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Midpalatal Suture Maturation Stage Evaluation In Young Adults

Anna Maria Betlej
University of Alabama at Birmingham

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by

ANNA M BETLEJ

NADA SOUCCAR, COMMITTEE CHAIR
WILLIAM HARRELL
AMJAD JAVED
CHUNG HOW KAU

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ANNA M BETLEJ

ORTHODONTICS

ABSTRACT

Rapid palatal expansion (RPE) is a gold standard treatment for posterior unilateral and bilateral crossbites or limited buccal overjet in patients with constricted maxilla. Midpalatal suture fusion is a limitation for obtaining the skeletal results and avoiding dental side effects. It is generally believed that midpalatal suture interlock increases significantly after the pubertal growth spurt. However, in the literature there are reported cases of successful midpalatal suture split in older adults. Individual cone-beam computed tomography (CBCT) assessment of midpalatal suture maturation was proposed by Angelieri et al. Since RPE treatment approach is commonly used it is important to understand the possibility of finding non-fused suture in older patients.

Objective: To determine the prevalence of midpalatal suture maturation stages in patients 16-35 years old and within the age subgroups and to compare the midpalatal suture maturation stages between male and female in corresponding age subgroups.

Methods: For this cross-sectional study 232 CBCT scans of adult male and female patients aged between 16 and 35 years old were evaluated. These patients had CBCT taken as a part of their pre-orthodontic records. Patients excluded from this study had a history of previous orthodontic treatment that included any palatal expansion or maxillary surgery, patients with syndromes, patients with cleft lip and/or palate, patients with systemic disease or medications affecting bone metabolism, maxillofacial trauma, presence of noise or blurry images on CBCT scans. The CBCTs that fulfill the criteria will be divided into

subgroups based on two criteria, their sex (female, male) and age (16-20, 21-25, 26-30, 31-35). Patients were also classified according to their growth pattern to normodivergent, hypodivergent and hypedivergent subgroups.

Results: The prevalence of stage C was the highest and accounted for 44.8%. The prevalence of stage E was 28.9%. The prevalence stage D was 24.6%. The prevalence of stage B was 1.7%. None of the evaluated sample had stage A. There is a correlation ($p = 0.03$) between midpalatal suture maturation and the age group. There is no significant difference between males and females group. There is a trend that in hypodivergent samples, midpalatal suture matures faster.

Conclusions: In samples aged 16-25, the majority of the samples have a non-fused midpalatal suture. In samples aged 26-35, the majority of the samples have a fused midpalatal suture. Hypodivergent samples' midpalatal sutures tend to mature faster than normodivergent and hyperdivergent groups.

Keywords: midpalatal suture, maturation stages, adults

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LITERATURE REVIEW

History of Rapid Palatal Expansion

Rapid Palatal Expansion (RPE) was first reported in 1860 by E.C. Angell. He published an article in *Dental Cosmos* about the orthopedic effect of opening the mid-palatal suture (MPS) when trying to gain space in the crowded dentition of a fourteen-year-old female patient. (1) That theory was initially rejected because of difficulties in maintaining good oral hygiene and uncontrolled force levels when utilizing jackscrews. After the long span of time when rapid palatal expansion was not being used as an orthodontic treatment modality, the method was eventually reintroduced in the 1960s when radiology was popularized. Rapid Palatal Expansion regained popularity in the orthodontic field through Andrew Haas' work after over 100 years of its initial launching. (2,3)

Biological Background of Sutures and Sutural Expansion

Sutures are defined by Pritchard et al. as "the entire complex of cellular and fibrous tissues intervening between, and surrounding, the definitive bone edges". (4) Sutural cranial growth is a form of intramembranous periosteal bone formation. Two adjacent cranial bones interlock in a zipper-like articulation and they form a suture. Sutures are composed of fibrous tissue which connects cranial bones. Sutures serve as growth sites so they lack innate growth potential but they respond to outside influencing factors under certain

circumstances resulting is bone modelling. (5) If mechanical force is applied to the bone at the sutural level and results in bone separation, i.e. rapid palatal expanding device, the new bone forms in the gap and therefore the size of the bone increases. Sutural growth potential function ceases when they ossify. The MPS contributes to transverse maxillary growth, particularly that of the palate. (6–9) It is important to understand the biological process occurring in the sutures in order to realize the benefits, but also the risks, of RPE. The sutural response to the force applied by rapid palatal expanders was examined by Cleall et al. on a group Macacus rhesus monkeys. Researchers found out that the space which occurred between palatal bones, as a result of expansion, healed quickly: midpalatal suture morphology was similar to the control 3 months into retention but the adjacent bone was immature, however, 6 months into retention there was no difference between the study sample and the control . (10) Cate et al. reported similar results in terms of connective tissue response to applied force. (11) Sutural complex functional activity is described by two populations of cells, osteocytic and fibrocytic. Natural development of the suture and rapid sutural expansion showed many similarities because both the processes occur by separating the joint. Ignoring inflammation in case of rapid expansion, the suture's response consists of osteogenesis and fibrillogenesis followed by remodeling. Injury occurring during rapid expansion could leave scars, which usually happens in other tissues. However, sutural fibroblasts are able to remodel and regenerate sutures. (4,11) Haas was studying rapid palatal expansion on animals and built the basis for other researchers to investigate the topic in humans. (2,3) Finally, in 1972, Melsen published an article about radiographic and histological changes that result from rapid palatal expansion in young adolescents. Evaluation of radiographs taken 6-week post-expansion revealed that the mid-

palatal suture area was radiographically indistinguishable in comparison to the pre-treatment radiographs of the same area. Nevertheless, there was a difference in histological activity between treated group and untreated controls. In treated patients, osteoblasts along the margins of the bone were significantly active. (12) In another histological study by Melsen, autopsy material from boys and girls ages 0-18 years old was analyzed and it was found that transverse growth of midpalatal suture continued up to 16 years old in girls and 18 years old in boys. She described that postnatal development of the midpalatal suture can be divided into three stages. In the first stage the suture is short, wide and Y-shaped, in the second stage it becomes more sinuous and in the third stage suture is heavily interdigitated. Mid-palatal suture interlock increases with suture maturation, making skeletal expansion more difficult. (13) The mid-palatal suture starts its closure during the juvenile age, with a substantial degree of fusion noticeable in the third decade of life. (14,15)

