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Evaluating the Association Between the Size of Adenoids/Tonsils and Craniofacial Skeletal Relationship in Children

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Evaluating the Association Between the Size of Adenoids/Tonsils and Craniofacial Skeletal Relationship in Children

by  
Katherine Lovell

THESIS

Submitted in partial satisfaction of the requirements for degree of  
MASTER OF SCIENCE

in

Oral and Craniofacial Sciences

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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Evaluating the Association Between the Size of Adenoids/Tonsils and Craniofacial  
Skeletal Relationship in Children

Kate Lovell

ABSTRACT

Adenoid and tonsillar hypertrophy are major contributors to pediatric obstructive sleep apnea (OSA). While Rapid Palatal Expansion (RPE) has been associated with reductions in lymphoid tissue size, the skeletal relationship with adenoid and tonsillar volume remains unclear. This study aims to quantify volumetric changes in adenoids and tonsils following RPE treatment and assess skeletal relationships using cone beam computed tomography (CBCT) and Artificial Intelligence (AI)-assisted landmarking.

A retrospective cohort study was conducted on 95 pediatric patients (mean age: 8 years; range: 4–15) with tonsillar hypertrophy (grade 3 or 4). Patients were divided into a control group (n=30) and an expansion group (n=65). The expansion group underwent RPE using a Hyrax expander, activated at 0.25 mm/day for 4 to 6 weeks. Final CBCT scans (T2) were obtained an average of 16.1 months after initial scans (T1). Volumetric analysis of adenoid and tonsillar tissue was performed using Anatomage Invivo 6. Skeletal relationships were evaluated with Diagnocat AI software. Paired t-tests and Wilcoxon rank-sum tests were used for statistical analysis ( $p < 0.05$ ).

The expansion group demonstrated statistically significant reductions in adenoid and tonsil volumes compared to controls. There were 86% and 92% of expansion patients who showed volume decreases in adenoids and tonsils, respectively. Average reductions were 12.4% ( $382.04 \text{ mm}^3$ ) for adenoids and 29.0% ( $1767.75 \text{ mm}^3$ ) for tonsils, with individual reductions up to 51.6% and 75.4%. The control group showed no

significant change. Out of the 95 patients there was an increase in adenoid and/or tonsillar volume in 10 patients. Each of these patients was analyzed for ANB, SNA, SNB, SN-MP, gonial angle, total airway volume, and cross-section of the minimum airway.

RPE significantly reduces adenoid and tonsillar volume, suggesting a long-term airway benefit in pediatric patients. Ongoing analysis will explore skeletal predictors of treatment response to refine patient selection for airway-focused orthodontic care.

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## LIST OF ABBREVIATIONS

AI: artificial intelligence

CBCT: cone beam computed tomography

CNN: convolutional neural network

OSA: obstructive sleep apnea

RPE: rapid palatal expander

SDB: sleep disordered breathing

# 1. INTRODUCTION

## 1.1 Preface

The adenoids and tonsils are a part of Waldeyer's ring, which is composed of the lingual and tubal tonsils, along with the adenoids and palatine tonsils. The tonsils are the first line of defense of pathogens entering the oral or the nasal cavity. Following a normal growth pattern, the tonsils typically increase in size until about 4 years old, then decrease in size throughout adolescence (1). While the direct cause of adenotonsillar hypertrophy is not known, and increased size can be caused by allergies, infections, gastroesophageal reflux, as well as irritants including secondhand smoke and pollution (2). With increased tonsillar size, there is obstruction into the airway, leading to an increased risk of sleep disordered breathing (SDB). This can range from mouth breathing, snoring, upper airway resistance syndrome to severe obstructive sleep apnea.

## 1.2 Adenotonsillar hypertrophy

Adenoid and tonsillar hypertrophy are major contributors to pediatric obstructive sleep apnea (OSA) along with obesity, craniofacial abnormalities, and neuromuscular disorders (3, 4). The prevalence of adenoid and tonsillar hypertrophy is 34.36% and 11% respectively in the population (5, 6). Typical symptoms of adenotonsillar hypertrophy are mouth breathing, snoring, nasal congestion, and recurring otitis media. An increased size of the adenoids and tonsils will lead to an obstructed airway, which contributes to upper airway dysfunction. Pediatric OSA can be attributed with

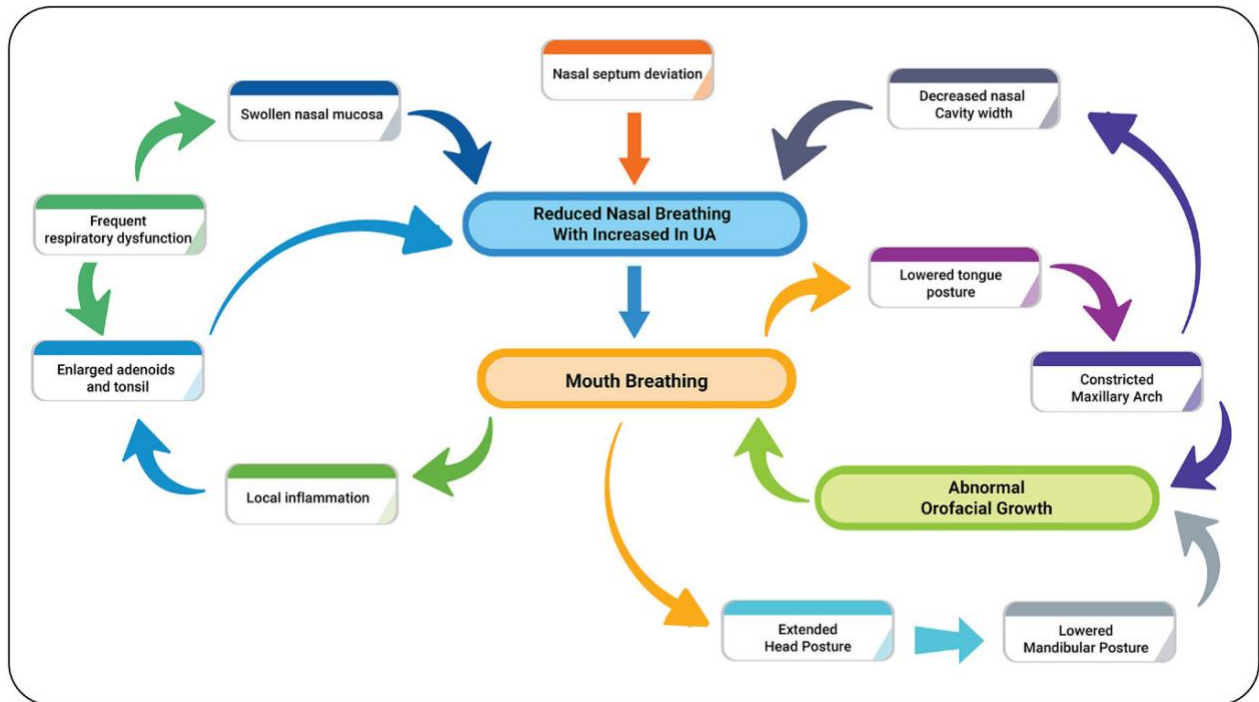
hyperactivity, insomnia, depression, and other psychiatric problems which can ultimately lead to behavioral problems (7). Tonsillectomy is recommended as the first line of treatment in children with tonsillar hypertrophy by the American Academy of Pediatrics and the American Academy of Otolaryngology Head and Neck Surgery (8, 9).

