# Growth of the Cranial Base in Craniosynostosis

JOAN T. RICHTSMEIER, PH.D.
HANNAH M. GRAUSZ, A.B.
G. ROBERT MORRIS, PH.D.
JEFFREY L. MARSH, M.D.
MICHAEL W. VANNIER, M.D.

**The configuration of the neurocranium has long been used as a diagnostic tool in assessing infants with abnormal head shape. In the case of craniosynostosis, a characteristic shape is caused by a constraint placed on growth of the neurocranium by prematurely closed sutures and secondary accomodation to that constraint. This investigation is a preliminary test of our hypotheses of growth of the cranial base under these constraints. Three dimensional landmark coordinate data were collected from pre-, peri-, and postoperative CT scans of eleven patients from The Cleft Palate and Craniofacial Deformities Institute, St. Louis, MO. These data were used in two sets of analytical comparisons. Comparisons of preoperative and perioperative morphology were taken to represent preoperative growth, while comparisons of perioperative to postoperative CT scans represent postoperative growth. Finite-element scaling analysis (FESA) and Euclidean distance matrix analysis (EDMA) were used to make these comparisons. Our results show that in cases involving premature closure of the metopic, sagittal, and bilateral coronal sutures, predictions about growth of the cranial base made prior to analysis prove correct. In these forms of craniosynostosis there are characteristic and consistent changes in the cranial base in both pre- and postoperative growth. Preoperative and postoperative growth in patients diagnosed with unicoronal synostosis show a greater degree of individual variability and do not follow a predictable pattern.**

KEY WORDS: *morphogenesis, growth, cranial base, three-dimensional, computed tomography, craniosynostosis, finite-element scaling analysis, Euclidean distance matrix analysis*

Previous research focusing on craniosynostosis has shown several relationships. Primarily, we know that a neurocranial morphology is associated with various forms of premature suture closure. First noted by Virchow (1851), this relationship was explained as resulting from inhibited growth across fused suture(s), and compensatory growth of the neurocranium along the length of the closed sutures and local to patent sutures. Fundamentals of this explanation are still accepted as sound, but new observations and interpretations are adding to our current understanding of the production of neurocranial shape in craniosynostosis. For example, Jane and Persing (1986) have reported that compensatory growth seems to occur on only one side of the suture unless the suture is continuous. The authors conclude that compensatory growth does not strictly follow Virchow's predictions.

Previous research has also related basicranial morphology to premature neurocranial suture closure. This relationship was first studied and identified in autopsy and dry skull studies (Kreiborg et al, 1976; Kreiborg and Bjork, 1981, 1982; Anton, 1989), and has been studied recently using three-dimensional (3D) computed tomographic (CT) reconstructions (Marsh and Vannier, 1986, 1989; Marsh et al, 1986).

Reports from neurologic and plastic surgeons indicate that given certain conditions, a process of normalization (which does not mean that a normal shape will necessarily result) of

Dr. Richtsmeier is Assistant Professor of Cell Biology and Anatomy at the Johns Hopkins University School of Medicine. Hannah Grausz is a doctoral candidate in the Department of Cell Biology and Anatomy, Program in Functional Anatomy and Evolution, The Johns Hopkins University School of Medicine. Dr. Morris is Assistant Professor of Civil Engineering at the G.W.C. Whiting School of Engineering, The Johns Hopkins University. Dr. Marsh is Professor of Surgery, Plastic and Reconstructive, Associate Professor of Surgery in Pediatrics, and Medical Director of the Cleft Palate and Craniofacial Deformities Institute at The Washington University School of Medicine. Dr. Vannier is Professor of Radiology at the Mallinckrodt Institute of Radiology at The Washington University Medical Center.

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Reprint requests: Joan T. Richtsmeier, Ph.D., Dept. of Cell Biology and Anatomy, The Johns Hopkins University, School of Medicine, 725 N. Wolfe Street, Baltimore, MD 21205.

neurocranial skull shape may occur after surgical suture release (Jane & Persing, 1986).

Given the structural and hypothesized functional relationships (Moss, 1960, 1973) between the neuro- and basicranium, a predictable association between the specific suture closed and growth of the cranial base before and after surgery might be anticipated. Predictions may be based on a review of the current literature and the postulate that the cranial base and the neurocranium conform to one another in order to provide functional protection for the growing brain. Predictions may be "tested" by comparing them to results of three-dimensional analyses of growth of the cranial base in children diagnosed with various forms of premature suture closure. The testing of such predictions may be offered as a relatively new approach to the study of growth. The purpose of this study is to understand the effect of neurocranial surgery on the magnitude and direction of growth of the cranial base. Two morphometric techniques used to quantify the differences between forms are briefly described and the results of our analyses are presented.

## Study Design and Predictions of Cranial Base Growth

Landmark data were collected from longitudinal sets of computed tomographic (CT) scans from individual patients to quantify and describe growth of the cranial base in three dimensions. Two comparisons were made for each patient. Firstly, landmarks collected from a preoperative CT scan are compared to homologous landmarks collected from a "perioperative" scan. The timing of the perioperative scan varied from individual to individual in terms of its temporal relationship to the actual date of surgery, but usually was within the first postoperative week (see Table 1 for exact timing of CT scanning and surgery). Secondly, landmarks were collected from the perioperative scan and compared to homologous landmarks located on a postoperative scan of the same individual. In most cases, the postoperative CT was taken approximately 1 year after surgery. Each comparison used two quantitative techniques: finite-element scaling analysis and Euclidean distance matrix analysis (see below). For each

**TABLE 1 CT Scan and Surgical Procedure Information for Patients Diagnosed with Craniosynostosis**

| *Suture Synostosed* | *Case* | *Age at Surgery (months-days)* | *Age at Scan (months-days)* | *Surgical Procedure* |
|---|---|---|---|---|
| Metopic | 1* | 3-5 | 1-12<br>3-12<br>15-19 | Metopic and bicoronal craniectomy, frontal bone revision, bilateral superolateral orbital advancement |
| | 2 | 3-29 | 2-7<br>4-5<br>16-21 | Metopic and bicoronal craniectomy, frontal bone revision, bilateral superolateral orbital advancement |
| | 3 | 8-0 | 5-28<br>8-6<br>19-22 | Metopic and bicoronal craniectomy, frontal bone revision, bilateral superolateral orbital advancement |
| Sagittal | 1* | 7-22 | 7-21<br>8-13<br>19-21 | Extended sagittal strip craniectomy |
| | 2 | 2-30 | 2-29<br>3-7<br>15-9 | Extended sagittal strip craniectomy |
| Bircoronal craniectomy | 1* | 2-26 | 2-4<br>3-2<br>14-8 | Extended bicoronal frontal bone revision, bilateral superolateral orbital advancement |
| | 2 | 4-13 | 2-18<br>4-19<br>7-23 | Extended bicoronal craniectomy, perisagittal craniectomy, frontal bone revision, bilateral superolateral orbital advancement |
| | 3 | 3-18 | 3-15<br>4-13<br>17-10 | Extended bicoronal craniectomy, frontal bone revision, bilateral superolateral orbital advancement and mesial translocation |
| Right unicoronal unilateral | 1 | 4-6 | 4-4<br>4-11<br>15-21 | Extended bicoronal craniectomy, frontal bone revision, superolateral orbital advancement |
| | 2 | 6-8 | 5-20<br>6-24<br>18-1 | Extended bicoronal craniectomy, frontal bone revision, unilateral superolateral orbital advancement |
| | 3* | 2-26 | 1-21<br>3-21<br>14-30 | Extended bicoronal craniectomy, frontal bone revision, unilateral superolateral orbital advancement |

