Three-Dimensional Morphological Analysis of Isolated Metopic Synostosis

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ABSTRACT

Morphological differences were quantified in three-dimensions among individuals with untreated isolated metopic synostosis and between those individuals and similar aged-matched normal dry skulls to test two hypotheses: first, that the dysmorphology is a self-correcting condition; and second, that a lack of vertical growth of the skull produces this dysmorphology.

Three-dimensional (3D) coordinates were recorded for 22 craniofacial landmarks from CT scans of 15 metopic patients, ranging from 5- to 32-months-old, and of four normal dry skulls, ranging in age from 6- to 36-months-old. The patient population was diagnosed with isolated metopic synostosis at The Johns Hopkins Medical Institutions in Baltimore, Maryland or Children's Hospital in St. Louis, Missouri.

Comparisons between the metopic age groups indicate that the trigonocephalic phenotype worsens through time. Between 5 and 14 months, the neurocranium displays an increase in vertical growth. This was followed by a lack of vertical growth between 14 and 32 months. The face displays a lack of vertical growth from 5 to 14 months and an increase in vertical growth after 14 months. Comparisons between the metopic age groups and the normal skulls indicate that the trigonocephalic head is taller superoinferiorly and longer anteroposteriorly. Relative to the normal phenotype, the inferior temporal region in the metopic phenotype is narrow.

These findings enabled the rejection of both hypotheses and localized form differences between normal and metopic phenotypes. Based on these results, we suggest that the trigonocephalic phenotype worsens with age and the amount of vertical growth that produces the trigonocephalic phenotype varies throughout growth with respect to location within the skull and age. Anat Rec 256:177–188, 1999. © 1999 Wiley-Liss, Inc.

Key words: **trigonocephaly; craniosynostosis; metopic suture; Euclidean Distance Matrix Analysis; craniofacial growth**

The metopic suture normally closes between 1 and 2 years of age and is usually obliterated by 3 years, but can remain patent as late as 7 years of age (Sperber, 1989). Premature closure of the metopic suture produces a less common form of nonsyndromic craniosynostosis (.04–1 per 1,000 live births) that results in a triangular-shaped neurocranium to which the descriptive term trigonocephaly has been applied (Anderson et al., 1962; Cohen, 1986). Depending upon the timing and extent of suture

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closure, a patient may present with a range of dysmorphologies including an isolated midline ridge or a large keel-shaped prominence overlying the metopic suture, ethmoidal hypoplasia, orbital hypotelorism, a shortened anterior cranial fossa, bitemporal narrowing, and biparietal widening (Anderson, 1981; Anderson et al., 1962; Eppley and Sadove, 1994; Friede et al., 1990; Posnick et al., 1994; Sadove et al., 1990). Unfortunately, there are very few quantitative descriptions of trigonocephaly produced by uncomplicated metopic craniosynostosis and those that do exist are two-dimensional in nature (Anderson, 1981; Anderson et al., 1962; Dominguez et al., 1981; Eppley and Sadove, 1994; Friede et al., 1990; Kolar and Salter, 1997; Posnick et al., 1994; Sadove et al., 1990). Since metopic synostosis is generally accepted as the cause of trigonocephaly (Friede et al., 1990; Cohen, 1986; Dominguez et al., 1981; Currarino and Silverman, 1960), we consider trigonocephaly to be synonymous with metopic synostosis.

Dominguez et al. (1981) concluded from qualitative observations of head shape that trigonocephaly is a self-correcting deformity and therefore recommended conservative, i.e., nonsurgical, management. In contrast, Friede et al. (1990) concluded from quantitative assessments of anteroposterior radiographs analyzed by cephalometric superimpositions of the forehead and three orbital landmarks, that trigonocephaly was not a self-correcting deformity. Friede and coworkers found that relative to a normal control group, patients with trigonocephaly experienced increases in orbital width, without changes in orbital height through time. The authors hypothesized that landmarks digitized from computed tomography (CT) scans might better address the question of whether the dysmorphologies accompanying metopic synostosis are self-correcting with age.

Posnick et al. (1994) conducted a more detailed study of trigonocephaly using linear distances measured on CT images. Their analysis of preoperative patients documented a narrow intercoronal, intertemporal, and anteromedial interorbital distance, as well as a narrow interorbital distance and hypotelorism, indicating that a fused metopic suture impacts the upper face in addition to the anterior neurocranium. Relative to a group of patients with metopic synostosis that did not undergo any surgical manipulations, the authors found that their surgical method resulted in normalization of forehead morphology but failed to correct dysmorphologies in the lateral orbital and temporal regions. From these results, the authors concluded that trigonocephaly was not a self-correcting deformity.

Kolar and Salter (1997) evaluated trigonocephalic morphology in a sample of 50 preoperative metopic synostosis patients, divided into two age groups (2–6 months and 7–69 months). Their results confirmed the classic dysmorphologies of trigonocephaly while also demonstrating that the cephalic index, width of the cranial base, and ear size and shape are unaffected in metopic synostosis. The authors suggested that a lack of vertical growth of the face and neurocranium is the most significant factor in producing the dysmorphologies associated with metopic synostosis.

Our study uses Euclidean Distance Matrix Analysis (EDMA) and three-dimensional (3D) landmark data collected from computed tomographic (CT) images of preoperative patients diagnosed with uncomplicated metopic synostosis to test two hypotheses: (1) that trigonocephaly is a self-correcting deformity and (2) that a reduction in vertical growth of the neurocranium and face is associated with trigonocephaly. If the first hypothesis is rejected by demonstrating that trigonocephaly worsens with age, we will examine how the dysmorphologies associated with metopic synostosis progress with age by testing the second hypothesis. If the second hypothesis is rejected, we will determine along which directional axes disproportionate growth occurs.

An idealized study constructed to test the first hypothesis would compare the development of trigonocephalic morphology using a longitudinal sample of nonsyndromic metopic synostosis individuals and a sample of age-matched normal individuals. If trigonocephaly was self-correcting, the form of the trigonocephalic skull would become more similar to the normal skull through time. Longitudinal samples of normal or trigonocephalic children were not available. Instead, we employ small cross-sectional samples of 3D-CT reconstructions of normal dry skulls and trigonocephalic patients. Although our small sample size questions the significance of statistical tests for differences between the normal dry skulls and our trigonocephaly patients, we present the comparisons for two reasons. First, they are important in understanding how trigonocephalic dysmorphology relates to normal craniofacial morphology. Second, there are no published studies to date that compare preoperative trigonocephalic form to normal craniofacial form in three dimensions.