Tonsillectomies are associated with improvements in three particular aspects of a children's life: neurocognition, behavior, and quality of life (10). Neurocognitive skills are associated with memory, attention, mental flexibility, and intelligence (11). Behavioral problems that arise from pediatric OSA are hyperactivity, irritability, increased aggression, reduced attention, as well as emotional and peer problems (12). Quality of life was found to be improved after tonsillectomy in areas such as sleep disturbance, physical and emotional symptoms, daytime functions, and caregiver concerns (13). It is clear that enlarged adenoids and tonsils can negatively impact a child's overall health and development.

### 1.3 Craniofacial complex

When left untreated, the craniofacial complex will continue to be affected, ultimately growing into characterized SDB phenotype. This typical phenotype is characterized by a constricted maxilla, retrognathic mandible with a clockwise rotation, and excess vertical growth as seen in figure 1 (14). Any reduction in the skeletal dimensions can affect the space allocation for the lymphoid tissues; therefore, enlarged adenoids and tonsils can affect the craniofacial development due to impaired nasal breathing as well as abnormal orofacial growth (15). An experiment completed on Rhesus monkeys found that when nasal breathing is impaired, the facial skeleton,

dental occlusion, and neuromusculature, differed from those who maintained nasal breathing (16, 17, 18). Facial anatomic structures can be a risk factor for SDB due to its limit with nasal breathing (19). It is important to restore nasal breathing in order to maintain ideal skeletal characteristics throughout development to help facilitate adequate nasal airflow.



**Figure 1.** Influence of sleep-disordered breathing on orofacial growth

#### 1.4 Previous studies

Researchers have previously studied orthodontic therapeutic effects that aid in a positive impact on the craniofacial patterns associated with SDB. Orthodontists can target specific structures throughout craniofacial growth to manipulate the facial skeleton (20). One study found that RPE significantly increased the cross-sectional dimension of the nasal cavity along with the nasopharynx, improving the quality of life in mouth breathers by opening the midpalatal suture (21). RPE has been also found to

provide a statistically significant increase with the nasal width (22). Using RPE at critical time points throughout growth can guide facial structures to order to facilitate breathing and help alleviate or prevent the onset of pediatric SDB (23). Our previous study developed a method to measure the adenoids and tonsils on CBCT scans and found that a possible long-term benefit of RPE led to a reduction in both the adenoids and tonsils after treatment (24).

## 2. HYPOTHESIS

Hypothesis ( $H_a$ ): There is an association between skeletal relationship and reduction in adenoids and tonsils through the use of RPE.

Null Hypothesis ( $H_0$ ): There is not an association between skeletal relationship and reduction in adenoids and tonsils through the use of RPE.

### 3. SPECIFIC AIMS

#### AIM #1:

To analyze the skeletal relationship with adenoids and tonsils.

#### AIM #2:

To measure additional patients for both adenoids and tonsils along with skeletal measurements.

#### AIM #3

To analyze treatment responders vs non-responders.

## 4. MATERIALS AND METHODS

### 4.1 Funding

The National Institutes of Health provided funding for the project, under the leadership of Dr. Christine Hong.

### 4.2 Sample size

In this retrospective cohort study, a total of 95 pediatric patients (mean age: 8, range: 4-15, 43 males and 52 females) who had tonsillar hypertrophy (size 3 and 4) were included and divided into a control group (n=30) and expansion group (n=65). The control group did not undergo any treatment. The expansion group underwent expansion using a conventional Hyrax expander, activated 0.25mm per day for 4 to 6 weeks. Final CBCT scans (T2) were performed 16.1 months after the initial scan (T1). Volumetric analysis of adenoid and palatine tonsils was performed using a combination of bony and soft tissue landmarks in CBCT scans through Anatomage Invivo 6 imaging software. AI landmarking was used to evaluate skeletal relationships through Diagnocat software. Distribution of the patient data can be found in Table 1.

Paired t-tests using the Wilcoxon rank sum test were used to evaluate the difference between the initial and final adenoid and tonsil volumes. P-values less than 0.05 were considered statistically significant.

**Table 1.** Patient demographics

Characteristic	Total		Expansion (N=65)		Control (N=30)		p-value*
	Median	(IQR)	Median	(IQR)	Median	(IQR)	
Age in years	8	(7, 9)	8	(7, 9)	7	(6, 9)	0.25
Gender, n (%)							0.25
Male	43	(45.3)	32	(49.2)	11	(36.7)	
Female	52	(54.7)	33	(50.8)	19	(63.3)	

