

INSTITUTO UNIVERSITÁRIO EGAS MONIZ

MESTRADO INTEGRADO EM MEDICINA DENTÁRIA

SKELETAL AGE AND THE RELATIONSHIP TO MIDPALATAL SUTURE MATURATION STAGES. A RETROSPECTIVE RADIOGRAPHIC STUDY IN A PORTUGUESE POPULATION

Trabalho submetido por
Joaquim Johan Fernandes Faerovig
para a obtenção do grau de Mestre em Medicina Dentária

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Trabalho orientado por
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ABSTRACT

Objetivos: O objetivo primário deste estudo foi avaliar o grau de correlação entre a idade cronológica (IC), maturação das vertebra cervicais (CVM) e maturação da sutura media palatina (MPSM) numa população Portuguesa. Um objetivo secundário foi avaliar o método CVM como um indicador preditivo na estimativa do grau de MPSM.

Materiais e Métodos: Foram analisadas 33 telerradiografias laterais e tomografias computadorizadas de feixe cónico (TCFC) de pacientes entre os 9 e 29 anos (20 femininas e 13 masculinos). Os estádios de CVM foram avaliados nas telerradiografias laterais e classificados de acordo com o método modificado de Baccetti et al. (CVS1 – CVS6). Os estádios de MPSM foram avaliados em TCFC's de acordo com o sistema de classificação de Angelieri et al. (Estádios A – E). A ordem de correlação de Spearman e o teste de desempenho diagnostico foram aplicados, com o nível de significância de $p < 0.05$.

Resultados: Foi encontrada uma correlação fraca entre a IC e os estádios da MPSM. Foi observada uma correlação positiva, mas moderada, entre a IC e a CVM, considerando ambos os sexos ($r=0.625$, $p < 0.001$), embora mais forte nos masculinos ($r=0.872$, $p < 0.001$) em comparação com as mulheres ($r=0.463$, $p=0.040$). Foi observada uma correlação moderada entre a CVM e a MPS para a amostra total ($r=0.433$, $p=0.012$) e para o sexo masculino ($r=0.603$, $p=0.029$). No teste de desempenho diagnostico, apenas no caso da CVS5 e CVS6 para a avaliação dos estádios D e E da MPS foi observado um valor LHR positivo superior a 10, indicando um aumento elevado e frequentemente conclusivo da probabilidade de a CVM corresponder a um estágio específico da MPS.

Conclusões: A IC não é um bom preditor dos estádios de MPSM entre adolescentes e jovens adultos. O método CVM pode ser um bom preditor de MPSM na fase pós-puberal.

Palavras-chave: Tomografia computadorizada de feixe cónico; maturação sutura media palatina; idade esquelética; expansão maxilar rápida.

SUMMARY

Objectives: The primary aim of this study was to evaluate the degree of correlation between chronological age (CA), cervical vertebrae maturation (CVM) and midpalatal suture maturation (MPSM) in a Portuguese population. A secondary objective was to evaluate the CVM method as a predictive indicator in estimating the degree of MPSM.

Materials and Methods: Thirty-three lateral cephalograms and cone beam computed tomography (CBCT) scans from patients aged 9-29 years (20 females and 13 males) were analysed. The CVM stages were assessed on the lateral cephalograms and classified according to the modified method of Baccetti et al. (CVS1 - CVS6). The MPSM stages were evaluated on CBCTs according to Angelieri et al.'s classification system (Stages A - E). Spearman's rank correlation order and diagnostic performance test were applied to the dataset, with the significance level at $p < 0.05$.

Results: A poor correlation was found between CA and stages of MPS. A positive but moderate correlation was observed between CA and CVM, considering both sexes ($r = 0.625$, $p < 0.001$), although stronger in males ($r = 0.872$, $p < 0.001$) compared to females ($r = 0.463$, $p = 0.040$). A moderate correlation was observed between CVM and MPS for the total sample ($r = 0.433$, $p = 0.012$) and males ($r = 0.603$, $p = 0.029$). The diagnostic performance test indicated that only in the case of CVS5 and CVS6 for the assessment of MPS stages D and E, a positive likelihood ratio (LHR) value greater than 10 was observed, indicating a high and often conclusive increase in the likelihood that the CVM corresponds to a specific maturational stage of the MPS.

Conclusion: CA is not a good indicator of the MPSM stage among adolescents and young adults. The CVM method can be a good predictor of MPSM in the post-pubertal stages of maturation.

Keywords: Cone-beam computed tomography; midpalatal suture maturation; skeletal age; rapid maxillary expansion.

GENERAL TABLE OF CONTENTS

<i>I. Introduction.....</i>	13
1. Contextualization/Justification	13
<i>II. Review of Literature</i>	18
2.1. Maxillary expansion.....	18
2.1.1. Indications for Maxillary Expansion.....	19
2.1.2. Expansion Modalities.....	19
2.1.3. Role of the MPS in Maxillary Expansion.....	20
2.1.4. Separation of the Hemimaxillae.....	20
2.1.5. Age-Related Differences of MPS Maturation	20
2.1.6. Expansion in primary and early mixed dentition.....	21
2.1.7. Expansion in adolescents	21
2.1.8. Expansion in Skeletally Mature Patients	22
2.1.9. Decision-Making Between RME and SARME/Le Fort I.....	23
2.2. Growth and Development	23
2.2.1. Development of the Palate	23
2.2.2. Embryology and Formation of the Human Palate and the Mid-Palatal Suture.....	24
2.2.3. Formation of the Primary Palate	25
2.2.4. Formation of the Secondary Palate	25
2.2.5. Formation of the MPS	25
2.3. Importance of Growth and Development in Orthodontics	26
2.3.1. Growth Indicators.....	28
2.4. Radiographic Methods and Skeletal Age Assessment.....	29
2.4.1. Evolution of Radiographic Tools and Diagnostic Technology	29
2.4.2. Computed Tomography (CT)	30
2.4.3. CBCT Imaging	30
2.4.4. Radiographic Analysis of Skeletal Maturity.....	31
2.4.5. Hand and Wrist Maturation Method	31
2.4.6. Third Finger Middle Phalanx Maturation Method	32
2.4.7. Dental Development.....	32
2.4.8. CVM Method.....	33
2.4.9. CVM Method Limitations	36
2.4.10. Objective Alternatives of CVM Classification.....	37
2.4.11. Midpalatal Suture Maturation.....	38
2.4.12. MPS Maturation - Limitations	39
<i>III. Objectives</i>	45
3.1 Research Hypothesis.....	45
<i>IV. Materials and Methods</i>	47
4.1. Investigation Methodology	47
4.2. Participants.....	47
4.3. Image acquisition	48
4.4. Radiologic examination.....	49
4.4.1. Image standardization of CBCTs	49
4.4.2. Standardization of the Axial Cross-Sectional Slice Used for Sutural Assessment	49

4.4.3. MPS Staging	50
4.5. CVM Assessment	51
4.6. Statistical analysis	52
<i>V. Results</i>	55
5.1. Measurement repeatability	55
5.2. Sample description.....	55
5.3. MPS Stages	56
5.4 CVM stages.....	59
5.5. Cross-tabulation analysis	61
5.6. Correlations	62
5.7. Diagnostic Performance	64
<i>VI. Discussion</i>	66
6.1. MPSM and CVM Sample Description	67
6.2. Description of MPSM related to CVM.....	68
6.3. Correlations	69
6.3.1. Age versus MPSM or CVM.....	69
6.3.2 CVM versus MPSM.....	70
6.5. LIMITATIONS OF THE STUDY	72
<i>VIII. BIBLIOGRAPHY</i>	74
<i>IX. ANNEXES</i>	81

LIST OF FIGURES

Figure 1. The two clinical forms of a constricted maxilla.....	18
Figure 2. Schematic drawing of the vertebral bodies of C2, C3 and C4 in the CVM staging system, (Adapted from Baccetti et al., 2002).....	35
Figure 3. Schematic drawing of MPS stages (Adapted from Angelieri et al. 2017)	38
Figure 4. Standardisation of CBCT images in all three planes A - Coronal, B – Axial and C - Sagittal).....	50
Figure 5. The classification of MPS stages A to E according to its morphology, visible on the axial cross-sectional slices.....	51
Figure 6. CVM stages, CVS1 through CVS6.....	52

LIST OF TABLES

Table 1. Previous studies regarding similar topics	40
Table 2. Age and gender distribution.....	56
Table 3. Distribution of the sample based on MPS maturation, mean age and gender. 57	
Table 4. Distribution of the sample based on MPS maturation, age and gender.....	58
Table 5. CVM distribution according to age and gender.....	59
Table 6. Distribution of the sample based on CVM stages, age and gender.	60
Table 7. Crosstabulation of CVM and MPS stages in females.....	61
Table 8. Crosstabulation of CVM and MPS stages in males.....	62
Table 9. Spearman rank correlation coefficients for the total sample.	63
Table 10. Spearman rank correlation coefficients for females.	63
Table 11. Spearman rank correlation coefficient for males.....	64
Table 12. Diagnostic performance parameters of CVM stages for the identification of MPS stages	65

LIST OF ABBREVIATIONS AND ACRONYMS

IUEM – Instituto Universitário Egas Moniz

MPS – Midpalatal Suture

RME – Rapid Maxillary Expansion

MARPE – Miniscrew Assisted Rapid Palatal Expansion

SARME – Surgically Assisted Rapid Maxillary Expansion

CA – Chronological Age

3D – Three-dimensional

CBCT – Cone Beam Computed Tomography

2D – Two-dimensional

ALADA – As Low as Diagnostically Acceptable

ALADAIP - As Low as Diagnostically Acceptable being Indication oriented and Patient Specific

FOV – Field of View

CVM – Cervical Vertebrae Maturation

CVS – Cervical Vertebrae Stage

CT – Computed Tomography

HWM – Hand Wrist Method

MPM – Middle Phalanx Maturation

AI – Artificial Intelligence

LHR – Likelihood Ratio

MPSM – Midpalatal Suture Maturation

I. Introduction

1. Contextualization/Justification

Maxillary constriction is a transverse anomaly present in various dento-skeletal deformities, including unilateral or bilateral posterior crossbites, and narrow, tapered, or high palatal arch normally associated with dental crowding (Baccetti et al., 2000). Chronic mouth breathing and open mouth posture may lead to an underdeveloped transverse maxilla, among other factors (Profitt et al., 2019). Recent randomized clinical trials state that the use of pacifiers is also associated with posterior crossbites, especially when its use is prolonged for more than a year (Arpalahti et al., 2024).

In 1860, Edward Angel first established the concept that the maxilla could be expanded by opening the midpalatal suture (MPS). A century later, Haas published the results of a study on the rapid expansion of a maxillary dental arch by opening the MPS (Haas, 1961). Since then, Rapid Maxillary Expansion (RME) has been used as an orthopaedic course of action to treat maxillary transverse deficiencies.

In the late stage of adolescence and early adulthood, the level of bone interdigitation in the MPS increases significantly requiring a greater magnitude of force for separation. The routine application of RME, therefore, is limited to growing patients (Baccetti et al., 2001; Sur & Taneja., 2008), as complications in patients with a complete fusion of the MPS may lead to clinical failure. These complications may involve severe pain, gingival recession and accentuated vestibular posterior teeth tipping leading to overhanging palatal cusps, buccal root resorption, fenestration of the buccal cortex, palatal tissue ulceration or necrosis, and instability of the expansion (Rungcharassaeng et al., 2007; Yildirim., 2019; Haas., 1980). Therefore, treating transversal maxillary deficiencies in skeletally mature patients becomes challenging. In these cases, skeletal anchorage methods may be needed to widen the maxilla transversally. A Miniscrew-Assisted RME (MARPE) might be recommended (Kapetanovic et al., 2021). In adults with complete MPS ossification, more invasive

treatment modalities might be necessary to attain maxillary skeletal transversal expansion that includes surgical procedures such as multi-segment Le Fort I osteotomies by opening the MPS, namely the Surgically Assisted RME (SARME) (Baccetti et al., 2001; Suri & Taneja., 2008).

Conflicting opinions are found in the literature regarding the success of RME alone versus SARME in correcting maxillary transverse deficiencies in skeletally matured patients. Chronological age (CA) has been regarded as a determinant factor in the choice of treatment approach between RME and SARME/Le Fort I osteotomy (Angelieri., 2017).

Histological investigations on autopsy material have demonstrated a significant discrepancy in the correlation between CA and the MPS ossification stage (Melsen., 1972). There is a lack of consensus regarding the time of MPS fusion, with various studies indicating different ages at which sutural closure occurs. Consequently, various age limits have been recommended for surgical intervention, further disorientating a clear cutoff age limit at which SARME is indicated. Further confusion is added by the several case reports showing success. (Persson & Thilander., 1977; Epker & Wolford., 1980; Timms & Vero., 1981; Alpern & Yurosko., 1987; Mossaz et al., 1992; Mommaerts., 1999).

The assessment of the MPS maturational stage for each patient is important to determine the appropriate treatment modality and timing of intervention, as so far, no well-defined CA cutoff point for the indication of MARPE or SARME for adolescents and young patients is available. There is no consensus relative to the age limit regarding the initiation and evolution of MPS maturation (MPSM) (Lee et al., 2004; Angelieri et al., 2013).

Radiographic evaluation of the MPS skeletal maturation stage has become a widely used approach for predicting the timing of individual pubertal growth, estimating

growth velocity and the amount of growth remaining. The hand-wrist radiograph has been considered the most standardised method for evaluating individual skeletal maturity, comparing a patient's bones in a hand and wrist with those in published atlases (Greulich & Pyle., 1959; Cavallo et al., 2021). Three-dimensional (3D) Cone Beam Computed Tomography (CBCT) is now available, allowing for individual evaluation of the MPSM stage in living subjects, providing more reliable clinical data for the decision-making process in the treatment of skeletal maxillary constriction between using RME alone or SARME in late adolescents and young adults, thus determining the ideal intervention time (Angelieri et al., 2017).

Angelieri et al. suggested a method for individual assessment of the MPS using CBCT, where the maturational stages were classified from A-E according to morphological characteristics (Angelieri et al., 2013). CBCT has the advantage of isolating the MPS without the overlapping sequences of other anatomical structures, facilitating visual inspection of sutural morphology. However, CBCT is not yet a routine radiological examination carried out in dental clinics (Mallya & White., 2013). In addition, the use of CBCT involves exposure to doses of ionizing radiation 10-100 times higher than those involved in the traditional two-dimensional (2D) cephalogram image (Mallya., 2015), so this examination should be used with caution.

Both hand-wrist radiographs and the CBCT examination used in the Angelieri et al. method, require additional X-ray exposure. Following the ALADA principle, now further refined to ALADAIP by the DIMITRA group in 2017, entails the obligation to minimize the radiation dose to patients and surroundings to As Low As Diagnostically Acceptable being Indication-oriented and Patient-specific. Indication-oriented, referring to the imaging protocol that should be tailored to a specific clinical indication or investigative question, and Patient-specific, where the imaging parameters should be adjusted according to the individual patient (age, size, medical history). These principles emphasize the importance of clear justification for each radiographic scan, with careful consideration of radiation dose in relation to diagnostic needs (Berkhout., 2015; Oenning et al., 2018).

To avoid additional radiation exposure, some researchers explored to relate maturation with skeletal and dental features other than the bones in the hand and wrist (O'Reilly & Yanniello., 1988; Uysal et al., 2004). According to several authors (Hellsing., 1991), dental development indicators only are not a reliable predictive indicator of a patient's stage of skeletal development. Due to the wide variation in the chronological timing of pubertal growth spurt, CA is also an unreliable predictor of the pubertal spurt (Luz et al., 2022).

Studies have demonstrated that the use of Cervical Vertebrae Maturation (CVM), visible on the lateral cephalogram, for estimation of adolescent growth spurt is effective as a biological indicator of skeletal maturity in addition to both in body height and mandibular size (Franchi et al., 2000). By assessing the CVM through the lateral cephalogram, a radiograph routinely used in orthodontic practice for diagnosis and treatment planning, clinicians could reduce the overall ionizing radiation exposure of their patients. Following this logic, researchers sought to investigate the relationship between CVM on lateral cephalograms and the maturational stages of the MPS. Angelieri et al. (2015) conducted a study using Brazilian and American subjects and concluded that in the early phase of skeletal maturation, CVM phases can be used to diagnose the MPS maturational stages, avoiding the need for CBCT imaging. In the post-pubertal period, however, the same study reported that CBCT may be indicated for the assessment of the MPS maturation when deciding between conventional RME and SARME. They also stated that if the CVM stage cannot be assessed, CA may be a viable alternative to predict MPSM stages (Angelieri et al., 2015).

