

# Facial Malformation in Crouzon's Syndrome Is Consistent with Cranial Base Development in Time and Space

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**Background:** In Crouzon's syndrome, cranial base deformities begin sequentially in the anterior cranial fossa initially, and later to the posterior cranial base. Facial characteristics are likely related to cranial base development. The temporal correlation between cranial base development and facial features is in need of clarification in Crouzon's patients, to clarify initial sites of deformity, which may impact surgical decision making.

**Methods:** Thirty-six computed tomography scans of unoperated Crouzon's syndrome patients and 54 controls were included and divided into 5 age-subgroups. All the planes used for analysis were set as perpendicular to a defined "midplane" to offset the confounding factor caused by potential asymmetry.

**Results:** The angle between Sella-Nasion plane and Frankfort horizontal plane was significantly increased before 6 months of age ( $P = 0.014$ ), with an average 70% ( $P < 0.001$ ) increase ultimately into adulthood. The angle between SN and maxillary plane and the angle between Sella-Nasion and occlusal planes increased consistently through infancy to adulthood (124% and 42%, respectively, both  $P < 0.001$ ). The relative angle of mandibular plane to Frankfort horizontal plane increased before 6 months (28%,  $P = 0.007$ ) with a peak timeframe from 2 to 18 years. Facial lateral curvature related measurements indicate the whole face is inclined posteriorly and inferiorly direction in relation to the anterior cranial base.

**Conclusion:** Crouzon's facial malformation development is synchronous and positionally correlational with cranial base deformity. It transmitted from orbit to mandible, with the most evident morphologic changes are in the orbit and midface. (*Plast Reconstr Surg Glob Open* 2018;6:e1963; doi: 10.1097/GOX.0000000000001963; Published online 4 October 2018.)

## INTRODUCTION

Craniosynostosis, exophthalmos, hypoplastic midface, and mandibular prognathism characterize Crouzon's syndrome.<sup>1-6</sup> In recent years, 3-dimensional morphometrics

methods have provided a better understanding of structural characteristics of these facial malformations. As facial characteristics are likely to be related to cranial base development,<sup>7,8</sup> this connection needs to be clarified further in pathologic conditions such as Crouzon's syndrome, to clarify which are primary and secondary deformities to understand pathogenesis of the deformity and anatomic trail of influence.

In our previous study of Crouzon's syndrome, cranial base deformity was noted to begin in the anterior cranial fossa, and with further growth deformity was evident in posterior cranial vault. This resulted in a more severe deformation in the posterior fossa. In view of the developmental position, correlation between facial and cranial

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base structure,<sup>8,10,11</sup> the question may be asked, does the more severe posterior skull base deformity cause a more significant corresponding facial deformity?

The purpose of this study was to examine this question and define the interactive craniofacial influences which change with age, by objectively analyzing craniofacial, temporal developments in a series of unoperated Crouzon’s syndrome patients.

**PATIENTS AND METHODS**

This is a longitudinal study performed in accordance with the Yale University Human Investigation Committee (HIC 1101007932). Computed tomographic scans were obtained from all subjects without any previous surgical intervention. Thirty-six preoperative computed tomographic scans of Crouzon’s syndrome patients, and 54 age- and sex-matched, controls without confounding disease were included. All the computed tomography scans are divided into 5 subgroups based on age: 0–6 months, 6 months to 2 years, 2 to 6 years, 6–18 years, and 18–62 years old. Age and sex were rematched in each age-subgroup to confirm comparability. Demographic information was tabulated.

Digital Imaging and Communications in Medicine data were digitized and manipulated using Mimics and 3-matics software (version 19.0; Materialise, Leuven, Belgium). Before the initial data acquisition for this study, the observer (X.L.) went measurements training until the Pearson correlation coefficients of both interobserver (compared with a practiced observer) at 0.95, and intraobserver error was less than 0.05. All the landmark points, generated lines, angles, and planes were chosen and produced twice by the same observer, in both Crouzon’s syndrome and control groups, with independent verification by 3 additional observers (A.F., R.S., and J.P.).

