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# Midpalatal Suture Maturation and Cervical Vertebrae Maturation:

# A CBCT Comparative Study

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# Midpalatal Suture Maturation and Cervical Vertebrae Maturation: A CBCT Comparative Study

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ABSTRACT

Introduction: Orthodontists routinely use rapid maxillary expansion for the correction of crossbites, dental crowding and maxillary atresia. In order to decide which procedure and timing is more adequate for the maxillary expansion, midpalatal suture maturation classifications have been proposed.

Purpose: The aim of this study was to determine whether predicting the maturation of the midpalatal suture is achievable by classifying the cervical vertebral maturation.

Methodology: The Angelieri *et al.* and Baccetti *et al.* scales were used to access the midpalatal suture maturation and cervical vertebrae maturation, respectively. There were analyzed cephalograms and axial sections from cone-beam computed tomography of 76 individuals (32 males and 44 females with a mean age of 18,8 ± 11,6 years). The two scales were also recoded, based on the three clinical interpretations, in order to have the same number of classes.

Results: Weighted Cohen's Kappa coefficient on both scales was greater than or equal to 0.90 for both inter-observer and intra-observer error assessment. The values of the Spearman's Correlation Coefficient (0.477) and the Intraclass Correlation Coefficient (0.642) show a moderate association between the evaluations produced by the two scales non-recoded. The scales recoded showed a reasonable agreement, with weighted Cohen's Kappa coefficient of 0.372 (95%CI: 0.166-0.580) and an agreement percentage between the classifications of 53.9%.

Conclusions: Either Baccetti *et al.* or Angelieri *et al.* methods have very good reproducibility. Both scales shown a moderate agreement in non-recoded system and reasonable agreement in the recoded system. Therefore, it is possible to conclude that to ensure the validity of using the Baccetti *et al.* method to predict the midpalatal suture maturation stage, more clinical studies are required and in the second system it is evident that there is a loss of information when the recoding is applied.

## RESUMO

Introdução: Os ortodontistas usam rotineiramente a expansão rápida da maxila para correção de mordidas cruzadas, apinhamento dentário e atresia maxilar. Para decidir qual o procedimento mais adequado para a expansão maxilar, foram propostas classificações da maturação da sutura palatina mediana.

Objetivos: O objetivo deste estudo foi determinar se é possível prever a maturação da sutura palatina mediana classificando a maturação vertebral cervical.

Metodologia: As escalas de Angelieri *et al.* e Baccetti *et al* foram usadas para aceder à maturação da sutura média palatina e das vertebras cervicais, respetivamente. Foram analisadas telerradiografias e cortes axiais de tomografias computorizadas de feixe cónico de 76 indivíduos (32 homens e 44 mulheres com idade média de 18,8 ± 11,6 anos) de uma amostra. As duas escalas foram também recodificadas, com base em três opções clínicas possíveis, para que ambas tenham o mesmo número de classes.

Resultados: O coeficiente Kappa de Cohen ponderado em ambas as escalas foi maior ou igual a 0,90, quer para a avaliação de erros inter-observadores e quer intra-observadores. Os valores do coeficiente de correlação de Spearman (0,477) e do coeficiente de correlação intraclasse (0,642) mostram a existência de uma associação moderada entre as avaliações produzidas pelas duas escalas não recodificadas. As escalas recodificadas apresentaram concordância razoável, com coeficiente de Kappa de Cohen de 0,372 (IC-95%: 0,166-0,580) e uma percentagem de concordância entre as classificações de 53,9%.

Conclusões: Quer o método de Baccetti *et al.* ou de Angelieri *et al*. têm uma reprodutibilidade muito boa. Ambas as escalas mostraram concordância moderada no sistema não recodificado e concordância razoável no sistema recodificado. Portanto, é possível concluir que, no primeiro sistema, deve haver mais estudos clínicos para garantir a validade do uso do método de Baccetti *et al.* para prever o estadio de maturação da sutura palatina mediana e, no segundo sistema, é evidente a perda de informações na recodificação.

## KEY-WORDS

maxillary expansion, midpalatal suture maturation, CBCT (Cone-Bean-Computed-Tomography), cervical vertebrae maturation, Baccetti's CVM method, Angelieri MPS method.

ABBREVIATIONS:

2D – two dimensions

3D – three dimensions

95%CI – 95% confidence interval

CBCT – cone-beam computed tomography

CVM – Cervical Vertebrae Maturation

DICOM – Digital Imaging and Communications in Medicine

SD – Standard deviation

ICC – Intraclass correlation coefficient

M – mean

MARPE – microimplant-assisted rapid palatal expansion

MPS – midpalatal suture

p – significance value of statistical tests

R – Spearman correlation coefficient

RME – rapid maxillary expansion

SARME – surgical assisted rapid maxillary expansion

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# INTRODUCTION

# I. INTRODUCTION

## 1.1 Maxillary growth

There are many factors that influence the growth rate: climate, genetic conditioning, nutrition, race, hormonal disturbances and environmental influences[1, 2]. Breastfeeding for less than six months have negative effect on the maxillary growth, no upper arch space in the deciduous dentition and may result in malocclusion such as posterior crossbite[3]. Slim and elevated palatal vault, unilateral or bilateral crossbite and potential dental crowding due to the contraction of the dental arches are characteristics of transverse maxillary constriction [4].

## 1.2 Treatment options for transverse maxillary constriction

The separation of the midpalatal suture (MPS) can be produced by non-surgical methods or surgical methods. Regarding the speed of the maxillary expansion, it can be rapid or slow[5]. Some examples of this sort of treatments are: rapid maxillary expansion (RME), surgical assisted rapid maxillary expansion (SARME) and microimplant-assisted rapid palatal expansion (MARPE) [6-8]. Clinically, orthodontists routinely use RME, in growing patients, for the correction of crossbites, dental crowding and maxillary atresia [6, 7, 9, 10]. Although, there is no consensus in the literature about the time point to shift from RME to SARME [6, 7], the last procedure mentioned has been suggested for patients older than 14[7], 16[1, 7], 20[1, 7] or 25[7] years of age. In contrast, other studies suggests that RME should be presented before puberty and that SARME should be done after adolescence [6]. Furthermore, sex was also reported as an influencing factor in the maturational stages[2, 8, 10-14], SARME was indicated for females older than 20 years and in males older than 25 years [7]. Additionally, authors have found a 54 year old patient with a not fused MPS [15] and patients with more than 19 year old with the MPS fully maturated[12, 15]. Then, the choice between the surgical or non-surgical methods depends on the MPS maturation stage [16].

Therefore, chronological age is not reliable for the decision between surgical or non-surgical methods[8, 10, 11, 13, 14, 16-19]. In order to help the decision-making process in the procedure selection for the maxillary expansion, midpalatal suture maturation classifications have been proposed.

## 1.3 Midpalatal suture maturation

Maxillary expansion can be made without surgery using removable or fixed non-surgical appliances, when the MPS is not fully maturated, not fused [8, 10]. Nevertheless, if the interdigitation of the MPS increases from posterior to anterior area of the suture, as occurs with the maturation, different treatment methods can be adopted[8, 10, 14, 15, 18-23] considering the MPS maturation.

Since chronological age is unreliable for defining the developmental stage of the suture [6, 16, 19, 24], there were proposed several methods its classification.

### 1.3.1 Classification methods

Multiple authors proposed numerous modalities for assessing MPS maturation such as:

- Revelo B. and Fishman L., in 1994, operated with standardized occlusal radiographs and measures between three points of the palate[20];
- Korbmacher *et al.*, in 2007, used micro-CT to quantify the MPS and showed substantial inter-individual and intra-sutural variation [18];
- Franchi *et al.,* in 2010, used low-dose computed tomography to assess the MPS before and after RME [25];
- Sumer *et al.,* in 2012, used ultrasonography to analyze the MPS in patients undergoing SARME [26];
- Angelieri *et al.,* in 2013, made use of cone-beam computed tomography (CBCT) to classify the MPS maturation allowing the diagnosis of its' anteroposterior characteristics [14];
- Kwak *et al*., in 2015, used fractal analysis to evaluate the MPS maturation proving to be an objective and quantitative method [21].

Of all this methods, Angelieri *et al.* [14] was selected for being the most studied in the literature. Angelieri *et al.* proposed five maturational stages (A-E) based on the degree of fusion of the MPS with CBCT images.

## 1.4 Cervical vertebrae maturation

Evaluation of skeletal maturity and identification of the pubertal peak in craniofacial growth can be done evaluating the cervical vertebrae maturation (CVM) [9, 23, 27, 28].

### 1.4.1 Classification methods

Hassel and Farman[29], in 1995, proposed six CVM stages: iniciation, acceleration, transition, deceleration, maturation and completion. In 2002, Baccetti *et al*.[30] presented five stages similar to Hassel and Farman but allowing two variations for each stage. In 2005, Baccetti *et al.*[31] added a 6th stage. When compared with Hassel-Farman method, Baccetti *et al.* method showed the best results[23]. Of all these methods, Baccetti *et al.* was selected for being the most studied in the literature and more actual.

## 1.5 Cone Beam Computed Tomography

CBCT is being used to visualize structures, such as the midpalatal suture, in 3-dimensional images, avoiding overlapping adjacent structures [8, 9, 14, 16, 32] with a low radiation exposure when in contrast to the medical computed tomography [14]. CBCT has diagnostic advantages over 2-dimensional images, so is being used for a correct orthodontic diagnosis and treatment planning[16]. CBCT helps to provide the information necessary to decide which technique (RME or SARME) is more adequate, considering the midpalatal suture maturation [16].

## 1.6 Aim of the study

The aim of this study was to determine whether predicting the maturation of the midpalatal suture is achievable by categorizing the cervical vertebral maturation, with Angelieri *et al.* and Baccetti *et al.* methods, respectively.

Null hypothesis: there is no correlation between the MPS maturation and the CVM using the Angelieri *et al.* and Baccetti *et al.* methods, respectively.

Null hypothesis: there is no correlation between the recoded MPS maturation classification (Angelieri *et al.*) and CVM classification (Baccetti *et al.*).

# MATERIALS AND METHODS

# II. MATERIALS AND METHODS

## 1.1 Type of study

This study is a cross sectional epidemiological, retrospective study by means of observational and descriptive analysis.

## 1.2 Time frame of the study

This present investigation was conducted from November 2019 to May 2020.

## 1.3 Literature research

The literature research about this topic was made by a research in the electronic data bases to obtain up-to-date and relevant scientific material. The data bases searched were: Pubmed, Scopus and Scielo. The key words and combination used were: “Cervical vertebral maturation AND maxillary expansion”, “Cervical Vertebrae Maturation”, “Midpalatal suture maturation AND cervical vertebrae maturation”, “Rapid maxillary expansion AND maturation”, “Rapid maxillary expansion”.

### 1.3.1 Inclusion criteria

- Systematic Reviews, Meta-Analysis, Journal Articles, Clinical Trials, Controlled and Randomized Clinical Trials;
- Studies made in humans;
- English and Portuguese articles;
- Articles published in the last 10 years;
- Other publications considered highly relevant to the study.