Types and Designs of Expanders

The main purpose of RPE is to provide an orthopedic effect by separating two maxillary bones at the MPS level. To facilitate this process, it is necessary to apply the force that is heavy enough to split the suture. In addition to the orthopedic outcome, the force applied to the MPS through the jackscrew expander also influences the dental position of the buccal segmnets, as teeth are localized within the bone which is being moved buccally. It is important to understand the mechanism of that concurrent tooth movement to try to prevent undesired dental movements, and at the same time, enhance beneficial effects. In RPE, the force is administered using a jackscrew that is located a high as possible in the palatal vault, and aligned with the midline of the palatal bones, thus coinciding with the MPS. Since the

screw should be as close as possible to the maxillary center of resistance, it should be relatively small. At the same time, a smaller screw expands less than a larger one and therefore leads to less overall expansion dimensions. The screw position is sometimes limited by the morphology of the palatal vault. When the palatal vault is very narrow, it may be impossible to open the screw without impinging into the palatal soft tissue. However, sometimes the compromised size and position of the jackscrew is unavoidable in patients with very high and narrow palatal vaults, which leads to a modified delivery of force, because the expander's arms and bands are almost on the same plane and the force is mostly transmitted to the teeth, and not to the suture. Araugio et al. published a finite elements study on the dental effects of RPE in the context of different screw positions with respect to the center of resistance of the upper first molars. There was buccal tipping when the jackscrew was positioned below the center of resistance (CR), no tipping when the screw was at the level of CR and even palatal tipping in case of high screw position (above CR of the first upper molar). Different types of RPE were designed to minimize undesired tooth movement concurrent with suture opening. (16) The main difference between them is the way they are attached to the teeth. Bonded expanders use acrylic splints covering the occlusal surfaces of upper posterior teeth bilaterally. Banded expanders are attached to two or four teeth (molar and/or premolar) by bands. Haas believed that mid-palatal suture opening should be supported not only by teeth, but also by bone. That is why Haas-type RPE, in addition to four bands cemented on teeth, also consists of acrylic supports contacting the palatal mucosa between the teeth and the jackscrew. (17) Wertz believed that such additional bony support will favor relapse prevention when compared to purely teeth-supported RPE. (18) Later, other modalities of jackscrew expanders became

available. One of them, bonded RPE, is attached to the maxillary teeth by acrylic splints which cover occlusal surface of those teeth. This type was believed to cause less vertical changes but it was proven in the literature that there is no difference between bonded and banded RPE in regards of the outcome in vertical dimension. (19) Recently, the technology has impacted the work flow of dentistry and CAD/CAM (computer-aided design and computer-aided manufacturing) RPE's are successfully used. (20) There are also other maxillary expansion modalities are more invasive than conventional jackscrew expansion protocols but can be a more predictable choice in the older patient population. Those approaches include miniscrew-assisted rapid palatal expansion (MARPE) and surgically assisted rapid palatal expansion (SARPE). MARPE was introduced in 2010 by Lee et al. (21) This approach is the most recent treatment modality of RPE but it has gained popularity among orthodontists. One of the reasons for its wide acceptance among clinicians is the fact that the procedure does not require the involvement of an oral surgeon. Miniscrews (also known as temporary anchorage devices -TADs) are inserted in the palate after administrating local anesthesia. Depending on the author, different designs are being proposed. (22–26) The number of miniscrews incorporated into the appliance vary from 2 to 4. Those miniscrews anchor the appliance to the palate and therefore enable the force to be applied directly to the bone. However, some authors recommend that the appliance should not only to be anchored to the bone but also to the teeth. In such case, the jackscrew, additionally to being connected to palatal bone, is also connected to teeth via arms extending from the jackscrew, in a similar fashion as in traditional RPE designs. The main difference between conventional RPE and MARPE is the use of TADs that anchor the appliance to the palatal bone and therefore are able to deliver more force directly in the

sutural region with limited dental side effects when compared to conventional RPE. If conventional RPE is used when mid-palatal suture is fused, the potential side effects - such as buccal crown tipping, dehiscence, marginal bone loss, acute pain, palatal mucous necrosis and expansion failure or poor long-term expansion stability – are more likely to occur. (27,28). Another RPE approach involves surgical procedure that is typically performed under general anesthesia and involves the surgical split of MPS along with the cuts to circummaxillary sutures. After cuts are made, the jackscrew expander is cemented in the mouth and tested for its effectiveness in opening the midpalatal suture intraoperatively. This procedure is known as surgically assisted rapid palatal expansion (SARPE) and has more risks associated with the procedure than traditional RPE or MARPE, is overall more painful and expensive. (29,30)

Indications for Rapid Palatal Expansion

There are several indications for treating patients with RPE. The main one is the transverse maxillary deficiency, resulting in unilateral or bilateral posterior crossbites. Unilateral posterior crossbite is usually associated with mandibular lateral shift which is often solved by rapid palatal expansion. (18) Maxillary deficiency in the transverse dimension can affect patients with normal anteroposterior relationships, as much as patients with maxillary deficiency in all three planes and in skeletal and dental class II and class III patients. In class III patients, RPE is often used to disarticulate circummaxillary sutures and facilitate better outcome when using protraction face mask for correcting the skeletal class III in growing patients. (31) In case of class II patients, who often have also transverse maxillary deficiency, when attempting the antero-posterior correction of the underlying skeletal

discrepancy by growth modification and when the correction is successfully achieved, those patients often finish with tight buccal occlusion due to insufficient transverse dimension of maxilla in relation to the mandible. Transverse maxillary deficiency is also associated with problems other than posterior skeletal crossbite like dental crowding, narrowed airways, mouth breathing, altered tongue position. (32–34)