Abbreviation and definitions of measurements, and detailed anatomic planes setting process were shown in Table 1 and Supplemental Digital contents 1-3 (see figure, Supplemental Digital Content 1, which displays all the planes used in this study were set as perpendicular to the midplane to offset the confounding factors caused by potential asymmetry, <http://links.lww.com/PRSGO/A885>; see figure, Supplemental Digital Content 2, which displays the “interactive rotate” function in 3-matic was used to

close the mouth for who underwent general anesthesia, and therefore had open-mouth posture during computed tomography scanning, <http://links.lww.com/PRSGO/A886>; see table, Supplemental Digital Content 3, which displays the definition of landmarks, cephalometric distances, ratios, angles, and planes, <http://links.lww.com/PRSGO/A887>; see table, Supplemental Digital Content 4, which displays measurements results in age subgroups analyses, <http://links.lww.com/PRSGO/A888>).

Statistical analyses were carried out in Microsoft Excel (v.2016, Microsoft Corp., Redmond, Wash.). *t* Test was used for comparison of continuous variables. All statistical tests were 2-sided, statistical significance was set at  $P < 0.05$ .

**RESULTS**

**Demographic Data**

A total of 90 computed tomographic scans were included (Crouzon,  $n = 36$ ; control,  $n = 54$ ). The 5 age subgroups consisted of 0–6 months, 6 months to 2 years, 2–6 years, 6–18 years, and 18–62 years old. The mean age of the 2 groups was as follows: Crouzon,  $10.84 \pm 14.70$  years with a range from 3 days to 62 years old; and control,  $8.53 \pm 13.22$  years with a range from 5 days to 62 years old. The Crouzon’s group consisted of 14 males and 22 females, and in the control group were 29 males and 25 females (Table 2).

**Craniofacial Planes Angular Measurements  
Angular Analysis Based on Sella-Nasion Plane**

Before 6 months of age, the angle between Sella-Nasion plane (SN; Table 3) and Frankfort horizontal plane (FH) was significantly increased 144% ( $P = 0.013$ ), with an average 70% increasing ( $P < 0.001$ ) in whole life of Crouzon’s syndrome compared with controls. The angle between SN and maxillary plane (Mx) and the angle between SN and occlusal plane (Occ) increased consistently through infancy to adulthood with the most marked increase from 6 months to 2 years (104%,  $P = 0.003$ ) and from 6 years to 18 years old [60% ( $P = 0.014$ )] when compared with age- and sex-matched controls. The angle between SN and mandibular plane (MP) increased  $7.64^\circ$  ( $P = 0.036$ ) before 6 years old, and increased twice that amount subsequently [peak time at 6–18 years (44%,  $P = 0.002$ )]. The angle between SN and mandibular ramus plane (MRP) had increased in the 2–6 years age group and between

**Table 1. Definition of Anatomic Planes**

Abbreviation	Variable	Definition
SN	Sella-Nasion plane	The plane passing through sella and nasion landmarks and perpendicular to midsagittal plane
FH	Frankfort horizontal Plane	The Frankfort horizontal plane is defined by a plane that passes the midpoint of both Orbita (Orbitar and Orbital) landmarks and the midpoint of the two Porion (Porionr and Porionl) landmarks, and perpendicular to midsagittal plane
Mx	Maxillary plane	The maxillary plane is defined by a plane that passes the anterior nasal spine and posterior nasal spine landmarks, and perpendicular to midsagittal plane
Occ	Occlusal plane	The occlusal plane is defined by a plane that passes the mean of upper and lower incisor landmarks in both sides and the mean of upper and lower molar landmarks in both side, and perpendicular to midsagittal plane
MP	Mandibular plane	The mandibular plane is defined by a plane that passes the menton and the mean of both Gonion landmarks, and perpendicular to midsagittal plane
MRP	Mandible ramus plane	The plane passes the mean of bilateral gonions and the mean of bilateral condylions, and is perpendicular to midsagittal plane