#### 1.3.2 Exclusion criteria:

- Leak of the key-words on the abstract;
- Leak of methods to assess the skeletal age;

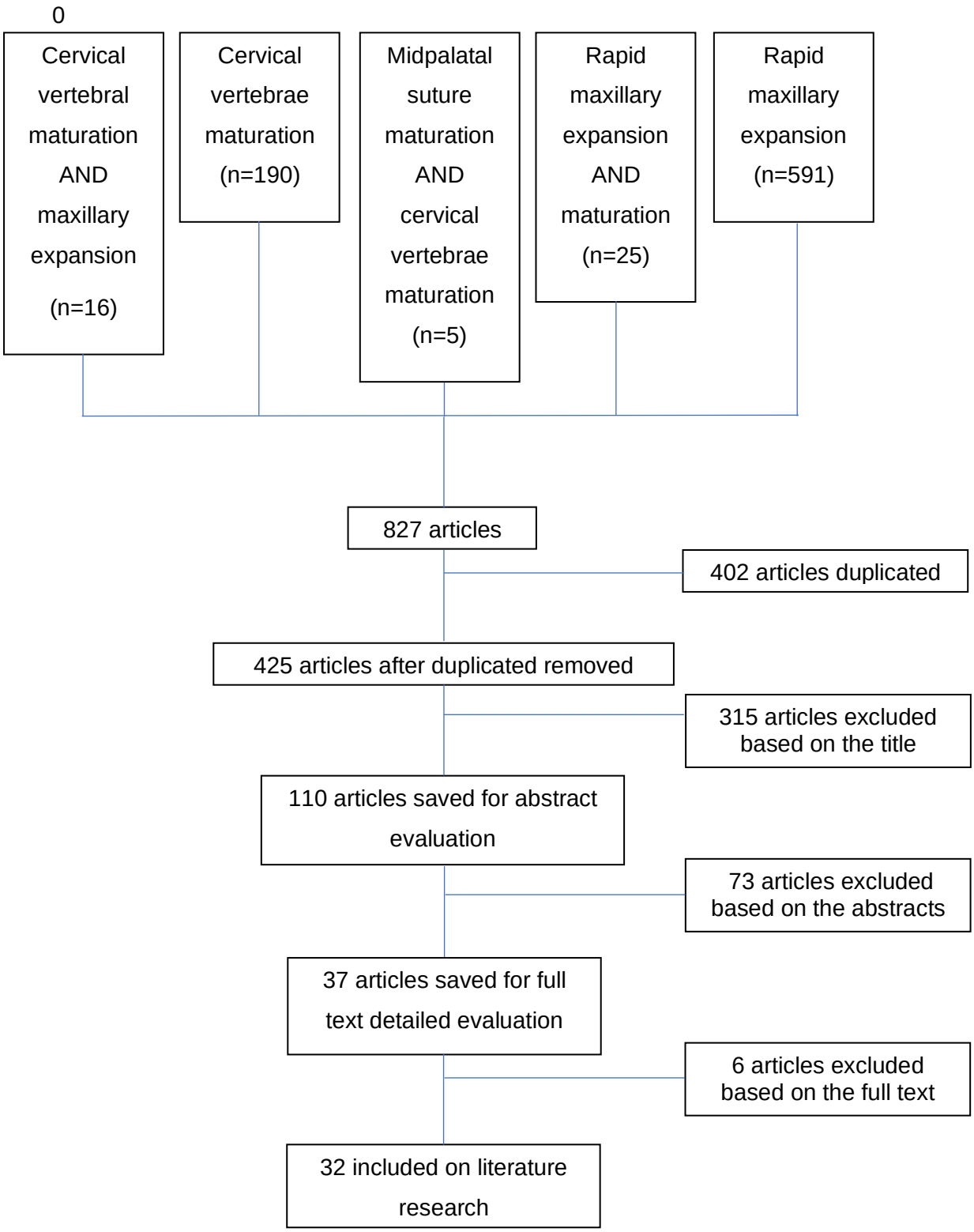



*Figure 1. Method of literature research.*

## 1.4 Sample

The sample consisted of patients who sought orthodontic treatment in a private clinic and had a CBCT made for orthodontic diagnosis. The methodology for determination the sample size is described in the Statistical Analysis chapter.

### 1.4.1 Eligibility Criteria

#### 1.4.1.1 Inclusion criteria

- No age limit;
- Good quality CBCT images.

#### 1.4.1.2 Exclusion criteria

- History of previous orthodontic treatment;
- Omission of any diagnostic data, including CBCT images;
- Poor-quality images that were difficult to distinguish;
- Congenital cleft lip and palate;
- Craniofacial syndromes;
- Growth related problematic conditions.

### 1.4.2 Sample characterization

Sample was classified in terms of: sex, age, facial biotype and skeletal class.

### 1.4.3 Ethical considerations

This study was approved by the Responsible for Access to Information of a Private Clinic, the Data Protection Unit of U.PORTO and the Ethics Committee's of FMDUP (Annexes 1.2,1.3,1.4)

Individual anonymity was guaranteed, i.e., all records were coded, and none identifying information was collected.

The records were used exclusively in the present research.

The present investigation did not generate any physical or emotional discomfort to the participants, since it is a cross-sectional descriptive and observational

epidemiological study with the use of retrospective data using complementary diagnostic performed in the context of orthodontic treatment.

The use of patients' personal data throughout the investigation was assessed by the University of Porto Personal Data Protection (Annex 1.4). However, since the participants were patients of the private clinic, the approval for the use of personal data was obtained by the responsible for access to information (Annex 1.3).

### 1.4.4 Funding and competing interests

The study doesn't have any financial or economical purpose, having only academic purposes.

The author has no conflicts of interest to declare.

## 1.5 Data collection and analysis protocol summary

Patients' who met the inclusion criteria were selected and their CBCT scan were imported to the private clinic computer, protected by password, with a coded identification (eg ID01) to guarantee anonymity. CBCT scans were analyzed using the Planmeca Romexis® software (Planmeca Oy, Helsinky, Finland) and there were no changes in the contrast, brightness, or size of the CBCT images.

The observation of the CBCT scans were made by two examiners (author and student, both in the last year of the Dental Medicine Integrated Master of the Dental Medicine Faculty, Porto University). The examiners were trained and calibrated. It was completed a calibration exercise, to ensure that the examiners understood the method, by analyzing 20 patients that were not included in this study.

Afterward, the axial sections of CBCT scans and cephalogram image of 76 patients were classified by the two examiners. Subsequently, after two weeks, 30 CBCT were selected randomly using the Microsoft® Excel® Random tool to repeat the evaluation to estimate the intra-observer error.

Data was organized in Microsoft® Excel® program (Microsoft Office, New Mexico, U.S.A) and analyzed using the Statistical Package for the Social Sciences® (SPSS), version 24 for Windows® (IBM Corp. Released 2016).

## 1.6 Cone-Beam Computed Tomography

For CBCT, the Planmeca ProMax® 3D Mid model (Planmeca Oy, Helsinky, Finland) was used. The computerized tomography scanner offers the capacity to include 3D imaging along with 2D panoramic and cephalograms in a single unit.

All CBCT exams were performed at the same private clinic using the following radiographic equipment:

- Name: Planmeca ProMax ® 3D Mid;
- Sensor type: flat screen;
- Focal Spot: 0,5mm, fixed anode;
- Voxel size: 0,4mm;
- Image acquisition: 200/360 degree rotation;
- Type of exposure: pulsed;
- Volume size: 200x170 mm;
- Type of reconstruction: cylindrical.

*Figure 2. Image of Planmeca ProMax® 3D Mid model. Adapted from Panmeca (2014). Planmeca USA. https://www.planmeca.com/na/imaging/3d-imaging/planmeca-promax-3d-mid/*

The CBCT settings:

- Anode voltage: 60-90 kV, 60-120kV;
- Anode Current: 1-14 mA;
- Exposure time: 9-33 s.

### 1.6.1 Patient preparation

Every subject was asked to remove any type of jewelry, metal or clothing that interfered with the head and neck region. Each patient was standing, with their hands placed on the palm rest (Figure 3) and the head with the mid sagittal plane perpendicular to the ground and Frankfurt horizontal plane (superior aspect of the external auditory canal to infraorbital rim line) parallel to the ground, in maximum intercuspation.

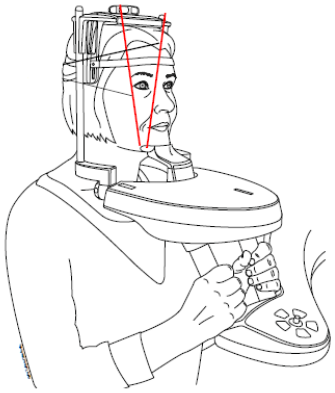


*Figure 3. Patients' ideal position during CBCT imaging. Adapted from Planmeca., Planmeca Promax® 3D Plus & 3D Mid with ProTouch. User's manual 3D imaging, p. 35*

### 1.6.2 Image collection and file import

Afterwards, the information was reconstructed automatically in three-dimensional images in DICOM (Digital Imaging and Communications in Medicine) format. The CBCT images were imported to Planmeca Romexis® software (Planmeca Oy, Helsinky, Finland) to be visualized, oriented and analyzed (Figure 4). The whole collection of reconstructed images of one patient was named "volume".

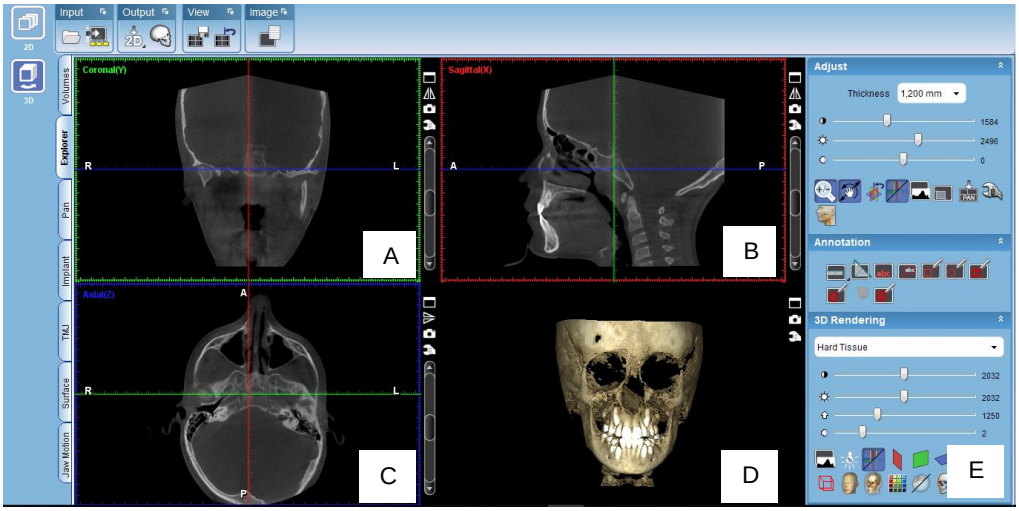



*Figure 4. Preview Window CBCT of a patient (Planmeca Romexis®). A- Coronal plane view; B- Sagital plane view; C- Axial plane view; D- 3D reconstruction; E- Image tools.*

### 1.6.3 Midpalatal suture image

#### 1.6.3.1 Volume orientation

In order to standardize the CBCT images all volumes were oriented. In the axial view, the vertical line of the cursor (red line) was matched to the axis of the palatal plane line (anterior nasal spine – posterior nasal spine) (Figure 4C). Simultaneously, on the coronal view (Figure 4A), the vertical line of the cursor (red line) was matched to the nasal septum, and the horizontal line of the cursor (blue line) was oriented parallel to the palatal plane. To simplify the observation of the axial cross-sectional planar view of the MPS, the horizontal line of the cursor would intersect the middle of the palate in the sagittal plane (Figure 4B).