#### 4.3 Inclusion and exclusion criteria

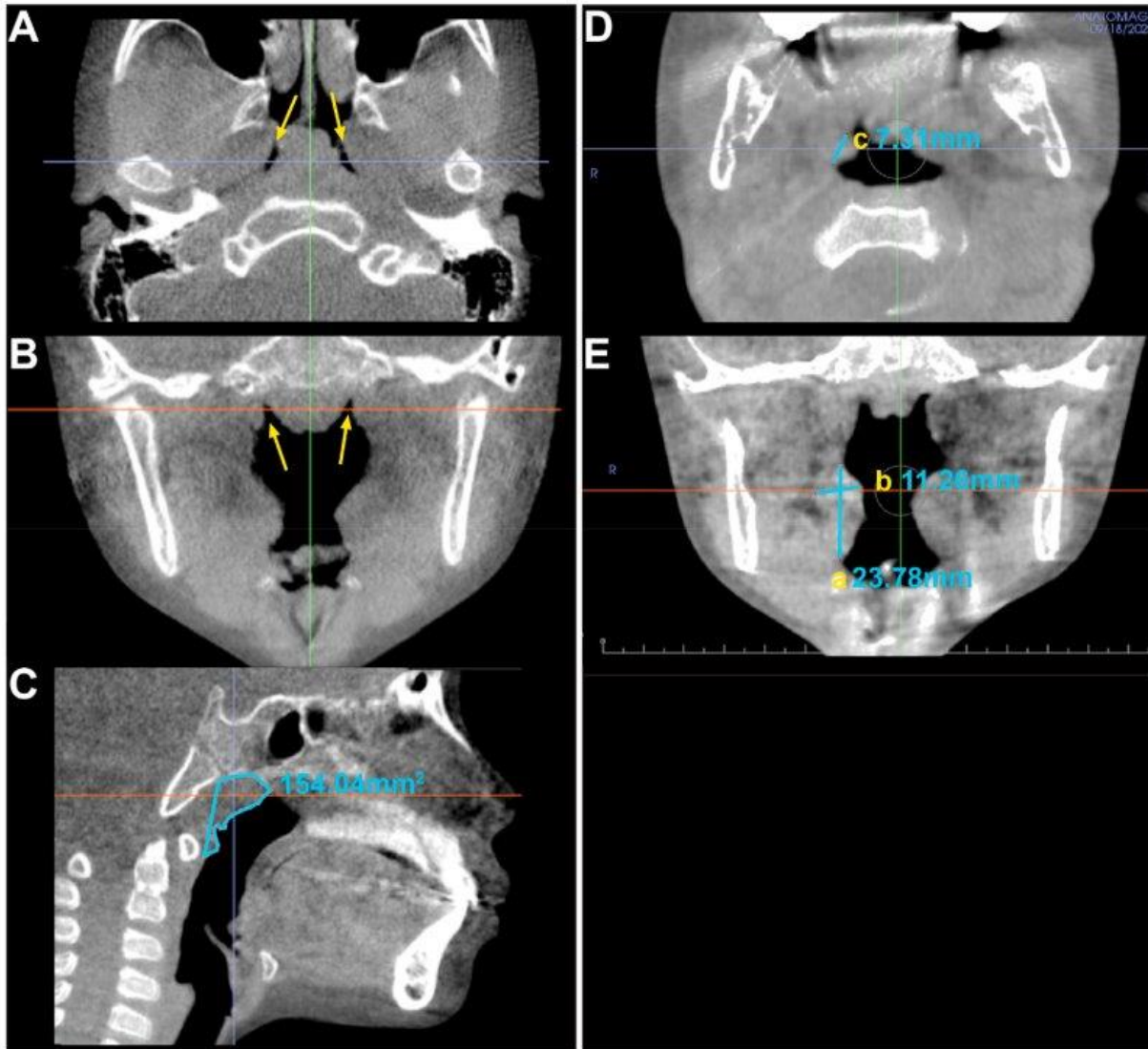
Inclusion criteria were patients with clinical indications for RPE with adenoid and tonsillar hypertrophy of grade 3 and 4. Exclusion criteria were patients with craniofacial anomalies such as cleft lip and palate, patients with severe hypertrophy of either the adenoids or the tonsils leading to obliteration of essential anatomical landmarks to perform the measurements, patients 16 years or older, patients with history of tonsillectomy and/or adenoidectomy, and patients who had a surgical or mini-implant assisted palatal expansion. The exclusion criteria for aim 1 only included patients whose landmarks were not visible on a lateral cephalogram for skeletal measurements.

#### 4.4 Measuring the adenoids and tonsils

Our previous paper delineates how to measure the tonsils on CBCT using a combination of bony and soft tissue landmarks, which is also the methodology used in this paper to measure the lymphatic tissue (24). Invivo 6 Advanced 3D Imaging Software (version 6.0; Anatomage, San Jose, California) was used to measure the lymphoid tissue. For adenoid measurements, the lateral limit consisted of the Fossae of Rosenmuller, the superior limit was the inferior surface of the sphenoid bone, the inferior

limit was the inferior plane of the atlas (C1) vertebra. The adenoid tissue that was projected anteriorly into the airway up to vomer was included in the measurement. The midsagittal slice is used to isolate the periphery. Figure 2 delineates the adenoid measurements in the axial (A), coronal (B), and sagittal at midsagittal plane (C). The volume was calculated using Cavalieri's principle with each section at 0.5mm intervals then summed up for the total volume (25). The following calculation was used for the adenoid volume:  $V = t \times \Sigma A$  where  $t$  is the section thickness and the interval of consecutive sections while  $\Sigma A$  is the total sectional area of consecutive sections (24).

For the palatine tonsils, the mathematical formula  $a*b*c*0.523$  was used to measure the tonsillar volume with the maximum vertical ("a"), transverse ("b"), and depth ("c") (26). The vertical and transverse dimensions were measured on the coronal view, while the depth was measured on the axial view. Figure 2 delineates the tonsil measurements in the axial (D) slice illustrates the depth (c) while the coronal slice (E) illustrates the vertical (a) and transverse (b) measurements. The vertical measurement was represented by the indentation into the lateral pharyngeal wall of the upper and lower tonsil. The transverse measurement was taken from the parapharyngeal fat pad to the tonsil's medial periphery. The depth was at the point of maximum hypertrophy for the left and right tonsil separately using the axial slice taken from the anterior and posterior indentation into the lateral pharyngeal wall (24).

