MIDFACIAL AND DENTAL CHANGES ASSOCIATED WITH POSITIVE AIRWAY PRESSURE IN CHILDREN AND ADOLESCENTS WITH SLEEP-DISORDERED BREATHING

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Abstract

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Introduction: The use of Positive Airway Pressure (PAP) for treatment of pediatric Sleep Disordered Breathing (SDB) is an increasingly widespread therapy that currently lacks longitudinal data to describe how mask pressure impacts the developing facial skeleton. Early reports have described a possible causal association between PAP usage and maxillary retrusion, but limited outcome reports and lack of established correlative assessment tools highlight the need for systematic research. The aims of this study were to examine the difference in midfacial growth between pediatric subjects with underlying craniofacial diagnoses that were prescribed PAP for SDB and were compliant vs. non-compliant with PAP therapy, and to explore correlations between demographic, medical, and sleep study variables with rate of annual facial change. **Methods:** This was a retrospective cohort study. Review of Craniofacial Center and Sleep Disorders Center records was performed to identify patients who were prescribed PAP for SDB with serial cephalographic images obtained as part of routine clinical care for concomitant craniofacial diagnosis. Lateral cephalometric analysis was used to determine mean annual change in midfacial structures from T1 to T2 in subjects with and without PAP compliance. Annual rate of change of cephalometric measurements for the compliant subjects were compared to non-compliant subjects. **Results**: 50 subjects (28 male, 22 female; mean age, 10.42) were compliant with PAP therapy (>20 hour/wk., >6 months) for an average of 2.57 years. The control group comprised 50 non-compliant subjects (29 male, 21 female; mean age, 8.53). Subjects who were compliant with PAP experienced negative mean annual change for all midface measurements compared to non-compliant subjects (SNA: -.57°, .56°; ANS-PNS: -.41mm, .95mm; SN-PP: -1.15°, .09°; A-SN': .40mm, 1.56mm; A-SN'perp: -.41mm, .8mm), and increased change in maxillary incisor measurements (U1-SN: 2.41°, -.51°; U1-PP: .10°, -.47°). **Conclusions**: Pressure to the midface from compliant PAP use during childhood may hinder normal facial growth, resulting in maxillary retrusion, counterclockwise tipping of the palatal plane, and flaring of the maxillary incisors.

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DEDICATION

To my parents, Dr. William Roberts and Dr. Tanja de Marsche,

for their endless love, support, and inspiration.

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INTRODUCTION

Sleep-Disordered Breathing (SDB) refers to a spectrum of conditions characterized by upper airway obstruction, abnormal respiratory patterns and fragmented sleep, ranging from Primary Snoring to severe Obstructive Sleep Apnea (OSA). The prevalence of OSA in children ages 2-6 is around 2-5%, and estimates for Primary Snoring are as high as 17%.[1, 2] Untreated SDB is a potentially disabling disorder that can be associated with early and significant morbidity, including neurocognitive deficits and decreased academic performance, behavioral and mood difficulties, cardiovascular impact including hypertension, hypercoagulability, and cardiac dysfunction, and chronic systemic inflammation with metabolic abnormalities.[3-5] Thus, treatment of SDB is imperative for maximizing a child's developmental potential and overall health. Adenotonsillectomy to remove large tonsils and adenoids is a first-line treatment for children with SDB, and for children with underlying midface hypoplasia even normal-sized tonsils and adenoids can contribute to airway obstruction.[2] If the underlying craniofacial condition is very severe, adenotonsillectomy may not be sufficient to resolve SDB. Positive Airway Pressure (PAP), either continuous or bi-level, has become an increasingly popular choice of therapy when adenotonsillectomy is unsuccessful in treating the condition, and for populations that do not respond well to surgery, including those with obesity and underlying neurologic co-morbidities.[6, 7]

PAP treats SDB at night by applying positive pressure via an external nasal mask, which creates a pneumatic stent in the upper airway and prevents airway collapse. There are three main styles of PAP masks: full-face masks, which cover the nose and mouth; nasal masks, which form a triangle around the nose; and nasal pillows, which

rest inside the nostrils. This study focuses on patients prescribed nasal masks, although it is possible for patients to change their mask design without notifying their prescribing doctor. Efficacy of nasal-PAP is dependent on creating an airtight seal around the nasal interface, placing a significant amount of pressure on the surrounding tissue and bones.

It has been hypothesized that the prolonged application of orthopedic forces from a nasal PAP mask could cause midfacial retrusion in growing children. Assuming that all children grow in a positive direction (away from cranial base) in the midface region, any evidence of active midface retrusion over time suggests the negative pressure effect of the PAP mask. Children with an underlying tendency for midface deficiency, such as from a craniofacial syndrome or operated cleft lip/palate, would likely display relative midface retrusion even without PAP usage.[8-10] Nasal mask pressure may enhance this underdeveloped appearance, however, by inhibiting midface growth or by actively pushing midfacial structures backward during the growth phase. Ironically, maxillary retrusion may lead to a more narrowed upper airway, potentially worsening the inherent SDB that PAP is attempting to treat.

