Cone-Beam Computed Tomography Analysis of Nasal Septum Changes Caused by Rapid Maxillary Expansion in Adolescent Patients with Mild to Moderate Septal Deviation

by

Tehnia Aziz

A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Science
in

Medical Sciences - Orthodontics

University of Alberta

Abstract

Objectives: The objective of this thesis was to analyze cone beam computed tomography (CBCT) images to measure potential changes in nasal septal deviation (NSD) from rapid maxillary expansion (RME) treatment in a sample of adolescent patients.

Methods: This retrospective study involved 26 patients that incidentally presented with mild to severe septal deviation and treated for transverse maxillary constriction with RME. A control group of 7 patients was also identified without RME treatment that presented with mild to severe baseline deviation. CBCT images were taken at T1 (before appliance insertion) and T3 (6 months after appliance removal) and were analyzed to measure changes in nasal septal deviation.

Results: Repeated measures ANOVA and non-parametric Wilcoxon related samples test resulted in no significant changes in NSD with or without RME treatment and irrespective of baseline deviation.

Conclusion: Rapid maxillary expansion treatment did not result in significant changes in NSD.

Preface

This thesis is an original work of Tehnia Aziz. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Board, project name "Analysis of two and three dimensional changes of nasal septum from rapid palatal expansion in adolescent patients with mild to moderate to nasal septal deviation", Number: Pro 00041136, Date: September 10th, 2013.

Chapter 2 of this thesis has been published as Aziz T, Biron V, Ansari K, and Flores-Mir C, "Measurement tools for the diagnosis of nasal septal deviation: a systematic review", *Journal of Otolaryngology, Head and Neck Surgery* 2014, vol 43, issue 1, doi:10.1186/1916-0216-43-11. I was responsible for the data collection and analysis as well as the manuscript composition. Ansari K assisted with the data collection and contributed to manuscript edits. Biron V formatted and contributed to manuscript edits. Flores-Mir C was involved with concept framework and manuscript edits.

Chapter 3 of this thesis has been published as Aziz T, Ansari K, Lagravere MO, Major MP, Flores-Mir C, "Effect of non-surgical maxillary expansion on the nasal septum deviation: a systematic review", *Progress in Orthodontics*. 2015;16:15. doi:10.1186/s40510-015-0084-y. I was responsible for the data collection and analysis as well as the manuscript composition. Ansari K assisted with the data collection and contributed to manuscript edits. Major M and Lagravere MO formatted and contributed to manuscript edits. Flores-Mir C was involved with concept framework and manuscript edits.

Acknowledgements

Thank you to my “dream” thesis committee of Drs. Flores-Mir, Lagravere and M Major for the thesis concept, valuable feedback and constant encouragement. I could not have done this project without your support. A special thanks to my supervisor and my mentor Dr. C Flores-Mir for putting up with me for the last five years and supervising two master degrees with such patience and kindness.

I wish I had words to thank my best friend and husband Kal, not only being my biggest source of inspiration in life, but also for the numerous hours he spent in fruition of this thesis project, even after long days of work and numerous other commitments.

To my amazing mother, who put everything on hold in her life just to better mine. To pack up everything, leave her professional life and move halfway across the world to help me is something I can never repay her for.

And, how could I forget to acknowledge the three joys of my life, Aahil, Almir and Aaira………because my world is so much of a better place with their loving hugs, smile and kisses.

Table of Contents

Appendices

List of Tables

List of Figures

List of Abbreviations

AR	Acoustic Rhinometry
BAME	Bone Anchored Maxillary Expander
CBCT	Cone Beam Computed Tomography
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
EMBASE	Database (Experta Medica Database**)**
MCA	Minimal Cross sectional Area
MEDLINE	Database (Medical literature Analysis and Retrieval System Online)
MPR	Multi Planar Reconstruction
NAR	Nasal Airway Resistance
NPV	Negative Predictive Value
NSD	Nasal Septal Deviation
NSSA	Nasal Spectral Sound Analysis
OR	Odiosoft-Rhino
PNIF	Peak Nasal Inspiratory Flow
PPV	Positive Predictive Value
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
RCT	Randomized Controlled Trial
RMM	Rhinomanometry
RME	Rapid Maxillary Expansion
SN	Sensitivity
SP	Specificity
TAME	Tooth Anchored Maxillary Expander
VAS	Visual Analog Score

Chapter 1

Introduction and Literature Review

1.1 Introduction- Statement of Problem

Rapid maxillary expansion (RME) is routinely used in orthodontic treatment to correct transverse maxillary constriction by opening of the mid-palatal suture (1). Inadequacy of nasal airway can necessitate mouth breathing, causing moderate to severe maxillary constriction, vertical skeletal growth pattern characterized by long anterior lower face height, bilateral maxillary cross-bite, high arched palate, low tongue posture and incompetent lips (2,3). Moss (4) has hypothesized that nasal breathing is a requirement for proper growth and development of the craniofacial complex. According to his functional matrix theory, nasal airflow is a continuous stimulus for lowering of the palate and for lateral maxillary growth, indicating a close relationship between nasal breathing and dentofacial morphology. Several studies (3,5-8) have investigated the effects of RME on nasal airway and have reported some beneficial side effects, that may include increase in nasal cavity size vertically due to lowering of the palatal floor and horizontally due to lateral displacement of the nasal walls. Some studies have hypothesized that an increase in the vertical dimensions of the nose from RME may also increase the length of the nasal septum thereby correcting nasal septal deviation (9-11). Further investigation of this potential effect would be beneficial, because septal cartilage can act as a growth center in early development, its deviation can cause distortion of the maxillary complex towards the deviated side (10). To our knowledge, only two studies (10,11) utilizing coronal views from posterior anterior radiographs have reported a favorable improvement of septal deviation post palatal expansion in growing patients. However, analysis of a three-dimensional structure in a single two-dimensional coronal view is rudimentary at best. Major limitation of these studies was lack of standardization in the study design. In other words, it was unclear whether both pre and post expansion radiographs measured the septal change at a set landmark. Although, improvement in nasal septum was reported post expansion, it was not clear whether the change was same at the same anatomical location. Furthermore, the septal changes could not be measured in entirety in a single 2-D coronal view.

Cone beam computed tomography (CBCT) has recently gained popularity in orthodontics in imaging of the dentofacial structures due to its accessibility, relatively low cost and radiation exposure compared to conventional computed tomography (CT) (12). Nasal breathing is a pre requisite for proper growth of the craniofacial complex. Moderate to severe nasal septal deviation (NSD) can cause nasal obstruction, implying that clinically significant NSD can have irreversible repercussions on growth and development of craniofacial structures. Whether RME is beneficial in reducing the effect of nasal obstruction from deviated nasal septum in growing patients has not been investigated intensively. Therefore, the purpose of this study is to analyze nasal septal changes in 3-D and to improve our understanding of the effects of RME on nasal septum.

1.2 Research Question

Does nasal septal deviation as objectively measured from CBCT images in coronal and axial views, improve in adolescent patients with rapid maxillary expansion treatment compared to a cohort of patients with nasal septal deviation but without rapid maxillary treatment?

1.3 Hypothesis

$H_{0:}$ There is no difference in nasal septum deviation as measured in coronal and axial views on CBCT between an adolescent patient cohort who received rapid maxillary expansion and a cohort that did not receive rapid maxillary expansion as part of their orthodontic treatment regimen

$H_{A:}$ There is a difference in nasal septum deviation as measured in coronal and axial views on CBCT between an adolescent patient cohort who received RME and a cohort that did not receive rapid maxillary expansion as part of their orthodontic treatment regimen

1.4 Literature Review

1.4.1 Role of Nasal Septum

The nasal septum is an important functional and aesthetic structure of the nose. It is responsible for regulating airflow through the nose while lending shape to the nasal dorsum and caudal aspect of the nose. The 10-15 degree junction between the nasal septum and the caudal border of the upper lateral cartilage in the anterior part of the nose forms the functionally important “internal nasal valve ”. The internal nasal valve generates greatest resistance in the respiratory tract, and therefore is a major flow-limiting segment. This allows the inspired airflow to be slowed and changed into appropriately directed laminar airflow stream, allowing for optimal modification of the inspired air by the nasal cavum. The nasal cavum’s lateral walls consists of three turbinates surrounding sinus drainage pathways that increase the surface area of the mucosa available to warm and humidify the inspired air for optimal gaseous exchange in the lungs. Without nasal septum this would not be possible.

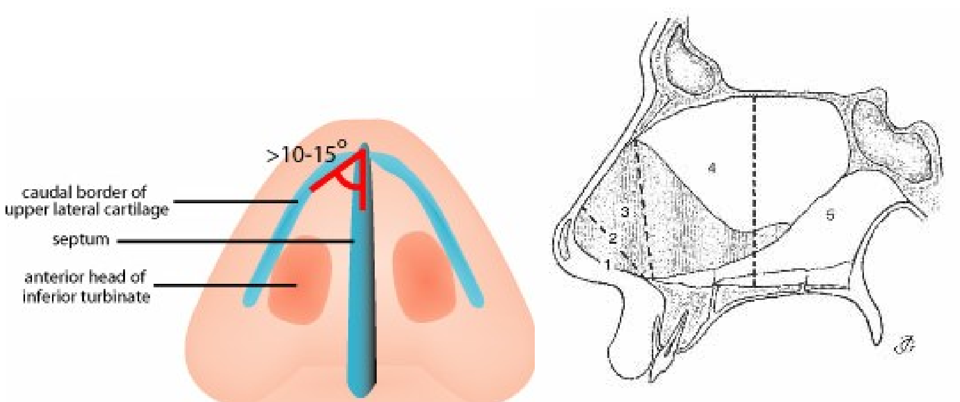


Figure 1. 1 (Left) 2 (Right): Internal Nasal Valve

Figure 1: Axial view (looking into the nasal cavity from inferior aspect)

Angle between the Nasal septum and Upper lateral cartilage

Figure 2: Sagittal view of the Nasal Septum

Area 1: Nostril. Area 2: Nasal valve. Area 3: Area underneath the bony and cartilaginous vault, also called the attic. Area 4: Anterior aspect of the nasal cavity including the heads of the turbinates and the infundibulum. Area 5: Posterior aspect of the nasal cavity, including the tails of the turbinates. (Adapted from Egbert H et al. Incorrect terminology in nasal anatomy and surgery, suggestions for improvement. Rhinology, 2003; 41:129-133)

Intrinsically, the nasal septum consists of cartilage and bone that is covered by mucous membranes. The perpendicular plate of ethmoid joins inferiorly with the Vomer bone forming a "V-like" junction. The quadrangular septal cartilage attaches to the "V-like" junction and projects anteriorly to form the external nose. Perpendicular plate of the ethmoid, vomer and quadrangular septal cartilage make up bulk of the nasal septum and are situated medially. There are other minor contributions of the septal anatomy as well. Anteriorly and superiorly, the perpendicular plate of the ethmoid articulates with the nasal spine of the frontal bone and the midline fusion of the nasal bones. The posterior border of the perpendicular plate of ethmoid is the sphenoid crest. The vomer joins the nasal crest of the palatine bone in the most posterior and inferior aspect of the nasal septum (13).

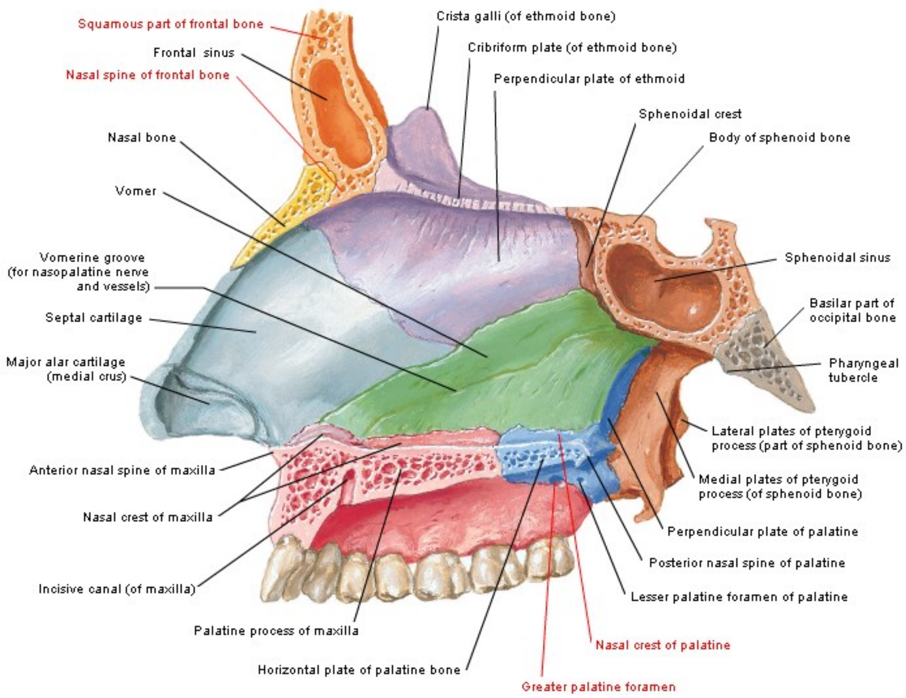


Figure 1.2 : Anatomy of the Nasal Septum

Nasal septal deviation (NSD) is defined as deviation of the either the bony or cartilaginous septum or both. The earliest investigation reported 80% of humans having some degree of septal deviation. An examination of 2,112 adult skulls in the late 1970's found only 21% of nasal septum to be straight with 37% of septa to be deviated and 42% as kinked. Kinking was considered when septal deformity involved spur formation of the vomer, perpendicular plate of ethmoid and/or the quadrilateral cartilage(14).

Prevalence range of NSD in neonates has been reported as one (15) to roughly twenty percent (16). In school aged children (6-15 years) it was documented as 20% when assessed on occipitomental projection radiographs, whereas the clinical diagnosis of NSD was made in approximately 10% of the same cohort of children (17). Thus far, there appears to be no consensus on diagnosis of nasal septal deviation by a single diagnostic tool or a universal protocol, which explains the large ranges reported in prevalence.

Septal deviation can arise from a multitude of factors. Any disturbance in the embryologic development of the nasal complex can lead to a deviated nasal septum. Increased intra uterine pressure and trauma during birth could be another cause. Kawalski et al investigated the prevalence of septal deviations in newborns and found that it can be as high as 22% in children delivered vaginally, while birth from a Caesarean section resulted in a low 4% rate (16). Other causes could include trauma from injuries, genetic connective tissue disorders such as Marfan syndrome (18), infections or nasal cavity neoplasms (19). Anomalies of the sinonasal complex such as nasal polyps, concha bullosa, or turbinate enlargement have been reported to contribute to septal deviation (20). Morphological changes of the nasomaxillary complex have also been implicated in having an effect on nasal septum. One study (21) has suggested asymmetry of the nasal floor from irregular maxillary shape to be the cause of a certain types of deviations. Another (22) hypothesized that a long caudal process of the quadrangular lamina can be associated with septal deformities more than a short one. Furthermore, long sphenoidal process of the septal cartilage, a remnant cartilaginous tail of the nasal septum resulting from its delayed ossification can also be associated with septal deviation (23).

Deviated nasal septum can result in nasal obstruction and crooked nose deformity. In cases of extreme deviation, laminar airflow is disturbed which adversely affects vital respiratory functions of the nasal cavity such as warming, humidifying and filtering of the inspired air (13). A deviation as small as 3 mm in the anterior nasal valve area can alter airflow and increase nasal resistance (24). A patent nasal airway in infants is requirement for proper feeding and any impediment in nasal breathing can lead to choking and hypoxia (16). In adults, the nasal obstruction from deviated nasal septum causes turbulent nasal airflow precipitating in dryness and crusting of the nose, frequent nosebleeds and recurrent sinusitis (25). Long face syndrome could be another sequelae of chronic mouth breathing due to septal deviation. Patients would manifest a retrognathic maxilla, posterior rotation of the mandible, increased lower facial height, lip incompetence, narrow alar base and dental malocclusions (26)

Effect of septal deviation on nasal airflow was demonstrated in decongested and untreated nasal cavities. Septal deviations as small as 3mm at the internal nasal valve area (narrowest portion of the nasal cavity) produced increases in nasal resistance and conversely decreased airflow. This finding is congruent with Poiseuille 's law, which suggests that small decrease in diameter of nasal airway will result in exponential decreases to the fourth power in airflow. As one progresses distally in the nasal cavity, it's cross sectional area increases. Therefore, obstructions of 5 mm from NSD found more posteriorly had a lesser effect on nasal resistance. In decongested noses, 3mm of NSD in the anterior region had no effect, but 4mm of deviation significantly increased nasal airway resistance in both control and decongested patients. The reason being that decongestion reduces mucosal engorgement in the area of nasal lumen, making it less sensitive to changes in cross sectional area. It is the anterior part of the nose that is extremely vulnerable to even minor changes (1mm) in the diameter of the nasal lumen (24). Magnusson et al inferred that small changes in cross sectional area in the anterior most area of the nose i.e. nasal valve area, may play a vital role in subjective sensation of nasal obstruction (5).

1.4.2 Quantification/ Classification of Nasal Septal Deviation

There appears to be a lack of consensus on the current classification systems of septal deviation. Both quantitative and qualitative approaches have been utilized, with numerical methods focusing on quantifying the severity of NSD based on nasal airway resistance (27). The earliest qualitative systems classification system was were based on rudimentary subjective visual observations, dividing NSD's into two categories, namely kinked and deviated, without much focus on the anatomical location (14). Later, a refined classification system by Mladina et al (28) illustrated seven types of septal deviation based on location that were easily identified on a clinical examination (Figure 1.3). These are described as follows:

Type 1. Unilateral vertical septal ridge in the valve region of the nose that does not reach the valve and therefore does not change the valve angle. This type of deviation plays a minor role in nasal pathology and might not be clinically significant.

Type 2. Unilateral vertical septal ridge in the valve region that touches the nasal valve and therefore reduces the valve angle.

Type 3. Unilateral vertical ridge that is located more deeply in the nasal cavity, opposite to the head of the middle turbinate

Type 4. S-shaped deformity of the nasal septum. Bilateral deformity consisting of type 2 on one side and type 3 on the other.

Type 5. Horizontal septal spur that sticks laterally and deeply into the nasal cavity. The opposite side of the nasal cavity is flat.

Type 6. Large unilateral intermaxillary wing with a "gutter" between it and the rest of the septum on one side. Contralateral side has an anteriorly positioned basal septal crest.

Type 7. Variable combination of types 1-6.

This study also concluded that the most common septal deviation was Type 3 (20.4%). Type 2 and 1 have similar incidence (16.4% and 16.2 %

respectively). Type 5 was (14%) and Types 6,4,7 were less frequent (9.4%, 8.7% and 4.1% respectively). However, a major criticism of this classification system was that that it only describes the shape of the nasal septum without any consideration to concomitant nasal pathology. Baumann et al (29) circumvented this limitation by defining six types of septal deviation with frequent and concurrent pathologies of the middle and inferior turbinates. This classification system is described in Table 1.1 and Figure 1.4.

1.4.3 Maxillary Expansion and Nasal Cavity Changes

Transverse maxillary constriction is a common skeletal deformity encountered in orthodontic practice with prevalence ranging from 2.7 – 23.3 % (30). Depending on its severity, unilateral or bilateral posterior cross bite occurs along with crowding of the dental arches, high arched palate, elevation of the nasal floor and oral breathing pattern (2). Maxillary transverse expansion is mainly employed in orthodontics to correct the transverse maxillary deficiency, posterior crossbite and dental crowding. This can be accomplished by a variety of appliances and treatment protocols with different rates of expansion according to patient's age and needs (31). Rapid maxillary expansion (RME) works by separation of the two halves of the palatal bones across the median palatal suture due to a lateral force from the appliance (32). Both the zygomatic and sphenoid bones of the cranial base are met with resistance during expansion, therefore the separation of maxillary bones occurs in a triangular manner, with apex towards the nasal cavity and base at the same level as the palatine process (33) resulting in more opening anteriorly than posteriorly (34).

The effect of rapid maxillary expansion on the nasal cavity was reported as early as 1961 when Haas (33) discovered that widening the maxilla from expansion resulted in an increased nasal width of 2-4.5mm with an expansion protocol of 0.4 to 0.5mm per day for 12 to 27 days in his patient cohort. It was postulated that the alteration in nasal dimensions following RME is related to the lateral movement of the nasal walls (33), increase in vertical dimension of the nasal cavity secondary to inferior rotation of the palate (32) and correction of deviated nasal septum (11). Due to the triangular expansion of the naso-maxillary complex with sutural opening maximal in anterior palate region, there is greatest improvement in airway patency at the internal nasal valve region with concomitant increase in inter-alar width (35). In other words, RME is considered to modify the nasal valve area, which represents the narrowest nasal cross-sectional area, and therefore greatest contributor to nasal airway resistance during breathing. Interestingly, patients with maxillary deficiency in the transverse dimension also have small nasal cross-sectional areas (36), which can explain the reason for maxillary expansion having a positive effect on nasal airway. Rhinomanometric evaluation has demonstrated that even a minor alteration in the nasal valve region can cause a disproportionately large change in the nasal airway resistance. Conversely, large changes in the posterior part of the nasal cavity cause disproportionately small changes in nasal resistance (37). In other words, rapid palatal expansion can decrease nasal airway resistance as it preferentially targets the anterior and inferior aspect of the nose leading to decrease in nasal airway resistance (38). However, there is significant variability in individual responses and there appears to be a weak correlation between decrease in nasal airway resistance and subjective improvement in nasal function (5).

Numerous studies have attempted to quantify changes in the nasal region from RME. Earlier studies quantified nasal changes on posterior anterior (PA) cephalograms. Da Silva et al documented a mean increase in intranasal width of 2.08 mm in his cohort of 8-year old patients post RME based on posterior anterior (PA) radiographs (39). Similarly, another study reported a mean gain of 1.06 mm in the maximum diameter of the lower nasal cavity and an increase in nasal height after RME treatment in teenagers (40). Hershey et al (41) reported an increase in transverse dimension of the anterior part of the nasal cavity from 1 to 3 mm when the region of maxillary molar/premolar region was expanded from 8-11 mm. The greatest reduction of nasal airway resistance occurred in patients with substantial initial nasal airway resistance (NAR). Although, in these patients NAR was stable during the 3-month retention period, it was also noted that some patients did not respond to RME with decrease in nasal resistance. It was hypothesized that those patients had persistent nasal obstruction from either mucosal swelling from environmental allergens, frequent upper respiratory tract infections and/or adenoid hypertrophy.

Due to individual variation in treatment response to RME, improvement in nasal airway resistance from it is not unanimously agreed upon in the literature (42). It was proposed that growth of the facial structures could decrease nasal resistance by approximately 0.1cm H_2O/L/sec per year (43). Although, this effect is minimal over a year, high forces resulting from palatal expansion could induce internal remodeling of the bones of the nasal cavity. In fact, some resorption of internal nasal cavity is a consequence of normal growth and development. Upper airway lymphoid tissue shrinkage was another reason for decrease in nasal airway resistance (at age 10) (42). Enoki et al (34) suggested that although there is an increase in the size and volume of the nasal cavity from RME resulting in a decrease in nasal airway resistance, there could be compensatory inferior turbinate hypertrophy nullifying the decrease in overall nasal airway resistance. In other words, this compensatory inferior turbinate hypertrophy negates any increases in the minimal cross sectional area at the nasal valve area region from RME, and was offered as an explanation for the conflicting results in the literature (34).

It has been documented that nasal width increases more if RME is done before the growth spurt (2.3mm) versus at or after the peak growth (1.5mm). Incomplete calcification of the midpalatal suture in growing patients translates into ease of displacement of the lateral walls of the nasal cavity (3). Rapid maxillary expansion treatment in mixed dentition i.e. prior to midpalatal suture closure has greater improvement in nasal airway resistance due to greater likelihood of skeletal change (nearly 50%) as opposed to during adolescence when the change is mostly dental. Although the orthopedic effect of RME is usually noted in the anterior and inferior portion of the nasal cavity, improvement in posterior and superior regions have been identified in the children younger than 12 years of age (8). A recently published systematic review concluded that there is "moderate" evidence in the literature to suggest that RME treatment during the growth increases the nasal cavity width, decreases the nasal airway resistance and therefore improves nasal airflow. In addition, stability of changes can be observed for at least 11 months. However, due to individual variation in treatment response further investigation is warranted and maxillary expansion for the sole purpose of improving nasal breathing should not be done without an a comprehensive assessment and input by an otolaryngologist (6).