* Indicates cases illustrated in Figures 3 to 10.

case, results of the comparison of the preoperative with the perioperative scan were interpreted as representative of preoperative growth, while results of the second comparison, the perioperative with the postoperative scan, were interpreted as representative of postoperative growth. Although the exact surgical procedure varied from patient to patient, the cranial base was never directly manipulated. All infants underwent craniotomy with partial calvarectomy including removal of the synostosed suture(s). Infants with metopic and bicoronal synostosis also had bilateral superolateral orbital recontouring and repositioning. Superolateral orbital manipulation was unilateral for infants with unicoronal synostosis. No orbital manipulation was performed in infants with sagittal synostosis (See Table 1).

In the following presentation of our predictions of pre- and postoperative patterns of growth in various forms of synostosis and the discussion of our analytical results, we describe growth by analytical comparison of morphologies. Differences between forms are described in terms of magnitudes of change in specific anatomic directions over periods of time. Although information on both magnitude and direction of change is necessary for understanding growth patterns, the two do not necessarily behave in a cooperative fashion. In other words, direction and magnitude can be affected in ways that appear uncoupled, even though they are responding to the same stimuli during growth. This is an important distinction when discussing compensatory growth in craniosynostosis. Premature closure of a suture places a constraint on growth of the craniofacial complex that is not present in normal children. When we speak of compensatory growth we are not referring to the "catch-up growth" that is observed after the removal of an insult attributed to inadequate nutrition or disease. Compensatory growth in craniosynostosis refers to redirected growth; growth that occurs in directions and/or magnitudes consistent with the removal of a physical constraint placed on the system. This redirected growth, which may be very different from normal, provides for continued functional and structural integrity of the growing system.

## Predictions of Cranial Base Growth

In the following discussion of predictions of growth of the cranial base in craniosynostosis, reference will be made only to growth local to the landmarks listed in Table 2.

**Metopic synostosis**: Preoperative growth as measured between the preoperative and perioperative scan would be expected to show a lack of expansion along the mediolateral (ML) axis local to the landmarks of the anterior cranial base. Landmarks more posteriorly placed would be expected to show a disproportionate amount of growth along the ML and anteroposterior (AP) axis. Postoperative growth would be expected to show similar magnitudes of growth at all landmarks.

**TABLE 2 Key to Landmark Locations Visualized on CT Slices and Used in Analysis**

| | |
|---|---|
| Petrous intersection | Superior-most point at which the medial tip or apex of the petrous temporal abuts with the basisphenoid/basiocciput |
| Internal acoustic meatus | Center to the entrance of this canal on the posterior surface of the petrous temporal |
| Foramen ovale | Center of this foramen on the internal aspect of the middle cranial fossa or, in younger individuals, the center of the common foramen ovale and spinosum |
| Superior orbital fissure | Inferior-most point of superior orbital fissure |
| Anterior clinoid process | Most medial, psoterior aspect of the anterior clinoid process |
| Carotid canal | Center of the exterior mouth of the canal on the inferior surface of the petrous temporal bone |

All landmarks are bilateral.

**Sagittal synostosis**: Sagittal synostosis would be expected to affect all cranial base landmarks uniformly. Disproportionate growth would be expected to occur along the AP axis preoperatively with little or no growth along the ML and superoinferior (SI) axes. After surgery, growth would be expected to be uniform along all axes at all landmarks.

**Bilateral coronal synostosis**: Expected preoperative growth local to the anterior cranial base would be reduced in magnitude relative to growth of the posterior cranial base and would occur primarily along the ML and SI axes. Growth local to those landmarks located on the more posterior portion of the cranial base would reflect compensatory growth of greater magnitude directed primarily along the superoinferior and mediolateral axes. Postoperatively, magnitudes of growth would be equivalent across all landmarks studied. Direction of growth of the anterior cranial base might show catch-up growth specifically along the AP axis, or uniformly along all axes.

**Unilateral coronal synostosis**: Expected growth in unilateral coronal synostosis would be essentially the same as that described for bilateral coronal synostosis, except that growth would be restricted to the ipsilateral side. There would be a marked difference in magnitude and direction of growth between the ipsilateral and contralateral sides, the latter being greater in magnitude. In addition, laterally directed compensatory growth would be expected to occur on the more posteriorly placed landmarks on the ipsilateral side preoperatively but be reduced postoperatively. Growth of the contralateral side would show some lateral compensatory growth preoperatively and no compensatory growth postoperatively.

In the following sections of this paper, an explanation of the approach used to quantify growth of the cranial base in craniosynostosis is provided, and the analytical results are

compared to our predictions. It is stressed that the analytical results can only be accepted as preliminary because the sample size is small. Nonetheless, these analyses are a first step in understanding the kinematics of cranial base growth in craniosynostosis.

## METHOD

### Data Collection: 3D Data from CT Slices

There are two ways to obtain 3D coordinate data from CT scans at this time. Three-dimensional coordinates of biologic loci can be collected from 3D reconstructed images according to voxel location. Alternatively, using high resolution CT scans (2-mm slices), landmarks can be located on a single slice in 2 dimensions according to pixel row and column. Using pixel location, the third dimension is assigned according to table position of the slice on which the landmark is located. The Z coordinate of a landmark can be approximated to the closest millimeter when a landmark appears to be located within the thickness of a slice. Hildebolt et al, (1990) have completed a study that suggests the superiority of measurements from 3D-CT reconstructions over those obtained directly from original CT slices. However, Hildebolt's study uses a very small sample of skulls (N = 5) to test for the accuracy of data obtained from the two modalities of data collection and analyzes measurement error of linear distances, not three-dimensional landmark coordinate locations. Our experience has shown that characteristics of specific landmarks (sutural intersections versus foramina versus bony protuberances) make them more or less prone to error using one or the other modality of data collection. Currently, there is no compelling evidence for favoring one form of landmark coordinate data collection over the other. At the initiation of this project, collecting data from CT slices was the technique available to us and we chose to continue using this method for the sake of consistency throughout the duration of the project. Currently we are systematically studying data collected using the two methods in order to determine the source and magnitude of error associated with each data collection technique (Grausz, personal communication).

Data were collected from all scans for a single individual by one of two investigators (JTR, HMG) with expert knowledge of cross-sectional craniofacial anatomy. A total of 36 landmarks were collected initially. Data was collected from each scan at least twice by the same investigator and the coordinates compared. If there was variation in location of landmark placement by more than 2 mm between the two independent data collection sessions, the two investigators involved in data collection reviewed the scan as a team. After discussion, data was again collected by the original observer. If the landmark could still not be located within 2 mm of the agreed location, the landmark was dropped. The twelve landmarks used in this analysis represented a subset of biologic loci that could be located on slice data with a high degree of repeatability with errors in location of less than 2 mm. In most cases, the intraobserver error was within 1 millimeter.

