Original Article

Craniofacial Morphology in Prematurely Born Children

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ABSTRACT

Objective: To test the null hypothesis that there is no difference between the craniofacial morphology of prematurely born children and that of matched full-term born controls.

Materials and Methods: White children 8 to 10 years of age, born at the University Hospitals of Lund and Malmö and living in the same part of Sweden, were included. One group consisted of 36 very preterm children, born during gestational weeks 29 to 32; the other group included 36 extremely preterm children, who were born before the 29th gestational week. Subjects were compared with a control group of 31 full-term children, who were matched for gender, age, nationality, and living area. One lateral head radiograph was taken for each child, and the cephalometric analysis included 15 angular and 11 linear variables. Also, the height, weight, and head circumference of each child were registered.

Results: A significantly shorter anterior cranial base and a less convex skeletal profile were found among extremely preterm children, and significantly shorter maxillary length was noted in both extremely preterm and very preterm groups as compared with full-term children. The lower incisors were significantly more retroclined and retruded in the extremely preterm group compared with the very preterm group and the full-term control group. Extremely preterm children were significantly shorter, and both extremely preterm and very preterm children had significantly lower weight and smaller head circumference compared with full-term children.

Conclusion: The null hypothesis was rejected because several craniofacial parameters differed significantly between preterm and full-term born control children. (*Angle Orthod.* 2009;79: 276–283.)

KEY WORDS: Premature birth; Craniofacial morphology; Cephalometric analysis

INTRODUCTION

The great improvement that has occurred in neonatal health and intensive care during the past two decades has led to increasing survival of very preterm (VPT) infants born during gestational weeks 29 to 32 and of extremely preterm (EPT) infants born before the 29th gestational week.[1–4] Once survival is assured, concern becomes focused on growth and development of these infants.

Many studies have indicated that VPT and EPT children experience significant growth failure in their early childhood,[5,6] and that compensatory catch-up growth occurs up to the time of adolescence.[1,6,7] However, most of the children in these studies remained significantly shorter, had lower weight, and had a smaller head circumference compared with full-term controls.[1,6,7] Also, higher frequencies of oral defects seen as palatal grooving, high-arched palate, prenormal occlusion, and palatal asymmetry have been reported in preterm children compared with full-term controls.[8,9] A recent investigation concluded that the prevalence of malocclusion traits and the professionally assessed need for orthodontic treatment were greater in a group of preterm children than in a control group of full-term children.[10]

It is recognized that the mechanisms that regulate craniofacial growth and development include complex interactions between genes, hormones, nutrients, and epigenetic factors that produce the final craniofacial morphology, and any disturbances in this mechanism may result in a deviating growth pattern.[11,12] However, according to the literature, it is unknown whether prematurely born children are at risk of altered craniofa-

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Accepted: April 2008. Submitted: March 2008.