Although there are numerous reports of the effects of RME on nasal airway, there is a dearth of studies in the literature on the effect of RME on nasal septum. Earliest finding of this effect came from Gray (11), whereby a subjective visualization of PA radiographs depicted an improvement in the "curve" of deviated nasal septum after RME treatment. The sample size in this study consisted of 310 patients ranging from ages 4-24 years of age with majority (86%) of the patients under the ages of 12. This implies that a greater degree of skeletal change was noted in this cohort due to patent mid palatal suture. Subjective improvement of nasal airway was also reported in these patients with improvement stable at 6 months post expansion. Approximately 80 percent of patients reporting switching from mouth to nasal breathing post expansion with a significant reduction (roughly 60%) in colds, sore throats, ear infections and nasal allergies. It was hypothesized that improvement of nasal ventilation from RME prevented dryness and crusting of the nasal mucosa thereby reducing recurrent upper airway infections. Improved ciliary function and normal nasal cycle function were among other benefits noted from increased nasal airflow resulting from RME. More recently, Farronato et al recruited 100 growing patients (ages 5-9 years, average 7.62 +/- 0.7) presenting with transverse maxillary constriction and measured an increase of 2.3mm in the width of the nasal cavity with a 94% reduction in the septal deviation. The NSD correction was noted in the inferior and middle half of the nasal cavity when compared to a non-expansion control group. Septal correction was measured by placing points on superior, middle and inferior segment of the septum as visualized from pre and post expansion PA cephalograms. Distances between these landmarks and distance (deviation) of these landmarks from an imaginary straight line in coronal view was measured. The resulting change was quantified as millimeter and as a percentage. Patient sample in this study had septal deviation of at least 1mm in middle/ inferior third of the septum as visualized as a deflection in the vertical path from superior to inferior on PA (coronal view) X-rays(10).

1.4.4 CBCT

Two-dimensional (2-D) imaging such as panoramic and cephalometric radiography is routinely used in an orthodontic practice for diagnosis and treatment planning. In 2-D radiography a parallel relationship needs to be established between the object and the image plane. Since X-ray beams are non-parallel, size of anatomical structures are dependent on distance between the focus, object and X-ray film (44). Tsao et al (45) have reported image foreshortening of as much as 69 percent and elongation of as much as 7 percent. Magnification errors, superimposition of anatomical structures and geometric distortion are suggested as additional drawbacks of 2-D radiography (44). Therefore, measurement of 3-D structures in 2-D view results in an unreliable analysis of craniofacial structures.

To overcome these limitations 3-D methods of imaging were introduced. Conventional computed tomography (CT) has a limited function in dentistry due to its high cost, lack of accessibility and high radiation dose (46). Conversely, quick scan time, lower radiation dose, acquisition of different volume sizes, image accuracy and accessibility of cone beam computed tomography (CBCT) images have made this 3-D diagnostic modality extremely attractive in craniofacial imaging.

CBCT utilizes an x-ray source (and detector) that usually rotates 360 degrees around the head to obtain multiple images. Single projection images or “basis images” are obtained at certain degree intervals, which are then translated by software algorithms to form 3-D volumetric data. This allows for creation of 2-D images in axial, sagittal, coronal, oblique planes and even curved planes through a process called multi-planar formatting (12). The software gathers raw images and the reconstructs them into viewable format. Voxels are the smallest subunit of the digital volume created by the software after scan reconstruction. CBCT voxels are isotropic, i.e. equal in x, y and z dimension and their size ranges from 0.07 to 0.40 millimeters per side (47). Therefore, due to its high resolution and diagnostic reliability, the use of CBCT in dentistry is recommended for TMJ joint evaluations, 3-D viewing of nasopharyngeal airway, assessment of impacted teeth, supernumerary teeth and root morphology/ resorption. In addition, analysis of space, size and volume of craniofacial structures by digitizing markers in 3-D coordinates can be used to evaluate maxillofacial growth changes in 3-D and in planning treatment outcome for orthognathic surgery (46,48).

1.4.5 Accuracy of CBCT in Craniofacial Imaging

Imaging from CBCT can enable analysis of the size, shape and volume differences in structures from growth or treatment results (49). Utilizing digital imaging and communications in medicine (DICOM) volume in the multiplanar reformation (MPR) mode, three-dimensional measurements and landmark identification can be made accurately made from CBCT (48). Linear measurements of dry human skulls from 3-D volumetric reconstruction demonstrated a mean difference of 1.13% (+/- SD= 1.47%) between physical skull measurements and imaging measurements. Some measurements from CBCT were statistically different than from the actual measurements, but the difference was not considered clinically significant(50).

1.5 Conclusions

The positive effect of RME on nasal airway resistance has been well documented in the literature, but its role in correction of septal deviation has not been intensively researched. No studies have evaluated the potential effect of RME on NSD with 3-D imaging. Comprehending the response of NSD from maxillary expansion if it indeed exists could assist clinicians in its making treatment decisions in the future. With the advent of 3-D CBCT imaging, it is likely that we will gain a better understanding of the role of RME in correcting NSD.

Figure 1.3: Classification system by Mladina et al.

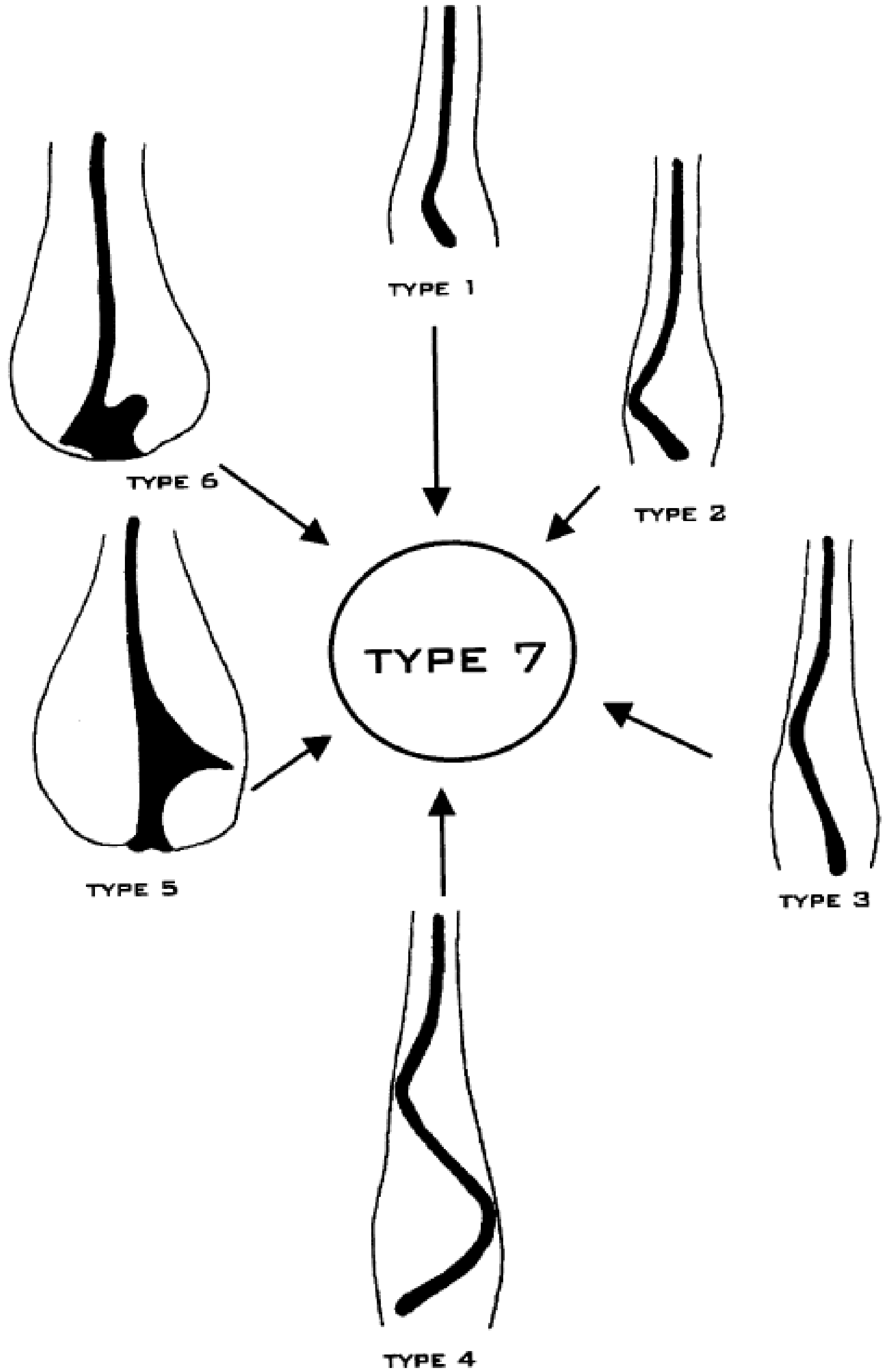


Figure 1. Types 1-4 are bird's eye view, whereas type 5 and 6 are in anterior posterior view.

Figure 1.4 :Baumann classification of Nasal Septal Deviation

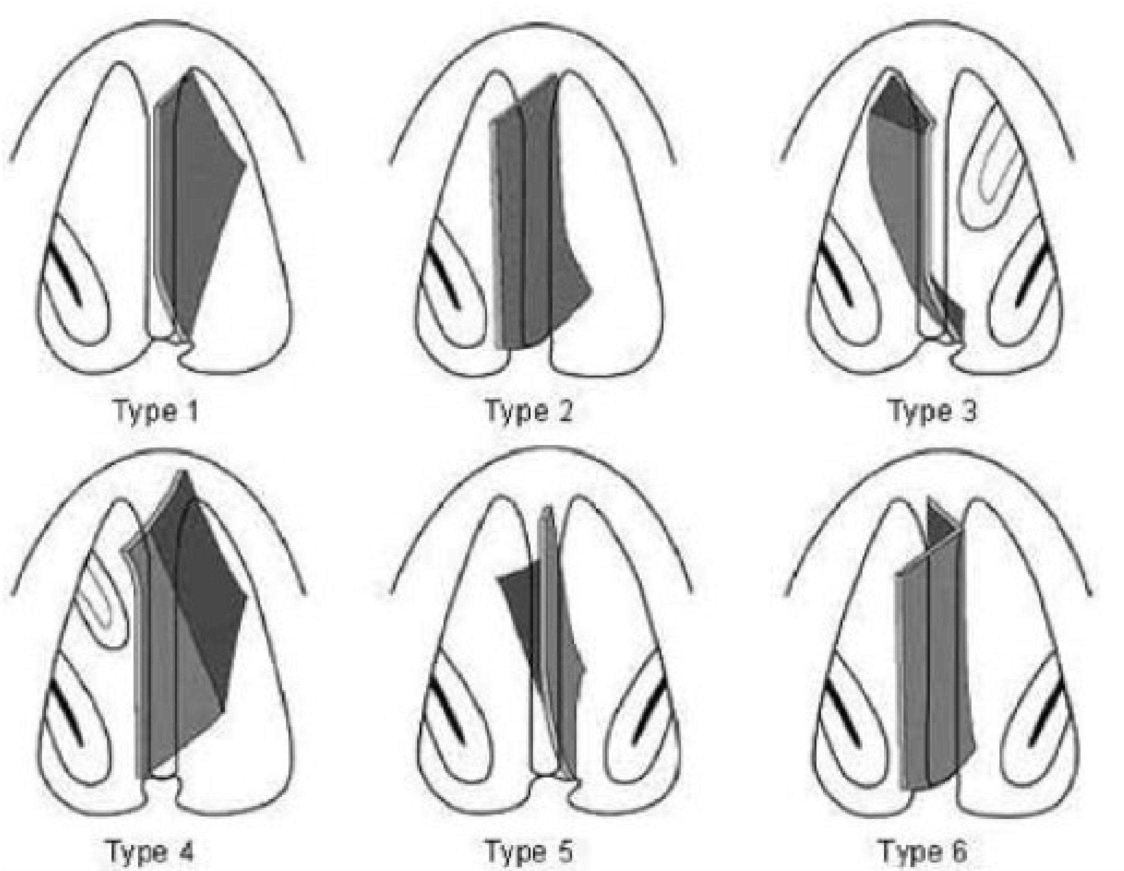
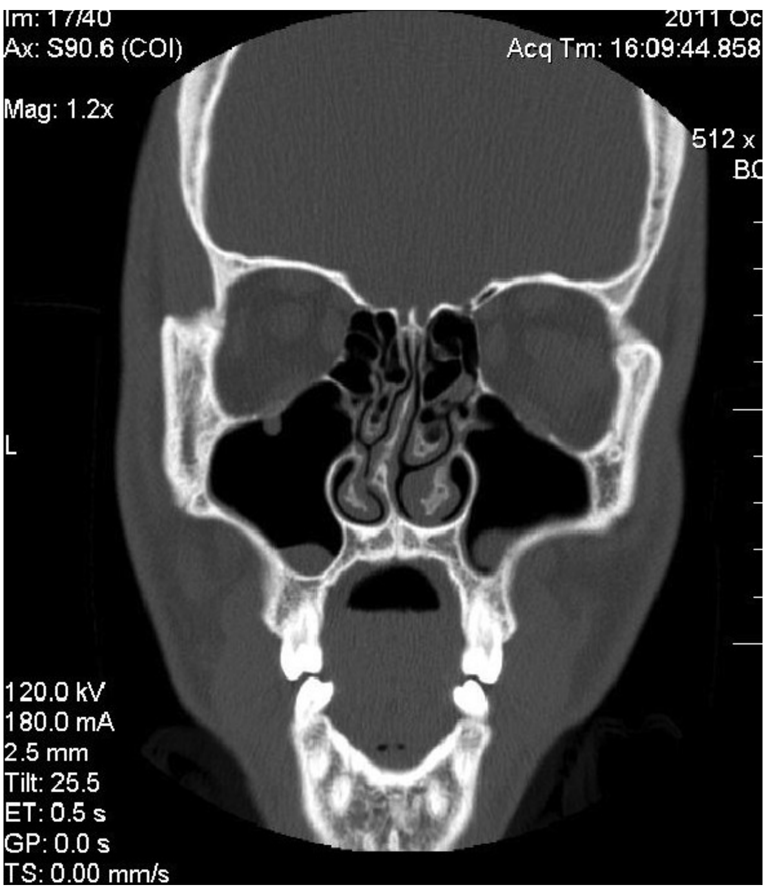


Table 1.1: Classification of Septal Deviation (Baumann and Baumann 2007)

Types of Septal Deviation	Septal pathology	Concomitant pathology
1	Septal crest	Contralateral turbinate hyperplasia, vomeral spur
2	Cartilaginous deviated nose	Ipsilateral turbinate hyperplasia
3	High septal deviation	Bilateral turbinate hyperplasia, contralateral concha bullosa
4	Caudally inclined septum	Contralateral turbinate hyperplasia, contralateral concha bullosa
5	Septal crest	Bilateral turbinate hyperplasia
6	Caudally inclined septum	Bilateral turbinate hyperplasia

Figure 1.5: Deviated Nasal Septum on CT scan



1.6 References

(1) Haas AJ. THE TREATMENT OF MAXILLARY DEFICIENCY BY OPENING THE MIDPALATAL SUTURE. Angle Orthod 1965 Jul;35:200-217.

(2) Laptook T. Conductive hearing loss and rapid maxillary expansion. Report of a case. Am J Orthod 1981 Sep;80(3):325-331.

(3) Baccetti T, Franchi L, Cameron CG, McNamara JA,Jr. Treatment timing for rapid maxillary expansion. Angle Orthod 2001 Oct;71(5):343-350.

(4) Moss-Salentijn L. Melvin L. Moss and the functional matrix. J Dent Res 1997 Dec;76(12):1814-1817.

(5) Magnusson A, Bjerklin K, Nilsson P, Jonsson F, Marcusson A. Nasal cavity size, airway resistance, and subjective sensation after surgically assisted rapid maxillary expansion: a prospective longitudinal study. American Journal of Orthodontics & Dentofacial Orthopedics 2011 Nov;140(5):641-651.

(6) Baratieri C, Alves M,Jr, de Souza MM, de Souza Araujo MT, Maia LC. Does rapid maxillary expansion have long-term effects on airway dimensions and breathing? American Journal of Orthodontics & Dentofacial Orthopedics 2011 Aug;140(2):146-156.

(7) Oliveira De Felippe NL, Da Silveira AC, Viana G, Kusnoto B, Smith B, Evans CA. Relationship between rapid maxillary expansion and nasal cavity size and airway resistance: short- and long-term effects. American Journal of Orthodontics & Dentofacial Orthopedics 2008 Sep;134(3):370-382.

(8) Monini S, Malagola C, Villa MP, Tripodi C, Tarentini S, Malagnino I, et al. Rapid maxillary expansion for the treatment of nasal obstruction in children younger than 12 years. Archives of Otolaryngology -- Head & Neck Surgery 2009 Jan;135(1):22-27.

(9) Bicakci AA, Agar U, Sokucu O, Babacan H, Doruk C. Nasal airway changes due to rapid maxillary expansion timing. Angle Orthod 2005 Jan;75(1):1-6.

(10) Farronato G, Giannini L, Galbiati G, Maspero C. RME: influences on the nasal septum. Minerva Stomatol 2012 Apr;61(4):125-134.

(11) Gray LP. Results of 310 cases of rapid maxillary expansion selected for medical reasons. Journal of Laryngology & Otology 1975 Jun;89(6):601-614.

(12) Scarfe WC, Farman AG, Sukovic P. Clinical applications of cone-beam computed tomography in dental practice. J Can Dent Assoc 2006 Feb;72(1):75-80.

(13) Cummings CW et al editor. Otolaryngology--head & neck surgery. Elsevier Mosby; St Louis, Missouri; 3rd edition, Vol 2: 1998, chp 50.

(14) Gray LP. Deviated nasal septum. Incidence and etiology. Annals of Otology, Rhinology, & Laryngology - Supplement 1978 May-Jun;87(3 Pt 3 Suppl 50):3-20.

(15) Podoshin L, Gertner R, Fradis M, Berger A. Incidence and treatment of deviation of nasal septum in newborns. Ear Nose Throat J 1991 Aug;70(8):485-487.

(16) Kawalski H, Spiewak P. How septum deformations in newborns occur. Int J Pediatr Otorhinolaryngol 1998 Jun 1;44(1):23-30.

(17) Haapaniemi JJ, Suonpaa JT, Salmivalli AJ, Tuominen J. Prevalence of septal deviations in school-aged children. Rhinology 1995 Mar;33(1):1-3.

(18) Finkbohner R, Johnston D, Crawford ES, Coselli J, Milewicz DM. Marfan syndrome. Long-term survival and complications after aortic aneurysm repair. Circulation 1995 Feb 1;91(3):728-733.

(19) Pirsig W. Growth of the deviated septum and its influence on midfacial development. Facial Plastic Surgery 1992 Oct;8(4):224-232.

(20) Aktas D, Kalcioglu MT, Kutlu R, Ozturan O, Oncel S. The relationship between the concha bullosa, nasal septal deviation and sinusitis. Rhinology 2003 Jun;41(2):103-106.

(21) Mladina R. The role of maxillar morphology in the development of pathological septal deformities. Rhinology 1987 Sep;25(3):199-205.

(22) Mladina R, Krajina Z. The influence of the caudal process on the formation of septal deformities. Rhinology 1989 Jun;27(2):113-118.

(23) Kim J, Kim SW, Kim SW, Cho JH, Park YJ. Role of the sphenoidal process of the septal cartilage in the development of septal deviation. Otolaryngology - Head & Neck Surgery 2012 Jan;146(1):151-155.

(24) Cole P, Chaban R, Naito K, Oprysk D. The obstructive nasal septum. Effect of simulated deviations on nasal airflow resistance. Archives of Otolaryngology -- Head & Neck Surgery 1988 Apr;114(4):410-412.

(25) Sooknundun M, Kacker SK, Bhatia R, Deka RC. Nasal septal deviation: effective intervention and long term follow-up. Int J Pediatr Otorhinolaryngol 1986 Nov;12(1):65-72.

(26) Vig KW. Nasal obstruction and facial growth: the strength of evidence for clinical assumptions. American Journal of Orthodontics & Dentofacial Orthopedics 1998 Jun;113(6):603-611.

(27) D'Ascanio L, Lancione C, Pompa G, Rebuffini E, Mansi N, Manzini M. Craniofacial growth in children with nasal septum deviation: a cephalometric comparative study. Int J Pediatr Otorhinolaryngol 2010 Oct;74(10):1180-1183.

(28) Mladina R, Cujic E, Subaric M, Vukovic K. Nasal septal deformities in ear, nose, and throat patients: an international study. Am J Otolaryngol 2008 Mar-Apr;29(2):75-82.

(29) Baumann I, Baumann H. A new classification of septal deviations. Rhinology 2007 Sep;45(3):220-223.

(30) Kilic N, Oktay H. Effects of rapid maxillary expansion on nasal breathing and some naso-respiratory and breathing problems in growing children: a literature review. Int J Pediatr Otorhinolaryngol 2008 Nov;72(11):1595-1601.

(31) Proffit WR, Fields Jr HW, Sarver DM. Contemporary orthodontics. : Elsevier Health Sciences; 2006.

(32) Haas AJ. Palatal expansion: just the beginning of dentofacial orthopedics. Am J Orthod 1970 Mar;57(3):219-255.

(33) Haas AJ. Rapid expansion of the maxillary dental arch and nasal cavity by opening the midpalatal suture. Angle Orthod 1961;31(2):73-90.

(34) Enoki C, Valera FC, Lessa FC, Elias AM, Matsumoto MA, Anselmo-Lima WT. Effect of rapid maxillary expansion on the dimension of the nasal cavity and on nasal air resistance. Int J Pediatr Otorhinolaryngol 2006 Jul;70(7):1225-1230.

(35) Warren DW, Hershey HG, Turvey TA, Hinton VA, Hairfield WM. The nasal airway following maxillary expansion. American Journal of Orthodontics & Dentofacial Orthopedics 1987 Feb;91(2):111-116.

(36) Baraldi CE, Pretto SM, Puricelli E. Evaluation of surgically assisted maxillary expansion using acoustic rhinometry and postero-anterior cephalometry. International Journal of Oral & Maxillofacial Surgery 2007 Apr;36(4):305-309.

(37) Kase Y, Hilberg O, Pedersen OF. Posture and nasal patency: evaluation by acoustic rhinometry. Acta Otolaryngol 1994 Jan;114(1):70-74.

(38) Wertz RA. Changes in nasal airflow incident to rapid maxillary expansion. Angle Orthod 1968 Jan;38(1):1-11.

(39) da Silva Filho OG, Montes LA, Torelly LF. Rapid maxillary expansion in the deciduous and mixed dentition evaluated through posteroanterior cephalometric analysis. American Journal of Orthodontics & Dentofacial Orthopedics 1995 Mar;107(3):268-275.

(40) Cross DL, McDonald JP. Effect of rapid maxillary expansion on skeletal, dental, and nasal structures: a postero-anterior cephalometric study. Eur J Orthod 2000 Oct;22(5):519-528.

(41) Hershey HG, Stewart BL, Warren DW. Changes in nasal airway resistance associated with rapid maxillary expansion. Am J Orthod 1976 Mar;69(3):274-284.

(42) Hartgerink DV, Vig PS, Abbott DW. The effect of rapid maxillary expansion on nasal airway resistance. American Journal of Orthodontics & Dentofacial Orthopedics 1987 Nov;92(5):381-389.

(43) Principato JJ, Wolf P. Pediatric nasal resistance. Laryngoscope 1985 Sep;95(9 Pt 1):1067-1069.

(44) Adams GL, Gansky SA, Miller AJ, Harrell WE,Jr, Hatcher DC. Comparison between traditional 2-dimensional cephalometry and a 3-dimensional approach on human dry skulls. American Journal of Orthodontics & Dentofacial Orthopedics 2004 Oct;126(4):397-409.

(45) Tsao DH, Kazanoglu A, McCasland JP. Measurability of radiographic images. Am J Orthod 1983 Sep;84(3):212-216.

(46) Silva MA, Wolf U, Heinicke F, Bumann A, Visser H, Hirsch E. Cone-beam computed tomography for routine orthodontic treatment planning: a radiation dose evaluation. American Journal of Orthodontics & Dentofacial Orthopedics 2008 May;133(5):640.e1-640.e5.

(47) Hatcher DC. Operational principles for cone-beam computed tomography. J Am Dent Assoc 2010 Oct;141(Suppl 3):3S-6S.

(48) Kapila S, Conley RS, Harrell WE,Jr. The current status of cone beam computed tomography imaging in orthodontics. Dento-Maxillo-Facial Radiology 2011 Jan;40(1):24-34.

(49) Stratemann SA, Huang JC, Maki K, Hatcher DC, Miller AJ. Evaluating the mandible with cone-beam computed tomography. American Journal of Orthodontics & Dentofacial Orthopedics 2010 Apr;137(4 Suppl):S58-70.

(50) Periago DR, Scarfe WC, Moshiri M, Scheetz JP, Silveira AM, Farman AG. Linear accuracy and reliability of cone beam CT derived 3-dimensional images constructed using an orthodontic volumetric rendering program. Angle Orthod 2008 May;78(3):387-395.

Chapter 2

Measurement Tools for the Diagnosis of Nasal Septal Deviation: A Systematic Review

2.1 Introduction:

Nasal septal deviation (NSD) is a common diagnosis made by otolaryngologists but is one that is not usually based on objective measurements. As a result, there can be a significant inter-observer variability in terms of diagnosing the condition, verifying its precise location, quantifying the degree of deviation, and assessing its clinical impact on patients. This subjectivity can lead to unnecessary surgical treatments, patient complications and low patient satisfaction rates. In the current era of evidence-based medicine, society demands that surgical interventions demonstrate clinically significant improvements. Since there is no consensus agreement about diagnosing NSD objectively, interventions treating NSD lack a strong evidence base. Interventions not supported by evidence-based medicine are at risk of being curtailed by publicly funded healthcare systems.