Aside from case reports, there are only a few studies in the literature focused on this topic, despite a rapidly increasing prescription rate for nasal PAP in children.[11-15] A cross-sectional study by Fauroux et al[15] reported facial flattening in 68% and clear maxillary retrusion in 37% of children aged 0-18 years using PAP, with a stronger association linked to longer nighttime use. Tsuda et al[13] documented measurable maxillary retrusion and remodeling in adults after 2 years of nasal PAP use using lateral cephalograms, which is remarkable considering the subjects had reached skeletal maturity. Korayem et al[14] evaluated children with and without PAP therapy

and identified no significant differences in craniofacial morphology between the groups and found no association between craniofacial change and length of PAP therapy.

Of the 1800 children currently undergoing treatment with PAP at the Sleep Disorders Center at Seattle Children's Hospital, approximately 200-250 are also being followed in the Craniofacial Clinic. This highlights the need to document the long-term effects of PAP therapy, as the very treatment being prescribed for SDB may result in decreased airway space and lead to reconstructive surgical repair, at significant personal and medical costs. This study attempts to characterize and quantify the physical effects of PAP therapy to the growing midface and maxillary dentition in a sample of children and adolescents with SDB. We hypothesize that those compliant with PAP will have more evidence of midface retrusion, as well as secondary dentoalveolar changes, when compared to those non-compliant with PAP as measured by objective cephalographic findings over time.

MATERIALS AND METHODS

In this retrospective cohort study approved by the Seattle Children's Hospital IRB, medical records from the Craniofacial Center and Sleep Disorders Center of Seattle Children's Hospital were reviewed. Medical and surgical histories, and diagnostic testing/imaging results were extracted.

Inclusion criteria for all subjects were as follows: (1) age, 0-18 years; (2) diagnosis by a sleep specialist of sleep disordered breathing and prescription of PAP via a nasal mask, either continuous or bi-level, following baseline polysomnography per usual clinical practice at the Sleep Disorders Center at Seattle Children's Hospital; (3)

medical-grade CT scan or lateral cephalogram at T1 (within 12 months of PAP prescription) and T2 (>6 months after T1 and >6 months of PAP compliance or non-compliance). Since it is rare for children to have 3D or 2D facial imaging unless they are undergoing orthodontic treatment or treatment for a craniofacial anomaly, all subjects with primary craniofacial diagnoses were included. Exclusion criteria were as follows: (1) maxillary orthognathic surgical treatment (LeFort 1, 2, or 3) occurring between T1 and T2, (2) poor quality imaging, (3) insufficient CPAP compliance data.

Sleep Variables

All subjects underwent diagnostic polysomnography (PSG) as part of their clinical care. PSG was performed at Seattle Children's Sleep Disorders Center, an accredited pediatric-specific facility. Polysomnography (PSG) lasted at least 6 hours and was performed in a private darkened room free of distraction with a parent or guardian present. The following physiologic parameters were monitored: electroencephalogram, electro-oculogram, submental and anterior tibialis electromyograms, electrocardiogram, oronasal airflow measured by thermistor and pressure transducer, expired end-tidal carbon dioxide, oxygen saturation via pulse oximeter, and thoracic and abdominal movement. All data were recorded into a computer-based acquisition and analysis program (XLTEK, Natus ® Oakville, Ontario, Canada or Rembrandt®, Buffalo, New York), scored by one certified technician, and interpreted by a board certified sleep medicine physician in accordance with AASM guidelines.[16] The Apnea Hypopnea Index (AHI) was defined as the total number of respiratory disturbances averaged per hour of total sleep time, and further divided

into those caused by obstructive apneas/hypopneas (physical barrier to breathing pattern) and those caused by central apnea (neurologic disruption to breathing pattern).

Determination of compliance with PAP was based on objective real-time data retrieved from an online database (EncoreAnywhere v 2.23.5.3, Philips Respironics) as well as subjective documentation in the medical record. Subjects were considered compliant if their record demonstrated PAP usage of at least 4 hours per night on 70% of nights for a minimum of 6 months.[17] Those who were not compliant with PAP remained in the study as comparative control participants. It was not possible to precisely calculate total hours of PAP usage or average mask pressure for each subject due to inconsistencies in the objective data available.

Cephalometric Analysis

Medical-grade CTs that were obtained in DICOM3 format were converted to 2-dimensional lateral cephalometric images using Dolphin 3D software (Dolphin imaging, Chatsworth, CA). Digital and scanned film cephalograms from individual image sources were also used when no CT was available for a given time point. All images were calibrated for image size standardization, randomized, and traced with Dolphin Imaging software by a single blinded operator (S.R.). Twenty radiographs were re-measured and the intra-observer error was measured to be 0.7°, 0.9mm, and 0.6mm for SNA(°), A-SN'(mm), and A-SN'perp(mm) by Dahlberg's estimator. Standard cephalometric landmarks were used and a custom analysis was generated using measurements relevant to the anterior-posterior and vertical position of the maxilla