Another study conducted on Brazilian subjects by Luz et al. concluded that the CVM method can be used to predict the early maturational stages of the MPS. In more advanced stages of maturity, however, evaluation of the MPS by tomography is suggested (Luz et al., 2022). Gorucu-Coskuner et al. in a study with a Turkish population, concluded that neither CVM nor CA could be used as a convenient tool to determine the stages of MPSM. However, this study was limited to a small sample size (Gorucu-Coskuner & Taner et al., 2018).

No similar studies have been conducted on a Portuguese population; it seems, therefore advantageous, to investigate the degree of correlation between CA and CVM and MPS in Portuguese children and adolescents. Furthermore, it would be interesting to investigate the validity of CVM for the assessment of skeletal maturity as a method to predict MPS maturational stages when choosing the appropriate maxillary expansion procedures.

II. Review of Literature

2.1. Maxillary expansion

Maxillary constriction is a transversal skeletal anomaly frequently observed in orthodontic patients and may be associated with dental crowding, unilateral or bilateral posterior crossbite and or, other occlusal disharmonies (Proffit et al., 2003). A constricted maxilla may also lead to a reduction in size of nasal airways, and mouth-breathing individuals have been described to possess a high palatal vault and a narrow and V-shaped maxillary arch (Kiliç & Oktay., 2008). In 1860, Angel introduced the concept of maxillary expansion by opening the MPS (Angell., 1860) and Haas in 1961 made RME a commonly used procedure to correct a transverse maxillary deficiency in growing patients (Haas., 1961; Zuccati et al., 2013). Since then, maxillary expansion has become a routinely used orthodontic procedure to correct transverse maxillary deficiencies.

A constricted maxilla is usually presented in two clinical forms: endoalveolism and endognathy (Figure 1). Endoalveolism is a dento-alveolar anomaly. The alveolar process is inclined lingually with no deformity of the underlying basal bone. While endognathy, is a basal anomaly, where the maxilla is narrow at a skeletal level, with the alveolar process presenting a normal orientation (Proffit et al., 2019).

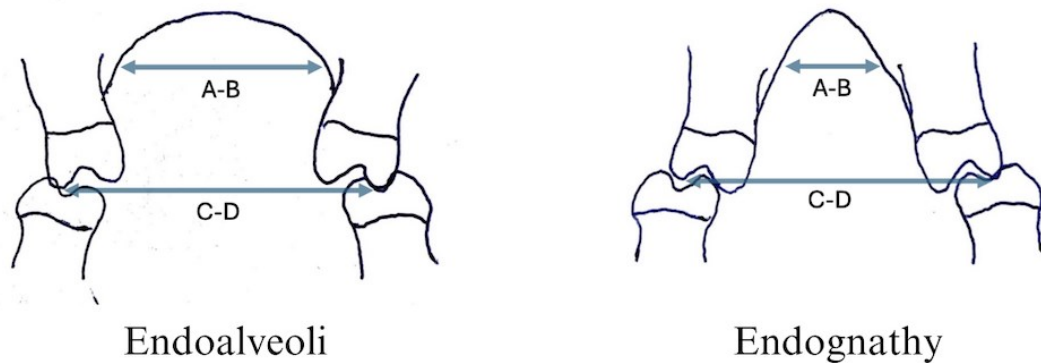


Figure 1. The two clinical forms of a constricted maxilla

2.1.1. Indications for Maxillary Expansion

Indications for maxillary expansion include the correction of crossbites, whether they are unilateral or bilateral posterior crossbites, dental and/or skeletal, true or functional. This is especially true in cases of V-shaped maxillary arch and deep palate; it also involves the correction of anterior crossbites associated with functional deviations or traumatic occlusion. Another common indication is the elimination of dental crowding by increasing the arch perimeter. Maxillary expansion is also used for the correction of axially inclined posterior teeth and increased buccal corridors, being also a facilitator for the correction of distocclusion on the lateral segments (Baccetti et al., 2001; Profitt et al., 2019)

2.1.2. Expansion Modalities

In generic terms, maxillary expansion can be split into three categories: passive, orthodontic, and orthopaedic/skeletal expansion. Passive expansion may be achieved by reducing cheek and lip pressure upon the dentition. This will create an imbalance between the forces of the tongue and the cheeks/lips that act passively upon the teeth, resulting in buccal movement of the teeth. Examples of orthodontic appliances for passive expansion are the Fränkel appliance and the Lip Bumper.

Orthodontic or dento-alveolar expansion is achieved by mechanically widening the dental arch. The dento-alveolar process is forced to tip buccally, increasing the maxillary transverse width and arch perimeter. Slower force application will give enough time for teeth to move along relative to their supporting bone (Profitt et al., 2019).

With orthopaedic expansion, the increase in transversal dimension is achieved at a skeletal level by opening the MPS usually with a fixed or removable appliance with a hyrax screw. Techniques and protocols for maxillary expansion vary, including slow

maxillary expansion, RME, SARME and MARPE (Agarwal & Mathur., 2010; Kapetanovic et al., 2021).

2.1.3. Role of the MPS in Maxillary Expansion

The MPS serves a vital role in the maxillary expansion, particularly in procedures such as RME, as it is one of the most important regions of resistance to expansion of the maxilla (Lee et al., 2014; Priyadarshini et al., 2017). The MPS is a key anatomical feature in the intermaxillary sutural system consisting of soft connective tissue, connecting the two mineralized maxillary bone halves (Mao., 2003).

2.1.4. Separation of the Hemimaxillae

The primary mechanism of RME involves the application of lateral forces to the maxillary bones, causing the separation of the hemimaxilla (maxillary halves) at the MPS. This separation allows for the expansion of the maxilla and subsequently, an increase in the transversal dimension of the dental arch (Isfeld et al., 2017; Zeng et al., 2023). The space created following the mechanical separation of the suture is initially filled with tissue fluids and haemorrhage. At this point, the expansion is particularly unstable, so the expansion device is compelled to be kept in place for three to four months. By then, new bone has formed and filled the sutural space. This bone deposition ensures the long-term stabilisation of the skeletal expansion, providing a permanent increase in maxillary width (Isfeld et al., 2017; Profitt et al., 2019).

2.1.5. Age-Related Differences of MPS Maturation

According to Baccetti et al. (2001), the success of RME is highly dependent on the level of maturation of the MPS. Younger patients with a lower level of MPSM (pre-pubertal peak) typically experience more predictable and stable expansion outcomes when compared to older patients whose MPS may be more calcified and more resistant to mechanical forces (Baccetti et al., 2001; Sayar & Kılınc., 2019).

2.1.6. Expansion in primary and early mixed dentition

In children with primary or early mixed dentition, the level of sutural interdigitation is low. Skeletal expansion has the best prognosis when the MPS is not fused or only has minor initial bridging, offering little mechanical resistance. Therefore, light forces are enough to slowly open the suture, with an activation protocol of 1 millimeter per week. Almost any expansion device can open the MPS in children up to 9 and 10 years of age, with removable appliances and lingual arches generating between 450 and 900 grams of pressure (Profitt et al., 2019).

2.1.7. Expansion in adolescents

With increasing age, the sutural interdigitation of the MPS becomes tighter, increasing its mechanical resistance. Heavier orthopaedic forces are needed to break and separate the two maxillary halves. RME is an orthodontic expansion procedure, using a fixed, tooth-borne expansion device to transmit heavy forces across the suture, usually done before the complete fusion of the maxillary complex sutures. An incorporated jackscrew is rotated, generating lateral forces that are transmitted to the supporting structures. A centimetre or more of expansion can be obtained in two to three weeks by applying 4,5 to 9 kilograms of force across the suture at an activation rate of 0,5 millimetres per day (two-quarter turns of the screw). It is important to understand that dento-alveolar effects will always be present with any tooth-supported expansion device. Therefore, the theory with rapid force application is to transfer the force to the MPS before the teeth have time to move along their supporting bone (Profitt et al., 2019). This will decrease dental movement while maximizing changes at the skeletal level. A slow expansion modality would be likely to just move the teeth with minimal skeletal effects. The amount of undesired orthodontic movement (buccal tipping of anchor teeth) and its side effects are proportional to patient age and skeletal maturation. Therefore, adolescents tend to have greater tooth inclination and buccal bone dehiscence and, less orthopaedic expansion than children (Baccetti et al., 2001).

As the MPS reaches complete fusion, the mechanical resistance of the sutural structures reaches a point where the opening by orthopaedic forces alone becomes more difficult. The inevitable existence of circum-maxillary sutural resistance and dental anchorage presents a risk of unwanted effects of RME procedures (Profitt et al., 2019; Yildirim., 2019).

2.1.8. Expansion in Skeletally Mature Patients

In skeletally mature patients, the probability of successful maxillary expansion decreases as sutures close and the resistance to mechanical forces increases. RME prognosis is therefore associated to the level of maxillary suture interdigitation: the greater the interdigitation and the more numerous the synostoses presented at the sutures, the lower the chances of splitting the maxilla without surgical intervention (Knaup et al., 2004; Angelieri et al., 2016). The amount of undesired orthodontic movement (buccal tipping of anchor teeth) and its side effects are proportional to patient age and skeletal maturation. Therefore, adolescents tend to have greater tooth inclination and buccal bone dehiscence and, less orthopaedic expansion than children (Profitt et al., 2019).

Studies have demonstrated that only approximately 50% of the expansion achieved by RME in children is skeletal, the percentage dramatically decreasing to 35% in adolescent patients. The transverse maxillary growth being the first craniofacial dimension to cease growing, with the maxillary sutures closing around 14 to 15 years in females, and 15 to 16 years in males (Korn & Baumrind., 1990; Profitt et al., 2019). Studies on treatment timing (Baccetti et al., 2001) show that treatment of late adolescent patients results in significantly less increase in the skeletal width of the maxilla and more dentoalveolar effects. The heavy force load during expansion is transmitted to the anchored teeth and may result in complications such as fenestration and dehiscence of the vestibular cortical bone, loss of periodontal attachment and gingival recession, root resorption, buccal tooth tipping, and instability of the expansion achieved (Rungcharassaeng et al., 2007; Yildirim 2019; Haas 1980).

Studies also show that the fusion of the MPS shows great variability (Korbmacher et al., 2007; Knaup et al., 2004) with consequent different degrees of resistance to suture opening and consequent unpredictable skeletal effects of RME with more unwanted dental movement. Mini-implant-assisted RPE (MARPE), a non-surgical procedure is recommended (Kapetanovic et al., 2021) when more resistance to suture opening is predicted. More invasive mechanics may be required to achieve skeletal expansion in patients with complete ossification of the MPS, namely SARME (Baccetti et al., 2001).

2.1.9. Decision-Making Between RME and SARME/Le Fort I

Surgical procedures, such as SARME or LeFort I osteotomies have been recommended for the treatment of maxillary deficiencies in adults (Alpern & Yurosko., 1987). CA has been considered a fundamental factor for the decision-making between RME alone and surgical assistance. However, the existing variability in the literature regarding the ideal age for surgically assisted procedures indicates that CA is an unreliable indicator for deciding between the two modalities (Angelieri et al., 2016) The individual assessment of the maturational stage of the MPS on CBCTs gives the clinician more reliable data when deciding if RME alone is possible or not (Angelieri et al., 2013).

2.2. Growth and Development

2.2.1. Development of the Palate

The human palate is an intricate structure dividing the nasal and oral cavities and forming the roof of the mouth. Its existence is important in several physiological functions, such as speech and articulation, deglutition, respiration and breastfeeding. The palate undergoes complex morphological changes during embryogenesis to achieve its final conformation. It is divided into an anterior immobile hard bony segment and a posterior mobile soft palate that does not contain bone (Burdi & Faist., 1967; Hammond & Dixon., 2022).

Hard Palate

The hard palate consists of the anterior two-thirds of the palate. It is a hard, immobile bone segment whose underlying osseous structures consist of the palatine processes of the maxilla and horizontal plates of the palatine bone (Burdi & Faist., 1967; Hammond & Dixon., 2022).

Soft Palate

The soft palate is the posterior last third of the palate and is a posterior continuation of the hard palate. It consists of muscle fibres and connective tissue covered by a mucous membrane consisting of a stratified squamous epithelium with secretory salivary glands. Unlike the hard palate, the soft palate is very flexible and does not contain any bony structures (Burdi & Faist., 1967; Hammond & Dixon., 2022).

2.2.2. Embryology and Formation of the Human Palate and the Mid-Palatal Suture

Embryology is necessary to understand the growth and development of various anatomical structures relevant to orthodontics and will help us understand the anomalies associated with their malformation. The human palate and the MPS play pivotal roles in craniofacial development as they are crucial for proper mouth functions, facial aesthetics and overall health. Embryological development and the formation of these structures are, therefore, pertinent to orthodontics and growth modification (Burdi & Faist., 1967; Hammond & Dixon., 2022).

Embryologic formation of the human palate is a highly orchestrated process that involves the integration of multiple embryonic structures and signalling pathways. It is broadly divided into the development of the primary and secondary palates (Burdi & Faist., 1967).

2.2.3. Formation of the Primary Palate

The facial region of the mammalian embryo originates mainly from the frontonasal prominence. The palate forms from the fusion of several embryonic structures, leading to the creation of both the primary and secondary palates. The primary palate starts developing around the fifth week of gestation from the intermaxillary segment, which forms through the medial nasal prominences. This segment evolves into the philtrum of the upper lip, the premaxillary part of the maxilla, and the anterior part of the hard palate, which houses the incisor teeth (Burdi & Faist., 1967; Hammond & Dixon., 2022).

2.2.4. Formation of the Secondary Palate

The secondary palate begins to develop in the sixth week of gestation and develops from the lateral palatine processes of the maxillary prominences. These processes initially grow downward on either side of the tongue. During the seventh or eighth week of gestation, the processes elevate to a horizontal position and begin to grow towards each other above the tongue (Burdi & Faist., 1967; Hammond & Dixon., 2022).

2.2.5. Formation of the MPS

By the end of the ninth week, the two palatal shelves approach each other and fuse by fibrous connective tissue in an anteroposterior direction at the midline, forming the secondary palate, which constitutes most of the hard and soft palates. This fusion down the midline is known as the MPS. Subsequently, at 12 weeks, the primary and secondary palates merge alongside the nasal septum. The MPS functions as a “growth centre” of the maxilla, and insufficient growth at this location can result in malocclusion and dental crowding (Shibusawa et al., 2021). During infancy and childhood, this suture remains patent, allowing for transverse growth of the maxilla. The suture is characterised by a fibrous connective tissue that eventually ossifies in a posteroanterior

direction with age, contributing to maxillary arch stabilisation (Hammond & Dixon., 2022).

2.3. Importance of Growth and Development in Orthodontics

Understanding the growth of the oro-facial region is important when planning orthodontic treatment. Skeletal maturation is an integral part of individual patterns of growth and development. Variation in the maturation status is closely associated with deviation in the timing and magnitude of growth (Baccetti et al., 2001; Cavallo et al., 2021). Due to individual variations in timing, duration, and velocity of growth, skeletal age assessment is essential in formulating viable orthodontic treatment plans. Clinical decisions regarding the use of extra-oral traction forces, functional appliances, extraction versus non-extraction treatments or orthognathic surgery are at least based on growth considerations (Baccetti et al., 2001; Profitt., 2019).

In orthodontics, growth and development are important in determining treatment options and intervention time for preadolescent children and adolescents. Growth modification principles are vital for an effective orthodontic treatment, particularly in growing patients (Baccetti et al., 2001). Growth refers to the natural progression of bone and tissue development, influenced by both genetic and environmental factors (Kelly & Eisman., 1990). Growth modification, however, aims to guide the natural course of development to correct skeletal discrepancies. Growth modification is achieved with appliances that influence the growth of the jaw and other facial bones, ensuring proper alignment and occlusion. Some growth modification procedures should be done before adolescence, whereas other procedures are much more effective and efficient if done in adolescents (Profitt et al., 2019).

Principles of growth modification rely on the timing of intervention, exploiting periods of accelerated and intense growth such as during puberty, to maximise treatment efficacy. By understanding and applying these principles, orthodontists can correct

malocclusions and other dental disharmonies more efficiently, potentially reducing the need for surgical interventions later in life (Baccetti et al., 2001).