MATERIALS AND METHODS

Sample and Landmark Data

Our cross-sectional sample consists of preoperative 3D-CT images of 16 infants (10 males and six females) that were diagnosed with isolated metopic synostosis at either The Johns Hopkins Medical Institutions in Baltimore, Maryland, or St. Louis Children's Hospital in St. Louis, Missouri. Our sample of normal dry skulls ($n = 4$) were selected from the Bosma Collection (Shapiro and Richtsmeier, 1997) to approximately match the age distribution of our clinical sample. The skulls from the Bosma Collection underwent CT scanning using a standard research protocol (Shapiro and Richtsmeier, 1997). The patient scans were obtained from the respective institutions following their respective protocols. Three-dimensional coordinates of 22 neurocranial and facial landmarks (Table 1 and Fig. 1) were collected from 3D-CT reconstructions of images of the Bosma skulls and each patient using REMEDI, a 3D-rendering and visualization software package developed by the Centre for Information-Enhanced Medicine, National University of Singapore. Our patient population was divided into three age groups and are named according to the mean age calculated for each group: 5 months, 14 months, and 32 months (Table 2). Two groups were formed from the sample of dry skulls: a 14 norm ($n = 2$; mean age of 12 ± 3 months) and a 32 norm ($n = 2$; mean age of 35 ± 6 months). There were no normal skulls available to create a 5 norm group to compare to the 5 month metopic group.

Since these data are cross-sectional, we cannot study growth in its strictest sense. However, we are accepting the comparison of chronological age groups as representative changes in morphology due to growth through time.

Hypotheses and Predictions

The first hypothesis states that trigonocephaly is a self-correcting deformity. This hypothesis was tested by

TABLE 1. List of landmarks digitized from 3D-CT reconstructions*

Landmark number	Landmark abbreviation	Landmark and abbreviation name
1	nas	nasion
2, 3	fzj	frontal-zygomatic junction posterior (r & l)
4, 5	ptnp	pterion posterior, frontal-zygo-matic-parietal intersection (r & l)
6, 7	ast	asterion (r & l)
8, 9	sphsq	intersection parietosphenoid and squasmosal sutures (r & l)
10, 11	boss	basi-occipital-sphenoid synchondrosis, lateral on occipital margin (r & l)
12	bas	basion
13	lam	lambda
14, 15	iam	internal auditory meatus (r & l)
16, 17	acp	anterior clinoid process (r & l)
18	glab	outer calvaria at glabella
19	sella	sella
20	brg	bregma
21, 22	tzj	temporal-zygomatic junction, inferior surface of the suture

*These landmarks are illustrated in Figure 1.

comparing the 5 month to the 14 month group and the 14 month to the 32 month group. The criteria required to reject this hypothesis include quantitative observations that indicate an increasing triangular head shape and reduction of bitemporal and interorbital distances over time (Table 3).

The second hypothesis states that a lack of vertical growth of the face and neurocranium is primarily responsible for the production of the dysmorphologies associated with trigonocephaly. To test this hypothesis, the form comparisons between the 5 month and 14 month group, and the 14 month and 32 month group were examined to determine those axes (anteroposterior, superoinferior, or mediolateral along which disproportionate growth occurs.

Finally, we used EDMA to compare the 14 month to the 14 norm group and the 32 month group to the 32 norm group. Since EDMA uses nonparametric procedures to calculate significant differences between two groups, we report the *P*-values and confidence intervals and remind the reader that a study with larger samples may or may not confirm our results. Results from these analyses will suggest whether or not this dysmorphology increases with age and will illustrate those differences that exist between normal and trigonocephalic phenotypes.

Method of Analyses

Euclidean Distance Matrix Analysis (EDMA) is a landmark-based method that compares forms and/or growth patterns between two populations in two or three dimensions (Lele and Cole, 1996; Lele and Richtsmeier, 1991, 1995; Richtsmeier et al., 1998). EDMA compares forms by first calculating a mean form matrix (FM) from landmark coordinate data for each population then tests for significant differences between them using nonparametric bootstrap procedures (Lele and Richtsmeier, 1991). A FM contains mean linear distances computed for all landmark pairs within each population. The FMs for two populations are compared by computing a form difference matrix (FDM). Simply, the FDM reports a ratio (population 1/population 2) of like linear distances calculated for all landmark pairs within each population. In this study, we are trying to determine the changes in form that occur during growth and how these changes contribute to the dysmorphologies of trigonocephaly. To do this, we compared the 5 month to the 14 month group to summarize those changes that take place from 5 to 14 months. We also compared the 14 month to the 32 month group to quantify the changes that occur during this 18-month period.

When like inter-landmark distances are the same between the two groups, the FDM ratio equals 1. If an inter-landmark distance in the numerator group is larger relative to that same inter-landmark distance in the denominator group, the FDM ratio will be greater than 1. If an inter-landmark distance in the numerator group is smaller relative to that same inter-landmark distance in the denominator group, the FDM ratio will be less than 1. The actual value of the FDM provides a relative measure of a specific linear distance in the two populations being compared. The further the value of the FDM ratio is from 1, the greater the difference is for a given inter-landmark distance between the two populations.

A nonparametric bootstrap algorithm tests for significant differences in overall shape of the two samples being compared ($P \leq 0.05$; Lele and Richtsmeier, 1991). Another nonparametric procedure calculates confidence intervals for each linear distance to determine which linear distances are significantly different between the two samples ($\alpha = 0.10$; Lele and Richtsmeier, 1995). This provides a test for localized differences between the two groups.

Growth patterns can also be compared using EDMA (Richtsmeier and Lele, 1993). Instead of comparing two mean forms, two growth intervals are compared. For example, in this study, there are three age groups (Table 2). The pattern of growth that occurs between the 5 month and 14 month groups (hereafter referred to as the 5–14 month interval) will be compared to the growth pattern that occurs between the 14 month and 32 month groups (hereafter referred to as the 14–32 month interval).

EDMA compares growth patterns between two age intervals in a series of steps. First, a form matrix (FM) is calculated for each sample being considered: 5 month, 14 month, and 32 month groups. Next, the pattern of growth that occurs within the 5–14 month interval is expressed as a growth matrix (GM) by comparing the FMS of the 5 month and 14 month groups. A GM reports a ratio of like linear distances for every possible landmark pair (using the older sample values in the numerator) and therefore is mathematically equivalent to a FDM. Another GM is created for the 14–32 month interval. Finally, the patterns of growth between the 5–14 month and 14–32 month intervals are contrasted by calculating a growth difference matrix (GDM). The GDM compares the two GMs by calculating a ratio of the change recorded for each linear distance in the two age intervals. This ratio uses the value of the GM calculated for the older age interval in the numerator (14–32 month interval) and the value of the GM calculated for the younger age interval in the denominator (5–14 month interval). If the growth observed for an inter-landmark distance in the older interval (the numerator) is greater than growth of the same inter-landmark distance in the younger age interval (denominator), the ratio will be greater than 1. This indicates that local growth experienced in the older interval is relatively