and anterior cranial base, and to the inclination of the palate and maxillary incisors. We were most interested in the amount of change in facial structures over time in compliant vs. noncompliant subjects, rather than the absolute values of the cephalometric measurements at each time point. Therefore, the results are given as annual rates of change, i.e. millimeters or degrees of change per year, for each measurement. For measurements involving the inclination of the maxillary incisor, patients with braces at any point between T1 and T2 were excluded. Since the PAP mask has direct contact with the bridge of the nose and the maxilla, cephalometric measurements were chosen that specifically isolate the position of the maxilla (A-point, anterior nasal spine, posterior nasal spine) and upper incisor (U1) in reference to the anterior cranial base (sella and nasion) (Figure 1). A-SN' and A-SN'perp are measurements that define the distance vertically in mm from A-point to a constructed line that is 7° below S-N (called SN', or SN "prime"), and horizontally from A-point to a constructed line perpendicular to SN'. SN' is an approximation for the Frankford-Horizontal line, which gives a better representation of the true horizontal plane, from which A-point can be plotted as if on an x,y axis (Figure 2). For all of the midface measurements chosen, expected rate of growth is a positive value (trajectory away from cranial base). Thus, results expressed as a negative value, or a smaller value when compared to the control group, represent midfacial structures being pushed backward or retarded in their growth, relative to cranial base over time. Mandibular measurements were not included due to inconsistent imaging (mandible not fully captured, or CT taken under general anesthesia with mouth open). The following measurements were chosen for analysis:

1. SNA (degrees): *anteroposterior projection of anterior maxilla relative to nasion*
2. S-N (mm): *length of anterior cranial base*
3. ANS-PNS (mm): *length of maxilla*
4. SN-PP (degrees): *angulation of palatal plane relative to anterior cranial base*
5. Ba-S-N (degrees): *degree of flexure of cranial base*
6. A-SN' (mm): *vertical distance from anterior maxilla to the S-N prime line (SN-7')*
7. A-SN'perp (mm)*: anteroposterior distance from anterior maxilla to a line perpendicular to the S-N prime line (SN-7')*
8. U1- SN (degrees): *inclination of upper incisor relative to anterior cranial base*
9. U1-PP (degrees): *inclination of upper incisor relative to palatal plane*

Statistical Analysis

Data were analyzed using SPSS software (version 13.00; SPSS, Chicago, Ill). Baseline characteristics and imaging results were compared using t-tests between compliant and non-compliant groups. Comparisons were adjusted for age, gender, and primary craniofacial diagnosis. Further analyses of cephalometric changes were done by age groups (<8 years, 8-15 years, >15 years). Multivariate regression analysis was used to relate change in cephalometric measurements to underlying severity of SDB and BMI. For this descriptive study, significance was set at $p<0.05$.

RESULTS

A search of the database for patients prescribed PAP and also seen in the Craniofacial Clinic at SCH yielded 217 patients. Of these, 98 (56 male, 42 female,

mean age 9.11), or 45.2%, were considered compliant with PAP and 119 (74 male, 45 female, mean age 8.37), or 54.8%, were considered non-compliant (Table 1). Reasons for non-compliance included: patient unable to tolerate PAP (n=49), PAP usage less than compliance criteria (n=28), PAP used compliantly for less than 6 months (n=23), patient did not start PAP for undocumented reason (n=10), adenotonsillectomy after PAP prescription (n=4), tracheotomy performed (n=3), or oral appliance prescribed (n=2). 3D or 2D imaging at T1 and T2 was found for 136 subjects. Thirty-six subjects were excluded from this study (n=18 for maxillary surgery between T1 and T2; n=13 for inadequate record of compliance, n=5 for poor quality radiographs,). Final data analyses and results were based on the remaining 100 subjects (57 male, 43 female, ages 0-18).

Baseline characteristics of the two groups are provided in Tables 2 and 3. The only statistical differences between the compliant and non-compliant groups were age at T1 and Total Arousal Index. Compliant subjects were 10.42 years old on average whereas non-compliant were 8.53 years old ($p<0.05$); and compliant subjects experienced mean 24.85 cortical arousals/hour whereas non-compliant subjects experienced mean 17.04 arousals/hour. There was fairly even distribution of underlying diagnoses in this cohort, with low prevalence of pre-PAP orthognathic surgeries. Nearly all subjects in both groups underwent pre-PAP adenotonsillectomy (data not shown). Follow-up time between images was 2.57 years (±1.17) for the compliant group and 2.45 years (±1.26) for the non-compliant group.

Rates of cephalometric changes for nearly every measurement differed between the two groups, with the PAP compliant group generally showing more negative or smaller changes over time, consistent with more midface retrusion. Compliant

subjects overall experienced decreased mean annual changes to midface projection. Compliant PAP subjects also experienced increased mean annual change for flaring of the upper incisor. Differences between groups were larger when the data were adjusted for age, gender, and primary craniofacial diagnosis (Table 4). Although significant pressure from the PAP mask has been reported to be exerted on the bridge of the nose (N point),[18] the mean change in cranial base length (S-N) was not different between groups.