The nasal septum is a midline support structure of the nasal cavity. Aside from being a key support mechanism of the nose and a major determinant of its shape, the space between the septum and lateral walls of the nasal cavity regulates nasal airflow and respiration. Within the nasal cavity, a straight septum enables laminar airflow, allowing the inspired air to be warmed, cleaned and humidified and thus optimized for gas exchange. Conversely, a deviated nasal septum can contribute to various degrees of nasal obstruction and altered nasal respiration (1,2).

Deviation of the nasal septum is a common structural cause of nasal obstruction and can arise from dislocation of the quadriangular cartilage from its bony boundaries, or from an intrinsic deformity affecting the vomer, perpendicular plate of ethmoid and/or the quadrilateral cartilage itself (3). In neonates, prevalence of septal deviation can vary from 1.45% (4) to 6.3% (5). A recent study (6) analyzed the prevalence of septal deviations in newborns and found that it can be as high as 22% in children delivered vaginally, while birth from a caesarean section resulted in only 4% NSD. Trauma to the septum from vaginal birth was suggested to be a common cause of NSD. The prevalence of NSD in school-aged children aged 6-15 years was roughly 20% when assessed on occipitomental projection radiographs, while a positive clinical diagnosis was made in approximately 10% of the same cohort of children (7).

Overall, the etiology of NSD can be classified as congenital, genetic effects causing aberrant growth, trauma (8), infection, or even mass effect from nasal cavity neoplasms (9). A recent study suggested that a long sphenoid process of the septal cartilage could also contribute to NSD (10).

Depending on the severity and location of NSD in adults, it can lead to mouth breathing, nasal crusting, epistaxis, and sinusitis (11). In infants, severe and bilateral NSD can result in poor feeding/ and or choking from food in the respiratory tract (6). Dental findings of patients with nasal obstruction resulting from NSD have been reported as Class 2 malocclusion with increased anterior facial height, retrognathic maxilla and mandible with increased overjet and constricted transverse maxillary dimension (12).

The wide range of reported incidences of NSD mentioned above is largely due to a lack of standardized objective criteria for making the diagnosis of NSD. However, other mitigating factors such as presence of turbinate hypertrophy, rhinitis, nasal valve collapse, nasal cycle and the complexity of the three dimensional geometry of the nasal cavity make the diagnosis even more challenging. Essentially, there seems to be no acceptable protocol for establishing the diagnosis of NSD. Diagnostic tests namely acoustic rhinometry (AR), rhinomanometry (RMM) and nasal spectral sound analysis (NSSA) have been documented in the literature to assess septal deviation. Acoustic rhinometry (AR) assesses nasal patency based on the measurement of acoustic reflection of a sound signal in the nose by structures within the nasal cavity. Rhinomanometry provides a dynamic physiologic assessment of the nose by measuring transnasal pressure and nasal volume airflow to calculate nasal resistance. Nasal sound spectral analysis (NSSA) can provide an indirect method of dynamically assessing nasal airflow by analyzing noise in the nasal cavity caused by turbulent nasal airflow. (1)

The purpose of this systematic review is to investigate the diagnostic modalities utilized to assess NSD. To our knowledge, no such review has been conducted, and considering the clinical manifestations and consequences of NSD, it would be beneficial to have an evidence-based diagnostic schema for NSD.

2.2 Methods

An electronic database search was conducted with the assistance of a senior librarian specializing in health sciences database searches. The electronic databases were MEDLINE (from 1966 to second week of August 2013), EMBASE (from 1966 to second week of August 2013), Web of Science (from 1945 to second week of August 2013) and all Evidence Based Medicine Reviews Files (EBMR); Cochrane Database of Systematic Review (CDSR), Cochrane Central Register of Controlled Trials (CCTR), Cochrane Methodology Register (CMR), Database of Abstracts of Reviews of Effects (DARE), American College of Physicians Journal Club (ACP Journal Club), Health Technology Assessments (HTA), NHS Economic Evaluation Database (NHSEED) until the second quarter of 2013. The search terms used in database searches were 'nasal septum', 'deviation', 'diagnosis', 'nose deformities' and 'nose malformation' (Appendix A). The following inclusion criteria were used to initially select studies from the abstracts and titles located through electronic database search.

Inclusion criteria consisted the following: human studies only, no case reports or conference proceedings, abstracts that discussed diagnosis of nasal obstruction with reference to septal deviation and no neonatal studies. Since the diagnosis and etiology of septal deviation in neonates is considered a separate entity it was not included in this systematic review.

Two authors (T.A. and K.A.) independently reviewed the title and abstracts of the database searches. Full text of all studies that appeared to meet the inclusion criteria were retrieved along with ones that had insufficient information in the abstracts to make a final decision regarding their inclusion. The references of retrieved articles were also manually searched for additional studies that could be included in the systematic review. The authors (T.A and K. A) independently assessed full articles obtained for inclusion in the systematic review and any disagreement was settled through discussion until a consensus was reached.

The following exclusion criteria were finally applied to the studies after retrieval of full text of articles: Any concurrent sino-nasal pathology in patients that would preclude diagnosis of nasal septal deviation was excluded, examples of such conditions included, but not limited to, were septal perforation, chronic rhinitis, chonal atresia, enlarged turbinates, nasal polyps etc; computer simulations of airflow to mimic septal deviation were not included, as these were not in vivo studies; studies including patients with prior septal surgery were not included, as this would reduce the detection rate of diagnosing nasal septal deviation; patients that did not receive any topical nasal decongestant prior to administering the diagnostic test were not included in this study. Minimizing mucosal swelling of septum will reduce the false positive rates of detecting nasal septal deviation.

Methodological scoring to assess quality of included studies was performed through use of the updated Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (13) (see Appendix B). It was established that the quality assessment would be through analysis of individual components and not the overall quality score.

2.3 Results

The flow chart of the electronic database search and final selection of studies to be included in the systematic review is outlined (Figure 1). Online searches resulted in 23 abstracts (14-37) after removal of duplicates that resulted from overlap of studies between the electronic databases. Fifteen studies were excluded (13-27) after full review of the articles and reasons for their exclusion are listed in Table 2.1. This resulted in a total of 8 studies (29-36) to be included in this systematic review. Key details of the included studies are listed in Table 2.2. Three studies (29, 31, 32) discussed the analysis of nasal sound intensity on expiration (31), inspiration (29) and both inspiration/expiration (32) in 2000-4000Hz frequency interval as diagnostic modality for nasal septal deviation. It was suggested in two of these studies that there was a positive correlation between severity of NSD and in intensity of nasal sounds (29,31). Three other articles (30,34,35) concluded that acoustic rhinometry (AR) was a reliable tool in diagnosing anterio-caudal NSDs (34,35). One study (30) concluded that the sensitivity of AR in detecting anterio-caudal septal deviations is 57 % and specificity is 70% when assessing even minor septal deviations that are visible on CT scans, but might not be clinically relevant. Another study (35) concluded that acoustic rhinometry could detect NSD due to statistically significant differences in the cross sectional areas and nasal cavity volumes between obstructed and unobstructed sides of the nose. One article on rhinomanometry concluded that it has limited diagnostic value in the clinical setting due to its ability to only diagnose major septal deviations in the anterior region and these were found only in a minority of the sample patients (33). Finally, one study (36) concluded that physical examination from nasal endoscopy/ anterior rhinoscopy is an accurate method of diagnosing septal deviation patients requiring septal surgery.

Results from QUADAS-2 tool are listed in Table 2.3. Most studies selected patients that were representative of the ones receiving the test in a clinical setting and clearly described selection criteria (low risk of bias and lack of applicability concerns for patient selection domain). Most of them described execution of index test to enable replication (high applicability of index test domain). However, none except one study (34) identified and explained patient withdrawal (high risk of bias for flow and timing domain). In all studies except one (36), index tests were performed with the knowledge of the reference tests (high risk of bias for index test).

2.4 Discussion

Nasal septal deviation (NSD) is a common clinical entity encountered in general otolaryngology-head and neck surgery. Upon review of the literature, no single test was identified as a gold standard of diagnosis of septal deviation. The diagnosis of NSD is generally ascertained after assimilating information gathered from a variety of sources including the patient's history, physical examination of the nose and anterior rhinoscopy, nasal endoscopy, and imaging (30).

Ideally, surgical interventions should be supported on strong evidence based medicine, with a diagnosis based on objective testing and criteria. Clinical inquiry from patients usually lacks sensitivity and specificity, especially as an isolated diagnostic tool in detecting NSD, possibly due to the presence of numerous co-existing and confounding pathologies. Anterior rhinoscopy and nasal endoscopy performed in the decongested state can diagnose the location and severity of nasal septal deviations, but it is an uncomfortable test that is subject to significant inter-rater variability (1,30). Imaging studies such as CT scans and MRIs can provide accurate three-dimensional diagnosis of NSD but are typically utilized in the clinical arena to assess paranasal pathology (i.e. sinusitis) rather than isolated NSD (1,30).

As accurate as they can be in diagnosing NSD, the former exposes patients unnecessarily to radiation while both modalities can be expensive (30). More readily available and less expensive diagnostic modalities have been created to objectively assess the nasal cavity patency. These diagnostic tests included in this systematic review are acoustic rhinometry (30, 34, 35), rhinomanometry (32, 33,34) and nasal sound spectral analysis (29,31, 32) all carried out in the decongested state.

Acoustic rhinometry (AR) assesses nasal patency based on the measurement of acoustic reflection of a sound signal in the nose by structures within the nasal cavity. AR analyses the initial and reflected sound waves creating a plot of the cross sectional area of the nasal cavity as a function of the distance from the nasal cavity entrance (34). Once this data is obtained, nasal volumes can also be calculated using AR. Unlike anterior rhinoscopy and nasal endoscopy, AR provides objective data. Typical minimal cross sectional areas (MCA) are encountered as defined distances from the anterior nasal aperture. In one study (30), they were defined as MCA 1 at 2 cm represents the anterior end of the inferior turbinate and internal nasal valve; MCA 2 at 4 cm represents the anterior part of the middle turbinate; and MCA 3 at 6 cm represents the middle portion of the middle turbinate. This study along with two other (34,35) on acoustic rhinometry concluded that AR becomes less accurate when measurements are made past MCA 1 of the anterior nasal cavity and are completely unreliable past MCA 3. Because

MCA 1 in fact represents the internal nasal valve area of the external nose, which is the narrowest part of the nasal passage, it is the most susceptible nasal airflow obstruction in the setting of NSD (37). Diminished accuracy of AR past the anterior portion of the inferior nasal turbinate (around 2cm distance from the nostril) could also be due to complicated intranasal anatomy posteriorly that leads to dispersion of acoustic energy (30). In fact, Mamikoglu et al (30) compared acoustic rhinometry and CT scan in diagnosing NSD, and found a positive correlation between MCA 1 and CT results. In particular, it was determined that the sensitivity of detecting anterior NSD is 54% while the specificity was 70%. Most of these deviations in this study were classified as “mild”. Sensitivity and specificity would have been higher if the study contained a greater proportion of patients with more severe NSDs. However, unlike physical exam and imaging, acoustic rhinometry cannot distinguish DNS from other obstructing nasal pathology.

While AR provides a static view of the nasal cavity, rhinomanometry (RMM) provides a dynamic physiologic assessment of the nose. Based on the laws of fluid dynamics, it quantifies nasal ventilation by measuring transnasal pressure and nasal volume airflow to calculate nasal resistance (34). Nasal resistance is an internationally accepted index of nasal patency (38). Huygen et al (33) concluded that minor deviations may defy detection by rhinomanometry as the detection rate (22%) of septal deviation was very similar the false positive rate of 24%. Furthermore, they found that RMM was most accurate in identifying larger NSDs in the anterior flow limiting regions of the nose including the nasal vestibule and valve area. Similarly, another study (34) on RMM reported that it is a sensitive tool in identifying septal deviations in anterior part of the nasal cavity, but was unable to determine the location of NSD. Although RMM quantifies the functional impact on nasal flow mechanics caused by these larger anterior based NSD, these anterior NSDs are nevertheless more easily diagnosed by simply performing anterior rhinoscopy. In fact, almost all studies in this systematic review had patients undergo assessment with anterior rhinoscopy and nasal endoscopy to detect severity and location of septal deviation prior to administration of the index test.

In contrast to administering RMM, which can be cumbersome and time consuming (29), nasal sound spectral analysis (NSSA) with Odiosoft-Rhino (OR) can provide an indirect method of dynamically assessing nasal airflow. NSSA analyses noise in the nasal cavity caused by turbulent nasal airflow. It is also easy and inexpensive to conduct (29). Unlike AR and RMM, NSSA does not require any nasal cannulation, which distorts the nasal cavity, and could skew the measurements (29,32). In order to accurately quantify this noise, NSSA must be conducted in a quiet room, a minor limitation of this test that is also incidentally experienced with AR. Like AR and RMM, each side of the nasal cavity can be evaluated independently, so side differences can be noted. In essence, one would expect that greater the physical nasal obstruction, greater the turbulent airflow, and louder the noise detected on NSSA testing. One study (29) found a significant difference between nasal inspiratory sound intensity of the NSD patient group and normal controls. The sensitivity and specificity were 86% and 83% respectively in terms of diagnosing isolated NSD. This study (29) also found a correlation between the severity of the deflection and the intensity of the inspiratory nasal sound in the 2000 to 4000 Hz interval. In a cohort with unilateral NSD in another study (31), expiratory sounds at the 2000-4000 Hz and 4000-6000 Hz intervals were found to be significantly louder on the deviated side than the other side of the nose. In same group of patients, Tahamilar et al (31) found a positive correlation between visual analog scores assessing the subjective feeling of nasal obstruction and expiratory NSSA measurements and also a direct correlation between the severity of NSD and expiratory NSSA. Furthermore, expiratory NSSA positively correlated with AR findings at MCA 1 region of the nose, that being the internal nasal valve flow limiting segment of the anterior nose. In one study (29) NSSA was compared with peak nasal inspiratory flow (PNIF). PNIF is another measurement of nasal airflow that is obtained with a portable inspiratory flowmeter. This study found a statistically significant lower PNIF values in the NSD group compared to normal controls and a positive correlation with NSSA. According to this paper (29) sensitivity and specificity of PNIF is 79% and 77% respectively for detecting NSDs. However, a limitation of NSSA (and RMM) is that the actual location of the NSD could not be ascertained. A recently published systematic review evaluated the efficacy of septoplasty for treatment of nasal obstruction concluded that AR, RMM and PINF are all valid objective measures to assess nasal patency in patients undergoing surgery (39).

Standardized criteria for assessing the symptom of nasal obstruction caused by NSD can be quantified using validated visual analog scales. However, the results from subjective assessments of nasal obstruction from visual analog scores (VAS) are flawed in patients with chronic DNS who may have simply become accustomed to breathing with limited nasal airflow. This was demonstrated in a study (35) found that only 30 out of 77 patients with significant nasal septal deviation complained subjectively of nasal obstruction. Conversely, out of 89 rhinoscopically normal patients 32 had subjective complaints of nasal obstruction, making VAS for assessing nasal obstruction caused by NSD challenging. There are a number of reasons why there is poor correlation between the subjective sensation of nasal obstruction and objective tests of nasal obstruction; the foremost being is that nasal sensation is relatively poorly understood (28). Studies included in this systematic review were assessed by QUADAS-2 and several methodological flaws were identified. One major limitation of these diagnostic studies was that anterior rhinoscopy, nasal endoscopy and/or CT scans were conducted to make the diagnosis of NSD prior to the use of diagnostic modalities such as acoustic rhinometry, rhinomanometry and nasal sound analysis (high risk of bias for index test). It was not clear in most studies whether the same examiner conducted all the diagnostic tests. Only one study (32) reported blinding of the examiner for the diagnostic tests conducted. This could lead to review bias (34) whereby interpretation of the results of the diagnostic test such as acoustic rhinometry could be altered by the knowledge of the results from nasal endoscopy and may lead to increased diagnostic accuracy of index tests.

2.5 Conclusions

In summary, diagnostic modalities such as acoustic rhinometry, rhinomanometry and nasal spectral sound analysis may be useful in identifying NSD in anterior region of the nasal cavity, but these tests alone add little value to diagnosis. Compared to anterior rhinoscopy, nasal endoscopy, and imaging, the above mentioned index tests lack sensitivity and specificity in identifying the presence, location, and severity of NSD.

Table 2.1 Studies Excluded from Systematic Review

Study	Reason for exclusion
Cho GS et al[14]	Discussed association between subjective sensation of nasal obstruction with respect to different locations in the nose with lack of reference to diagnosis of nasal septal deviation
Liu T et al[15]	Computer simulations of nasal airflow in nasal obstruction/ septal deviation.
Chen XB at al[16]	Computer simulations of nasal airflow in nasal obstruction/septal deviation.
Hanif J et al[17]	Little reference to diagnosis of septal deviation, discussed quantification of severity of nasal septum for future surgery.
Filho DI et al[18]	Little or no reference to diagnosis of nasal septal deviation.
Cole P et al[19]	Computer simulations of nasal airflow in nasal obstruction/septal deviation.
Farhadi, M[20]	Unclear on inclusion of patients with only septal deviation/ nasal obstruction from other causes.
Kahveci OK[21]	Only addressed efficacy of NOSE scale in patients receiving septal surgery.
Rujanavej V et al[22]	Diagnosis of septal deviation made with concurrent nasal obstruction and sinonasal disease.
Gogniashvilli G et al[23]	Prevalence study of physiological/ pathological septal deviation.
Garcia GJ et al[24]	Computer simulations of nasal airflow in nasal obstruction/septal deviation.
Pirila T et al [25]	Discussed patient satisfaction with septoplasty, without reference to diagnosis of septal deviation.
Chandra RK et al[26]	Review of nasal obstruction.
Benninger MS[27]	Excluded patients with nasal septal deviation.
Cuddihy PJ et al[28]	Almost half of the sample of patients had concurrent rhinitis.

Figure 2. 1 Summary of Systematic Review Process

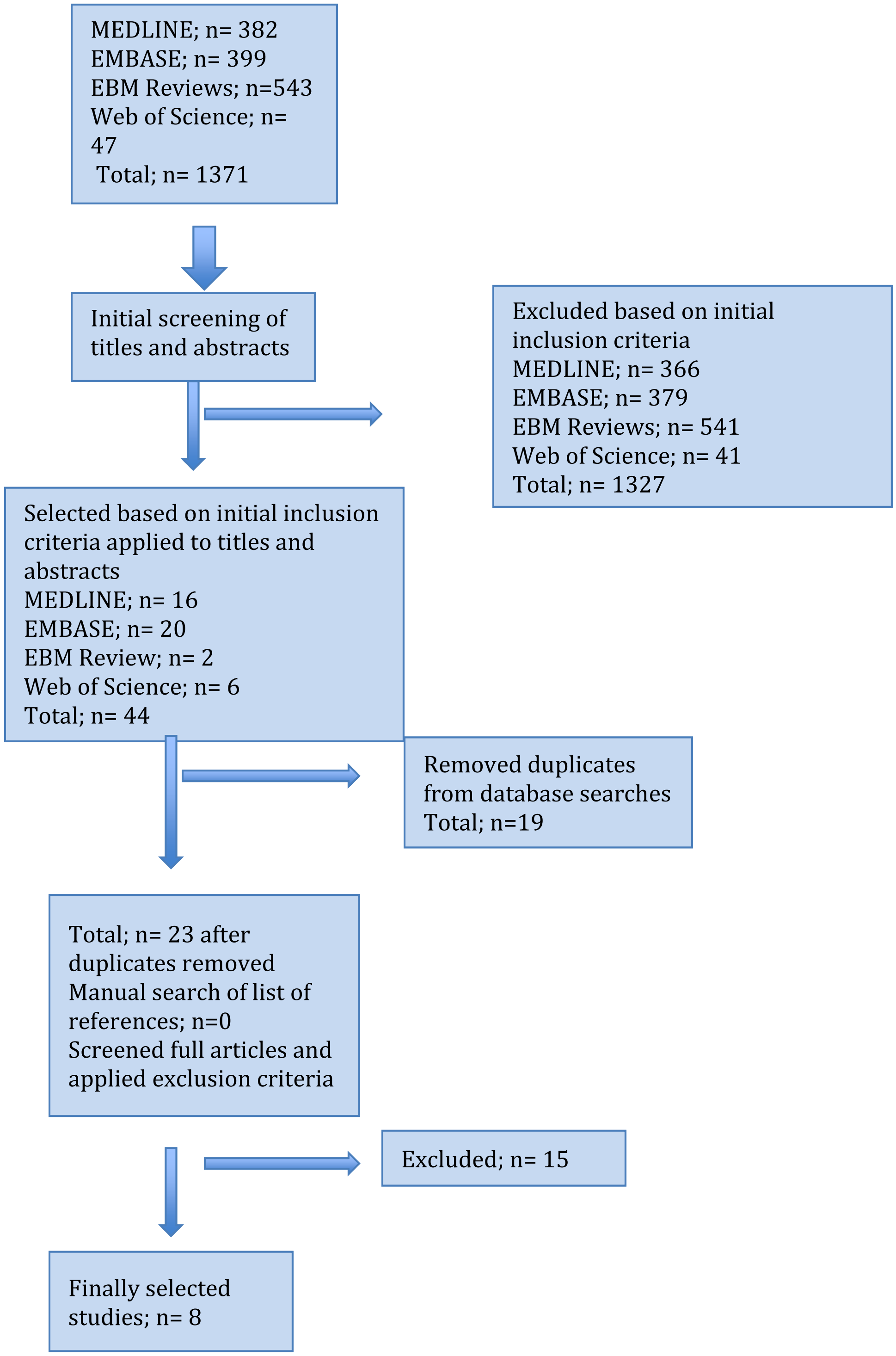


Table 2.2 Summary of Studies Included in Systematic Review

Study	Study group	Control group	Diagnostic Measure(s)	Sensitivity (SN)/ Specificity (SP)	Results
Choi et al[29]	n=43 Ages 18 to 48 years (mean 35 +/- 13 yrs)	n=40 Ages 20 to 50 years (mean 32+/-24 years)	NSSA compared with PNIF and VAS	SN=86% and SP= 83% for NSSA in septal deviation patients at 2000-4000Hz interval. SN=79% and SP=78 % for PNIF	Correlation between PNIF and NSSA for frequency interval 2000-4000 Hz in deviated patients (r= 0.72, p<0.01)
Mamikoglu et al[30]	n= 24 Ages 14 to 67years (median 36)	No control group	AR compared with CT scans, MCA measured at 2, 4 and 6 cm from the nostril	SN of AR in detecting anterior septal deviations is 57 % and SP is 70% when assessing minor septal deviations seen on CT	AR and CT correlate well if deviation present at a distance of 2 cm from anterior nose (r= 0.73, p<0.001). Correlation decreases past 4 cm and AR is not accurate beyond 6 cm
Tahamiler et al[31]	n= 61 Ages 18 to 66 years (mean 32 +/- 11)	No control group	Comparison between AR and VAS using OR at 200-6000Hz (MCA 1 measured 2.2cm from anterior nose)	Not mentioned	Weak correlation but significant results for OR at 2000-4000Hz and 4000-6000 Hz interval (r= 0.5, p<0.01) with AR for 2.2 cm from the vestibule for ipsilateral deviation. Between VAS and OR at 2000-4000Hz (r= 0.41, p<0.01) for ipsilateral deviation
Tahamiler et al[32]	n= 68, Ages 18 to 54 years, (mean 32)	n=61 Ages 17 to 56 years, (mean 34)	Expiratory /inspiratory nasal sound with OR, Compared with VAS and RMM	None mentioned	OR correlates well with VAS/ RMM and can be a useful tool in measuring nasal patency at 2000-4000 Hz interval (p< 0.0001)
Huygen et al[33]	n= 193, no ages given. (Site of septal deviation; vestibule, valve, anterior-superior portion /central and posterior areas)	n=33, 21-67 years of age	RMM (mean flow at transnasal pressure of 150 Pa) vs rhinoscopic measurement of deviation	None mentioned	RMM is a poor tool for localization of deviation. Had 80% detection rate for only severe deviations in nasal vestibule and valve
Szucs et al[34]	n=50 Ages 18 to 64 years, (mean 33) Group 1, n=8 severe septal deviation anterior	n=15	RMM and AR. Inspiratory and expiratory nasal airway resistance (NAR) at 75	Both AR and RMM show sensitivity in diagnosis of severe and moderate septal deviation in the anterior part of nasal	p <0.05 for MCA, Volume and NAR at 75 and 150 Pa for anterior septal deviation. p> 0.05 for MCA, Volume, and NAR at 75

	nasal cavity up to 2.5 cm from columella, Cottle area I and II Group 2, n=14 moderate deviation, anterior nasal cavity Cottle area I and II Group 3, n= 12, middle nasal cavity between 2.5 to 4.5 cm from columella, Cottle area IV Group 4, n= 16, posterior nasal cavity, between 4.5 to 8 cm from columella Cottle area V (see figure)		and 150 Pa measured for RMM. MCA and volume of nasal cavity at deviation measured by AR	cavity. Not sensitive enough in middle/ posterior deviations	and 150 Pa for middle and posterior deviations
Huang et al[35]	n=77 (significant septal deviation); Ages 19-74 years, mean age=39	n=89 Ages 19-74 years, mean age=39	AR; Mean MCA (anterior 1-5cm from the anterior nose) Total V (between points at the nostril to 5cm into the nose)	No sensitivity values given but concluded AR is a sensitive tool to determine structural abnormality	mMCA (p=0.001) and Total V (p=0.04) measured on the narrower side was smaller than in the wider part of nasal cavity
Sedaghat et al[36]	n=137 74 males, 63 females mean age= 42 years All had septal deviation	No control group	Nasal endoscopy, anterior rhinoscopy, physical exam	SN=86.9% and SP= 91.8 %	PPV=93.6 % and NPV=96.4% for septal surgery. Clinical assessment of patients with deviated nasal septum is accurate in predicting them needing medical intervention

AR Acoustic Rhinometry, *CT* computed tomography, *MCA* Minimal cross sectional area (mMCA: mean minimal cross sectional area, average of right and left nostrils), *NAR* nasal airway resistance *NSSA* nasal sound spectral analysis, *NPV* negative predictive value, *OR* Odiosoft-Rhino, *PNIF* peak nasal inspiratory flow, *PPV* positive predictive value, *RMM* rhinomanometry, *V* Total Volume (average of right and left nostrils), *VAS* Visual analogue score.

