

3D Orthodontic Imaging to detect midfacial retrusion in children on non-invasive positive pressure ventilation (NPPV) therapy

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Research Article

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Abstract

Purpose

To determine the presence and magnitude of mid-face hypoplasia (retrusion) using 3D photography to measure facial convexity angle in children using non-invasive positive pressure (NPPV) therapies through a nasal mask.

Methods

Stereophotogrammetry and biometric data were collected at baseline and at follow-up from children aged 0–12 years who were being treated with NPPV for a period of 0.6–4.0 years. Analyses evaluated the changes in facial convexity parameters and included comparisons according to duration of use, compliance (non-compliant considered 'NC control' group), and the presence of syndromes or craniofacial abnormalities.

Results

Eighteen children aged 0.1–11.5 years were studied: 13 compliant constituting the 'NPPV' group, 5 non-compliant as the 'NC control' group. Change in facial convexity angle ranged from – 6.6% to 8.3%. Within the NPPV group, 69% experienced midfacial hypoplastic changes, with a higher proportion amongst those without syndromes or craniofacial abnormalities (89% vs 25%), whilst amongst the NC controls and those who had craniofacial abnormalities, a greater proportion of hyperplastic changes (80% and 86% respectively) was evident.

Conclusion

Using 3D-imaging, this preliminary study showed that up to 69% of children who were compliant with NPPV therapy, developed some degree of midfacial retrusion, particularly those without underlying syndromes or craniofacial abnormalities.

Introduction

Non-invasive positive pressure therapy (NPPV) is predominantly delivered by nasal masks as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiLevel). However, concerns have arisen regarding the side effects on facial growth of such treatments with particular concern about the development of midfacial hypoplasia, in children (Reviewed in Bariani et al (1)). Midfacial hypoplasia refers to the relative flattening/retrusion of central face structures (2). However, difficulties with obtaining frequent x-rays of sufficient quality for measuring multiple orthodontic landmarks in children, along with a lack of consensus about the relevant amount of retrusion (and which landmarks would be relevant) to clinically indicate mid-face hypoplasia means that it currently remains a subjective diagnosis.

The soft tissue angle of facial convexity is defined by the soft tissue glabella (the most prominent point of the area of skin between eyebrows above the nose on the mid sagittal plane), subnasale (the point where the nasal septum and upper lip meet on the mid sagittal line), and soft tissue pogonion (the most prominent point on the chin on the mid sagittal plane) (Fig. 1A). This measure has been used to assess craniofacial changes from orthodontic surgeries (3–5), and holds potential as a method to detect midfacial hypoplasia in 3D images (6). However, there is a lack of literature exploring its use in the assessment of changes with NPPV treatments.

The relationship between long-term NPPV use and midfacial hypoplasia in children was first suggested in two case studies (7, 8). Two subsequent cohort studies using cephalometric radiographs verified this relationship in pediatrics (9, 10) while another did so in an adult population (11). Only one cohort study reported no association of NPVV and midfacial changes (12), with suggestion that the lack of change was due to the restricted sample size and short duration of the post-NPVV measure; 6 months vs > 15 months when compared to the other 3 studies (reviewed in Bariani et al. (1)).

The aim of this study was to determine if measuring the soft tissue angle of convexity with 3D stereophotogrammetry, would detect the development of midfacial hypoplasia in children using NPPV through a nasal mask. Our analysis is conducted on two groups of children with those having normal craniofacial features compared to those with syndromes or craniofacial abnormalities. Further analysis was undertaken to determine any relationship with compliance with therapy, with those who were non-compliant (NC) considered as not using the NPPV sufficiently to induce a change and hence constituted as 'NC controls'. That group was compared to those who still used the therapy as the NPPV group.

Methods

Patients, Polysomnography (PSG) and NPPV compliance

Details of the methods pertaining to patient recruitment and polysomnography (PSG) have been detailed (6). The cohort of children in this study are a subset of (6) and were those for whom follow-up 3D imaging was available longitudinally. The 3D images and PSG were undertaken as part of the clinical assessment of suspected sleep disordered breathing after review by a Paediatric sleep physician. OSA severity was classified using obstructive apnea hypopnea index (OAHl), with < 1 considered as OAHl negative, 1-<5 as mild, 5-<10 as moderate and > 10 as severe (13, 14). Ethics approval was obtained from NSW Sydney Children's Hospital Network Health Ethics committee for the study (2019/ETH00036).

The methods of initiation of NPPV therapy and obtaining compliance data within our department have been described in detail previously (15). Patients who were considered compliant and constituted the 'NPPV' group used NPPV for at least 4 h/night for the majority of nights (interpreted as at least 70% of total compliance data provided), with a minimum of 4 weeks data available (16).