Regression analysis was used to test for an interaction between age group and rate of facial change, however sample size in each age group was not large enough and variability was too high to detect a significant difference between age groups (Table 5). Further regression analyses were performed looking at underlying severity of SDB variables and BMI with cephalometric changes and no significant correlations were found (Table 6). Complete raw data is presented in Table 7.

DISCUSSION

Compliance data for nighttime PAP usage is scarcely documented in the Sleep Medicine literature. For the initial craniofacial population in this study (n=217), 45.2% of all subjects were compliant with PAP, meaning the device was used at least 4 hours per night on 70% of nights for a minimum of 6 months. The average age of compliant subjects was 9.2 for males (n= 56) and 9.0 for females (n=42), whereas the average age of non-compliant subjects was 8.3 for males (n=74) and 8.5 for females (n=45). It is reasonable to assume that older patients may be more tolerant of wearing a PAP mask while sleeping, although the overall compliance rate is low.

As hypothesized, subjects with adequate cephalographic imaging who were compliant with nighttime PAP (n=50) experienced a significant amount of midface growth restriction in comparison to non-compliant controls (n=50). In fact, the mean data for compliant subjects in our sample reflects active retrusion of the midface, meaning that midfacial structures of many subjects were actually pushed backwards from where they started, whereas non-compliant controls showed overall forward midface growth. For example, A-SN'perp decreased by an average of -0.41mm per year in the compliant group, whereas A-SN'perp increased by 0.8mm annually in the non-compliant group. Decreases in SNA and A-SN'perp describe restriction of maxillary growth in an anteroposterior direction. Decreased ANS-PNS suggests resorption of the anterior maxilla in response to PAP mask pressure, although this measurement should be interpreted with caution, as PNS is often a difficult point to reliably identify on a lateral cephalogram. Decreased rate of change in A-SN', a vertical measurement, suggests that PAP may restrict the normal downward growth of the anterior maxilla.

Previous studies have not addressed the potential for negative change in palatal plane inclination as a result of PAP, which might result in skeletal and dental effects such as anterior open bite and concomitant clockwise rotation of the mandible. In our sample, compliant subjects averaged a negative change in SN-PP over time (degrees per year), suggesting a counterclockwise rotation of the palatal plane with reference to anterior cranial base. The upper incisor also increased in proclination, as evident by an increase in both U1-SN and U1-PP (the non-compliant group showed a slight retroclination of the upper incisor over time). Tsuda et al showed the opposite effect on upper incisor inclination in a study of adults using nasal PAP for >2 years.[13]

The most significant outlier in this sample in terms of SNA, or the subject that showed the most negative change in SNA in response to compliant PAP use, was also the youngest compliant subject in the sample (male, age 1.05 years at PAP prescription). This subject had unilateral cleft lip and palate and an Apnea-Hypopnea Index of 9.3 events per hour. After 2.52 years of compliant PAP use, this subject exhibited a negative change in SNA of -8.9 degrees, an increase in A-SN' of 4.2mm, and a negative change in A-SN'perp of -0.5mm. For comparison, only one other subject in this study was under two years old when prescribed PAP and she was non-compliant with PAP (female, age 1.08 years, branchial arch anomaly, AHI=16.7). After 2.23 years, she exhibited a change in SNA of -2.3 degrees, an increase in A-SN' of 11.8mm, and a positive change in A-SN'perp of 4.1mm. The most significant outlier in terms of A-SN'perp (horizontal change of A-point in mm), was a compliant male with unilateral cleft lip and palate, age 6.32 years at PAP prescription and AHI of 17. After 2.20 years of PAP use, change in SNA was -4 degrees, change in A-SN' was 3.5mm, and change in A-SN'perp was -3.9mm. A similar non-compliant patient (female, age 5.32, bilateral cleft lip and palate, AHI=1.4) exhibited positive change in SNA of 2.8 degrees, change in A-SN' of 1.4mm, and change in A-SN'perp of 3.9mm after 3.09 years. Although childhood growth is complicated by many underlying variables, including amount and quality of sleep, it is apparent that PAP mask pressure over multiple years resulted in negative, or backwards movement of midface landmarks in these compliant one and six-year olds.

Chronologic age, rather than skeletal age, was used in this study and may not be an accurate determinant of childhood and adolescent growth spurts. It is likely that PAP use during periods of rapid facial growth, such as the pubertal growth spurt, is

the most detrimental to the developing midface. In our sample, although subjects in the 8-15 age group showed less absolute negative change than compliant subjects in the younger and older age groups, the data reflect a decreased rate of positive growth compared to control and normal subjects during a time of expected accelerated positive growth (Table 5). Further research is needed to detect differences in rates of facial change between age groups.