Table 2.3 Methodological Assessment of Included Studies Using Quality Assessment of Diagnostic Accuracy Studies-2

Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Choi et al[29]	LR	HR	LR	HR	U	LR	LR
Mamikoglu et al[30]	LR	HR	LR	HR	U	U	LR
Tahamiler et al[31]	LR	HR	LR	HR	LR	LR	LR
Tahamiler et al[32]	LR	HR	LR	HR	LR	LR	LR
Huygen et al[33]	LR	HR	LR	HR	LR	U	LR
Szucs et al[34]	LR	HR	LR	LR	LR	LR	LR
Huang et al[35]	U	HR	LR	HR	U	LR	LR
Sedaghat et al[36]	LR	LR	U	HR	LR	LR	LR

L=Low Risk, H=High Risk, ? =Unclear Risk

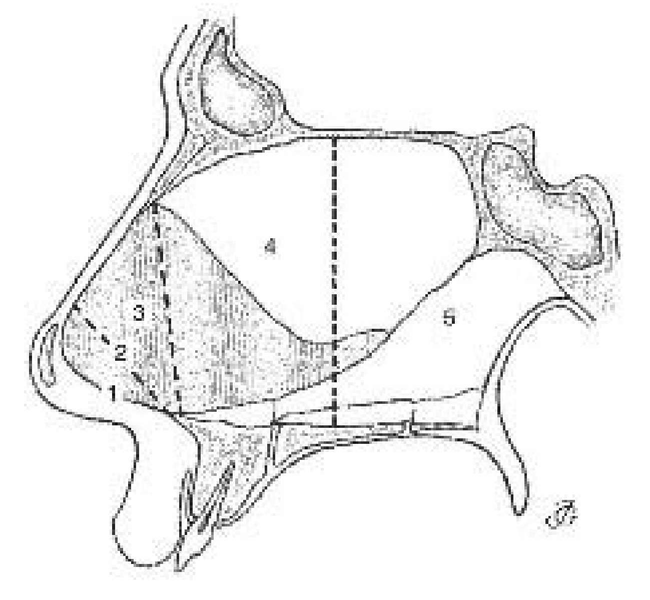


Figure 2.2 Areas of the nasal cavity according to Cottle. Area 1: nostril. Area 2: nasal valve. Area 3: area underneath the bony and cartilaginous vault, also called the attic. Area 4: anterior aspect of the nasal cavity including the heads of the turbinates and the infundibulum. Area 5: the posterior aspect of the nasal cavity, including the tails of the turbinates. (Adapted from Egbert H et al. Incorrect terminology in nasal anatomy and surgery, suggestions for improvement. Rhinology, 2003; 41:129-133)

2.6 References

1. Cummings CW, Fredrickson JM, Harker LA, Krause CJ, Richardson MA, Schuller DE. Otolaryngology Head and Surgery. St Louis, Missouri; 3rd edition, Vol 2: 1998 (Chps 42 and 50).

2. Neskey D, Eloy JA, Casiano RR. Nasal, septal, and turbinate anatomy and embryology. *Otolarygngol Clin N Amer* 2009;42(2):193-205

3. Gray LP. Deviated nasal septum. Incidence and etiology. *Ann Oto Rhinol Larngol Suppl* 1978;50:1-20

4. Jeppesen F, Winfield I. Dislocation of the nasal septal cartilage in the newborn. *Acta Obstetr Gynecol Scand* 1972;51:5-15

5. Alpini D, Corti A, Brusa E, Bini A. Septal deviation in newborn infants. *Int J Pediatr Otorhinolaryngol* 1986;11:103-107

6. Kawalski H and Spiewak P. How septum deformations in newborns occur. *Int J Pediatr Otorhinolaryngol* 1998; 44(1): 23-30

7. Haapaniemi J, Suonpää JT, Salmivalli AJ, Tuominen J. Prevalence of septal deviations in school-aged children. *Rhinology* 1995; *33*(1):1-3

8. Finkbohner R, Johnston D, Crawford ES, Coselli J, Milewicz DM. Marfan syndrome long-term survival and complications after aortic aneurysm repair. *Circulation* 1995;91(3):728-733

9. Pirsig W. Growth of the deviated septum and its influence on midfacial development. *Fac Plast Surg* 1992 8(4): 224-232

10. Kim J, Kim SW, Kim SW, Cho JH, and Park YJ. Role of the Sphenoidal Process of the Septal Cartilage in the Development of Septal Deviation. *Otolaryngol Head Neck Surg* 2012;146(1):151-155

11. Sooknundun M, Kacker SK, Bhatia R, and Deka RC. Nasal septal deviation: effective intervention and long term follow-up. *Int Journal of Pediatr Otorhinolaryngol* 1986;12(1): 65-72

12. D'Ascanio L, Lancione C, Pompa G, Rebuffini E, Mansi N, and Manzini M.Craniofacial growth in children with nasal septum deviation: a cephalometric comparative study. *Int J Pediatr Otorhinolaryngol* 2010;74(10): 1180-1183

13. Whiting P, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ,

Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM;QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Inter Med* 2011;155(8):529-36

14. Cho GS, Kim JH, Jang YJ. Correlation of nasal obstruction with nasal cross-sectional area measured by computed tomography in patients with nasal septal deviation. *Ann Otol Rhinol Laryngol* 2012;*121*(4):239-245

15 . Liu T, Han D, Wang J, Tan J, Zang H, Wang T, Yunchuan L,Cui S. Effects of septal deviation on the airflow characteristics: Using computational fluid dynamics models. *Acta Oto-laryngologica* 2012:*132*:290-298

16. Chen XB, Lee HP, Chong H, Fook V, Wang D. Assessment of septal deviation effects on nasal air flow: a computational fluid dynamics model. *Laryngoscope* 2009;*119*:1730-1736

17. Hanif J, Jawad SS, Eccles R. A study to assess the usefulness of a portable spirometer to quantify the severity of nasal septal deviation. *Rhinology* 2003;*41*:11-15

18. Filho DI, Raveli DB, Raveli RB, Loffredo LCML, Gandini LG. A comparison of nasopharyngeal endoscopy and lateral cephalometric radiography in the diagnosis of nasopharyngeal airway obstruction. *Am J Orthod Dentofacial Orthop* 2001;*120*:348-352

19. Cole P, Chaban R, Naito K, Oprysk, D. The obstructive nasal septum: effect of simulated deviations on nasal airflow resistance. *Arch Otolaryngol Head Neck Surg* 1988;*114*(4): 410-412

20. Farhadi M, Ghanbari H, Izadi, F et al. Role of spirometry in detection of nasal obstruction. *J Laryngol Otol* 2013:127:271-273

21. Kahveci OK, Miman MC, Yucel A, Yucedag F, Okur, E, Altuntas, A.The efficiency of Nose Obstruction Symptom Evaluation (NOSE) scale on patients with nasal septal deviation. *Auris Nasus Larynx* 2012; *39*(3):275-279

22. Rujanavej V, Snidvongs K, Chusakul S, Aeumjaturapat S. The validity of peak nasal inspiratory flow as a screening tool for nasal obstruction. *J Med Assoc Thai 2012;95*(9):1205-1210

23. Gogniashvilli G, Steinmeier E, Mlynski, G, Beule AG. Physiologic and pathologic septal deviations: subjective and objective functional rhinologic findings. *Rhinology* 2011;*49*(1):24-29

24. Garcia GJ, Rhee JS, Senior BA, Kimbell JS. Septal deviation and nasal resistance: an investigation using virtual surgery and computational fluid

dynamics. *Am J of Rhinol Allergy* 2010;*24*:e46-e53

25. Pirila T, Tikanto J. Acoustic rhinometry and rhinomanometry in the preoperative screening of septal surgery patients. *Am J Rhinol Allergy* 2009;*23*(6):605-609

26. Chandra RK, Patadia MO, Raviv J. Diagnosis of nasal airway obstruction. *Otolaryngol Clin North Am* 2009;*42*(2):207-225

27. Benninger MS. Nasal endoscopy: its role in office diagnosis. *Am J Rhinol 1997;11*:177-180

28. Cuddihy PJ, Eccles, R. The use of nasal spirometry as an objective measure of nasal septal deviation and the effectiveness of septal surgery. *Clin Otolaryngol* 2003; *28*(4): 325-330

29. Choi H, Park IH, Yoon HG, Lee HM. Diagnostic accuracy evaluation of nasal sound spectral analysis compared with peak nasal inspiratory flow in nasal septal deviation. *Am J Rhinol Allergy* 2011;*25*(2):e86-e89.

30. Mamikoglu , Houser S, Akbar I, Ng B, Corey J P. Acoustic rhinometry and computed tomography scans for the diagnosis of nasal septal deviation, with clinical correlation. *Otolaryngol Head Neck Surg* 2000;*123*(1): 61-68

31. Tahamiler R, Canakcioglu S, Yilmaz S, Dirican, A. Expiratory nasal sound analysis as a new method for evaluation of nasal obstruction in patients with nasal septal deviation: comparison of expiratory nasal sounds from both deviated and normal nasal cavity. *J Laryngol Otol* 2008;*122*(02):150-154.

32. Tahamiler R, Alimoglu Y, Canakcioglu S. Comparison of Odiosoft-Rhino and rhinomanometry in evaluation of nasal patency. *Rhinology* 2011;*49*(1):41-45

33. Huygen PL, Klaassen AB, De Leeuw TJ, Wentges, RT. Rhinomanometric detection rate of rhinoscopically-assessed septal deviations. *Rhinology* 1992;*30*(3):177-181

34. Szucs E, Clement PA. Acoustic rhinometry and rhinomanometry in the evaluation of nasal patency of patients with nasal septal deviation. *Amer J Rhinology* 1998; *12*(5):345-352

35. Huang ZL, Wang DY, Zhang PC, Dong F, Yeoh KH. Evaluation of nasal cavity by acoustic rhinometry in Chinese, Malay and Indian ethnic groups. *Acta oto-laryngologica* 2001;*121*(7):844-848.

36. Sedaghat AR, Busaba NY, Cunningham MJ, Kieff D. Clinical assessment is an accurate predictor of which patients will need septoplasty. *Laryngoscope* 2013;123:48-52

37. Cole PC, Chaban R. Naito K, Oprysk D. The obstructive nasal septum. *Arch Otolaryngol Head and Neck Surg* 1988;114:410-412

38. Clement PAR. Committee report on standardization of rhinomanometry. *Rhinology* 1984;22:151-5

39. Moore M, Eccles R: Objective evidence for the efficacy of surgical management of the deviated septum as a treatment for chronic nasal obstruction: a systematic review.

Chapter 3

Effect of rapid maxillary expansion on the nasal septum deviation: a systematic review

3.1 Introduction

The nasal septum is an important functional and aesthetic structure of the nose. It is responsible for regulating airflow through the nose while lending shape and support to the nasal dorsum and caudal aspect of the nose. Within the nasal cavity, a straight septum enables laminar airflow, allowing the inspired air to be warmed, cleaned and humidified and thus optimized for gas exchange at the alveoli in the lungs. Conversely, a deviated nasal septum can contribute to various degrees of nasal obstruction and altered nasal respiration (1).

Nasal septal deviation (NSD) is defined as deviation of the either the bony or cartilaginous septum or both from the midline. Although, the earliest investigation reported 80% of humans having some degree of septal deviation (2), more recent numbers in adults range around 65% (3). Prevalence range of NSD in neonates has been reported between one (4) to roughly twenty percent (5). In school aged children (6-15 years) it was documented as 20% when assessed on occipitomental projection radiographs, whereas the clinical diagnosis of NSD was made in approximately 10% of the same cohort of children (6).

Nasal obstruction from a deviated nasal septum may cause turbulent nasal airflow precipitating in dryness and crusting of the nose, frequent nosebleeds and recurrent sinusitis (7). Furthermore, during developmental years inadequacy of the nasal airway can necessitate chronic mouth breathing, causing moderate to severe maxillary constriction, and a vertical skeletal growth pattern characterized by long anterior lower face height, bilateral maxillary crossbite, high arched palate, low tongue posture and incompetent lips (8,9). In addition, it has been hypothesized that nasal breathing is a requirement for proper growth and development of the craniofacial complex (10). According to the functional matrix theory, nasal airflow is a continuous stimulus for lowering of the palate and for lateral maxillary growth, indicating a close relationship between nasal breathing and dentofacial morphology.

Rapid maxillary expansion (RME) is routinely used in orthodontic treatment to correct transverse maxillary constriction by opening of the midpalatal suture (11). It works by separation of the two halves of the palatal bones across the median palatal suture due to a lateral force from the appliance (12). Both the zygomatic and sphenoid bones of the cranial base are met with resistance during expansion. Therefore the separation of maxillary bones occurs in a triangular manner, with apex towards the nasal cavity and base at the same level as the palatine process (13) resulting in more opening anteriorly than posteriorly (14). Thus one can extrapolate that there will be greatest improvement in the caliber of the anterior rate limiting nasal valve area from RME compared to other regions of the nasal cavity. Some studies have reported correction of septal deviation as an incidental finding from

RME (15,16). To our knowledge, no review of the literature has been conducted to investigate this finding. Therefore, the purpose of this systematic review is to methodically analyze the available literature concerning the effects of RME on nasal septal deviation.

3.2 Methods

Several databases were searched electronically with the help of a senior librarian specializing in health sciences database searches. The searched electronic databases were MEDLINE (from 1966 to fourth week of May 2014, OVID), EMBASE (from 1974 to fourth week of May 2014, OVID), Web of Science (from 1945 to fourth week of May 2014, Thomson Reuters), Cochrane Database of Systematic Review (CDSR), Cochrane Central Register of Controlled Trials (CCTR), Cochrane Methodology Register (CMR), Database of Abstracts of Reviews of Effects (DARE), American College of Physicians Journal Club (ACP Journal Club), Health Technology Assessments (HTA) and NHS Economic Evaluation Database (NHSEED) until the second quarter of 2014. The MeSH search terms used in database searches were 'nasal septum', 'palatal expansion', and 'maxillary expansion', 'orthodontic device' and 'palatal expansion technique'.

Two authors (T.A. and K.A.) independently reviewed the title and abstracts of the database searches. Abstracts from human studies that discussed orthopedic effect on nasal septum from non-surgical palatal expansion were included at the initial selection phase. Full text of all studies that appeared to meet the inclusion criteria were retrieved along with ones that had insufficient information in the abstracts to make a final decision regarding their inclusion. The references of retrieved articles were also manually searched for additional studies that could be included in the systematic review. The authors (T.A and K.A) independently assessed full articles obtained for inclusion in the systematic review and any disagreement was settled through discussion until a consensus was reached.

The following exclusion criteria were finally applied to the studies after retrieval of full text of articles:

1. No case reports
2. Studies that reported presence of any concurrent sino-nasal pathology in their patient sample that would preclude visualization of nasal septum before or after RPE treatment were excluded (examples of such conditions included, but not limited to, were septal perforation, enlarged turbinates and nasal polyps etc).
3. Studies that merely reported a visual change in NSD as an incidental finding and did not implement protocols to methodically measure nasal septum pre and post expansion were also excluded.

Methodological scoring to assess the quality of included studies was also performed independently by two authors (T.A and K.A) through Methodological Index for non-Randomized Studies (MINORS) checklist (17). Any disagreement in individual scores was settled through discussion till the final consensus was reached. Although an overall quality score was tabulated, it was established that the quality assessment would be mostly through analysis of individual components.

3.3 Results

The flow chart of the electronic database searches and final selection of studies to be included in the systematic review is outlined in Figure 3.1. Online searches resulted in 6 potential abstracts (15,16,18-21) after removal of duplicates that resulted from overlap of studies between the electronic databases. Four studies (16,18-20) were later excluded after full review of the articles and reasons for their exclusion are listed in Table 3.1. This resulted in only two studies (15,21) to be included in this systematic review. Key details of the included studies are listed in Table 3.2.

One study (15) reported straightening of the nasal septum by approximately 94% in the middle and the inferior third of nasal cavity from RME. Correction in NSD was confirmed by a reduction in the amplitude of septal deviation as measured in millimeters from the mid sagittal plane. The included sample were 100 children aged 5 to 9 years. RME was accomplished through hyrax activated twice a day for 15 days.

Another study (21) reported no positional change in the nasal septum from RME. In this study, nasal septal angle was measured in degrees from the mid sagittal plane. The sample consisted of 10 children aged 13-17 years with occlusal coverage hyrax appliance. Expansion protocol in this cohort was twice a-day hyrax activation for 2-3 weeks.

Results from MINORS (17) are listed in Table 3.3. Total scores for both studies were the same. Both included studies stated clear objectives (Item 1) and assessed outcomes according to the aim of the study (Item 4) with appropriate statistical analysis (Item 12). Both studies included patients according to predetermined exclusion/ inclusion criteria and measurement protocols (Items 3, 4). However, unbiased assessment of outcome variable was not fulfilled by either study (Item 5). In addition, patients that could have been lost to follow up were not reported by either study (Item 7). Neither study conducted a prospective sample size calculation from effect size (Item 8) or had baseline equivalence of control and treatment groups (Item 10). One study (21) recruited the control group from data archives, therefore the criteria of contemporary control and treatment groups was not fulfilled (Item 10).

3.4 Discussion

Nasal breathing is a pre requisite for proper growth of the craniofacial complex. Moderate to severe nasal septal deviation (NSD) can cause clinically significant nasal obstruction, resulting in irreversible repercussions on the growth and development of craniofacial structures.

The purpose of this systematic review is to investigate the effect of rapid maxillary expansion on nasal septal deviation.

Historically, RME was believed to primarily affect airway function through changes to nasal volume. For example, Haas (13) reported RME resulted in an increased nasal width of 2-4.5mm with an expansion protocol of 0.4 to 0.5 mm per day for 12 to 27 days in his patient cohort. It was postulated that the alteration in nasal dimensions following RME are related to the lateral movement of the nasal walls, increase in the vertical dimension of the nasal cavity secondary to inferior rotation of the palate (12).

Like Haas, many investigators have focused on changes in nasal volume or the secondary effect of changing nasal airflow resistance after RME. These studies yielded inconclusive findings. Some demonstrated positive nasal changes after RME (22,23), others found no difference (24), while some found such small differences that the clinical relevance was questioned (25,26). However, more clinically directed inquiry, such as subjective patient experience (27,28) and polysomnography changes with sleep apnea (29) have provided growing support to functional airway benefits of RME.

Since changes in nasal volume alone seem inconclusive to account for the effects of RME, alternative explanations are now being explored, such as changes in the nasal septum. Data from computational fluid dynamic studies that have modeled nasal septal deviations have been valuable in providing (30,31) comprehensive information on nasal airflow characteristics. These studies concluded that anterior and inferior septal deviations increase nasal resistance more than posterior and superior septal deviations (30,31). Consequently, significant septal deviations in the posterior nasal cavity can occur without significant increase in nasal airway resistance. The reason for this finding is due to the fact that in healthy nasal passages majority of the airflow is at the height of the nasal floor and area between inferior and middle turbinates, with less than 15 % of nasal airflow at superior part of the nasal cavity (30). Rapid maxillary expansion affects nasal airway because it is considered to modify the nasal valve area, which represents the narrowest nasal cross-sectional area. In other words, nasal valve area is the greatest contributor to nasal airway resistance during breathing.

Interestingly, patients with maxillary deficiency in the transverse dimension also have small nasal cross-sectional areas (32), which can explain the reason for maxillary expansion having a potentially positive effect on nasal airway. Further investigation of the possibility of RME correcting NSD would be valuable, considering the undesirable sequelea of NSD on nasal breathing, which can consequently affect craniofacial development. In addition, septal cartilage can act as a growth center in early development; its deviation can cause distortion of the maxillary complex towards the deviated side (15).

Although, there are numerous reports of the effects of RME on nasal airway, only a few of those studies have hypothesized that RME “straightens” the nasal septum thereby correcting nasal septal deviation (15,16,33). Earliest finding of this effect came from Gray (16), whereby he noted an improvement in the “curve” of the deviated nasal septum after RME treatment from subjective visualization of posterior anterior radiographs. The sample size in this study consisted of 310 patients ranging from 4-24 years of age with majority (86%) of the patients under the ages of 12. Subjective improvement of nasal airway was reported in these patients with improvement stable at 6 months post expansion. Approximately 80 percent of patients reporting switching from mouth to nasal breathing post expansion with a significant reduction (roughly 60%) in colds, sore throats, ear infections and nasal allergies. It was hypothesized that improvement of nasal ventilation from RME prevented dryness and crusting of the nasal mucosa thereby reducing recurrent upper airway infections. Improved ciliary function and normal nasal cycle function were among other benefits purported from increased nasal airflow resulting from RME. However, this study was excluded from our systematic review since the conclusions were based on visual and subjective assessment of X-rays without any objective quantification of change or appropriate statistical analysis.

Only two studies (15,21) were finally included in this systematic review after conducting electronic searches of several databases. Both analyzed the change in nasal septal deviation from RME in two-dimensional coronal views from posterior anterior cephalograms. Farronato et al (15) recruited 100 growing patients (ages 5-9 years, average 7.62 +/- 0.7) presenting with transverse maxillary constriction and measured an increase of 2.3 mm in the width of the nasal cavity and reported 94% reduction in the septal deviation from RME. The NSD correction was noted in the inferior and middle half of the nasal cavity when compared to a non-expansion control group. Septal correction in this study was measured by placing points on superior, middle and inferior segments of the septum as visualized from pre and post expansion PA cephalograms. Distances between these landmarks were measured along with maximum amplitude of deviation from an imaginary midline in coronal view. The resulting change was quantified in millimeters and as a percentage. Patient sample in this study had septal deviation of at least 1mm in middle/ inferior third of the septum as visualized as a deflection in the vertical path from superior to inferior on PA (coronal view) X-rays. However, the results from the other included paper (21) were contradictory to the aforementioned study. The latter study reported no change in NSD from RME in an older cohort of patients (ages 13-17 years).

It has been documented that RME efficacy is greater when done before the growth spurt (2.3mm) versus at or after the peak growth (1.5mm) (9). Incomplete calcification of the midpalatal suture in growing patients translates into ease of displacement of the lateral walls of the nasal cavity

(9). Rapid maxillary expansion treatment in mixed dentition i.e. prior to midpalatal suture closure has greater improvement in nasal airway resistance due to greater likelihood of skeletal change (nearly 50 %) as opposed to during adolescence when the change is mostly dental. However, to our knowledge, no study has investigated the effect of slow or semi-rapid expansion on nasal airway or structures.

Methodological quality of studies included in this systematic review was analyzed using MINORS checklist. Although, both studies had similar total scores (7.5/12) suggesting moderate level of evidence, there were a few methodological flaws. Both stated clear objectives and assessed outcomes according to the aim of the study, however, the outcome assessor was not blinded and the reasons for lack of blinding were not mentioned. There was also no prospective sample size calculation, and the reasoning behind this was not elucidated. It is ambiguous whether the baseline characteristics of the control and treatment groups were equivalent. Farronato et al (15) included a “control” group having no septal deviation and without RME. It would be difficult to ascertain the effect of an intervention such as RME, without a comparable baseline nasal septal deviation in control and treatment groups. Although, the Altug-Atac et al (21) did report including an age matched untreated control group, the comparison was historical, because the control group was recruited from archived patient database.

Furthermore, it is unclear whether the control group and RME group had similar baseline nasal septal deviation for accurate comparison.

Due to lack of literature in this area, it would be beneficial to plan future studies in preadolescent patient population presenting with transverse maxillary deficiency. Aim of the aforementioned study would be to methodically measure NSD in a three-dimensional view at set landmarks instead of an isolated pre and post PA cephalogram image.