#### 1.6.3.2 Image preparation

When the palate is flattened it is possible to obtain an image of the entire suture in one slice.

If the palate is considered a curve, the suture maturation stage must be evaluated in two distinct slices, one of the anterior region and one of the posterior region of the palate (*Figure 5*).

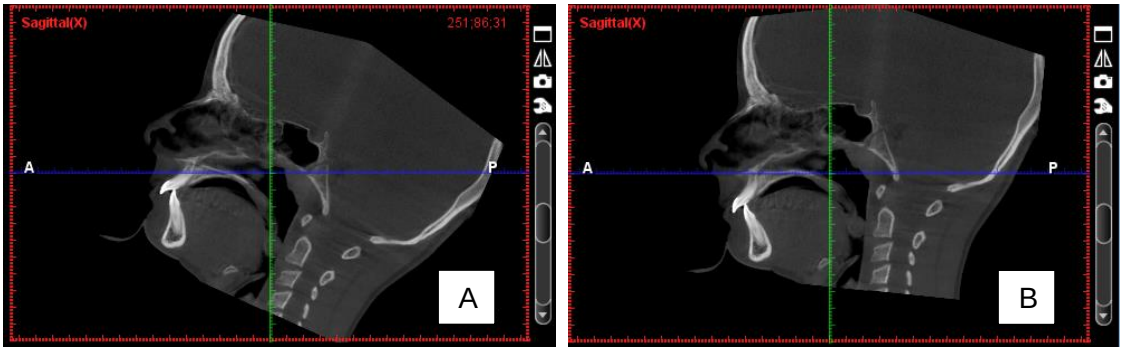



*Figure 5. Patient with curved palate. A- Anterior slice orientation; B- Posterior slice orientation.*

In patients with a very thick palate, the suture maturation stage must be analyzed in the two most central axial slices, and the slice with the highest maturation stage should be considered in the study (*Figure 6*).

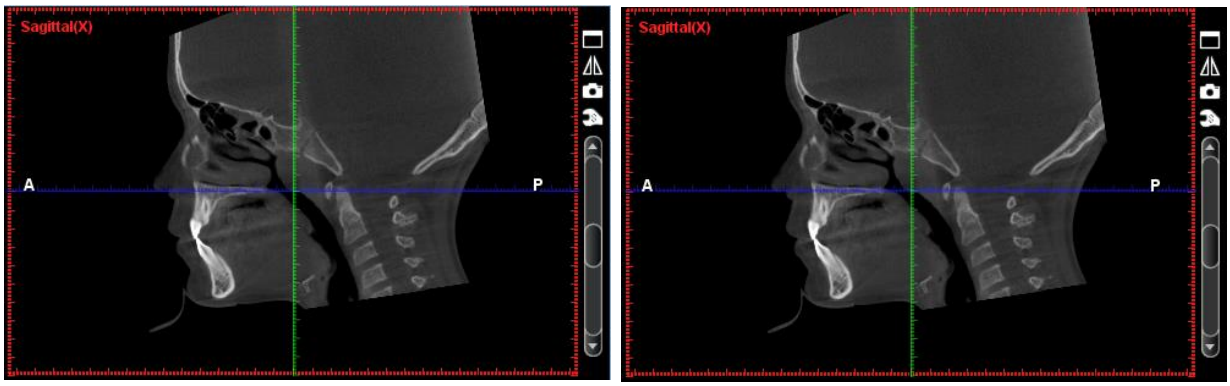



*Figure 6. Patient with a thick palate.*

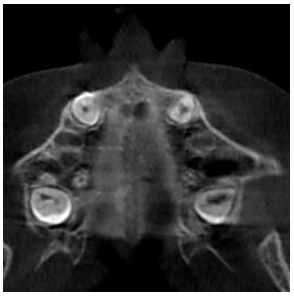
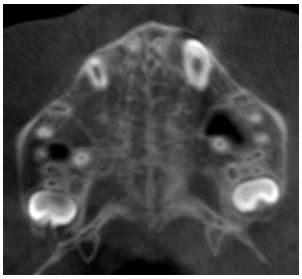
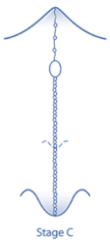
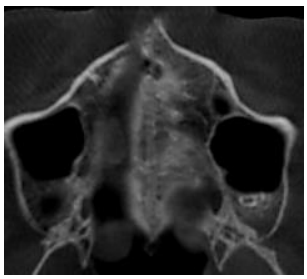
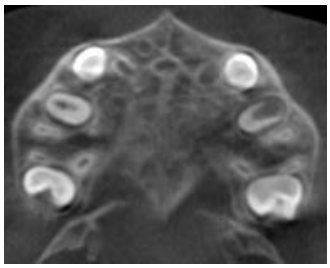
### 1.6.3.3 Image export

CBCT images were taken by a screen capture of the axial plane view showing the MPS and saved in a Microsoft® PowerPoint® presentation (Microsoft Office, New Mexico, U.S.A). Every image was arranged on a slide with an identification code (eg. ID01).

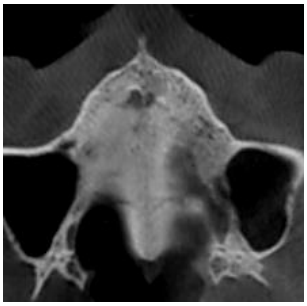
#### 1.1.1.1 Midpalatal suture maturation classification according to Angelieri *et al.* [14]

All images were classified according to the Angelieri *et al.* method.

*Table I.Stages of midpalatal suture maturation*

| | | |
|---|---|---|
|   | Stage A: midpalatal suture is very nearly a straight radiopaque line (high density- white) with little or without interdigitation. |  |
|   | Stage B: midpalatal suture adopts an uneven shape and seems a sinuous high-density line. Patients can have minor areas where two parallel sinuous, radiopaque lines near each other and divided by small, radiolucent (low density) spaces. |  |
|   | Stage C: midpalatal suture assumes two parallel wavy radiopaque line near each other, divided by small, radiolucent spaces in the palatine and maxillary bones. The suture might have either a straight or irregular shape. |  |
|   | Stage D: fusion of the palatine bone in the midpalatal suture has occurred, starting in posterior and going forwards. The midpalatal suture disappears with the fusion but in the maxillary portion of the suture, can be seen two radiopaque (high-density) lines divided by a small, radiolucent spaces. |  |


Stage E: fusion of the midpalatal suture in the maxillary bone. The radiopaque line disappears, or at minimum, it appears in a portion of the maxillary bone. There is no alteration in the rest of the palate.



### 1.6.4 Cervical Vertebrae image

#### 1.6.4.1 Cephalogram preparation

Profile cephalogram is a lateral radiograph of the skull and is a relevant diagnostic aid in orthodontics. This exam allows the evaluation of different characteristics and parameters of the profile of each individual. These parameters allow orthodontist to assess dental and skeletal characteristics in the vertical and anteroposterior directions and then compare them with previously defined standard measures, providing a diagnosis and treatment.

In the preview window of Planmeca Romexis® software it was created a virtual cephalogram by clicking the image presented in Figure 7. Then the cephalogram was automatically created, Figure 8.

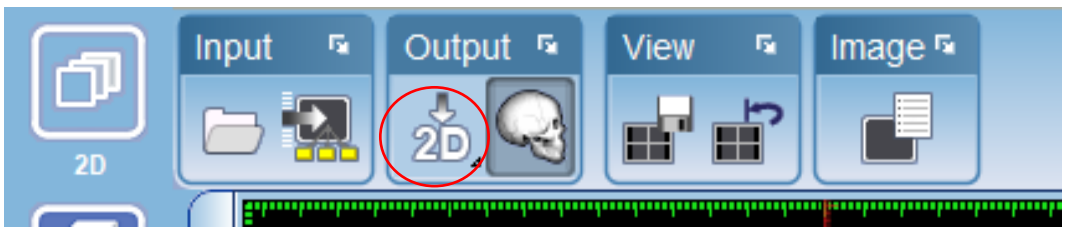



*Figure 7. Virtual ceph (create a virtual cephalogram image from the volume)*


*Figure 8. Virtual Cephalometric Image*

### 1.6.4.2 **Export cephalogram**

Images were taken by a screen capture of the virtual cephalometric and saved in a Microsoft® PowerPoint® presentation (Microsoft Office, New Mexico, U.S.A). Every image was arranged on a slide with an identification code.

### **1.6.4.3 Cephalometric study method**

The cephalometric tracing and analysis values were preformed using a computer software, Nemoceph® Dental Studio. This program allows to obtain the values throught cephalometric traces and specific analyzes integrated in the program. All cephalometric measurements were performed by the orthodontist as part of a diagnosis of each clinical case. The facial biotype and skeletal relationship of each individual were also determined. It was applied the Rickets analysis (Annex 1.1).

### **1.6.4.4 Cervical vertebrae maturation classification according to Baccetti T. *et al*.[31]**

All vertebral images were classified according to the Baccetti T. *et al.* method.

*Table II. Stages of cervical vertebral maturation*

| | | |
|---|---|---|
|  CS1 | Stage 1: the inferior margins of the three vertebrae (C2 to C4) are plane. Vertebrae C3 and C4 outline is trapezoid. |  |
|  CS2 | Stage 2: the inferior margin of C2 has a concavity. The rest of the vertebrae (C3 and C4) have the same form, trapezoid. |  |
|  CS3 | Stage 3: the inferior margins of C2 and C3 have a concavity. The C3 and C4 outline may be trapezoid or rectangular horizontal. |  |
|  CS4 | Stage 4: the inferior margins of C2, C3 and C4 have a concavity. The outlines of C3 and C4 are a horizontal rectangle. |  |

| | | |
|---|---|---|
|  CS5 | Stage 5: the inferior margins of C2, C3, and C4 still have a concavity. At least one of C3 or C4 outlines is a square. Otherwise, the outline of the other vertebra is still a horizonal rectangle. |  |
|  CS6 | Stage 6: the inferior margins od C2, C3 and C4 still have a concavity. At least one of C3 or C4 outlines is a vertical rectangle. Otherwise, the outline of the other vertebra is a square. |  |

## 1.7 Statistical Analysis

The sample size was estimated by specifying a test power of 80% (1 - β = 0.80, where β is the Type II error) and a significance level of 5% (α = 0.05, where α is the Type I error), following the directions of Bujang & Baharum [33].

Under these conditions, considering the ordinal scales under study, a minimum sample of 74 patients is required to detect a weighted Cohen's Kappa Coefficient of 0.60, corresponding to good agreement, assuming that the frequencies of each category of answers is not equal.