Stereophotogrammetry (3D imaging) and change after NPPV use

Our hospital's photography department used their standard 3D imaging protocol to conduct the 3D imaging and the detailed methodology has been described previously (6). The 3DMD software (3dMDvultus Inc. 4.0) was used to measure the desired soft tissue measurements by first manually identifying landmarks (Glabella, Nasion, Subnasale, Pogonion, and Menton (Fig. 1A)), and using the inbuilt angle and distance calculators to measure the facial convexity angle (17). This angle was chosen as the single measure of interest for our study due to the stability of the contributing landmarks (Glabella, Subnasale, Pogonion) with age, and previous documentation of < 1.5mm change identified in these locations between ages 3 and 6 years, compared to alternative locations used in soft tissue analogues of the Sella-Nasion A and B (SNA and SBA) angles which show more than double that change with age (18).

Each imaging session using the stereophotogrammetry set up (depicted in Fig. 1B), produced between two and ten images and, as such, the average measurement for each patient across each session was used in the analysis. Given the subjectivity of the landmarks, repeated measurements were conducted by the primary author and the intraclass correlation coefficient (ICC) calculated. For pre-treatment sessions, the single-measure ICC was 0.98 (95% CI: 0.95–

0.99) while for post-treatment sessions it was 0.95 (95% CI: 0.87–0.98), consistent with high reproducibility between measurements.

The difference in facial convexity angle (in degrees ($^{\circ}$)) was computed by subtracting the latest measure from the earliest baseline measure prior to NPPV initiation. This difference was computed to derive the percent change (%). A positive difference in the degree of facial convexity indicated hypoplasia (retrusion), while a negative difference indicates hyperplasia (protrusion) (19).

Statistical analysis

Statistical analysis was performed using R studio (R version 4.3.3, R Foundation for Statistical Computing, Vienna, Austria). A p-value ≤ 0.05 was considered significant. Summary statistics of numerical variables are presented as mean $\pm$ standard deviation (SD) with medians also provided in the tables. Categorical variables are presented as frequency (%).

Given the small sample size and non-normal distribution of data, non-parametric tests were chosen for all analyses. Comparisons between the NPPV and NC groups were conducted using the Wilcoxon rank-sum test for all continuous numerical variables. Fisher's exact test (with the Freeman-Halton extension for 2x3 tables) was used to assess differences in the proportion of patients showing retrusion versus protrusion in facial convexity angle, based on compliance and craniofacial status. To evaluate changes over time within individuals, the Wilcoxon signed-rank test was applied to compare baseline and follow-up measurements. Confidence intervals were reported at the 95% level for group comparisons; however, 88% confidence intervals were used in subgroup analyses with limited sample sizes as the discrete signed-rank test necessitates only exact quantiles are achievable, and as such, the closest admissible level, not exceeding the desired 95% confidence interval level, was chosen (20).

Results

Dataset characteristics

Of the total 113 children initially included in the baseline study (6), 95 were lost to follow-up or did not have a second 3D image. As such, 18 children remained for final analysis in this study. These 18 children were found to be representative of the initial cohort with regards to their anthropometric demographics, PSG data, and facial convexity angle whereby $p > 0.05$ for all parameters when compared to the 95 children (Supplementary Table 1).

At the time of the initial 3D imaging, the 18 children were aged between 0.05 and 11.5 years, 56% were male, 50% were less than 1 year of age, and 50% had severe OSA (Supplementary Table 2). Participants were classified according to the Australian Standard Classification of Cultural and Ethnic Groups (ASCCEG) classification system as Caucasian ($n = 10$), Asian ($n = 5$), or Middle Eastern/African ($n = 3$) due to potential for ethnic disparities (21). Review of the medical records identified 7 children as having a craniofacial anomaly including Trisomy 21, secondary to a car vehicle accident, Pierre Robin sequence (note this is associated with mandibular, not maxillary hypoplasia), Pompe's disease and Chromosomal deletion (Table 1).

The NPPV use was 67% CPAP, 17% BiLevel and 17% not used (Supplementary Table 2) with the average duration of use being 1.8 years, (range 0.4-4.0 years, Table 1). Compliance data identified 13 (72%) as compliant (Supplementary Table 2), thus constituting our NPPV study cohort.

NPPV compared to NC controls demographics and Sleep parameters

There was no difference in anthropometric measures between the NPPV and NC groups at baseline (Table 2), but for PSG data, the NPPV cohort had higher AHI ($p = 0.07$), lower oxygen saturation ($p = 0.08$), and both baseline and maximum CO_2 levels were higher ($p = 0.02$, and $p = 0.04$, respectively) (Table 2).