3.5 Conclusions

The question of whether RME is beneficial in reducing the effect of nasal obstruction from deviated nasal septum in growing patients has not been intensively investigated. Thus far, the limited available evidence suggests a potentially positive effect in childhood, but no significant change in adulthood from RME in patients with NSD. However, the risk of bias was moderate and the clinical significance of reported changes may be considered questionable.

Figure 3.1 Summary of Systematic Review Process

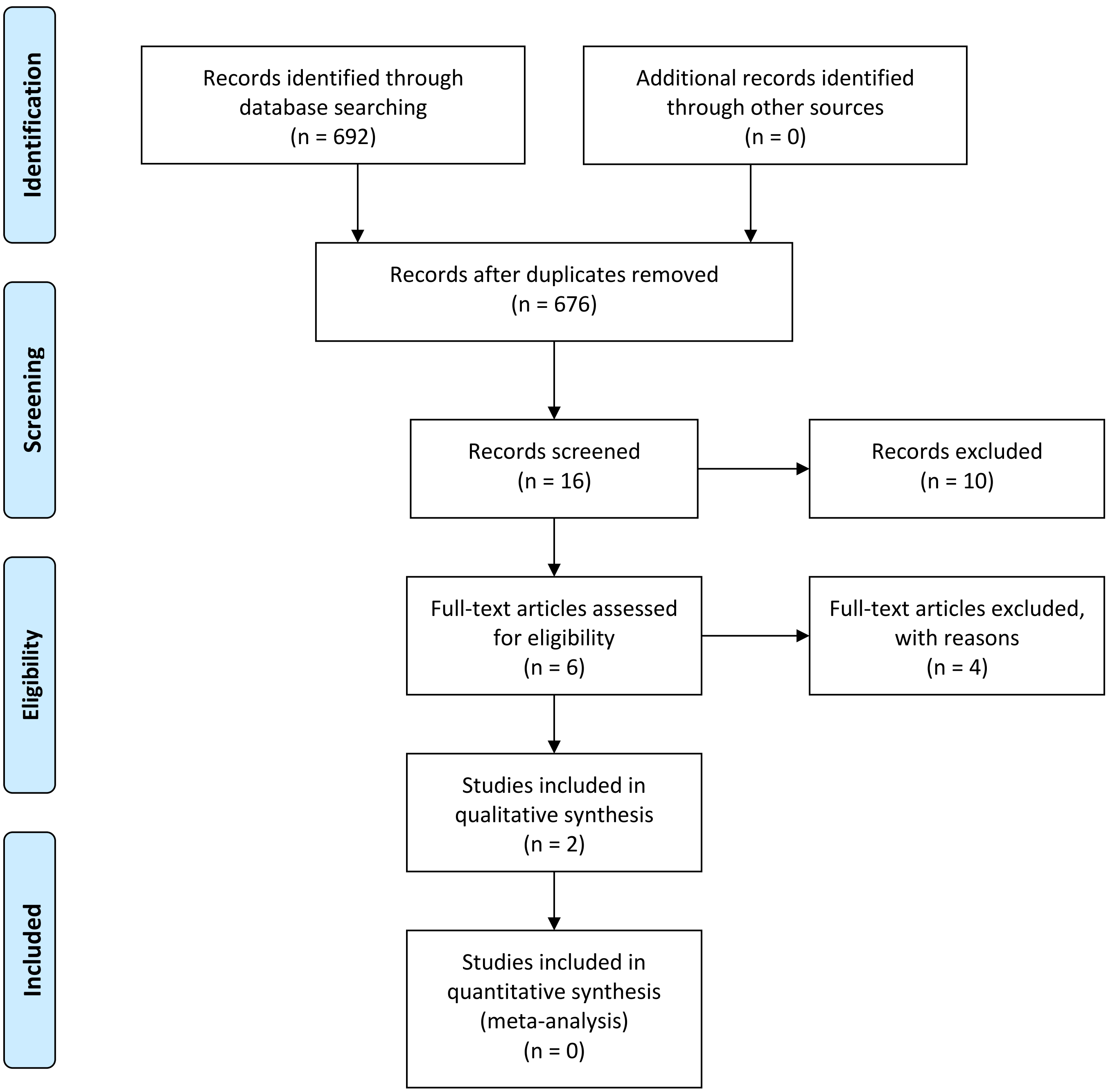


Table 3.1 Excluded Studies and Reason for their Exclusion

Studies Excluded	Reason for Exclusion
Baydas et al (18)	No mention of nasal septum
Schwarz et al (19)	Only surgical RME discussed with respect to changes in nasal septum
Gray LP (20)	Reported a visual change in nasal septum from RME without employing methods to measure the change
Gray LP (16)	Reported a visual change in nasal septum from RME without employing methods to measure the change

Table 3. 2 Characteristics of Included Studies

Study	Baseline characteristics of treatment group	Baseline characteristics of Control Group	RME Protocol	Measurement of the Nasal Septum	Results
Farronato et al (15)	N=100 Ages 5-9 years (mean =7.62 years, SD= 0.7) Nasal septal deviation (NSD) of more than 1mm as seen on PA radiographs (amplitude of deviation)	N=40 Ages 5-9 years (mean 7.62, SD= 0.7) Not treated with RME Not clear if they presented with NSD	Hyrax expander 1 turn (0.25mm) twice a day for 15 days	Amplitude of NSD measured on Frontal/PA cephalograms as millimeter distance between midline axis of symmetry and deviated nasal septum. Measurements taken before appliance insertion (T0), at appliance removal (T1) and 6 months after appliance removal (T2)	94 % reduction in amplitude of NSD from RME in middle and lower third of the nasal cavity from T0 to T2.
Altug-Atac et al (21)	n=10 Ages 13-17 years (mean =15 years) Nasal septal angle (from mid sagittal plane=1.05 degrees (S.D=0.91)	n=10 Ages 13-17 years (mean =15 years) Not treated with RME Nasal septal angle 0.78 (SD=1.23)	Occlusal coverage Hyrax type expander with 2 turns a day for 2-3 weeks	Measured in degrees as angle between the nasal septum mid sagittal plane on Frontal/PA cephalograms Measurements taken prior to appliance insertion and after 12 weeks active expansion	No significant positional change in nasal septum from RME

Table 3.3 Methodological Quality Assessment of Included Studies by MINORS

Methodological Item	Farronato et al (15)	Score	Altug-Atac et al (21)	Score
1. A clearly stated aim	Yes	1	Yes	1
2. Inclusion of consecutive patients	Yes	1	Yes	1
3. Prospective collection of data	Yes	1	Yes	1
4. Endpoints appropriate to the aim of the study	Yes	1	Yes	1
5. Unbiased assessment of the study endpoint	No	0	No	0
6. Follow up period appropriate for the aim of the study	Yes	1	Yes	1
7. Loss to follow up less than 5%	Unclear	0.5	Unclear	0.5
8. Prospective calculation of study size	No	0	No	0
9. An adequate control group	No	0	Unclear	0.5
10. Contemporary groups	Yes	1	No	0
11. Baseline equivalence of groups	No	0	Unclear	0.5
12. Adequate statistical analysis	Yes	1	Yes	1
Total Score		7.5		7.5

Score Key: Yes = 1, No = 0, Unclear = 0.5

3. 6 References

(1) Cummings CW et al editor. Otolaryngology--head & neck surgery. 4th ed. Philadelphia, Pa: Elsevier Mosby; 2005.

(2) Gray LP. Deviated nasal septum. Incidence and etiology. Annals of Otology, Rhinology, & Laryngology - Supplement 1978 May-Jun;87(3 Pt 3 Suppl 50):3-20.

(3) Stallman JS, Lobo JN, Som PM. The incidence of concha bullosa and its relationship to nasal septal deviation and paranasal sinus disease. Ajnr: American Journal of Neuroradiology 2004 Oct;25(9):1613-1618.

(4) Podoshin L, Gertner R, Fradis M, Berger A. Incidence and treatment of deviation of nasal septum in newborns. Ear Nose Throat J 1991 Aug;70(8):485-487.

(5) Kawalski H, Spiewak P. How septum deformations in newborns occur. Int J Pediatr Otorhinolaryngol 1998 Jun 1;44(1):23-30.

(6) Haapaniemi JJ, Suonpaa JT, Salmivalli AJ, Tuominen J. Prevalence of septal deviations in school-aged children. Rhinology 1995 Mar;33(1):1-3.

(7) Sooknundun M, Kacker SK, Bhatia R, Deka RC. Nasal septal deviation: effective intervention and long term follow-up. Int J Pediatr Otorhinolaryngol 1986 Nov;12(1):65-72.

(8) Laptook T. Conductive hearing loss and rapid maxillary expansion. Report of a case. Am J Orthod 1981 Sep;80(3):325-331.

(9) Baccetti T, Franchi L, Cameron CG, McNamara JA,Jr. Treatment timing for rapid maxillary expansion. Angle Orthod 2001 Oct;71(5):343-350.

(10) Moss-Salentijn L. Melvin L. Moss and the functional matrix. J Dent Res 1997 Dec;76(12):1814-1817.

(11) Haas AJ. The treatment of maxillary deficiency by opening the midpalatal suture. Angle Orthod 1965 Jul;35:200-217.

(12) Haas AJ. Palatal expansion: just the beginning of dentofacial orthopedics. Am J Orthod 1970 Mar;57(3):219-255.

(13) Haas AJ. Rapid expansion of the maxillary dental arch and nasal cavity by opening the midpalatal suture. Angle Orthod 1961;31(2):73-90.

(14) Enoki C, Valera FC, Lessa FC, Elias AM, Matsumoto MA, Anselmo-Lima WT. Effect of rapid maxillary expansion on the dimension of the nasal cavity and on nasal air resistance. Int J Pediatr Otorhinolaryngol 2006 Jul;70(7):1225-1230.

(15) Farronato G, Giannini L, Galbiati G, Maspero C. RME: influences on the nasal septum. Minerva Stomatol 2012 Apr;61(4):125-134.

(16) Gray LP. Results of 310 cases of rapid maxillary expansion selected for medical reasons. Journal of Laryngology & Otology 1975 Jun;89(6):601-614.

(17) Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ J Surg 2003 Sep;73(9):712-716.

(18) Baydas B, Yavuz I, Uslu H, Dagsuyu IM, Ceylan I. Nonsurgical rapid maxillary expansion effects on craniofacial structures in young adult females. A bone scintigraphy study. Angle Orthod 2006 Sep;76(5):759-767.

(19) Schwarz GM, Thrash J, Byrd DL, Jacobs JD. Tomographic assessment of nasal septal changes following surgical-orthodontic rapid maxillary expansion. Am J Orthod 1985 1985;87(1):39-45.

(20) Gray LP, Brogan WF. Septal deformity malocclusion and rapid maxillary expansion. Orthodontist 1972;4(1):2-14.

(21) Altug-Atac AT, Atac MS, Kurt G, Karasud HA. Changes in nasal structures following orthopaedic and surgically assisted rapid maxillary expansion. International Journal of Oral & Maxillofacial Surgery 2010 Feb;39(2):129-135.

(22) Baratieri C, Alves M,Jr, de Souza MM, de Souza Araujo MT, Maia LC. Does rapid maxillary expansion have long-term effects on airway dimensions and breathing? American Journal of Orthodontics & Dentofacial Orthopedics 2011 Aug;140(2):146-156.

(23) Smith T, Ghoneima A, Stewart K, Liu S, Eckert G, Halum S, et al. Three-dimensional computed tomography analysis of airway volume changes after rapid maxillary expansion. American Journal of Orthodontics & Dentofacial Orthopedics 2012 May;141(5):618-626.

(24) Gordon JM, Rosenblatt M, Witmans M, Carey JP, Heo G, Major PW, et al. Rapid palatal expansion effects on nasal airway dimensions as measured by acoustic rhinometry. A systematic review. Angle Orthod 2009 Sep;79(5):1000-1007.

(25) Ceroni Compadretti G, Tasca I, Alessandri-Bonetti G, Peri S, D'Addario A. Acoustic rhinometric measurements in children undergoing rapid maxillary expansion. Int J Pediatr Otorhinolaryngol 2006 Jan;70(1):27-34.

(26) Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012 Sep;130(3):e714-55.

(27) Doruk C, Sokucu O, Sezer H, Canbay EI. Evaluation of nasal airway resistance during rapid maxillary expansion using acoustic rhinometry. Eur J Orthod 2004 Aug;26(4):397-401.

(28) Oliveira De Felippe NL, Da Silveira AC, Viana G, Kusnoto B, Smith B, Evans CA. Relationship between rapid maxillary expansion and nasal cavity size and airway resistance: short- and long-term effects. American Journal of Orthodontics & Dentofacial Orthopedics 2008 Sep;134(3):370-382.

(29) Guilleminault C, Monteyrol PJ, Huynh NT, Pirelli P, Quo S, Li K. Adeno-tonsillectomy and rapid maxillary distraction in pre-pubertal children, a pilot study. Sleep & Breathing 2011 May;15(2):173-177.

(30) Garcia GJ, Rhee JS, Senior BA, Kimbell JS. Septal deviation and nasal resistance: an investigation using virtual surgery and computational fluid dynamics. American Journal of Rhinology & Allergy 2010 Jan-Feb;24(1):e46-53.

(31) Liu T, Han D, Wang J, Tan J, Zang H, Wang T, et al. Effects of septal deviation on the airflow characteristics: using computational fluid dynamics models. Acta Otolaryngol 2012 Mar;132(3):290-298.

(32) Baraldi CE, Pretto SM, Puricelli E. Evaluation of surgically assisted maxillary expansion using acoustic rhinometry and postero-anterior cephalometry. International Journal of Oral & Maxillofacial Surgery 2007 Apr;36(4):305-309.

(33) Bicakci AA, Agar U, Sokucu O, Babacan H, Doruk C. Nasal airway changes due to rapid maxillary expansion timing. Angle Orthod 2005 Jan;75(1):1-6.

Chapter 4
Nasal Septal Changes in Adolescent Patients treated with Rapid Maxillary Expansion as assessed through Cone Beam Computed Tomography

4.1 Introduction

The reciprocal effects of nasal breathing on craniofacial development have been intensively investigated in the literature. According to Moss' functional theory, nasal respiration enables normal growth and development of the craniofacial structures(1). Moss hypothesized that undisturbed nasal airflow is a continuous stimulus for lowering of the palate and for lateral maxillary growth, indicating a close relationship between nasal breathing and dentofacial morphology. Altered respiration patterns resulted in forward tongue positioning, lowered mandibular posture, and downward displacement of the maxilla with extrusion of posterior teeth. The mandible rotates clockwise increasing the lower facial height, and there is a concurrent relative shortening of the mandibular ramus along with an increase in the gonial angle. (2)

Nasal septal deviation (NSD) is defined as deviation of the either the bony or cartilaginous septum or both from the facial midline. In humans, significant nasal obstruction caused by NSD can affect nasal airflow and can increase nasal airway resistance, leading to the craniofacial changes reported by Harvold (2). These changes consist of a long face syndrome characterized by narrow maxilla, steep mandibular plane, retrognathic mandible, increased lower face height, lip incompetence, constricted alar bases and typically malocclusion consisting of a posterior crossbite (3).

Rapid maxillary expansion (RME) is routinely used in orthodontics to treat transverse maxillary constriction, posterior dental crossbite and crowding (4). Sutural opening effect of RME can be described as a rotation hinge, whereby the base of the hinge is at the floor of the nasal cavity and the point of rotation is at the top of the nose. It can therefore be hypothesized that as the nasal floor or roof of the palate lowers down with RME there is a concomitant increase of vertical nasal dimensions that could straighten a deviated septum. Although, several studies have investigated the effect of RME on nasal cavity size and airway (5-10), there is lack of research on the changes caused by RME of the nasal septum. Reports have suggested RME may affect the nasal septum(7,11,12). Gray first reported septum changes when he discovered that RME treatment also appeared to improve NSD (7). More recently, Farronato *et al* (11) reported a 94% reduction in septal deviation from RME in children aged 5-9 years presenting with transverse maxillary constriction. The NSD correction was noted in the inferior and middle half of the nasal cavity when compared to a non-expansion control group.

To our knowledge, all previous reports utilized two-dimensional radiology (7,11,12) to assess nasal septal changes produced during RME and had significant methodological limitations. Two studies reported a favourable improvement of septal deviation after RME (7,11) treatment in growing patients while one (12) reported no change in non growing patients aged

15-19 years of age. However, these studies had some major limitations. There was lack of standardization in the study design and the nasal septum was measured at one snap shot radiographic image instead of its entirety along different points along the septum. It was also unclear whether both pre and post expansion radiographs measured the septal change at a set landmark. Although, improvement in nasal septum was reported post expansion, it was not clear whether the change was the same at each anatomical location along the nasal septum. Considering the importance of nasal breathing in development of craniofacial structures, it would be beneficial to ascertain if RME can reliably improve NSD and hence its detrimental effects on nasal breathing. Therefore, the objective of this study is to analyze three- dimensional changes of the nasal septum from maxillary expansion in an adolescent patient cohort. The utilization of three-dimensional imaging should overcome some of the limitations of previously conducted research.

4.2 Hypothesis

$H_{0:}$ There is no difference in nasal septum deviation as measured in coronal and axial views on CBCT between an adolescent patient cohort who received rapid maxillary expansion and a cohort that did not receive rapid maxillary expansion as part of their orthodontic treatment regimen

$H_{A:}$ There is a difference in nasal septum deviation as measured in coronal and axial views on CBCT between an adolescent patient cohort who received

RME and a cohort that did not receive rapid maxillary expansion as part of their orthodontic treatment regimen

4.3 Material and Methods

This retrospective study met ethics requirement by approval by the University of Alberta Health Research Ethics Board (study ID Pro00041136 - See Appendix B).

Patient samples were obtained from a previously conducted randomized clinical trial at the Department of Dentistry at University of Alberta during an 18-month period. A total of 33 patients with varying degrees of NSD at T1 (i.e. prior to RME treatment) were selected from an available pool of CBCT images of 120 patients through a brief visual inspection of the entire nasal septum for each patient. Patients with mild and moderate to severe nasal septal deviation were identified from transverse and coronal views of cone beam computed tomography (CBCT) records taken prior to treatment (T1) with RME (or without RME for control patients). Based on a previous publication (13) the septal deviation was considered moderate to severe if the deflection of the nasal septum from the mid-sagittal plane was greater than 9 degrees and mild if deviation was less than or equal to 8 degrees in any isolated CBCT image. Although septal deviation in degrees was used to categorize the sample based on the severity of NSD, it was the “degree of tortuosity” i.e. ratio of curved septum to imaginary straight septum that was used as an outcome measure in this study.

The final sample consisted of:

14 patients (10 females, 4 males) treated with RME with moderate/ severe NSD at T1 (more than 9 degrees).

12 patients (6 females, 6 males) treated with RME with mild NSD at T1 (less than 9 degrees)

7 untreated patients (3 females, 4 males) with RME with moderate to severe NSD (control group)

The control group was overall a year younger than both treatment groups (control group age range 12-13 years and treatment group age 14 years) (14). Maxillary expansion was carried out by either by bone-anchored expander (BAME) or tooth anchored maxillary expander (TAME).

Maxillary expansion was carried out in both BAME (14 patients) and TAME (12 patients) by activation twice a day (0.25 mm per turn, 0.5 mm daily) until posterior dental crossbite overcorrection by twenty percent was achieved (maxillary lingual cusps overlapping with lingual inclines of mandibular buccal cusps) and retained for 6 months. Bone anchored maxillary group received 2 mini screws on the palate between the permanent first molars and premolars (length, 12 mm; diameter, 1.5 mm; Straumann GBR-System, Andover, Mass) and an expansion screw (Palex II

Extra-Mini Expander, Summit Orthodontic Services, Munroe Falls, Ohio). The expansion and retention protocol was the same in both groups after expansion. Both groups had CBCT images taken 4 times (baseline [T1], after activation of the appliance [T2], after removal of the appliance [6 months, T3], and before fixed bonding [12 months, T4]). Only CBCT images taken at T1 and T3 were analyzed for this study. The goal of this study was not to analyze an immediate change in NSD from RME but to allow for 6-month relapse from RME prior to measuring NSD. (For detailed information on the methods of the previously conducted randomized trial, please refer to reference (14).

All CBCT images were taken with either a NewTom (18 patients at T1 and T3) or an iCAT machine (15 patients at T1 and T3). Images were converted to DICOM format software with a voxel size of 0.25 mm. All images at T1 and T3 for each patient were then uploaded to OsiriX DICOM Viewer (v.5.8 32 bit, Pixmeo, Geneva, Switzerland). Based on a previous publication(15):

1. Seven images (3 in axial and 4 in coronal views) were identified in the 3-D viewer/2-D orthogonal MPR mode in OsiriX for each patient in the sagittal view (Table 4. 1, Figures 4.1).

2. Based on five anatomical landmarks on sagittal view, three axial (A1, A2, A3) and four coronal DICOM images (C1, C2, C3, C4) for each patient at each time point were isolated. Seven DICOM images (A1, A2, A3, C1, C2, C3, C4) were obtained according to each landmark isolated in sagittal view per

patient at each time point (14 images for one patient considering T1 and T3).

3. These five anatomical landmarks in sagittal view were anterior most point of nasal bone (image A1, C1), perpendicular plate and vomer junction (image A2, C4), anterior nasal spine (image C2), crista galli (image C3), halfway point between anterior nasal spine and perpendicular plate/vomer junction (image A3).

For example, to isolate image A1 (and C1)

a. The most anterior point of the nasal bone is identified in the sagittal view on OsiriX (Figure 4. 1, Table 4.1). When the cursor is placed on this landmark, corresponding axial and coronal images were generated (Figure 4.2). The image generated in axial view is called A1 (corresponding to anterior most point on the nasal bone) and C1 for coronal view (corresponding to anterior most point of the nasal bone).
b. Similarly, when the cursor was placed on perpendicular plate of ethmoid and vomer junction images A2 and C4 corresponding to axial and coronal view were generated respectively (Figure 4.3). The image generated in axial view is called A2 (corresponding to perpendicular plate of ethmoid and vomer junction) and C4 for coronal view (corresponding to perpendicular plate of ethmoid and vomer junction).

c. See Figures 4.4 to 4.6 for images generated from anterior part of the nasal bone (coronal image C2, Figure 4.4), crista galli (coronal image C3, Figure 4.5) and halfway point (axial image A3, Figure 4.6) respectively.

Landmarks were chosen due to their ease of identification based on anatomical locations and to reasonably cover the boundaries of normal septal anatomy in anterior-posterior and inferior to superior directions. Landmark A3 was the only landmark not identified by an anatomical structure (15).

Table 4.1 Descriptions of the Landmarks in Sagittal View for Coronal and Axial Image Generation

Landmarks/ points selected on DICOM images in Sagittal view	Anatomical location
A1*	Most anterior point of nasal bone (axial view)
A2	Junction of perpendicular plate of Ethmoid bone and Vomer (axial view)
A3	Midway Point between A2 (C4) and C2. Anatomically found between the anterior nasal spine and Vomer/ perpendicular plate of Ethmoid junction in vertical direction (axial view)
C1*	Anterior point of nasal bone (coronal view)
C2	Most anterior point of anterior nasal spine (coronal view)
C3	Mid point of Crista galli (coronal view)
C4	Junction of perpendicular plate of Ethmoid bone and Vomer (coronal view)

- A stands for axial landmarks and C stands for coronal landmarks.
- Although A1 and C1 are same anatomical landmarks in sagittal view, On A1 slice/image nasal septum is measured in anterior to posterior. On C1 slice, it is measured from to inferior to superior view.