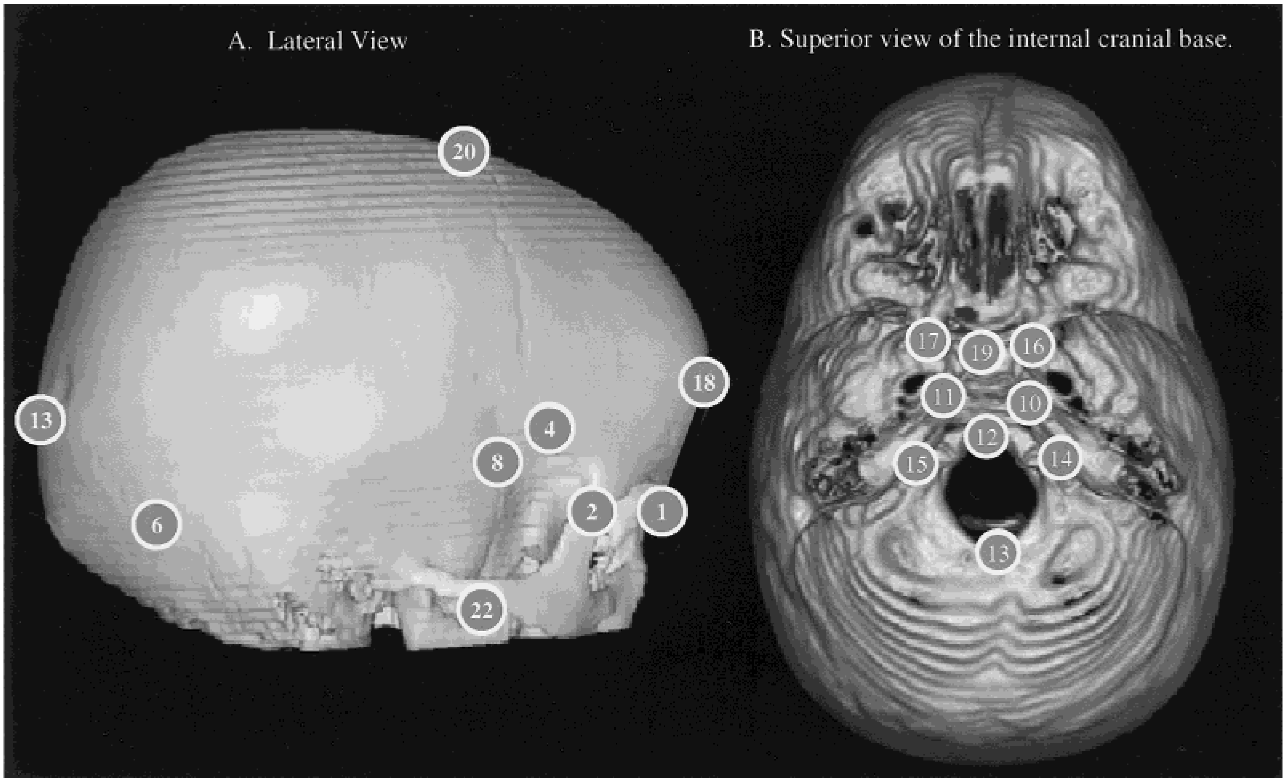

Fig. 1. The landmarks listed in Table 1 are illustrated. **A:** Only right-sided landmark for landmarks that occur bilaterally are illustrated. **B:** Landmarks along the endocranial surface of the basicranium.

TABLE 2. Sample sizes and age distributions for the metopic patients and dry skulls

Metopic developmental age samples	Age in weeks
5 month group (mean age = 23.3 weeks, about 5 months)	
Patient 1	13
Patient 2	17
Patient 3	20
Patient 4	28
Patient 5	38
14 month group (mean age = 57.6 weeks; about 14 months)	
Patient 6	41
Patient 7	42
Patient 8	43
Patient 9	60
Patient 10	78
Patient 11	82
32 month group (mean age = 131.75 weeks; about 32 months)	
Patient 12	99
Patient 13	104
Patient 14	151
Patient 15	173
Normal developmental age samples	
14 norm (mean age = 12 ± 6 months, n = 2)	
32 norm (mean age = 35 ± 6 months; n = 2)	

greater than that experienced during the younger interval. If the ratio is less than 1, then the amount of growth experienced local to an inter-landmark distance in the older interval is less than the amount of growth experienced by that same inter-landmark distance in the younger interval. The collection of these localized values enables comparison of growth patterns.

TABLE 3. Traits associated with metopic synostosis that were used to test the hypothesis that trigonocephaly is a self-correcting deformity*

Morphological trait	Linear distance (abbreviation, number)
Interorbital breadth	rfzj-lfzj (1–2)
Superior bitemporal breadth	rptn-lptn (4–5)
Inferior bitemporal breadth	rsphsq-lsphsq (8–9)
Height of the lateral orbit wall	rtzj-rfzj (21–2); ltzj-lfzj (22–3)
Anteroposterior length of the skull	lam-brg (13–20); lam-glab (13–18); rast-glab (6–18);
Triangular configuration of the skull	last-glab (7–18); rfzj-glab (2–18); lfzj-glab (3–18); rptn-glab (4–18); lptn-glab (5–18)

*Locations of landmark numbers are illustrated in Figure 1 and defined in Table 1.

RESULTS

Form Differences

To test the hypothesis that trigonocephaly is a self-correcting deformity, the 5 month group was compared to the 14 month group and the 14 month group was compared to the 32 month group. These comparisons describe form changes of the trigonocephalic skull through time. Given our chosen level of significance, the 5 month and 14 month groups are similar in shape (P = .081). However, there are regions of localized differences between the 5 month and 14 month groups as indicated by confidence intervals ($\alpha = 0.10$). Linear distances that display no form change from 5 to 14 months are not shown and indicate regions of the skull that do not change significantly during this interval. (EDMA outputs are available upon request.)

The linear distances that define interorbital breadth (Fig. 2B, 2–3) and superior bitemporal breath (Fig. 2B, 4–5) increase, widening the upper face and forehead in the 14 month group, relative to the 5 month group. The oblique measure of the zygomatic bones in part reflect the dimensions of the lateral orbital walls (Fig. 2A, 22-2, 23-3) and are larger in the 14 month group. Differential growth of other linear distances that describe the triangular configuration of the neurocranium (Table 3) are also larger and in the 14 month group, relative to the 5 month group (Fig. 2A, 6–18, 18–20; Fig. 2C, 6–7, 14–15). Linear distances between the frontozygomatic junctions and glabella (Fig. 2B, 2–18, 3–18) and nasion and glabella (Fig. 2B, 1–18) possess no form changes. This suggests that the upper face and forehead remain unchanged along the superoinferior axis, between the 5 and 14 months. The posterior cranial fossa displays the greatest magnitudes of difference, localized along mediolateral axes (Fig. 2C). There are no form differences along endocranial surfaces of the anterior and middle neurocranium (Fig. 2C,D). The posterior third of the neurocranium widens faster than the middle of the neurocranium and face while the length of the neurocranium increases faster than the width of the anterior and middle neurocranium, maintaining and enhancing trigonocephalic dysmorphologies.