**Table 2. Age and Gender Distributions of Crouzon Syndrome Group and Controls Shown by 5 Age Subgroups**

Age Group	Crouzon	Control	P
0–0.5			
Number	7	14	
Age ± SD (y)	0.19±0.18	0.17±0.13	0.76
Sex			
Male	3	8	
Female	4	6	
0.5–2			
Number	6	12	
Age ± SD (y)	0.96±0.35	1.01±0.30	0.77
Sex			
Male	3	7	
Female	3	5	
2–6			
Number	9	11	
Age ± SD (y)	4.51±1.37	4.26±1.58	0.72
Sex			
Male	3	6	
Female	6	5	
6–18			
Number	7	8	
Age ± SD (y)	12.16±4.24	11.25±4.78	0.70
Sex			
Male	4	5	
Female	3	3	
18–62			
Number	7	9	
Age ± SD (y)	36.86±12.48	34.35±12.00	0.70
Sex			
Male	1	3	
Female	6	6	
0–62			
Number	36	54	
Age ± SD (y)	10.84±14.70	8.53±13.22	0.45
Sex			
Male	14	29	
Female	22	25	

6 and 18 years by 11% and 14%, as compared with controls ( $P = 0.01$  and  $P = 0.02$ , respectively; Fig. 1; Supplemental Digital Content 4).

**Angular Analysis Based on Frankfort Horizontal Plane**

The angle between FH and Occ had a slight increase by 2.73° ( $P = 0.019$ ) on average with a significant difference at 6–18 years. The increase of the angle between Mx and FH developed between 6 months to 2 years by 7.14° ( $P = 0.007$ ). The relative angle of MP to FH increased before 6 months by 5.26° ( $P = 0.006$ ) with a plateau period from 2 years to 18 years by over 10° increase ( $P = 0.001$ ). The angle between MRP and FH only increased 6.38° in the 2- to 6-year-old Crouzon's patients [ $P = 0.03$ ; see figure, Supplemental Digital Content 5, which displays angular analysis based on Frankfort horizontal plane show the relative angles of middle and lower face changing by age in Crouzon syndrome (16-year-old, female) compared with control (16-year-old, female), <http://links.lww.com/PRSGO/A889>].

**Angular Analysis of Adjacent Planes**

The angle between SN and MRP consists of 5 angles, the SN-FH, FH-Mx, Mx-Occ, Occ-MP, and MP-MRP angles (Fig. 2). Although the largest SN-MRP angle only slightly increased from 2 to 18 years of age, the 5 angles included in it, changed significantly throughout development. As above, the angle between SN and FH increased before

**Table 3. Measurements Results in Full Age Range (0–62 Years of Age) Comparison**

Index	Crouzon		Control		P
	AVE	STD	AVE	STD	
Angular analysis based on Sella-Nasion plane					
SN-FH	10.44	5.36	6.14	3.55	< 0.001*
SN-Mx	13.63	5.76	6.09	4.16	< 0.001*
SN-Occ	21.43	5.14	15.12	5.91	< 0.001*
SN-MP	43.42	8.80	31.48	6.98	< 0.001*
SN-MRP	86.31	12.27	78.58	10.02	0.003*
Angular analysis based on Frankfort horizontal plane					
FH-Mx	3.19	4.95	0.05†	4.10	0.002*
FH-Occ	11.17	4.87	8.44	5.66	0.020‡
FH-MP	32.93	7.81	25.09	5.23	< 0.001*
FH-MRP	76.06	10.54	72.63	8.10	0.112
Angles of adjacent planes					
Mx-Occ	8.36	4.74	8.91	5.66	0.631
Occ-PI/MP	22.41	7.77	15.96	6.77	< 0.001*
Mp-MRP	43.82	7.33	46.30	10.07	0.201
Cephalometric angles					
SNA	74.08	6.68	85.66	4.42	< 0.001*
SNB	75.13	6.21	80.77	5.33	< 0.001*
ANB	1.06§	5.84	4.90	3.15	< 0.001*
N-S-PPMR/L	80.48	7.37	76.85	4.29	0.011‡
N-S-ARR/L	109.25	4.36	106.23	3.84	0.001*
N-A-Pog	170.51	9.56	168.90	7.76	0.42
N-S-GN	70.82	6.78	61.06	6.21	< 0.001*
S-N-Pog	73.77	6.18	80.69	5.40	< 0.001*
Linear measurements					
S-N	52.88	7.35	55.98	10.85	0.110
S-ANS	59.49	10.15	66.45	14.01	0.008*
S-A	57.47	10.06	66.20	14.32	0.001*
S-B	80.01	19.75	83.68	21.59	0.432
S-Pog	86.40	23.41	90.31	24.20	0.469
S-GN	89.35	23.61	92.31	24.44	0.586
S-PNS	28.81	7.18	35.22	9.37	< 0.001*
S-GO	52.42	14.86	56.15	16.00	0.275
S-AR	40.76	7.36	45.31	7.24	0.006*
ANS-BA	68.89	10.68	79.11	14.32	< 0.001*
ANS-N	36.25	9.40	35.66	10.22	0.779
ANS-MEN	54.49	16.47	50.23	16.02	0.251
N-Men	90.48	25.11	85.83	25.40	0.417
N-ANS/S-PNS	1.27	0.22	1.01	0.11	< 0.001*
ANS-Men/N-Men	0.60	0.05	0.58	0.03	0.095
S-GO/N-Men	0.60	0.06	0.67	0.05	< 0.001*
Wit's	2.93§	6.69	2.55	2.70	< 0.001*