 DOI: 10.2319/030108-124.1

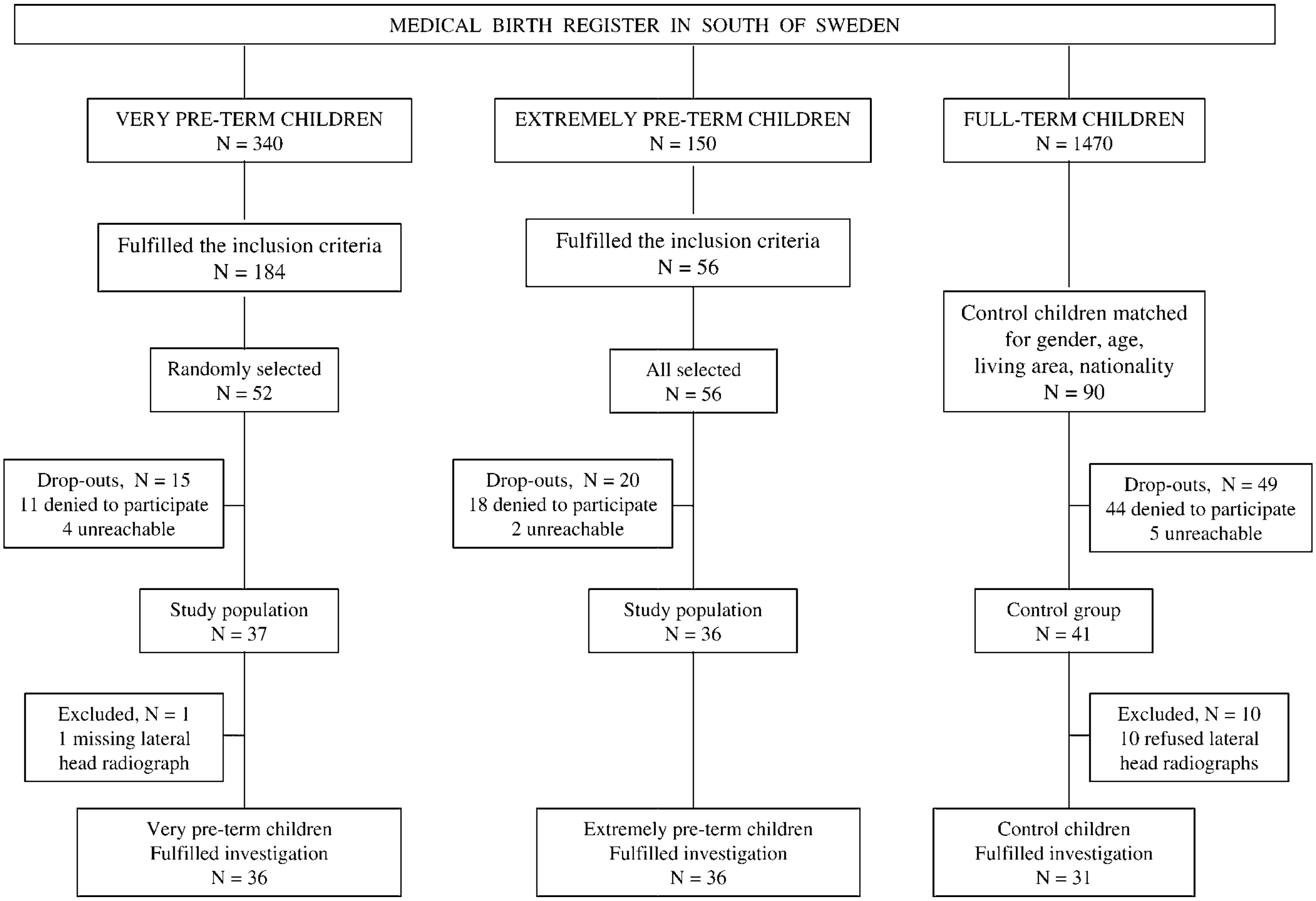

Figure 1. Flow chart showing the recruitment of preterm and full-term participants.

cial morphology.[8] Therefore, the aim of this study was to evaluate the craniofacial morphology in extremely and very preterm born 8- to 10-year-old children and to compare these findings with those in matched full-term born controls. The null hypothesis was that craniofacial morphology would not differ between preterm and full-term children.

MATERIALS AND METHODS

Subjects

Recruitment of preterm and full-term control children is described in Figure 1. This study was approved by the Ethics Committee of the University of Lund, Sweden, and after permission had been obtained from the National Epidemiologic Center of the Swedish National Board of Health and Welfare, access to the Medical Birth Register was obtained. An epidemiologist at the Department of Epidemiology, University of Lund, performed the selection from the register and created a data file over all children born during gestational weeks 23 to 32 from 1992 through 1996 in the County of Skane, Sweden. These files contained information about gestational age, birth weight, gender, ethnic background, birth at hospital, and living area for 340 VPT children and 150 EPT children.

Included for participation in the study were white children 8 to 10 years of age who were born at the University Hospitals of Lund and Malmö and now were living in the southwest part of the County of Skane. Children with syndromes or with neuromuscular disorders (eg, cerebral palsy) were excluded (two VPT and seven EPT children). Written information about the study was sent to the parents, and after 1 to 2 weeks, parents were called by telephone and were given information and an opportunity to ask questions about the study. Those who had not responded within 3 weeks were sent a mail reminder. After this, no further attempt was made to contact the families. Informed consent was obtained for each participant and was confirmed in writing by at least one parent. Among the group of EPT children, 56 fulfilled the inclusion criteria and were invited to participate. Among the 184 VPT children who fulfilled the inclusion criteria, 52 children were randomly selected and were asked to participate in the study. The study population consisted