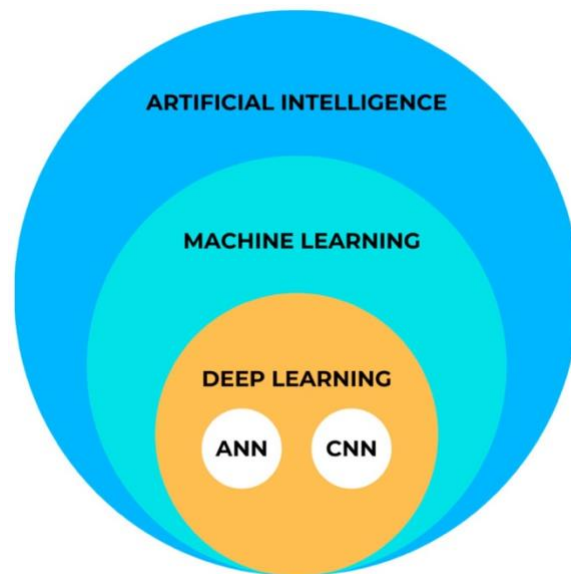


**Figure 2.** Adenoid and tonsillar measurements

#### 4.5 Artificial intelligence and cephalometric tracing

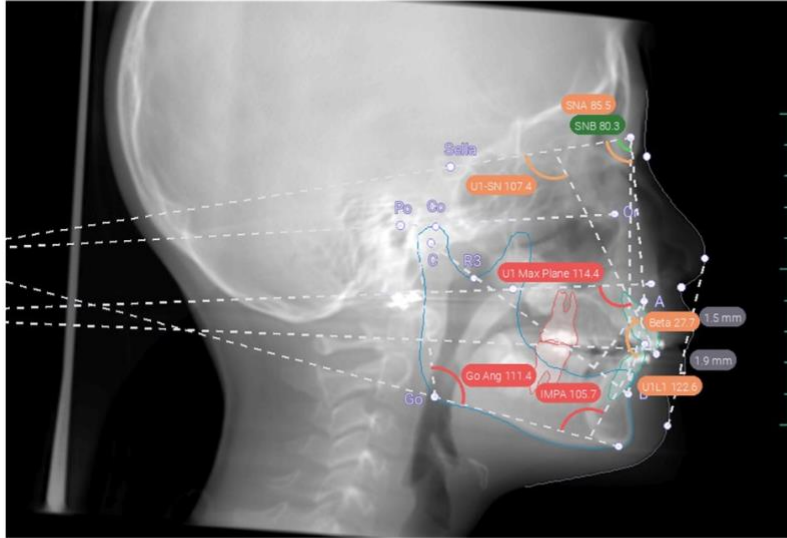
Artificial Intelligence can be used for accurate skeletal orthodontic diagnosis presented on a CBCT reconstructed lateral cephalogram. A study was conducted with 5,890 lateral cephalograms with a multimodal convolutional neural network (CNN) model and was found to have >90% sensitivity, specificity, and accuracy compared to clinical performance (27). CNN is a type of artificial intelligence that specifically analyzes visual data to extract information, as seen in Figure 3. Other studies have also

found no statistically significant difference between AI cephalometric analysis and landmarks that were conducted by human examiners (28, 29). In our study, we used the AI-driven platform, Diagnocat (Diagnocat, Ltd., San Francisco, CA, USA) to perform the diagnostic measurements on the lateral cephalograms constructed from CBCT input.



**Figure 3.** Simplified AI diagram

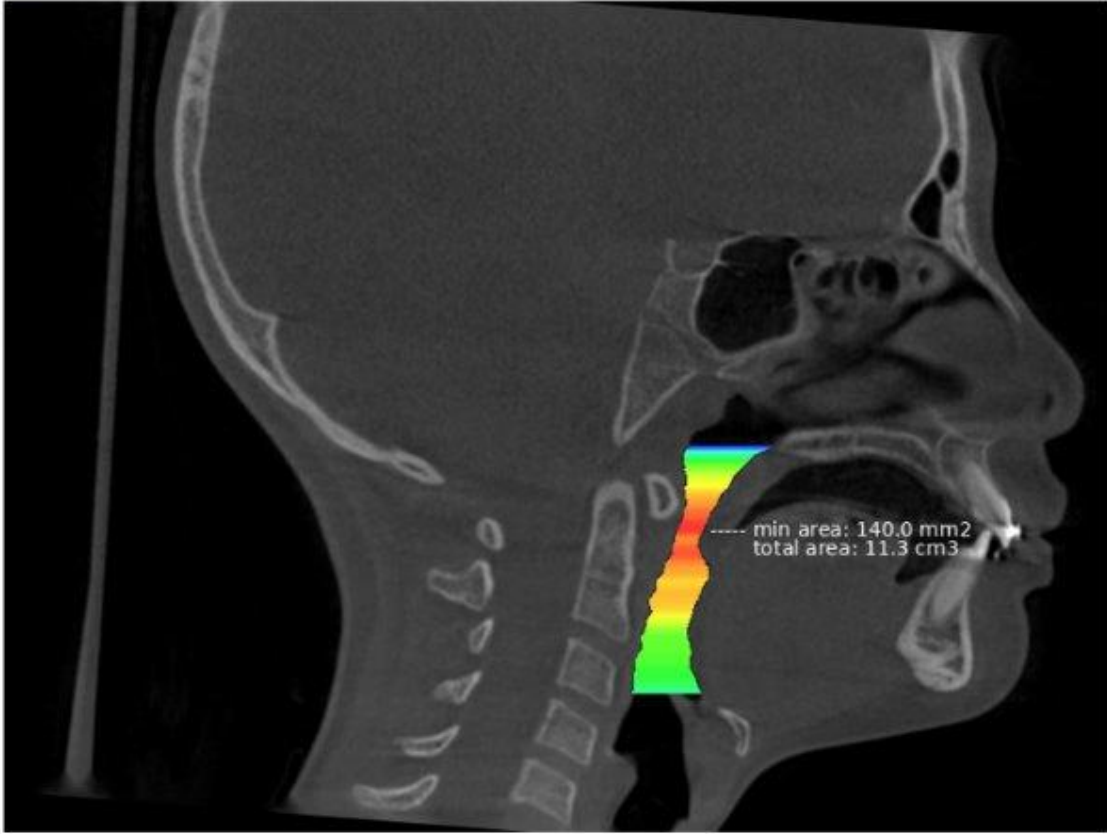
An example of the measurements taken from Diagnocat, along with the airway cross-section can be found in Figure 4 and 5. For our study, we chose to measure specific landmarks on the lateral cephalogram which were: ANB, SNA, SNB, SN-MP, gonial angle, total airway volume, and cross-section of the minimum airway. Diagnocat measures both left and right sides for the lateral cephalograms; in our study we recorded the average of both the left and right side for each skeletal landmark. Each measurement was taken at the initial and final timepoints. For aim 1, if a landmark was not visible on the lateral cephalogram, the patient was not included in the results.