Information related to the ideal time for treatment of maxillary transverse deficiency with an orthopaedic device is considerably based on studies on the growth and maturation of the intermaxillary sutural system (Baccetti et al., 2001). Melsen's study on autopsy material histologically examined the maturation of the MPS at different developmental stages. It showed that the transversal growth of the MPS continued up to the age of 16 in girls, and 18 in boys. Based on morphology, the development of the MPS could be divided into three stages. In the first stage, the suture was short, broad, and Y-shaped; in the second, the course was more sinuous; and in the third interdigitation was so heavy that a separation of the two halves of the maxilla would not be possible without fracturing the interdigitated processes (Melsen., 1975). In another study in 1982, Melsen & Melsen also included observations of the "adult" stage of the suture, noting the formations of bony bridges and synostoses across the suture (Melsen & Melsen., 1982). These histological data may conclude that patients showing an advanced stage of skeletal maturation may have difficulties undergoing orthopaedic maxillary expansion. (Kapetanovic et al., 2021). In patients with complete MPS ossification, more invasive mechanics might be necessary to attain skeletal expansion; namely SARME (Baccetti et al., 2001).

Persson & Thilander (1977) observed fusion of the MPS in patients from 15-19 years of age. On the other hand, patients at the ages of 27, 32, 54 and 71 years have been reported to show no signs of fusion of the MPS (Persson & Thilander., 1977; Knaup et al., 2004; Korbmacher et al., 2007). Similarly, SARPE has been recommended for individuals older than 14 years of age (Mommaerts., 1999), 16 years (Epker & Wolford., 1980), 20 years (Mossaz et al., 1992), or 25 yearold (Timms & Vero., 1981). Alpern and Yurosko observed a significant difference in CA between males and females for the fusion of the MPS. The same authors recommended using SARPE instead of RME for female patients older than 20 and males over 25. (Alpern & Yurosko., 1987).

The lack of a clear cutoff age limit at which SARPE is indicated, further confusion has been added by several case reports showing successful orthopaedic maxillary expansion in much older patients (Handelman., 1997; Handelman et al., 2000). Findings such as these indicate that the variability in the developmental stages of fusion of the MPS is not directly related to CA, especially in young adults (Angelieri et al., 2013).

2.3.1. Growth Indicators

The question of when to initiate treatment is intimately linked to the identification of phases of accelerated or intense growth that can contribute notably to the treatment outcomes of skeletal discrepancies (Baccetti et al. 2002). Identification of these specific prepubertal, pubertal, and postpubertal growth phases can be assessed through various growth indicators (Cavallo et al., 2021). Characteristics such as CA, dental development, height, weight, and skeletal maturity are common maturational indices that have been used to identify the various stages of growth and development in young orthodontic patients (Hassel & Farman., 1995).

CA

Extensive reports say that the average age for the onset and peak of pubertal growth in stature is approximately 12 to 14 years in boys, and 10 to 12 years in girls (Tanner et al., 1976). Nevertheless, high variability has been seen among individual subjects, limiting its diagnostic accuracy. It is to be considered that the onset of pubertal growth is influenced by several factors, which include ethnicity and genetic factors, nutrition and socioeconomic status (Parent et al., 2003). Clinical relevancy of CA as an indicator for pubertal growth phases in individual patients therefore becomes unreliable and very limited (Baccetti et al., 2006).

2.4. Radiographic Methods and Skeletal Age Assessment

Skeletal maturation is manifested by an orderly and repeatable series of identifiable alterations in the skeleton's appearance during childhood. Those changes include the timing and sequence of the appearance of centres of ossification, specific reshaping in bone contours, and the timing and succession of the ultimate closure of the growth plates. Skeletal maturation can be evaluated radiographically by comparing the radiographic aspect of portions of an individual child's skeleton with the standardised appearance in a comparable population of children at different phases of their development towards maturity (Zerin & Hernandez., 1991; Cavallo et al., 2021).

2.4.1. Evolution of Radiographic Tools and Diagnostic Technology

Diagnostic technology has witnessed an extreme advancement across all its branches in the last decades. The evolution of complementary diagnostic tools in the form of image screening has come a long way since 1895, when Wilhelm Conrad Röntgen accidentally discovered an image cast from a cathode ray generator and later proposed its medical use by taking a picture of his wife's hand, clearly revealing her wedding ring and bones (Pauwels., 2020). He coined the term X-ray. A few decades later in the 1920s, Broadbent and Todd developed a roentgenographic craniostat, which was later improved in 1931 when Broadbent and Hofrath simultaneously and independently introduced a standardized method for the production of cephalometric radiographic images (Broadbent., 1931), which remained comparatively unaltered until recent times.

Broadbent's discovery captured the imagination of orthodontists and cephalometric radiography became rapidly an essential diagnostic tool in orthodontics when Moyers (Moyers., 1988) defined cephalometry as a radiographic technique to project the human head into a geometric design. Cephalograms have since been widely used in clinical practice as an investigative technique to evaluate growth and treatment responses in patients.

2.4.2. Computed Tomography (CT)

Cross-sectional imaging became more important in dentistry with the introduction of CT imaging techniques. CT was becoming an essential tool for dentists to have in their diagnostic arsenal, and it may be used in many different dental specialities. However, there are some disadvantages to CT devices. The devices are expensive and not available in every hospital and produce too high radiation dose to be suitable for most dental and orthodontic applications. Foreign objects like prosthetics and other restorative materials create artefacts, and lesions far away from the cross-section can be skipped (Karatas & Toy., 2014).

Recently, with the availability of three-dimensional (3D) diagnostic imaging using cone beam computed tomography (CBCT), it is possible to isolate and individually assess the maturational stages of the MPS on live subjects, to determine ideal intervention timing for RME (Karatas & Toy., 2014; Pauwels., 2020; Angelieri et al., 2017).

2.4.3 CBCT Imaging

CBCT imaging provides a 3D volumetric data construction of dental and surrounding maxillofacial anatomical structures with dimensional accuracy and isotropic resolution (ADA., 2012), i.e., the spatial resolution in the trans axial plane (X-Y plane) and the longitudinal direction (Z direction) are equivalent. The technique consists of the use of a rectangular or round cone-shaped X-ray beam. The CBCT uses a collimated X-ray source with a round or pyramidal-shaped beam, where the X-ray source and the reciprocating area detector revolve 360° around the patient's head, which is stabilized by a head holder capturing the field of view (FOV) of the patient (Pauwels et al., 2015). Single projection images known as “basis” images are acquired at certain degree intervals, capturing the exposed tissues. These basis images are similar to lateral cephalometric radiographic images in which each image is slightly offset. This series of projection images is referred to as the projection data. The projection data is fed to the software, and sophisticated algorithms, including back-filtered projection, are applied to the image data to generate a 3D volumetric data set which is used for a primary

reconstruction of images of the three orthogonal planes (axial, sagittal and coronal) (Kumar et al., 2015).

CBCT has the advantage of isolating the MPS without overlapping other anatomical structures, facilitating visual inspection of sutural morphology. CBCT devices differ between models and fabricants, with differences in patient positioning, exposure time, resolution, radiation dose and clinical ease of use. The CBCT devices and various fabricants provide different FOV settings, varying in the extent of tissue coverage exposed to scanning, allowing for specific diagnostic needs. With these cone-beam systems, clinicians may achieve 3D images with very low radiation doses at a time (Karatas & Toy., 2014; Pauwels., 2020).

2.4.4. Radiographic Analysis of Skeletal Maturity

The individual assessment of growth stages and maturation using radiographic analysis has become a widely used approach to predict the timing of pubertal growth, to estimate growth velocity and the amount of growth remaining in growing patients. Skeletal maturation can be assessed radiographically by recurring to several methods, including the hand-wrist maturation (HWM) method, third finger middle phalanx maturation (MPM), dental maturation, CVM and MPS maturation (MPSM) (Zerin & Hernandez, 1991; Cavallo et al., 2021; Augusto et al., 2022).

2.4.5. Hand and Wrist Maturation Method

What is considered to be the most common method for the assessment of skeletal maturation is the hand and wrist method (HWM) (Cavallo et al, 2021). Generally, there are two approaches to the assessment of the hand-wrist radiograph. The first method comprises the two comparison methods of Greulich & Pyle and Tanner et al. The Greulich & Pyle method uses an atlas as a standard of comparison. The atlas is composed of plates of “typical” hand-wrist radiographs at six months intervals of chronologic age. Each bone of the subject’s hand and wrist is compared with the

corresponding bones in published atlases and is assigned an age in months (Greulich & Pyle., 1959. Tanner et al's method also compares an individual's bones in the hand and wrist with radiographic standards of skeletal maturity in "normal" children of similar age and sex (Tanner et al., 1983).

The second common method of assessment of the hand-wrist radiograph uses specific indicators to relate maturation to the pubertal growth curve, which focuses on the individual evaluation of maturation rather than on mean values. A series of indicators have been described in the literature including the onset of calcification of the sesamoid, state of calcification of the hook of the hamate, and staging of the middle phalanges of the third finger (Bowden., 1976; Fishman., 1979; Demirjian et al., 1985).

2.4.6. Third Finger Middle Phalanx Maturation Method

The third finger middle phalanx maturation (MPM) method is another technique used to evaluate skeletal growth. It involves examining the middle phalanx of the third finger using a radiographic image of the hand to evaluate the stages of bone development. Perinetti et al. proposed a method based on previous descriptions by Fishman, Hägg & Taranger, and Rahagopal & Kansal, with modifications (Perinetti et al., 2016).

2.4.7. Dental Development

Dental maturation is a form of skeletal age assessment which may easily be gauged through the evaluation of tooth formation (Demirjian et al., 1973) and can be carried out on panoramic or even intra-oral radiographs that are routinely used in dental practice. The most common dental maturation method is the one proposed by Demirjian et al., (1973), which comprises eight stages from A to H according to tooth formation and is applicable to any tooth. Previous reports show there is a high degree of correlation between dental maturation and the hand-wrist method (Chertkow., 1980).

2.4.8. CVM Method

During the last decades, the CVM method has gained increased interest among orthodontists as a method of assessing skeletal maturity and identifying pubertal growth spurts. Initially proposed by Hassel & Farman, and subsequently modified according to Baccetti et al. the CVM method analyses the morphological changes in the second (C2), third (C3) and fourth (C4) cervical vertebrae as shown in lateral cephalometric radiographs. The CVM method categorises skeletal development into 6 stages based on vertebral morphology (CVS1 to CVS6) as shown in Figure 2 below. Features of the CVM method, as described by Franchi & coworkers include that in nearly 95% of North American subjects, growth interval stages between CVS3 and CVS4 coincide with the pubertal peak in both mandibular growth and body height (Baccetti et al., 2015). Furthermore, the reproducibility of this method for the identification of CVM stages is as high as 98.6%. The method is useful in anticipating the pubertal peak in mandibular growth, as the peak has not been reached if either CVS1 or CVS2 is recorded in an individual patient. (Franchi et al., 2000; Baccetti et al 2002; Baccetti et al., 2005).

CVS1

The lower border of the second, third and fourth vertebrae (C2, C3 and C4) are flat and may be slightly convex. The vertebral bodies of C3 and C4 are trapezoidal in shape, the superior surface slopes downward and forward, with the posterior border being taller than the anterior border. This stage occurs from approximately the time of eruption of the deciduous teeth until about two years before the peak of craniofacial skeletal growth. In some patients, C3 and C4 may appear rectangular and vertically short, resembling an ice hockey puck. Maximum facial adaptations occur in the midfacial region as the sutures are more open and around 80% to 100% of growth is expected. Therefore, this stage is clinically significant as research indicates that the optimal moment of intervention with facial mask therapy is at CVS1 (McNamara & Franchi, 2018; Franchi et al., 2000; Baccetti et al., 2002; Baccetti et al., 2005).

CVS2

This stage is characterised by a visible concavity along the inferior border of C2. The lower borders of C3 and C4 remain flat, both retaining their trapezoidal shape, similar to a “wedge of cheese”. CVS2 can be seen as the “get ready” phase. Nearly 65% to 80% of growth is predicted as the interval of peak mandibular growth is expected to initiate within a year after this stage becomes evident (Franchi et al., 2000; Baccetti et al., 2002; Baccetti et al., 2005).

CVS3

The third stage is identified by visible notching of the inferior borders of C2 and C3 while the inferior border of C4 remains flat. Most bodies of C3 and C4 continue to maintain a trapezoidal shape, although in some instances either C3 or C4 may take on a more rectangular horizontal shape. At this stage, maximum craniofacial growth velocity (around 25% to 65%) is to be expected (Franchi et al., 2000; Baccetti et al., 2002; Baccetti et al., 2005).

CVS4

In CVS4, all three cervical bodies (C2, C3 and C4) show evident concavities along their inferior borders. The shape of C3 and C4 becomes particularly important as both bodies assume a more rectangular horizontal shape. During CVS4, continued accelerated craniofacial growth (10% to 25%) is to be anticipated (Franchi et al., 2000; Baccetti et al., 2002; Baccetti et al., 2005).

CVS5

The fifth stage can be differentiated from CVS4 by the shapes of C3 and C4, with at least one of these bodies becoming square. If not square, the body of the other

cervical vertebra is rectangular/horizontal. All three cervical bodies have notches, so the presence of notching is no longer important in the differential diagnosis. When one reaches this stage substantial craniofacial growth has been attained, and merely 5% to 10% of residual growth could be expected (Franchi et al., 2000; Baccetti et al., 2002; Baccetti et al., 2005).

CVS6

The CVS6 is the most challenging to determine. The length of the posterior border is longer than the inferior border. Sometimes, measurements are required to determine which of the borders is longer. Cortical bone appears to be better delineated in CVS6 than in CVS5. Little or no growth is anticipated. It is reported that 17% of females never reach CVS6 (Franchi et al., 2000; Baccetti et al., 2002; Baccetti et al., 2005).

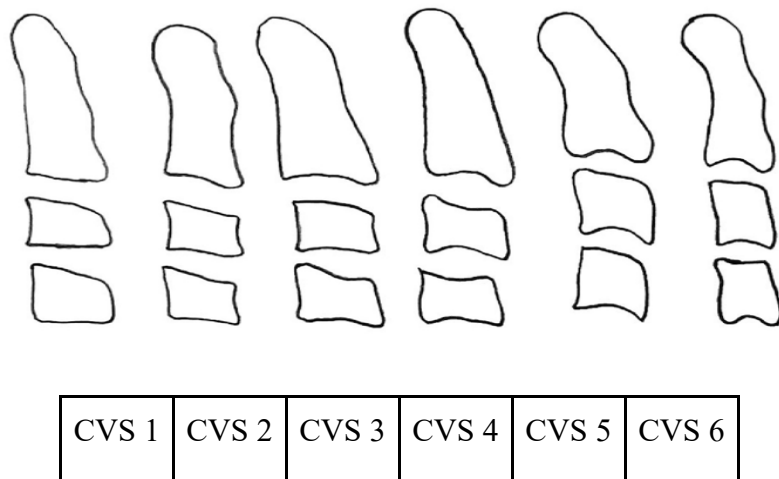


Figure 2. Schematic drawing of the vertebral bodies of C2, C3 and C4 in the CVM staging system, (Adapted from Baccetti et al., 2002).

The main features of the CVM method, as described previously by Franchi and colleagues, encompass several significant features that add to its utility in orthodontic practice. In nearly 95% of North American subjects, the growth interval identified by the CVM method aligns with the pubertal peak in both mandibular growth and body height (Baccetti et al., 2002). Secondly, the cervical vertebrae are visible on the lateral cephalometric scans routinely undertaken in orthodontic practice. Moreover, the appraisal of the shape of the cervical vertebrae is straightforward. The CVM method's ease of use is further complemented by its high reproducibility, as trained examiners achieve a classification accuracy of approximately 98% (Franchi et al., 2000; Baccetti et al., 2005). Nevertheless, some limitations affect the CVM method's reliability and applicability.

2.4.9 CVM Method Limitations

One of the primary criticisms of the CVM method is its reproducibility. Studies have indicated that the method may yield inconsistent results, particularly due to the subjective nature of the staging process. Some studies reported good reproducibility (Uysal et al., 2006; Lai et al., 2008), while others reported reproducibility issues. The subjective description of the stages resulted in disagreement between the observers (Gabirel et al., 2009; Nestman et al., 2011). This subjectivity was reported to cause low inter-examiner agreement (less than 50%) (Schoretsanti et al., 2021). This poor reproducibility was mainly attributed to the level of training, clinical experience, and the evaluation method itself (Perinetti et al., 2014; Rongo et al., 2015; Cericato et al., 2015).