Figure 4. 1 Location of Axial and Coronal Images from Anatomical Landmarks in Sagittal View

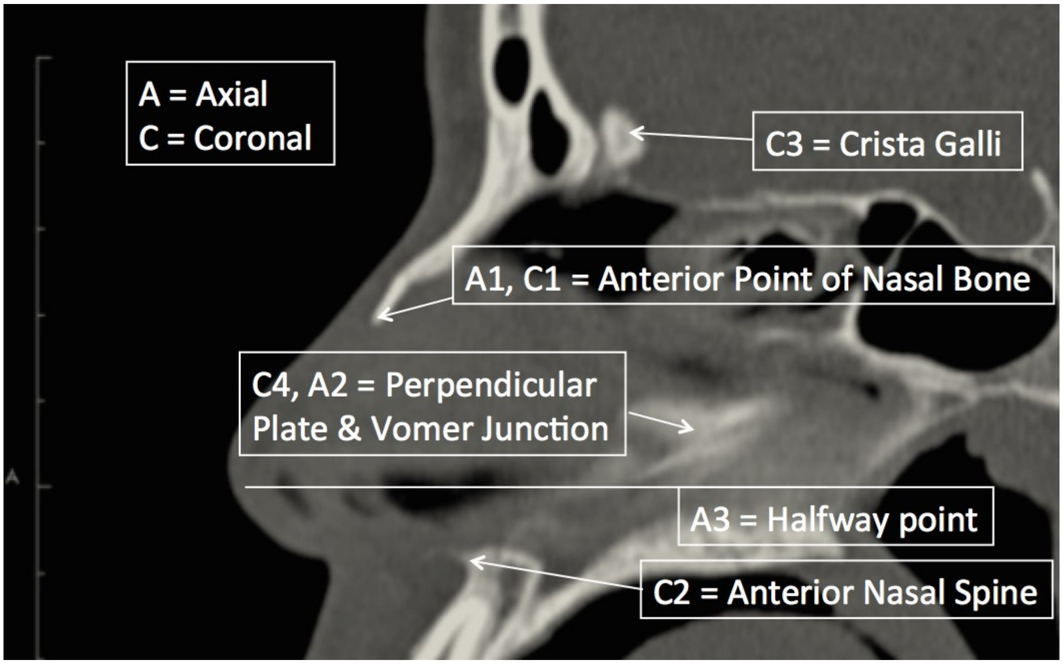


Figure 4.2 OsiriX (2-D Orthogonal MPR mode) for Axial and Coronal Images Based on Sagittal Landmark A1/C1

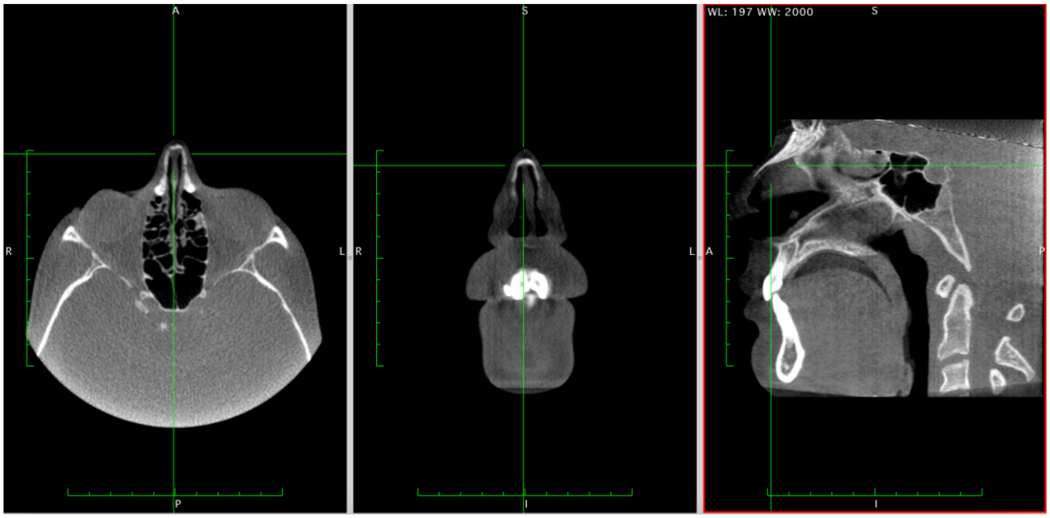


Figure 4.3 OsiriX (2-D Orthogonal MPR mode) for Axial and Coronal Images Based on Sagittal Landmark A2/C4

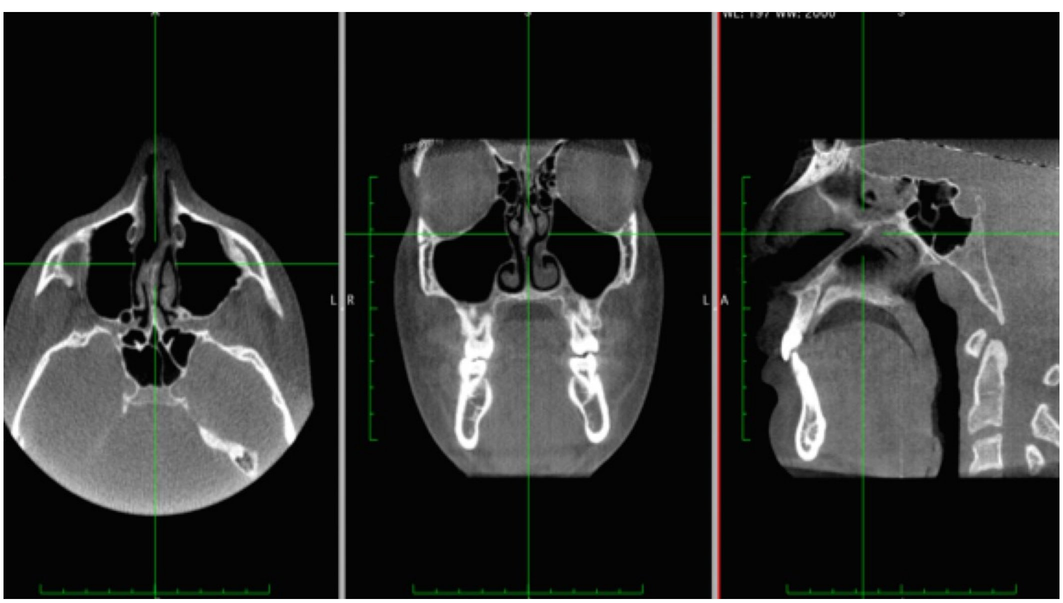


Figure 4.4 OsiriX Image in Coronal View based on Sagittal Landmark C2

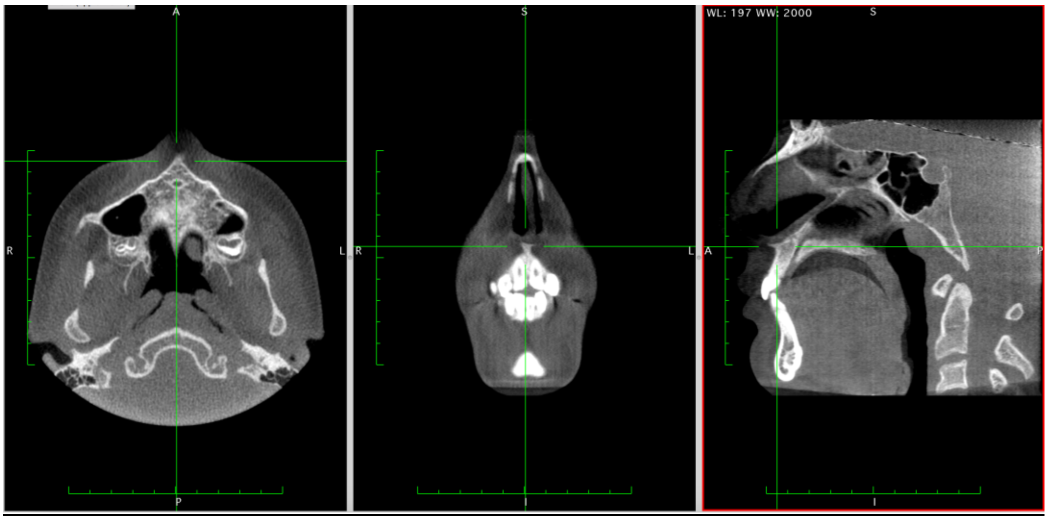


Figure 4.5 OsiriX Image in Coronal View based on Sagittal Landmark C3

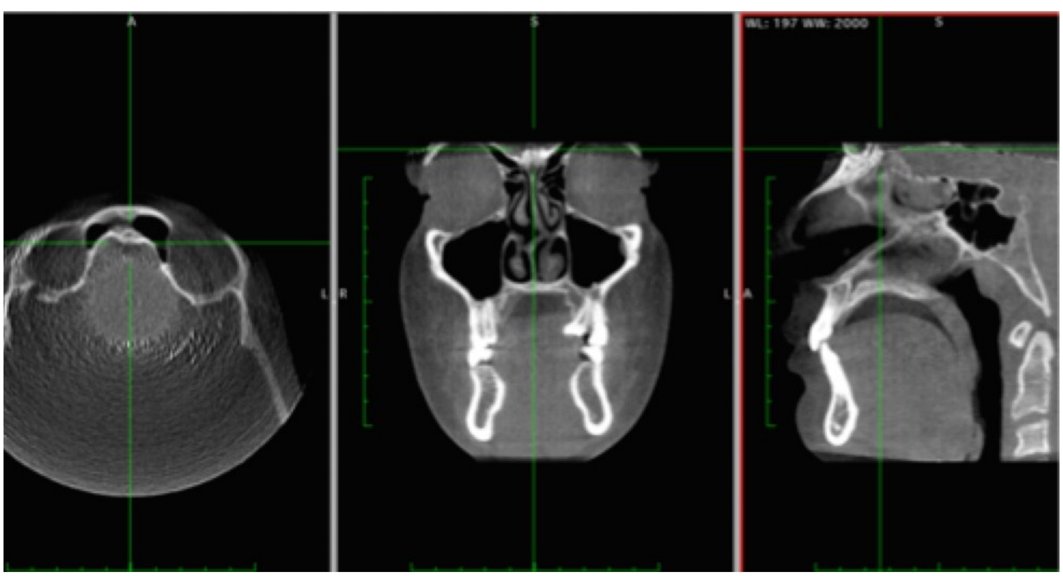
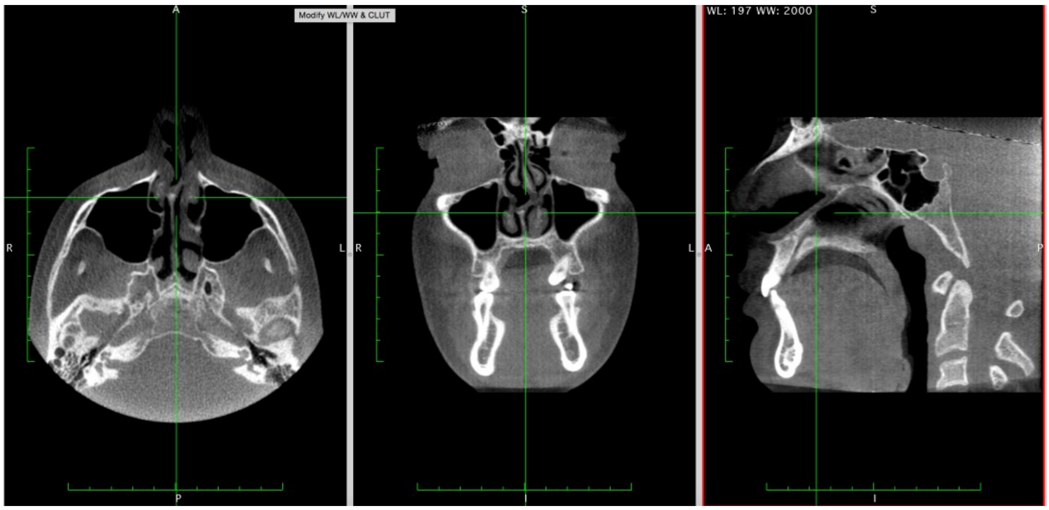


Figure 4.6 OsiriX Image in Coronal View based on Sagittal Landmark A3



Landmarked images were then transferred to MATLAB (MathWorks R2013b, Natick, Massachusetts) for systematic NSD tracing and analysis. The study investigator did input the time point (T1 or T3 DICOM image) in the MATLAB software, but was blinded to the degree of septal deviation or whether it was a treatment or control patient. The software code was adapted to this study by the same computer engineer who originally created the computer analysis(15). This software enabled the septum to be systematically traced and analyzed.

During analysis in MATLAB, the axial images (A1, A2, A3) were traced from anterior to posterior direction.

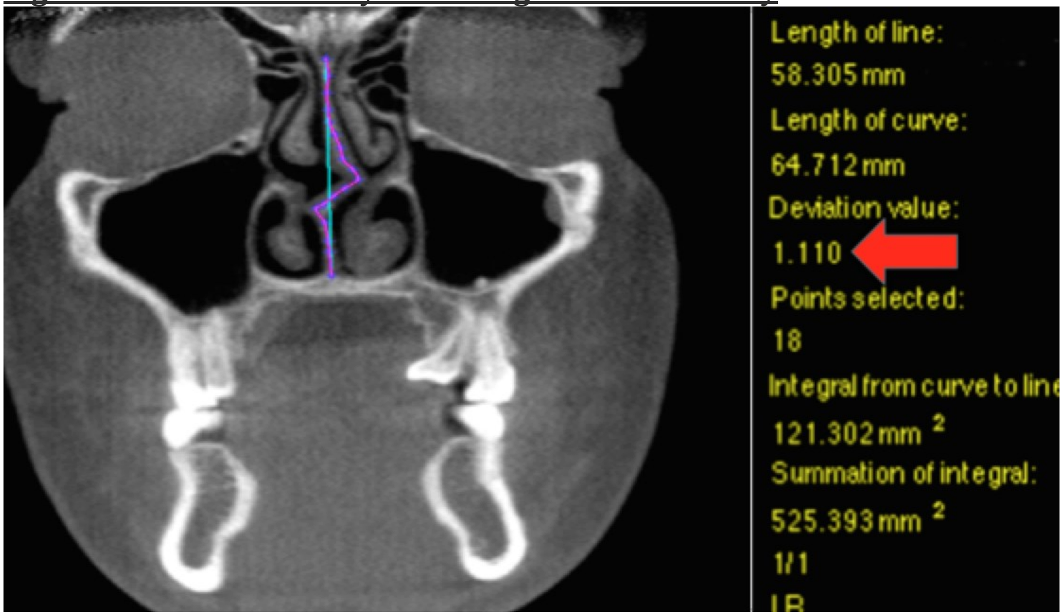
1. For example, the axial image A1, the nasal septum was systematically traced by placing points approximately 1-2 mm apart along its anterior posterior course.
2. Similarly, in coronal images (C1, C2, C3, C4) the nasal septum was

traced in entirety from superior to inferior direction by placing points digitally 1-2mm apart.

3. The data from NSD measurements done in MATLAB software was automatically transferred to a comma separated value (csv) spreadsheet. Once data analysis was complete, data was further copied to excel spreadsheet for ease of statistical analysis with SPSS program.

For the present study, NSD was quantified based on the “degree of tortuosity” or ratio of length of the curve of the length of an imaginary line in the mid sagittal plane (see Figure 4.7, red arrow points to ratio). In other words, the degree of tortuosity is an absolute measurement of the degree of septal deviation from the midline at each identified landmark in both coronal and/or axial views. Measurements for NSD ratios generated in MATLAB are included in a table in Appendix D.

Figure 4.7 MATLAB Analysis for Degree of Tortuosity



**Deviation value is "degree of tortuosity" It is the curved (purple) line to straight (blue) line. Deviation value of 1.11/1 could also mean 11% deviation*

4.4 Statistical Tests

4.4.1 Reliability and Measurement Error

Intra-rater reliability and measurement errors were conducted for identification of 5 landmarks in the sagittal plane in OsiriX. Reliability and measurement error was also conducted for tracing NSD course in MATLAB for 10 randomly selected patients. Reliability was done twice since data for this study was collected in two separate steps, one as identification of anatomical landmarks in sagittal view in OsiriX and then as NSD measurements in MATLAB (from the selected DICOMs based on landmark identification/image isolation in OsiriX). All measurements were repeated three times with at least 5 days apart. Landmark identification was done in OsiriX with X, Y and Z coordinates noted for anterior point of the nasal bone (image A1/ C1), vomer and perpendicular plate junction (image A2/C4), anterior nasal spine (image C2), crista galli (image C3), and halfway point between anterior nasal spine and vomer/perpendicular plate junction (image A3). Nasal septum measurements in MATLAB for each image (A1, A2, A3, C1, C2, C3 and C4) were also recorded. Intra-class correlation with consistency under two-way mixed model was tabulated in SPSS for both anatomical landmark identification in OsiriX and nasal septum measurements in MATLAB.

4.4.2 Tests for Main study

The purpose of this study was to investigate a change (if any) in nasal septum deviation that may have occurred from rapid maxillary expansion treatment. Statistical analysis was carried out using SPSS (version 21) using alpha=0.05. Repeated measures ANOVA test was utilized with 2 within-subject factors and 1 between-subject factor. Baseline septal deviation of "mild" and "moderate to severe" was considered between subjects factor. Time (T1 and T3, 2 levels) and spatial images (A1, A2, A3, C1, C2, C3 and C4, 7 levels) were the two within subject factors. Non-parametric Wilcoxon signed ranked test using Bonferroni corrected alpha =(0.05/7= 0.007) were also performed to analyze changes when model assumptions were not met with repeated measures ANOVA.

4.5 Results

The intra-class correlation coefficients and corresponding confidence interval (95%) for both OsiriX landmark identification and MATLAB NSD measurements are listed in Tables 4.2 and 4.3. Location of most landmarks indicated good agreement (16) between parameters by high ICC values (>0.8). Minimum, maximum and mean measurement error for both Osirix landmark identification and MATLAB NSD ratios are listed in Tables 4.4 and 4.5. Mean measurement error in OsiriX was in the range of 0.5 – 2.2 mm with the A3 having the largest error in all coordinates (1.96 to 2.2mm). Difference between landmark coordinates in OsiriX measured at three different time points for reliability was not greater than 4 mm. MATLAB NSD ratios at all landmarks were less than 0.02.

Multiple outliers with A2, C3 and C4 being the most common locations for NSD is apparent from the descriptive box plot of NSD at baseline and after treatment (Figure 4.8). All model assumptions for repeated measures ANOVA were violated. The Q-Q plot of Mahalanobis distance for outliers based on difference between T1 and T3 depicted lack of normal distribution since the data points did not conform around a 45-degree line (Figure 4.9). Linearity amongst landmarks was not present at baseline either (T1) as visualized by generalized scattered distribution between landmarks (Figure 4.10). Mauchly Test of Sphericity was significant which indicated violation of the sphericity assumption; therefore degrees of freedom were corrected with Greenhouse-Geisser correction. There was no significant difference in NSD between time F (1,24)=0.2, p=0.659. There was also a lack of evidence for difference in NSD at spatial images A1, A2, A3, C1, C2, C3, C4 with time (time*spatial), F statistic (2.93, 70.24)= 0.205, p=0.889 (Figure 4.11). Partial eta square was 0.008 for time*spatial accounting for only 0.8 % of variance explained by the effect of RME on NSD at the 7 landmarks. Baseline septal deviation of mild or moderate to severe had no effect change at spatial landmarks with time (baseline deviation*spatial*time) either with F (2.93, 70.24)=1.85, p=0.147, accounting for only 7% of variance in NSD. The final model was kept with the three- way interaction term since it contained the hypothesis for this study. In addition there was no major difference in p-values and test statistics when the three- way interaction term was removed.

All model assumptions for repeated measures ANOVA were violated; therefore, non-parametric testing was conducted. In addition, equal variance assumption was also violated for other parametric testing. Box plot of raw data of mild and moderate to severe NSD group shows multiple outliers and a large variation between the two groups at baseline (i.e. a difference of >2 times the range between groups, Figure 4.12). Wilcoxon signed rank test was employed to assess median change in NSD from T1 to T3 at images A1, A2, A3, C1, C2, C3, C4. No significant change was identified (p value> 0.071, alpha=0.007). Alpha was divided by 7 since comparison at each image was done individually (Table 4.4). Wilcoxon signed rank test was also done to examine if there was a change in NSD between T1 and T3 in the control, group of 7 patients without RME treatment. There was no significant change between a 6-month time difference either ($p>0.091$, Alpha= 0.007).

4.6 Discussion

The purpose of this retrospective study was to investigate the effect of rapid maxillary expansion treatment on patients presenting with nasal septal deviation. RME was conducted in these patients solely for the treatment of transverse maxillary deficiency, whereby NSD was discovered as an incidental finding on their CBCT images prior to treatment. There is no "gold standard" test to diagnose septal deviation (17) and different protocols for measuring septal deviation have been identified in the literature. Although septal deviation in degrees was used to categorize the sample based on the severity of NSD, it was the "degree of tortuosity" that was utilized as a continuous outcome measure in this study. Degree of tortuosity measurement is ratio of the length of the curve of the deviated septum to the length of an ideal straight septum. This measurement solely measured the nasal septum in isolation and did not classify or include other confounding nasal pathology that could be the reason for the septal deviation, such as turbinate hypertrophy or mucosal swelling. Therefore, this measurement method was well suited to the objective of our study.

Owing to retrospective nature of the study and the available CBCT records of patients that have undergone RME, the sample size for was less than ideal. Nevertheless, our findings were similar to a recently conducted study (12) in two dimensions, whereby no change in nasal septal deviation was identified pre and post maxillary expansion on adolescent patients. On the other hand, this study was different than the previous one (12), since the analysis of septal deviation was based on three-dimensional measurements on CBCT as opposed to two- dimensional on a posterior-anterior cephalogram. To date, this study appears to be the only one comparing the effect of RME on NSD utilizing three-dimensional analysis of CBCT images.

The main finding of this investigation was that rapid maxillary expansion had no effect on patients that had nasal septal deviation at baseline, as measured at consistent spatial landmarks in axial and coronal views. Furthermore, mild or severe baseline deviation had no statistically significant effect on NSD change as measured at set landmarks. The time difference between T1 and T3 in the treatment group was similar to that of the control group; both groups did not have any statistically significant change in NSD over a 6-month period. Although, parametric tests were conducted in spite of violated model assumptions, non-parametric testing method was also employed, given its simplicity of use in studies with a small sample size, where model assumptions were violated. Despite the suitability of non-parametric statistical testing methods to our study, they have inherent disadvantage of less power. Less power means that the chance of detecting a true effect is diminished (18).

Therefore, to arbitrarily accept that RME has no effect on NSD should be interpreted with some caution. Relatively small sample size in conjunction with great variability (large standard deviation) in individual patient NSD measurements as visualized from presence of numerous outliers from the scatter plots could make the effect of RME treatment on NSD challenging. In other words, due to the large individual variation among the patients recruited in this study, it could be that the true effect of RME treatment on NSD is difficult to discern. In fact, four patients out of a sample of twenty-six (15%) depicted a visual improvement in NSD from RME at mostly the coronal location of C3 (one at A3) (See Figures 4.13 to 4.16). This finding suggests that change at image C3 is clinically relevant. However, we assume that NSD at anterior locations, such as at images A1 and C1, would have a higher clinical significance due their close proximity to the major airflow limiting area of the anterior nasal valve area. Visual improvement in only four patients presenting with moderate to severe NSD, but not in others parallels the conclusions of Harvold's primate study (2). For that study, the experimental protocol and sample characteristics were standardized, the animals responded and adapted to nasal obstruction quite differently. In fact, based on the statistical model only 7% of variance in NSD could be attributed to RME treatment.

It has been proposed that early intervention with RME (i.e. before suture starts closing) in pre-pubescence would result in a greater skeletal than a dental change (19). Given that all patients in this study were adolescents, it is possible that lack of statistically significant change in NSD from RME was the result of adolescent patients having greater interdigitation of surrounding sutures. In addition, increased bone density (calcification) of surrounding craniofacial structures in adolescence can offer greater resistance to skeletal change from RME. In contrast, in patients with mixed and deciduous dentition, studies have reported the effect of RME to be attributed to between one half to two-thirds skeletal change(19,20). In fact, the studies that reported favourable effect of RME on NSD consisted of patients recruited prior to their adolescent growth spurt (7,11).

Although there is a lack of studies examining the effect of RME on NSD, there are several studies investigating the influence of RME treatment on the nasal airway (5-9). However, there still lies a great deal of ambiguity in the literature with respect to nasal airway changes from RME due to conflicting findings. This ambiguity could be attributed due to different expansion protocols, different measurement methods to assess nasal airway change, patients with varying degrees of skeletal maturation of patients being treated, individual patient variation with or without concurrent pathologies such as infections and allergies causing mucosal edema.

Due to the great anatomical complexity of a dynamic structure such as the nose, it is not surprising that there appears to be a lack of consensus. Airflow through each of the nasal passages is not equal. Some regions are subjected to high velocity airflow while other areas are exposed to low flow currents. Mostly, it is the internal nasal valve region, the nasal septum and the anterior end of the inferior turbinates that are subjected to higher velocity airflow (21). Moreover, the variation in airflow is further accentuated by the effect of nasal cycle, whereby there is a shift in the majority of nasal airflow between the right and left nasal passage every 2-4 hours (22). The physiological benefits of the nasal cycle are to allow rest and recovery of the nasal epithelium, protecting it from any drying or the temperature effects of the nasal airflow (23). Thus, one can expect significant temporal variation in nasal airflow measurement on a particular side of the nasal cavity due to intermittent patient swelling of the nasal mucosa. This results from physiological and cyclic effects of nasal cycle and could even be due to allergy from airborne particles. Since no topical decongestant was used prior to imaging at either time point the confounding effect of mucosal swelling on our measurements cannot be condoned. Decongestion reduces mucosal engorgement in the area of nasal lumen, making nasal airflow less sensitive to decreases in cross sectional area. It is the anterior part of the nose that is extremely vulnerable to even minor changes (1mm) in the diameter of the nasal lumen (24). It was challenging to isolate the nasal septum from the superimposition of mucosal edema in some patients in our sample. For the purpose of standardization, the midpoint of the nasal septum with its overlying mucosa was taken for all measurements.

It has been suggested that small decreases in the cross sectional area in the anterior most area of the nose (i.e. nasal valve area, may play a vital role in the subjective sensation of nasal obstruction (25). Since RME treatment affects the anterior and inferior aspect of the nasal cavity, it would be worthwhile to investigate the effect of RME on the associated subjective improvement in nasal breathing in these patients through validated quality of life questionnaires such as the nasal obstruction symptom evaluation (NOSE) scale (26).