Facial Convexity Angle

Facial convexity angle ranged from $159\text{--}178^\circ$ at baseline and $157\text{--}178^\circ$ at follow-up (Fig. 2A). All children showed a change in facial convexity angle (Fig. 2A), with changes ranging from -11.1° to $+13.4^\circ$, equating to a magnitude percent change from 0.1 to 8.3% (Table 1). In total, regardless of NPPV use, duration, and/or craniofacial status, 10 (56%) children had an increase in the angle of facial convexity (retrusion, suggesting the development of midfacial hypoplasia) and 8 (44%) a decrease (protrusion, indicative of midfacial hyperplasia or mandibular retrusion) (Table 3, Fig. 2A). Correlation analyses indicated no relationship between the percent change in angle convexity with the time between imaging or age at follow-up (Supplementary Fig. 1 A&B).

Applying the analysis according to the presence or absence of syndromes or craniofacial abnormalities, a retrusion in obtuse angle of facial convexity was evident in 9 (82%) children without a syndrome or craniofacial abnormality but a protrusion for 6 (86%) for those with a syndrome or craniofacial abnormality ($p = 0.01$) (Table 3).

Effects of NPPV on Facial Convexity Angle

The median facial convexity angle within the NPPV group did not differ to that of NC controls either at baseline ($p = 0.58$, Table 4) or follow-up ($p = 0.17$, Table 4). The median difference in facial convexity angle in the NPPV group was $+3.1$ while in the NC control group, it was -1.0 , thus being in the opposite direction (Table 4), yet this did not reach statistical significance ($p = 0.20$).

Within the NPPV group, 9 (69%) had a retrusion in convexity angle compared to 1 (20%) of the NC control group, regardless of whether they had syndromes or craniofacial abnormalities ($p = 0.12$, Table 3). Focusing on the non-syndromes/non-craniofacial abnormalities cohort, this equated to 8/9 (89%) NPPV (Fig. 2B) vs 1/2 (50%) NC control ($p = 0.35$). Interestingly, the one NPPV non-syndromic/non-craniofacial child for who a protrusion in angle was evident (case #3, Fig. 2B), it was the largest protrusion amongst our study cohort, with the degree of change equating to 6.6% (Table 1).

In terms of percentage change in facial convexity, children using NPPV experienced the greatest magnitude of changes with a median of $+1.9\%$ vs -0.7% in NC controls (Fig. 2C). The retrusion was specifically amongst the non-craniofacial cohort with a median of $+3.5\%$ change while for those in the craniofacial group, this was a protrusion with median -0.8% (Fig. 2c). Correlation analyses focusing on the 9 NPPV non-craniofacial cohort indicated no relationship between the percent change in angle convexity with the length of time between imaging or the age at follow-up (Supplementary Fig. 1 C&D).

Comparing 3D imaging data parameters at baseline and follow-up within NPPV group, applying the Wilcoxon signed-rank test showed that despite 69% of NPPV users (and amongst those, 89% of the those without syndromes or craniofacial abnormalities) exhibited a retrusion in facial convexity, the median difference of the angle change was not significant for NPPV ($p = 0.09$), nor the non-craniofacial NPPV subset ($p = 0.07$) (Table 4), most likely due to the restricted sample size ($n = 13$ and 9 respectively). Additional facial convexity measurements within the NPPV cohort showed some statistically significant changes, in particular nason to menton, subnasale to menton, and nose base

width ($p \leq 0.02$, Supplementary Table 3), but these are most likely influenced by age-related facial growth and anatomical changes on these distance-based variables.

When stratifying data according to threshold limits of percent change of angle (Table 5), 62% of NPPV children had a > 1% change compared to 20% for the NC control group (Table 5). A change of > 3.5% was exclusive to NPPV users, equating to 46%, with rates higher in NPPV users without craniofacial abnormalities (56% vs 25%, Table 5). A > 5% change was exclusive to NPPV users without craniofacial abnormalities and was evident in 23% of children. Further breakdown according to OSA severity showed of the patients with severe OSA at baseline, 57% exceeded > 3.5% change compared with only 33% of children with mild or moderate severity (Table 5). For additional breakdown based on the magnitude of changes, please refer to Supplement Table 4.

Discussion

The present study provides additional evidence to support the suspected development of midfacial changes with prolonged NPPV use in children. Additional analyses indicated that the effect was more pronounced in children without syndromes or craniofacial abnormalities, and in those with more severe OSA at baseline.