\* $P < 0.01$ .

†The angle rotated anticlockwise from FH plane.

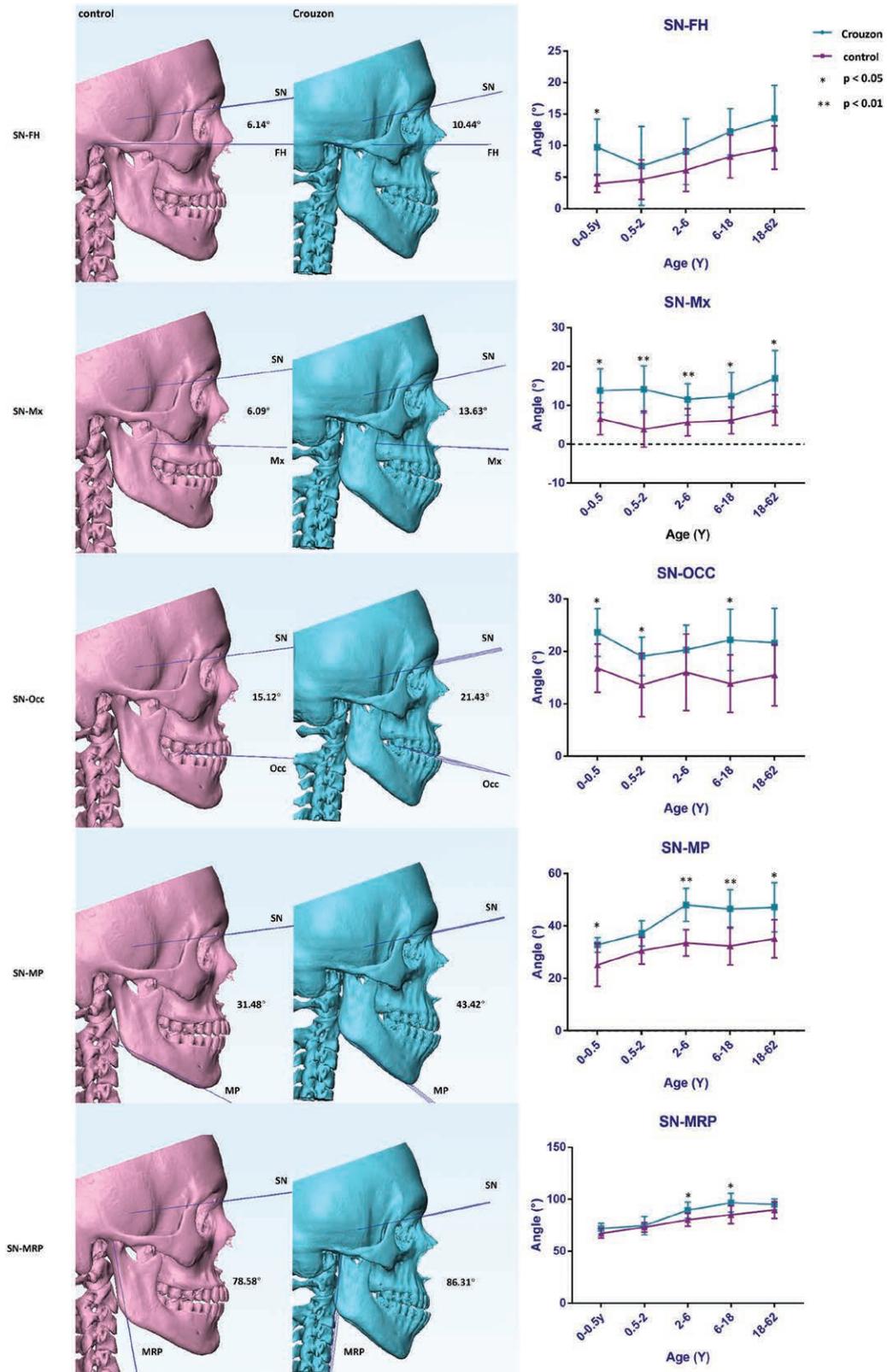
‡ $P < 0.05$ .