For intra-observer error assessment, a random subsample of 30 patients from the 74 study participants was selected. To evaluate the measurement error (inter-observer and intra-observer) and to study the agreement between the Angelieri *et al*.[14] and Baccetti *et al*.[31] classifications, the weighted Cohen's Kappa coefficient[34] was used. This coefficient assumes the maximum value of 1 in the case of perfect agreement between two measurements. The further away from 1, the lower the agreement. The coefficient value is influenced by the magnitude of the discrepancy between two evaluations: the greater the difference between the two evaluations, the greater the penalty in the coefficient value. For the classification of agreement between the pairs of measurements, the cut-off points proposed by Altman[35] were considered:

- weak (<0.20);
- reasonable (0.21 - 0.40);
- moderate (0.41 - 0.60);
- good (0.61 - 0.80);
- very good (> 0.80).

In addition to the weighted Cohen's Kappa coefficient, the percentages of agreement between the pairs of evaluations are also presented.

To calculate the weighted Cohen's Kappa coefficient, we used the package psych version of 2017, (Revelle, Illinois, U.S.A) available in program R - version 3.3.2 of 2017 (R Core Team, Vienna, Austria) [36].

The significance of the association of scale classifications with sex and age was assessed using the Chi-square test and the Spearman correlation coefficient, respectively. A significance level of 5% was considered, i.e., associations were considered statistically significant when the significance value was less than 0.05 ($p < 0.05$).

### 1.7.1 Recodification

The two scales do not have the same number of categories, therefore, to study the agreement between the Angelieri *et al.* and Baccetti *et al.* scales, both scales were recoded according to the literature and on the treatment decision [7]:

Angelieri *et al.* Method:

- Category A - stages A and B: it is possible to expand;
- Category B - stage C: possible but treatment success more doubtful;
- Category C - stages D and E: expansion is not possible.

Baccetti *et al.* Method:

- Category A - stages 1, 2 and 3: it is possible to expand;
- Category B - stage 4: possible but treatment success more doubtful;
- Category C - stages 5 and 6: expansion is not possible.

# RESULTS

# III. RESULTS

## 1.1 Sample

The sample consisted of 76 patients, mainly female (57.9%), aged between 7 and 58 years, with an average age of 18.0 years. The predominant age group was from 10 years to 15 years (47.4%). Of the 76 patients, 30 (39.5%) are skeletal Class I, 33 (43.4%) are Class II and 13 (17.1%) are Class III. Regarding the facial biotype, 27 (35.5%) were dolichofacial, 25 (32.9%) mesofacial and 24 (31.6%) brachyfacial. (Table III,

Figure *9*, Figure 10, Figure 11 and Figure 12).

*Table III. Characterization of the sample regarding sex, age, skeletal class and facial biotype (N = 76)*

| | Categories | n | % |
|---|---|---|---|
| Sex | Female | 44 | 57.9% |
| | Male | 32 | 42.1% |
| **Age** (years) | < 10 years | 10 | 13.2% |
| Minimum = 7 | 10 - 15 years | 36 | 47.4% |
| Maximum = 58 | 16 - 20 years | 8 | 10.5% |
| Mean = 18.8 | 20 - 30 years | 10 | 13.2% |
| Standard deviation = 11.6 | > 30 years | 12 | 15.8% |
| Skeletal Class | Class I | 30 | 39.5% |
| | Class II | 33 | 43.4% |
| | Class III | 13 | 17.1% |
| Facial Biotype | Dolichofacial | 27 | 35.5% |
| | Mesofacial | 25 | 32.9% |
| | Brachyfacial | 24 | 31.6% |

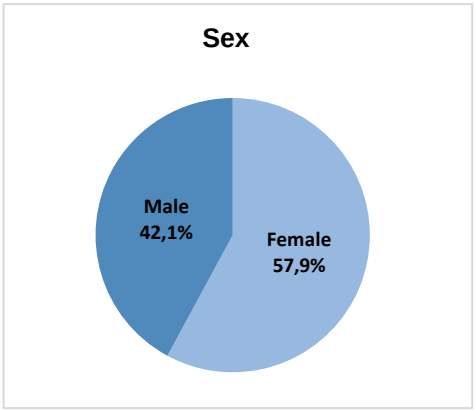



*Figure 9. Sample characterization regarding sex (N = 76).*

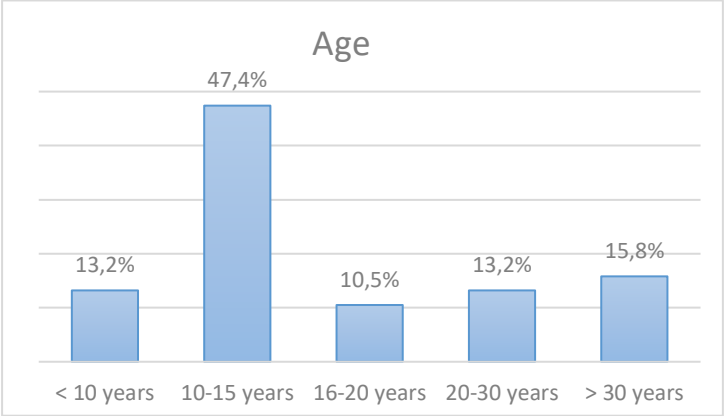



*Figure 10. Sample characterization regarding sex and age (N = 76).*

There are no significant differences between female and male patients regarding age, neither in the means, with a significance value of Student's T Test of 0.431, nor in the distribution by age group, with a Chi-square test significance value of 0.295 (Table IV). The age of female patients varies between 7 and 48 years, with an average of 19.7 years (SD = 11.9), and male between 8 and 58 years, with an average of 17.6 years (SD = 11.3).

*Table IV. Comparison of sex with age.*

| Age | Sex | | p |
|---|---|---|---|
| | Female (n = 44) | Male (n = 32) | |
| Minimum - Maximum | 7 - 48 | 8 - 58 | |
| Mean | 19.7 | 17.6 | p = 0.431 |
| Standard Deviation | 11.9 | 11.3 | |
| < 10 anos | 7 (15.9%) | 3 (9.4%) | |
| 10-15 anos | 18 (40.9%) | 18 (56.3%) | |
| 16-20 anos | 3 (6.8%) | 5 (15.6%) | p = 0.295 |
| 20-30 anos | 7 (15.9%) | 3 (9.4%) | |
| > 30 anos | 9 (20.5%) | 3 (9.4%) | |

## 1.2 Facial biotype

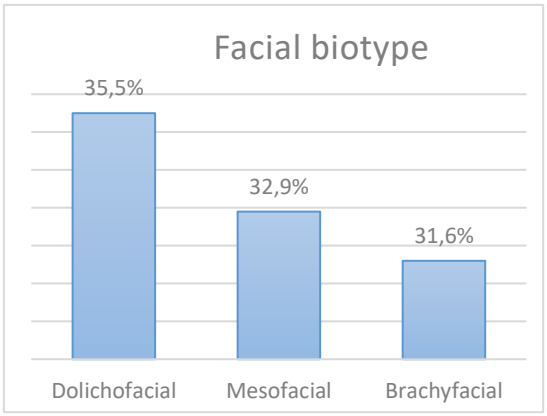



*Figure 11. Sample characterization regarding facial biotype (N=76).*

*Table V. Sample characterization by facial biotype and distribution by gender (percentage of each biotype by gender).*

| | DOLICHOFACIAL | MESOFACIAL | BRACHYFACIAL | TOTAL |
|---|---|---|---|---|
| **MALE** | 13 (40.6%) | 6 (18.8%) | 13 (40.6%) | 32 (100.0%) |
| **FEMALE** | 14 (31.8%) | 19 (43.2%) | 11 (25.0%) | 44 (100.0%) |
| **TOTAL** | 27 (35.5%) | 25 (32.9%) | 24 (31.6%) | 76 (100.0%) |

## 1.3 Skeletal Class

Concerning the skeletal class, Class II was the most prevalent (Figure 12). The male population is mostly Class II (50,0%) and the female population is frequently Class I (50,0%) (Table *VI*).

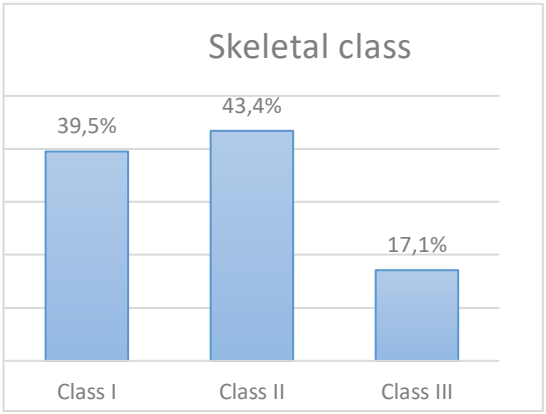



*Figure 12. Sample characterization regarding skeletal class (N=76).*

*Table VI. Sample characterization by skeletal class and distribution by sex (percentage of each skeletal class by sex)*

| | CLASS I | CLASS II | CLASS III | TOTAL |
|---|---|---|---|---|
| **MALE** | 8 (25.0%) | 16 (50.0%) | 8 (25.0%) | 32 (100.0%) |
| **FEMALE** | 22 (50.0%) | 17 (38.6%) | 5 (11.4%) | 44 (100.0%) |
| **TOTAL** | 30 (39.5%) | 33 (43.4%) | 13 (17.1%) | 76 (100.0%) |

*Table VII. Comparison of skeletal class with facial biotype.*

| | CLASS I | CLASS II | CLASS III | TOTAL |
|---|---|---|---|---|
| **DOLICHOFACIAL** | 9 (33.3%) | 15 (55.6%) | 3 (11.1%) | 27 (100.0%) |
| **MESOFACIAL** | 14 (56.0%) | 9 (36.0%) | 2 (8.0%) | 25 (100.0%) |
| **BRACHYFACIAL** | 7 (29.2%) | 9 (37.5%) | 8 (33.3%) | 24 (100.0%) |
| **TOTAL** | 30 (39.5%) | 33 (43.4%) | 13 (17.1%) | 76 (100.0%) |

## 1.4 Association of facial biotype and skeletal Class with suture maturation

Regarding the association of facial biotype and skeletal Class, there was a high percentage of stage D, in Angelieri *et al* scale, in brachyfacial patients (45,8%) and Class III patients (53,8%) (*Table VIIITable VII* and *Table IX*).