Table 1. Hard and Soft Tissue Reference Points

Hard Tissue Reference Points		
ai	apex inferius	The apex of the root of the most prominent lower incisor
ar	articulare	Intersection between the contour of the external cranial base and the dorsal contour of the condylar head
as	apex superius	The apex of the root of the most prominent upper incisor
ba	basion	The most posteroinferior point on the margin of the foramen magnum
gn	gnathion	The lowest point of the mandibular symphysis
go	gonion	The most posteroinferior point on the angle of the mandible
ii	incision inferius	The midpoint of the incisal edge of the most prominent lower central incisor
is	incision superius	The midpoint of the incisal edge of the most prominent upper central incisor
n	nasion	The most anterior point of the frontonasal suture
pg	pogonion	The most anterior point of the mandibular symphysis
pm	pterygomaxillare	The intersection between the nasal floor and the posterior contour of the maxilla
s	sella	The center of the sella turcica
sm	supramentale	The most posterior point on the anterior contour of the lower alveolar process
sp	spinal point	The apex of the anterior nasal spine
ss	subspinale	The most posterior point on the anterior contour of the upper alveolar process
tgo	gonion, tangent point	The intersection between the mandibular and the ramus line
Soft Tissue Reference Points		
N	Soft tissue nasale	Soft tissue point corresponding to the hard tissue point nasion
PG	Soft tissue pogonion	The most prominent point of the chin
PN	Pronasale	The most prominent point of the nose
PLi	Prolabium inferior	The most prominent point of the lower lip
PLs	Prolabium superior	The most prominent point of the upper lip
SN	Subnasale	The deepest point in the nasolabial sulcus

finally of 36 EPT children and 36 VPT children. Nonparticipants are described in the flow chart (Figure 1).

The control group also was recruited from the Medical Birth Register. A full-term normal birth weight child who was born at the same hospital, was of the same gender and nationality, had come from the same living area, and was nearest in birth month (±1 month) to the preterm child was selected. To be included, the control children had to have no history of oral or nasal intubation, and children with syndromes or with neuromuscular disorders were excluded (one child). Three control participants were identified for every preterm child. If the family did not respond or refused to participate, a second family and, if necessary, a third family were contacted. It was decided that at least one control should be included for every two preterm children. Ninety control children were consecutively asked to participate, but five were unreachable and 44 declined to participate. Furthermore, 10 control children refused the lateral head radiograph examination; thus, the control group finally consisted of 31 children (Figure 1).

Methods

One lateral head radiograph was taken for each child. Radiographs were taken with the subjects seated, the head fixed in the cephalostat with ear-rods and support on the forehead, the teeth in central occlusion, and the lips closed in a relaxed position. All lateral head radiographs were taken from 2002 to 2005 at the Department of Radiology, Faculty of Odontology, Malmö University, Malmö, Sweden. The x-ray unit used was a Cranex 3+ Ceph (Soredex Co, Helsinki, Finland) with a Kodak Lanex 320 intensifying screen (Eastman Kodak Co, Rochester, New York). All measurements were corrected for the enlargement (10%) and were converted to life size. Landmarks, reference lines, and measurements used were based mainly on those defined and described by Björk[13] and Thilander et al.[14] The most important reference points, reference lines, and variables used are described and shown in Tables 1 through 3 and Figure 2.

All measurements on radiographs were documented to the nearest 0.5 degree for angles and 0.5 mm for distances. Images of bilateral structures were bisected. The cephalograms were scored and coded by an independent person, and the examiner who conducted the measurement analysis of the cephalograms was unaware of the group to which the child belonged.

Height, weight, and head circumference of each child were registered. Height was measured to the nearest 0.5 cm with a stadiometer attached to the wall. Weight was measured on a digital scale with an accuracy of 0.1 kg, whereas head circumference was measured in the maximum fronto-occipital plane with a nonextensible plastic-coated tape measure. Sucking habits and swallowing pattern were registered. Overbite and overjet were registered on study casts. Measurements were taken with a stainless steel ruler to the nearest 0.5 mm.