Landmark identification in Osirix and NSD ratios in MATLAB were indicative of good reliability. It was ascertained that identifying the location of landmark A3 with certainty was challenging. It was the only landmark that was not associated with a hard tissue anatomical structure and rough approximation in space was made on all DICOMS without a ruler to accurately measure the half waypoint between anterior nasal spine and the vomer and perpendicular plate junction. Although, the reliability at A3 for both OsiriX and in turn MATLAB was suggestive of good reliability, the mean measurement error of close to 4 mm was reported in x, y and z coordinates. The accuracy of the bony landmark identification on cadaveric human skulls is superior to measurements made on radiographic images of live patients. However, landmark determination accuracy on radiographic imaging is affected by patient motion, unstandardized head positioning, metal artifacts and soft tissue superimposition (27). All the above-mentioned factors could impact landmark identification in our patient sample. Segmentation is a technique that mitigates some of these inaccuracies. It is the foundation of three- dimensional imaging such as CBCT, which allows for an easier analysis of a desired area by suppression of surrounding anatomical structures. Anatomic landmarks of the craniofacial region whose accuracy may be affected by poor segmentation consist of anterior nasal spine (ANS), posterior nasal spine (PNS), porion, condylion and point A. However, based on our reliability readings, we did not was encounter this in our analysis, whereby the high ICC values for landmark C2 (ANS) was indicative of good reliability.

One major limitation in landmark identification for this study was the generalized scatter/noise identified on some CBCT images and lack of standardized head position in five patients between Time 1 and Time 3. Since reliability was reasonably good, we are not concerned with the scatter leading to a major difficulty in landmark identification. In addition, we do not assume the lack of standardized head position to be a major drawback of the study since we measured the ratio of the length of the nasal septal deviation to the length of the ideal nasal septum as opposed to cross sectional areas between deviated and non-deviated sides. Cross sectional areas measured at each landmark could confounded if the head positions digressed from the natural head position or a position parallel to Frankfort horizontal plane between T1 and T3.

4.7 Conclusions

In a small sample of adolescent patients rapid maxillary expansion does not result in a significant change in nasal septal deviation in adolescent patients. Although, this research study did not provide strong evidence to suggest that RME treatment has any effect on NSD in adolescent patients, the results of our findings should be interpreted with caution due to small sample size and large variation amongst individual patient characteristics.

Table 4.2 Intra-Rater Reliability for Anatomical Landmark Identification in Sagittal View in OsiriX

Landmark	X-Coordinate	Y-Coordinate	Z-Coordinate
A1/C1	0.980 (0.943-0.995)	0.974 (0.925-0.993)	0.994 (0.983-0.998)
A2/C4	0.963(0.897-0.990)	0.974 (0.926-0.993)	0.986 (0.959-0.996)
A3	0.941 (0.839-0.984)	0.929 (0.810-0.980)	0.988 (0.965-0.997)
C2	0.980(0.943-0.995)	0.978 (0.937-0.994)	0.990 (0.971-0.997)
C3	0.998 (0.993-0.999)	0.973 (0.924-0.993)	0.986 (0.959-0.996)

Table 4.3 Intra-Rater Reliability for MATLAB NSD Tracing Measurements

Landmark /Slice	ICC	Confidence Interval
A1	0.948	(0.871-0.983)
A2	0.993	(0.982-0.998)
A3	0.872	(0.702-0.957)
C1	0.947	(0.867-0.983)
C2	0.914	(0.791-0.972)
C3	0.904	(0.771-0.969)
C4	0.941	(0.854-0.981)

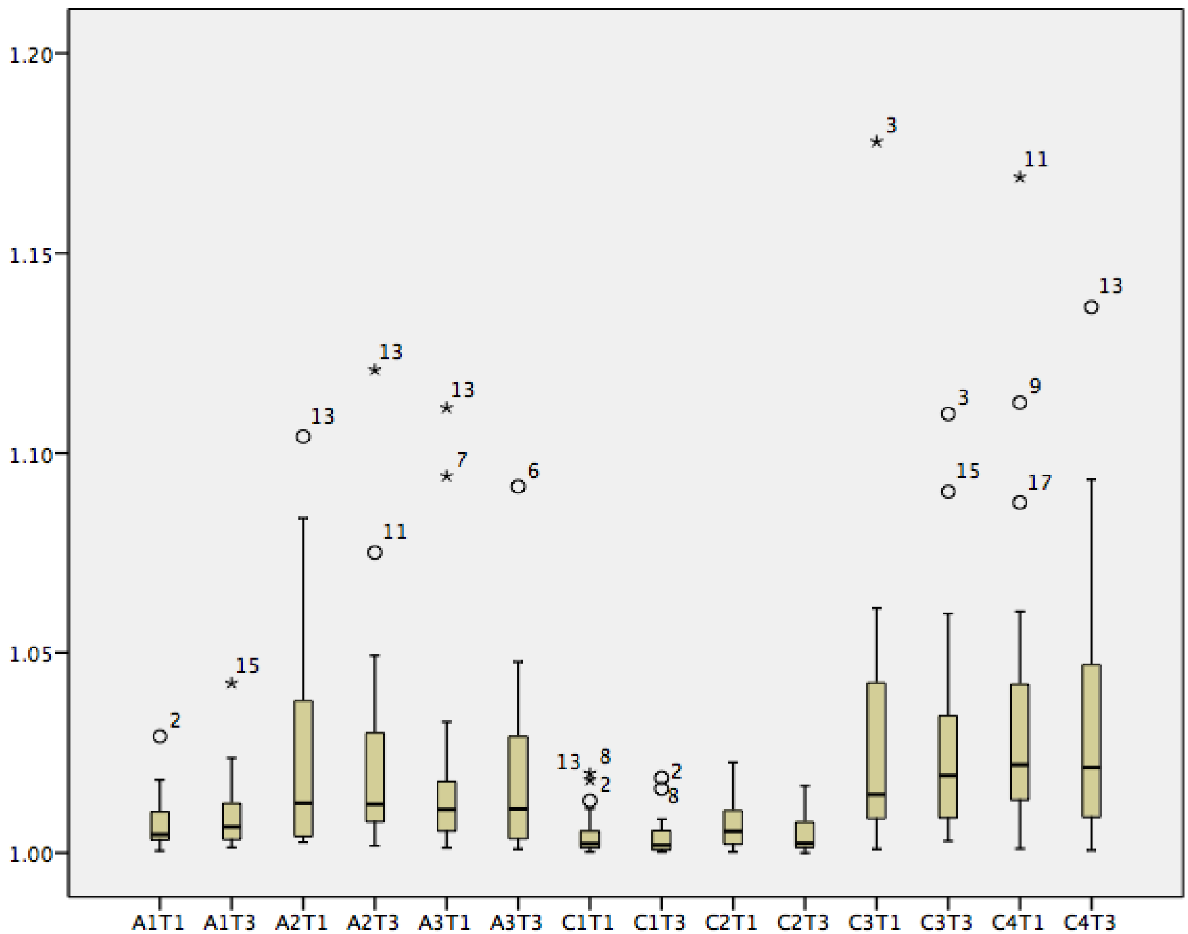
Table 4.4 Measurement Error in millimeters for Anatomical Landmark Identification in Sagittal View in OsiriX

Landmark	X coordinate	Y coordinate	Z coordinate
A1/C1	1.11(0-2.24)	1.23 (0.38-2.77)	1.23 (0.41-2.67)
A2/C4	1.32(0.3-3.64)	1.44(0.37-2.73)	1.78 (0.09-3.43)
A3	1.96 (0.67-3.71)	2.2 (1.25-3.27)	2.03 (0.48-3.49)
C2	1.58 (0.56-3.25)	1.52 (0.23-3.14)	1.61 (0.13-3.65)
C3	0.52 (0.28-0.84)	1.89 (0.59-3.51)	1.64 (0.41-3.61)

Table 4.5 Measurement Error for MATLAB NSD ratio at Each Image

Image	Mean Ratio
A1	0.0016
A2	0.0042
A3	0.0069
C1	0.0025
C2	0.0023
C3	0.0166
C4	0.0090

Figure 4.8 Descriptive Plot of Nasal Septal Deviation at T1 and T3



<u>Figure 4.9 Normality Plot with Mahalanobis Distance</u>

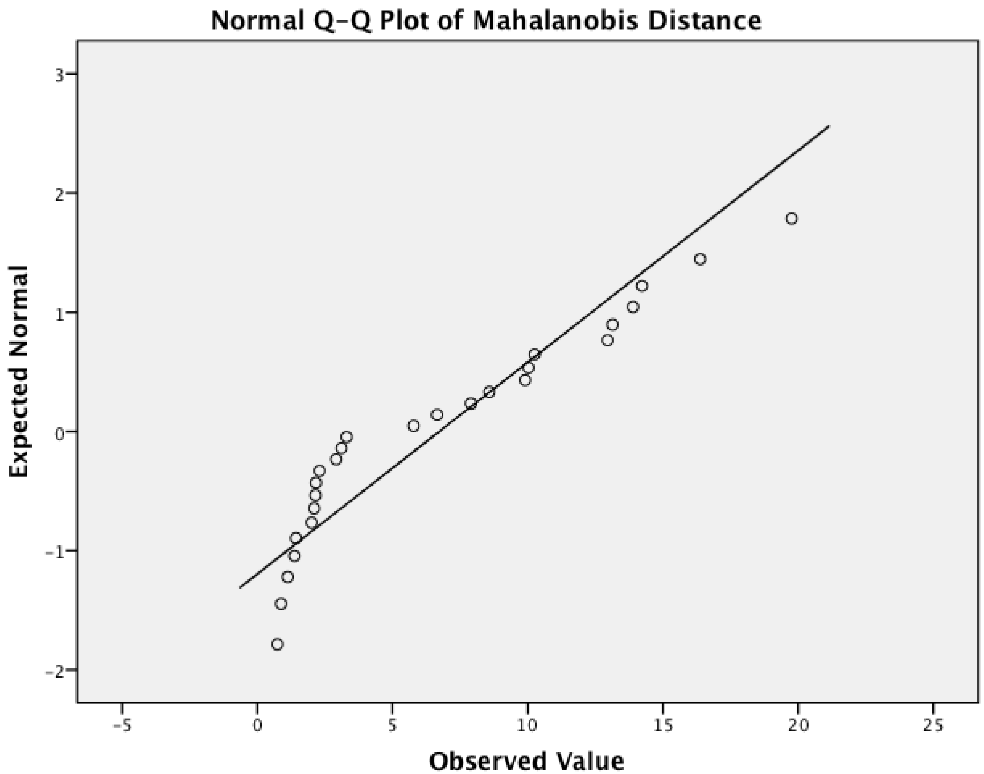


Figure 4.10 Linearity Assumption for Repeated Measures ANOVA

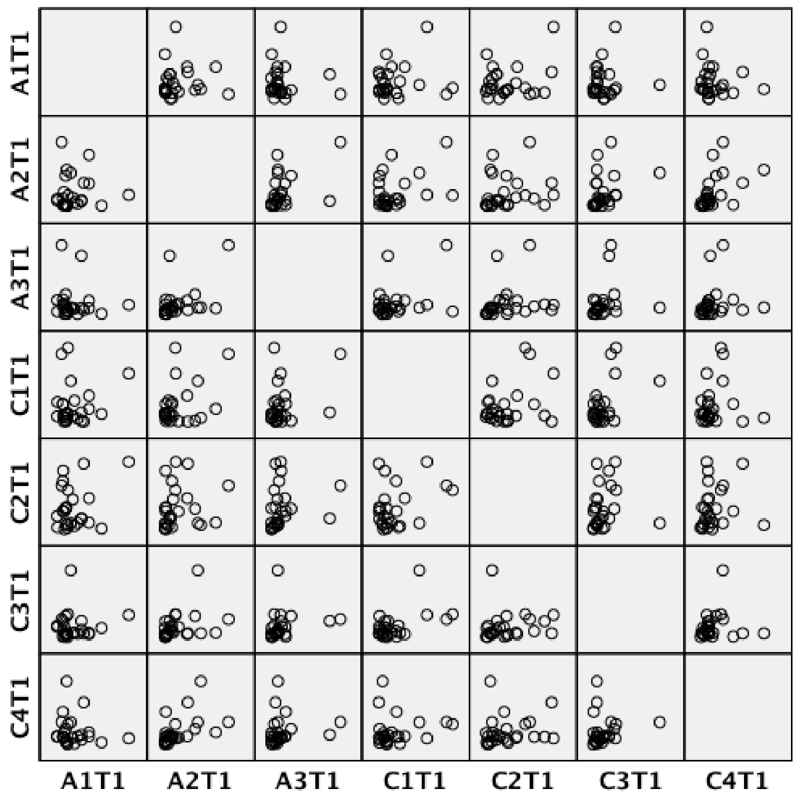


Table 4.6 Non Parametric testing with Wilcoxon Signed Rank Test

Septal Deviation Change after Maxillary expansion at Landmark	P-value
A1	0.221
A2	0.780
A3	0.253
C1	0.722
C2	0.071
C3	0.409
C4	0.849

Figure 4.11 NSD Change at Coronal and Axial Images with RME treatment (T1 to T3)

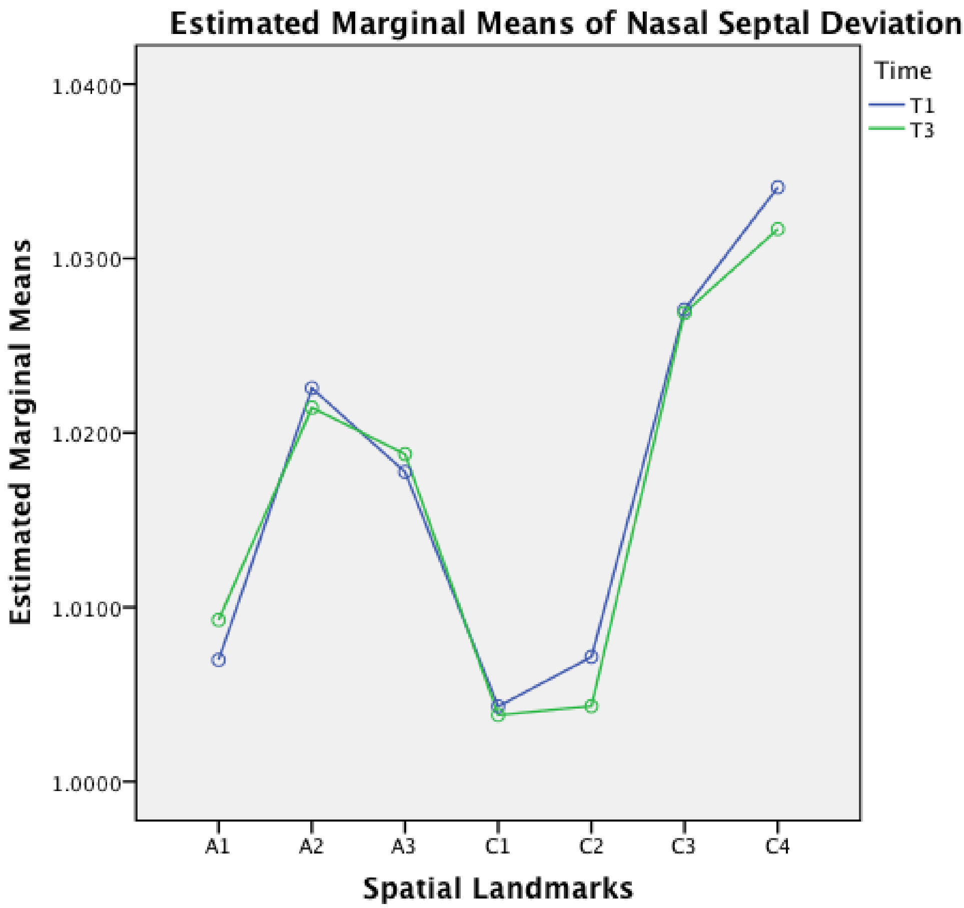
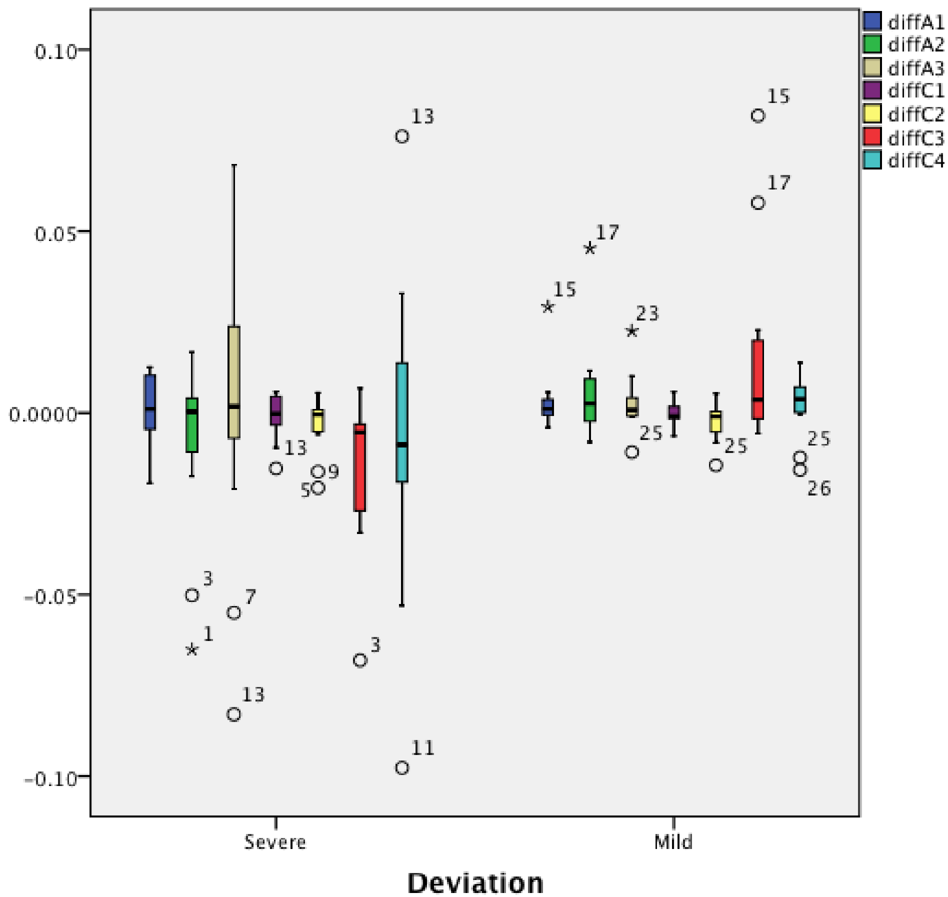


Figure 4.12 Equal Variance Assumption for Parametric Tests



NSD Change in 4 patients from T1 (first) to T3 (second image)

<u>Figure 4.13 Change at Landmark C4 for Patient 1</u>

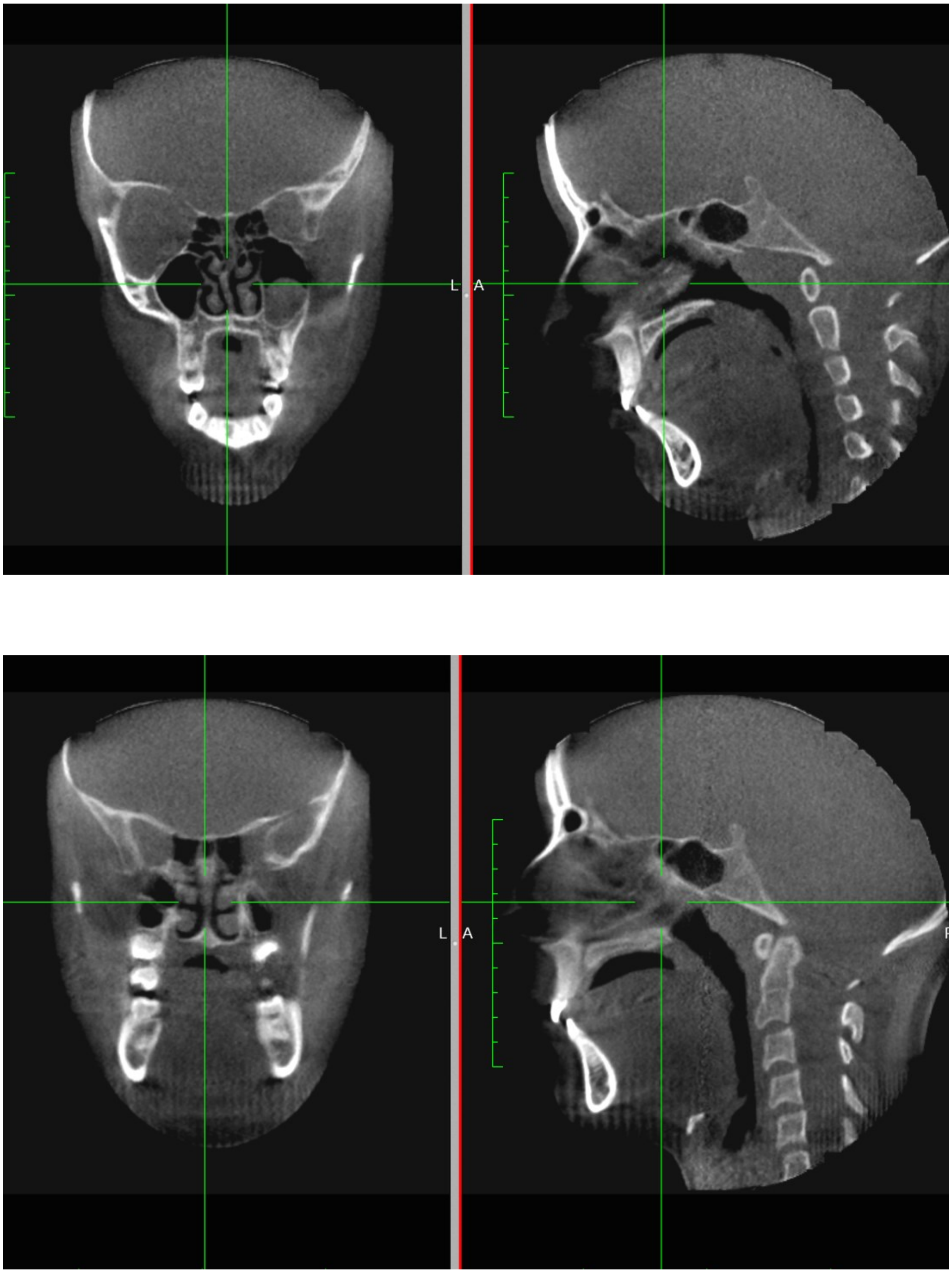
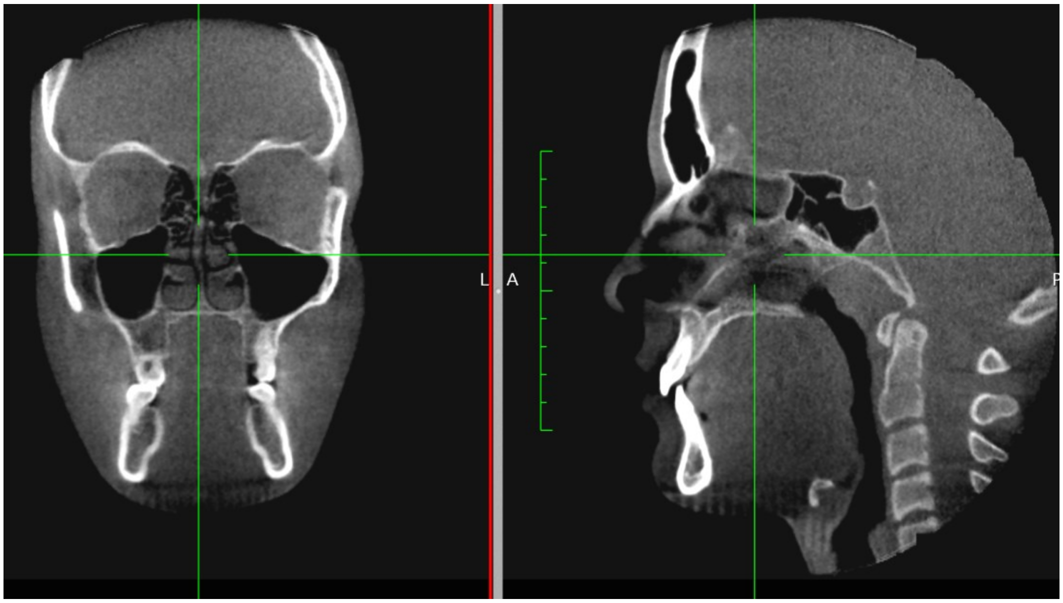