Name	Value R	Norm	Dev R
<b>Vertical Relationship</b>			
SN-MP	24.2	32 ± 2	5.8
FH-OP	5.5	9 ± 4	-
Go Ang	111.4	130 ± 7	11.6
Mid Height	47.3	49 ± 4	-
Low Height	52.7	50 ± 5	-
<b>A-Po Relationship</b>			
Beta	27.7	31 ± 2	1.3
Wits	3.9	0 ± 1	2.9
NSeAr	117.1	124 ± 5	1.9
SNA	85.5	82 ± 2	1.5
SNB	80.3	80 ± 2	-
ANB	5.2	2 ± 2	1.2
MP	61.2	71 ± 2	7.8
S-N	58.6	70 ± 3	8.4
<b>Soft</b>			
ULip to Eline	1.5	-4 ± 2	3.5
LLip to Eline	1.9	-2 ± 2	1.9
<b>Incisor Relationship</b>			
Overjet	3.8	3 ± 1	-
Overbite	3.2	3 ± 1	-
U1-SN	107.4	105 ± 2	0.4
U1-PP	114.4	110 ± 2	2.4
U1-TVL (ANS)	1.6	0 ± 1	0.6
Interincisal	122.6	130 ± 6	1.4
Li-MP	105.7	90 ± 5	10.7
Shimbashi	15.8	18 ± 1	1.2

Moderate 1-2 deviations    Severe >2 deviations

Figure 4. Lateral cephalogram measured using AI

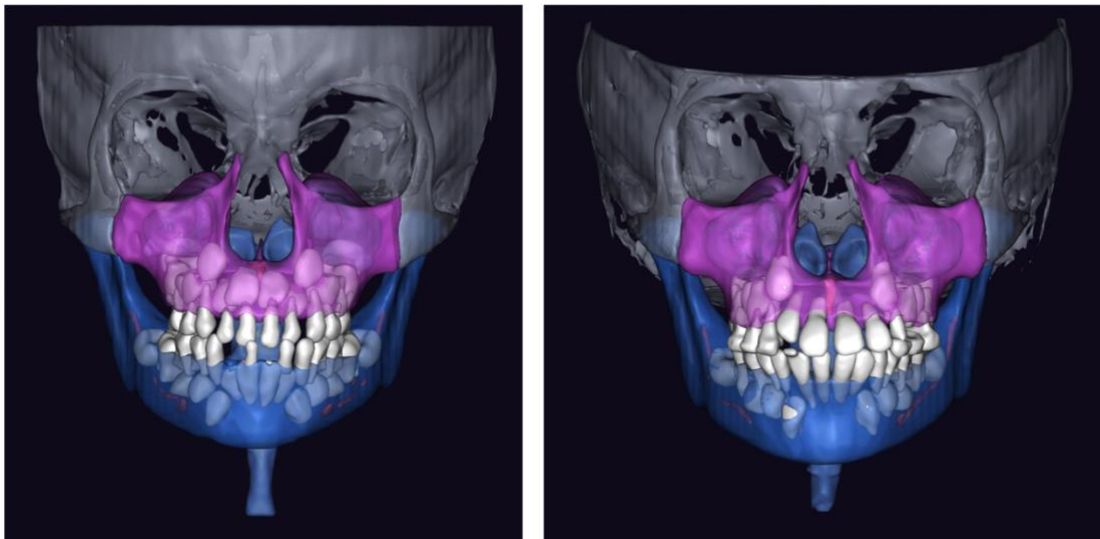


**Figure 5.** Airway cross-section measured using AI

## 5. RESULTS

### 5.1 Analyzing the skeletal relationship with adenoids and tonsils

Each of the 95 patients were measured for ANB, SNA, SNB, SN-MP, gonial angle, total airway volume, and cross-section of the minimum airway. Of the 95 patients, 70 patients had skeletal landmarks that were visible on the lateral cephalogram; for example, patients were excluded if nasion was cut off in the CBCT. For aim 1, there were 22 control patients and 48 expansion patients. The expansion group (n=48) had a smaller ANB, SNA, SNB, SN-MP, gonial angle, and airway minimum compared to the control group (n=22) at the initial timepoint. After expansion, the median value of the airway total increased at the final timepoint and was larger than the control group. Figure 6 shows the skeletal changes using a 3D rendering of a patient who underwent RPE. Table 2 and 3 demonstrate the skeletal landmarks before treatment (T1) and after treatment (T2) in both the control group and expansion group.



**Figure 6.** Skeletal changes shown with a 3D rendering using Diagnocat

**Table 2.** Skeletal landmarks before treatment (T1) and after treatment (T2) in the control group

Control (N=22)						
	Initial		Final		Difference	
	Median	(IQR)	Median	(IQR)	Median	(IQR)
SNMP	36.1	(33.4, 38.6)	34.1	(32.4, 36.3)	-1.32	(-2.65, -0.45)
Go Angle	130.8	(126.7, 134)	128.3	(123.9, 130.5)	-1.42	(-3.5, -0.10)
SNA	82.8	(80.5, 84.6)	83	(81.2, 84.9)	0.60	(-0.60, 1.40)
SNB	79.1	(76.5, 81.2)	78.7	(76.8, 80.9)	0.35	(-0.90, 1.3)
ANB	4.1	(2.2, 5.5)	4.7	(3.4, 5.5)	-0.25	(-0.90, 1.8)
Airway total	77.1	(54.1, 97.5)	72.4	(48.2, 90.4)	-2.4	(-22.5, 16.3)
Airway minimum	9.1	(6.9, 10.8)	8.5	(6.9, 12.2)	0.45	(-2.0, 1.8)

**Table 3.** Skeletal landmarks before treatment (T1) and after treatment (T2) in the expansion group

Expansion (N=48)						
	Initial		Final		Difference	
	Median	(IQR)	Median	(IQR)	Median	(IQR)
SNMP	32.3	(29.5, 36.1)	32.1	(29.4, 36.3)	-0.07	(-1.57, 0.85)
Go Angle	128.1	(124.3, 131.3)	127.1	(123.4, 131.5)	-0.25	(-0.85, 0.65)
SNA	81.4	(78.8, 84.2)	81.6	(78.6, 83.9)	0.05	(-0.5, 0.95)
SNB	77.2	(75.6, 80.7)	77.7	(75.2, 81.1)	-0.05	(-0.55, 1.15)
ANB	3.7	(2.6, 5.1)	3.4	(1.9, 5.1)	0	(-0.95, 0.40)
Airway total	79.2	(59.6, 125.8)	119.1	(82.8, 193.1)	25.2	(-19.7, 95.9)
Airway minimum	8.6	(7.3, 10.9)	11.2	(9.5, 15.8)	2.2	(0.10, 6.65)

## 5.2 Adenoid and tonsillar volume before and after treatment

Compared to the control group (n=30), the expansion group (n=65) experienced a statistically significant decrease in both adenoid and tonsil volume. There was non-statistically significant increase in volume from T1 to T2 for the control group. For the expansion group, 86% and 92% of patients experienced significant reduction in adenoid and tonsil volume, respectively. Fifty-six out of the 65 patients experienced a decrease in adenoid volume, while 60 out of the 65 patients demonstrated a decrease in tonsil volume. The average volume decrease of adenoids was 12.4% while that of tonsils was 29.0%. The patients had up to 51.6% and 75.4% reduction in adenoid and tonsil size,

respectively, following RPE orthodontic treatment. The median and IQR (interquartile range) are used to describe the data due to the outliers present.