Previous studies have utilized cephalometric radiographs or CT scans and hard tissue measurements to evaluate midfacial changes in OSA patients (9, 11). The alternative approach presented in this paper uses 3D imaging. This has only recently emerged as a method to assess OSA severity in cross-sectional analysis, replacing the standard lateral photograph (3, 4, 22, 23). However, few studies have utilised 3D imaging to track facial growth over time (19), and there is still a lack of normative soft tissue measurement standards based on age and gender. Additionally, it remains unclear which measurement landmarks are most suitable for monitoring midfacial hypoplasia. 3D imaging has the specific benefits of allowing measurement of midline structures without the need for an ideal lateral image nor does it use ionizing radiation, offering the potential to overcome the limitations of common imaging modalities (particularly in children). That said, a caveat is that although it is 3D imaging, the majority of the measures are 2D, based on previous imaging modalities. Volumetric measures would be required to fulfil the 3D criteria to its fullest extent and this is currently limited in the literature due to a lack of normative volumetric datasets and the absence of validated anatomical definitions (24).

An association between midfacial hypoplasia and the development of OSA has been reported (1, 25). Children with syndromes and craniofacial abnormalities, such as Trisomy 21, which affect midfacial development, have increased risk for OSA (26). Improvement in OSA severity with midfacial advancement surgery has been reported, such that patients have a lower AHI post-operatively (25, 27). Our study identified that retrusive midfacial changes occurred in children without preexisting syndromes or craniofacial abnormalities compliant with NPPV therapies where there was a greater number of children who experienced a retrusion in obtuse angle of facial convexity amongst those compliant to NPPV therapy compared to the non-compliant patients who were more likely to experience protrusion, consistent with the findings of Roberts et al.,(9). Although this outcome was not correlated with duration of NPPV use, the development of midfacial hypoplasia from NPPV use is likely attributed to the prolonged exertion of force on the (growing) facial bones, which may be further related to the tightness of head and face straps attached to the facial mask used by our children, hypothesised to lead to altered growth and structural changes over time (7, 8). Moreover, the magnitude of change, being > 3.5% from baseline exclusively in over 50% of NPPV users, provides a tangible threshold for future comparative studies and analysis.

The severity of OSA influences the treatment pressures used, because treatment pressures increase with disease severity, likely contributing more to facial remodelling (7, 8). In our patient group, greater retrusion of midfacial structures occurred in the patients with severe OSA although the restricted sample size did not allow statistical

correlation. This suggests that OSA higher treatment pressures may increase the degree of retrusion, although an alternative hypothesis is that the underlying pathophysiology of severe OSA itself may be linked to the pattern of facial growth which requires further study to test.

Limitations of Study

The major limitation of the current study is the small number of children studied resulting in subgroup analyses that are underpowered and as such, the data would be considered preliminary at this stage. As with all cephalometry studies, the accuracy of these measurements is dependent on the correct alignment of the jaw which is limited in practice in the paediatric population, especially infants aged 0–12 months (who made up 50% of our cohort) a developmental stage where head control is limited. Despite this, 3D photos remove the requirement for the specific midline imaging required in x-rays, and our ICC values showed excellent reproducibility amongst the images taken with tight standard deviations per child. The profile of the current study lacked an age-matched untreated control group, given these would not clinically be recommended for 3D imaging, and was skewed towards severe OSA as this group of patients are by definition, more likely to be placed on long-term NPPV therapy. Future prospective study would be required to account for these.

Conclusion

Using 3D stereophotogrammetry, this preliminary study showed that up to 69% of children who were compliant with NPPV therapy had some degree of midfacial retrusion during ongoing NPPV use. This proportion was higher amongst those without underlying syndromes or craniofacial abnormalities, being 82%. Over half of these children showed a magnitude of change in facial convexity angle ranging from > 3.5-5%. The study confirms the potential of 3D photography to monitor changes in facial growth in the pediatric population, however, future studies to assess additional and/or confounding variables will require expanded sample size and inclusion of untreated controls.

Abbreviations

AASM
American Academy of Sleep Medicine
AHI
apnoea-hypopnoea index
BiLevel
Bilevel positive pressure therapy
CHW
Children's Hospital at Westmead
CPAP
continuous positive airway pressure
CT
Computerised Tomography
ECG
electrocardiogram
EEG
electroencephalogram
EMG
electromyographic

EOG
electrooculographic
MRI
magnetic resonance imaging
NPPV
non-invasive positive pressure
NREM
non-rapid eye movement
OAHl
obstructive apnoea hypopnoea index
OSA
Obstructive sleep apnoea
PSG
polysomnography
REM
rapid eye movement

Declarations

Statements and Declarations

All authors have seen and approved the manuscript. All authors report no conflicts of interest. The research was conducted at The Children's Hospital at Westmead, NSW, Australia.