Variability in visual training and interpretation among different examiners can lead to discrepancies in staging, as evidenced by studies showing poor reproducibility in clinical settings (McNamara & Franchi, 2018; Lucchese et al., 2022).

The CVM method also lacks a definitive description in the literature, leading to the lack of standardisation and contributing to variability in practice. Different studies have employed various criteria for staging, leading to confusion and potential

assessment inaccuracy (McNamara & Franchi, 2018; Hassel & Farman, 2021). Many studies using the CVM method have not established rigorous selection criteria for their subjects, which can introduce bias. For example, several investigations might overlook important factors like race, systemic diseases and syndromes that affect growth and development, thus compromising the validity of the findings (Hassel & Farman, 2021; Lucchese et al., 2022). Furthermore, the duration of each maturation stage in the CVM method can be variable and unpredictable, limiting its clinical applicability, especially in identifying the timing of growth spurts in individual patients (Perinetti et al., 2018).

2.4.10 Objective Alternatives of CVM Classification

Alternative staging systems that aim to improve reproducibility and reduce subjectivity have been proposed. An objective staging system was established, using linear and angular measurements that were traced and digitized on cephalometric analysis of the cervical vertebrae's morphology (Baccetti et al., 2005).

Recently, the application of Artificial Intelligence (AI) in determining CVM stages represents a significant advancement in objective classification methods. AI algorithms, particularly those leveraging machine learning and deep learning techniques, can analyse cervical vertebrae images with high precision and consistency, reducing human error and inter-observer variability. Additionally, using AI can streamline the process which allows for rapid processing of large datasets, benefiting clinical and research applications (Zhou et al., 2021; Atici et al., 2023).

With the emergence of artificial intelligence (AI), studies have been conducted on using AI to estimate CVM stages. Shoari et al. (2024) conducted a study to estimate stages of mandibular growth based on the CVM in lateral cephalograms by means of AI. The AI model designed in their study could be employed as a diagnostic aid tool along with other growth indicators to estimate mandibular growth. Their model had the highest accuracy (87,5%) in estimating pre-pubertal and pubertal stages (Shoari et al., 2024).

2.4.11 Midpalatal Suture Maturation (MPSM)

There is a lack of consensus regarding the minimum age for surgical assistance for the treatment of transverse maxillary deficiencies, mainly because of the large variability in the CA of MPS fusion (Angelieri et al., 2017). To provide more reliable clinical information for decision-making between RME alone and SARPE modalities, Angelieri et al. proposed a method for individual assessment of the MPS morphology using CBCT in late adolescents and young adults (Angelieri et al., 2013). Stages of MPS maturation were classified from A to E and described according to morphological characteristics (Figure 3) visible on axial cross-sectional slices.

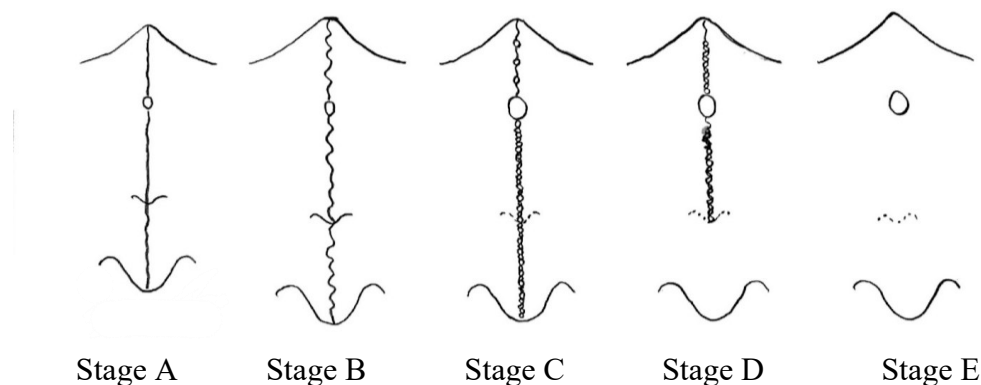


Figure 3. Schematic drawing of MPS maturational stages A - E (Adapted from Angelieri et al. 2013)

- **Stage A** is characterised by a straight, high-density radiopaque sutural line with little or no interdigitation.
- **Stage B** is identified as a high-density scalloped line. Patients at stage B may also present small areas where two parallel, high-density scalloped lines are close to each other, separated by areas of small low-density spaces.

- **Stage C** is visualized as two parallel, radiopaque, high-density scalloped lines that are close to each other, separated in some areas by small low-density spaces.
- **Stage D** is seen as two scalloped, high-density lines at the midline on the maxillary portion of the palate, but the midpalatal suture cannot be identified in the palatine bone. The suture can still be seen as two high-density lines separated by small low-density spaces.
- **Stage E**, sutural fusion has occurred in the maxilla. The midpalatal suture cannot be identified, and the para-sutural bone density is the same as in other regions of the palate.

2.4.12 MPSM - Limitations

The use of the CBCT radiological examination to assess the degree of MPS maturation, however, involves exposure to doses of ionizing radiation 10-100 times higher than those involved in the traditional two-dimensional cephalogram image (Mallya., 2015), so this examination should be used with caution. Other skeletal age assessments, such as the hand-wrist radiograph, have been the most commonly used method for orthodontists to evaluate the different stages of skeletal maturity and pubertal growth (Uysal et al., 2006; Flores-Mir et al., 2004). Furthermore, CBCT is not yet a routine radiological examination (Mallya & White., 2013), so it seems advantageous to investigate the degree of correlation between skeletal maturation, as assessed by the stages of maturation of the cervical vertebrae (CVM) in the cephalogram image, and the degree of maturation of the MPS.

Both the hand-wrist method and Angelieri's CBCT method do, however, require additional X-ray exposure. As a way of avoiding this additional radiation exposure, some researchers sought to relate maturation with skeletal and dental features other than the bones in the hand and wrist (O'Reilly & Yanniello., 1988; Uysal et al., 2004).

2.5 Previous studies

The following table presents a list of the more important studies related to the present investigation that evaluated MPS and CVM maturation stages in different populations using CBCTs and lateral cephalograms. None of the following investigations is identical to the present study. However, there are similarities between the methodologies which the present study follows.

Table 1. Previous studies regarding similar topics

Author/date	Aims/Objectives	Methodology	Results/Discussion
Uysal et al., (2006)	<ol style="list-style-type: none"> 1. Investigate the relationship between CA and CVM 2. Identify the relationship between chronologic and maturation stage evaluated by hand-wrist radiographs 3. To determine whether CVM correlates with maturation indicated by hand-wrist X-ray in a Turkish population 	Lateral cephalometric scans and hand-wrist radiographs of 503 subjects (290 female, 213 males; ages between 5.3 – 24.1 years)	The CVM maturation stages are clinically useful maturity indicators of pubertal growth in Turkish subjects.
Angelieri et al. (2013)	To present a novel classification method for individual assessment of midpalatal suture morphology using CBCT images.	<p>Cone-beam computed tomography images from 140 subjects (ages, 5.6-58.4 years) were examined to define the radiographic stages of midpalatal suture maturation. Five stages of maturation of the midpalatal suture were identified and defined</p> <p>Intraexaminer and interexaminer agreements were evaluated by weighted kappa tests.</p>	<p>Stages A and B typically were observed up to 13 years of age, whereas stage C was noted primarily from 11 to 17 years but occasionally in younger and older age groups. Fusion of the palatine (stage D) and maxillary (stage E) regions of the midpalatal suture was completed after 11 years only in girls. From 14 to 17 years, 3 of 13 (23%) boys showed fusion only in the palatine bone (stage D).</p> <p>This new classification method has the potential to avoid the side effects of rapid maxillary expansion failure or unnecessary surgically assisted rapid maxillary expansion for late adolescents and young adults.</p>

Perinetti et al. (2014)	To evaluate diagnostic accuracy and repeatability of the visual assessment of the cervical vertebrae maturation (CVM) stages.	Ten operators underwent training sessions in visual assessment of CVM staging. Subsequently, they were asked to stage 72 cases equally divided into the six stages. Such assessment was repeated twice in two sessions (T1 and T2) 4 weeks apart. A reference standard for each case was created according to a cephalometric analysis of both the concavities and shapes of the cervical vertebrae.	Visual assessment of the CVM stages is accurate and repeatable to a satisfactory level. About one in three cases remain misclassified; disagreement is generally limited to one stage and is mostly seen in stages 4 and 5.
Angelieri et al., (2015)	To analyze the diagnostic performance of the cervical vertebrae maturation (CVM) method in estimating accurately the stages of midpalatal suture (MPS) maturation.	Cone beam computed tomography (CBCT) of 142 subjects (84 female, 58 male, mean age 14.8 +/-9.7 years) Visual analysis of CVM and MPS stages by 2 calibrated examiners.	Most CVM stages can be used for the diagnosis of the stages of maturation of the MPS, so CBCT imaging may not be necessary. In the post pubertal period, assessment of the MPS maturation using CBCT may be indicated in deciding between conventional RME and SARME.
Jang et al. (2016)	To determine whether predicting maturation of the midpalatal suture is possible by classifying its morphology on cone-beam computed tomography (CBCT) images and to investigate relationships with other developmental age indices.	The morphology of the midpalatal suture was assessed by using CBCT images of 99 patients. Axial plane images of the midpalatal suture were classified into five stages according to the classification scheme. To make the assessment more accurate, the morphology and fusion of the midpalatal suture were additionally investigated on coronal cross-sectional planar images and volume-rendered images. Bone age was evaluated using the hand and wrist method (HWM) and cervical vertebrae method (CVM); dental age (Hellman's index), sex, and CA were also assessed. To evaluate relationships among variables, Spearman's rho rank test was performed along with crosstabs using contingency coefficients.	Among developmental age indices, the HWM and CVM showed strong correlations and high associations, suggesting that they can be useful in assessing maturation of the midpalatal suture.
Tonello et al. (2017)	To evaluate the maturation stages of the midpalatal sutures in children aged 11 to 15 years old, and to identify the status of suture maturation in these subjects to use as a comparison for the prognosis of maxillary expansion in older patients.	Tomographic images in axial sections of the midpalatal sutures from 84 children (40 boys, 44 girls; ages, 11-15 years) were classified using a scale denoting the maturation stage of the midpalatal suture (A, B, C, D, and E). The chi-square test was applied to evaluate suture stages by sex and age groups.	The results of this study, which showed dominant prevalence of stage C, suggest that conventional, nonsurgical rapid maxillary expansion performed in patients over 15 years old is justified by a satisfactory prognosis when assessment of the sutural status indicates stage C.
Angelieri et al., (2017)	To evaluate midpalatal suture maturation in adults, as observed in cone beam computed tomography (CBCT) images	CBCT scans from 78 subjects (64 female and 14 male, age range from 18 to 66 years) were evaluated. Midpalatal suture maturation was verified on the central cross-sectional	The majority of the adults presented a fused midpalatal suture in the palatine (stage D) and/or maxillary bones (stage E). However, the midpalatal suture was not fused in 12% of the subjects. Sex and CA were not significant predictors of the

Skeletal Age and the Relationship to Midpalatal Suture Maturation Stages. A Retrospective Radiographic Study in a Portuguese Population.

		axial slice in the superior–inferior dimension of the palate, using methods validated previously. Intra-examiner agreement was analyzed by weighted kappa test.	maturational stages of the midpalatal suture. The individual assessment of midpalatal suture maturation by way of CBCT images may provide reliable information critical to making the clinical decision between rapid maxillary expansion and surgically assisted rapid maxillary expansion for the treatment of maxillary atresia in adults.
Gorucu-Coskuner et al. (2018)	To evaluate the stages of midpalatal suture (MPS) maturation in patients older than 15 years, and to determine the correlation between the stage of MPS maturation and cervical vertebrae maturation (CVM).	Cone-beam computed tomography (CBCT) scans of 50 patients (29 female and 21 male; mean age, 19.79 ± 4.09 years) were evaluated. Good quality CBCT images from 15–30-year-old patients for evaluation of impacted canines or determination of orthognathic surgery were selected. The CBCT images were evaluated at two different time intervals for determination of the stages of MPS and CVM. The stages of MPS maturation were classified as A, B, C, D, or E using the axial sections by using a method validated previously. The stages of CVM were classified using sagittal sections of the CBCT images. Intra-examiner agreement was assessed using the Kappa test. The correlations between MPS maturation and CA and CVM were assessed using Spearman’s rank correlation analysis.	The limitation of our study was a small sample size, and, on the basis of our results, neither CVM nor CA could be used as a convenient tool to determine the stage of MPS maturation in 15–30-year-old patients.
Jimenez-Valvida et al. (2019)	The aim of this study was to evaluate the midpalatal suture maturation stages in adolescents and young adults using cone-beam computed tomography (CBCT)	200 CBCT scans of individuals aged 10 to 25 years old (95 males and 105 females) divided into three groups, adolescents ($n = 48$), post-adolescents ($n = 52$), and young adults ($n = 100$). The midpalatal suture maturation stage evaluation according to Angieleri’s method, using cross-sectional axial slice. Two previously calibrated examiners analyzed the images and classified according to five different maturation stages. A, B, and C stages were considered with open midpalatal suture, and D and E were considered without open midpalatal suture. Association tests were performed using chi-square test also, and a binary logistic regression was evaluated ($P < 0.05$).	The possibility to find midpalatal suture opening in post-adolescents and young adults is approximately 20%, greater than the orthodontists considered years ago. Furthermore, men are more likely to present midpalatal suture opening. These implications might be considered by the orthodontists when RME treatment is required. Besides, the ossification of the middle palatal suture is very variable; thereby, the use of CBCT might be recommended to evaluate the midpalatal suture opening and therefore to verify the possibility of maxillary disjunction.
Mahidan et al. (2020)	To evaluate the correlation of skeletal age based on cervical vertebrae maturation (CVM) stage	A cross-sectional analytic study. A total number of 93 samples were included. Samples were taken from	The results demonstrated that CVM stages had a significant but moderate positive correlation with the maturation of MPS. Until CS3, the

	and midpalatal suture (MPS) maturation in an Iranian population.	patients who were in CS3 to CS6 stages of CVM who had cone-beam computed tomography, lateral cephalometry based on inclusion criteria. The maturation of MPS was assessed based on the cone-beam computed tomography images. In the classification of maturation of MPS, there are five stages (A–E) and the suture fusion occurs in stage D. In stage E, the suture is fused completely. The CVM stage (CS1–6) was also assessed based on the lateral cephalograms. Data were analyzed using Spearman correlation with a significance level of 0.05.	MPS has not been fused and in CS6 the MPS is fused definitely.
Lucchese et al. (2022),	The present systematic review was carried out to evaluate both qualitatively and quantitatively the effectiveness of the cervical vertebral maturation (CVM) method in predicting the pubertal growth spurt.	PubMed, PMC, Scopus, SciELO, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science databases were searched. The research included every article published from 1970 to June 2019, featuring the keywords: (“cervical vertebrae” OR (“cervical” AND “vertebrae”) AND (“orthodontics” OR “growth and development” OR (“growth” AND “development”) OR (“growth”).	Overall, the CVM method can be considered an effective method and may be used with other skeletal indices for the radiographic assessment of skeletal maturity, and also to identify the growth peak in growing patients.
Luiz et al. (2022)	To evaluate and correlate the CVM and MPS maturation methods in patients aged from 11 to 14 years old, and investigate if CVM method can be predictive of the midpalatal suture maturation stage	42 CBCT and lateral cephalometric scans of children aged 11 to 14 years of age. Images were evaluated by two investigators. Kappa coefficient was calculated to estimate intra and inter-examiner agreement. Spearman correlation test was performed to evaluate the correlation between methods, age and gender. To evaluate the diagnostic performance of the CVM and MPS methods, the likelihood ratio (LHR positive) was applied.	The CVM method can be used as a predictor of the maturation stages of the midpalatal suture in the early stages of maturity. In more advanced stages, the evaluation of the palatal suture by tomography is suggested.
Yang et al. (2024)	To evaluate the midpalatal suture (MPS) maturation stages using the cone-beam computed tomography classification method in Chinese children aged 5-10 years, adolescents aged 11-15 years, and postadolescents aged 16-20 years and identify a correlation between maturation stage and age and sex.	Axial sections of tomographic images from 717 participants (369 female and 348 male participants) aged 5-20 years were used to classify the maturation stage of the MPS (stages A, B, C, D, and E). Kappa statistics were used to evaluate the measurement error. The chi-square test was applied to analyze the differences	The classification method is informative for clinical judgment of MPS maturation. Of the participants, 69.4%, aged 5-20 years, are in stages A, B, and C. The distribution of Chinese participants in advanced stages of the maturation stage increases with age. Female patients generally experience earlier MPS maturation than male patients, particularly those aged 11-20 years.