§B point was in front of A point.

6 months of age, and the angle between FH and Mx increased from 6 to 2 years of age. The Mx-Occ remained stable or even decreased slightly with time when compared with controls. The Occ-MP angle increased 4.8° ( $P = 0.008$ ) before 6 months with minor decrease between 6 months to 2 years, and then the angle increased again, by 10.21° at 2–6 years ( $P = 0.002$ ), 5.86° at 6–18 years ( $P = 0.004$ ), and 6.22° over 18 years ( $P = 0.045$ ), respectively. The MP-MRP angle is stable except a decrease by 6.21° at 2–6 years ( $P = 0.002$ ).

**Cephalometric Angular Measurements**

The SNA showed a persistent decrease from birth to 62 years old by 11.58°, yielding statistical significance ( $P < 0.001$ ). The SNB decreased 10.87° ( $P = 0.002$ ) before 6 months and at adulthood remained decreased at 5.56° ( $P < 0.001$ ). The ANB decreased after 6 months by 5.97° on average ( $P < 0.001$ ) with the peak change after 18 years old.



**Fig. 1.** Angular analysis based on Sella-Nasion plane show the relative angles of planes to cranial base changing by age in Crozon syndrome (16-year-old, female) compared with control (16-year-old, female). The degrees marked in the left 2 columns are the average degrees of 0- to 62-year-old in controls (pink) and Crozon syndrome (blue).