### Subjects

The eleven patients used in this study presented with previously untreated craniosynostosis. They were evaluated with high resolution CT scans and treated by a single surgeon (JLM) at the Cleft Palate and Craniofacial Deformities Institute (CPCDI) of Washington University Medical Center. CT scanning was done under the supervision of a single radiologist (MWV) at the Mallinckrodt Institute of Radiology. Patients were chosen from patient records of the CPCDI on the basis of diagnosis and availability of pre-, peri-, and postoperative scans. Data from other patients are currently available and can be included in future research. Table 1 summarizes the patient data used in analysis organized by diagnosis.

### Method of Analysis

To understand the effect of surgical suture release on growth of the cranial base, two morphometric techniques, finite-element scaling analysis (FESA) and Euclidean distance matrix analysis (EDMA), were used. Both FESA and EDMA were applied to each data set to quantify growth as the difference between a single individual measured at various points in time. The usefulness of these methods in the study of craniofacial growth has been demonstrated elsewhere (Richtsmeier and Lele, 1990).

#### *FESA*

This method, based on engineering principles, was first introduced for the study of biologic form by Lewis et al (1980). A biologic object is divided into smaller geometric forms called finite elements. In this study we have modeled the cranial base as two contiguous hexahedral elements (Fig. 1). The location of each vertex is defined by the coordinate of a biologically meaningful landmark (see Table 2) that can be reliably located on each of the forms considered in the comparison.

FESA compares forms in order to determine the amount of change required to produce a target (older) morphology from an original (younger) morphology. The difference between forms is estimated from information on the location of landmarks at the vertices of the elements and the actual connectivity of these landmarks in the construction of the elements. The measurements produced are expressed in terms of strain (Lewis et al, 1980) local to each of the landmarks used to define the element. This means that information from surrounding landmarks is used to produce local measures of form change and that the design of elements for study is a critical part of FESA. Elements should be designed to encompass biologically homogenous areas; obvious morphologic

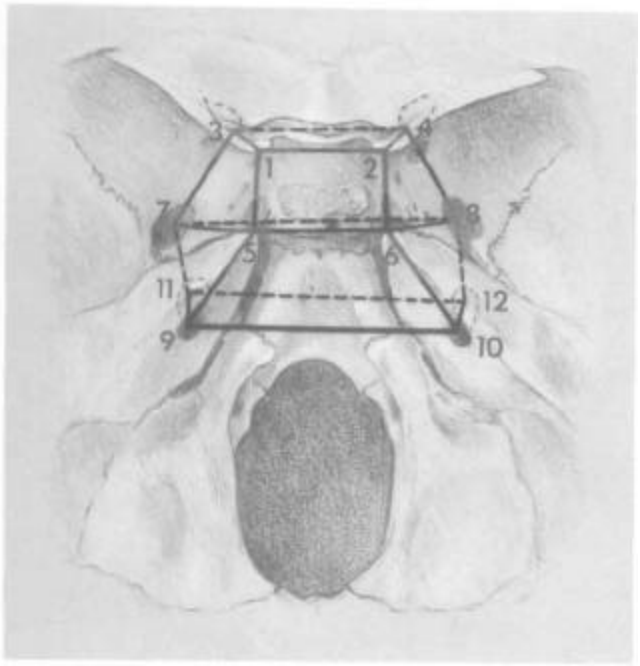


**FIGURE 1 Cranial base modeled as two contiguous finite elements. Numbers identify the landmark used in analysis as pictured in Figures 3 through 10. For clarification, the numbering system is as follows: 1,2 - right, left anterior clinoid process; 3,4 - right, left superior orbital fissure; 5,6 - right, left petrous intersection; 7,8 - right, left foramen ovale; 9,10 - right, left internal acoustic meatus; 11,12 - right, left carotid canal.**

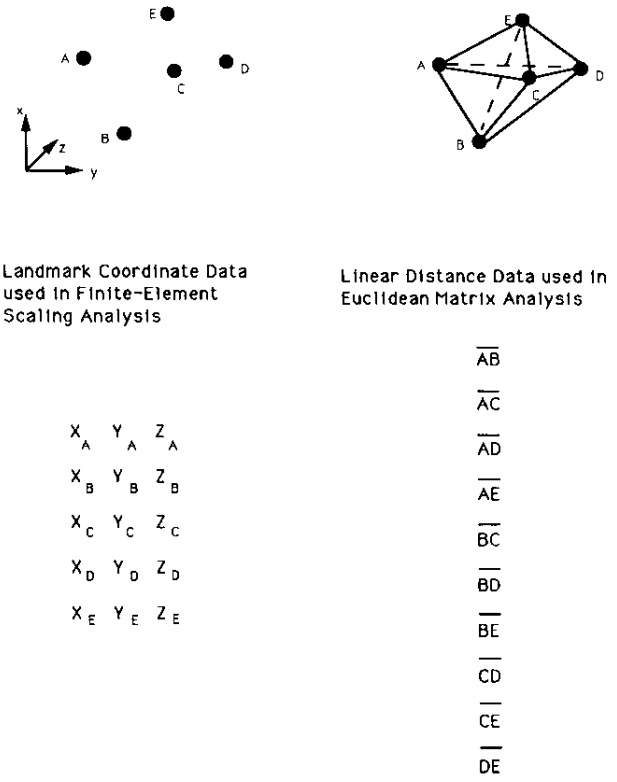


**FIGURE 2 Any form can be archived by a series of landmark coordinates or the matrix of all possible linear distances between landmarks. FESA uses landmark coordinates data for analysis while EDMA uses the matrix of all possible linear distances calculated from the original coordinate data for analysis. These represent equivalent ways to describe a geometric form.**

discontinuities should be used as boundaries for elements and not be encompassed within an element. The implications and potential dangers of improper element design in the application of FESA has been discussed by Lele (1991) and Richtsmeier et al (1990).

FESA produces information about the directions and magnitude of change at each landmark. Directional information can be rotated to a coordinate system consistent with anatomic directions (AP, ML, SI) for ease of interpretation. Detailed discussion of the mathematics of FESA and its application in the study of growth are available from several sources (Skalak et al, 1982; Lozanoff and Diewert, 1986; Richtsmeier and Cheverud, 1986; Cheverud and Richtsmeier, 1986; Richtsmeier et al, 1989).

In this study, we used landmark data from a preoperative CT scan as the initial form and compared it to homologous landmark data from a scan of the same individual taken at a later age, perioperatively (the target form). The results of this analysis were interpreted as a representation of preoperative growth that occurs local to each landmark. A second analysis uses this same perioperative scan as the initial object and compares it to landmark data from a scan of the same individual taken postoperatively (the target form). This comparison represents postoperative growth local to the landmarks considered. Individuals are grouped by diagnosed craniosynostosis and each group is considered independently.