The majority of subjects in this study had relative midface deficiency at T1 resulting from various craniofacial conditions. Subjects age 6-16 in this study had average SNA measurements of 75.5° for males (n=43) and 77.0° for females (n=28), whereas non-syndromic patients age 6-16 would be expected to have SNA measurements of 81.0° for males and 81.2° for females on average, based on cephalometric standards from the University of Michigan growth studies.[19] For S-N (mm), subjects age 6-16 in this study had average measurements of 63.4mm for males and 64.0mm for females, compared to 77.8mm for non-syndromic males and 74mm for non-syndromic females. Annual change in midfacial measurements for subjects in this study reveals an overall slower midfacial growth rate in craniofacial patients compared to the non-syndromic standards. For example, annual change in S-N in this study's population was 0.17 for all compliant patients and 0.49 for all non-compliant patients, whereas non-syndromic children age 6-16 undergo annual change in S-N of 0.9mm on average. Underlying craniofacial diagnosis was not shown to be a major factor in the degree of midface retrusion caused by PAP in this study. A system of grouping syndromes according to degree of midface deficiency might minimize confounding factors in a future study.

When interpreting these results, consideration should be given to the high variability in underlying craniofacial diagnoses, age, and time between T1 and T2 in this sample. Additionally, although a nasal mask interface was prescribed to each patient in this study, various mask designs may have been worn, as patients often interact directly with the PAP mask supplier to find a mask that fits most comfortably. Another limitation of this study includes variation in image format - although CT was the primary source of imaging, digital and film cephalograms were also included, which may have contributed to minor error in image size calibration.[20] Lastly, a future prospective study should ensure that T1 corresponds to the exact commencement of PAP, and that T2 correlates to the exact end of PAP, or a set time after T1. This would provide a more precise baseline analysis and ensure that follow-up analysis precludes any recovery, or "catch-up" growth of the midface after PAP is discontinued.

PAP is currently the most frequently prescribed therapy for patients with severe SDB who do not respond well to adenotonsillectomy. When used consistently for greater than 2 years, PAP has been shown to cause midfacial retrusion in adults, so it is not surprising that PAP could impair the developing midface of a child or adolescent.[13] PAP has, however, been proven to be highly effective in treating SDB and sleep apnea in children, and so the potential negative side effects of PAP on the pediatric midface must be weighed against the advantageous effects of PAP, including improvement in daytime sleepiness, temperament, school performance, and reducing the potential for related medical conditions.[7, 21] When prescribed for children, duration of PAP treatment is usually for several years or until airways have enlarged via somatic growth. It may also be life-long, depending on the underlying associated

condition. The clinical significance of potential midface retrusion should be determined for each patient prescribed nasal PAP. Evaluation and monitoring by an orthodontist throughout PAP therapy is recommended to detect dental changes, as well as negative skeletal and facial effects that may lead to worsening of potential airway obstruction. Protraction headgear or "facemask", an orthodontic treatment used to protract the midface and maxillary dentition, may be a viable treatment option for patients showing midface retrusion resulting from PAP.

A subsequent prospective, perhaps multi-center, study should include a description of the pressure setting of the PAP machine, with distinction between continuous and bi-level pressure. Additionally, 3-D analysis of airway volume may determine whether compliant PAP usage puts patients at risk for overall upper airway constriction that could potentially worsen SDB symptoms and require continued therapy with PAP or orthognathic surgery. 3dMD facial imaging and intraoral scanning of the dentition could also be used to document soft tissue and dental changes more precisely, in three dimensions, and without radiation over multiple time points.

CONCLUSION

In this study, 45.2% of all subjects were compliant with PAP therapy. Craniofacial measures based on cephalometric analysis indicated statistically significant decreases in annual rates of change for all craniofacial measurements related to growth of the midface in compliant vs. noncompliant subjects. Compliant patients showed overall maxillary retrusion, counterclockwise tipping of the palatal plane, and flaring of the maxillary incisors over an average of 2.5 years of PAP therapy. Additional studies are needed to further assess clinical factors such as the timing and duration of PAP

therapy and their correlation to surrogate endpoints related to pediatric midface development. Based on the preliminary findings of this study, patients prescribed PAP for SDB should be monitored for facial and dental effects related to the applied PAP mask pressure over time. These findings indicate a need for greater collaboration between sleep medicine physicians and their orthodontic colleagues. Standardized cephalometric lateral head films could assist clinicians in diagnosing PAP-related midface change over time.