*Table VIII. Association of facial biotype with suture maturation (N = 76).*

| | **Dolichofacial** (n = 27) | **Mesofacial** (n = 25) | **Brachyfacial** (n = 24) | **Total** (n = 76) |
|---|---|---|---|---|
| **Angelieri** | | | | |
| Stage A | 4 (14.8%) | 0 (0.0%) | 0 (0.0%) | 4 (5.3%) |
| Stage B | 9 (33.3%) | 7 (28.0%) | 3 (12.5%) | 19 (25.0%) |
| Stage C | 7 (25.9%) | 3 (12.0%) | 4 (16.7%) | 14 (18.4%) |
| Stage D | 3 (11.1%) | 8 (32.0%) | 11 (45.8%) | 22 (28.9%) |
| Stage E | 4 (14.8%) | 7 (28.0%) | 6 (25.0%) | 17 (22.4%) |
| **Baccetti** | | | | |
| Stage 1 | 1 (3.7%) | 4 (16.0%) | 0 (0.0%) | 5 (6.6%) |
| Stage 2 | 7 (25.9%) | 2 (8.0%) | 4 (16.7%) | 13 (17.1%) |
| Stage 3 | 4 (14.8%) | 3 (12.0%) | 3 (12.5%) | 10 (13.2%) |
| Stage 4 | 8 (29.6%) | 5 (20.0%) | 7 (29.2%) | 20 (26.3%) |
| Stage 5 | 3 (11.1%) | 7 (28.0%) | 5 (20.8%) | 15 (19.7%) |
| Stage 6 | 4 (14.8%) | 4 (16.0%) | 5 (20.8%) | 13 (17.1%) |

*Table IX. Association of skeletal class with suture maturation (N = 76).*

| | **Class I** (n = 30) | **Class II** (n = 33) | **Class III** (n = 13) | **Total** (n = 76) |
|---|---|---|---|---|
| **Angelieri** | | | | |
| Stage A | 2 (6.7%) | 2 (6.1%) | 0 (0.0%) | 4 (5.3%) |
| Stage B | 8 (26.7%) | 9 (27.3%) | 2 (15.4%) | 19 (25.0%) |
| Stage C | 6 (20.0%) | 7 (21.2%) | 1 (7.7%) | 14 (18.4%) |
| Stage D | 5 (16.7%) | 10 (30.3%) | 7 (53.8%) | 22 (28.9%) |
| Stage E | 9 (30.0%) | 5 (15.2%) | 3 (23.1%) | 17 (22.4%) |
| **Baccetti** | | | | |
| Stage 1 | 2 (6.7%) | 3 (9.1%) | 0 (0.0%) | 5 (6.6%) |
| Stage 2 | 5 (16.7%) | 4 (12.1%) | 4 (30.8%) | 13 (17.1%) |
| Stage 3 | 4 (13.3%) | 5 (15.2%) | 1 (7.7%) | 10 (13.2%) |
| Stage 4 | 7 (23.3%) | 9 (27.3%) | 4 (30.8%) | 20 (26.3%) |
| Stage 5 | 6 (20.0%) | 8 (24.2%) | 1 (7.7%) | 15 (19.7%) |
| Stage 6 | 6 (20.0%) | 4 (12.1%) | 3 (23.1%) | 13 (17.1%) |

## 1.5 Sistematic error assessment

To evaluate the measurement error, the 76 participants' evaluations were made by two observers - inter-observer error analysis. In addition to this assessment, each observer repeated the classifications of 30 participants (39.5% of the sample, randomly selected) - intra-observer error analysis. Results are shown in Table X, Table XI, Table XII, Table XIII, Table XIV and Table XV.

### 1.5.1 Angelieri *et al.* scale

Weighted Cohen's Kappa coefficient on Angelieri *et al.* scale was greater than or equal to 0.90 for both inter-observer and intra-observer error assessment (in both

observers). Agreement percentages greater than 86% were verified in all cases. These results lead to the conclusion that there is a high agreement between measurements, with no measurement error on the Angelieri et al. scale (Table X, Table XI, Table XII).

*Table X. Data from the study of the inter-observer error of the Angelieri et al. scale (N = 76).*

| | | Observer 2 | | | | | Total |
|---|---|---|---|---|---|---|---|
| | | Stage A | Stage B | Stage C | Stage D | Stage E | |
| Observer 1 | Stage A | 3 | 0 | 0 | 1 | 0 | 4 |
| | Stage B | 0 | 17 | 1 | 1 | 0 | 19 |
| | Stage C | 0 | 0 | 12 | 1 | 1 | 14 |
| | Stage D | 0 | 0 | 1 | 20 | 1 | 22 |
| | Stage E | 0 | 0 | 0 | 2 | 15 | 17 |
| | Total | 3 | 17 | 14 | 25 | 17 | 76 |

Weighted Kappa = 0.895; Agreement percentage: 88.2% (67/76)

*Table XI. Data from the study of the intra-observer error of the Angelieri et al. scale - observer 1(N = 30)*

| | | 2nd analysis | | | | | Total |
|---|---|---|---|---|---|---|---|
| | | Stage A | Stage B | Stage C | Stage D | Stage E | |
| 1st analysis | Stage A | 0 | 0 | 0 | 0 | 0 | 0 |
| | Stage B | 0 | 6 | 0 | 0 | 0 | 6 |
| | Stage C | 0 | 0 | 6 | 1 | 0 | 7 |
| | Stage D | 0 | 0 | 2 | 6 | 1 | 9 |
| | Stage E | 0 | 0 | 0 | 0 | 8 | 8 |
| | Total | 0 | 6 | 8 | 7 | 9 | 30 |

Weighted Kappa = 0.944; Agreement percentage: 86.7% (26/30)

*Table XII. Data from the study of the intra-observer error of the Angelieri et al. scale - observer 2 (N = 30).*

| | | 2nd analysis | | | | | Total |
|---|---|---|---|---|---|---|---|
| | | Stage A | Stage B | Stage C | Stage D | Stage E | |
| 1st analysis | Stage A | 0 | 0 | 0 | 0 | 0 | 0 |
| | Stage B | 0 | 4 | 1 | 0 | 0 | 5 |
| | Stage C | 0 | 0 | 7 | 0 | 0 | 7 |
| | Stage D | 0 | 1 | 0 | 8 | 1 | 10 |
| | Stage E | 0 | 0 | 0 | 0 | 8 | 8 |
| | Total | 0 | 5 | 8 | 8 | 9 | 30 |
| Weighted Kappa = 0.909; Agreement percentage: 90.0% (27/30) | | | | | | | |

### 1.5.2 Baccetti *et al.* Scale

Regarding the Baccetti *et al.* scale (Table XII, Table XIII and Table XIV), the Weighted Cohen's Kappa Coefficient (≥ 0.96) and the agreement percentages (> 80%) in the inter-observer and intra-observer evaluations show that, also on this scale, there wasn't a measurement error.

*Table XIII. Data from the study of the inter-observer error of the Baccetti et al. scale (N = 76)*

| | | Observer 2 | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Stage 5 | Stage 6 | |
| Observer 1 | Stage 1 | 5 | 0 | 0 | 0 | 0 | 0 | 5 |
| | Stage 2 | 0 | 13 | 0 | 0 | 0 | 0 | 13 |
| | Stage 3 | 0 | 2 | 8 | 0 | 0 | 0 | 10 |
| | Stage 4 | 0 | 0 | 3 | 14 | 3 | 0 | 20 |
| | Stage 5 | 0 | 0 | 0 | 2 | 12 | 1 | 15 |
| | Stage 6 | 0 | 0 | 0 | 0 | 3 | 10 | 13 |
| | Total | 5 | 15 | 11 | 16 | 18 | 11 | 76 |
| Weighted Kappa = 0.960; Agreement percentage: 81.6% (62/76) | | | | | | | | |

*Table XIV. Data from the study of intra-observer error of the Baccetti et al. scale – observer 1 (N = 30)*

| | | 2nd analysis | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Stage 5 | Stage 6 | |
| 1st analysis | Stage 1 | 2 | 1 | 0 | 0 | 0 | 0 | 3 |
| | Stage 2 | 0 | 2 | 1 | 0 | 0 | 0 | 3 |
| | Stage 3 | 0 | 0 | 3 | 0 | 0 | 0 | 3 |
| | Stage 4 | 0 | 0 | 1 | 6 | 1 | 0 | 8 |
| | Stage 5 | 0 | 0 | 0 | 0 | 7 | 0 | 7 |
| | Stage 6 | 0 | 0 | 0 | 0 | 1 | 5 | 6 |
| | Total | 2 | 3 | 5 | 6 | 9 | 5 | 30 |

Weighted Kappa = 0.963; Agreement percentage: 83.3% (25/30)

*Table XV. Data from the study of intra-observer error of the Baccetti et al. scale – observer 2 (N = 30)*

| | | Observer 2 | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Stage 5 | Stage 6 | |
| 1st analysis | Stage 1 | 3 | 0 | 0 | 0 | 0 | 0 | 3 |
| | Stage 2 | 0 | 4 | 0 | 0 | 0 | 0 | 4 |
| | Stage 3 | 0 | 0 | 2 | 0 | 0 | 0 | 2 |
| | Stage 4 | 0 | 0 | 0 | 8 | 0 | 0 | 8 |
| | Stage 5 | 0 | 0 | 0 | 0 | 9 | 0 | 9 |
| | Stage 6 | 0 | 0 | 0 | 0 | 0 | 4 | 4 |
| | Total | 3 | 4 | 2 | 8 | 9 | 4 | 30 |

Weighted Kappa = 1.000; Agreement percentage: 100.0% (30/30)

## 1.6 Characterization and association with sex and age

### 1.6.1 Characterization

The characterization of the Angelieri *et al*. and Baccetti *et al.* scale classifications is presented in Table XVI and Figure 13.

Considering the evaluation obtained by the Angelieri *et al.* scale, about half of the participants (51.3%) are in stages D (28.9%) or E (22.4%). There are still 18.4% in Stage C, 25.0% in Stage B and 5.3% in Stage A.

According to the Baccetti *et al*. scale, more than half (63.2%) are in stages 4 (26.3%), 5 (19.7%) or 6 (17.1%). There were 6.6% in Stage 1, 17.1% in Stage 2, 13.2% in Stage 3.

*Table XVI. Characterization of the sample regarding the Angelieri et al. and Baccetti et al. scale classifications (N = 76).*

| | Classification | n | % |
|---|---|---|---|
| Angelieri *et al.* | Stage A | 4 | 5.3% |
| | Stage B | 19 | 25.0% |
| | Stage C | 14 | 18.4% |
| | Stage D | 22 | 28.9% |
| | Stage E | 17 | 22.4% |
| Baccetti *et al.* | Stage 1 | 5 | 6.6% |
| | Stage 2 | 13 | 17.1% |
| | Stage 3 | 10 | 13.2% |
| | Stage 4 | 20 | 26.3% |
| | Stage 5 | 15 | 19.7% |
| | Stage 6 | 13 | 17.1% |

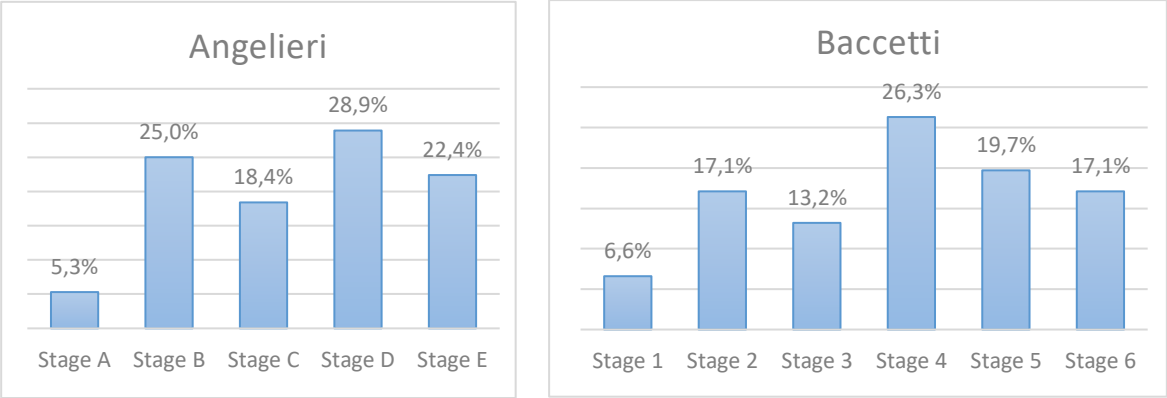



*Figure 13. Characterization of the sample regarding the Angelieri et al. and Baccetti et al. scale classifications (N = 76).*

### 1.6.2 Association with sex and age

The results in Table XVII show that, based on the Angelieri *et al.* scale classification, there is no statistically significant association with sex (p = 0.685), in other words, the distribution by different stages is similar in female and male participants.