### *EDMA*

This method for the comparison of forms was proposed by Lele (1991) and has been applied in several studies of craniofacial morphology (Richtsmeier and Lele, 1990; Grausz, 1990; Corner and Richtsmeier, 1991). EDMA uses landmark coordinate data to calculate all possible linear distances between landmarks. The matrix that describes a form based on landmark data is referred to as a Euclidean distance matrix or a form matrix. The relative location of all landmarks can be reconstructed in entirety from landmark coordinate data (as used in FESA) or from the Euclidean distance matrix (Fig. 2).

In applying EDMA, there are two Euclidean distance matrices. One represents the initial morphology, the other represents the target morphology. EDMA compares these Euclidean distance matrices by systematically comparing pairs of homologous linear distances as a ratio. The matrix of these ratios is called a form difference matrix. Inspection of the form difference matrix allows us to determine how the two forms differ by identifying those linear distances that are most and least different between the forms being compared.

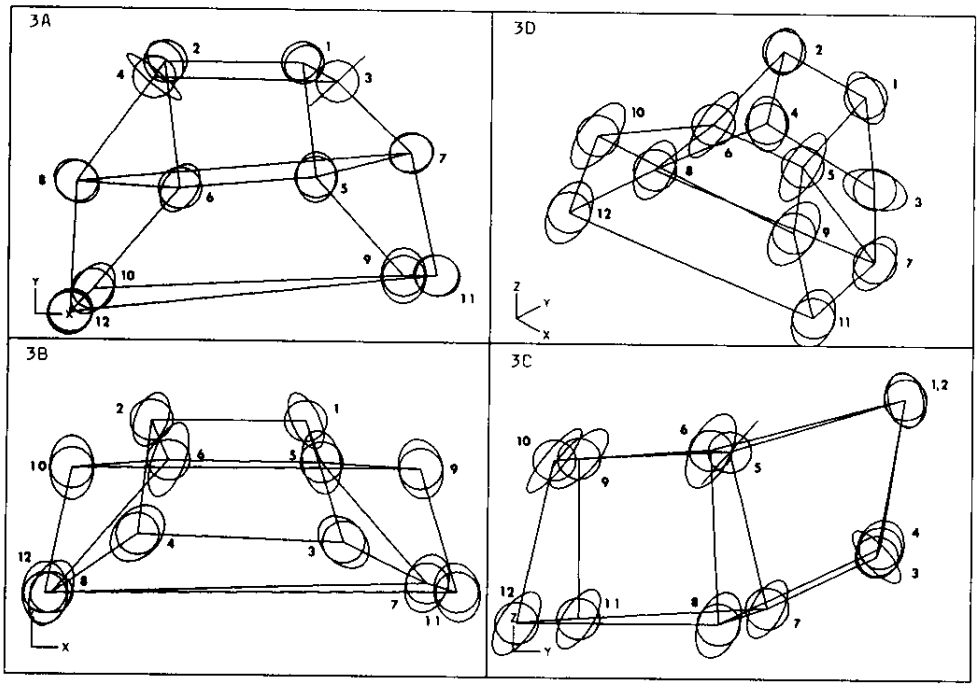


**FIGURE 3 Graphical representation of preoperative growth in metopic synostosis, as calculated by FESA. Numbers identify landmarks as enumerated in Figure 1. The X axis runs approximately mediolaterally, the Y axis runs approximately anteroposteriorly, and the Z axis runs approximately superoinferiorly. Because the X axis was placed collinear with a line connecting landmarks 1 and 2, they appear to overlie each other on the lateral view. Graphic displays of 3D analysis are projected onto four 2-dimensional planes. Tracing counterclockwise and starting in the upper left hand corner the views displayed are: *A*, superior view consistent with the perspective shown in Figure 2; *B*, posterior view looking through the back of the cranial base toward the anterior aspect; *C*, lateral view, the right side of the cranial base being closest to the observer; and *D*, oblique view from a posterosuperior perspective on the right side. Location of landmarks represents the older form in every comparison. Circles centered around each landmark represent the condition of no form change local to the landmark in deforming the younger into the older morphology. Ellipses that overlie the circles represent the magnitude and direction of change local to that landmark. For example, in *C*, all posteriorly placed landmarks show an increase along an axis that is oriented from posteroinferior to anterosuperior. Growth can also produce a reduction in dimensions along a particular axis. When this occurs, the minimum radius of the ellipse is smaller than the radius of the circle that represents no change. *C*, a reduction is seen along the axis oriented from posterosuperior to anteroinferior local to the landmarks on the posterior cranial base. In fact, reduction is so great in this direction local to landmark 5 that the ellipse has collapsed to a line. Figures 3 through 10 were produced by FIESCA software (Morris, 1989).**

If all elements of the form difference matrix are equal to 1 then there is no difference between the samples being compared. If all elements are not equal to 1, but are constant across the matrix, then the difference between the samples can be attributed exclusively to size. Those ratios that are less than 1 indicate that the linear distance is larger in the target form while ratios greater than 1 indicate a smaller linear distance in the target form. When the form difference matrix consists of numbers of varying values, differences between the forms are due to both size and shape.

In its simplest form, EDMA is a method based on inspection of the ratio matrix. Lele and Richtsmeier (1991) provide a method for identifying those landmarks that are most influential in discriminating one form from the other using EDMA. Because the problem addressed and sample sizes used here are not appropriate for statistical analysis, no statistical treatment of the data was included.

EDMA was applied in the same way as FESA. The form difference matrix that summarized the comparison of the preoperative scan with the perioperative scan was interpreted as representative of preoperative growth. The form difference matrix that compared the perioperative scan with the postoperative scan was interpreted as representing postoperative growth.

Detailed comparison of EDMA and FESA as applied in a study of craniofacial growth was reported by Richtsmeier and Lele (1990). In our current study, EDMA results were found to be in general agreement with FESA results and are therefore presented jointly. The accompanying figures are graphic representations of the comparison of forms using FESA. Output of EDMA is extremely cumbersome, so the results are presented in a discussion format. Analytical results of data analysis (computerized output) are available from the senior author on request.