To further test the hypothesis that trigonocephaly worsens with age, the 14 month group was compared to the 32 month group. In this comparison, there were significant differences ($P = 0.03$) in the overall form of the trigonocephalic skulls. Figure 3A–D illustrates linear distances that are significantly different between the 14 month and 32 month groups as indicated by confidence intervals ($\alpha = 0.10$). (EDMA outputs are available upon request.)

In the 14 month to 32 month group comparison, the linear distance between nasion and glabella displays the largest magnitude of form difference (Fig. 3B, 1–18). In fact, all the linear distances listed in the last row in Table 3 are much larger in the 32 month group, relative to the 14 month group. Superior bitemporal breadth (Fig. 3B, 4–5) remains unchanged between the 14 month and 32 month group, while inferior bitemporal breadth becomes narrower in the 32 month group as a result of an increase in the linear dimensions that surround it (Fig. 3B, 8–9). Linear distances indicative of anteroposterior lengthening of the skull as defined in Table 3 show no form changes. However, linear distances that cross the middle cranial fossa connecting endocranial landmarks with glabella suggest an anteroposterior lengthening of the anterior and middle cranial fossae (Fig. 3D).

To test the hypothesis that the dysmorphologies associated with trigonocephaly are produced by a lack of vertical growth of the face and neurocranium, the previous form comparisons (Figs. 2A–D, 3A–D) were inspected to determine along which axes form changes were occurring. In the first form comparison (5–14 months), increases in superoinferior and anteroposterior form changes dominate the neurocranium (Fig. 2A). A disproportionate amount of change occurs along the mediolateral axis in the face (Fig. 2B) and posterior skull base (Fig. 2C). The greatest magnitudes of change occur in the neurocranium along oblique axes (Fig. 2A, 1–18; 6–18; 6–20, 13–20, 16–20) that have superoinferior (vertical) as well as anteroposterior (horizontal) components. In the neurocranium, there is an increase in vertical and horizontal dimensions, but the face displays a lack of vertical change over this interval.

In the second comparison (14–32 month), there are no superoinferior changes occurring in the neurocranium (Fig. 3A), indicating a lack of vertical growth. However, several linear distances connecting facial landmarks to glabella lie along oblique superoinferior and anterosuperior axes suggesting changes in the vertical dimensions of the face (Fig. 3B, 22–18, 23–18, 1–18; 2–18, 3–18, 4–2, 3–5). During this age interval, changes in the neurocranium do not occur along the superoinferior axis. However, the face shows changes that are oriented along oblique superoinferior and anteroposterior axes.

Growth Comparisons

Since the previous results suggest that trigonocephaly worsens with age, we compared the pattern of growth for the 5–14 month (younger age) interval with the pattern of growth for the 14–32 month (older age) interval. Confidence intervals ($\alpha = 0.10$) were used to determine localized differences between the growth patterns of these two intervals (Fig. 4A–D). Solid lines represent linear distances that experience significantly more growth in the older age interval relative to the younger age interval. Dotted lines represent linear distances that experience significantly less growth during the older age interval relative to the younger age interval. Distances between landmarks that are not labeled display no differences in the magnitude of growth between the two intervals. While there is considerably less time in the younger age interval (9 months) relative to the older age interval (18 months), our results indicate that more growth is occurring within the younger age interval reflecting the higher rates of relative growth documented in the craniofacial complex during the first year of postnatal life (Burdi, 1969; Enlow, 1986; Sperber, 1989).

In the older age interval, the anterior neurocranium and forehead experience relatively less growth along oblique (superoinferior and anteroposterior) and mediolateral axes with three exceptions (Fig. 4A–D). Large increases of growth are observed for the older age interval between nasion and glabella (Fig. 4A,B, 1–18) and the frontozygomatic junctions and glabella (Fig. 4B, 2–18, 3–18). The older age interval also exhibits relatively less growth between the intersections of the left and right parietosphenoid and squasmosal sutures (Fig. 4B, 7–8) and the left and right pterions with nasion (Fig. 4B, 1–4, 1–5). These patterns narrow the temporal region, enhancing the triangular dimensions of the trigonocephalic skull in the older age interval. Additionally, decreases in growth between the left and right parietosphenoid and squasmosal sutures with nasion (Fig. 4B, 1–8, 1–7) also enhance the triangular dimensions of the forehead in the older age interval.

The middle cranial fossa grows relatively less along oblique (Fig. 4D, 14–16, 15–17) and mediolateral (Fig. 4D, 14–15) axes in the older age interval. The anterior cranial fossa displays relatively more growth along the anteroposterior axis (Fig. 4D, 16–18, 16–17) in the older age interval, while the inferior aspect of the posterior skull (Fig. 4C) shows age related differences in growth. There are no differences in growth patterns within the posterior cranial fossa (Fig. 4D).

The anterior neurocranium and forehead are dominated by patterns of growth decreases (Fig. 4A,B) in the older age