Table 4 and 5 describe the data and demonstrate a statistically significant difference ( $p < 0.0001$  for the control group and  $p < 0.001$  for the expansion group) before and after treatment in the adenoid and tonsillar volume.

**Table 4.** Adenoid and tonsil measurements before treatment (T1) and after treatment (T2) in the control group

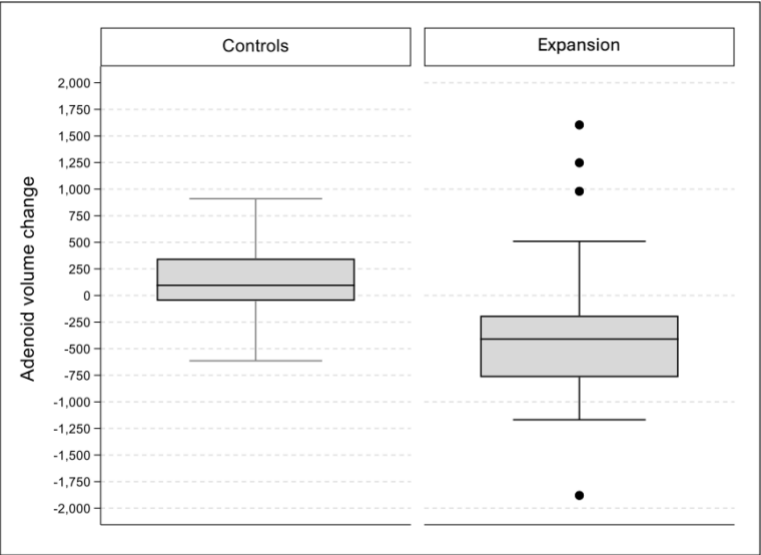
Control (N=30)						
	Adenoid			Palatine Tonsils		
	T1	T2	$\Delta$	T1	T2	$\Delta$
Average (mm <sup>3</sup> )	5483.97	5693.76	104.89	4821.83	5357.62	535.79
SD	2145.21	2175.24	315.69	2351	2495.09	1773.07
Minimum Value	2390.64	1335.235	-613.75	1369.42	2131.44	-5161.91
Maximum Value	10263.91	10210.84	909.84	11313.67	11534	5846.38
P-Value	<0.0001			<0.0001		
* p-values calculated using the Wilcoxon rank sum test						

**Table 5.** Adenoid and tonsil measurements before treatment (T1) and after treatment (T2) in the expansion group

Expansion (N=65)						
	Adenoid			Palatine Tonsils		
	T1	T2	$\Delta$	T1	T2	$\Delta$
Average (mm <sup>3</sup> )	5689.66	4925.58	-382.04	5382.29	3614.54	-1767.75
SD	1966.41	1959.44	561.64	2190.77	1445.52	1859.47
Minimum Value	1973.32	2015.51	-1879.92	2547.20	1614.56	-8083.46
Maximum Value	12113.25	10252.48	1603.82	13974.37	10248.95	1855.87
P-Value	<0.001			<0.001		
* p-values calculated using the Wilcoxon rank sum test						

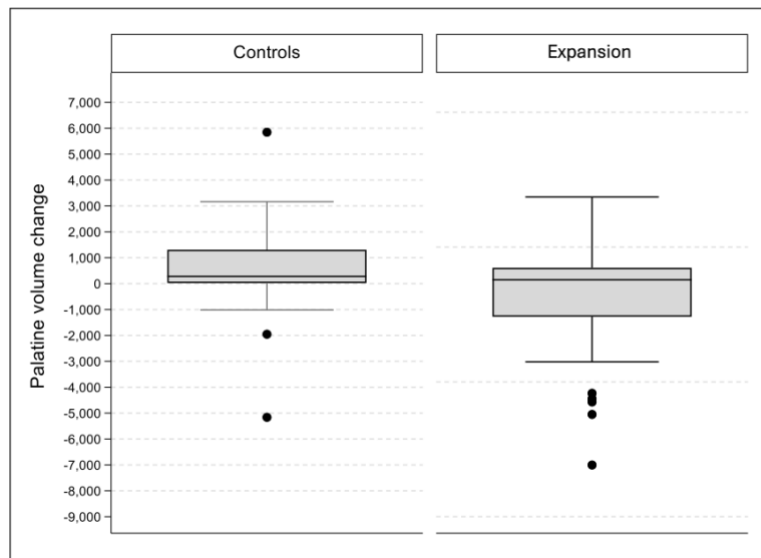
Overall, within the expansion group, the average volume reduction of adenoids was 12.4% (382.04mm<sup>3</sup>). There were 3 outliers in the expansion group that were above the normal distribution, who greatly increased in adenoid volume. There was 1 outlier

below the normal distribution, who greatly decreased in adenoid volume. This can be seen in Figure 7 which is a box plot describing the distribution of the data.



**Figure 7.** Adenoid volumetric measurements

Figure 8 describes the distribution of the data for the tonsil measurements. Overall, within the expansion group, the average volume reduction of tonsils was 29.0% (1767.75 mm<sup>3</sup>). There was a total of 3 outliers in the control group: 1 above and 2 below the normal distribution, who increased and decreased in tonsillar volume, respectively. There were 5 outliers in the expansion group that were below the normal distribution, who greatly decreased in tonsillar volume.