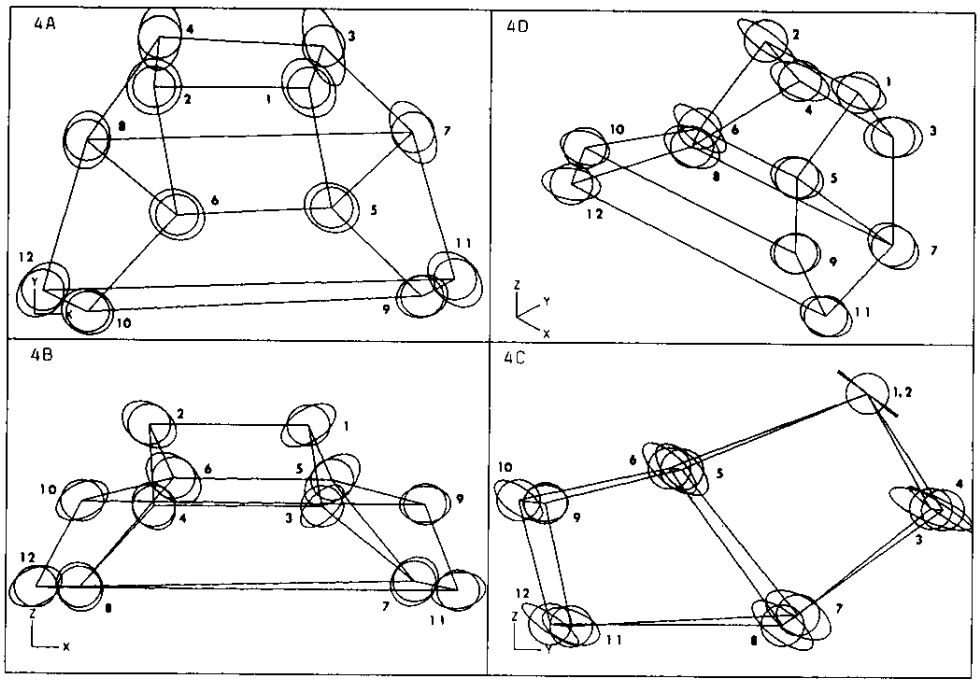


**FIGURE 4 Postoperative growth in metopic synostosis. (See Fig. 3 legend for further explanation.)**

## RESULTS

### Metopic Synostosis

Analysis of preoperative growth in metopic synostosis (Fig. 3) showed distinct patterns for the landmarks of the anterior and posterior cranial base. It is not the fossa because the carotid canal location was taken on the exterior of the basicranium. Fossa refers only to the interior of the cranium. The anterior-most landmarks (the superior orbital fissures and the anterior clinoid processes) showed marked reduction in size along the AP axis with growth but an increase in size along the SI axis. In all cases, asymmetry in growth of the cranial base was noted. Magnitudes of change were consistently greater on one side in every individual. The landmarks of the posterior cranial base, the carotid canals, and the internal acoustic meati showed a significantly greater magnitude of preoperative growth than the landmarks of the anterior cranial base. Most of the change at these posterior landmarks is in the SI direction with a large component of AP change. EDMA confirms these findings, particularly the high degree of change local to the carotid canals.

In the middle cranial base there is a less consistent pattern of preoperative directional change among the landmarks than in the anterior cranial fossa. However, the petrous intersections are consistently included in those linear distances that change least in the EDMA analyses of the patients with metopic synostosis. In one case, the petrous intersections and foramina ovale showed reduction along the AP axis and increase along the SI axis during preoperative growth (Case 1 in Table 1). In another case, there was an increase in AP growth (Case 2) and very little change at all in the third case. One possible explanation for the variability in growth patterns of the middle cranial base is the age of the individual at surgery. The individual who exhibited the least change in the middle cranial base (Case 3 in Table 1) was considerably older than the two children showing more exaggerated changes at these landmarks. The variation in growth kinematics at the landmarks in the middle cranial base in differently aged individuals may indicate changes in plasticity of the dysmorphic region through time.

In the comparison of the perioperative scan with the postoperative scan (Fig. 4), changes at all points across the cranial base were striking in their uniformity of magnitude and direction. The asymmetry in preoperative growth is not seen in postoperative growth. Every landmark showed maximal change along an axis that stretched from posterosuperior to anteroinferior (see Fig. 4C). A large increase in size along the ML axis was also found. The increase in ML growth was least apparent in the region of the superior orbital fissures and anterior clinoid processes in all cases, possibly indicating a slow rebound in compensatory growth at these landmarks after suture release. This response appears to be independent of the age of the individual as all three patients exhibited the same pattern in magnitude of change.

### Sagittal Synostosis

Analysis of preoperative growth of children diagnosed with sagittal synostosis showed almost no change along the ML