However, there were significant sex differences when considering the Baccetti *et al.* scale rating (p = 0.005). The frequency analysis shows that the percentages of patients in stages 1, 2 and 3 are higher in male than in female patients, and the opposite in percentages in stages 4, 5 and 6.

*Table XVII. Association between sex and the Angelieri et al. and Baccetti et al. scales (N = 76).*

| | Classification | Female (n = 44) | Male (n = 32) |
|---|---|---|---|
| Angelieri *et al.* | Stage A | 6.8% (n = 3) | 3.1% (n = 1) |
| | Stage B | 22.7% (n = 10) | 28.1% (n = 9) |
| | Stage C | 15.9% (n = 7) | 21.9% (n = 7) |
| | Stage D | 27.3% (n = 12) | 31.3% (n = 10) |
| | Stage E | 27.3% (n = 12) | 15.6% (n = 5) |
| Chi-square test | | p = 0.685 | |
| Baccetti *et al.* | Stage 1 | 4.5% (n = 2) | 9.4% (n = 3) |
| | Stage 2 | 9.1% (n = 4) | 28.1% (n = 9) |
| | Stage 3 | 4.5% (n = 2) | 25.0% (n = 8) |
| | Stage 4 | 36.4% (n = 16) | 12.5% (n = 4) |
| | Stage 5 | 25.0% (n = 11) | 12.5% (n = 4) |
| | Stage 6 | 20.5% (n = 9) | 12.5% (n = 4) |
| Chi-square test | | p = 0.005 | |

Age Spearman's Correlation Coefficient values with the Angelieri *et al.* scale show the existence of a weak positive correlation (R = 0.201, p = 0.082). The correlation with the Baccetti *et al.* scale classification (R = 0.581, p <0.001) is strong positive and statistically significant, indicating that the higher the age, the higher the stage.

## 1.7 Correlation between Baccetti et al. and Angelieri et. al methods

The results of the study of the agreement between the Angelieri *et al.* and Baccetti *et al.* scales are presented in Table XVIII. The values of the Spearman's Correlation Coefficient (R = 0.477) and the Intraclass Correlation Coefficient (ICC=0.642) show the existence of a moderate (correlation) association between the evaluations produced by the two scales.

*Table XVIII. Agreement between the Angelieri et al. and Baccetti et al. scales (N = 76).*

| | | **Angelieri *et al.*** | | | | | **Total** |
|---|---|---|---|---|---|---|---|
| | | **Stage A** | **Stage B** | **Stage C** | **Stage D** | **Stage E** | |
| **Baccetti *et al.*** | **Stage 1** | 1 | 3 | 1 | 0 | 0 | 5 |
| | **Stage 2** | 2 | 5 | 2 | 3 | 1 | 13 |
| | **Stage 3** | 0 | 2 | 3 | 4 | 1 | 10 |
| | **Stage 4** | 1 | 5 | 6 | 5 | 3 | 20 |
| | **Stage 5** | 0 | 3 | 1 | 4 | 7 | 15 |
| | **Stage 6** | 0 | 1 | 1 | 6 | 5 | 13 |
| | **Total** | 4 | 19 | 14 | 22 | 17 | 76 |
| **ICC = 0.642; Spearman's Correlation Coefficient: 0.477** ($p < 0.001$) | | | | | | | |

## 1.8 Agreement between Angelieri *et al.* and Baccetti *et al.* scales recoded

The results of the study of agreement between the Angelieri *et al.* and Baccetti *et al.* scales (Table XIX and Figure 14) show a reasonable agreement, with weighted Cohen's Kappa coefficient of 0.372 (95%CI: 0.166-0.580) and a percentage of agreement between the classifications of 53.9%.

Compared to the Angelieri *et al.* method, the Baccetti *et al.* method led to a higher percentage of patients being classified in category A (favorable: 36.8% vs. 30.3%) and category B (doubtful: 26.3% vs. 18.4%). In contrast, the Angelieri *et al.* method ranked fewer patients of category C (unfavorable: 36.8% vs. 51.3%).

Table XIX. Agreement between Angelieri *et al.* and Baccetti *et al.* scales (N = 76).

| | | BACCETTI *ET AL.* | | | Total |
|---|---|---|---|---|---|
| | | A (favorable) | B (doubtful) | C (unfavorable) | |
| ANGELIERI *ET AL.* | A (favorable) | 13 | 6 | 4 | 23 (30.3%) |
| | B (doubtful) | 6 | 6 | 2 | 14 (18.4%) |
| | C (unfavorable) | 9 | 8 | 22 | 39 (51.3%) |
| | Total | 28 (36.8%) | 20 (26.3%) | 28 (36.8%) | 76 |
| Weighted Kappa = 0.372 (95%CI: 0.166-0.580); Agreement percentage: 53.9% (41/76) | | | | | |

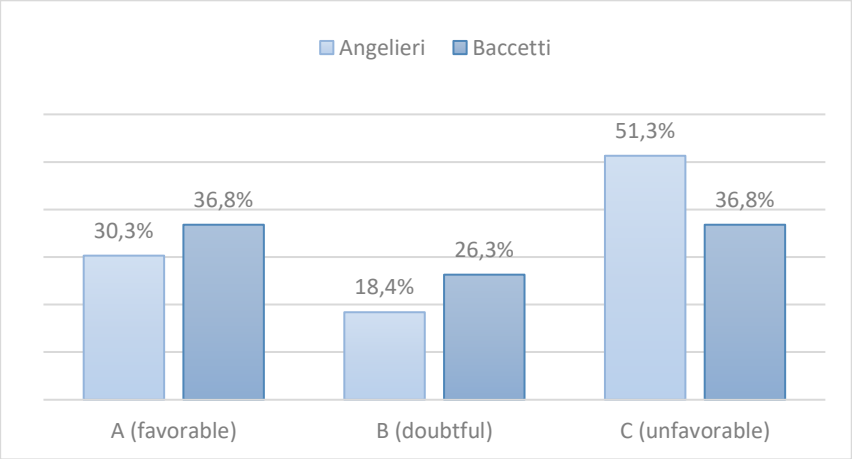



*Figure 14. Classification according to the new categories of the Angelieri et al. and Baccetti et al. scales (N = 76).*

# DISCUSSION

# IV. DISCUSSION

Since chronological age is not reliable for predicting the development stage of the MPS [6, 16, 19, 24], the evaluation of the MPS maturation by a diagnostic method, before the RME, is important, for the patient safety. Diagnostic methods must be reliable, safe and scientifically studied. For these reason both, Angelieri *et al.* and Baccetti *et al.* methods were chosen for this investigation [14, 28].

## 1.1 State of Art

Although RME can lead to the increase of maxillary width, buccal and palatal intermolar width[22], when is not properly planned can lead to RME failure. There are side-effects after the RME failure such as: accentuated buccal inclination of the maxillary posterior teeth, periodontal damage and palate necrosis[7, 12]. The increased resistance to RME can be affected by the pronounced interdigitation of the MPS (have a tendency to be from posterior to anterior) and the circummaxillary structures which increases the rigidity of the maxillary bones [8, 10, 14, 15, 18, 19, 21-24].

## 1.2 Sample

The sample size calculation is a crucial aspect in structuring the investigation. In fact, the analyzed systematic reviews allow to identify studies with very different samples, in characterization and in number. In this study, the sample size was calculated in order to have a test power of 80% and a significance level of 5%. For this purpose, considering the ordinal scales under study, a minimum sample of 74 patients is required to detect a weighted Cohen's Kappa Coefficient of 0.60 (corresponding to good agreement).

The sample composed by 76 patients randomly selected from an orthodontic practice that met the inclusion criteria. Of these patients, 44 were females and 32 were males, between 7 and 58 years old. The sample was higher than most of the studies found in literature. Grunheid *et al.* [16] worked with a total of 30 orthodontic patients (17 female and 13 male), Isfeld's *et al.* [17] sample was formed by 63 preadolescent and adolescent patients and Baccetti *et al.*[24], in 2001, from all filters applied, result 42 patients (25 female and 17 male). Additionally, Gueutier *et al.* [19], Sumer *et al.*[26], Franchi *et al.*[25] and Korbmacher *et al.*[18]used a sample less than 30 individuals.

Concerning the CVM, Baccetti *et al.* [30] analyzed 214 patients' cephalograms and Hassel and Farman[29] evaluated 220 cephalograms and hand-wrist radiographs of

subjects between 8 and 18 years old. Regarding the authors that attempted different technologies to assess the MPS maturation, Kwak *et al.* [21] had a sample of 131 adult patients, Korbmacher *et al.* [18] documented 28 human-palate specimens, Sumer *et al.* [26] recorded the MPS after SARME in 3 patients, Franchi *et al.* [25] studied the MPS with a sample of 17 prepubertal subjects and Angelieri *et al.* [14] examined 140 patients CBCT.

Although some authors describe sex as a direct influencing factor for bone maturation[8, 10, 11], Angelieri *et al.* [13] refers that the maturation of the MPS was not affected significantly by sex nor age. Therefore, the fact that the sample is arbitrary does not influence the outcomes. The design of the present study didn't allow to take conclusions about the association between sex, chronological age and bone maturation stage. Considering chronological age, Angelieri *et al.* scale showed a weak positive correlation. In the other hand, Baccetti *et al.* scale demonstrated a strong positive and statistically significant correlation between the scale and the chronological age. This result was similar to the findings of Ramirez-Velasquez *et al.* [2]. Even though, there is a significant sex difference when considering the Baccetti *et al.* scale rating, the higher percentage of advanced CVM maturation stages (4,5,6) appeared in female patients.

## 1.3 Methodology and methods

Concerning the literature research, apart from the articles found in the literature, there were included in this study the articles published by Revelo B. and Fishman L. [20] and Hassel et al.[29], despite the fact they didn't fit these criteria, since they are considered gold standard, regarding the subject of this thesis.

The fact that the two examiners have never used Angelieri *et al.* method and Baccetti *et al.* method was sidestepped by the intensive exercises with training material and calibration[14, 30, 31]. The CBCT and the cephalogram were cropped showing only the areas of interest (MPS and cervical vertebrae), to prevent any additional information that might influence the observer during the evaluation, this way the bias was avoided. Additionally, it is crucial to emphasize that the number of examiners was low, and the diagnosis is subjective and conditioned by the image quality and experience of the examiners with these methods. The amount of training reflects in reproducibility[37], otherwise can lead to inaccuracies in the diagnosis.

Since the two methods do not have the same number of categories, both scales were recoded to have the same number of categories concerning the treatment decision. The recoded scale is supported by Angelieri *et al*. in stage A and B is possible to widening the maxilla orthopedically, but in stage C there is an increase of the sutural resistance,

therefore the outcome is more doubtful than in the previous stages [6, 7]. This methodology was reliable analyzing the inter-observer results (88.2% in Angelieri *et al.* scale and 81.6% in Baccetti *et al.* scale).