Human Ethics and Consent to Participate

Ethics approval for the study was obtained from NSW Sydney Children's Hospital Network Health Ethics committee (2019/ETH00036), based on the National Health and Medical Research Council

(NHMRC) National Statement on Ethical Conduct in Human Research in accordance with the Declaration of Helsinki. Informed consent to participate in the research was obtained by the parent(s).

Author contributions

Gemma Tyler: Methodology, Data Curation and analysis, Writing—original draft.

Rita Machaalani: Conceptualization, Data analysis, Writing – review and editing.

Karen Waters: Methodology, Data analysis, Writing – review and editing.

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Clinical trial number

Not applicable.

Data availability

The data presented in the study is available from the corresponding author upon reasonable request.

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Tables

Table 1: Demographic and facial convexity data per participant ordered according to sex and age separated by absence or presence of craniofacial abnormality.

ID	Sex	Ethnicity	Age at initial 3D imaging evaluation (years)	Time between 3D imaging (years)	OSA Severity	Type of NPPV & pressure	Compliance assessment	Change in facial convexity angle, ° (%)
No Craniofacial abnormality								
1	Male	Caucasian	0.1	2.2	Mild	CPAP 5	Compliant	3.1 (1.9)
2	Male	Middle eastern	0.1	0.8	Severe	Not used	Not Compliant	-1.0 (0.7)
3	Male	Caucasian	0.1	0.6	Severe	CPAP 6	Compliant	-11.1 (6.6)
4	Male	Caucasian	0.4	4.0	Moderate	CPAP 10	Compliant	9.3 (5.5)
5	Male	Caucasian	0.6	0.6	Moderate	CPAP 6	Compliant	0.4 (0.2)
6	Male	Caucasian	3.7	3.5	Moderate	BIPAP 10/5	Compliant	2.3 (1.4)
7	Female	Asian	0.2	0.4	Severe	CPAP 6	Compliant	6.8 (4.1)
8	Female	Caucasian	0.5	2.1	Mild	CPAP 6	Compliant	13.4 (8.3)
9	Female	Asian	5.4	2.6	Moderate	CPAP 8	Not Compliant	5.2 (3.2)
10	Female	Middle eastern	9.0	1.3	Severe	CPAP 6	Compliant	11.2 (6.9)
11	Female	Caucasian	11.5	1.6	Severe	BIPAP 16/6	Compliant	5.9 (3.5)
Craniofacial abnormality present								
12	Male Trisomy 21	Asian	0.1	1.1	Severe	CPAP 6.5	Compliant	7.4 (4.4)
13	Male Trisomy 21	Caucasian	1.2	0.6	Severe	CPAP 5	Compliant	-1.9 (1.1)
14	Male Motor vehicle accident	Middle eastern	6.6	1.8	Severe	CPAP 8	Compliant	-0.9 (0.5)
15	Male Apert's syndrome	Caucasian	9.9	1.6	Mild	Not used	Not Compliant	-2.9 (1.7)
16	Female Pierre robin	Asian	1.0	1.0	Severe	Not used	Not Compliant	-0.2 (0.1)
17	Female Pompe's	Asian	4.0	2.2	Moderate	BIPAP 25/12	Compliant	-2.5 (1.4)

18	Female Chromosomal short arm 5 deletion	Caucasian	7.7	3.7	Mild	Not used	Not Compliant	-2.9 (1.6)
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Table 2: Demographics and sleep study comparison between NPPV and NC control group at baseline and follow-up sleep studies.

	NC control (n=5)		NPPV (n=13)		
	Mean $\pm$ SD	Median	Mean $\pm$ SD	Median	P-value
Baseline					
Age (years)	3.5 $\pm$ 2.8	5.0	2.7 $\pm$ 3.8	0.9	0.44
Weight (kg)	17.9 $\pm$ 13.0	19.1	14.4 $\pm$ 12.2	9.9	0.78
Height (cm)	101.8 $\pm$ 42.3	117.0	78.3 $\pm$ 29.4	66.0	0.37
AHI	10.7 $\pm$ 7.5	13.3	31.1 $\pm$ 7.7	22.5	0.07
OAHl	7.3 $\pm$ 5.6	8.3	16.0 $\pm$ 21.1	11.3	0.44
Baseline SpO ₂ (%)	97.3 $\pm$ 1.7	98.0	95.5 $\pm$ 2.1	96.0	0.08
Min SpO ₂ (%)	83.6 $\pm$ 13.9	91.0	83.1 $\pm$ 7.6	87.0	0.35
Baseline TcCO ₂ (%)	42.2 $\pm$ 4.6	40.0	49.3 $\pm$ 5.4	49.0	0.02
Max TcCO ₂ (%)	48.0 $\pm$ 6.6	44.0	57.0 $\pm$ 8.1	57.9	0.04

AHI = apnoea hypopnea index, OAHl = obstructive apnoea hypopnea index, SpO₂ = oxyhaemoglobin saturation, TcCO₂= transcutaneous carbon dioxide, SD= standard deviation.