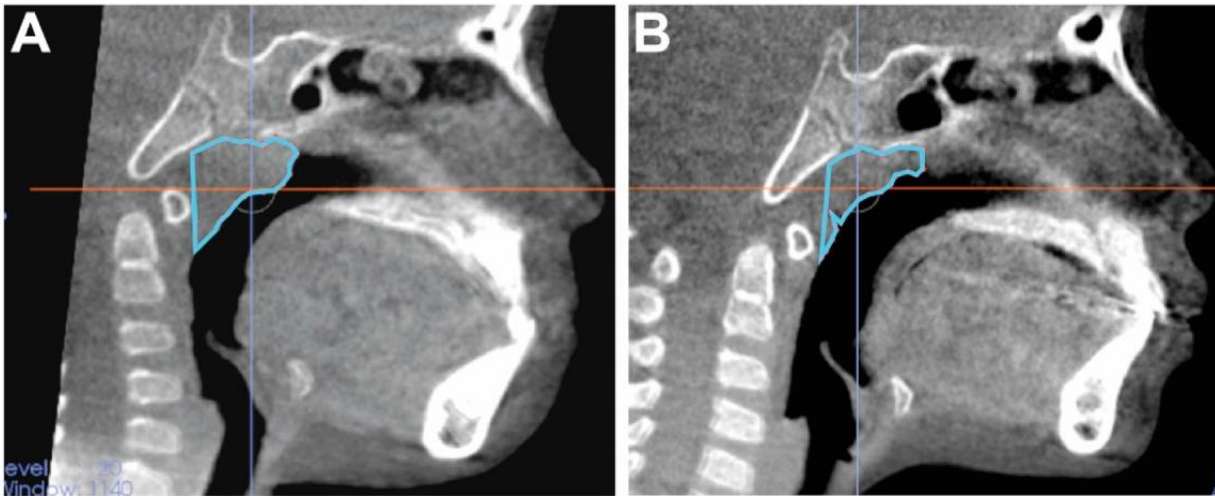


**Figure 8.** Tonsil volumetric measurements

### 5.3 Adenoid treatment responders vs non-responders

In our study, 86% of patients experienced a significant reduction in adenoid volume after RPE treatment. Figure 9 depicts the adenoid volume decrease most patients experienced in CBCT sagittal slices of T1 (A) and T2 (B). The top 5 patients with the greatest adenoid volume decrease had their CBCT reviewed, as well as reviewed their skeletal measurements. These patients had a decrease in adenoid volume ranging from a decrease of 41.00% to 51.58%. While the skeletal

measurements did not indicate a specific pattern, it was found that 4 of the 5 patients had mucus present in their sinuses in the initial CBCT. This could possibly represent that these patients experienced a great decrease in their adenoid volume due to the presence of an infection or allergen that was causing irritation and potential inflammation of the adenoids.



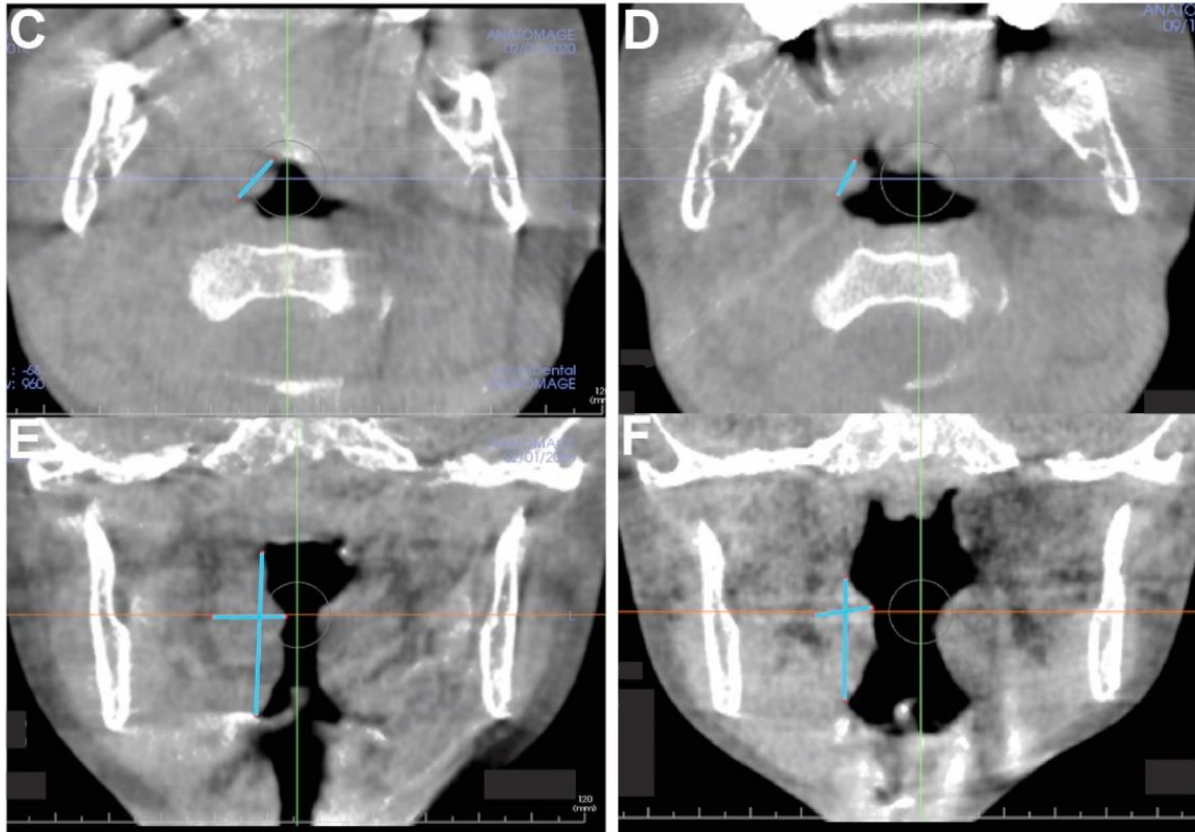
**Figure 9.** Representative CBCT sagittal slices of T1 (A) and T2 (B) for adenoid volume changes

This study further investigated potential reasons as to the reason why certain patients experienced an increase in adenoid volume, while others were outliers and experienced a larger decrease in adenoid volume. Overall, there were a total of 9 patients composed of 5 males and 4 females, who experienced an increase in their adenoids. There were 5 patients who experienced an increase in adenoid volume that was less than 23%, ranging from an increase of 8.51% to 22.35% after RPE treatment. The sinuses of these 5 patients were clear, indicating that there were no active sinus infections during the initial or final timepoints. The remaining 4 patients experienced an increase of adenoid volume ranging from 51.61% to 57.20%. Upon reviewing the CBCT

scans, 2 of the 9 patients had sinusitis and mucus present in the maxillary sinuses in the initial and final scans. This could factor into the hypertrophy of the lymphoid tissue due to active inflammation present.

#### 5.4 Tonsil treatment responders vs non-responders

This study found that 92% of patients who experienced a significant reduction in tonsil volume. Figure 10 depicts the tonsil volume decrease that most patients experienced in the CBCT axial slices of T1 (C) and T2 (D) and coronal slices of T1 (E) and T2 (F). The top 5 patients with the greatest decrease in their tonsil volume had their CBCT reviewed from the initial and final timepoints, as well as their skeletal measurements. There was not a specific pattern found with the skeletal measurements, looking skeletal class I, II, or III, SNA, SNB, gonial angle, and SN-MP. Of the 5 patients, there was one who had sinusitis present both at the initial and final timepoints. These patients experienced a decrease in tonsil volume ranging from a decrease of 58.51% to 75.43% after RPE treatment. There is no clear indication as to why these patients were outliers and experienced a significant decrease in their tonsil volume.