Midpalatal Suture Growth Evaluation

Age is a limiting factor in achieving the skeletal expansion of maxilla. If expansion is attempted when sutures are ossified and the growth has ceased, it is not always possible to split the palatal suture. (35) Determining the maturation of facial sutures has been a challenge for many years. Low correlation scores between skeletal and chronological age have been reported by Fishman and therefore individual growth assessment was recommended. (36) Hand wrist radiographs are the gold standard method used to determine the skeletal age of the growing patient. Carpal radiograph analysis utilizes 11 indicators of bone maturity. They appear on the hand wrist x-ray successively until the end of adolescence. However, while mandibular growth has been correlated to the maturation of carpal bones, the correlation does not apply to the maxilla. (37) The midpalatal suture maturation assessment was attempted by using occlusal radiographs but it turned to be unreliable due to the vomer and other nasal structures superimposing on the palatal suture area, together with the problem of the direction of the beam in relation to sutural path. (38) This limitation can lead to misinterpretation of the degree of sutural fusion. In 2013, Angelieri et al. proposed an individual evaluation method for midpalatal suture. Five maturation stages, A-E, were determined by observing the suture on CBCT scans. (39)

According to this classification sutural resistance is gradually increasing from stage A to E. In stages A and B suture is not fused and the RPE would result in greatest skeletal expansion. In stage C suture is mainly not fused but some areas of fusion may be observed. In stages D and E there is significant fusion of the suture and surgical expansion approach is indicated. In 2017, Grunheid et al. studied different methods to predict the skeletal response to RPE in 30 patients treated with maxillary expansion. They concluded that the method based on the density ratio of the suture had the best correlation with amount of achieved skeletal expansion when compared to chronological ages and maturational stages. (40) However, this study had some limitations including its retrospective design, limited sample size, different expansion protocols and timing of evaluation of the post-treatment effects.

Treatment Timing for Rapid Palatal Expansion

Rapid palatal expansion (RPE) is an orthopedic intervention that requires relatively heavy forces to facilitate the opening of the midpalatal suture. As a result of applying heavy forces to the maxillary bone through the activation of jackscrew anchored to maxillary teeth, the collagenous fibers stretch and new bone forms between the two halves of maxilla. As this newly formed bone matures, the maxilla is expanded and the transverse maxillary deficiency is being addressed. (28) The recommended timing for non-invasive treatment of transverse maxillary deficiencies using conventional RPE is relatively early in life and usually takes place before the growth spurt. (27,28) However, it was reported in the literature that MPS maturation is weakly correlated with chronological age and sex. (39) Currently, RPE is a gold standard in treating maxillary transverse deficiency in a young

patient population with various malocclusions. (29) The dental side effects related to RPE treatment are most noticeable when conventional RPE is used in patients whose midpalatal suture fusion reaches more advanced stages (41). MARPE was introduced to limit those dental side effects by delivering the force directly to the bone. It is reported to be successfully used in patients after their pubertal growth peak. The reported success rate of MARPE in adult patients between 16-26 years old has been reported to vary between 84.2% to 86.96%. (21,42) Therefore, while MARPE is more successful at splitting the palatal suture in young adults when compared to RPE, a percentage of adult patients still need to be treated with a surgical approach. (43) MARPE has not been widely accepted by clinicians mainly due to skepticism regarding the chances of splitting the fused suture, but also due to the TADs inserting procedure being involved. In case of SARPE, age is not a limiting factor since the suture is separated surgically and the jackscrew is used to perform the expansion with the pace that enables bone to fill the gap and heal in more biological pace and with less relapse involved, when comparing to traditional segmented Le Fort 1 osteotomy. (29)

Skeletal Effects of RPE

Because multiple problems that are addressed by the RPE treatment are dental manifestations of underlying skeletal discrepancies, it is essential to assess the changes in skeleton and the force system delivered by RPE. Many research projects were designed to study this topic. Krebs found that treatment with RPE influences maxilla rotation in both horizontal and frontal plane. (44) Wertz evaluated the effects of RPE treatment on patients, and additionally two supplemental dried skulls for comparison. It was observed that due to

the fact that the location of the center of resistance is close to the fronto-maxillary suture, the maxillary arch does a downward movement during mid-palatal suture opening with RPE and both alveolar halves of the maxilla, tip buccally. This gives the effects of pyramidal shape of sutural opening with the tip of the pyramid in nasal cavity. (45) Haas studied cephalometric radiographs and found a 0° to 2.5° increase in SNA angle values. Initial outcomes were not indicating the predictable results. In Wertz's study, sixty patients treated with RPE Haas-type appliance were examined. Assessment of cephalometric radiographs showed a small maxillary downward displacement, with usual little forward movement, but occasional distal displacement. Vertical displacement of the maxilla was variable, sometimes moving superiorly and in other instances moving inferiorly. Wertz found the mandibular plane angle to nearly always open with RPE treatment. This effect was attributed to the occlusal interferences caused during expansion. Considering stability, Wertz found that the mandibular plane angle almost always returned to close to pre-treatment values. ANB measurements were irregular, and so was the inclination of the maxillary incisors. Regarding differences in terms of the age of the patients, Wertz found that younger patients had a greater component of skeletal changes than those who were older at the beginning of treatment. Wertz found no gender-based differences in response to RPE treatment. (18) Another study by Sarver and Johnston evaluated maxillary displacement differences with bonded and banded expanders. The study was driven by the investigators' aspiration to prevent unwanted skeletal changes in certain facial types. (46) Many orthodontic patients have combined skeletal problems that might include open-bite tendency, Class II, and long faces. Such patients can be candidates for RPE treatment as they may have constricted maxillary bones. However, care needs to be taken to limit