Table 2. Hard and Soft Tissue Reference Lines

Hard Tissue Reference Lines	
Nasion-sella line (NSL)	A line from sella to nasion
Sella-basion line (s-ba)	A line from sella to basion
Nasion-subspinale line (n-ss)	A line from nasion to subspinale
Nasion-supramentale line (n-sm)	A line from nasion to supramentale
Nasion-pogonion line (n-pg)	A line from nasion to pogonion
Subspinale to pogonion (ss-pg)	A line from subspinale to pogonion
Nasal line (NL)	A line through the spinale and pterygomaxillare
Mandibular line (ML)	A line passing from the gonion through the gnathion on the mandible
Ramus line (ar-tgo)	A tanget to the posterior border of the mandibular ramus and through the articulare
Axis of upper incisor (ILs)	A line from is to the apex
Axis of lower incisor (ILi)	A line from ii to the apex
Soft Tissue Reference Lines	
E-line (EL)	A line from soft tissue pogonion to pronasale
Nasion-subnasale (N-SN)	A line from soft tissue nasion to subnasale
Subnasale-pogonion (SN-PG)	A line from subnasale to soft tissue pogonion

Method Error Analysis

Twenty randomly selected cephalograms were traced on two separate occasions. No significant mean differences between the two series of records were found with the use of paired *t*-tests. Method errors according to the Dahlberg formula[15] ranged from 0.4 to 1.0 degree and from 0.3 to 0.9 mm, except for the variable soft tissue profile (N-SN-PG), for which the error was 1.2 degrees.

Statistical Analysis

All data were analyzed with the Statistical Package for the Social Sciences (SPSS, SPSS Inc, Chicago, Ill) version 13.0 software program. A sample size calculation was performed, and it was considered sufficient to enroll at least 22 children in each group, which would yield a power of 90% to discover an estimated evident mean difference of 3 degrees (±3 degrees) in terms of angular variables and 3 mm (±3 mm) in terms of linear variables measured on lateral head radiographs.

The arithmetic mean and standard deviation (SD) were calculated for each cephalometric variable, and one-way analysis of variance (ANOVA) with Tukey's post-hoc test was used to test differences between groups. Analysis of covariance was used when corrections were made for the following background variables: gender, age, sucking habits, swallowing pattern, height, weight, and head circumference. Differences with probabilities of less than 5% ($P < .05$) were considered to be statistically significant.

RESULTS

The mean gestational age for EPT and VPT children was 26.8 and 30.8 weeks, whereas the value for birth weight was 939.5 and 1634.7 g, respectively. The corresponding average values for full-term control children were 39.9 weeks and 3592.3 g (Table 4). At the time of examination, the chronological mean age of EPT and VPT children was 9.2 and 9.4 years, and 9.5 years for full-term controls, with no significant difference noted among the three groups (Table 4). EPT children were significantly shorter, and both EPT and VPT children had significantly lower weight and smaller head circumference compared with full-term control children (Table 4). When corrections were made for gender, it was found that in all three groups, the girls had significantly smaller head circumferences compared with the boys.

Participants with an ongoing sucking habit or swallowing with tongue thrust were few, and no significant difference was noted between groups. None of the children in the three groups reported any history of orthodontic treatment. According to the analysis of nonparticipants, these did not differ from the final groups in terms of age, gender, ethnic origin, or living area.

Cephalometric Data

Skeletal variables. Results from the cephalometric analysis are presented in Table 5. The length of the anterior cranial base (n-s) was significantly shorter in the EPT group than in the full-term group, and the skeletal profile (n-ss-pg) was significantly less convex in the EPT group than in the full-term group (Table 5). Maxillary length (sp-pm) was significantly shorter in both the EPT and VPT groups than in the full-term group (Table 5).

When corrections were made for gender, it was found that in all three groups, the length of the anterior cranial base (n-s) was significantly shorter for girls than for boys. The cranial base angle (n-s-ba) was significantly larger for girls in all three groups. No other

Table 3. Hard and Soft Tissue Variables

Skeletal, degrees	
Sagittal	
n-s-ba	Cranial base angle
s-n-ss	Maxillary position in relation to anterior cranial base
s-n-sm	Mandibular position in relation to anterior cranial base
ss-n-sm	Jaw relationship
s-n-pg	Mandibular chin in relation to anterior cranial base
n-ss-pg	Facial profile/profile convexity
Vertical	
NL/NSL	Maxillary plane angle relative to anterior cranial base
ML/NSL	Mandibular plane angle relative to anterior cranial base
NL/ML	Jaw relationship
ar-go-gn	Mandibular jaw angle
Skeletal, mm	
Sagittal	
n-s	Anterior cranial base length
s-ba	Posterior cranial base length
sp-pm	Maxillary length
ar-pg	Mandibular length
Vertical	
n-gn	Total anterior facial height
n-sp′	Upper anterior facial height
sp′-gn	Lower anterior facial height
n-sp′/sp′-gn (%)	Ratio upper/lower facial height
Dental, degrees	
ILi/ILs	Interincisal angle
ILs/NSL	Upper incisor proclination relative to anterior cranial base
ILs/NL	Upper incisor proclination relative to maxillary base
ILi/ML	Lower incisor proclination relative to mandibular base
Dental, mm	
is to ss-pg	Protrusion of the upper incisor
ii to ss-pg	Protrusion of the lower incisor
Soft tissue, degree	
N-SN-PG	Facial profile/profile convexity
Soft tissue, mm	
PLs to EL	Protrusion of the upper lip
PLi to EL	Protrusion of the lower lip