Figure 4.14 Change at Landmark C4 for Patient 2



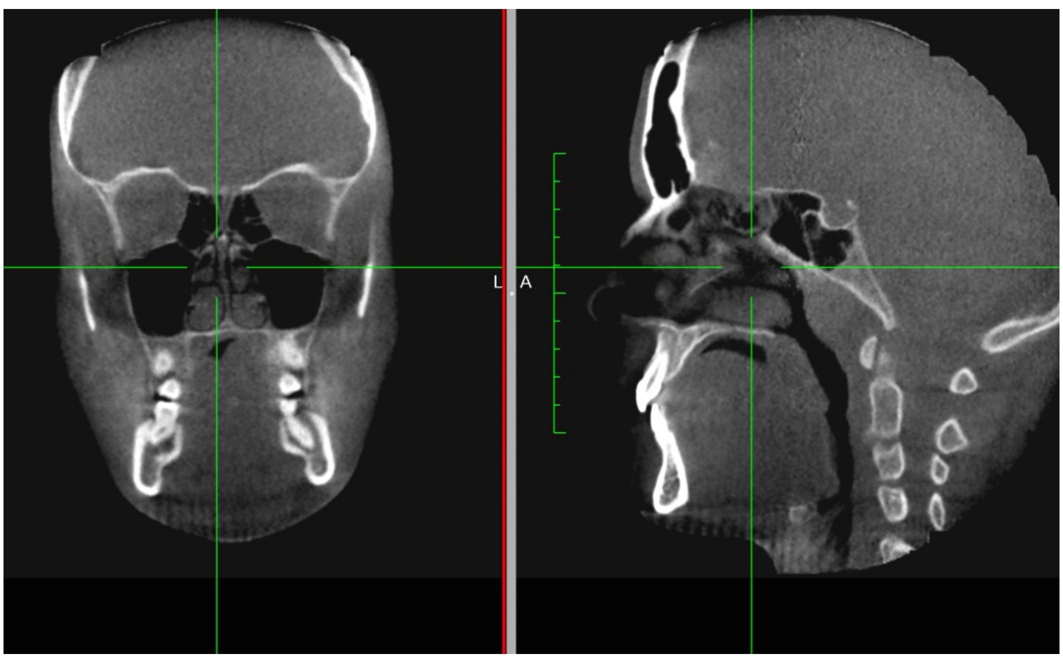
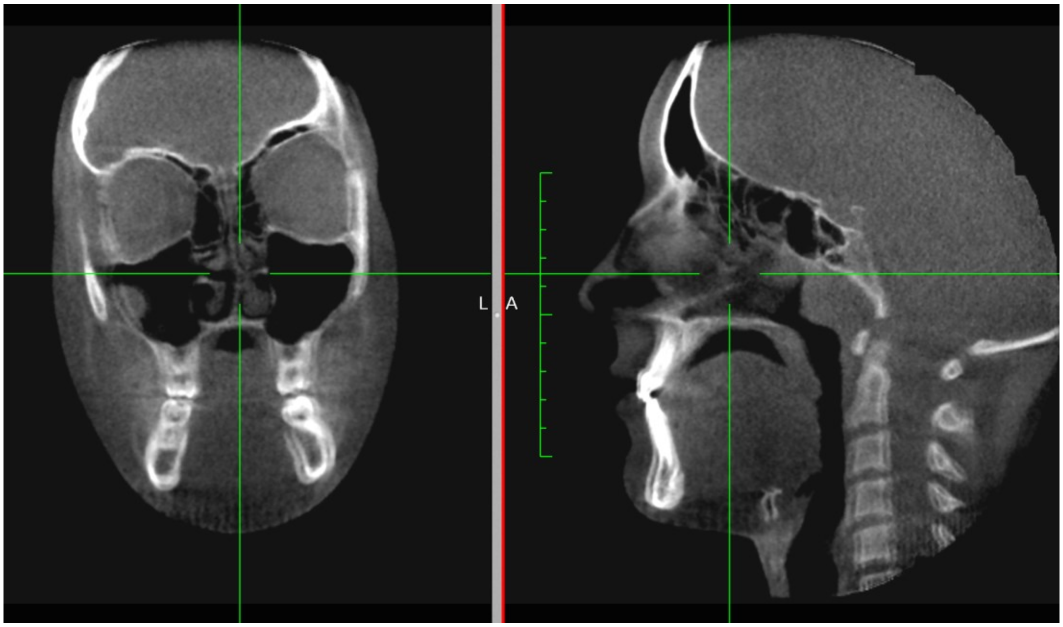


Figure 4.15 Change at Landmark C4 for Patient 3



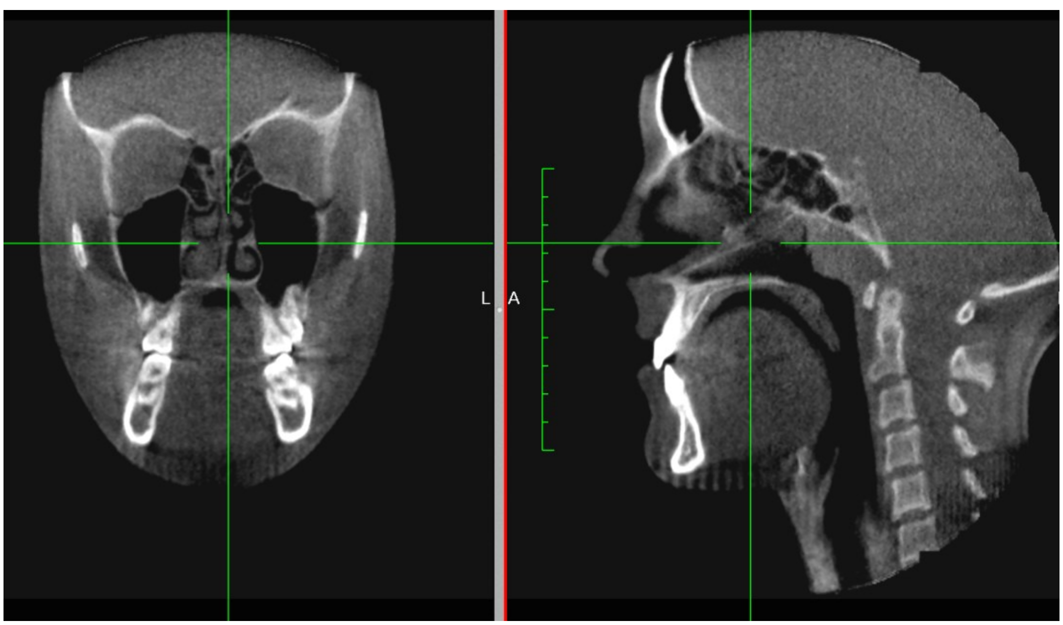
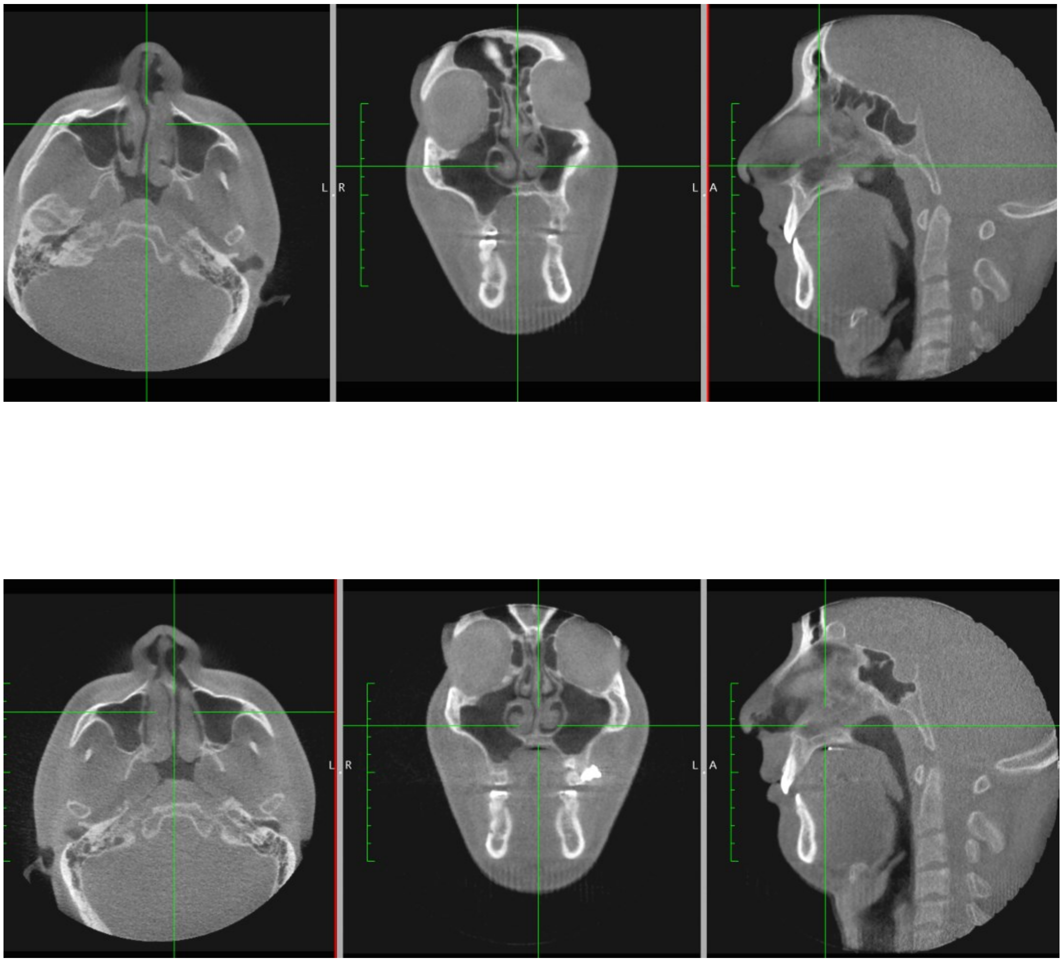


Figure 4.16 Change at Landmark A3 for Patient 4



4.8 References

(1) Moss-Salentijn L. Melvin L. Moss and the functional matrix. J Dent Res 1997 Dec;76(12):1814-1817.

(2) Harvold EP, Tomer BS, Vargervik K, Chierici G. Primate experiments on oral respiration. Am J Orthod 1981 Apr;79(4):359-372.

(3) Vig KW. Nasal obstruction and facial growth: the strength of evidence for clinical assumptions. American Journal of Orthodontics & Dentofacial Orthopedics 1998 Jun;113(6):603-611.

(4) Proffit WR, Fields Jr HW, Sarver DM. Contemporary orthodontics. : Elsevier Health Sciences; 2006.

(5) Enoki C, Valera FC, Lessa FC, Elias AM, Matsumoto MA, Anselmo-Lima WT. Effect of rapid maxillary expansion on the dimension of the nasal cavity and on nasal air resistance. Int J Pediatr Otorhinolaryngol 2006 Jul;70(7):1225-1230.

(6) Kilic N, Oktay H. Effects of rapid maxillary expansion on nasal breathing and some naso-respiratory and breathing problems in growing children: a literature review. Int J Pediatr Otorhinolaryngol 2008 Nov;72(11):1595-1601.

(7) Gray LP. Results of 310 cases of rapid maxillary expansion selected for medical reasons. Journal of Laryngology & Otology 1975 Jun;89(6):601-614.

(8) Baratieri C, Alves M,Jr, de Souza MM, de Souza Araujo MT, Maia LC. Does rapid maxillary expansion have long-term effects on airway dimensions and breathing? American Journal of Orthodontics & Dentofacial Orthopedics 2011 Aug;140(2):146-156.

(9) Bicakci AA, Agar U, Sokucu O, Babacan H, Doruk C. Nasal airway changes due to rapid maxillary expansion timing. Angle Orthod 2005 Jan;75(1):1-6.

(10) Baccetti T, Franchi L, Cameron CG, McNamara JA,Jr. Treatment timing for rapid maxillary expansion. Angle Orthod 2001 Oct;71(5):343-350.

(11) Farronato G, Giannini L, Galbiati G, Maspero C. RME: influences on the nasal septum. Minerva Stomatol 2012 Apr;61(4):125-134.

(12) Altug-Atac AT, Atac MS, Kurt G, Karasud HA. Changes in nasal structures following orthopaedic and surgically assisted rapid maxillary expansion. International Journal of Oral & Maxillofacial Surgery 2010 Feb;39(2):129-135.

(13) Setlur J, Goyal P. Relationship between septal body size and septal deviation. American journal of rhinology & allergy 2011;25(6):397-400.

(14) Lagravere MO, Carey J, Heo G, Toogood RW, Major PW. Transverse, vertical, and anteroposterior changes from bone-anchored maxillary expansion vs traditional rapid maxillary expansion: a randomized clinical trial. American Journal of Orthodontics & Dentofacial Orthopedics 2010 discussion 304-5; Mar;137(3):304.e1-304.12.

(15) Lin JK, Wheatley FC, Handwerker J, Harris NJ, Wong BJ. Analyzing Nasal Septal Deviations to Develop a New Classification System: A Computed Tomography Study Using MATLAB and OsiriX. JAMA facial plastic surgery 2014.

(16) Portney L, Watkins M. Foundations of clinical research: applications to practice. Prentice Hall, Upper Saddle River 2008.

(17) Aziz T, Biron VL, Ansari K, Flores-Mir C. Measurement tools for the diagnosis of nasal septal deviation: a systematic review. Journal of Otolaryngology: Head and Neck Surgery 2014;43:11.

(18) Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, et al. Power failure: why small sample size undermines the reliability of neuroscience. Nature Reviews Neuroscience 2013 May;14(5):365-376.

(19) Monini S, Malagola C, Villa MP, Tripodi C, Tarentini S, Malagnino I, et al. Rapid maxillary expansion for the treatment of nasal obstruction in children younger than 12 years. Archives of Otolaryngology -- Head & Neck Surgery 2009 Jan;135(1):22-27.

(20) Haas AJ. Palatal expansion: just the beginning of dentofacial orthopedics. Am J Orthod 1970 Mar;57(3):219-255.

(21) Eccles R. Nasal airflow in health and disease. Acta Otolaryngol 2000 Aug;120(5):580-595.

(22) Flanagan P, Eccles R. Spontaneous changes of unilateral nasal airflow in man. A re-examination of the 'nasal cycle'. Acta Otolaryngol 1997 Jul;117(4):590-595.

(23) Boyce J, Eccles R. Do chronic changes in nasal airflow have any physiological or pathological effect on the nose and paranasal sinuses? A systematic review. Clinical Otolaryngology 2006 Feb;31(1):15-19.

(24) Cole P, Chaban R, Naito K, Oprysk D. The obstructive nasal septum. Effect of simulated deviations on nasal airflow resistance. Archives of Otolaryngology -- Head & Neck Surgery 1988 Apr;114(4):410-412.

(25) Magnusson A, Bjerklin K, Nilsson P, Jonsson F, Marcusson A. Nasal cavity size, airway resistance, and subjective sensation after surgically assisted rapid maxillary expansion: a prospective longitudinal study. American Journal of Orthodontics & Dentofacial Orthopedics 2011 Nov;140(5):641-651.

(26) Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. Otolaryngology - Head & Neck Surgery 2004 Feb;130(2):157-163.

(27) Periago DR, Scarfe WC, Moshiri M, Scheetz JP, Silveira AM, Farman AG. Linear accuracy and reliability of cone beam CT derived 3-dimensional images constructed using an orthodontic volumetric rendering program. Angle Orthod 2008 May;78(3):387-395.

Chapter 5
Final Discussion and Future Recommendations

5.1 Final Discussion

The objective of this thesis was to obtain a better understanding of the potential effect of rapid maxillary expansion (RME) on nasal septal deviation (NSD). Although, improvement in NSD from RME has been reported as an incidental finding in a few studies(1,2), there is a lack of research with standardized protocols and low risk of bias to quantify the change. This thesis study differs from two prior studies in a two ways: first, it analyzes the change in NSD systematically in three dimensions instead of measuring septal deviation on a snapshot of one anatomical location in a two-dimensional PA cephalogram; secondly, it includes a control group that presented with baseline severe septal deviation, but did not have RME treatment.

The main finding of this investigation was that RME had no statistical and meaningful effect on NSD as measured at DICOM slices in axial and coronal views. Furthermore, mild or severe baseline NSD had no statistically significant effect on NSD change from RME treatment. In addition, control group of seven patients with baseline deviation of moderate to severe NSD did not have any statistically significant change from RME. The evaluation time was similar between treatment and control groups. Patients in this study could be not be randomly allocated to a treatment or control group owing to the retrospective study design. Only association inferences could be made due to the study design. Population inference could not be ascertained since the sample for this study was not randomly selected from the population. Instead, patients in this study were recruited from the Orthodontic Graduate Clinic who were undergoing evaluation of cross bite treatment and were incidentally noted to have NSD on CBCT images.

The earliest report of a positive effect of RME on NSD came from Gray (1) whereby a subjective visualization of PA radiographs depicted an improvement in the "curve" of deviated nasal septum after RME treatment. A large sample size along with majority (86%) of patients under 12 years of age worked in this study's favour. Subjective improvement of nasal airway was also reported in these patients with improvement stable at 6 months post expansion. Similarly, Farronato et al (2) recruited 100 growing patients (5-9 years) presenting with transverse maxillary constriction and reported a 94% reduction in the septal deviation in the inferior and middle half of the nasal cavity when compared to a non-expansion control group. A systematic review was conducted to evaluate NSD changes produced by RME (chapter 3). It reported a potentially positive effect in childhood, but no significant change in post adolescent patients presenting with NSD and treated with RME. However, the conclusions in the systematic review were drawn from only two included studies. This reflects the dearth of literature elucidating the effect of RME on NSD.

5.2 Future Recommendations

- Patients included in this study were retrospectively recruited from a previously conducted randomized control trial. Most of the patients in this trial were treated with rapid maxillary expansion, but only those patients that had NSD as an incidental radiographic finding were recruited. Therefore, the sample size was dependent on number of subjects that had radiographic evidence of NSD within the sample cohort. Although, it could be beneficial to recruit a larger sample of patients through multidisciplinary orthodontic/ otolaryngology clinics to smooth out the effect of numerous outliers in this sample. It is also possible that a larger sample will show no change since the mean NSD values at baseline in all groups were very closely overlapped.

- RME is proposed to have more skeletal change (possibly NSD change as well) as opposed to dental change if conducted prior to adolescence (2,3). It is possible that no change in NSD was identified in our sample due to skeletal maturity. It would be beneficial to recruit a younger sample for a future study.

- Randomized control trial design provides the higher level of evidence/low risk of bias than a retrospective study design.

Investigation of the effect of RME on NSD through a RCT would add to our current understanding of this area.

- The methods protocol of the previously conducted randomized clinical trial did not include use of decongestants prior to imaging, since it was not required for the study design/research question. Use of decongestants would eliminate the effects of nasal mucosa from nasal cycle, allergy and infection and enable better visualization of the nasal septum for analysis.

- Although some studies (4-6)have reported a subjective improvement in breathing after maxillary expansion. It is still unclear whether RME would lead to a clinical improvement in breathing in patients with moderate to severe NSD. To employ validated scales such as the nasal obstruction symptom evaluation, NOSE questionnaire (7) for subjective sensation of breathing in patients with RME treatment would be valuable. Furthermore, quantification of changes in nasal resistance and airflow characteristics in patients presenting with NSD and RME treatment would further enhance the understanding of the effect of RME on NSD. In other words, it is possible that the change in NSD from RME may not be significant visually, but can be clinically relevant if patients do report a subjective improvement in breathing.

5.3 References

(1) Gray LP. Results of 310 cases of rapid maxillary expansion selected for medical reasons. Journal of Laryngology & Otology 1975 Jun;89(6):601-614.

(2) Farronato G, Giannini L, Galbiati G, Maspero C. RME: influences on the nasal septum. Minerva Stomatol 2012 Apr;61(4):125-134.

(3) Monini S, Malagola C, Villa MP, Tripodi C, Tarentini S, Malagnino I, et al. Rapid maxillary expansion for the treatment of nasal obstruction in children younger than 12 years. Archives of Otolaryngology -- Head & Neck Surgery 2009 Jan;135(1):22-27.

(4) Oliveira De Felippe NL, Da Silveira AC, Viana G, Kusnoto B, Smith B, Evans CA. Relationship between rapid maxillary expansion and nasal cavity size and airway resistance: short- and long-term effects. American Journal of Orthodontics & Dentofacial Orthopedics 2008 Sep;134(3):370-382.

(5) Magnusson A, Bjerklin K, Nilsson P, Jonsson F, Marcusson A. Nasal cavity size, airway resistance, and subjective sensation after surgically assisted rapid maxillary expansion: a prospective longitudinal study. American Journal of Orthodontics & Dentofacial Orthopedics 2011 Nov;140(5):641-651.

(6) Hershey HG, Stewart BL, Warren DW. Changes in nasal airway resistance associated with rapid maxillary expansion. Am J Orthod 1976 Mar;69(3):274-284.

(7) Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. Otolaryngology - Head & Neck Surgery 2004 Feb;130(2):157-163.

Appendices

Appendix A: Database Searches

MEDLINE/EMBASE and EMBR	Web of Science
1. Exp Nasal Septum/ 2. Exp Nose deformities/ 3. Deviat*.mp 4. Exp Diagnosis/ 5. Diagnos*.mp A. 1 OR 2 AND 3 B. 4 OR 5 Combine A and B	Nasal septal deviation* (Topic) AND Diagnosis* (Topic)

Appendix B: QUADAS-2 Tool

Table 1. **Risk of Bias and Applicability Judgments in QUADAS-2**

Domain	Patient Selection	Index Test	Reference Standard	Flow and Timing
Description	Describe methods of patient selection Describe included patients (previous testing, presentation, intended use of index test, and setting)	Describe the index test and how it was conducted and interpreted	Describe the reference standard and how it was conducted and interpreted	Describe any patients who did not receive the index tests or reference standard or who were excluded from the 2 × 2 table (refer to flow diagram) Describe the interval and any interventions between index tests and the reference standard
Signaling questions (yes, no, or unclear)	Was a consecutive or random sample of patients enrolled? Was a case–control design avoided? Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? If a threshold was used, was it prespecified?	Is the reference standard likely to correctly classify the target condition? Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index tests and reference standard? Did all patients receive a reference standard? Did all patients receive the same reference standard? Were all patients included in the analysis?
Risk of bias (high, low, or unclear)	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns about applicability (high, low, or unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or its interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	

(Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies. Ann Intern Med. 2011;155:529-536)

Appendix C: Ethics Approval

Approval

Date:	September 10, 2013
Study ID:	Pro00041136
Principal Investigator:	Carlos Flores Mir
Study Title:	Analysis of two- and three-dimensional changes of nasal septal during rapid palatal expansion in adolescent patients with mild to moderate nasal septal deviation
Approval Expiry Date:	September 9, 2014
Sponsor/Funding Agency:	McIntyre Fund - Division of Orthodontics - Department of Dentistry

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel . Your application has been reviewed and approved on behalf of the committee.

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. It has been determined that the research described in the ethics application is a secondary review of previously collected research data for which subject consent for access to personally identifiable health information would not be reasonable, feasible or practical. Subject consent therefore is not required for access to personally identifiable health information described in the ethics application.

In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (September 9, 2014), you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health approvals should be directed to (780) 407-604. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,

Dr. Glen J. Pearson, BSc, BScPhm, PharmD, FCSHP
Chair, Health Research Ethics Board – Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Appendix D. Descriptive data from Chapter 4

Descriptive Statistics before RME Treatment for mild to severe NSD					
	N	Minimum	Maximum	Mean	Std. Deviation
A1T1	26	1.0005	1.0291	1.007027	.0062230
A2T1	26	1.0026	1.1041	1.023519	.0269405
A3T1	26	1.0012	1.1113	1.018408	.0261935
C1T1	26	1.0002	1.0198	1.004450	.0053398
C2T1	26	1.0002	1.0226	1.007258	.0068738
C3T1	26	1.0009	1.1779	1.028350	.0357671
C4T1	26	1.0010	1.1690	1.035069	.0379937

Descriptive Statistics after RME Treatment for mild to severe NSD					
	N	Minimum	Maximum	Mean	Std. Deviation
A1T3	26	1.0013	1.0424	1.009242	.0087029
A2T3	26	1.0017	1.1208	1.021881	.0259833
A3T3	26	1.0009	1.0916	1.019315	.0204643
C1T3	26	1.0002	1.0187	1.003935	.0046621
C2T3	26	1.0000	1.0167	1.004427	.0045804
C3T3	26	1.0029	1.1098	1.026985	.0260070
C4T3	26	1.0006	1.1365	1.032342	.0335468

Descriptive Statistics for control group at T1					
	N	Minimum	Maximum	Mean	Std. Deviation
A1T1	7	1.0015	1.0094	1.004500	.0026913
A2T1	7	1.0010	1.0431	1.023200	.0155147
A3T1	7	1.0003	1.0836	1.028314	.0273226
C1T1	7	1.0022	1.0358	1.008114	.0122553
C2T1	7	1.0008	1.0173	1.003743	.0060373
C3T1	7	1.0025	1.1278	1.044743	.0490479
C4T1	7	1.0094	1.1572	1.065243	.0545444

Descriptive Statistics for control group at T3					
	N	Minimum	Maximum	Mean	Std. Deviation
A1T3	7	1.0007	1.0436	1.010586	.0149514
A2T3	7	1.0014	1.0696	1.022114	.0238879
A3T3	7	1.0020	1.0534	1.020214	.0187834
C1T3	7	1.0006	1.0239	1.009600	.0111836
C2T3	7	1.0009	1.0288	1.008143	.0108371
C3T3	7	1.0013	1.1510	1.047800	.0498600
C4T3	7	1.0050	1.1280	1.037229	.0446749