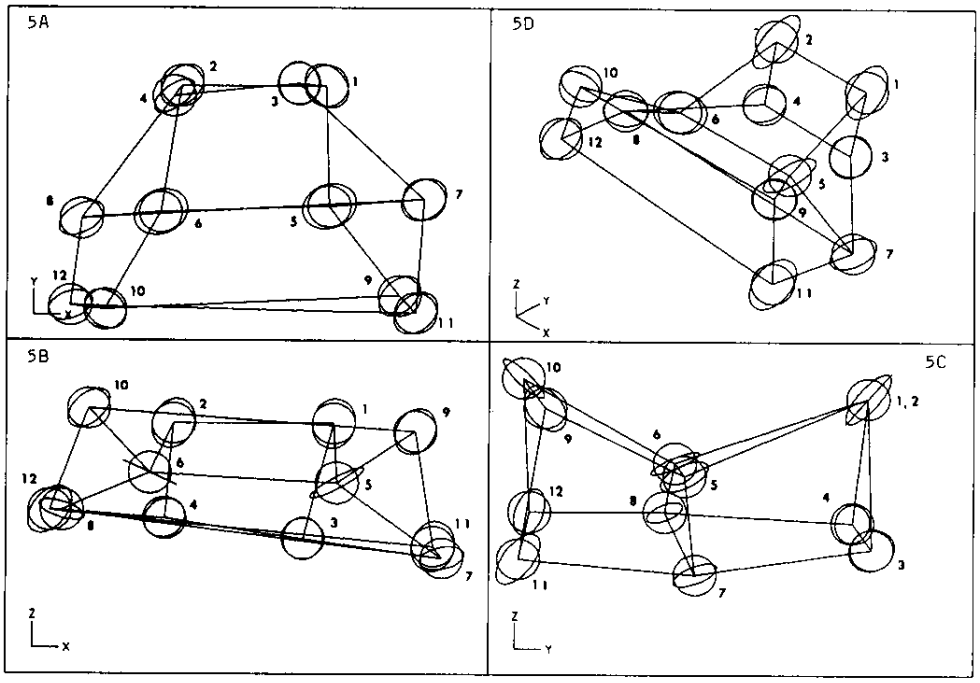


**FIGURE 5 Preoperative growth in sagittal synostosis. (See Fig. 3 legend for further explanation.)**

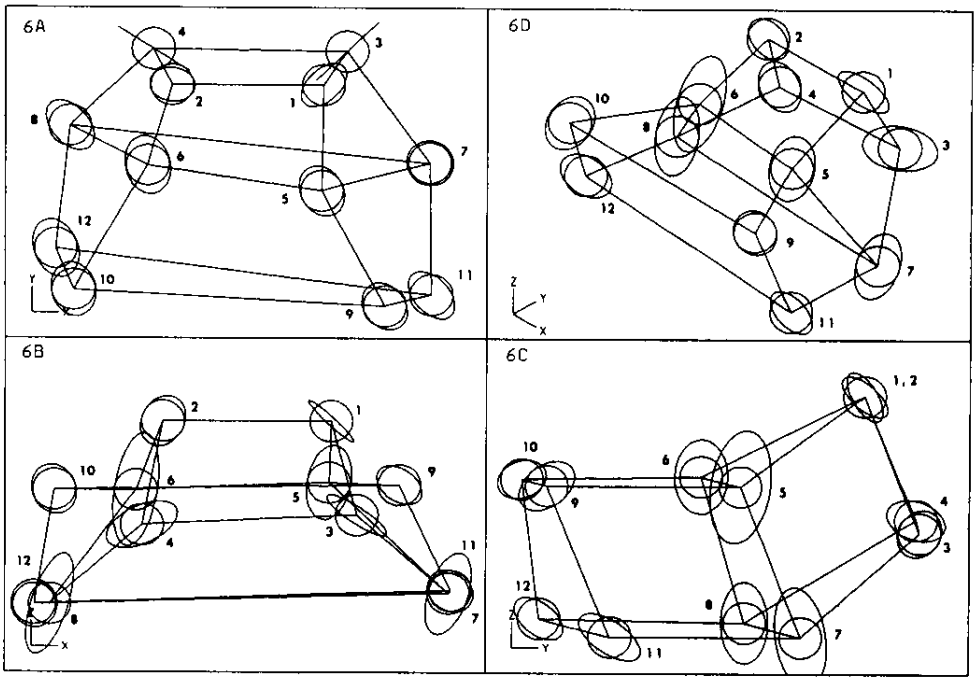


**FIGURE 6 Postoperative growth in sagittal synostosis. (See Fig. 3 legend for further explanation.)**

axis except for a small amount of ML expansion local to the foramen ovale and the petrous intersections (Figs. 5A and B). The greatest changes occurred along the AP axis, clearly seen in the landmarks of the posterior cranial base. Although AP is the principal direction of change at the anterior clinoid processes and superior orbital fissures, the degree of AP expansion of the anterior cranial base is small when compared to that occurring local to other landmarks of the cranial base. There is little growth in the SI direction during this preoperative period although a small amount of SI growth does occur

local to the most superior and posterior landmarks. Comparison of growth of the two patients showed similarities even though the discrepancy in their ages was large. This suggests that the pattern of growth determined by the constraints of a synostosed sagittal suture was less affected by the age of the individual than other forms of craniosynostosis.

Large changes in the direction and magnitude of growth in the cranial base can be seen during postoperative growth in sagittal synostosis, particularly in the middle cranial base (Fig. 6). At the petrous intersections and foramen ovale, there is marked growth in the SI direction as confirmed by EDMA. There is also AP growth at these same landmarks. Disproportionate amounts of growth in the SI direction were observed at the anterior clinoid processes, the superior orbital fissures, and the carotid canals. AP change was prominent at the anterior-most landmarks, especially at the superior orbital fissures. The lack of ML keep as is seen in the preoperative period continued in the postoperative year, possibly indicating a slow rebound.

### Bicoronal Synostosis

The magnitudes of shape change at all landmarks across the cranial base caused by growth during the preoperative interval in children diagnosed with bicoronal synostosis are very similar (Fig. 7). In the middle and posterior cranial base, size decreased along the AP axis, whereas a slight increase in the AP direction occurred local to the superior orbital fissures. The anterior clinoids exhibit little change in all directions, and no change along the AP axis. The middle and posterior cranial base landmarks showed growth mostly in the SI direction. This is especially true of the carotid canals, which showed the greatest magnitude of shape change of any of the landmarks. In one of the individuals, there is also a large magnitude of shape change at the petrous intersections and at foramina ovale (See Table 1 Case 2). EDMA substantiated a large amount of change at the carotid canals.

There were large differences between the preoperative and the postoperative periods in the children with bicoronal synostosis (Fig. 8). In the postoperative interval, every basicranial landmark showed a large amount of expansion in the AP direction, although this was not the principal direction of change in each patient. In one patient, growth occurred predominantly along the AP axis (Case 3), while in another there was also a large degree of change along the SI axis (Case 2). In all cases, there was substantial change at the posterior part of the cranial base, but varying amounts of change anteriorly. As in the preoperative period, the greatest magnitude of shape change occurred at the carotid canals, which was also reflected in the EDMA analysis.

### Unicoronal Synostosis

Unilateral coronal synostosis was the most difficult disorder to characterize because of the variation in growth patterns among individuals (Fig. 9). All of the preoperative comparisons showed differences between growth on the ipsilateral and contralateral sides (all patients studied had right coronal synostosis). On the ipsilateral side, there was absence of AP change, preoperatively except local to the anterior cranial base. The landmark demonstrating the greatest magnitude of change in all cases was the ipsilateral superior orbital fissure. This finding complements the observation of a recessed ipsilateral frontal bone and bossing of the contralateral frontal bone in unicoronal synostosis. Morphologically, the landmarks located on the petrous temporal bone were displaced laterally on the ipsilateral side, suggesting localized compensation (see Fig. 9). Magnitudes of shape change local to the middle and posterior cranial fossae landmarks were variable, sometimes greater on the ipsi- or contralateral side, or similar on the two sides. Size change during preoperative growth was equally variable at the middle and posterior fossae between individuals. In one case there was greater size change on the ipsilateral side of the entire cranial base (Case 3), in another case (Case 1) the contralateral side had greater change, and in Case 2 there was little difference between the sides. This last case may indicate the importance of the age of the patient at surgery. Case 2 was older than most patients who undergo corrective surgery for unicoronal synostosis. More growth was completed in this patient by the time the CT scans were taken so that the magnitudes of change during this period of time were not as profound as in the younger patients.

The postoperative growth in unicoronal synostosis (Fig. 10) was equally variable between individuals. In two of the three cases, growth was very similar across all landmarks, while in the third case (Case 3) the carotid canals showed a much greater rate of shape change than any other landmark. Growth occurred predominantly along the AP axis after suture release especially at the posterior part of the cranial base. There was also a major degree of SI growth. In the postoperative period, magnitudes of size and shape change were more similarly distributed between the ipsilateral and contralateral sides in all of the individuals, presenting a more symmetric final morphology than that seen preoperatively.

## Discussion

There is continued disagreement about whether the primary mechanism of craniosynostosis lies in the neurocranium or the cranial base. Previous research has demonstrated a characteristic basicranial morphology associated with specific premature neurocranial synostoses (Marsh and Vannier, 1986). Experimental animal studies (e.g. Babler and Persing, 1980; Persing et al, 1986a, 1986b; Persson et al, 1979) have documented induced deformities of the cranial base in normal rabbits that appear to follow the constraints of specific calvarial sutures. The human and animal findings suggest that there is a close functional relationship between the neurocranium and the cranial base. This study was initiated to

