et al 2016). Judgement by others about a person's integrity, social, and intellectual attractiveness were found to be strongly influenced by dental esthetics (Papio et al 2019).

5.1 Future Research

Perhaps measurements of the palatal depth in the posterior third, or posterior to the transverse palatine suture, should be considered instead in the P_d/P_l ratio since the MPS fuses in the posterior to anterior direction. A retrospective or prospective study could be designed to see whether MPS have expanded or can be expanded; this could be designed to compare if there is a difference between using a conventional digital lateral cephalogram and a CBCT generated lateral cephalogram.

Prospective study using the either or both maturational stages to make treatment decision and confirm whether the desired treatment effect was achieved regardless of chronological or skeletal age.

Using a maxillary expander with differential opening to activate the anterior maxilla first and measure the success and failure rate of subsequent posterior skeletal expansion.

There may be benefit to examine the dental and skeletal effect headgear or functional appliances have on patients with class II malocclusion at all ZMS maturational stages and CVM stages.

Future in vitro and in vivo studies with human biopsy specimen would be beneficial to determine the true accuracy and validity of using CBCT in measuring and/or visualizing the circummaxillary sutures.

5.2 Limitations

Since this is a cross-sectional study completed by a single operator at a single center, there is risk of systematic error. Based on this, the external validity of the findings should be interpreted with caution.

The class III malocclusion subjects were limited compared to class I and II malocclusion. Further studies with higher sample would better elucidate the MPS and ZMS status of class III malocclusion relative to CVM stages.

5.3 Application to Clinical Orthodontics

The information presented in this study could potentially provide insight in the clinical decision, based on the factors (age, gender, CVMS, maturational stages of the MPS) presented here, whether to decide between a conventional RME, MARPE, or SARPE to best avoid unwanted periodontal side effects that accompanies with these types of treatment.

6.0 Conclusion

According to the subjects observed in this sample, it can be concluded that:

1. Deeper and shorter palates are associated with an open MPS, and shallower and longer palates are associated with a closed MPS.
2. There is a strong association that if the ZMS is open, the MPS is open as well and when the ZMS is closed, the MPS is found to be open more than half the time.
3. When considering RME, the MPS maturation status should be evaluated starting at CVMS III since 25% of the time MPS is closed. Males tend to have a slightly higher chance of open MPS at CVMS V than females.
4. When maxillary protraction treatment is indicated, an individual's ZMS maturation status should be considered to be evaluated with CBCT since some closure has been observed even at CVMS I.
5. With respect to class I malocclusions:
    a. If only RME treatment is indicated, the MPS maturation status should be evaluated starting at CVMS III since 25% of the time the MPS is closed.
    b. In pseudo-class III malocclusion, in which RME with a facemask is indicated, the ZMS maturation status should be evaluated at least starting at CVMS II.
6. With respect to class II malocclusions:
    a. If only RME treatment is indicated, the MPS maturation status should be evaluated starting at CVMS III since 20% of the time MPS is closed at that CVM stage.
7. With respect to class III malocclusions:

a. Even though statistically significant association of sutural patency was found at the ZMS but not MPS for individuals with class III malocclusions, the data implies class III malocclusion treatment should be considered earlier and more proactively in young patients.
b. Information from this study in terms of class III malocclusions should be used with caution due to the low sample size of this subgroup.

8. There is no significant difference in the measured mean zygomatic widths.

The findings from this study may be applicable in treatment considerations for practitioners that do not have advanced imaging capabilities. For those that do, this information may indicate when to examine the MPS and ZMS more closely for their maturational status.