Skeletal Age and the Relationship to Midpalatal Suture Maturation Stages. A Retrospective Radiographic Study in a Portuguese Population.

		in the distribution of MPS stages by age group and by sex among all participants, as well as the adolescent group. The Fisher exact test was employed to assess the differences in MPS stage distribution by sex among children aged 5-10 years and among the postadolescent group. The Mann-Whitney U test was used to assess the potential variance in age distribution between stages C and D.	
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III. Objectives

The primary aim of this observational retrospective study was to evaluate and correlate the CVM and MPSM methods between age and sex in patients aged 9 to 30 years. This was accomplished by using lateral cephalometric radiographs and CBCT scans of the same patient to visually assess the morphological stages of maturation of the cervical vertebrae and the MPS.

The secondary objective was to evaluate the CVM method as a predictive indicator in estimating the degree of MPSM.

3.1 Research Hypothesis

In this study, the following research questions were defined, and the corresponding null hypothesis (H0) and alternative hypothesis (H1) were formulated:

1st Research Question - Is there any correlation between CA and stages of MPSM?

- H0: There is no correlation between CA and the stages of maturation of the MPS.
- H1: There is a correlation between CA and the stages of maturation of the MPS.

2nd Research Question - Is there any correlation between CA and stages of CVM?

- H0: There is no correlation between CA and the stages of CVM.
- H1: There is a correlation between CA and the stages of CVM.

3rd Research Question - Is there any correlation between the CVM stages and the level of MPSM?

- H0: There is no correlation between the CVM stages and the level of MPSM.
- H1: There is a correlation between the CVM stages and the level of MPSM.

IV. Materials and Methods

4.1. Investigation Methodology

The search of supporting bibliography and literature for this investigation was done using research databases such as Google Scholar and PubMed. Relevant books in the field of contemporary orthodontics were also utilized for the theoretical background. The keywords that were utilized were: *cone-beam computed tomography, midpalatal suture maturation, skeletal age, rapid maxillary expansion.*

The present study consists of two components: a theoretical component involving a narrative review of literature related to the research question, and an investigative component, which includes the assessment of skeletal age through CBCT, and lateral cephalometric radiographs based on established staging systems using Baccetti et al. and Angelieri et al. techniques. A second part of the investigative component was to correlate and evaluate the diagnostic performance of the CVM method as a predictive indicator for MPSM.

A retrospective observational 3D, radiographic study was carried out at the Dental Clinic of Egas Moniz School of Health & Science. This study was approved by the ethical committee of Egas Moniz School of Health & Science (PT-331/23 from 5 of January 2024) Informed consent was obtained from all patients before undertaking CBCT and cephalometric scans.

4.2. Participants

The available CBCT between January 2023 – July 2024 in the database of the Egas Moniz School Dental Clinics were searched for subjects which fulfilled the inclusion and exclusion criteria as follows.

The inclusion criteria were:

1. Individuals of Portuguese nationality.
2. Patients with CBCT and lateral cephalometric radiographs were taken at the same period.
3. Age range from 9 to 30 years.
4. Good quality CBCT image that includes the complete maxillary arch.

The exclusion criteria were:

1. Patients with previous or present orthodontic or orthopaedic treatment
2. Patients with cleft lip and palate or other craniofacial deformities
3. Patients with systemic diseases affecting bone metabolism
4. Patients with a history of maxillofacial trauma.

Only 33 subjects (13 male and 20 female) aged 9-30 years were acquired and included in this investigation. This number did not allow for calculating a sample size, therefore the present investigation is considered a pilot study used for a power calculation for a future study.

4.3. Image acquisition

All CBCT and cephalometric scans were taken and obtained from Planmeca Viso G7 (Planmeca, Helsinki, Finland). The CBCT images were required by clinicians for diagnostic purposes and treatment of these patients. Cephalometric scans were acquired from the orthodontic department. The following settings were used: 120kVp, 5 mA, large field of view (20 cm x 17 cm), exposure time of 30 seconds and slice thickness of 0.45 mm. The 3D images were constructed using the Planmeca Romexis Viewer, software version 6.0 (Helsinki, Finland).

4.4. Radiologic examination

All CBCT scans and cephalograms were analysed using the Planmeca Romexis Viewer software and further cropped and exported into a PowerPoint presentation with a black background. The researcher was trained by an expert in the field of interpreting CBCT data prior to continuing the analysis. Inter- and intra-operator reproducibility analyses were carried out at a two-week interval to assess the reliability and consistency of the assessments of the CVM method and the classification of the MPSM stages. The Cohen's weighted Kappa coefficient was used. A P-value less than 0.05 was considered statistically significant.

4.4.1. Image standardization of CBCTs

Head orientation and natural head position in all three planes of space was verified or corrected. The cursor (the position indicator) of the image analysis software was positioned along the patient's midsagittal plane in both the coronal and axial views. In the sagittal view, the patient's head was adjusted so that the anteroposterior long axis of the palate was horizontal. Orientation starts first with the midsagittal cut.

4.4.2. Standardization of the Axial Cross-Sectional Slice Used for Sutural Assessment

In the coronal view, the horizontal blue line was placed transversally across the hard palate. The vertical red line was placed along the nasal septum, perpendicular to the hard palate.

In the sagittal plane, the midsagittal cross-sectional slice was employed to place the palate horizontally, placing the software's horizontal blue line along the centre through the anterior and posterior nasal spine. In the axial cross-sectional slice, the software's red vertical line was also placed to pass through the anterior and posterior nasal spine. The horizontal green line on the axial slice is placed parallel to the transversal palatine suture.

After placing the vertical line along the palate, the central cross-sectional slice in the axial (superoinferior) dimension (ie, from the nasal to the oral surface) was employed for the classification of maturational stages of the MPS. For subjects with a curved palate, the palate was evaluated in 2 central cross-sectional axial slices, identifying the posterior and anterior regions of the MPS separately. For images showing a thicker palate, the palate was evaluated in the 2 most central axial slices. A curved palate was represented as a palate where the anterior and posterior segments cannot be visualized in the same axial slice, and therefore, sutural staging classification requires two slices (Angelieri et al., 2013). A thick palate was defined as a palate where the MPS can be assessed in more than three axial slices (oral, central, and nasal); for this reason, a thick palate might have two or more central slices.

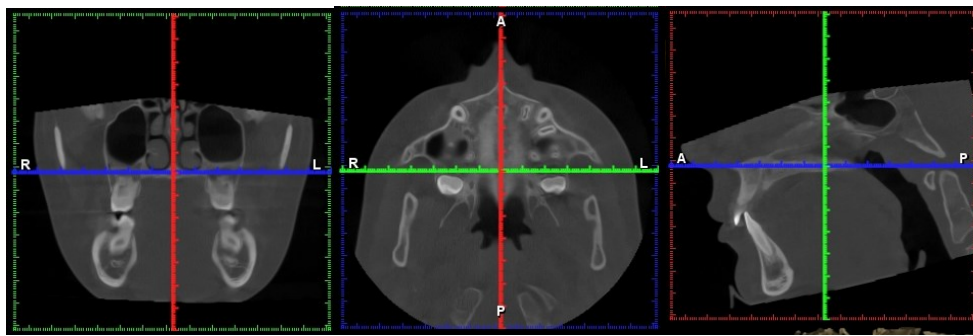


Figure 4. Standardisation of CBCT images in all three planes A - Coronal, B – Axial and C - Sagittal)

4.4.3. MPS Staging

Transverse CBCT axial cross-sections were used to classify five maturational stages of the MPS (A to E), following the Angelieri et al. methodology (Angelieri et al., 2013) (Figure 3).

(Figure 5). **Stage A** of the MPS morphology is defined by one generally straight high-density sutural line, with little or no interdigitation. **Stage B** is observed as a high-density scalloped line at the midline. Patients at stage B may also present some areas as two parallel, scalloped, high-density lines separated by small areas of low-density spaces. **Stage C** is visualized as two parallel, high-density scalloped lines close to each

other, separated by areas of small low-density spaces. **Stage D** is visualized as two parallel, high-density, scalloped lines on the midline of the maxillary portion of the palate, but the suture cannot be identified in the palatal bone. **Stage E**, sutural fusion has occurred in the maxilla. The suture cannot be identified at stage E, parasutural bone density is equal to other regions of the palate. Inter- and intra-operator reproducibility validity were carried out at a 2-week interval for visual analysis and classification.

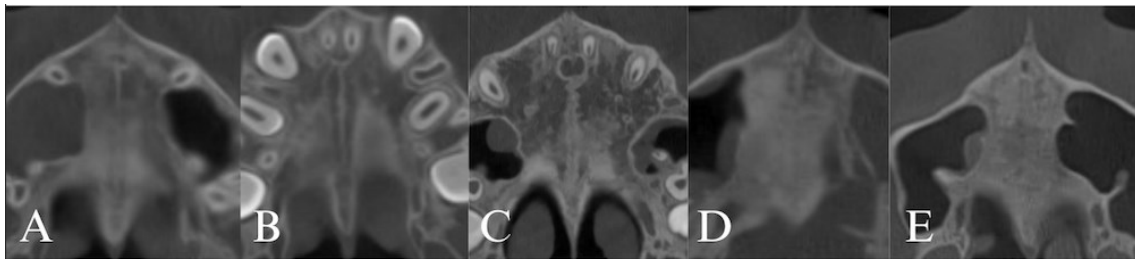


Figure 5. The classification of MPS stages A to E according to its morphology, visible on the CBCT axial cross-sectional slices.

4.5. CVM Assessment

Lateral cephalometric scans were used to assess the CVM stages. Stages CVS1, CVS2, CVS3, CVS4, CVS5 and CVS6 were assessed following the modified method of Baccetti et al. (2001). The morphology of the three cervical vertebrae (C2, C3 and C4), was evaluated by visual inspection. Two sets of morphological characteristics were analysed:

1 - The presence or absence of a concavity at the lower border of the body of C2, C3 and C4.

2 - Four basic shapes of the body of C3 and C4 were considered:

- Trapezoid (superior border is tapered from posterior to anterior)
- Rectangular horizontal (heights of the posterior and anterior border are equal; the superior and inferior borders are longer than the posterior and anterior borders)
- Squared (the posterior, anterior, superior and inferior borders are equal)

- Rectangular vertical (the posterior and anterior borders are longer than the superior and anterior borders)

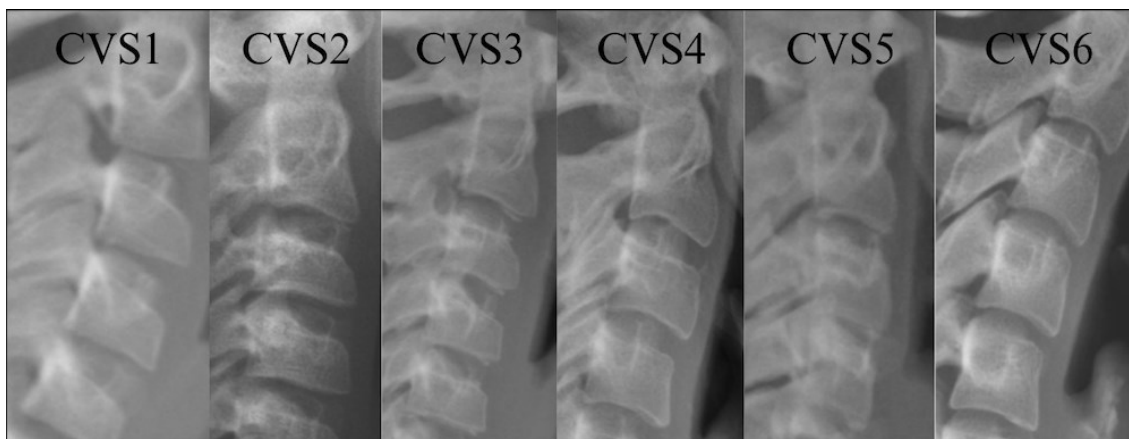


Figure 6. The CVM stages on lateral cephalograms, CVS1 through CVS6

Cervical vertebrae maturation staging system (Figure 6): **CVS1** (initiation)- inferior borders are flat on the second (C2), third (C3) and fourth (C4) vertebrae, vertebral bodies are wedge-shaped with anterior borders being shorter in height than the posterior borders. **CVS2** (acceleration)- concavities begin to develop on the inferior border of C2 and C3, bodies of C3 and C4 are nearly rectangular, inferior border of C4 still remains flat. **CVS3** (transition)- clear concavities develop on the inferior border of C2 and C3. **CVS4** (deceleration)- distinct concavities are visible on the inferior borders of C2, C3 and C4, bodies of all four cervical vertebrae are rectangular. **CVS5** (maturation) - vertebral bodies of C3 and C4 are nearly square, and spaces between vertebral bodies are reduced. **CVS6** (completion) - vertebral bodies of C3 and C4 are more vertical than horizontal.

4.6. Statistical analysis

Descriptive and inferential analyses were carried out using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, USA) version 28. The level of significance (P value) was determined to be at 5%. A weighted Kappa coefficient was calculated for the evaluation of inter- and intra-operator agreement for the CVM method

and the classification of the MPS maturation. The correlations between the MPS and the CVM stages were evaluated by the Spearman correlation test.

The correlation between skeletal maturity assessed with the CVM method and the maturational stages of the MPS was evaluated with a measure of diagnostic performance - the positive likelihood ratio

The properties of the CVM method as a diagnostic or screening tool for the diagnosis of the MPSM stages were described with the following diagnostic performance parameters: Sensitivity, Specificity, Predictive values and the Likelihood Ratios (LHR) (Attia., 2003). The positive predictive value of a test is the probability that the patient has the condition (in this case, a specific MPSM stage) when restricted to patients who have a specific finding (a specific CVM stage). The LHR is the probability that the condition (MPSM stage) is present in patients with the finding (CVM stage) divided by the probability that the same condition is present in patients without the finding and indicates the probability of the condition (MPSM stage) being diagnosed when the finding (CVM stage) is present. It combines both the sensitivity and specificity of the test and directly estimates how much a test result outcome changes the odds of having a condition. (Attia., 2003).

The LHR may range from 0 to infinity (McGee., 2002). A result of 1 indicates no diagnostic performance (ie, no relationship) whereas a result smaller than 1 is interpreted as a decrease in the likelihood of having the condition (negative relationship) (Deeks & Altman., 2004). An LHR greater than 1 indicates that the presence of the finding is associated with having the condition, and the bigger the number the stronger the association. An LHR between 1 and 2 is interpreted as an increase of 15% in the likelihood of having the condition and an LHR between 2 and 5 indicates a bigger increase (15%- 30%) in that likelihood. An LHR between 5 and 10 is interpreted as a moderate increase (30%-45%) in the likelihood of having the condition and LHRs above 10 indicate a large and conclusive increase in the likelihood of having the condition (ie, strong association) (McGee., 2002).

Due to the small number of participants in each maturational stage of both CVM and MPS, three groups were created for the calculation of diagnostic performance: Prepubertal stages CS1 and CS2 for the identification of MPS stages A and B, pubertal stage CS3 for the diagnosis of MPS stage C, and post-pubertal stages CS5 and CS6 for the assessment of MPS stages D and E.

V. Results

5.1. Measurement repeatability

The Cohen's weighted Kappa coefficient was calculated for evaluating intra-examiner reliability for the classification of CVM and MPSM was 0.948 and 0.812, respectively. For inter-examiner reproducibility evaluation, the Kappa coefficient was 0.944 for the CVM and 0.973 for the MPSM. This result indicates an almost perfect intra-examiner agreement according to Landis and Koch (Landis & Koch., 1977).

5.2. Sample description

The distribution of patients by age and gender is presented in Table 2. Among the 33 enrolled patients in the study, 20 were female patients with a mean age of 16.45 years (SD \pm 6.44). Females represented 60.6% of the total sample aged between 9 and 29 years. Among the females, 70% were 15 years old or younger and 30% older than 20 years old. The age range for male patients was between 10 and 28 years and the mean age was 15.46 (SD \pm 4.98). The mean age of the total sample was 16.6 (SD \pm 5.85).