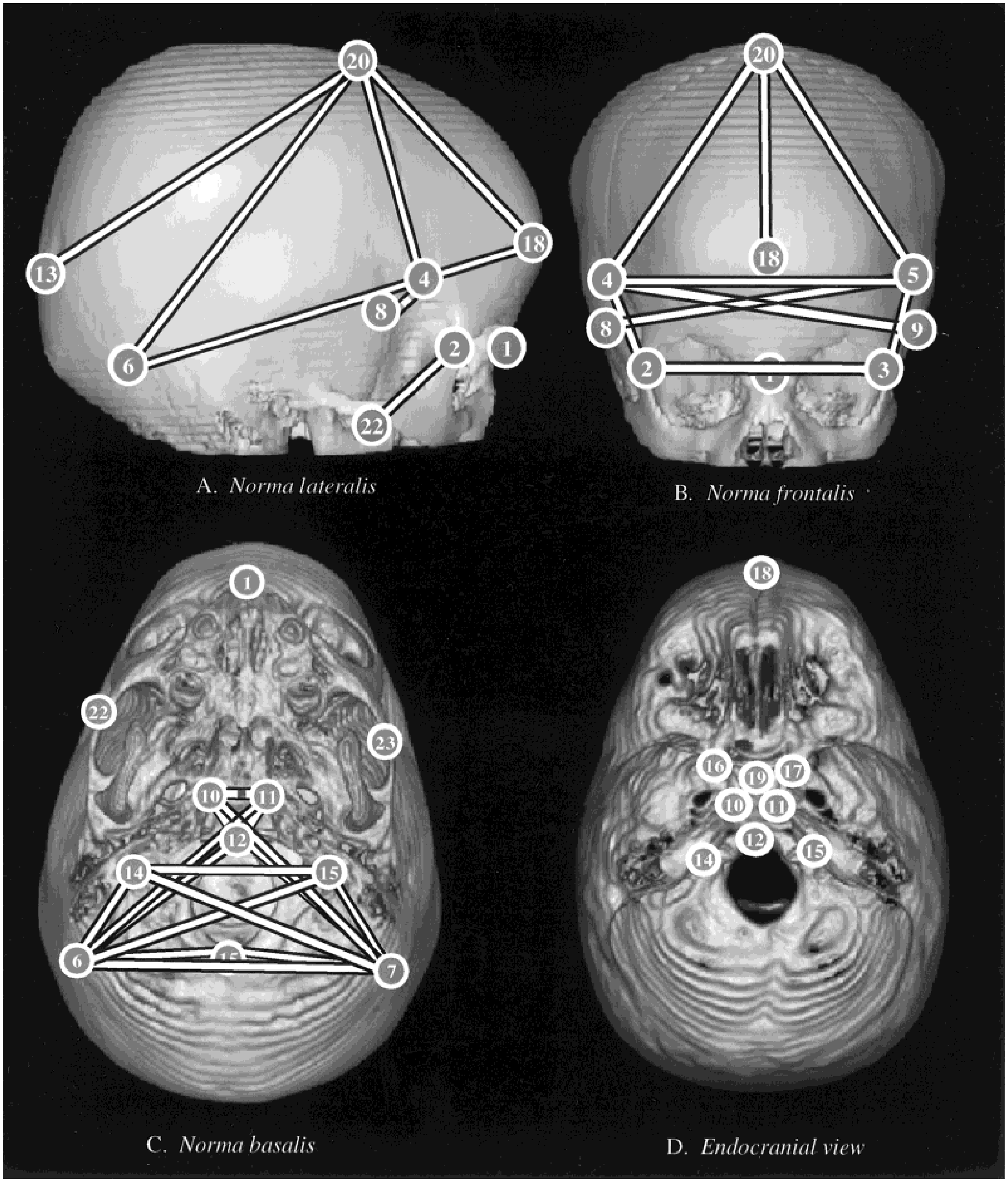

Fig. 2. Linear distances that were significantly different in the comparison between the 5 month and 14 month groups are illustrated on four 3D-CT reconstructions of a trigonocephalic skull. The views are: (**A**) lateral; (**B**) frontal; (**C**) inferior; (**D**) endocranial surface of the basicranium. Solid lines indicate linear distances that are greater in the 14 month group, while dotted lines indicate linear distances that are smaller in the 14 month group.

interval relative to the younger age interval. This pattern is also present in the posterior basicranium (Fig. 4C). The opposite is true for the upper face that displays relatively more growth along vertical dimensions in the older age interval (Fig. 4B, 1–18, 2–22, 3–23). Finally, there is a decrease in the breadth of the inferior temporal region (Fig. 3B, 7–8). These results suggest that patterns of differential growth produce the trigonocephalic phenotype.

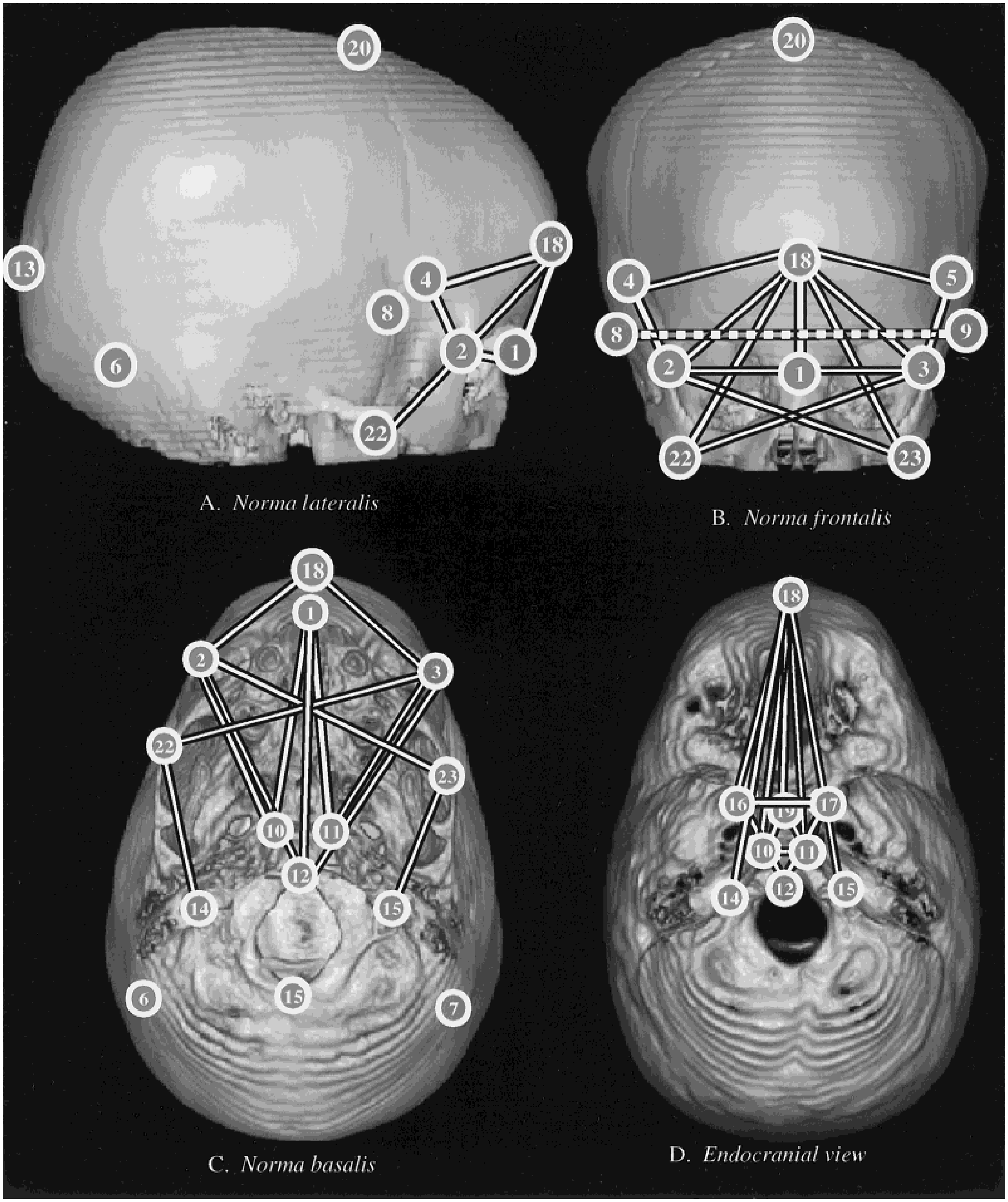

Fig. 3. Linear distances that were significantly different in the comparison between the 14 month and 32 month groups are illustrated on four 3D-CT reconstructions of a trigonocephalic skull. The views are: (**A**) lateral; (**B**) frontal; (**C**) inferior; (**D**) endocranial surface of the basicranium. Solid lines indicate linear distances that are greater in the 32 month group, while dotted lines indicate linear distances that are smaller in the 32 month group.