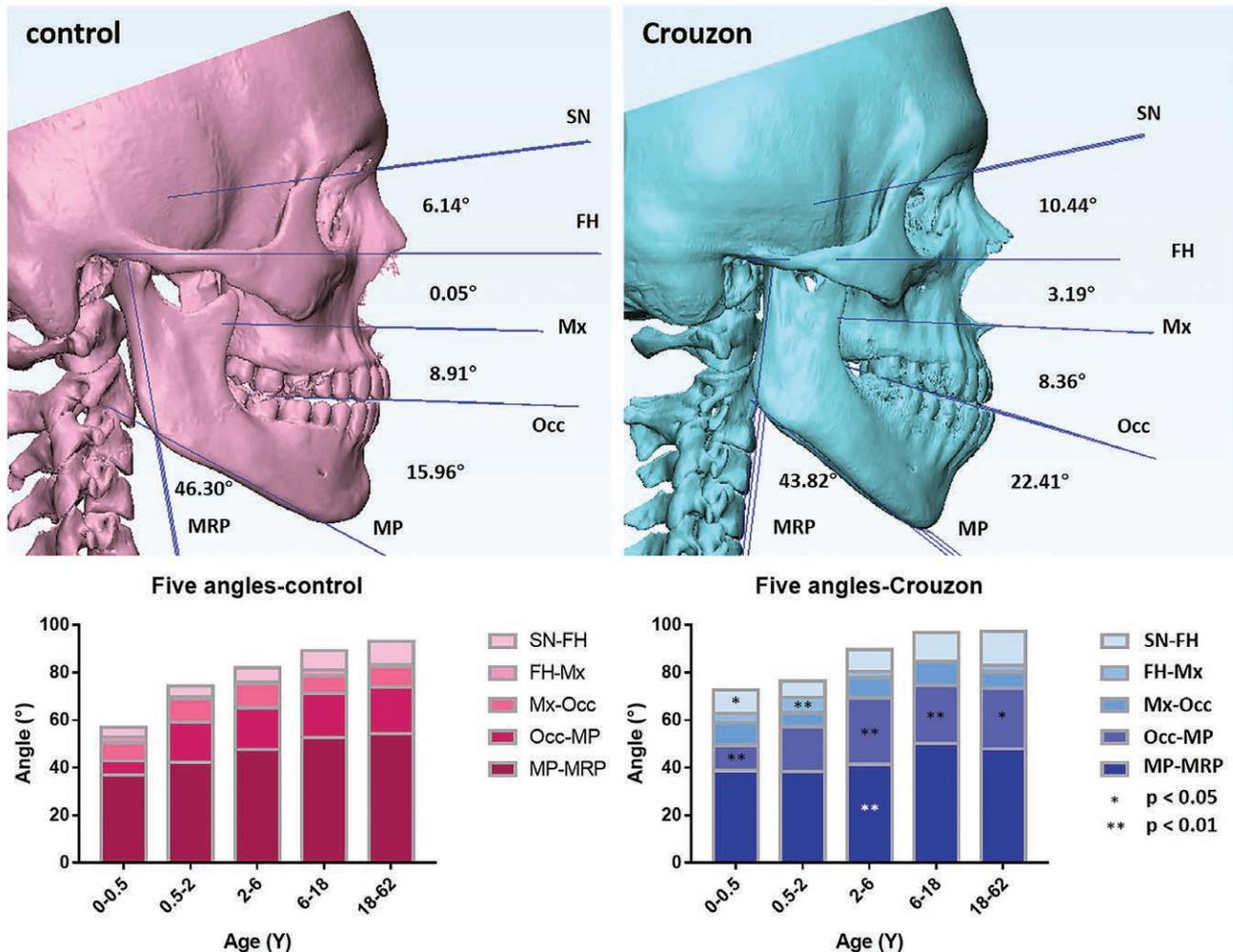


Fig. 2. Angular analyses of adjacent planes show the contribution of 5 angles included in SN-MRP changed by age.

The angle N-S-PP increased from 2 years old by 4.55° ( $P = 0.04$ ) to 18 years old by 8.16° ( $P = 0.015$ ) with an average increase of 3.64° ( $P = 0.011$ ). The angle N-S-AR increased 8.36° ( $P < 0.001$ ) before 6 months and got 3.01° ( $P = 0.002$ ) increase in adulthood.

The facial convexity angle (N-A-Pog) is unchanged in the whole age range in Crouzon's syndrome compared with controls. The N-S-GN angle increased before 6 months by 10.29° ( $P < 0.001$ ) to 18 years old by 11.95° ( $P = 0.003$ ). The S-N-Pog angle decreased early and developed before 6 months by 12.32° ( $P < 0.001$ ), with the final decrease of 6.92° ( $P < 0.001$ ; see figure, Supplemental Digital Content 6. Facial lateral curvature related cephalometric angles changing by age, <http://links.lww.com/PRSGO/A890>).

#### Linear Measurements

In the linear distances with sella as the anterior reference point, the distance S-A, S-Pog, and S-PNS decreased before 6 months by 6% ( $P = 0.039$ ), 11% ( $P = 0.039$ ), and 13% ( $P = 0.004$ ), respectively. After 6 months, all the other linear measurements share the sella as the reference anchor point, also shortened (see figure, Supplemental

Digital Content 7, which displays linear measurements represented with Sella or ANS as one end of the distance, <http://links.lww.com/PRSGO/A891>).

Specifically, with ANS as the reference point, ANS-BA shortened by approximately 20% after 6 months into adulthood ( $P < 0.001$ ). The length of ANS-N approximated normal throughout growth. The length of ANS-Men only increased 14% ( $P = 0.037$ ) before 6 months and 11% ( $P = 0.041$ ) between 2 and 6 years old. The whole facial height N-Men is unchanged compared with controls.

It is helpful to divide growth influences and effects into 2 parts, the upper and the lower facial structure. The ratio of the upper anterior facial height to upper posterior facial height (N-ANS/S-PNS) increased by 26% ( $P < 0.001$ ). The ratio of lower facial height to total facial height (ANS-Men/N-Men) remained stable. The ratio of posterior facial height to anterior facial height (S-Go/N-Men) decreased by 11% ( $P < 0.001$ ). The change of the occlusal relation index, the modified 3-D Wit's measurement (a projective linear measurement between the 3-D cephalometric hard tissue A point and B point landmarks that are projected perpendicular on the 3-D occlusal plane) is the most significant. It began before 6 months by 307%

( $P = 0.046$ ), increased 366% ( $P = 0.012$ ) at 6 months to 2 years, and achieved a 215% ( $P < 0.001$ ) increase throughout development compared with controls.