Table 3: Frequency for facial convexity changes and OSA severity based upon NPPV use and craniofacial status

	Total	NC control	NPPV	P-value	No Craniofacial abnormality	Craniofacial abnormality	P-value
<i>n values</i>	18	13	5		11	7	
<i>Facial Convexity Change, n (%)</i>							
<i>Retrusion</i>	10 (56)	1 (20)	9 (69)	0.12	9 (82)	1 (14)	0.01
<i>Protrusion</i>	8 (44)	4 (80)	4 (31)		2 (18)	6 (86)	
<i>OSA Severity, n (%)</i>							
<i>Mild</i>	4 (22)	2 (40)	2 (15)	0.64	2 (18)	2 (29)	0.68
<i>Moderate</i>	5 (28)	1 (20)	4 (31)		4 (36)	1 (14)	
<i>Severe</i>	9 (50)	2 (40)	7 (54)		5 (45)	4 (57)	

Table 4: Imaging data parameters at baseline and follow-up for NPPV and NC control cohorts.

	Baseline		Follow-up		Difference		95% Confidence Interval		
	Mean $\pm$ SD	Median	Mean $\pm$ SD	Median	Mean	Median	Lower bound	Upper bound	P value
NPPV Cohort									
Age (years)									
All cohort (n=13)	2.9 $\pm$ 3.9	0.6	4.6 $\pm$ 4.1	2.6	1.7 $\pm$ 1.1	1.6	0.9	2.3	<0.001
Non-craniofacial subset (n=9)	2.9 $\pm$ 4.4	0.5	4.7 $\pm$ 4.5	2.6	1.8 $\pm$ 1.3	1.6	0.6	2.8	0.004
Craniofacial subset (n=4)	3.0 $\pm$ 2.9	2.6	4.4 $\pm$ 3.5	4.0	1.4 $\pm$ 0.7	1.4	0.6*	2.2*	0.13
Facial Convexity Angle (°)									
All cohort (n=13)	168.3 $\pm$ 5.4	168.2	171.6 $\pm$ 6.0	172.1	3.3 $\pm$ 6.7	3.1	-0.9	7.4	0.09
Non-craniofacial subset (n=9)	166.1 $\pm$ 4.7	166.2	170.7 $\pm$ 6.8	172.1	4.6 $\pm$ 7.2	5.9	-2.1	10.1	0.07
Craniofacial subset (n=4)	173.1 $\pm$ 3.4	173.2	173.7 $\pm$ 3.2	173.9	0.5 $\pm$ 4.6	-1.4	-2.5*	7.4*	0.87
NC control Cohort									
Age (years)									
All cohort (n=5)	4.8 $\pm$ 4.2	5.4	6.7 $\pm$ 5.1	8.0	1.9 $\pm$ 1.2	1.6	0.8	3.7	0.06
P value ^{&}		0.64		0.58		0.64			
Facial Convexity Angle (°)									
All cohort (n=5)	167.0 $\pm$ 9.2	163.1	166.6 $\pm$ 7.8	168.3	-0.4 $\pm$ 3.3	-1.0	-2.9	5.2	0.63
P value ^{&}		0.58		0.17		0.20			

[&]Compared to NPPV All cohort (n=13) data using Wilcoxon rank sum test, *88% Confidence Interval

Table 5: Number of patients above various threshold values for percentage changes in facial convexity angle to detect midfacial hypoplasia from NPPV use, categorised by craniofacial status and OSA severity at baseline.