undesired skeletal effects already described by Wertz. (18) Sarver and Johnston found that the bonded appliance was effective in slightly tipping the posterior part of the palatal plane, causing a posterior movement of the maxillary central incisors, and a posterior and downward movement of the anterior portion of the maxilla. (46) Haas found it useful to utilize vertical pull chin cup for long-face patients, regardless of whether or not they are undergoing RPE treatment. He noticed that for patients undergoing therapy with RPE, the vertical pull chin cup is beneficial in order to control vertical dimension while opening the mid-palatal suture. (47) In addition to Haas, Schulz also focused on analyzing the effects of RPE on patients with tendency to excessive vertical growth. The results revealed that in the group of patients treated with RPE vertical pull chin cup and fixed appliance, there was significantly less change in vertical dimension in comparison to the group treated only with RPE and fixed appliance. (48) Cozza et al. assessed skeletal changes correlated with RPE in patients with class II with mixed dentition. The appliance was attached to the second primary molars. They noticed that at the time of RPE removal the total anterior facial height significantly increased in comparison to control group. (49) Lagravère et al. conducted a meta-analysis evaluating changes associated with RME and found that the mandibular plane angle was opening, and the values were statistically significant. (50)

Dental Effects of Rapid Palatal Expansion

Molar tipping is an apparent outcome of the treatment with RPE. There have been contradicting reports regarding the final angular position of the maxillary molars following expansion. Most of the researchers are in agreement that the molars that anchor the

RPE appliance tip buccally as a result of maxillary expansion. But there is a question whether the movement that is categorized as tipping at the beginning of expansion is a pure tipping or the combination of inclination and movement. (45) If we consider the fact that while opening mid-palatal suture the alveolar bones are rotating buccally, then what can be noticed is that the maxillary molars could present tipping movements due to the rotation o the maxillary segments in a buccal direction. As the teeth are located in that bone, they exhibit buccal tipping which might be a result of maxillary bone tipping and not by real tipping of the teeth. (51) Both maxillary and mandibular arch perimeter and arch depth have also been shown to increase immediately following RPE therapy, as well as after the second phase of the treatment which usually is completed with fixed appliances. (52) Patients with constricted maxillae who need maxillary expansion often have constricted lower arches as a compensation of narrowed upper arch. Constricted maxillary arch keeps mandible in "the trap" as the mandible cannot grow to the sides because of lack of space. (51) Almost 60 years ago, in 1959, Haas conducted a study on pigs and observed that while the maxilla is expanded buccally, the mandibular teeth followed the same pattern and also tipped buccally in the experimental group, while showing little change in the control group. The reason for lower teeth buccal tipping was probably the effect of many variables including a change of the musculature balance between the tongue, masseter and buccinator muscles, together with a modifications of the inclination dental planes following expansion. (2) In 1954, Brodie reported that "the interaction of the forces of these two antagonistic muscles masses would dictate the size and form of the arches as well as the axial inclination of the teeth". (53) The expanded maxilla occupies more space in the mouth which leads to a decrease of the pressure on the mandibular arch. Limited pressure from

buccinators enables the pressure from the tongue to increase and expand the mandibular dental arch into outward direction. This in turn allows pressure from the tongue to expand the mandibular teeth in a buccal direction. (2)

RATIONALE

It is widely accepted that RPE is commonly successful in patients before puberty. The problem arises when orthodontists treat older patients. In these patients, Angelieri recommends acquiring CBCT images to assess the maturation stage and therefore the degree of completed fusion of the MPS for each individual. (54) Orthodontists often do not consider non-surgical approaches for maxillary transverse deficiency treatment in non-growing adults due to common belief that the midpalatal suture is fused after puberty. The knowledge of what is the possibility to find a non-fused midpalatal suture in adults, can provide with the more evidenced-based decision in regards of the treatment options in non-growing patients with skeletal transverse maxillary deficiency and posterior crossbites. In patients whose age is within the range when the incidence of non-fused midpalatal suture indicates the chance for successful non-surgical approach, additional examination, including CBCT, can be justified and utilized.

SPECIFIC AIMS OF THE STUDY

Specific Aim 1: To determine the prevalence of midpalatal suture maturation stages in patients 16-35 years old and within the age subgroups.

Specific Aim 2: To compare the midpalatal suture maturation stages between male and female in corresponding age subgroups

NULL HYPOTHESIS

We hypothesize that there is no difference in the midpalatal suture maturation stages between age subgroups in patients aged 16 to 35.

MATERIAL AND METHODS

This study is approved by the University of Alabama Institutional Review Board for Human Use (IRB-300004529). For this retrospective study, 232 CBCT scans of adult patients aged between 16 and 35 years old were evaluated. The CBCT images consisted of de-identified pre-orthodontic records and were provided by two sources: orthodontic private practice in Alexander City, Alabama and the Department of Oral and Maxillofacial Radiology at University of Connecticut both using the same imaging machine: iCAT Next Generation (Imaging Sciences International, Hartfield, PA), FOV 16 x 13 cm, resolution 0.3 mm and isotropic voxels in all three planes of space. The following inclusion criteria were used in the chart review: (1) 16 to 35 years old male and female patients, (2) CBCT was taken prior to initiation of the orthodontic treatment , (3) CBCT including the entire maxilla. The exclusion criteria were: (1) previous orthodontic treatment that included any palatal expansion or maxillary surgery, (2) patients with syndromes, (3) patients with cleft lip and/or palate, (4) patients with systemic disease or medications affecting bone metabolism, (5) maxillofacial trauma, (6) presence of noise or blurry images on CBCT scans. The CBCTs that fulfilled the inclusion and exclusion criteria were divided into subgroups, (1) their sex (female, male), (2) age (16-20, 21-25, 26-30, 31-35), and (3) vertical skeletal growth pattern (hypodivergent, normodivergent and hyperdivergent). Due to the fact that multiple CBCT's did not have Nasion point captured in the scan, Frankfort-mandibular plane angle (FMA) was used to assess divergency. Samples with FMA between 20° and 30° were classified as normodivergent, samples with FMA larger than 30° were