Appendix A Supplemental Information

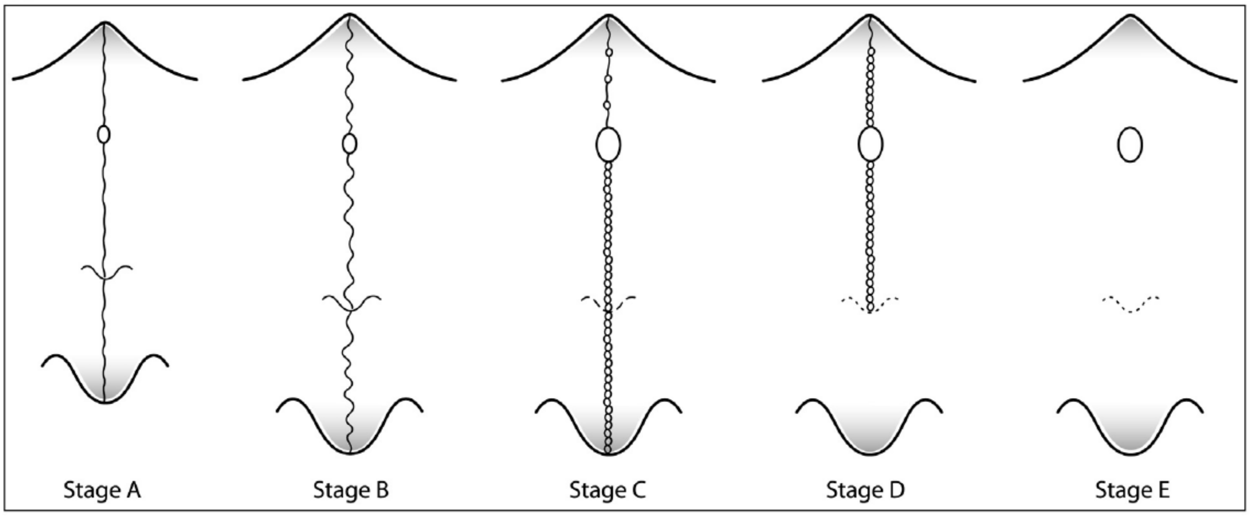

Figure 17. Schematic drawing of the MPS maturational stages (Angelieri et al. 2013)

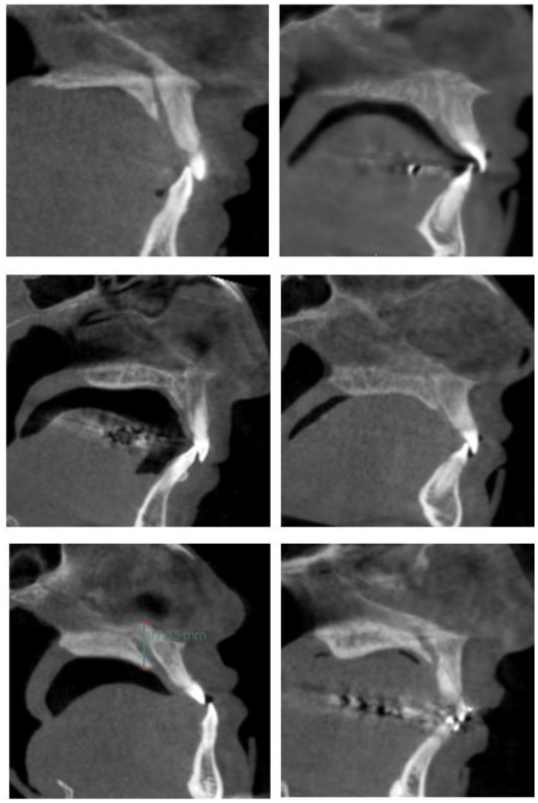

Figure 18. Midsagittal sections of the hard palate. Note the morphological differences in shape and thickness as well as the amount of cortical bone compared to cancellous bone.

Figure 19. Variation in the zygomatic widths in coronal sections. Note the sides with clear sinuses tend to have narrower widths than the sides with soft tissue presentation, which presents with wider widths.

Table 15. List of statistical comparisons in this study

Chi-Square comparisons	**Fisher's Exact Test**	**Rank sum comparisons**	**Paired t-test**
MPS vs CVMS	MPS vs CVMS in class I malocclusion	MPS vs Age	Right, left zygomatic width
MPS vs ZMS	MPS vs CVMS in class II malocclusion	ZMS vs Age	
ZMS vs CVMS	MPS vs CVMS in class III malocclusion	MPS vs P_d/P_l ratio	
ZMS vs CVMS in class II malocclusion	ZMS vs CVMS in class I malocclusion	ZMS vs P_d/P_l ratio	
	ZMS vs CVMS in class III malocclusion		
	CVMS vs MPS in males		
	CVMS vs MPS in females		
	CVMS vs ZMS in male		
	CVMS vs ZMS in females		

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