## 1.4 Results

According to Tonello *et al.* [10] stage C was the most often observed (53,84%) in his sample. Ladewig *et al.* [12] concluded that stage C, D, and E had the higher prevalence (91.9%). In this study, both female and male patients, stage D was the most prevalent (27.3% and 31.3%, respectively) in Angelieri *et al.* method (Table XVI).

Regarding Baccetti *et al.* method, Ramirez-Velasquez *et al.* and Angelieri *et al.*[2, 9] concluded that the stage 1 is the most prevalent. In this investigation, on the other hand, in Baccetti *et al.* scale, stage 2 was more often observed in males, and stage 4 in female, these findings are consistent with Jang HI *et al.* [8]. Spearman's Correlation Coefficient values for age with the Angelieri *et al.* scale show the existence of a weak positive correlation. The correlation with the Baccetti *et al*. scale classification was strong positive and statistically significant, indicating that the higher the age, the higher the stage as Ramirez-Velásquez [2] found.

### 1.4.1 Baccetti/Angelieri scales correlation non-recoded

The study of the agreement between the Angelieri *et al.* and Baccetti *et al.* scales showed the existence of a moderate association between the evaluations produced by the two scales, with the Spearman's Correlation Coefficient of 0.477 and the ICC (0.642).

The evidence is sufficient to reject the following null hypothesis: there is no correlation between the MPS maturation and the CVM using the Angelieri *et al.* and Baccetti *et al.* methods, respectively.

### 1.4.2 Baccetti/Angelieri scales recoded

Angelieri *et al.* method is based on five different stages and Baccetti *et al.* method consists in six stages. In order to compare these two scales directly, it was necessary to recode based on the treatment options. However, when there is recoding, information may be lost in the process, as there is a decrease in the number of scales.

The results of this study show a reasonable agreement between the Angelieri *et al.* and Baccetti *et al.* recoded scales, with weighted Cohen's Kappa coefficient of 0.372 (95%CI: 0.166-0.580) and a percentage of agreement between the classifications of 53.9%.

The evidence is not sufficient to reject the following null hypothesis:there is no correlation between the recoded MPS maturation classification (Angelieri *et al.*) and CVM classification (Baccetti *et al.*).

## 1.5 Study limitations and final considerations

To avoid subjecting the patient to more radiation, a 2D reconstruction of a 3D image was used, in this process there may have been loss of information, therefore there has to be a lot of attention when analyzing the reconstructed images. Although the results of this study have shown a moderate association between the scales, it's important to clarify that Baccetti *et al.* scale is usually applied in a 2D image and cervical vertebrae produce different images taking into account the incidence of x-ray.

Although it is important to study methods to access the MPS to procced with the treatment planning, this study is based on two theorical classifications. Therefore, it is important to study what happened after the separation of the MPS. It would be essential to know if the MPS behaves as this investigation concluded.

# CONCLUSION

# V. CONCLUSION

It was possible to conclude the following:

- The nonrecoded Angelieri *et al.* and Baccetti *et al.* scales have a moderate correlation.
- The recoded Angelieri *et al.* and Baccetti *et al.* scales show a reasonable agreement, showing that there was a significant loss of information in the recoding system.

# REFERENCES

# VI. REFERENCES

1. Szemraj A, Wojtaszek-Slominska A, Racka-Pilszak B. Is the cervical vertebral maturation (CVM) method effective enough to replace the hand-wrist maturation (HWM) method in determining skeletal maturation?-A systematic review. Eur J Radiol. 2018;102:125-8.

2. Ramirez-Velasquez M, Viloria-Avila TJ, Rodriguez DA, Rojas ME, Zambrano O. Maturation of cervical vertebrae and chronological age in children and adolescents. Acta Odontol Latinoam. 2018;31(3):125-30.

3. Chen X, Xia B, Ge L. Effects of breast-feeding duration, bottle-feeding duration and non-nutritive sucking habits on the occlusal characteristics of primary dentition. BMC Pediatr. 2015;15:46.

4. Di Vece L, Faleri G, Picciotti M, Guido L, Giorgetti R. Does a transverse maxillary deficit affect the cervical vertebrae? A pilot study. Am J Orthod Dentofacial Orthop. 2010;137(4):515-9.

5. Bishara SE, Staley RN. Maxillary expansion: Clinical implications. Am J Orthod Dentofacial Orthop. 1987;91(1):3-14.

6. Abo Samra D, Hadad R. Midpalatal suture: evaluation of the morphological maturation stages via bone density. Prog Orthod. 2018;19(1):29.

7. Angelieri F, Franchi L, Cevidanes LH, Bueno-Silva B, McNamara JA, Jr. Prediction of rapid maxillary expansion by assessing the maturation of the midpalatal suture on cone beam CT. Dental Press J Orthod. 2016;21(6):115-25.

8. Jang HI, Kim SC, Chae JM, Kang KH, Cho JW, Chang NY, et al. Relationship between maturation indices and morphology of the midpalatal suture obtained using cone-beam computed tomography images. Korean J Orthod. 2016;46(6):345-55.

9. Angelieri F, Franchi L, Cevidanes LH, McNamara JA, Jr. Diagnostic performance of skeletal maturity for the assessment of midpalatal suture maturation. Am J Orthod Dentofacial Orthop. 2015;148(6):1010-6.

10. Tonello DL, Ladewig VM, Guedes FP, Ferreira Conti ACC, Almeida-Pedrin RR, Capelozza-Filho L. Midpalatal suture maturation in 11- to 15-year-olds: A cone-beam computed tomographic study. Am J Orthod Dentofacial Orthop. 2017;152(1):42-8.

11. Armond MC, Generoso R, Falci SG, Ramos-Jorge ML, Marques LS. Skeletal maturation of the cervical vertebrae: association with various types of malocclusion. Braz Oral Res. 2012;26(2):145-50.

12. Ladewig VM, Capelozza-Filho L, Almeida-Pedrin RR, Guedes FP, de Almeida Cardoso M, de Castro Ferreira Conti AC. Tomographic evaluation of the maturation stage of the midpalatal suture in postadolescents. Am J Orthod Dentofacial Orthop. 2018;153(6):818-24.

13. Angelieri F, Franchi L, Cevidanes LHS, Goncalves JR, Nieri M, Wolford LM, et al. Cone beam computed tomography evaluation of midpalatal suture maturation in adults. Int J Oral Maxillofac Surg. 2017;46(12):1557-61.

14. Angelieri F, Cevidanes LH, Franchi L, Goncalves JR, Benavides E, McNamara JA, Jr. Midpalatal suture maturation: classification method for individual assessment before rapid maxillary expansion. Am J Orthod Dentofacial Orthop. 2013;144(5):759-69.

15. Knaup B, Yildizhan F, Wehrbein H. Age-related changes in the midpalatal suture. A histomorphometric study. J Orofac Orthop. 2004;65(6):467-74.

16. Grunheid T, Larson CE, Larson BE. Midpalatal suture density ratio: A novel predictor of skeletal response to rapid maxillary expansion. Am J Orthod Dentofacial Orthop. 2017;151(2):267-76.

17. Isfeld D, Flores-Mir C, Leon-Salazar V, Lagravere M. Evaluation of a novel palatal suture maturation classification as assessed by cone-beam computed tomography imaging of a pre- and postexpansion treatment cohort. Angle Orthod. 2019;89(2):252-61.

18. Korbmacher H, Schilling A, Puschel K, Amling M, Kahl-Nieke B. Age-dependent three-dimensional microcomputed tomography analysis of the human midpalatal suture. J Orofac Orthop. 2007;68(5):364-76.

19. Gueutier A, Pare A, Joly A, Laure B, de Pinieux G, Goga D. Rapid maxillary expansion in adults: Can multislice computed tomography help choose between orthopedic or surgical treatment? Rev Stomatol Chir Maxillofac Chir Orale. 2016;117(5):327-34.

20. Revelo B, Fishman LS. Maturational evaluation of ossification of the midpalatal suture. Am J Orthod Dentofacial Orthop. 1994;105(3):288-92.

21. Kwak KH, Kim SS, Kim YI, Kim YD. Quantitative evaluation of midpalatal suture maturation via fractal analysis. Korean J Orthod. 2016;46(5):323-30.

22. Sayar G, Kilinc DD. Rapid maxillary expansion outcomes according to midpalatal suture maturation levels. Prog Orthod. 2019;20(1):27.

23. Jaqueira LM, Armond MC, Pereira LJ, Alcantara CE, Marques LS. Determining skeletal maturation stage using cervical vertebrae: evaluation of three diagnostic methods. Braz Oral Res. 2010;24(4):433-7.

24. Baccetti T, Franchi L, Cameron CG, McNamara JA, Jr. Treatment timing for rapid maxillary expansion. Angle Orthod. 2001;71(5):343-50.

25. Franchi L, Baccetti T, Lione R, Fanucci E, Cozza P. Modifications of midpalatal sutural density induced by rapid maxillary expansion: A low-dose computed-tomography evaluation. Am J Orthod Dentofacial Orthop. 2010;137(4):486-8; discussion 12A-13A.

26. Sumer AP, Ozer M, Sumer M, Danaci M, Tokalak F, Telcioglu NT. Ultrasonography in the evaluation of midpalatal suture in surgically assisted rapid maxillary expansion. J Craniofac Surg. 2012;23(5):1375-7.

27. Franchi L, Baccetti T, McNamara JA, Jr. Mandibular growth as related to cervical vertebral maturation and body height. Am J Orthod Dentofacial Orthop. 2000;118(3):335-40.

28. Rainey BJ, Burnside G, Harrison JE. Reliability of cervical vertebral maturation staging. Am J Orthod Dentofacial Orthop. 2016;150(1):98-104.

29. Hassel B, Farman AG. Skeletal maturation evaluation using cervical vertebrae. Am J Orthod Dentofacial Orthop. 1995;107(1):58-66.

30. Baccetti T, Franchi L, McNamara JA, Jr. An improved version of the cervical vertebral maturation (CVM) method for the assessment of mandibular growth. Angle Orthod. 2002;72(4):316-23.

31. Baccetti T, Franchi L, McNamara JA, Jr. The Cervical Vertebral Maturation (CVM) Method for the Assessment of Optimal Treatment Timing in Dentofacial Orthopedics. Semin Orthod. 2005;11(3):119-29.

32. Isfeld D, Lagravere M, Leon-Salazar V, Flores-Mir C. Novel methodologies and technologies to assess mid-palatal suture maturation: a systematic review. Head Face Med. 2017;13(1):13.

33. Bujang MA BN. Guidelines of the minimum sample size requirements for Cohen's Kappa. Epidemiology Biostatistics and Public Health - 2017. 2017;14.

34. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol Bull. 1968;70(4):213-20.

35. Altman D. Practical statistics for medical research. London: Chapman and Hall1991.

36. Revelle WR. psych: Procedures for Personality and Psychological Research. Software. 1.7.8 ed. Northwestern University, Evanston, Illinois, USA2017.