classified as hyperdivergent, samples with FMA smaller than 20° were classified as hypodivergent. (55) CBCT scans were imported and evaluated in the Blue Sky Plan software (Blue Sky Bio, Libertyville, IL). Initially, the head was adjusted in the coronal, axial and sagittal views, for the best view of MSP. In the sagittal plane, the palate was positioned horizontally, parallel to the software's horizontal yellow lines. When a curved, deep palate was seen in a subject, two axial view slices were recorded for more accurate visualization of the midpalatal suture according the recommendations from previous studies. (39,56,57) For the most accurate mid-palatal suture assessment, in the multiplanar reconstruction screen, the head was manipulated so that the palatal plane was perpendicular to the vertical line in sagittal view. Once the head was positioned, the axial view images will be saved in JPEG format.

One examiner analyzed the images and classified the midpalatal suture maturation stage. Suture maturation assessment was conducted according to the method proposed by Angelieri et al.(39) The classification defines 5 stages of midpalatal suture maturation: A-E. (39) Stages A, B and C are considered to be open MPS, while stages D and E are considered to be with fused MPS.

In stage A, the MPS is almost a straight high-density sutural line with no or little interdigitation.

In stage B, the MPS has an irregular shape and appears as a scalloped high-density line. There can be also some small areas where 2 parallel, scalloped, high-density lines close to each other and separated by small low-density spaces are seen

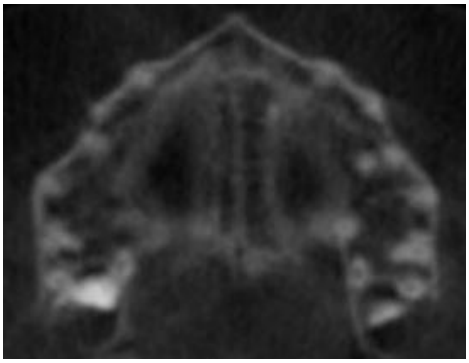

Figure 1 CBCT view of the midpalatal suture in stage B

In stage C, the MPS appears as 2 parallel, scalloped, high-density lines that are close to each other, separated by small low-density spaces in the maxillary and palatine bones (between the incisive foramen and the palatino-maxillary suture and posterior to the palatino-maxillary suture). The suture can be arranged in either a straight or an irregular pattern.

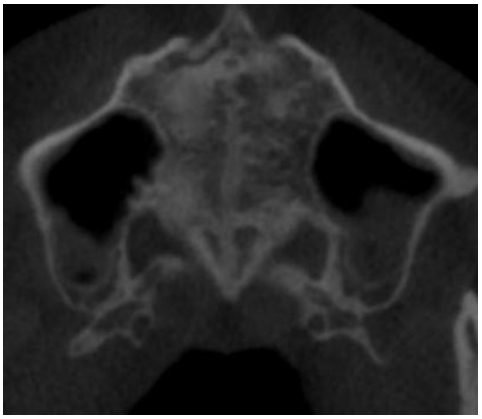

Figure 2 CBCT view of the midpalatal suture in stage C

In stage D, the fusion of the MPS has occurred in the palatine bone, with maturation progressing from posterior to anterior. In the palatine bone, the midpalatal suture cannot

be visualized at this stage, and the parasutural bone density is increased (high-density bone) compared with the density of the maxillary parasutural bone. In the maxillary portion of the suture, fusion has not yet occurred, and the suture still can be seen as 2 high density lines separated by small low-density spaces.

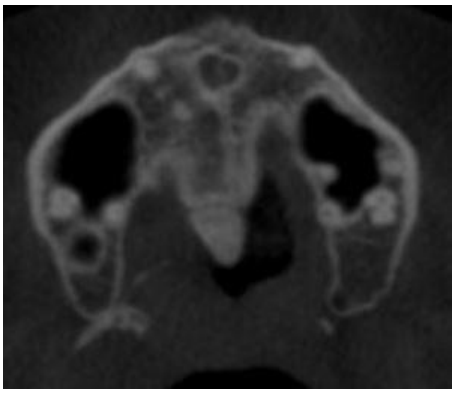

Figure 3 CBCT view of the midpalatal suture in stage D

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

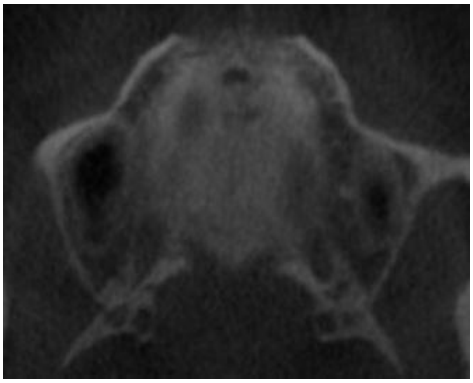

Figure 4 CBCT view of the midpalatal suture in stage E

Eight weeks later, 23 randomly selected CBCT's were analyzed again to evaluate the inter-rater reliability.

RESULTS

Evaluation of Intraexaminer Measurement Error

The agreement was measured by weighted kappa statistic with the value of 0.91 and 95% confidence interval (95%qw CI) of [0.79, 1.00], indicating a high reliability of the performed measurement and classification of midpalatal suture maturation stages.