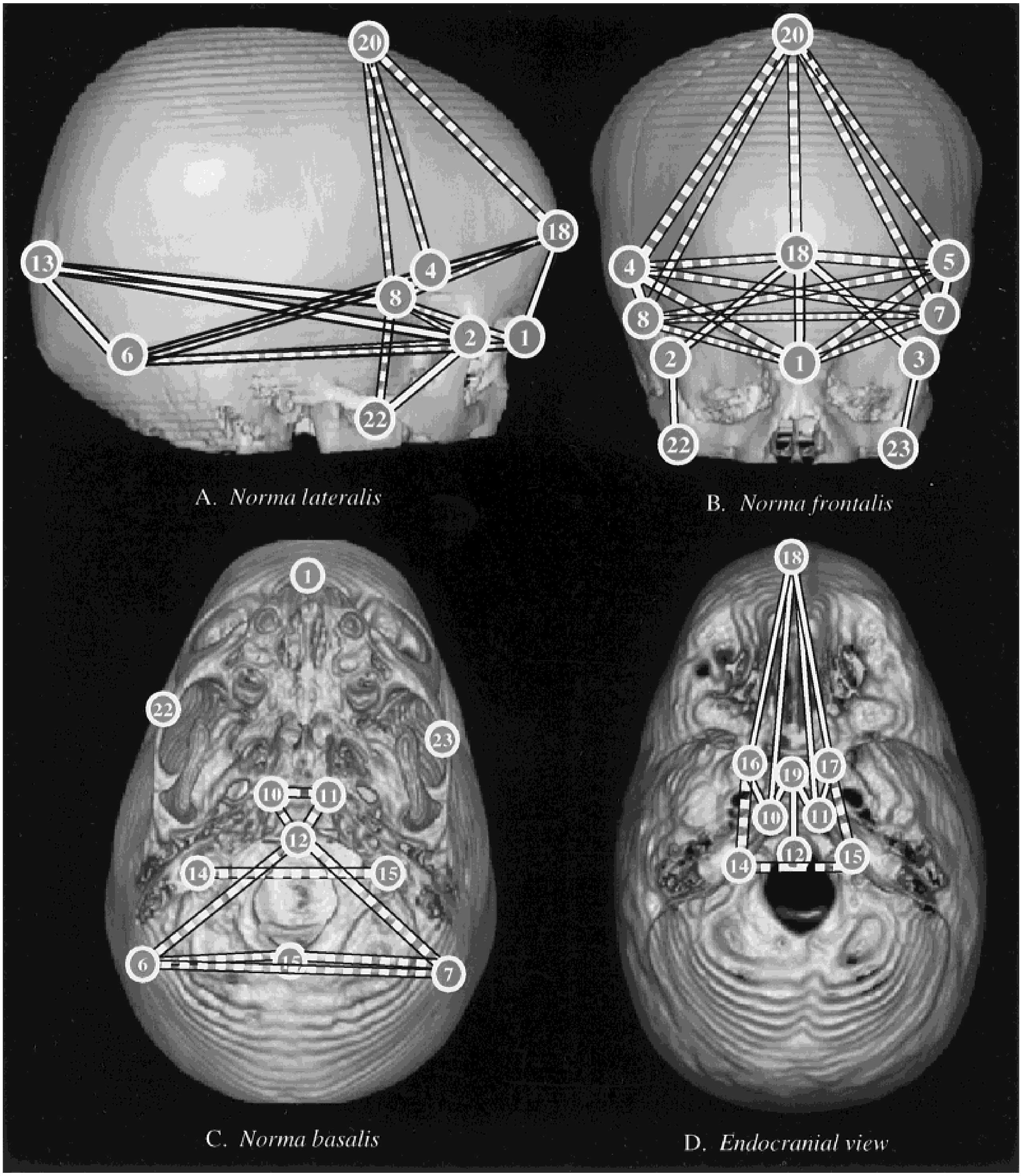

Fig. 4. Linear distances that displayed more growth in the comparison between the 5–14 month and 14–32 month intervals are illustrated on four 3D-CT reconstructions of a trigonocephalic skull. The views are: (**A**) lateral; (**B**) frontal; (**C**) inferior; (**D**) endocranial surface of the basicranium. Solid lines indicate linear distances that displayed significantly more growth in the 14–32 month interval, while dotted lines indicate linear distances that displayed significantly less growth in the 14–32 month interval.

Aged-Matched Form Comparisons

The reader is reminded that while nonparametric bootstrap procedures were used, statements about the statistical significance should be interpreted with caution. The overall form of the skull is significantly different ($P < 0.01$) between the metopic (14 month) and normal (14 norm) groups. Figure 5A–D illustrates the differences and similarities between the metopic (14 month) and normal (14 norm) groups. (EDMA outputs are available upon request.)

Overall, the metopic group is longer (anteroposteriorly) and taller (superoinferiorly) than the normal group. Linear distances that define the triangular dimensions of the trigonocephalic skull (Table 3; last row) are all larger in metopic group (Fig. 5A,B). Oblique linear distances containing anteroposterior and superoinferior components (Fig. 5C, D) also suggest that metopic group is longer anteroposteriorly and taller superoinferiorly, relative to the normal group. Interorbital, superior, and inferior bitemporal breadth display no differences between the normal and age-matched groups. Relative to the normal group, the metopic group displays an increase in vertical dimensions of the middle neurocranium (Fig. 5A, 20–22). Other linear distances that suggest an increase in vertical growth in the metopic group are oriented along oblique axes (Fig. 5A, 1–18, 6–20, 18–20; Fig. 5B, 2–22, 3–23). The anterior cranial base (Fig. 5D, 16–18, 17–18, 18–19) is longer while the posterior cranial base is shorter (Fig. 5D, 12–19) in the metopic group, relative to the normal group. These results suggest that a trigonocephalic skull is taller along a superoinferior axis, longer along an anteroposterior axis and wider than a normal skull at 14 months.

The overall form of the skull is significantly different ($P < 0.01$) between the metopic (32 month) and normal (32 norm) groups. Figure 6A–D illustrates the differences and similarities between the metopic and normal groups. Relative to the normal skull, the metopic skull is longer along the anteroposterior axis (Fig. 6A, 13–18, Fig. 6C, 1–15) and is comparatively narrow along a mediolateral axis (Fig. 6B, 8–9, 8–18, 9–18). Additionally, the linear distances that indicate an increase in the vertical dimensions of the neurocranium in the 14 month–14 norm comparison are maintained in this comparison. Finally, the middle cranial fossa is wider (Fig. 6D, 16–17) and the anterior cranial base is longer (Fig. 6D, 18–19) in the metopic group, relative to the normal group.