## DISCUSSION

Orbital dysmorphology, midface hypoplasia, and mandibular, relative prognathism, of Crouzon's syndromes have been previously reported.<sup>2,4,6,11-13</sup> As integral parts of a whole facial skeletal structure, changes in the above structures with growth, support the concept of a correlation between facial structure and skull base anatomy.<sup>7,8,14</sup> The present study was designed mainly on 3-D angular analysis of dominant craniofacial planes in Crouzon's syndrome, which is the first time this technique has been used in morphospace analysis, to our knowledge. Specifically, the midpoint of bilateral landmarks was used if a plane was produced by bilateral landmarks, to set all the planes as perpendicular to the sagittal plane and without lateral tilt. The angular and linear measurements developed from defined landmarks, to clarify the primary role that the cranial base plays on facial development, and the sequence of change in the skeleton, defined by age.

Plane angular analysis is based on SN and reflects the reference plane to document the changing position of facial structures relative to the cranial base. The markedly increased angle between SN and FH was the main recorded anatomical relationship anomaly that existed before 6 months; further changes are postulated to occur directly or indirectly thereafter related to this early developing abnormal relationship. This is consistent with Carr et al.,<sup>4</sup> who have shown that the orbit deformity of Crouzon's syndrome, developed in infancy. The widened and shortened anterior cranial fossa happens in the early development of the Crouzon's syndrome infant.<sup>15</sup> This increased SN-FH angular measurement is consistent, in time and space, with the anterior cranial fossa and its abnormal increased orbit height.<sup>11</sup>

In our previous study, related to cranial base development in Crouzon's patients, the deformity of anterior cranial fossa was influential in the development of posterior fossa deformity. Multiple studies show the relationship of midface deformity with middle cranial fossa, and the relation between the posterior cranial fossa dimensions, and that of the mandible.<sup>8-10</sup> Our previous study shows Crouzon's syndrome developed widened and shortened cranial base. The shortened cranial base length mainly began at anterior skull base and transmitted to posterior, resulting in kyphotic cranial base. As the deformity is passed posteriorly in the cranial base, the facial deformities do not change appreciably. This cranial base distortion is synchronous and positional related to facial malformation development, but the degree of severity is not inconsistent between cranial base and facial structures. Specifically, the mandible did not develop the most severe malformation, although its anatomical counterpart in the cranial base, the posterior cranial base, developed the most severe malformation.

In the current study, the position of the maxillary plane, occlusal plane and mandibular plane are inferiorly

and posteriorly rotated compared with anterior cranial base over time. The significantly increased angle of the MRP develops 2 years later than other planes. All the angles between above planes and Sella-Nasion plane statistically increase over time. This results in a longer face shape in Crouzon's syndrome as reported in previous work.<sup>1,6,16</sup>

As orbital dysmorphology is one of the main characteristics of Crouzon's syndrome,<sup>11,17</sup> analysis of the relative position between lower planes and Frankfort horizontal plane may clarify the influence of the orbit development on face shape. The most significantly increased angle regionally is between FH and the maxillary plane. This is consistent with the severe midface retrusion of Crouzon's syndrome previously reported.<sup>12</sup> Conjointly analyzing this with the shorten anteroposterior length of midface (shown in our linear measurements), and unchanged midface volume in Crouzon's syndrome,<sup>2</sup> reflect this hallmark facial deformity this occurs is without midface height reduction.

The angle analysis between adjacent planes show the absolute change of each facial structure between its adjacent, superior, and inferior planes. The angles MP-MRP and SN-MRP remain stable, while the angle of Occ-MP is increased. This indicates a counterclockwise occlusal plane, which is consistent with class III malocclusion and relative mandibular prognathism characteristic of Crouzon's syndrome.<sup>9,18</sup>

Facial lateral curvature related measurements indicate the whole face was inclined in a posterior direction in relation to the anterior cranial base. Decreased S-N-Pog, increased N-S-GN, and stable N-A-Pog manifest the holistic description of the posterior rotation of middle and lower face.<sup>19</sup>