Sample Demographics

The sample consisted of 232 subjects. It included 140 females and 92 males. The sample was divided into four age groups: 16-20, 21-25, 26-30, 31-35 years old. Each of this group consisted of: 93, 52, 42 and 45 CBCT scans respectively. The collected and evaluated CBCT scans included B, C, D and E midpalatal suture maturation stages consisting of 4, 104, 57 and 67 participants, respectively. In terms of growth status the sample included 82 normodivergent, 116 hypodivergent and 34 hyperdivergent participants. (Table 1).

Table 1

Sample Demographics

Variable	N	%
Sex		
F	140	60.3
M	92	39.7
AGE GROUP		
16-20	93	40.1
21-25	52	22.4
26-30	42	18.1
31-35	45	19.4
SUTURE		
B	4	1.7
C	104	44.8
D	57	24.6
E	67	28.9
GROWTH		
HYPER	34	14.7
HYPO	116	50.0
NORMO	82	35.3

Correlation of Age and Midpalatal Suture Maturation Stage in Males and Female

Chi-square test revealed that there is a significant association between the midpalatal suture maturation stage and age group. There is a significant correlation (p = 0.03) between midpalatal suture maturation stage and the age group. There is a trend that older groups display more advanced stages of sutural ossification and fusion.

Over 50% of patients in age groups 16-20 and 21-25 years old have the midpalatal suture maturation stage classified as B and C. On the other hand, over 50% of patients in age

groups 26-30 and 31-35 years old have the midpalatal suture maturation stage classified as D and E. None of the patients in the study was classified as stage A of midpalatal suture maturation and none of the patients in age groups 26-30 and 31-35 were classified as stage B of midpalatal suture maturation. In age group 31-35 years old, nearly 50% of the patients were had their midpalatal suture maturation stage classified as E. (Table 2).

Comparing males and females, both have similar trend in terms of the midpalatal suture maturation stage in each group age and it is very possible that there is no difference between them. (Table 3 and 4).

Table 2. Midpalatal maturation stages by age groups.

SUTURE BY AGE GROUP				
		SUTURE		
AGE GROUP	**B**	**C**	**D**	**E**
16-20	3 (3.23%)	49 (52.69%)	24 (25.81%)	17 (18.28%)
21-25	1 (1.92%)	27 (51.92%)	10 (19.23%)	14 (26.92%)
26-30	0 (0%)	14 (33.33%)	13 (30.95%)	15 (35.71%)
31-35	0 (0%)	14 (31.11%)	10 (22.22%)	21 (46.67%)
***p* = 0.03**				

Table 3. Midpalatal maturation stages by age group in females.

SUTURE BY AGE GROUP FOR FEMALE ONLY				
		SUTURE		
AGE GROUP	**B**	**C**	**D**	**E**
16-20	3 (5.56%)	29 (53.7%)	11 (20.37%)	11 (20.37%)
21-25	1 (2.63%)	19 (50%)	4 (10.53%)	14 (36.84%)
26-30	0 (0%)	9 (37.5%)	6 (25%)	9 (37.5%)
31-35	0 (0%)	7 (29.17%)	4 (16.67%)	13 (54.17%)
***p* = 0.1389**				

Table 4. Midpalatal maturation stages by age group in males.

SUTURE BY AGE GROUP FOR MALE ONLY				
		SUTURE		
AGE GROUP	B	C	D	E
16-20	0 (0%)	20 (51.28%)	13 (33.33%)	6 (15.38%)
21-25	0 (0%)	8 (57.14%)	6 (42.86%)	0 (0%)
26-30	0 (0%)	5 (27.78%)	7 (38.89%)	6 (33.33%)
31-35	0 (0%)	7 (33.33%)	6 (28.57%)	8 (38.1%)
***p* = 0.0969**				

Correlation of Age and Midpalatal Suture Maturation Stage in Normodivergent, Hypodivergent and Hyperdivergent Samples

When analyzing the midpalatal suture maturation stages and its correlation with the facial skeletal growth pattern, in the hypodivergent group there is a statistically significant correlation (p=0.0488) between the age of the patient and the sutural developmental stage. There is a noticeable trend that midpalatal suture in hypodivergent patients tend to mature faster when compared to normodivergent and hyperdivergent patient. In the youngest evaluated group age, 16-20 years old, over 60% of the patients have midpalatal suture maturation stage classified as D and E, whereas in hyperdivergent and normodivergent groups in the same age range, is it about 25% and 30% respectively. (Table 5, 6 and 7).

Table 5. Midpalatal maturation stages by age group in hyperdivergent sample

SUTURE BY AGE GROUP FOR GROWTH STATUS HYPERDIVERGENT				
		SUTURE		
AGE GROUP	B	C	D	E
16-20	1 (8.3%)	8 (66.7%)	2 (16.7%)	1 (8.3%)
21-25	0 (0%)	3 (30.0%)	2 (20.0%)	5 (50.0%)
26-30	0 (0%)	1 (33.3%)	0 (0%)	2 (66.7%)
31-35	0 (0%)	5 (55.6%)	1 (11.1%)	3 (33.3%)
***p* = 0.4884**				

Table 6. Midpalatal maturation stages by age group in hypodivergent sample.

SUTURE BY AGE GROUP FOR GROWTH STATUS HYPODIVERGENT				
		SUTURE		
AGE GROUP	B	C	D	E
16-20	1 (2.5%)	14 (35.0%)	16 (40.0%)	9 (22.5%)
21-25	1 (4.2%)	13 (54.2%)	7 (29.2%)	3 (12.5%)
26-30	0 (0%)	7 (25.9%)	10 (37.0%)	10 (37.0%)
31-35	0 (0%)	6 (24.0%)	5 (20.0%)	14 (56.0%)
***p* = 0.0488**				

Table 7. Midpalatal maturation stages by age group in normodivergent sample.