	Patient exceeding threshold (%)		
Threshold*	>1%	>3.5%	>5%
Craniofacial Status			
<i>Entire Cohort (n=18)</i>			
<i>NPPV (n=13)</i>	62	46	23
<i>NC control (n=5)</i>	20	0	0
<i>No Craniofacial Abnormality (n=11)</i>			
<i>NPPV (n=9)</i>	78	56	33
<i>NC control (n=2)</i>	50	0	0
<i>Craniofacial Abnormality (n=7)</i>			
<i>NPPV (n=4)</i>	25	25	0
<i>NC control (n=3)</i>	0	0	0
OSA Severity			
<i>Entire Cohort (n=18)</i>			
<i>Mild (n=4)</i>	50	25	25
<i>Moderate (n=5)</i>	60	20	20
<i>Severe (n=9)</i>	44	44	11
<i>NPPV (n=13)</i>			
<i>Mild (n=2)</i>	100	50	50
<i>Moderate (n=4)</i>	50	25	25
<i>Severe (n=7)</i>	57	57	14
<i>NC Control (n=5)</i>			
<i>Mild (n=2)</i>	0	0	0
<i>Moderate (n=1)</i>	100	0	0
<i>Severe (n=2)</i>	0	0	0

*only positive % changes are represented here as this represents hypoplasia. For the total magnitude of change (including negative values), please refer to Supplementary Table 3.

Figures

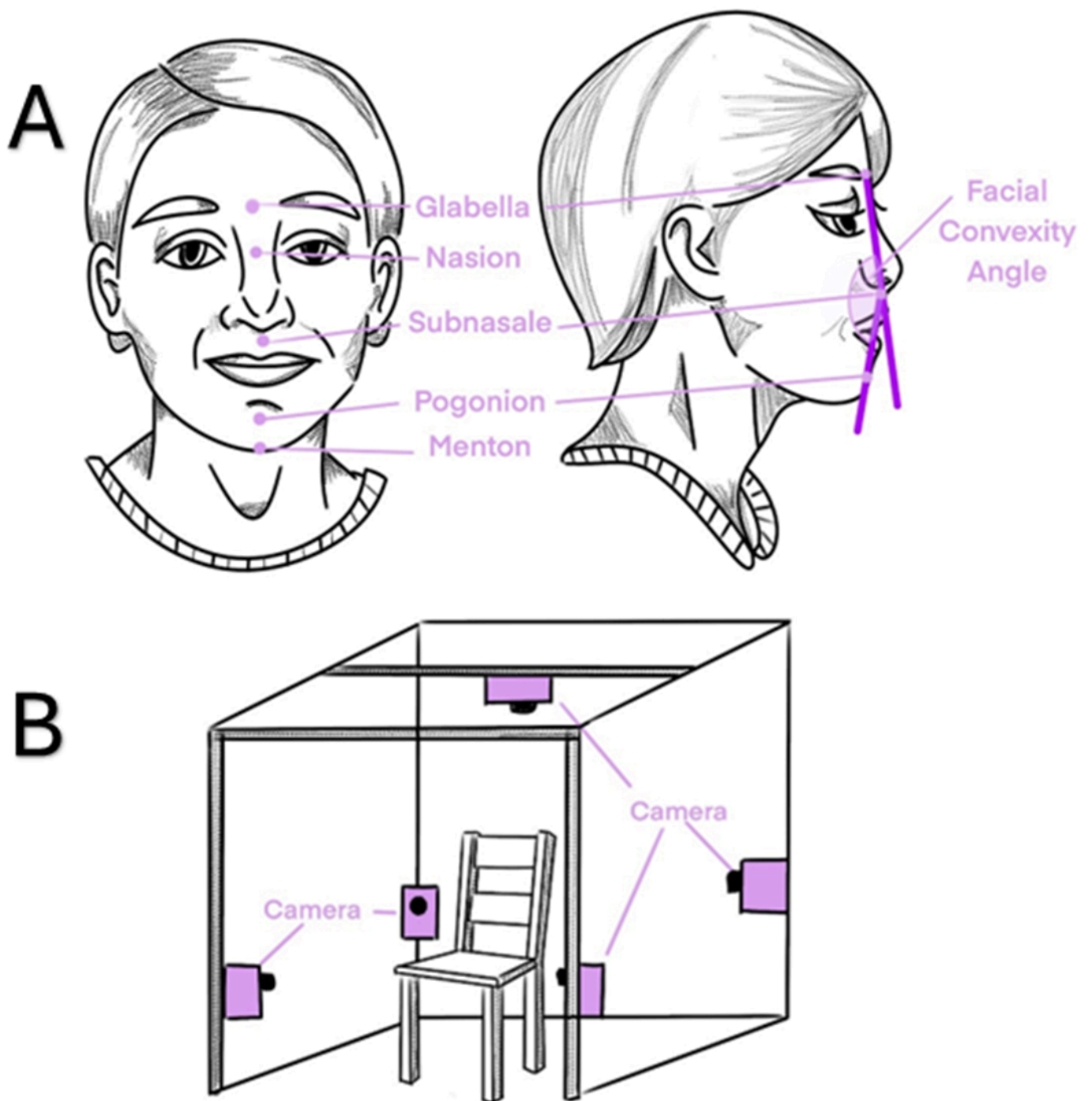


Figure 1

Stereophotogrammetry. (A) soft tissue landmarks including facial convexity angle, and (B) the stereophotogrammetry setup.