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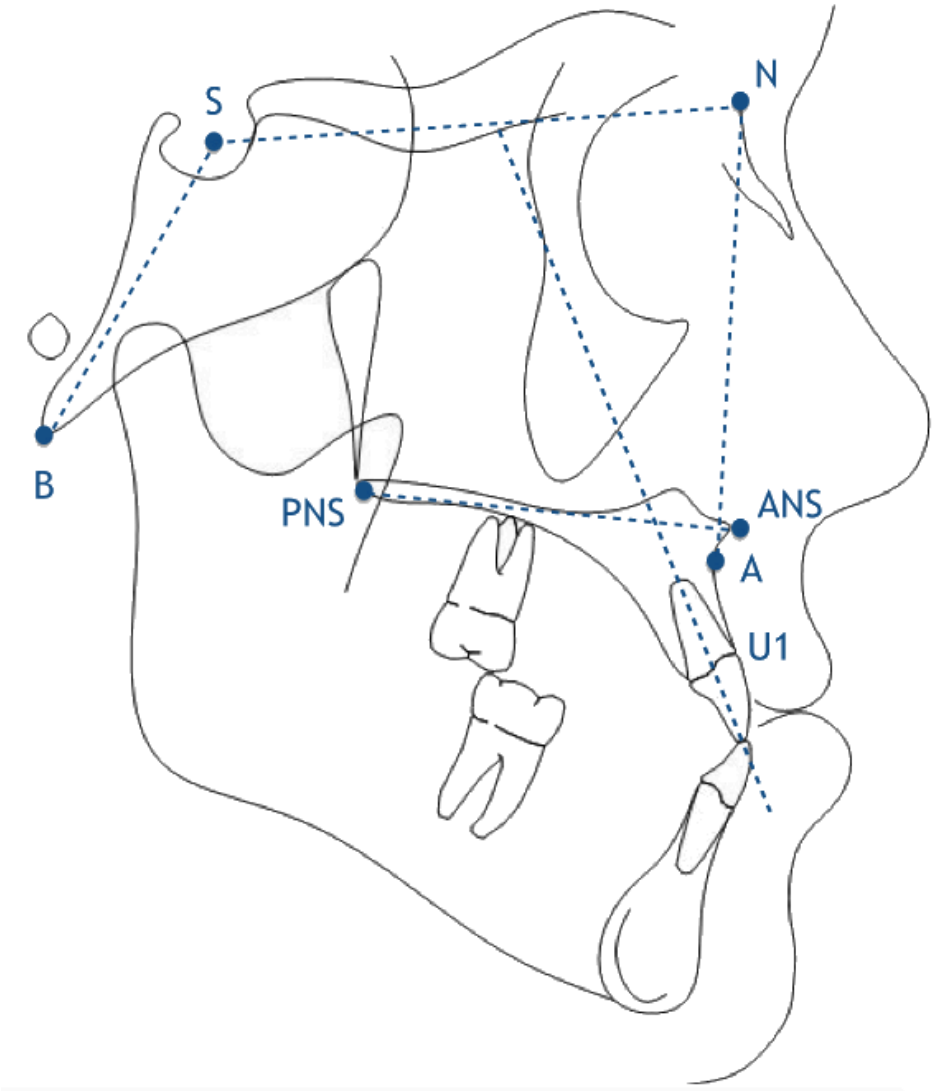
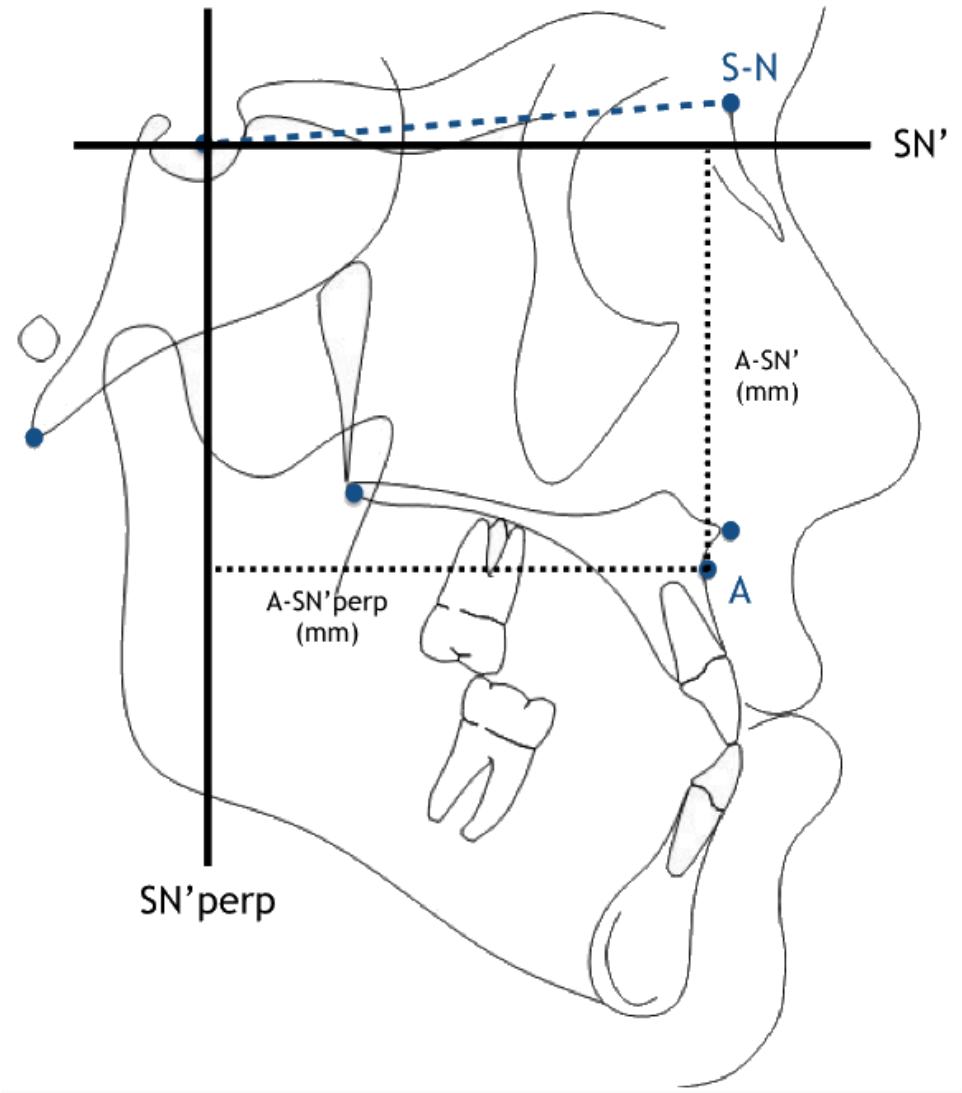
APPENDIX