SUTURE BY AGE GROUP FOR GROWTH STATUS NORMODIVERGENT				
		SUTURE		
AGE GROUP	B	C	D	E
16-20	1 (2.4%)	27 (65.9%)	6 (14.6%)	7 (17.1%)
21-25	0 (0%)	11 (61.1%)	1 (5.6%)	6 (33.3%)
26-30	0 (0%)	6 (50.0%)	3 (25.0%)	3 (25.0%)
31-35	0 (0%)	3 (27.3%)	4 (36.4%)	4 (36.4%)
***p* = 0.3562**				

DISCUSION

Rapid palatal expansion (RPE) is indicated as a part of orthodontic care particularly when treating posterior unilateral and bilateral crossbites or tight transverse relationship of posterior dentition. (58) Treatment options for those conditions include tooth-borne expanders with or without acrylic pad support, bone-borne expanders anchored in the bone by the temporary anchorage devices (TADs), surgically-assisted rapid palatal expansion, as well as traditional surgical approach in conjunction with LeFort 1 down fracture. (27,59) The clinical decision between these treatment modalities has traditionally been based on the patient's chronological age. While there have been different publications recommending surgically-assisted palatal expansion in select cases, there is no consensus in the literature regarding the age after which this approach is indicated. Recommendations range from patients being at least 14 years old (60), 20 years old (61) , or 25 years old (62). On the other hand, many published case reports show effective treatment outcomes in adult patients when using non-surgical rapid palatal expansion. (63–66) Unsuccessful attempts of rapid palatal expansion in older patients can lead to significant side effects, such as buccal crown tipping, dehiscence, marginal bone loss, acute pain, palatal mucous necrosis and expansion failure or poor long-term expansion stability. (27,28)

In 2013, Angelieri et al. proposed the individual assessment of midpalatal suture maturation stage by using a new classification based on the evaluation of the suture on CBCT scans. They recommended completing this assessment prior to making a surgical

versus non-surgical palatal expansion treatment decision in adolescents and young adults In this article, they reported great variability in terms of the timing or midpalatal suture fusion in relation to chronological age. (39)

In our study, we evaluated 232 patients aged 16 to 35 years and assessed their midpalatal suture maturation stage on the CBCT scans. We found stage C, where the MPS appears as 2 parallel, scalloped, high-density lines that are close to each other, separated by small low-density spaces in the maxillary and palatine bones to be the most frequent measurement of the sample (44.8%). Stage A was not found our sample. Moreover, our sample exhibited statistically significant correlation ($p = 0\ .03$) between midpalatal suture maturation stage and the age group. There is a trend that older groups display more advanced stages of sutural ossification and fusion.

Males and females in our sample were not significantly different from a timing of MPS maturation standpoint. Growth studies show that the transverse dimension matures first, and that males mature later than females, but our results did not demonstrate any difference between males and females. (5) The homogeneous results between males and females observed in this study could be due to an uneven distribution of males and females (39.7% and 60.3% respectively) in our data as well as the relatively small sample size. However, the male/female distribution of our sample is in accordance with the percentage of males versus females that seek orthodontic treatment as adults. (67)

When studying age group 16-20 years old, 52.69% of the MPS were classified as stage C maturation. There were 3.23% of subjects' images that were classified as stage B. Therefore, in 56% of the CBCT images in this age group, the midpalatal suture was not fused. This finding indicates that it would be possibility to successful attempt mid-palatal

suture split with a non-surgical approach. In this age group males and females exhibited asimilar trend in terms of distribution the midpalatal suture maturation stages. Valdivia et al.'s study found that the majority of males and females in the age group 16-20 years old exhibited D and E stages of midpalatal suture maturation stages, and that stages A-C (non-fused midpalatal suture) represented 41.7% of this age group. (68) In our study, the number of CBCT images in the 16-20 years old group is 93, whereas in the study by Valdivia et al. it is 52. Our results for males are consistent with the results of Ladewig et al. that found that the prevalence of stage C maturation stage in males of age group was 52.3%, whereas in our study it was 51.28%. For females, we found stage C in 53.7% of sample, whereas Ladewig et al. found stage C in 39.7%. (57) Those differences could be a result of environmental and genetic characteristic of the evaluated sample.

In the 21-25 years old age group, the majority of the sample (51.92%) was classified as stage C of midpalatal suture maturation development (50% of females and 57.14% of males). Stages D and E accounted for less than half of the sample in this age group (47.37% and 42.86% in females and males respectively). Therefore, in our study, over half of the sample aged 21-25 years exhibited non-fused midpalatal suture therefore indicating that a non-surgical approach could be attempted. In contrast to our study, Valdivia et al. found fused mid-palatal suture (stages D and E) in 90.6% of the females and 74.4% males in the 21-25 age group. Those differences could resulted from the variations in collected sample that are relatively small and therefore might not be the most accurate representation of the general population. In both of the studies, females displayed more advanced stages of midpalatal suture maturation in this age group. In our study, stage E was not observed in any male in the 21-25 years old group. This finding could be explained by the small

number of males in this age group (N=14). According to Tonello et al., stage C is stilfavorable for obtaining maxillary expansion successfully. He justified attempting non-surgical approach in stage C patients because in this study stage C was most prevalent (50%) in the age group that is considered to have predictable results when utilizing traditional RPE protocol. (56)

In age group 26-30, majority of the samples were evaluated to have closed mid-palatal suture and exhibiting stages D and E, with the prevalence 62.5% in females and 72.22% in males. Therefore, in our study 37.5% females and 27.78% males in aged 26-30 years had midpalatal suture that was not fused. This finding could explain published case reports where midpalatal suture split was achieved without surgical approach, typically utilizing mini-screw assisted rapid palatal expansion technique (23,24,42) This technique is a treatment of choice when attempting the non-surgical maxillary expansion in adults due to other factors contributing to resistance of maxillary bone to the expansion force. Even though the patients presented in such reports do not have a described classification of the MPS maturation, they could in fact present with non-fused sutures. Palatal expansion affects the entire maxilla and maxillary expansion is a three-dimensional process which is not limited to the palate. In order for midpalatal suture to open, the left and right maxillae need to separate and this movement is a rotational movement with the center of rotation located around orbits. (25) In the older age groups it is expected to see higher prevalence of stages D and E since they represent the advanced ossification stage and fusion of the suture, making sutural expansion more challenging. Case reports generally show successful palatal expansions in older patients, however they do not indicate that successful palatal expansion should be expected to be easily and commonly achieved.