Table 2. Age and gender distribution

Age (Years)	Gender		Total
	Female (%)	Male (%)	
9	1 (100)	-	1
10	1 (33.3)	2 (66.7)	3
11	2 (100)	-	2
12	2 (40)	3 (60)	5
13	1 (50)	1 (50)	2
14	6 (100)	-	6
15	1 (50)	1 (50)	2
16	-	1 (100)	1
17	-	2 (100)	2
19	-	1 (100)	1
20	-	1 (100)	1
21	1 (100)	-	1
22	1 (100)	-	1
23	1 (100)	-	1
28	1 (50)	1 (50)	2
29	2 (100)	-	2
Total	20 (60.6)	13 (39.4)	33
Mean Age (SD)	16.45 (6.44)	15.46 (4.98)	16.6 (5.85)

5.3. MPS Stages

The distribution of patients based on MPS maturation stage, mean age and gender is shown in Table 3. Table 4 shows the distribution based on the individual age for each gender. Of the total sample, 58% were in stage C with a mean age of 16.7 years old (SD 6.01) (Table 3). Among all females, 60% were in stage C, with a mean age of 16.9 years old (SD 6.57). No cases in MPSM stages A and E were documented among females. The female age range in Stage B was 9-21 years old and in Stage, C was 11-29 years old but no females between 16 – 20 years old were present in the sample (Table 4). Eight out of the 12 females (67%) in stage C were below 16 years old, and the other four (33%) were above 20 years old (Table 4). Of the total females, 70% were 15 years old or younger. Among these, 20% were in stage B, 40% in stage C and 10% in stage D. Forty per cent of total females were in Stage C between 11- 15 years old (Table 4). Among males, 54% were in stage C with a mean age of 16.28 years old (SD 5.5) (Table 3). All MPSM stages were documented among males. Four out of the 7 males (57%) in stage C were below 16 years old, two (29%) were 17 years old and one (14%) 28 years old (Table 4). Of the total males, 54% were 15 years old or younger. Among these, 14%

were in stage A, 29% in stage B and 57% in stage C. No male below 15 years of age was in PSM stage D, E. Forty-six per cent of total males were in stage C between 11-15 years old (Table 4). The male age range in stage C were 12 – 28 years old.

Table 3. Distribution of the sample based on MPS maturation, mean age and gender.

MPS stages	Gender				n (% of MPS) (% of total)	Total Age (SD)
	n (% of MPS) (% of total)	Female Mean Age (SD)	n (% of MPS) (% of total)	Male Mean Age (SD)		
A	0 (0)	-	1 (100) (7.7)	12 (0.0)	1 (100) (3)	12 (0.0)
B	6 (67) (30)	16.33 (7.74)	3 (33) (23.1)	13 (5.2)	9 (100) (27)	15.22 (6.85)
C	12 (63) (60)	16.91 (6.57)	7 (37) (53.8)	16.28 (5.5)	19 (100) (58)	16.68 (6.07)
D	2 (67) (10)	14 (0.0)	1 (33) (7.7)	16 (0.0)	3 (100) (9)	14.66 (1.15)
E	0 (0) (0)	-	1 (100) (7.7)	20 (0.0)	1 (100) (3)	20 (0.0)
Total	20 (60.6)	16.45 (6.44)	13 (39.4)	15.46 (4.98)	33 (100)	16.6 (5.58)

Table 4. Distribution of the sample based on MPS maturation, age and gender

Gender	MPS Maturation					Total
Females	A	B	C	D	E	
Age						
9	0	1	0	0	0	1
10	0	1	0	0	0	1
11	0	0	2	0	0	2
12	0	0	2	0	0	2
13	0	1	0	0	0	1
14	0	0	4	2	0	6
15	0	1	0	0	0	1
16	0	0	0	0	0	0
17	0	0	0	0	0	0
19	0	0	0	0	0	0
20	0	0	0	0	0	0
21	0	0	1	0	0	1
22	0	1	0	0	0	1
23	0	0	1	0	0	1
28	0	0	1	0	0	1
29	0	1	1	0	0	2
Total	0	6	12	2	0	20
Percent	0%	30%	60%	10%	0%	100%
Males	A	B	C	D	E	Total
Age						
9	0	0	0	0	0	0
10	0	2	0	0	0	2
11	0	0	0	0	0	0
12	1	0	2	0	0	3
13	0	0	1	0	0	1
14	0	0	0	0	0	0
15	0	0	1	0	0	1
16	0	0	0	1	0	1
17	0	0	2	0	0	2
19	0	1	0	0	0	1
20	0	0	0	0	1	1
21	0	0	0	0	0	0
22	0	0	0	0	0	0
23	0	0	0	0	0	0
28	0	0	1	0	0	1
29	0	0	0	0	0	0
Total	1	3	7	1	1	13
Percent	7.7%	23.1%	53.8%	7.7%	7.7%	100%

5.4 CVM stages

Table 5 shows the CVM assessment, according to mean age and gender and in Table 6, the distribution is based on the individual age. Considering the total sample, the CVM stage mainly represented was CVS4 with 27.3 %. CVS4 was also the most common stage among females, with 30% of females assessed to be in this maturation stage. No female participant was in the CVS3. Among males, as the mean age increased, so did the CVM stage (Table 5). The same was not observed among females. The mean age of females in CVS4 and CVS5 was 20.16 (SD 7.85) and 13.4 (SD 1.34) respectively (Table 5). Five females (25% of total females) in CVS5 and 2 (10% of total females) in CVS6 were below 15 years of age. It was observed that 18.2 % of the total sample was assessed as being in the maximum stage of cervical maturation, CVS6, and 83% of them were females.

Table 5. CVM distribution according to age and gender.

CVM stages	Gender				n (% of CVM) (% of total)	Total Age (SD)
	n (% of CVM) (% of total)	Female Age (SD)	n (% of CVM) (% of total)	Male Age (SD)		
CVS1	2 (40) (10)	10.5 (2.12)	3 (60) (23.1)	11.0 (1.73)	5 (100) (15.2)	10.8 (1.64)
CVS2	2 (50) (10)	10.5 (0.7)	2 (50) (15.4)	12 (0.00)	4 (100) (12.1)	11.25 (0.95)
CVS3	0 (0) (0)	-	1 (100) (7.7)	12 (0.00)	1 (100) (3)	12 (0.0)
CVS4	6 (67) (30)	20.16 (7.85)	3 (33) (23.1)	17.0 (2.00)	9 (100) (27.3)	19.1 (6.48)
CVS5	5 (63) (25)	13.4 (1.34)	3 (37) (23.1)	17.66 (2.08)	8 (100) (24.2)	15.0 (2.67)
CVS6	5 (83) (25)	19.8 (5.93)	1 (17) (7.7)	28 (0.00)	6 (100) (18.2)	21.16 (6.27)
Total	20 (60.6)	16.45 (6.44)	13 (39.4)	15.46 (4.98)	33 (100)	16.6 (5.58)

Table 6. Distribution of the sample based on CVM stages, age and gender.

Gender	CVM Stages						Total
Females	CVS1	CVS2	CVS3	CVS4	CVS5	CVS6	
Age							
9	1	0	0	0	0	0	1
10	0	1	0	0	0	0	1
11	0	1	0	0	1	0	2
12	1	0	0	1	0	0	2
13	0	0	0	1	0	0	1
14	0	0	0	0	4	2	6
15	0	0	0	1	0	0	1
16	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0
21	0	0	0	0	0	1	1
22	0	0	0	0	0	1	1
23	0	0	0	1	0	0	1
28	0	0	0	0	0	1	1
29	0	0	0	2	0	0	2
Total	2	2	0	6	5	5	20
Percent	10%	10%	0%	30%	25%	25%	100%
Males	CVS1	CVS2	CVS3	CVS4	CVS5	CVS6	Total
Age							
9	0	0	0	0	0	0	0
10	2	0	0	0	0	0	2
11	0	0	0	0	0	0	0
12	0	2	1	0	0	0	3
13	1	0	0	0	0	0	1
14	0	0	0	0	0	0	0
15	0	0	0	1	0	0	1
16	0	0	0	0	1	0	1
17	0	0	0	1	1	0	2
19	0	0	0	1	0	0	1
20	0	0	0	0	1	0	1
21	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0
28	0	0	0	0	0	1	1
29	0	0	0	0	0	0	0
Total	3	2	1	3	3	1	13
Percent	23.1%	15.4%	7.7%	23.1%	23.1%	7.7%	100%

5.5. Cross-tabulation analysis

The distribution of the MPSM stages according to CVM stages for females and males is reported in Table 7 and Table 8, respectively. In MPSM stage C, there were females and males in all CVM stages. This was not observed in the other MPSM stages A, B, D and E. The frequency of females in stage C increased with the increased CVM stage. The frequency of males in stage C, however, did not change with increased CVM stage. At CVS4, no females or males were observed at MPS stage D or E. Among males, it was observed that more advanced CVM stages show higher MPSM stages (Table 8). Among females, 10 % (2 / 20) were CVS5 and D and 20% (4 / 20) were CVS6 and C. Thirty percent of females (6 / 20) were in MPSM stage B. Of these 5% were in CV1, 5% in CV2, 15% in CV4 and 5% in CV6 (Table 7).

Table 7. Crosstabulation of CVM and MPS stages in females.

		MPS			Total
		B	C	D	
CVM					
CVS1	Count	1	1	0	2
	% within CVM	50.0%	50.0%	0.0%	100.0%
	% within MPS	16.7%	8.3%	0.0%	10.0%
	% of Total	5.0%	5.0%	0.0%	10.0%
CVS2	Count	1	1	0	2
	% within CVM	50.0%	50.0%	0.0%	100.0%
	% within MPS	16.7%	8.3%	0.0%	10.0%
	% of Total	5.0%	5.0%	0.0%	10.0%
CVS4	Count	3	3	0	6
	% within CVM	50.0%	50.0%	0.0%	100.0%
	% within MPS	50.0%	25.0%	0.0%	30.0%
	% of Total	15.0%	15.0%	0.0%	30.0%
CVS5	Count	0	3	2	5
	% within CVM	0.0%	60.0%	40.0%	100.0%
	% within MPS	0.0%	25.0%	100.0%	25.0%
	% of Total	0.0%	15.0%	10.0%	25.0%
CVS6	Count	1	4	0	5
	% within CVM	20.0%	80.0%	0.0%	100.0%
	% within MPS	16.7%	33.3%	0.0%	25.0%
	% of Total	5.0%	20.0%	0.0%	25.0%
Total	Count	6	12	2	20
	% within CVM	30.0%	60.0%	10.0%	100.0%
	% within MPS	100.0%	100.0%	100.0%	100.0%
	% of Total	30.0%	60.0%	10.0%	100.0%

Table 8. Crosstabulation of CVM and MPS stages in males.

		MPS					Total
		A	B	C	D	E	
CVM							
CVS1	Count	0	2	1	0	0	3
	% within CVM	0.0%	66.7%	33.3%	0.0%	0.0%	100.0%
	% within MPS	0.0%	66.7%	14.3%	0.0%	0.0%	23.1%
	% of Total	0.0%	15.4%	7.7%	0.0%	0.0%	23.1%
CVS2	Count	1	0	1	0	0	2
	% within CVM	50.0%	0.0%	50.0%	0.0%	0.0%	100.0%
	% within MPS	100.0%	0.0%	14.3%	0.0%	0.0%	15.4%
	% of Total	7.7%	0.0%	7.7%	0.0%	0.0%	15.4%
CVS3	Count	0	0	1	0	0	1
	% within CVM	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
	% within MPS	0.0%	0.0%	14.3%	0.0%	0.0%	7.7%
	% of Total	0.0%	0.0%	7.7%	0.0%	0.0%	7.7%
CVS4	Count	0	1	2	0	0	3
	% within CVM	0.0%	33.3%	66.7%	0.0%	0.0%	100.0%
	% within MPS	0.0%	33.3%	28.6%	0.0%	0.0%	23.1%
	% of Total	0.0%	7.7%	15.4%	0.0%	0.0%	23.1%
CVS5	Count	0	0	1	1	1	3
	% within CVM	0.0%	0.0%	33.3%	33.3%	33.3%	100.0%
	% within MPS	0.0%	0.0%	14.3%	100.0%	100.0%	23.1%
	% of Total	0.0%	0.0%	7.7%	7.7%	7.7%	23.1%
CVS6	Count	0	0	1	0	0	1
	% within CVM	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%
	% within MPS	0.0%	0.0%	14.3%	0.0%	0.0%	7.7%
	% of Total	0.0%	0.0%	7.7%	0.0%	0.0%	7.7%
Total	Count	1	3	7	1	1	13
	% within CVM	7.7%	23.1%	53.8%	7.7%	7.7%	100.0%
	% within MPS	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	% of Total	7.7%	23.1%	53.8%	7.7%	7.7%	100.0%

5.6. Correlations

Table 9 shows the Spearman Rank Order correlations for the total sample and Table 10 and Table 11 for the females and males respectively. No correlation was observed between CA and stages of MPS maturation regarding both sexes ($r = 0.248$, $p = 0.164$), males ($r = 0.515$, $p = 0.072$) or females ($r = 0.550$, $p = 0.817$). There was a positive but moderate correlation between CVM and CA considering both genders ($r = 0.625$, $p < 0.001$). The correlation was stronger in males ($r = 0.872$, $p < 0.001$) compared to females ($r = 0.463$, $p = 0.040$).

A moderate correlation was observed between the CVM and MPS maturational stages, for the total sample ($r = 0.433$, $p = 0.012$) and for males ($r = 0.603$, $p = 0.029$). There was no significant correlation between CVM and MPS among female subjects ($r = 0.343$, $p = 0.139$).

Table 9. Spearman rank correlation coefficients for the total sample.

		Both Genders		
		Age	MPS	CVM
Age	r	1.000	.248	.625**
	Sig. 2-(tailed)	-	.164	<.001
	N	33	33	33
MPS	r	.248	1.000	.433*
	Sig. 2-(tailed)	.164	-	.012
	N	33	33	33
CVM	r	.625**	.433*	1.000
	Sig. 2-(tailed)	<.001	.012	-
	N	33	33	33
** . Significant at the 0.01 level (2-tailed)				
* . Significant at the 0.05 level (2-tailed)				

Table 10. Spearman rank correlation coefficients for females.

		Females		
		Age	MPS	CVM
Age	r	1.000	.055	.463*
	Sig. 2-(tailed)	-	.817	.040
	N	20	20	20
MPS	r	.055	1.000	.343
	Sig. 2-(tailed)	.817	-	.139
	N	20	20	20
CVM	r	.463*	.343	1.000
	Sig. 2-(tailed)	.040	.139	-
	N	20	20	20
** . Significant at the 0.01 level (2-tailed)				
* . Significant at the 0.05 level (2-tailed)				

Table 11. Spearman rank correlation coefficient for males.

	Males			
		Age	MPS	CVM
Age	r	1.000	.0515	.872**
	Sig. 2-(tailed)	-	.072	<.001
	N	13	13	13
MPS	r	.0515	1.000	.603*
	Sig. 2-(tailed)	.072	-	.029
	N	13	13	13
CVM	r	.872*	.603*	1.000
	Sig. 2-(tailed)	<.001	.029	-
	N	13	13	13
** . Significant at the 0.01 level (2-tailed)				
* . Significant at the 0.05 level (2-tailed)				

5.7. Diagnostic Performance

The data from the CVM stages and the MPS stages were combined into three maturation categories: pre-pubertal, pubertal and post-pubertal. Stages CVS1 and CVS2 for the identification of MPS stages A and B (pre-pubertal), stage CVS3 for the diagnosis of MPS stage C (pubertal), and CVS5 and CVS6 for the assessment of MPS stages D and E (post-pubertal). Four diagnostic performance parameters were calculated for the different pubertal categories and presented in Table 12.

The positive LHR values of CVS1 and CVS2 for the diagnosis of stages A and B in the MPS maturation were between two and -five (2.67), indicating a small increase in the likelihood (15% - 30%) of detecting the MPS maturational stages A and B. The CVS3 showed a minimal increase (15%) in the likelihood of detecting the maturational stage C of the MPS. Only in the case of CVS5 and CVS6 for the assessment of MPS stages D and E, a positive LHR greater than 10 was observed, thus indicating a large and conclusive increase in the likelihood that CVM stages CVS5 and CVS6 corresponds to the maturational stage D and E of the MPS (McGee., 2002).