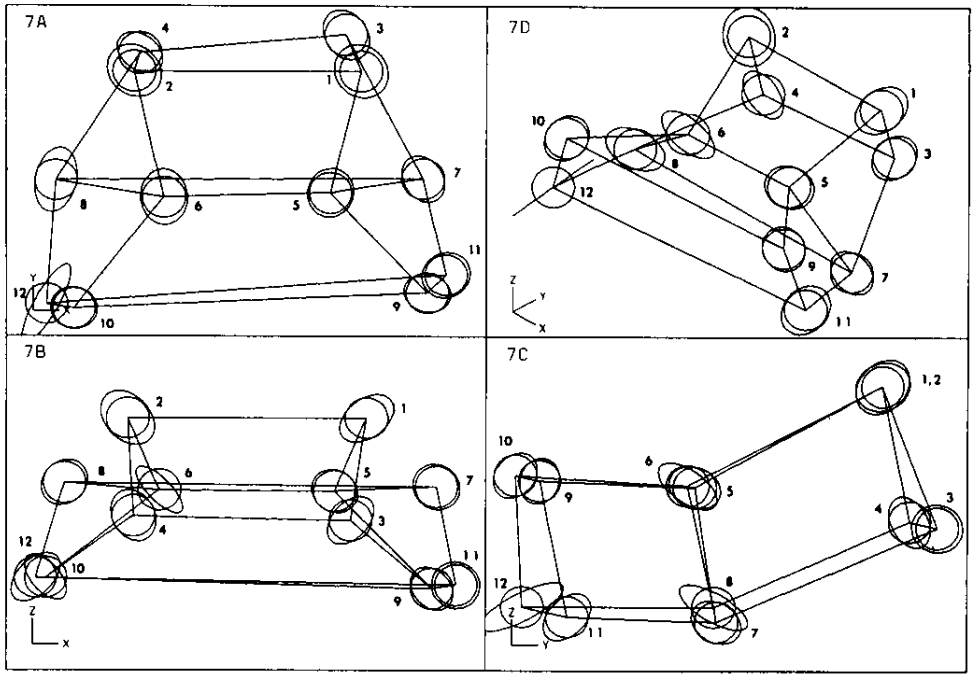


**FIGURE 7 Preoperative growth in bicoronal synostosis. (See Fig. 3 legend for further explanation.)**

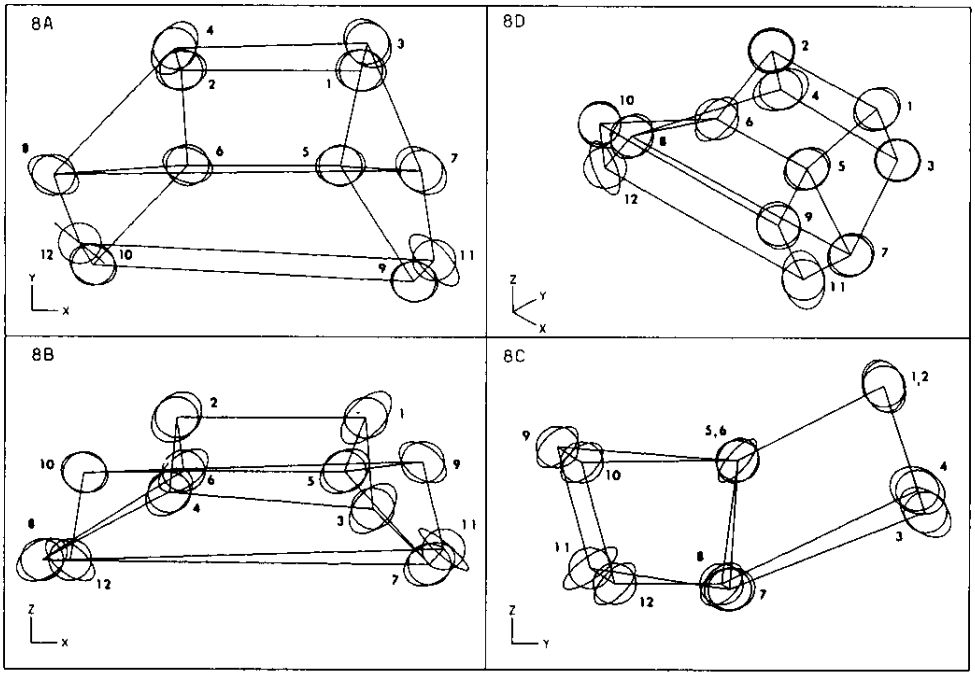


**FIGURE 8 Postoperative growth in bicoronal synostosis. (See Fig. 3 legend for further explanation.)**

determine if the proposed dynamic interrelationship between the neurocranium and cranial base could be demonstrated by observing the effect that surgery of the neurocranium has on growth and morphology of the cranial base.

The analytical results from this study are generally consistent with our predictions concerning growth patterns of the cranial base in three of the four types of craniosynostosis considered here. This suggests that our current understanding of the dynamics of craniofacial growth and the influence of premature suture closure on the development of the cranial