In the age group 31-35, majority of the patients had stages D and E, 70.84% of females and 66.57% of males. Those results are similar to the findings in the age group 26-30. This could suggest that after the age of 25 partial or complete fusion of midpalatal suture is more prevalent and therefore suture split less likely to be achieved without a surgical intervention. While this finding is in accordance with growth studies, it is interesting to note that, in our sample, in both males and females, around 30% of this age group was classified with stage C of midpalatal suture maturation indicating a possibility of achieving successful RPE without surgical intervention in these patients. Angelieri et al. in his study from 2017 evaluated midpalatal suture maturation stages in adults. The sample was divided into two groups, less than 30 year old and more than 30 years old. In the group that was older than 30 years old, stages D and E were found in 88% of sample. (69) In constrast, stages D and E were found in 68.9% of the CBCTs in the 31-35 group. (5) The recommendation is therefore to acquire a CBCT on adult patients who might benefit from rapid palatal expansion and grade their stage of MPS maturation regardless of age in order to develop the most appropriate treatment plan for their malocclusion.

In the recent study by Reis et al. published in 2020 they classified the midpalatal suture maturation in sample 15 to 40 years old males and females. (70) In this study, similarly to our, stage A of the midpalatal suture was not found. In study by Reis, stage B was found in 1.03% of sample, whereas in our study it was 1.72%. Stage C was found in 34.09% in study by Reis, whereas in our study in 44.82%. In study by Reis et al. stage D was found in 16.63% of sample, whereas in our it was 24.56%. Stage E was found in 48.25% of the sample in study by Reis et al, whereas it was found in 28.89% in our study. In the youngest age group, 16-20 years old, stage C was most prevalent in both of the studies. In the age

group 26-30 years old, stage E was the most prevalent in both of the studies. In the age group 31-36 years old, stage E was the most prevalent in both of the studies. In the age group 21-25 years old, in our study stage C was the most prevalent, whereas in study by Reis et al. it was stage E that was the most prevalent.Study by Reis et al. had larger sample size than our study (487 subjects and 232 respectively).

Our sample was also grouped by skeletal growth pattern and divided into normodivergent, hypodivergent and hyperdivergent subgroups. 116 (50%) CBCT images exhibited a hypodivergent skeletal pattern, 82 (35.3%) CBCT images were normodivergent and 34 samples (14.7%) were hyperdivergent. Due to relatively small sample size, those divergency groups were not further divided into males and females due to potential misleading conclusions that could be made after such categorization. In the hypodivergent group, there is a positive correlation between age group and midpalatal suture maturation stage. In the normo- and hyper- divergent groups, the correlation was not detected. In the youngest age group (16-20 years old), the observed trend is that in hypodivergent patients, the midpalatal suture matures earlier than in two other growth pattern groups. In the hypodivergent group, the non-fused midpalatal suture (stages A-C) was identified in 37.5% of the sample, in the normodivergent group it was identified in 68.3% of the sample and in the hyperdivergent group in 75% of cases. This finding is consistent with clinical experience of many clinicians that in short-faced patients it is more difficult to split the suture. It could be justified by the findings in the study by Vidalon et al. who found that individuals with a hypodivergent facial pattern have a higher height and cortical thickness of the palatal bone. (71) Similarly, Johari et al. concluded in his study that there was a

significant relationship between the mean cortical bone thickness and facial height with significantly less thickness in long faces compared to short faces. (72)

The current study had some limitations. First, the small sample size of the collected age, gender and divergency subgroups limits the generalizability of the results. Therefore, further studies with bigger sample sizes for each of the subgroups are needed to reevaluate the correlation of midpalatal suture with gender and divergency. Second, this study evaluated only the midpalatal suture maturation, whereas the previous studies indicated that several more cranio-facial complex sutures and structures, including pterygomaxillary suture and zygomatic buttress can affect the ability to open the midpalatal suture.(73,74)

CONCLUSIONS

In patients aged 16 to 35 years old, stage C of midpalatal suture maturation stage was found most frequently. In the 16-25 years age group, the majority of patients have a non-fused midpalatal suture. In the 26-35 age group, the majority of patients have a fused midpalatal suture. Hypodivergent samples' midpalatal sutures tend to mature faster than normodivergent and hyperdivergent groups. There is value is assessing the stage of mi-palatal suture maturation prior to committing to a surgical treatment plan, particularly in normo- and hyperdivergent patient.

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APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

470 Administration Building
701 20th Street South
Birmingham, AL 35294-0104
205.934.3789 | Fax 205.934.1301 | irb@uab.edu

NHSR DETERMINATION

TO: Betlej, Anna Maria

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance Number FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 21-Jan-2020

RE: IRB-300004529
Midpalatal Suture Maturation Evaluation in Young Adults.

The Office of the IRB has reviewed your Application for Not Human Subjects Research Designation for the above referenced project.

The reviewer has determined this project is not subject to FDA regulations and is not Human Subjects Research. Note that any changes to the project should be resubmitted to the Office of the IRB for determination.

if you have questions or concerns, please contact the Office of the IRB at 205-934-3789.

Additional Comments:

De-identified data from a non-research source

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