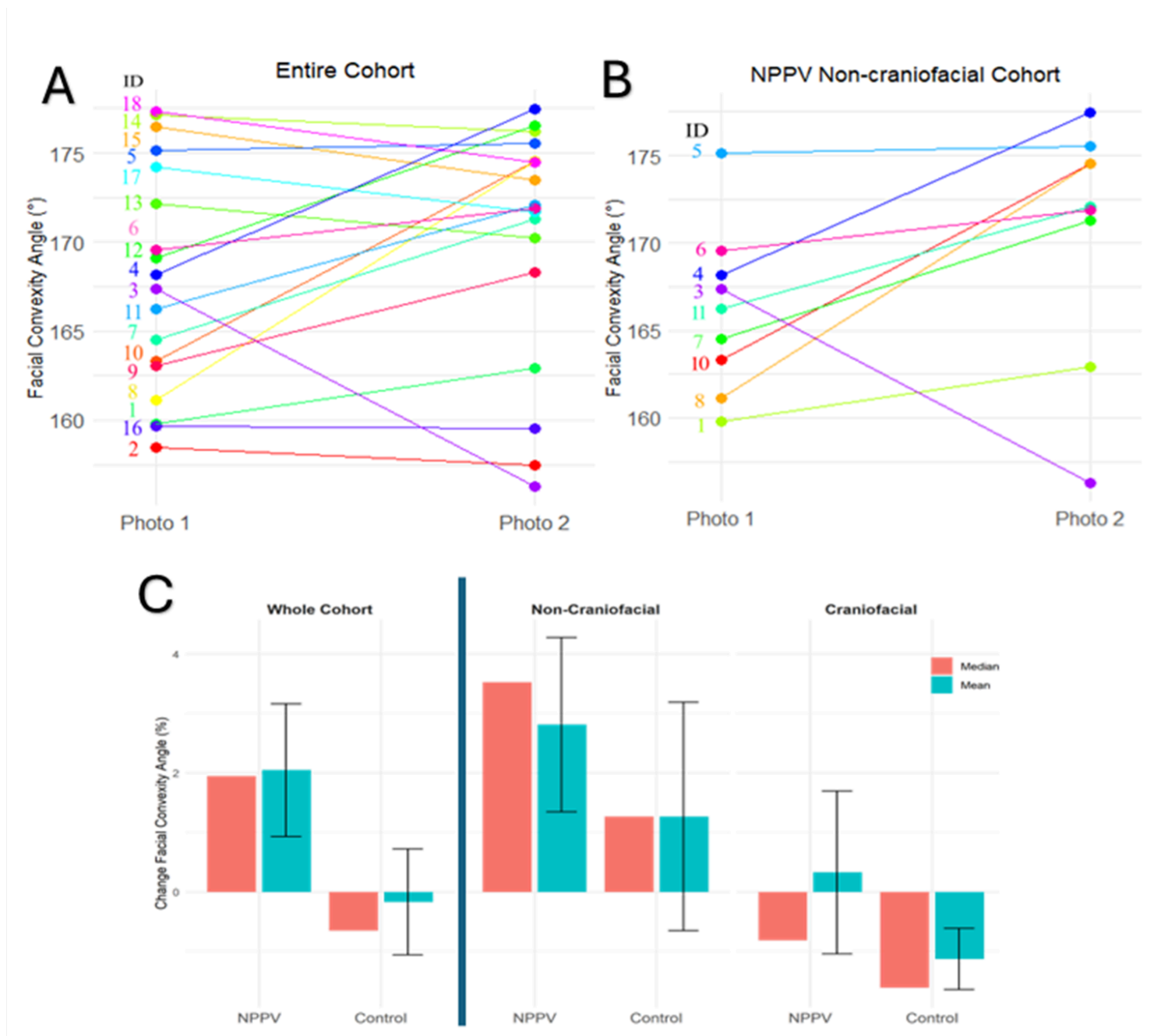


Figure 2

Changes in soft tissue angle of facial convexity. Individual representation of (A) Entire cohort, (B) NPPV non-craniofacial cohort, and [C] plot to show comparison in the mean and median percentage change of facial convexity angle of the NPPV vs NC control cohorts.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [3DNIVSupplementaryFile2026Submitted.docx](#)