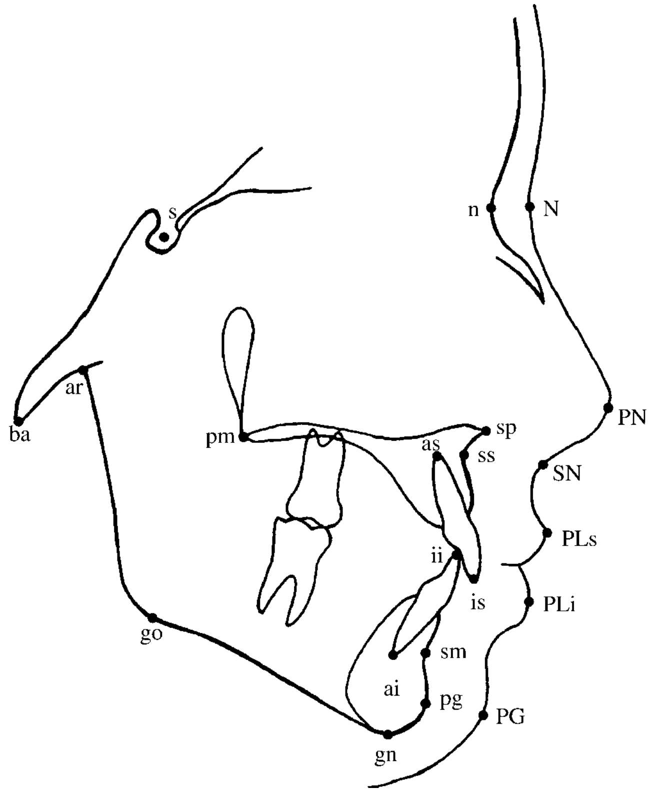

Figure 2. Hard and soft tissue cephalometric reference points; for definitions, see Table 1.

significant differences were noted between genders or among the three groups.

Dental variables. The lower incisors were significantly more retroclined (ILi/ML) and more retruded (ii to ss-pg) in the EPT group than in both the full-term and VPT groups. The mean interincisal angle (ILs/ILi) also was significantly larger in the EPT group than in the other two groups (Table 5). No other significant differences were reported among the three groups or between genders.

Soft tissue variables. The upper lip of VPT children was more protruded (PLs to EL) than that of the control group (Table 5). No other significant differences were found among the three groups or between genders.

DISCUSSION

The most pronounced differences were that extremely preterm children (EPT group) had a significantly shorter anterior cranial base and a less convex skeletal profile as compared with full-term children. A significantly shorter maxillary length was found in both the EPT and VPT groups compared with the full-term children. Furthermore, the lower incisors were significantly more retroclined and retruded in the EPT group than in the VPT group and in the full-term control group. Thus, the null hypothesis was rejected with respect to these numbers of craniofacial variables.

So far, this study is the only one that has evaluated craniofacial morphology in preterm children; therefore, comparisons with previous studies are not possible. Nevertheless, findings that the anterior cranial base and the maxilla were shorter in the EPT group correspond well with the significantly smaller head circumference in this group, and they also may explain the less convex skeletal profile found in this group. It was observed that the EPT children at 8 to 10 years of age

Table 4. General Characteristic Data of Extremely Preterm (EPT Group, A), Very Preterm (VPT Group, B), and Full-Term Control Children (FT Group, C)