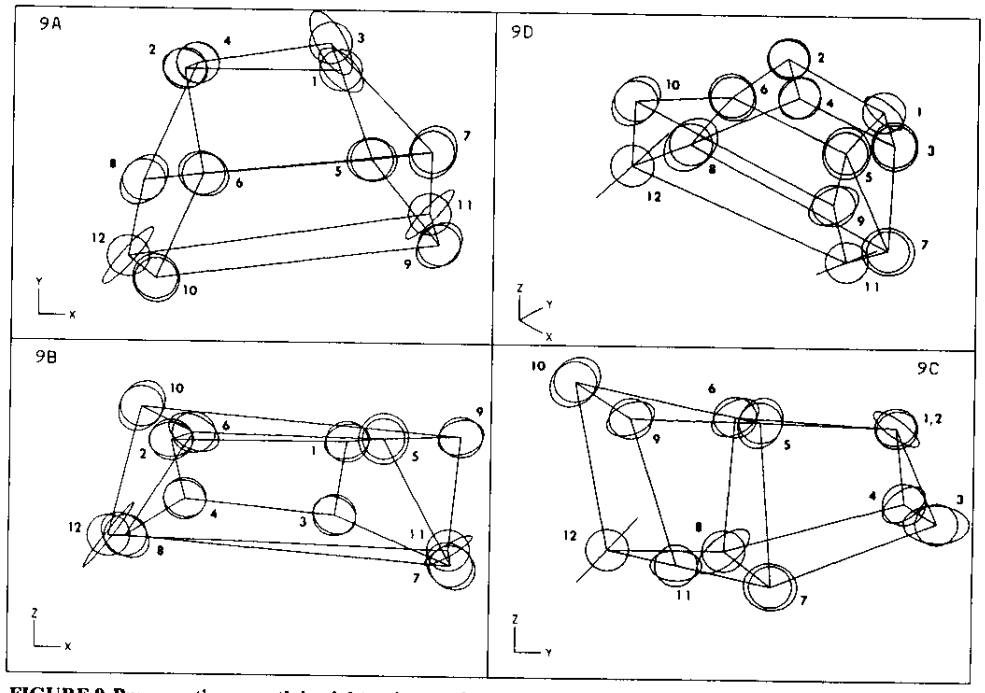


**FIGURE 9 Preoperative growth in right unicoronal synostosis. (See Fig. 3 legend for further explanation.)**

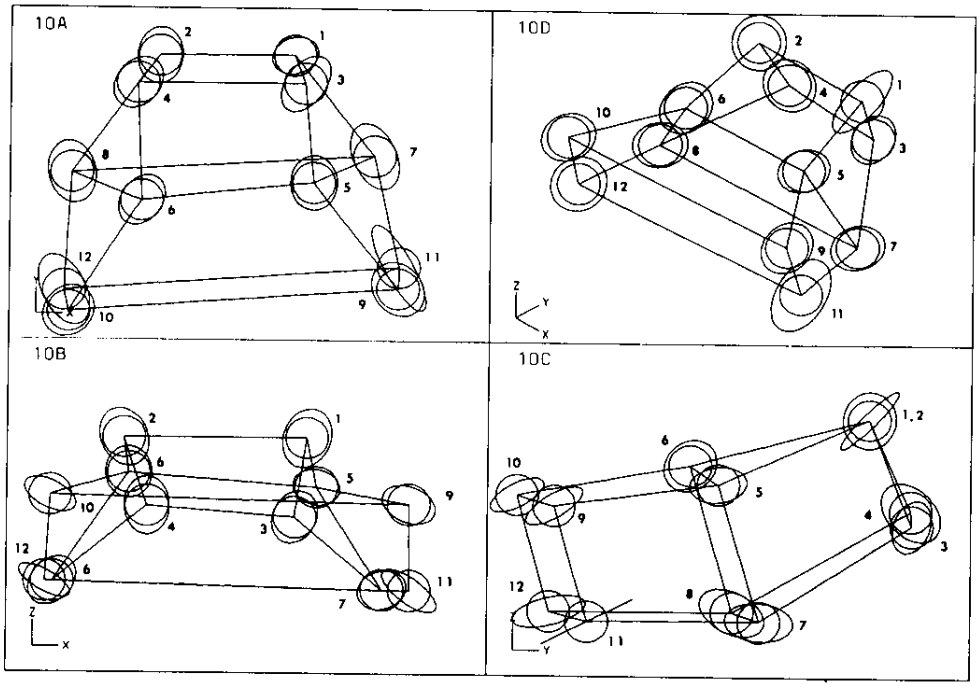


**FIGURE 10 Postoperative growth in right unicoronal synostosis. (See Fig. 3 legend for further explanation.)**

base is reasonable. However, there are no definitive answers. Nuances of the analysis of each case provide the basis for more questions, as well as clues to further understanding.

For example, we found consistent asymmetry in basicranial growth in patients with metopic synostosis. This was unexpected because the metopic suture is a midline structure. This may suggest unilateral involvement of other portions of the frontal bone (such as the orbital plate) in metopic synostosis. In addition, postoperative growth along the ML axis in metopic synostosis was less than expected local to the anterior

landmarks (closest to the site of the suture). Postoperative growth in sagittal synostosis showed a similar absence of an expected increase in ML expansion. This may suggest that a large percentage of ML growth of the cranial base occurs prenatally, or very early postnatally, and can not be recovered by postnatal suture release. Alternatively, the brains of infants with metopic and sagittal synostosis may have subnormal ML growth potential.

Analysis of preoperative growth in bicoronal synostosis demonstrates an actual decrease in size along the AP axis local to the middle and posterior portions of the cranial base. Whether or not bony material is actually being lost local to these landmarks by way of resorption is possible but cannot be determined by morphometric analyses. It is equally plausible that bone continues to form locally, but that the direction of growth has changed due to nonlocal adjustments occurring through displacement. The new directions of growth could result in a rearrangement of landmarks such that they lie closer to one another on the AP axis. Our morphometric techniques cannot provide information regarding how the more posteriorly placed landmarks have become more closely approximated, but the knowledge that they have done so allows us to form hypotheses and design experiments to identify processes that result in the final configuration.

Analysis of growth in unilateral coronal synostosis was not consistent. It is possible that the degree of variability in growth pattern among patients with unicoronal synostosis is in part related to individual variation in the degree of synostosis of the coronal-frontosphenoidal-sphenoethmoidal-frontozygomatic sutural ring (Burdi et al, 1986). Potential unilateral involvement of these basicranial sutures in unicoronal synostosis would not be affected by craniectomy. If involvement of the cranial base is not uniform in the unicoronal cases considered, this would also contribute to individual variability. We are not proposing that cranial base synostosis is absent in the other types of synostosis. Our results suggest, however, that unilateral involvement of cranial base sutures may be limited to cases of metopic and unicoronal synostosis. These impressions need to be evaluated by incorporation of a detailed study of cranial base suture status with the results presented here.

We must also question whether our model of preoperative and postoperative growth are representative subsets of these processes. We stress that we have looked at an extremely narrow window (in both sample size and temporal limits) of preoperative and postoperative growth. Increased sample size with longitudinal follow-up will provide a more comprehensive view of postoperative growth.

In full recognition of the practical limitations of the study presented here, we feel that our analyses support our predictions about the kinematics of cranial base growth in craniosynostosis. Our results support the idea of a structural and functional relationship between the neurocranium and basicranium and suggest direct communication between the two systems. The ultimate question is, what is the mechanism by which these two structures communicate to produce the highly integrated craniofacial complex? Although a great deal is known about growth at the cellular level, relatively little is known about morphogenesis or the way in which large structures take on particular shapes and sizes through the processes of growth and development. Ultimately, the use of morphometric techniques in the study of change in size and shape through time has a significant role to play in providing understanding of the highly integrated process of growth.

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# Commentary

Richtsmeier et al have presented a qualitative analysis of 11 patients with craniosynostosis followed pre- and postoperatively by 3D CT scanning. The well known difficulties in mathematical characterization of growth patterns of the basicranium are compounded when longitudenal follow-up of surgical patients is attempted.

The group of 11 patients was divided into 5 diagnostic categories (as shown in their Table 1) and underwent various surgical procedures. Each patient underwent CT scanning 1 to 8 weeks prior to, and 12 to 52 weeks following surgery. Landmark coordinate information was obtained by a stringent procedure, the spatial resolution of which was limited only by the resolution of the sampling grid. Two distinct mathematical analyses were carried out on the data set: finite element scaling analysis (FESA) and Euclidean distance matrix analysis (EDMA). The authors report that the two methods yield comparable results. They go on to conclude that growth of the basicranium following surgical release of fused calvarial sutures respects predictable patterns except in the cases of unilateral coronal synostosis.

A source of difficulty one encounters early in attempting such an analysis lies in the ambiguity in identifying and locating biologically meaningful landmarks. The set of landmarks chosen by the authors is well characterized radiologically. However, they implicitly acknowledge that partial volume average artifact may alter the assignment of location. They also are concerned that age-related growth may alter the 3D configuration of a specific landmark and hence affect the radiologic identification of its address. Of major concern, too, is the problem that some of the chosen landmarks, and their adjacency relationships, may fail to capture biologically useful information. Nevertheless, the pathways of landmark movement do vary systematically and hence carry some information.

Another difficulty in carrying out this analysis is the varying ages (2 to 8 months) of the patients at the time of surgery, as well as the varying pre- and postoperative time intervals. An open question remains concerning the choice of appropriate control data.

The authors have provided a well reasoned motivation for the development of a well characterized control population in which the normal growth curve of each of these adjacency relationships is documented. We eagerly await their subsequent work in which we expect that the disordered growth of the proband population can be understood relative to the "normal" controls.

This is a very thoughtful initial approach to a difficult and important clinical problem.

Allen Kantrowitz, M.D.
Director of Cranial Base Surgery
Montefiore Medical Center
Assistant Professor of Neurosurgery
Albert Einstein College of Medicine
Bronx, NY

Commentary reprint requests:
Allen Kantrowitz, M.D.
Department of Neurosurgery
Montefiore Medical Center
111 East 210th Street
Bronx, NY 10467.