37. Rongo R, Valleta R, Bucci R, Bonetti GA, Michelotti A, D'Antò V. Does clinical experience affect the reproducibility of cervical vertebrae maturation method? The Angle Orthodontist. 2015;85(5):841-7.

# ANNEXES

# VII. ANNEXES

## 1.1 Analysis and cephalometric

### 1.1.1 Points

- A point (A): Deepest point of the anterior maxilla concavity. It is the anterior limit of the maxilla.
- Anterior nasal spine (ANS): Most anterior point of the anterior nasal spine of the maxilla. It constitutes the previous reference of the palatal plane.
- Basion (Ba): Cranial point most antero-inferior foramen magnum. It represents the posterior limit of the skull base. It is the lowest point of the clivus.
- Condylar point (Dc): Midpoint of the mandibular condyle at the intersection of the skull base plane. It is the upper reference of the condylar axis.
- Gnation (Gn): Most antero-inferior point of the mandible, at the level of the median sagittal plane. It forms the lower reference of the facial axis of mandibular growth.
- Mandibular centroid (Xi): Point located in the geometric center of the mandibular upstream branch. Postero-inferior reference of the internal mandibular axes (body axis and condylar axis).
- Nasion (N): Most anterior cranial point of the frontonasal suture. It represents the anterior limit of the skull base.
- Pogonion (Pog): Most anterior point of the mandible, at the level of the median sagittal plane of the symphysis. It represents the anterior limit of the mandible.
- Porion (Po): The uppermost cranial point of the external auditory canal. Posterior reference of the horizontal of Fh.

- Pterygoid (Pt): Most superior point of the greater round foramen, located at the most posterior-superior point of the pterygomaxillary cleft. It serves as a reference for the study of jaw growth.
- Suborbital (Or): Lower cranial point of the lower external border of the orbital cavity. It consists of the previous reference of the horizontal Fh.
- Supra-pogonion (Pm): Point located at the convergence of the external cortex with the internal cortex of the chin bone at the level of the median sagittal plane of the mandibular symphysis. It forms the anterior reference of the mandibular body axis.

### 1.1.2 Planes and axis

- Frankfurt Plan (Fh): Plan resulting from the union of the points Po and Or. Helps to position the patient's head in a standardized position.
- Skull base plane (basocranial): Reference plane formed by the points Ba and Na.
- Axis of the mandibular body: Line formed by the points Xi and Pm.
- Condylar axis: Reference planes formed by the union of points Dc and Xi.
- Facial plane: Plan resulting from the union of the points N and Pog.

### 1.1.3 Ricketts analysis

- Facial convexity: distance from point A to the facial plane (N-Pog). Indicates the maxillomandibular relationship in the anteroposterior direction.

  Standard: 2mm ± 2mm at 9 years. Decreases 0.2 mm / year

- Lower Facial Height: angle formed between the points ANS), Xi and Pmwith vertex in Xi. Designates the vertical growth of the lower facial third.

  Norm: 47º ± 4º

- Facial depth: angle formed by the facial plane (N-Pog) with the Frankfurt plane (Po-Or). It allows to determine if the skeletal classes (II or III) are from mandibular bone, this variable being an anteroposterior indicator.

  Norm: 87º ± 3º at 9 years old. Increases 0.23º / year

- Facial axis: angle formed by the Ba-N and Pt-Gn planes. Indicates the position of the chin in the vertical direction. Relevant for the determination of the facial biotype and points the direction of facial growth.

  Norm: 90º ± 3.5º

- Mandibular arch: angle formed by the axis of the mandibular body (Xi-Pm) with the condylar axis (Xi-Dc). It allows to evaluate the degree of condyle inclination and the mandibular growth pattern.

  Norm: 26º ± 4º at 9 years old. Increases, 0.5º / year

- Angle of the Mandibular Plane: angle formed between the mandibular plane and the horizontal plane of Frankfurt. Necessary for the determination of the facial biotype.

  Norm: 26º ± 4º

To determine the facial biotype according to Ricketts it was necessary to analyze five different values: lower facial height, angle of the mandibular plane, facial axis, facial depth and mandibular arch. To classify the skeletal Class, it was necessary to analyze the cephalometric factor “facial convexity”:

- values between 0 and 4 mm: Class I pattern
- values above 4 mm: Class II pattern
- values below 0 mm: Class III pattern

## 1.2 Ethics Committee Approval

U.PORTO
FACULDADE DE MEDICINA DENTÁRIA
UNIVERSIDADE DO PORTO

Exmª Senhora
**Sofia Isabel Madeira Reis**
Faculdade de Medicina Dentária da U. Porto

Ref.ª 24 02 MAR 2020

**Assunto:** Parecer relativamente ao Projeto de Investigação nº 24/2019.
**(Midpalatal suture maturation and cervical vertebrae maturation: a CBCT comparative study).**

Informo V. Exa. que o projeto supracitado foi analisado na reunião da Comissão de Ética para a Saúde, da FMDUP, no dia 14 de fevereiro de 2020.

A Comissão de Ética é **favorável** à realização do projeto tal como apresentado.

O formulário definitivo de apresentação do trabalho, aprovado e carimbado pela Comissão de Ética para a Saúde, da FMDUP, acompanha a presente comunicação.

A Comissão de Ética recomenda a existência de um seguro de responsabilidade civil e relembra que a inexistência de seguro responsabiliza diretamente os investigadores.

**Subject:** Recommendation on the research project nº 24/2019.
**(Midpalatal suture maturation and cervical vertebrae maturation: a CBCT comparative study).**

I hereby inform that the aforementioned project was analyzed on the 14th day of february, 2020, by the Ethics Committee for Health of the Faculty of Dental Medicine,

The Ethics Committee is **favourable** to the project execution.

The final submission form approved and stamped by FMDUP's Ethics Committee for Health is attached.

The Ethics Committee recommends the existence of liability insurance and recalls that the absence of insurance directly holds researchers accountable.

Com os melhores cumprimentos,
A Presidente da Comissão de Ética para a Saúde, da FMDUP

Prof. Doutora Inês Alexandra Costa Morais Caldas

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## 1.3 RAI-Dental Clinic Director Approval

DENTEREAL
CLÍNICA DENTÁRIA

Porto, 04 de dezembro de 2019

Eugénio Joaquim Pereira Martins, Diretor Clínico da Dentereal Clinica Dentária de Vila Real Lda., sita na Rua Cândido Reis nº40, 5000-638 Vila Real, NIF 503214019, venho por este meio autorizar a estudante Sofia Isabel Madeira Reis a cedência dos dados clínicos necessários, conforme as considerações éticas que me são exigidas, para a realização do projeto intitulado por "Midpalatal Suture Maturation and Cervical Vertebrae Maturation: A CBCT Comparative Study" a realizar no âmbito da Unidade Curricular "Monografia de Investigação ou Relatório de Atividade Clínica" no Mestrado Integrado em Medicina Dentária na Faculdade de Medicina Dentária da Universidade do Porto.

Com os melhores cumprimentos,

(Prof. Doutor Eugénio Martins)

## 1.4 Data Protection Unit of U.PORTO Approval

| U.PORTO | Unidade de Proteção de Dados | DATA:10/01/2020 |
|---|---|---|

**PARECER A-2/2020**

| | |
|---|---|
| **Nome** | Sofia Isabel Madeira Reis |
| **Nº Mecanográfico** | 201602945 |
| **Unidade Orgânica** | Faculdade de Medicina Dentária da Universidade do Porto (FMDUP) |
| **Título** | "Midpalatal Suture Maturation and Cervical Vertebrae Maturation: a CBCT Comparative Study" |
| **Ticket Nº** | 2019112915000989 |

**Sumário do Pedido**

No âmbito da unidade curricular de "Monografia de Investigação ou Relatório de Atividade Clínica", integrada no plano de estudos do Mestrado Integrado em Medicina Dentária da FMDUP, pretende a requerente levar a cabo um estudo clínico sem intervenção, destinado a comparar dois métodos de avaliação da maturidade óssea, a partir de imagens de CBCT (Tomografia Computorizada de Feixe Cónico): a metodologia de Angelieri *et al.*, que envolve a classificação da maturação da sutura palatina, e a metodologia de Baccetti *et al.*, que avalia a maturação das vértebras cervicais. Pretende-se verificar se os dois métodos permitem a obtenção de resultados correlacionáveis.

A amostra será constituída por pacientes da Clínica Dentária Dentereal, que fornecerá os seguintes dados à investigadora, já expurgados de identificadores pessoais diretos: sexo, idade, existência ou não de aleitamento materno, telerradiografia obtida através da reconstrução de CBCT e cortes axiais de CBCT.

**Conclusões**

Considerando que,

**(1)** a Clínica Dentária Dentereal se configura como Responsável pelo Tratamento dos dados acima referidos, nos termos do art.º 4.º/7 do Regulamento Geral sobre a Proteção de Dados;

**(2)** foi autorizada pelo Diretor Clínico da referida clínica, a cedência desses dados;

**(3)** as operações de tratamento de dados a desenvolver pela requerente apenas incidirão sobre dados consideráveis anónimos, tendo em conta os meios atualmente colocados à disposição do Homem-médio para direta ou indiretamente identificar uma pessoa singular,

somos do parecer que o tratamento de dados acima referenciado não carece de autorização prévia do Senhor Reitor, pelo que poderá a requerente avançar com a sua realização, sem necessidade de mais formalismos.

**Anexos**

| | |
|---|---|
| **Anexo 1** | Autorização_Diretor_Clínico |

**a Encarregada da Proteção de Dados da Universidade do Porto**

Susana Rodrigues Pereira

**Doutora Susana Rodrigues Pereira**

Parecer A-2/2020| 1

## 1.5 Thesis Supervisor Approval

PARECER

**Monografia de Investigação/Relatório de Atividade Clínica**

Informo que o Trabalho de Monografia desenvolvido pela estudante Sofia Isabel Madeira Reis com o título "Midpalatal Suture Maturation and Cervical Vertebrae Maturation: A CBCT Comparative Study" está de acordo com as regras estipuladas na FMDUP, foi por mim conferido e encontra-se em condições de ser apresentado em provas públicas.

Porto, 20 de maio de 2020

O orientador

Prof. Doutor Eugénio Joaquim Pereira Martins

## 1.6 Thesis Co- Supervisor Approval

PARECER

**Monografia de Investigação/Relatório de Atividade Clínica**

Informo que o Trabalho de Monografia desenvolvido pela Sofia Isabel Madeira Reis com o título "Midpalatal Suture Maturation and Cervical Vertebrae Maturation: A CBCT Comparative Study" está de acordo com as regras estipuladas na FMDUP, foi por mim conferido e encontra-se em condições de ser apresentado em provas públicas.

Porto, 20 de maio de 2020

A co-orientadora

(Prof.ª Doutora Maria João Feio Ponces Ramalhão)

## 1.7 Researcher's Statement

DECLARAÇÃO

**Monografia de Investigação/Relatório de Atividade Clínica**

Declaro que o presente trabalho no âmbito de Monografia de Investigação/Relatório de Atividade Clínica, integrado no MIMD, da FMDUP, é da minha autoria e todas as fontes foram devidamente referenciadas.

Porto, 20 de maio de 2020

A investigadora

Sofia Isabel Madeira Reis

(Sofia Isabel Madeira Reis)