Although results from these cross-sectional age-matched comparisons are based upon very small sample sizes, they support the results from our previous analyses and suggest several interesting patterns of form differences. First, between 14 and 32 months, the trigonocephalic form maintains a larger anteroposterior length of the neurocranium relative to a normal form. Second, through time, the trigonocephalic form develops a narrow inferior temporal region along a mediolateral axis and the forehead maintains its triangular dimensions (i.e., it does not self-correct). Third, the cranial base lengthens between 14–32 months. Fourth, the trigonocephalic patients and normal skulls possess similar middle cranial fossa widths at 14 months. However, by 32 months the middle cranial fossa is wider in trigonocephalic patients, relative to the normal skulls.

DISCUSSION

Welcker (1862) divided trigonocephaly into two broad categories: (1) complex and (2) simple or isolated, i.e., not associated with any other craniofacial anomalies. The patients in our study were of the latter type with a sex ratio of three males to one female, agreeing with the male predominance of other reports (Anderson, 1981; Anderson et al., 1962; Cohen, 1986; Delashaw et al., 1986; Dhellemmes et al., 1986; Dominguez et al., 1981; Eppley and Sadove, 1994; Friede et al., 1990; Kolar and Salter, 1997; Shillito and Matson, 1968).

Dominguez et al. (1981) suggested that trigonocephaly is a self-correcting deformity that children “grow out” of. However, results from other investigations suggest that trigonocephaly is not a self-correcting deformity (Kolar and Salter, 1997; Posnick et al., 1994). Our analysis enabled rejection of the null hypothesis that trigonocephaly is a self-correcting deformity. Our results suggest that the wide range of dysmorphologies associated with trigonocephaly worsen with the advancing age of the child in the age period studied (5 months to 3 years).

Kolar and Salter (1997: pp. 346) suggest that “vertical growth restriction, as expressed in reduced auricular head height [vertex of the skull to porion] is one of the most significant components of overall anterior craniofacial growth anomalies in metopic synostosis.” Our results indicate that both increases and decreases in vertical growth of the skull are present in the development of trigonocephalic morphology. Specifically, while a lack of vertical growth in the neurocranium is not apparent until after 14 months, the neurocranium displays an increase of vertical growth between 5 and 14 months. During the 14 to 32 month interval, the face displays increases in vertical and anteroposterior growth. Finally, our results suggest that relative to age-matched normal skulls, there is an increase in the vertical dimensions of the neurocranium. From these results, we conclude that the dysmorphologies accompanying trigonocephaly result from increases and decreases in growth along superoinferior axes that are temporally sensitive and vary with respect to location within the craniofacial complex. These results are based upon cross-sectional data and may change when the hypothesis is tested with longitudinal data.

The effect that metopic synostosis has on the endocranium has been largely ignored. Between 5 and 14 months, there are no significant form changes occurring along endocranial aspects of the basicranium (Fig. 2D). Form changes are localized to the ectocranial surface along mediolateral and anteroposterior axes (Fig. 2C). Between 14 and 32 months, form changes occur along the endocranial surface of the basicranium (Fig. 3D). Relative to normal skulls, the cranial base lengthens and the middle cranial fossa widens with increasing age in metopic patients (Figs. 5D, 6D). These results suggest that the dysmorphologies associated with trigonocephaly are not limited to the upper face and neurocranium and that these differences are temporally sensitive.

Our comparison of growth patterns between the 5–14 month and 14–32 month trigonocephalic age intervals suggest that there is more growth occurring in the face and basicranium (Fig. 4D) in the younger age interval. This was not unexpected since growth rates are known to be elevated between 0–1 years relative to years 1–3 (Burdi, 1969; Enlow, 1986; Sperber, 1989). Those linear distances

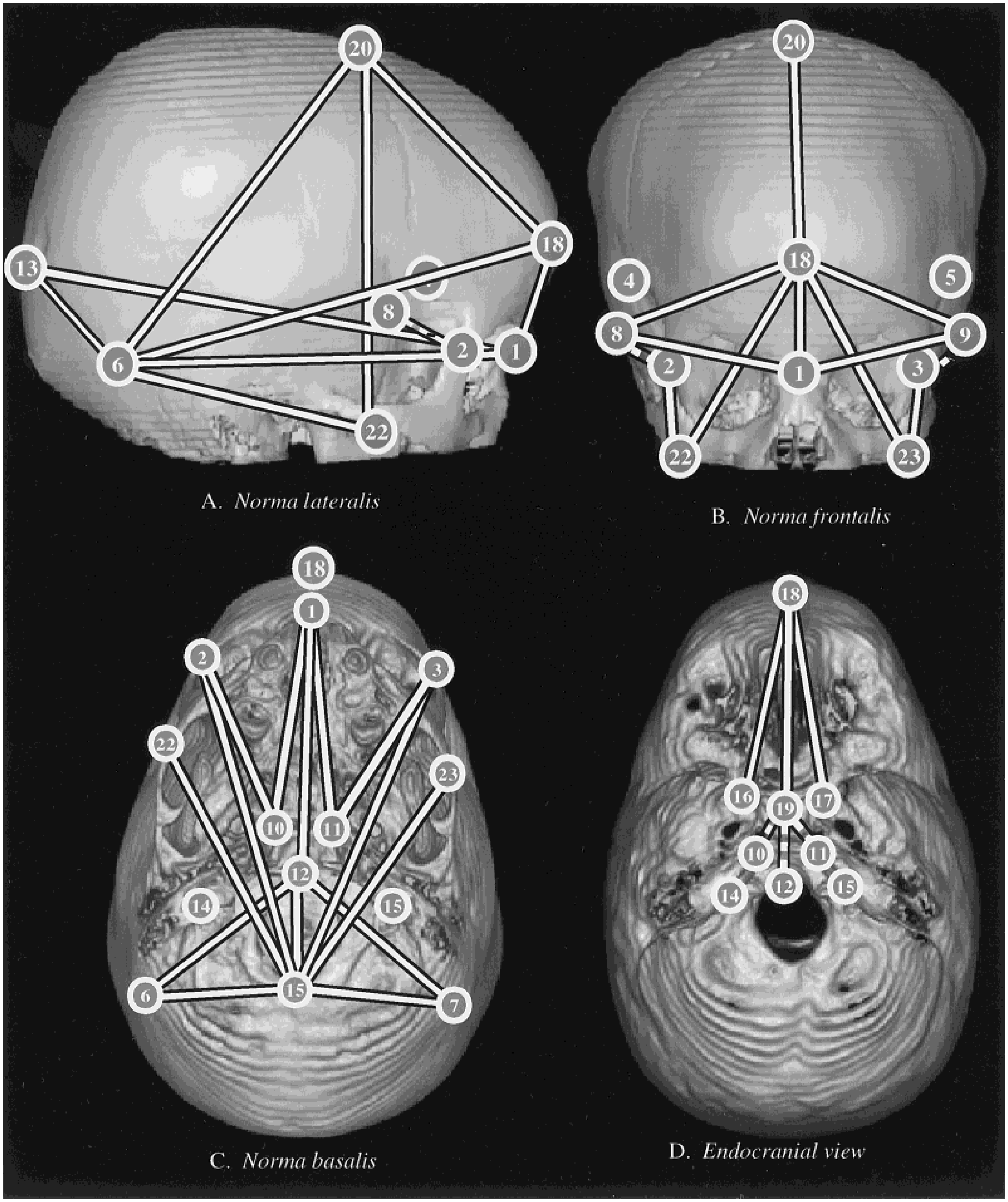

Fig. 5. Linear distances that are different in the comparison between the 14 month and 14 norm groups are illustrated on four 3D-CT reconstructions of a trigonocephalic skull. The views are: (**A**) lateral; (**B**) frontal; (**C**) inferior; (**D**) endocranial surface of the basicranium. Solid lines indicate linear distances that are greater in the 14 month group, while dotted lines indicate linear distances that are smaller in the 14 month group.