	EPT Group (A) (n = 36) Girls/Boys 11/25		VPT Group (B) (n = 36) Girls/Boys 16/20		FT Group (C) (n = 31) Girls/Boys 16/15		
	Mean	SD	Mean	SD	Mean	SD	Group Differences[a]
Variables at Birth							
Gestational age, wk	26.8	1	30.8	1.1	39.9	1	A,B/C:***, A/B:***
Birth weight, g	939.5	240.7	1634.7	344.7	3592.3	461.5	A,B/C:***, A/B:***
At Investigation							
Age, y	9.2	0.6	9.4	0.4	9.5	0.5	A,B/C and A/B: NS
Height, cm	133.6	8.1	137.2	6.2	140.7	6.7	A/C:***, A/B and B/C: NS
Weight, kg	29.5	6.8	32.7	7.5	37.8	7.2	A/C:***, B/C:*, A/B: NS
Head circumference, cm	52.2	1.5	52.8	1.6	53.6	1.3	A/C:***, B/C:*, A/B: NS

[a] NS indicates not significant; * $P < .05$; ** $P < .01$; *** $P < .001$.

were significantly shorter, and both EPT and VPT children had significantly lower weight and smaller head circumference compared with the full-term control children. These results correspond well with those reported after other investigations of EPT children.[1,7]

In a longitudinal cephalometric study of children with normal occlusion,[14] it was found that the position of the permanent incisors continuously achieved a more proclined position from 5 to 16 years of age. In the present study, the lower incisors were found to be significantly more retroclined in the EPT group compared to VPT and full-term control children. This fact may be explained by the early birth and the fact that catch-up has not yet been completely accomplished.

When corrections were made for gender, it was found that the anterior cranial base was larger in boys than in girls in all three groups, and a similar gender difference was reported earlier.[16,17] In addition, it was found that in all three groups, the girls had a significantly smaller head circumference compared with the boys. Recently, it was reported that extremely immature children (<26 weeks' gestation) had a significantly smaller head circumference than their full-term peers,[7] but in contrast to our results, these differences were more marked in boys than in girls.

The main strength of the present study was that two strictly divided groups of preterm children, according to gestational age and birth weight, were compared with a well-defined and matched control group of full-term children. It is well known from the literature that ethnic differences in facial traits have been observed, and that the dentofacial pattern changes during periods of active growth.[14,18] To reduce potential confounding factors, the age group was strictly defined, and only white children who originated from the same living area were included in the study; in this way, conditions were right for a homogeneous sample to be taken.

Deliberately, an age group of 8 to 10 years was selected, because from the time of birth to this age, a reasonable time has passed for possible catch-up growth among preterm children. Moreover, most often, this age group represents individuals that are in mixed dentition; therefore, the time is appropriate for starting assessment for orthodontic treatment need and selection of those who are to receive orthodontic treatment. From this viewpoint, it can be mentioned that none of the children examined had any history of previous orthodontic treatment.

The goal was to include one control for each preterm child, but this was not possible because many control families declined to participate because of lack of time. Nevertheless, according to the analysis of nonparticipants, these individuals did not differ from the final control group in terms of age, gender, ethnic origin, or living area. Even if the number of nonparticipants was high, the control group and the preterm groups included an adequate number of participants, according to the original performed sample size calculation. It can be noted that other studies have reported similar problems with recruiting full-term controls.[19,20]

Localization of reference points is the main source of error in cephalometrics. Because no systematic differences were observed in the location of reference points according to the repeated analysis of cephalograms, and because the size of the method error for each variable was low or acceptable, cephalometric analysis of the total sample in this study was considered valid.

CONCLUSIONS

- The null hypothesis was rejected because several craniofacial parameters differed significantly between preterm and full-term born control children.

ACKNOWLEDGMENTS

This study was supported by the Swedish Dental Society, the Swedish Patent Revenue Fund, the Skane County Council

Table 5. Cephalometric Measurements for Extremely Preterm (EPT Group, A), Very Preterm (VPT Group, B), and Full-Term Control Children (FT Group, C)[a]