In summary, the malformation development of Crouzon's skull base and facial structures are synchronous in spatial relation, but inconsistent in the degree of severity. Before 6 months of age, the increase of angles based on SN in Crouzon's syndrome patients is gradually noted from the top to the bottom of the facial skeleton. This strongly suggests, the earliest pathologic deformities begin at the top of the cranial skeleton at the anterior cranial base. Related to these deformities, there may be regional increased intracranial pressure, which influences structural development from anterior to the posterior cranial base. This would be augmented by brain growth anteriorly causing posterior translation of the bulk of brain tissue. The results of this study showed that the peak significant changes in cranial base to face angles were consistent with the downward movement of the maxilla. The severity of the deformation is also gradually reduced from top to bottom, shown as striking deformity in orbit and midface development, which then combines with relatively mild mandibular prognathism. The eventual maxillary and mandibular shapes are attributed to superimposition of influences of functional matrices and compensatory mechanisms and result in more evident deformity, with more visible morphologic changes of the face.<sup>19,20</sup> In addition, the angle most directly influencing midface projection is the middle cranial fossa point, as the center of the skull base, potentially, the strongest influence for change with skull and face deformity.

Furthermore, dental maturation has a significant growth influence on midface development. Reitsma et al.<sup>21,22</sup> reported severe early dental maturation delay in Crouzon's syndrome, until puberty. This could be caused by the hypogenetic maxillary and mandibular bone, and the supporting structure of dental arch. The diminished growth dental arch, in turn, may cause compensatory growth of mandible, with resulting class III malocclusion. However, the mandible is not the most obvious structural abnormality in Crouzon's syndrome, suggesting functional forces (eg, eating, chewing) may override compensatory growth influences intracranially. Coquerelle et al.<sup>23</sup> also reported the reorientation of both deciduous and permanent teeth are highly correlated with the mandibular morphology. This supports Moss's concept of functional matrices, being responsible for the primary morphogenetic and spatial influencing factors in mandibular growth.<sup>21</sup>

Implications for surgical treatment: our unpublished data<sup>9</sup> show the posterior vault expansion and whole cranial vault cranioplasty, at an early age can stop, or at least decelerate the progressively kyphotic cranial base angulation, while the anterior expansion (Monobloc) has less benefit in limiting abnormal cranial base angulation. There is consistent and progressive anatomic distortion of the skull base, which is inconsistent in the degree of severity of Crouzon's skull base and facial structures malformation, with differing types of skull surgeries. This also suggests the importance of the surgeries time sequence, that is, early posterior vault expansion reduces more overall skull deformity than later surgery. The different degree of correction with age, at surgery in both cranial base, and cranial vault surgical intervention (and possibly facial surgeries) provided to Crouzon's patients, could achieve a more normal growth pattern in the mature craniofacial appearance. A detailed intervention timing and sequence surgery plan for Crouzon's syndrome patients is in process. Facial surgeries may need to occur later in life than cranioplasty due to concerns related to hindering tooth and midface development. The vector correction is needed to be taken into consideration for the facial surgeries. To recover the counterclockwise rotated maxillary plane, may be a desired goal to rebuild the facial structures for Crouzon's syndrome patients. Therefore, accompanying the monobloc or LeFort osteotomy and advancement, a clockwise rotation controlled by distraction, may be influential. In addition, to fully utilize the functional accommodation, concept orthodontic treatment may be additive/augmentative to correct deformity in childhood or early adolescence.<sup>25-29</sup>

## CONCLUSIONS

Crouzon's skull base distortion and facial structure malformation development are synchronous in spatial relation, but inconsistent in the degree of severity in influencing individual bone/region structures. The time sequence for the development of facial deformity in Crouzon's syndrome is from the top to down (ie, cranial base to midface). The severity of deformity is also patterned in the same direction. The earliest facial structural change

in the region of the orbit, yet the most obvious deformity is the midface, with anteroposterior shortening and mediolateral widening of the maxilla. Although the posterior cranial fossa growth resulted in local deformities (which are severe in Crouzon's syndrome), its facial position counterpart, the mandible, did not produce the same obvious changes. The surgeries time sequence and the different degree of correction with age, of both cranial base or cranial vault surgical intervention and facial surgeries, are needed to be explored further. Functional factors of eating and breathing may likely override structural restrictions of bone growth in the cranial base.

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