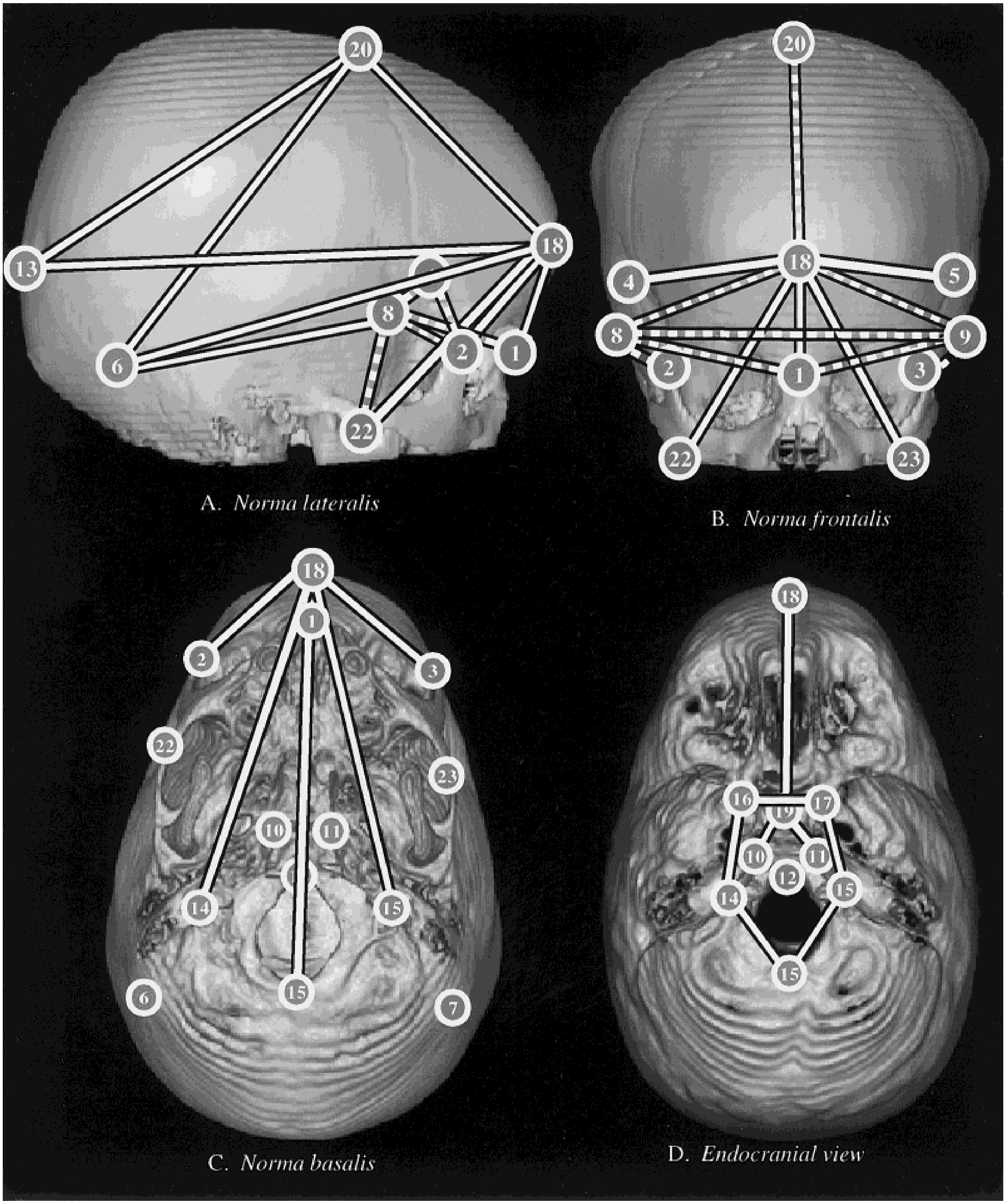

Fig. 6. Linear distances that are different in the comparison between the 32 month and 32 norm groups are illustrated on four 3D-CT reconstructions of a trigonocephalic skull. The views are: (**A**) lateral; (**B**) frontal; (**C**) inferior; (**D**) endocranial surface of the basicranium. Solid lines indicate linear distances that are greater in the 32 month group, while dotted lines indicate linear distances that are smaller in the 32 month group.

that show relatively greater increases in the older age interval reflect an anteroposterior lengthening of the neurocranium (Fig. 4A,D). These results, along with the previously discussed form comparisons, suggest that a lack of vertical growth is present only during the older age interval in trigonocephaly.

Data from other studies (Kolar and Salter, 1997; Posnick et al., 1994; Dominguez et al., 1981) are cross-sectional and lack a normal control group while our data are cross-sectional and include a small sample of normal dry skulls. Our results show that the form of the trigonocephalic skull is different from a normal skull and that these differences increase through time. These comparisons showed that relative to age-matched normal skulls, our trigonocephalic patients possess heads that are taller superoinferiorly and longer anteroposteriorly. Narrowing of the inferior temporal region follows increases in the anteroposterior length and superoinferior height of the neurocranium. Finally, linear distances that define the triangular dimensions of the forehead and face (Table 3, last row) increase through time in trigonocephalic patients relative to our age-matched normal skulls.

Our results indicate that trigonocephaly is not self-correcting and appears to worsen with age and illustrate that early growth of the trigonocephalic skull is characterized by vertical growth in the neurocranium and a lack of vertical growth in the face. Late growth is characterized by vertical growth in the face and a lack of vertical growth in the neurocranium. In light of these results, we cannot support the null hypothesis that a lack of vertical growth produces the trigonocephalic phenotype. We suggest that growth vectors that are temporally and regionally sensitive produce the trigonocephalic phenotype. Moreover, we found a temporal sequence of the development of the trigonocephalic phenotype; i.e., changes local to the neurocranium manifest themselves prior to those local to the forehead and orbits. Finally, these results indicate that dysmorphologies accompanying trigonocephaly are not restricted to the neurocranium and face, but are also present in the basicranium.

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