According to the four parameters of sensitivity, specificity, positive predictive value, and positive LHR (Table 12), the post-pubertal stages CS5 and CS6 showed the highest diagnostic performance for the identification of stages D and E in MPS maturation, with specificity and positive predictive values of 100%). However, the 95% confidence intervals for the positive LHRs of the CVM stages for the identification of MPS maturational stages were variable, with the widest range seen for CS5 and CS6 (0.99-infinity).

Table 12. Diagnostic performance parameters of CVM stages for the identification of MPS stages

	CS1 and CS2 Variable diagnosed: Stages A and B	CS3 Variable diagnosed: Stage C	CS5 and CS6 Variable diagnosed: Stages D and E
Sensitivity (%)	55.6 (25.3-81.4)	100 (5.5-100)	28.6 (12.0-28.6)
Specificity (%)	79.2 (67.8-88.9)	43.8 (40.8-43.8)	100 (87.8-100)
Positive Predictive Value (PPV) (%)	50.0 (22.8-73.2)	5.3 (0.3-5.3)	100 (42.1-100)
Positive Likelihood Ratio (LHR)	2.67 (0.79-7.30)	1.78 (0.09-1.78)	Inf. (0.99-Inf.)

Data presented as: value (95% CI).

VI. Discussion

This was a retrospective, 3D radiographic observational investigation undertaken on a sample of patients attending the Egas Moniz Dental Clinics. This was the first study performed on Portuguese subjects to evaluate and correlate the CVM and MPSM methods between age and sex in patients aged 9 to 30 years, and to further evaluate the CVM method as a predictive indicator for estimation of MPSM.

The use of conventional RME in adolescents and young adults is often unpredictable due to the variability in the rate and extent of fusion of the MPS in relation to CA (Melsen., 1972; Persson & Thilander., 1977;). The assessment of MPSM stages with CBCT images is a reliable method for predicting RME outcomes, without the often-confusing overlapping anatomical structures of the nose that usually occur when a 2D occlusal radiograph is used for diagnosis (Wehrbein & Yildizhan., 2001; Angelieri et al., 2013). On the other hand, the use of CBCT imaging is associated with higher costs and increased radiation exposure for patients.

The initiation of fusion of the MPS has been associated with the rate of skeletal growth and the transverse growth pattern of the maxilla (Persson & Thilander., 1977). Both skeletal and transverse maxillary growth patterns have been related to velocity curves of body height with similar periods of growth spurt and growth completion (Björk., 1966). In orthodontics, the evaluation of skeletal maturation and adolescent growth peak has been identified using the hand-wrist and CVM methods (Karlberg., 2002; Baccetti et al., 2005). It has been shown that the CVM method serves as a reliable biological indicator for somatic skeletal maturity in growing patients. The CVM method presents good reproducibility when specific training is provided, along with precise guidelines for assessing each CVM stage visually (Perinetti et al., 2014).

This study explored the degree of correlation between CVM, MPSM and chronologic age. Correlation analysis was made between CA and MPS and CVS maturation stages,

and between MPS and CVM stages. The relation between CVM and MPSM methods was also evaluated to determine the validity of the CVM to predict the MPSM stages.

6.1. MPSM and CVM Sample Description

The MPSM method results show that most of the total sample (56%) were in MPSM stage C with the highest prevalence observed in females (63%) with a mean age of 16.7 years old ($SD \pm 6.1$). Similarly, Luz et al. (2022) and Tonello et al. (2017) noticed a higher prevalence of stage C maturation and a higher prevalence among females, however at a younger age (around 12 years of age). On the other hand, Yang et al. (2024) found the highest percentage of stage C in the age group 16-20 years old. The relatively small sample size in this study and the different distribution of age groups may explain this age discrepancy as 30% of females were between 21 and 29 years old and the rest 70% were between 9 and 15 years old. For MPSM stages D and E, the prevalence in this study was 12 %, equally distributed between genders which are in disagreement with the higher prevalence of females reported by previous researchers with samples composed of participants with a similar (Jimenez-Valvida., 2019; Yang et al., 2024) or different age group (Luz et al., 2022; Gorucu-Coskuner et al., 2018; Tonello et al., 2017). Although aligning with previous studies reporting a higher percentage of MPSM stage C, conflicting prevalences by gender and age between the present study and previous ones reinforce the randomness between MPS maturation stages and chronological age.

The present study shows that CA in adults is not a reliable predictor for MPSM (some older patients presented less MPSM than younger ones). This was especially noticed among females. Even though a general increase in sutural closure with age was observed, CA alone did not determine the MPSM by itself, aligning with the findings reported by other similar studies (Gorucu-Coskuner et al., 2018). These findings encourage taking CBCT scans in young adults to identify the maturational stage of the MPS.

The CVM method shows that most of the sample (27.3%) were assessed as being in the CVS4 stage which is in agreement with previous studies (Luz et al., 2022; Gorucu-Coskuner., 2018; Perinetti et al., 2017). The distribution of CVM stages was different between genders with the females presenting a more advanced stage of maturation. This is in accordance with previous studies showing that, compared to females, the skeletal maturation in males is observed later (Luz et al., 2022). In the present study, the higher stages of maturation (CVS4, CVS5 and CVS6) were observed in 80% of females and in 54% of males. This extreme difference in frequency observed in the study may also result from the fact that the percentage of females and males in the sample above 20 years old was 30% and 8% respectively.

6.2. Description of MPSM related to CVM

No case of suture fusion (stage D and E) was found before CVS4 in this study. Similarly, previous studies have reported that MPS fusion starts from CVS4 (Angelieri et al., 2015; Jang et al., 2016). We may therefore state that the present study corroborates the inference that nonsurgical palatal expansion could be performed before stage CVS4 of CVM without the need to take CBCT.

Cases with unfused MPS were found in all stages of cervical vertebrae maturation in both genders in this study. Among the patients assessed as being in the CVS5 maturation stage, 50% were in MPS stage C. The total number of patients in CVS6 was 6 and none of them showed MPS fusion, as 83% were in MPS stage C and 17% in MPS stage B. This means that in the post-pubertal and young adulthood, MPS was not fused in at least half the patients, indicating that in those periods, conventional RME may still have a good prognosis. Similarly, Kwak et al., in a study with adult patients from Korea in CVS5 and CVS6 CVM stages, showed that the MPS was not fused in 61.9% of the CS5 and in 38.2% of the CS6 samples. In another study, the fusion of MPS was incomplete in 27% of male patients in CVS5 (Kwak et al., 2016).

6.3. Correlations

6.3.1. Age versus MPSM or CVM

A weak and non-significant correlation was observed between CA and MPSM stages ($r = 0.248$, $p = 0.164$). This finding was independent of gender. Therefore, the null hypothesis of the first research question is accepted. Similar findings were observed in a study with 42 Brazilian 11 to 14 years-old children (Luz et al 2022). In a study with an Iranian sample of 93 subjects, the Spearman correlation coefficient between age and MPSM stage was positive but weak (Mahidan et al., 2020). Differences in sample size and age between studies may explain the different significance of the results. Generally, these results confirm the indication that CA alone is not a statistically significant predictor of the maturational stages of the MPS and that a CBCT scan might be needed at any age before making the clinical decision between RME only or SARME/ LeFort osteotomy for maxillary expansion if age is the only biological indicator used to make that decision. In accordance with other studies, the correlation between age and MPS maturation was not significantly influenced by gender.

The results demonstrated a significant positive correlation, although moderate, between CA and CVM stages ($r = 0.625$, $p < 0.001$) indicating that when CA increases, the stage of CVM also advances (suggesting that skeletal maturity is related to chronological age). Thus, the null hypothesis of the second research question is rejected. Among males, the correlation was stronger than among females. The absence of females between 16 – 20 in the same may have biased this finding. These findings contradict with previous studies, showing no correlation between the reported two variables in children aged 11-14 years old (Luz et al 2022). The small age range of their sample may, however, explain the contradictory results with the present study.

6.3.2 CVM versus MPSM

In the current study, the correlation between CVM and MPS maturation stage was positive but moderate for the total sample ($r = 0.433$, $p = 0.012$) and males ($r = 0.603$, $p = 0.029$). No correlation was found among females ($r = 0.343$, $p = 0.139$). The significant positive correlation coefficient observed between the CVM stages and stages of MPSM, suggests that maturation of the MPS is related to skeletal growth. Hence the null hypothesis of the third research question is rejected. In a previous study with a sample of 93 Iranians, a positive but moderate correlation was found between CVM and MPSM stage both among males and females ($r = 0.754$ in male patients, $r = 0.691$ in female) (Mahidan et al., 2020). Females between 16- 20 years old were not represented in the present study, and that may have affected the results. Angelieri et al. assessment of 142 Brazilian and American subjects and Jang et al. evaluation of 99 Koreans revealed a strong correlation between both maturation staging methods ($r = 0.908$ and 0.874 , respectively) (Angelier et al., 2015; Jang et al., 2016). This contradicting outcome might have resulted from the different ethnic backgrounds, sample size and age range being investigated.

The results show a significant correlation between the CVM stages and chronological age. As per previous studies on this subject, the results of this study also indicate that CA is not a reliable indicator of MPSM. A significant correlation coefficient was noticed between the CVM stages and stages of MPS maturation, suggesting that MPSM is correlated to skeletal growth. The use of a definitive CVM stage for assessing the stages of MPSM was further explored with measures of diagnostic accuracy/performance, such as positive LHRs.

6.4. Diagnostic Performance

As explained earlier, a positive LHR value below (1) is clarified as a decrease in the likelihood of the explored condition (maturation stage of the MPS). Positive LHRs greater than (1) indicate that the test result (CVM stage) increases the possibility of the specific condition (maturation stage of the MPS). However, the test is considered to

be a reliable and conclusive diagnostic aid only if a positive LHR of (10) or more (Deeks & Altman., 2004).

The analysis of the values of positive LHRs of the CVM stages for the assessment of MPSM at different pubertal stages indicate that only CVS5 and CVS6 can be used for reliable identification of MPS stages D and E. From a clinical perspective, these results coincide with the fact that conventional RME undertaken in patients at CVS5 and CVS6 (post-pubertal peak) may become challenging due to partial fusion (Stage D) or complete fusion (Stage E) of the MPS. For patients in these two stages, a CBCT is recommended prior to making the clinical decision concerning conventional RME (still possible at stage C) or surgically assisted expansion (stages D and E).

Numerous studies have proposed using SARME to optimise maxillary expansion without substantial tooth movement, severe pain, mucosal ulceration or necrosis, increased vestibular tipping and gingival recession, which are expected complications of unsuccessful RME procedure (Rungcharassaeng et al., 2007; Yildirim 2019; Haas 1980). Our study, however, observed that 50% of the post-pubertal subjects at CVS5, and 83% of the subjects at CVS6 had stage C in MPSM, explaining the occasional clinical success of RME procedures in adult patients. One in three males at CS5 still had stage C of the MPSM, permitting achieving skeletal expansion using RME. Therefore, a CBCT is recommended to assess MPS morphology in the postpubertal stages CVS5 and CVS6.

Our results revealed that the prepubertal phases (CVS1 and CVS2) and pubertal phase (CVS3) of skeletal maturity cannot be used as reliable indicators for MPS stages A and B, and C, respectively. These results contradict the findings of a similar study conducted by Angelieri and co-workers (2015), where the CVM stages had positive LHR values greater than 10 for each of the three pubertal phases, thus serving as reliable and conclusive indicators of MPS maturational stages (Angelieri et al., 2015). This may be influenced by the much larger sample size obtained in their study (142

subjects). Therefore, caution is recommended in using prepubertal phases (CVS1 and CVS2) as reliable indicators for MPS stages A and B. In addition, the pubertal phase (CVS3) of skeletal maturity showed limited reliability in indicating the MPS stage C. These results are not in line with the findings of a similar study conducted by Angelieri and co-workers in 2015, where the CVM stages had positive LHR values greater than 10 for each of the three pubertal phases, thus serving as reliable and conclusive indicators of MPS maturational stages (Angelieri et al., 2015). Their larger sample size (142 subjects), the more comprehensive age range (5-58 years old) and the different ethnicity-examined subjects, may explain the different results.

6.5. Limitations of the Study

Being retrospective, the primary limitation of this study is the risk of bias that results from the convenience sampling due to subjects being omitted from the analysis based on incomplete data sets. Another strong limitation is the small sample size and consequent reduced power of the findings, as we don't know whether a larger sample size would have affected the significance of the results. Furthermore, the distribution of the age groups was not similar between genders; therefore, the data was mostly presented related to the respective gender. It should also be mentioned that some extent of subjectivity in assessing the maturation stages of the radiologic images might played a role in assessment accuracy. Further investigations on the matter are therefore recommended, with larger sample sizes to increase the power of findings, multicenter databases to yield a more representative basis regarding the whole population, and future-oriented prospective studies. While the subjective visual radiologic image examination showed an almost perfect calibration, an objective assessment method might help eliminate bias and avoid margin error with an increased method accuracy. With the surge of AI, promising scenarios of fast and reliable processing of large data sets may become part of an orthodontist's diagnostic arsenal in the future. Since at Egas Moniz School of Health and Science Dental Clinic, it is not a routine practice to have a register of patient nationality, it may in some cases be difficult to assert the ethnicity.

VII. CONCLUSION

Within the limitations of the present of the present study, we can conclude the following.

- Females below 16 years of age are more likely to present MPS closure than males
- MPSM stages show a wide variation in terms of chronological age, especially in females in late adolescence and young adulthood. These findings encourage taking CBCT scans to identify the maturational stage of the MPS in those age groups if age is the only biological indicator used in the decision to perform RME with or without surgical assistance.
- CVM has a moderate correlation to chronological age
- CVM has a moderate correlation to the MPSM method among male subjects
- CVM method can be a predictive indicator of the MPSM in the initial and final maturation stages: CVS1, CVS2 as predictive of stages A, B and CVS5, CVS6 as predictive of stages D, E.
- Further research with a bigger sample size should be done to further explore the validation of the CVM method as a predictor of MPS maturation.

VIII. BIBLIOGRAPHY

- Agarwal, A., & Mathur, R. (2010). Maxillary expansion. *International journal of clinical pediatric dentistry*, 3(3), 139.
- Alpern, M. C., & Yurosko, J. J. (1987). Rapid palatal expansion in adults: with and without surgery. *The Angle Orthodontist*, 57(3), 245-263.
- American Dental Association Council on Scientific Affairs. (2012). The use of cone-beam computed tomography in dentistry: an advisory statement from the American Dental Association Council on Scientific Affairs. *The journal of the American dental association*, 143(8), 899-902.
- Angell, E. E. (1860). Treatment of irregularity of the permanent or adult teeth. *Dental Cosmos*, 1, 540-544.
- Angelieri, F., Cevidanes, L. H., Franchi, L., Gonçalves, J. R., Benavides, E., & McNamara Jr, J. A. (2013). Midpalatal suture maturation: classification method for individual assessment before rapid maxillary expansion. *American Journal of Orthodontics and Dentofacial Orthopedics*, 144(5), 759-769.
- Angelieri, F., Franchi, L., Cevidanes, L. H., Bueno-Silva, B., & McNamara Jr, J. A. (2016). Prediction of rapid maxillary expansion by assessing the maturation of the midpalatal suture on cone beam CT. *Dental press journal of orthodontics*, 21(06), 115-125.
- Angelieri, F., Franchi, L., Cevidanes, L. H., & McNamara Jr, J. A. (2015). Diagnostic performance of skeletal maturity for the assessment of midpalatal suture maturation. *American Journal of Orthodontics and Dentofacial Orthopedics*, 148(6), 1010-1016.
- Angelieri, F., Franchi, L., Cevidanes, L. H. S., Gonçalves, J. R., Nieri, M., Wolford, L. M., & McNamara Jr, J. A. (2017). Cone beam computed tomography evaluation of midpalatal suture maturation in adults. *International journal of oral and maxillofacial surgery*, 46(12), 1557-1561.
- Arpalahti, I., Hänninen, K., Tolvanen, M., Varrelä, J., & Rice, D. P. (2024). The effect of early childhood non-nutritive sucking behavior including pacifiers on malocclusion: a randomized controlled trial. *European Journal of Orthodontics*, 46(5).
- Attia, J. (2003). Moving beyond sensitivity and specificity: using likelihood ratios to help interpret diagnostic tests. *Australian prescriber*, 26(5).
- Baccetti, T., Franchi, L., Cameron, C. G., & McNamara Jr, J. A. (2001). Treatment timing for rapid maxillary expansion. *The Angle Orthodontist*, 71(5), 343-350.
- Baccetti, T., Franchi, L., & McNamara Jr, J. A. (2002). An improved version of the cervical vertebral maturation (CVM) method for the assessment of mandibular growth. *The Angle Orthodontist*, 72(4), 316-323.