Figure 1: Cephalometric points used for analysis



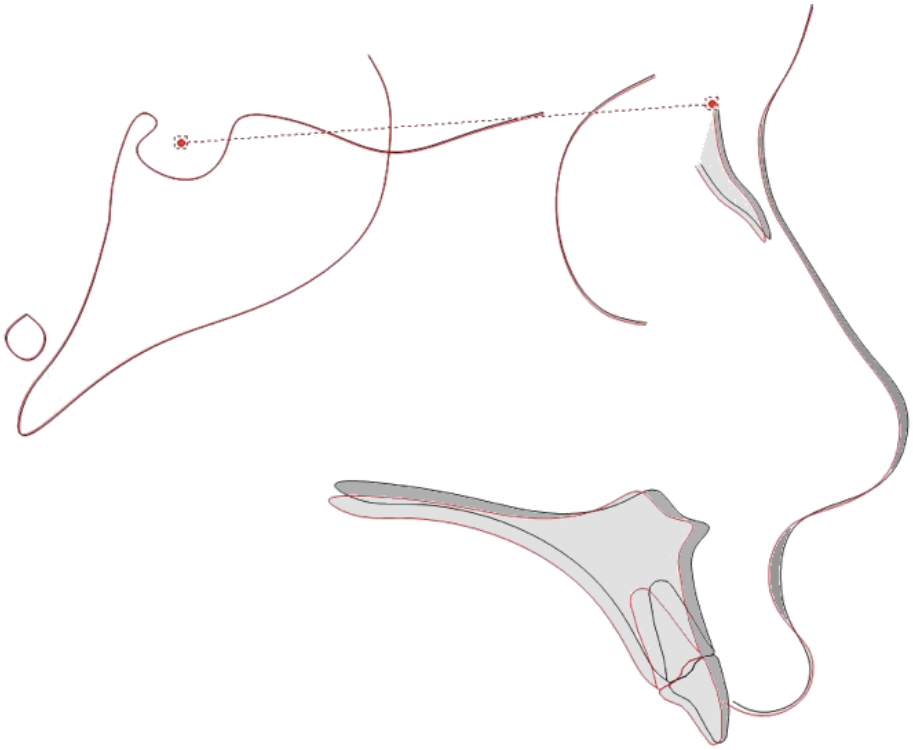
A=subspinale, ANS=anterior nasal spine, B=basion, N=nasion, PNS=posterior nasal spine, S=sella, U1=upper incisor