	EPT Group (A) (n = 36)		95% Confidence Interval for Mean		VPT Group (B) (n = 36)		95% Confidence Interval for Mean		FT Group (C) (n = 31)		95% Confidence Interval for Mean		
Variables	Mean	SD	Lower	Upper	Mean	SD	Lower	Upper	Mean	SD	Lower	Upper	Group Difference[b]
Skeletal, degrees													
Sagittal													
n-s-ba	129.9	4.2	128.5	131.3	130.6	5.5	128.8	132.5	129.9	4.5	128.2	131.5	NS
s-n-ss	81.1	5.5	79.2	82.9	81.3	3.4	80.2	82.5	82.8	3.9	81.4	84.2	NS
s-n-sm	78.1	4.1	76.7	79.5	77.7	3.4	76.6	78.9	78.6	3.9	77.2	80.1	NS
ss-n-sm	2.5	2.6	1.6	3.4	3.8	2.8	2.8	4.7	3.9	2.4	3.1	4.8	NS
s-n-pg	78.9	4	77.6	80.3	79	4.8	77.3	80.6	79	4.1	77.5	80.5	NS
n-ss-pg	176.3	6.2	174.2	178.4	173.2	5.5	171.4	175.1	172.1	5.6	170.1	174.2	A/C: $P = .011$
Vertical													
NL/NSL	4.8	3.5	3.7	6	5.6	3.7	4.3	6.8	5.3	2.5	4.3	6.2	NS
ML/NSL	33.8	5.6	31.9	35.7	34.8	5.7	32.9	36.8	33.1	5.9	31	35.3	NS
NL/ML	28.4	5	26.7	30.1	28.8	5.2	27.1	30.6	28.5	4.6	26.8	30.2	NS
ar-go-gn	126	6.3	123.8	128.1	126.5	6.3	124.4	128.6	127.6	6.6	125.1	130	NS
Skeletal, mm													
Sagittal													
n-s	64.4	4	63	65.7	64.9	3.6	63.7	66.1	66.7	3.5	65.4	68	A/C: $P = .029$
s-ba	42.8	3	41.7	43.8	43.2	3.9	41.9	44.5	43.2	3.2	42	44.4	NS
sp-pm	54.2	2.7	53.3	55.2	53.9	5.9	51.9	55.9	57.1	2.9	56	58.2	A/C: $P = .017$; B/C: $P = .007$
ar-pg	93.1	5.1	91.4	94.9	93.1	4.4	91.6	94.6	95.6	5.5	93.6	97.6	NS
Vertical													
n-gn	104.2	5.9	102.2	106.2	105.7	7.6	103.1	108.3	105.6	5.3	103.7	107.5	NS
n-sp′	47.3	3.5	46.1	48.4	48.1	5.7	46.2	50	46.9	2.7	45.9	47.8	NS
sp′-gn	56.9	3.6	55.7	58.1	57.6	4.6	56	59.2	58.7	3.7	57.3	60.1	NS
n-sp′/sp′-gn, %	83.2	6.4	81	85.4	84	13.2	79.6	88.5	80	5.6	77.9	82	NS
Dental, degrees													
ILi/ILs	136	8.6	133.1	138.9	130.2	9.9	126.8	133.5	128.4	8.9	125.1	131.2	A/C: $P = .003$; A/B: $P = .022$
ILs/NSL	103.8	5.6	101.9	105.7	103.1	6.8	100.8	105.4	105.5	6.3	103.2	107.8	NS
ILs/NL	108.9	5.5	107.1	110.8	108.3	7.3	105.8	110.7	110.8	5.6	108.7	112.8	NS
ILi/ML	87.3	7.1	84.9	89.7	93.6	5.6	91.7	95.4	93.5	7.5	90.8	96.3	A/C: $P = .001$; A/B: $P = .000$
Dental, mm													
ii to ss-pg	−0.2	1.6	−0.7	0.4	1.3	1.8	0.7	1.9	1.8	2	1	2.5	A/C: $P = .000$; A/B: $P = .003$
is to ss-pg	4.5	2.3	3.7	5.3	5.2	2.5	4.3	6.1	5.6	2.2	4.8	6.4	NS
Overbite	3.7	2.2	2.9	4.4	3.8	1.5	3.3	4.3	2.9	1.9	2.3	3.6	NS
Overjet	4.5	2.3	3.7	5.3	4.4	2.3	3.6	5.1	4.6	2.5	3.7	5.5	NS
Soft tissue, degrees													
N-SN-PG	162.3	5.4	160.4	164.1	160.4	8.2	157.6	163.2	160.7	7	158.1	163.2	NS
Soft tissue, mm													
PLs to EL	−1	2.5	−1.8	−0.2	−0.1	1.8	−0.7	0.6	−1.6	2.1	−2.3	−0.8	B/C: $P = .015$
PLi to EL	−0.2	2.7	−1.1	0.7	0.4	2.6	−0.5	1.3	−0.6	2.8	−1.6	0.4	NS

[a] Overjet and overbite were measured on study casts.
[b] NS indicates not significant.

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