- Baccetti, T., Franchi, L., & McNamara Jr, J. A. (2005). The cervical vertebral maturation (CVM) method for the assessment of optimal treatment timing in dentofacial orthopaedics. In *Seminars in Orthodontics*, 11, 3, pp. 119-129.
- Berkhout, W. E. (2015). The ALARA-principle. Backgrounds and enforcement in dental practices. *Nederlands tijdschrift voor tandheelkunde*, 122(5), 263-270
- Broadbent, B. H. (1931). A new x-ray technique and its application to orthodontia. *The Angle Orthodontist*, 1(2), 45-66.
- Burdi, A. R., & Faist, K. (1967). Morphogenesis of the palate in normal human embryos with special emphasis on the mechanisms involved. *American Journal of Anatomy*, 120(1), 149-159.
- Cavallo, F., Mohn, A., Chiarelli, F., & Giannini, C. (2021). Evaluation of bone age in children: a mini-review. *Frontiers in Pediatrics*, 9, 580314
- Chandrasekar, R., Chandrasekhar, S., Sundari, K. S., & Ravi, P. (2020). Development and validation of a formula for objective assessment of cervical vertebral bone age. *Progress in orthodontics*, 21, 1-8.
- Chertkow, S. (1980). Tooth mineralization as an indicator of the pubertal growth spurt. *American journal of orthodontics*, 77(1), 79-91.
- Deeks, J. J., & Altman, D. G. (2004). Diagnostic tests 4: likelihood ratios. *British Medical journal*, 329(7458), 168-169.
- Epker, B. N., & Wolford, L. (1980). Dentofacial deformities: surgical-orthodontic correction. *Mosby St. Louis*.
- Flores-Mir, C., Nebbe, B., & Major, P. W. (2004). Use of skeletal maturation based on hand-wrist radiographic analysis as a predictor of facial growth: a systematic review. *The Angle Orthodontist*, 74(1), 118-124.
- Franchi, L., Baccetti, T., & McNamara Jr, J. A. (2000). Mandibular growth as related to cervical vertebral maturation and body height. *American Journal of Orthodontics and Dentofacial Orthopedics*, 118(3), 335-340.
- Greulich, W., & Pyle, S. (1959). Radiographic ossification and the adolescent growth spurt. *American Journal of Orthodontics and Dentofacial Orthopedics*, 69, 611-9.
- Haas, A. J. (1980). Long-term posttreatment evaluation of rapid palatal expansion. *The Angle Orthodontist*, 50(3), 189-217.
- Haas, A. J. (1961). Rapid expansion of the maxillary dental arch and nasal cavity by opening the midpalatal suture. *The Angle Orthodontist*, 31(2), 73-90.

Skeletal Age and the Relationship to Midpalatal Suture Maturation Stages. A Retrospective Radiographic Study in a Portuguese Population.

Hammond, N. L., & Dixon, M. J. (2022). Revisiting the embryogenesis of lip and palate development. *Oral Diseases*, 28(5), 1306-1326.

Handelman, C. S. (1997). Nonsurgical rapid maxillary alveolar expansion in adults: a clinical evaluation. *The Angle Orthodontist*, 67(4), 291-308.

Handelman, C. S., Wang, L., BeGole, E. A., & Haas, A. J. (2000). Nonsurgical rapid maxillary expansion in adults: report on 47 cases using the Haas expander. *The Angle Orthodontist*, 70(2), 129-144.

Hassel, B., & Farman, A. G. (1995). Skeletal maturation evaluation using cervical vertebrae. *American Journal of Orthodontics and Dentofacial Orthopedics*, 107(1), 58-66.

Helsing, E. (1991). Cervical vertebral dimensions in 8-, 11-, and 15-year-old children. *Acta Odontologica Scandinavica*, 49(4), 207-213.

Isfeld, D., Lagravere, M., Leon-Salazar, V., & Flores-Mir, C. (2017). Novel methodologies and technologies to assess mid-palatal suture maturation: a systematic review. *Head & face medicine*, 13, 1-15.

Jang, H. I., Kim, S. C., Chae, J. M., Kang, K. H., Cho, J. W., Chang, N. Y., ... & Cho, J. H. (2016). Relationship between maturation indices and morphology of the midpalatal suture obtained using cone-beam computed tomography images. *The Korean Journal of Orthodontics*, 46(6), 345-355.

Jimenez-Valdivia, L. M., Malpartida-Carrillo, V., Rodríguez-Cárdenas, Y. A., Dias-Da Silveira, H. L., & Arriola-Guillén, L. E. (2019). Midpalatal suture maturation stage assessment in adolescents and young adults using cone-beam computed tomography. *Progress in orthodontics*, 20, 1-7.

Kapetanović, A., Theodorou, C. I., Bergé, S. J., Schols, J. G., & Xi, T. (2021). Efficacy of Miniscrew-Assisted Rapid Palatal Expansion (MARPE) in late adolescents and adults: a systematic review and meta-analysis. *European Journal of Orthodontics*, 43(3), 313-323.

Kiliç, N., & Oktay, H. (2008). Effects of rapid maxillary expansion on nasal breathing and some naso-respiratory and breathing problems in growing children: a literature review. *International Journal of Pediatric Otorhinolaryngology*, 72(11), 1595-1601.

Knaup, B., Yildizhan, F., & Wehrbein, H. (2004). Age-related changes in the midpalatal suture. A histomorphometric study. *Journal of Orofacial Orthopedics*, 65(6), 467-474.

Korbmacher, H., Schilling, A., Püschel, K., Amling, M., & Kahl-Nieke, B. (2007). Age-dependent three-dimensional microcomputed tomography analysis of the human midpalatal suture. *Journal of Orofacial Orthopedics*, 68(5), 364-376.

- Korn, E. L., & Baumrind, S. (1990). Transverse development of the human jaws between the ages of 8.5 and 15.5 years, studied longitudinally with use of implants. *Journal of Dental research*, 69(6), 1298-1306.
- Karatas, O. H., & Toy, E. (2014). Three-dimensional imaging techniques: A literature review. *European journal of dentistry*, 8(01), 132-140.
- Kumar, M., Shanavas, M., Sidappa, A., & Kiran, M. (2015). Cone beam computed tomography-know its secrets. *Journal of international oral health*, 7(2), 64.
- Kwak, K. H., Kim, S. S., Kim, Y. I., & Kim, Y. D. (2016). Quantitative evaluation of midpalatal suture maturation via fractal analysis. *Korean journal of orthodontics*, 46(5), 323.
- Landis, J. R., & Koch, G. G. (1977). An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. *Biometrics*, 363-374.
- Lee, S. C., Park, J. H., Bayome, M., Kim, K. B., Araujo, E. A., & Kook, Y. A. (2014). Effect of bone-borne rapid maxillary expanders with and without surgical assistance on the craniofacial structures using finite element analysis. *American Journal of Orthodontics and Dentofacial Orthopedics*, 145(5), 638-648.
- Liu, H., Feng, L., & Wang, L. (2023). Diagnostic value of cervical vertebral maturation stages for midpalatal suture maturation assessment: a study in the Chinese population. *BMC Oral Health*, 23(1), 504.
- Liu, S., Xu, T., & Zou, W. (2015). Effects of rapid maxillary expansion on the midpalatal suture: a systematic review. *European journal of orthodontics*, 37(6), 651-655.
- L'tanya, J. B., White Jr, R. P., Proffit, W. R., & Turvey, T. A. (1997). Segmental LeFort I osteotomy for management of transverse maxillary deficiency. *Journal of oral and maxillofacial surgery*, 55(7), 728-731.
- Mahdian, A., Safi, Y., Dalaie, K., Kavousinejad, S., & Behnaz, M. (2020). Correlation assessment of cervical vertebrae maturation stage and mid-palatal suture maturation in an Iranian population. *Journal of the World Federation of Orthodontists*, 9(3), 112-116.
- Mallya, S. M. (2015). Evidence and professional guidelines for appropriate use of cone beam computed tomography. *Journal of the California Dental Association*, 43(9), 512-520.
- Mallya, S. M., & White, S. C. (2013). The Nature of Ionizing Radiation and the Risks from Maxillofacial Cone Beam Computed Tomography. *Cone Beam Computed Tomography: Oral and Maxillofacial Diagnosis and Applications*, 25-41.

Skeletal Age and the Relationship to Midpalatal Suture Maturation Stages. A Retrospective Radiographic Study in a Portuguese Population.

- Mao, J. J., Wang, X., & Kopher, R. A. (2003). Biomechanics of craniofacial sutures: orthopedic implications. *The Angle Orthodontist*, 73(2), 128-135.
- Melsen, B. (1975). Palatal growth studied on human autopsy material: a histologic microradiographic study. *American journal of orthodontics*, 68(1), 42-54.
- Melsen, B., & Melsen, F. (1982). The postnatal development of the palatomaxillary region studied on human autopsy material. *American journal of orthodontics*, 82(4), 329-342.
- Mommaerts, M. Y. (1999). Transpalatal distraction as a method of maxillary expansion. *British Journal of Oral and Maxillofacial Surgery*, 37(4), 268-272.
- Mossaz, C. F., Byloff, F. K., & Richter, M. (1992). Unilateral and bilateral corticotomies for correction of maxillary transverse discrepancies. *The European Journal of Orthodontics*, 14(2), 110-116.
- Moyers, R. E. (1988). Analysis of the craniofacial skeleton. *Handbook of orthodontics*.
- Nalcaci, R. U. H. İ., Öztürk, F. A. T. İ. H., & Sökücü, O. (2010). A comparison of two-dimensional radiography and three-dimensional computed tomography in angular cephalometric measurements. *Dentomaxillofacial Radiology*, 39(2), 100-106.
- Oenning, A. C., Jacobs, R., & Salmon, B. (2021). ALADAIP, beyond ALARA and towards personalized optimization for paediatric cone-beam CT. *International Journal of Paediatric Dentistry*, 31(5), 676-678.
- O'Reilly, M. T., & Yanniello, G. J. (1988). Mandibular Growth Changes and Maturation of Cervical Vertebrae: —A Longitudinal Cephalometric Study. *The Angle Orthodontist*, 58(2), 179-184.
- Pauwels, R., Araki, K., Siewerdsen, J. H., & Thongvigitmanee, S. S. (2015). Technical aspects of dental CBCT: state of the art. *Dentomaxillofacial Radiology*, 44(1), 20140224.
- Pauwels, R. (2020). History of dental radiography: Evolution of 2D and 3D imaging modalities. *Medical Physics International*, 8(1), 235-77.
- Perinetti, G., Caprioglio, A., & Contardo, L. (2014). Visual assessment of the cervical vertebral maturation stages: A study of diagnostic accuracy and repeatability. *The Angle Orthodontist*, 84(6), 951-956.
- Perinetti, G., Contardo, L., Castaldo, A., McNamara Jr, J. A., & Franchi, L. (2016). Diagnostic reliability of the cervical vertebral maturation method and standing height in the identification of the mandibular growth spurt. *The Angle Orthodontist*, 86(4), 599-609.

- Priyadarshini, J., Mahesh, C. M., Chandrashekar, B. S., Sundara, A., Arun, A. V., & Reddy, V. P. (2017). Stress and displacement patterns in the craniofacial skeleton with rapid maxillary expansion—a finite element method study. *Progress in Orthodontics*, *18*, 1-8.
- Rungcharassaeng, K., Caruso, J. M., Kan, J. Y., Kim, J., & Taylor, G. (2007). Factors affecting buccal bone changes of maxillary posterior teeth after rapid maxillary expansion. *American Journal of Orthodontics and Dentofacial Orthopedics*, *132*(4), 428-e1.
- Sayar, G., & Kılınc, D. D. (2019). Rapid maxillary expansion outcomes according to midpalatal suture maturation levels. *Progress in orthodontics*, *20*, 1-7.
- Shah, N., Bansal, N., & Logani, A. (2014). Recent advances in imaging technologies in dentistry. *World journal of radiology*, *6*(10), 794.
- Shibusawa, N., Endo, Y., Morimoto, N., Takahashi, I., & Miura, T. (2021). Mathematical modeling of palatal suture pattern formation: morphological differences between sagittal and palatal sutures. *Scientific reports*, *11*(1), 8995.
- Suri, L., & Taneja, P. (2008). Surgically assisted rapid palatal expansion: a literature review. *American journal of orthodontics and dentofacial orthopedics*, *133*(2), 290-302.
- Tanner, J. M., Whitehouse, R. H., Marubini, E., & Resele, L. F. (1976). The adolescent growth spurt of boys and girls of the Harpenden growth study. *Annals of human biology*, *3*(2), 109-126.
- Timms, D. J. (1980). A study of basal movement with rapid maxillary expansion. *American journal of orthodontics*, *77*(5), 500-507.
- Timms, D. J., & Vero, D. (1981). The relationship of rapid maxillary expansion to surgery with special reference to midpalatal synostosis. *British Journal of Oral Surgery*, *19*(3), 180-196.
- Tiziano Baccetti, D., Lorenzo Franchi, D., Laura De Toffol, D., Bruno Ghiozzi, D., & Paola Cozza, M. (2006). The diagnostic performance of CA in the assessment of skeletal maturity. *Progress in Orthodontics*, *7*, 176-188.
- Tonello, D. L., de Miranda Ladewig, V., Guedes, F. P., Conti, A. C. D. C. F., Almeida-Pedrin, R. R., & Capelozza-Filho, L. (2017). Midpalatal suture maturation in 11-to 15-year-olds: A cone-beam computed tomographic study. *American journal of orthodontics and dentofacial orthopedics*, *152*(1), 42-48.
- Uysal, T., Ramoglu, S. I., Basciftci, F. A., & Sari, Z. (2006). CA and skeletal maturation of the cervical vertebrae and hand-wrist: is there a relationship? *American Journal of Orthodontics and Dentofacial Orthopedics*, *130*(5), 622-628.
- Wehrbein, H., & Yildizhan, F. (2001). The mid-palatal suture in young adults. A radiological-histological investigation. *The European Journal of Orthodontics*, *23*(2), 105-114.

Skeletal Age and the Relationship to Midpalatal Suture Maturation Stages. A Retrospective Radiographic Study in a Portuguese Population.

Yang, P., Zhu, M., Guo, Y., Su, C., Wang, Y., Bai, Y., & Zhang, N. (2024). Evaluation of midpalatal suture maturation stage in 5-to 20-year-olds using cone-beam computed tomography. *American Journal of Orthodontics and Dentofacial Orthopedics*.

DOI: [10.1016/j.ajodo.2024.07.019](https://doi.org/10.1016/j.ajodo.2024.07.019)

Yildirim, M., & Akin, M. (2019). Comparison of root resorption after bone-borne and tooth-borne rapid maxillary expansion evaluated with the use of microtomography. *American Journal of Orthodontics and Dentofacial Orthopedics*, 155(2), 182-190.

Zeng, W., Yan, S., Yi, Y., Chen, H., Sun, T., Zhang, Y., & Zhang, J. (2023). Long-term efficacy and stability of miniscrew-assisted rapid palatal expansion in mid to late adolescents and adults: a systematic review and meta-analysis. *BMC Oral Health*, 23(1), 829.

Zerin, J. M., & Hernandez, R. J. (1991). Approach to skeletal maturation. *Hand clinics*, 7(1), 53-62.

Zuccati, G., Casci, S., Doldo, T., & Clauser, C. (2013). Expansion of maxillary arches with crossbite: a systematic review of RCTs in the last 12 years. *The European Journal of Orthodontics*, 35(1), 29-37.

IX. ANNEXES



Comissão de Ética EGAS MONIZ

Plataforma: PT-331/23
Processo Interno nº 1352

Ex.mo Senhor
Joaquim Johan Fernandes Faerovig

Monte de Caparica, 25 de janeiro de 2024.

Ex.mo Senhor,

Em resposta ao Pedido de Parecer que submeteu à apreciação da Comissão de Ética da Egas Moniz, com o tema denominado **"Idade esquelética e sua relação com os estádios de maturação da sutura média palatina. Um estudo radiológico retrospectivo em população Portuguesa"**, foi aprovado.

A Presidente da Comissão de Ética da Egas Moniz

Profª Doutora Cidália de Castro

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