Figure 2: A-point plotted by A-SN' and A-SN'perp

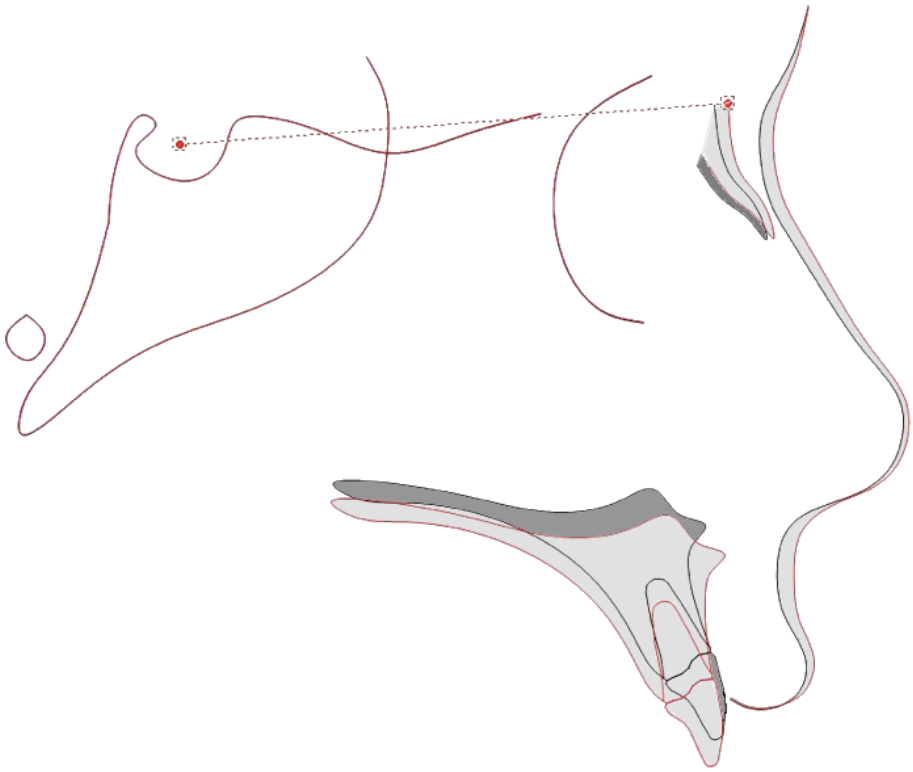


SN'=line 7 degrees below S-N line, SN'perp=line perpendicular to SN', A-SN'=vertical distance between A and SN' in mm, A-SN'perp=horizontal distance between A and SN'perp in mm

Figure 3: Superimpositions of baseline and follow-up data



A – COMPLIANT



B- NON-COMPLIANT

Average position of facial and dental structures at T1 (dark) and T2 (light), superimposed on sella-nasion line

Table 1: Overall compliance data (initial patient group, n=217)

		Compliant	Non-compliant
Total n		98	119
% of total n		45.2%	54.8%
Gender	male (n)	56	74
	female (n)	42	45
Age (yrs.) at PAP prescription	male	9.2	8.3
	female	9.0	8.5

Table 2: Demographic data with sleep study variables from initial polysomnography

	Compliant			Non-compliant		
	Valid N	Mean	Standard Deviation	Valid N	Mean	Standard Deviation
Age at PAP prescription	50	9.63	4.33	50	9.47	4.58
Age at T1*	50	10.42	4.35	50	8.53	4.43
T2-T1 (years)	50	2.57	1.17	50	2.45	1.26
Ht (cm)	50	129.72	26.43	50	128.91	29.16
Wt (kg)	50	34.23	18.83	50	34.84	21.19
BMI%	49	56.40	30.31	49	61.07	32.43
Sleep Efficiency (%)	47	80.49	17.15	49	79.53	12.33
Total Arousal Index*	48	24.85	21.43	47	17.04	14.1
Apnea Hypopnea Index	48	17.61	19.8	50	12.03	19.12
Mean ETCO2	46	42.61	4.53	44	43.7	4.45
Max ETCO2	41	49.51	5.07	42	49.71	5.11
Mean SaO2 (%)	48	96.55	1.27	50	96.61	1.27
Nadir SaO2 (%)	47	89.15	5.29	47	89.28	6.21

*Groups significantly different ($p < 0.05$) by *t* test

Table 3: Demographic data with medical history variables

		Compliant		Non-compliant	
		n	%	n	%
Gender	Male	28	56%	29	58%
	Female	22	44%	21	42%
Primary craniofacial diagnosis	Orofacial clefts	11	22%	17	34%
	Craniosynostosis	12	24%	9	18%
	Branchial arch anomalies	14	28%	14	28%
	Other	13	26%	10	20%
LeFort 1, 2, or 3 prior to PAP		4	8%	1	2%
Mandibular advancement prior to PAP		3	6%	3	6%

No significant differences ($p<0.05$) found between groups in any variable.

Table 4: Differences between groups: annual change in cephalometric measurements – adjusted for age at T1, gender, and primary craniofacial diagnosis

	Mean annual change (degrees or mm per year)		Unadjusted mean annual change (degrees or mm per year)				Adjusted mean annual change (degrees or mm per year)			
	Compliant	Non-compliant	Diff.	95% CI		p-value	Diff.	95% CI		p-value
SNA (°)	-0.57 ± .93	0.56 ± .77	-1.14	-1.47	-.80	<.001*	-1.21	-1.57	-.86	<.001*
SN (mm)	0.17 ± .69	0.49 ± 1.21	-.32	-.71	.07	.111	-.23	-.63	.17	.257
ANS-PNS (mm)	-0.41 ± .93	0.95 ± 1.25	-1.35	-1.79	-.91	<.001*	-1.43	-1.89	-.98	<.001*
SN-PP (°)	-1.15 ± 1.62	0.09 ± 1.69	-1.23	-1.89	-.57	<.001*	-1.33	-2.02	-.64	<.001*
Ba-S-N (°)	-0.05 ± .56	-0.20 ± 1.00	.15	-.17	.48	.351	.13	-.21	.48	.452
A-SN'(mm)	0.40 ± .94	1.56 ± 1.76	-1.16	-1.73	-.60	<.001*	-1.07	-1.60	-.54	<.001*
A-SN'perp (mm)	-0.41 ± .80	0.80 ± 1.16	-1.21	-1.61	-.82	<.001*	-1.18	-1.60	-.77	<.001*
U1 - SN (°)	2.14 ± 3.57	-0.51 ± 3.04	2.65	1.26	4.04	<.001*	3.05	1.60	4.51	<.001*
U1 - PP (°)	1.00 ± 3.39	-0.47 ± 2.98	1.47	.13	2.81	.032*	1.73	.32	3.15	.017*

*****$p<0.05$ by linear regression. Data are presented as means ± standard deviation