**Figure 10.** CBCT axial slices of T1 (C) and T2 (D) and coronal slices of T1 (E) and T2 (F) for palatine tonsil volume changes

There were 5 patients who experienced a tonsil increase, composed of 3 males and 2 females. The range of tonsil increase was 7.55% to 55.73% of volume following RPE treatment. One of these patients had mucus present in the maxillary sinuses at the final timepoint of treatment, possibly indicating active inflammation in the tonsils. There were no skeletal patterns found among these 5 patients to indicate a specific skeletal type who tended to have an increase in tonsil volume.

## 6. DISCUSSION

In children with a OSA and a high arch and narrow palate, RPE can be considered as an effective treatment (30). Our study demonstrates that 86% of patients experienced a significant decrease in adenoid volume, while 92% of patients experienced a reduction in tonsil volume following RPE treatment. This study further confirms our previous study that shows patients who undergo RPE treatment typically experience a significant reduction in the volume of adenoids and tonsils.

Of the 95 patients in this study who had their adenoids and tonsils measured, there were 70 patients who had skeletal landmarks visible on the CBCT to assess any skeletal relationship with the adenoids and tonsils. It was found that the adenoid group had a smaller SN-MP, gonial angle, SNA, SNB, and airway minimum compared to the control group at the initial timepoint. The median value of the airway increased after RPE treatment and was also larger than that of the control group median. This could be attributed to the fact that there is an increase in nasal volume at the level of the internal nasal valve (31). There is an association with skeletal and dental malocclusion and a larger tonsil size; one study found that patients with Class II dental malocclusion, while an isolated tonsil obstruction was found to be more with a Class III dental malocclusion (32). While our study found that the adenoid group tended to have smaller SN-MP, gonial angle, SNA, SNB, and airway minimum when compared to the control group, these changes are not statistically significant, and a larger sample size was needed before making any conclusions.

In this study, 95 patients were measured for their adenoid and tonsil size before and after RPE treatment. The majority of patients experienced a statistically significant

reduction in their adenoid and tonsil volume following treatment ( $p < 0.001$  for the control group and  $p < 0.0001$  for the expansion group). The average decrease in adenoid volume was 12.4%, and the average tonsil volume decrease was 29.0%. RPE expands the oral and nasal cavity volume which can aid in tongue posture leading to an improved pharyngeal airway. This can contribute to alleviate irritation of the lymphoid tissues with nasal breathing (33). Nasal breathing patients have greater pharyngeal airway and maxillary arch parameters than patients who mouth breathe (34). Patients who mouth breathe can have antigens trigger an immune response which can in turn cause tonsillar hypertrophy, as the tonsils do not have the protection from the filtration, humidification, and warming presented in nasal breathing. In children with SDB, they may benefit from RPE treatment, which can widen the oral and nasal cavity.

While 56 of the 65 patients experienced a significant decrease in adenoid volume after RPE treatment, there were patients who experienced an increase in adenoid volume. It was found that among the patients who experienced an increase in adenoid volume, 2 of the 9 patients had sinusitis as seen with excess mucus present in the maxillary sinuses in the initial and final CBCTs. Sinusitis is associated with enlarged adenoids, which could present as a possible reason these specific patients experienced an increase following RPE treatment (35). Similarly, the 4 of the 5 patients who experienced the greatest decrease in their adenoids also had sinusitis present in their initial CBCT. The patients could have had an active infection or allergen causing the hypertrophy of the adenoids, and after RPE treatment the hypertrophy decreased. There was no clear skeletal pattern associated with patients who had a large increase

or decrease in their adenoids; there also was no statistically significant difference in age or sex among these patients.

Sixty of the 65 patients demonstrated a decrease in tonsil volume following treatment. Of the 5 patients who experienced an increase in the tonsil volume, 2 patients had sinusitis at the time of the CBCT in the initial and/or final timepoints. This could possibly indicate an active infection or allergen present that would cause tonsillar hypertrophy. Sinusitis can be closely associated with enlarged tonsils, which could be a potential reason this patient experienced an increase in tonsil volume following RPE treatment (36). No skeletal pattern was found among these patients to indicate a specific skeletal type in patients who experienced an increase in tonsil volume. Additionally, the top 5 patients who experienced the greatest decrease in tonsil volume were analyzed for specific skeletal patterns and their CBCT was reviewed. One patient had sinusitis present at both the initial and final timepoints. There was no clear indication as to why these patients experienced a significant decrease in their tonsil volume. There was no statistically significant difference in age or sex between these patients who responded well to RPE treatment and those who did not.

To our knowledge, this is the second study to use low-radiation CBCT for volumetric measurement of the adenoid and tonsils. It is possible that the total volume was overestimated because of the poor contrast with soft tissues in a CBCT. It is possible that there was a greater reduction in the lymphoid tissues than what was analyzed in our study. MRI imaging provides better imaging to assess the soft tissues, which could present as a future direction of this study. It is common that patients who experience enlarged adenoids and/or tonsils are using anti-inflammatory medications;

one limitation of our study is that we were not able to record the patients' medications. Additionally, a larger population is needed to analyze skeletal landmarks in order to find a possible skeletal pattern associated with enlarged adenoids or tonsils.

## 7. CONCLUSIONS

Pediatric OSA has multiple contributors, one of which is adenoid and tonsillar hypertrophy. RPE is associated with a reduction in the lymphoid tissue, as shown in this and previous studies. Our study further investigated potential skeletal relationships with adenotonsillar hypertrophy through CBCT analysis and AI landmarking.

To our knowledge, this is one of the first studies to quantify the changes in adenoid and tonsils following RPE and exploring the potential skeletal patterns associated with enlarged lymphoid tissue. Patients were analyzed for ANB, SNA, SNB, gonial angle, SN-MP, total airway volume, and minimum airway cross-section. There were no statistically significant patterns associated with adenotonsillar size and skeletal relationship; however more investigation is needed to explore potential skeletal predictors.

This research also further investigated the patients who responded well to treatment and experienced a decrease in adenotonsillar volume, as well as non-responders who demonstrated an increase in adenoid and/or tonsil volume. CBCT analysis showed that most outlier patients who had a great increase or decrease in adenotonsillar volume were experiencing sinusitis during initial or final CBCT scans. However, after further analysis there was no skeletal pattern found among these outlier patients.

In this study, the majority of patients experienced a decrease in adenotonsillar volume following RPE treatment. Patients who present with a high arch, narrow palate, and adenotonsillar hypertrophy could benefit from RPE treatment, especially those with

SDB. This study provides pivotal insight into the therapeutic effect of RPE in pediatric OSA patients.

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