

# Image Corrected Cephalometric Analysis (ICCA): Design and Evaluation

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**Image corrected cephalometric analysis (ICCA) is a method for eliminating serial image parallax error. In a radiographic survey, image parallax is an inherent and random property of the two-dimensional image of the subject. Radiographs of the same subject taken at different times will be different in image parallax. This difference, parallax error, is routinely displayed between serial radiographic studies. Parallax error discourages the use of conventional serial cephalometric surveys for tracking and studying changes in discrete craniofacial structures lying outside the midsagittal plane, unilaterally disposed, or changing without bilateral symmetry. Anatomic outlines or discrete points of such structures would routinely display measurement perturbations caused by image parallax differences between surveys. The ICCA method eliminates this problem. Therefore, accurate serial measurements of bone marker point displacements are made possible with two-dimensional reconstructions of points lying in three-dimensional space. The method of ICCA was tested for accuracy by using zero time serial cephalometric surveys of five subjects. Mean implant error of 0.12 mm (SD = 0.1) was found between predicted (ICCA) and actual measured implant movement caused by the image parallax error. After applying this method, bone marker movements are unlikely to be caused by parallax error between conventional serial cephalometric studies. Furthermore, displacement growth can be related to the relocation of composite growth outlines and midline anatomic landmarks. One plagiocephaly case and one hemifacial microsomia case were used to demonstrate ICCA for growth and treatment effect documentation.**

**KEY WORDS:** *bone markers, cephalometric radiography, craniofacial displacement growth, image correction, parallax distortion*

By themselves, anatomic measurement points (landmarks) in early childhood are limited in number and often poorly defined because of surface morphology. They are also difficult to identify precisely because of rapid growth. Furthermore, as expressed in bony cortical drift, apposition, and deposition, remodelling growth mechanisms obscure displacement growth of component anatomy of the craniofacial skeleton. Therefore, using anatomic landmark points, bony component movements can not be accurately identified.

Metallic implants, vital staining, and radioisotopes are well-known methods of bone marking used to study cra-

niofacial growth. When metallic implants are placed in three-dimensional skeletal components, identifiable measurement points are obtained. Yet, accurate displacement measurements of tantalum implants are rarely possible in conventional serial cephalometric studies, because image parallax distortions routinely obfuscate the measurements. This study describes and tests the accuracy of a method to reconstruct conventional lateral cephalometric film images of tantalum implants to a constant image parallax distortion. Such reconstructions can be used to accurately identify bony component movements, not routinely obtainable by other methods. This method can be useful and important in the early life clinical management of craniostenosis, facial dysplasia, oral cleft, and other kinds of patients.

## LITERATURE REVIEW

Once implanted in bone, the biocompatibility of tantalum is an important factor contributing to constancy of position and possible osseointegration (Rune et al., 1980; Selvik, 1990). The contrast density of tantalum is well suited for x-ray imaging (Selvik, 1990). In combination with radiographic techniques, metallic implants are uniquely suited to studying displacement growth of im-

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planted component anatomy within the craniofacial complex (Björk, 1955).

Cephalometric radiography standardized image distortion by fixing source to image-receptor distance (SID), and anode, object and film spatial positions to a head holder (Broadbent, 1931). Most difficult to consistently control is head position in a cephalostat. Between films, implants lying outside the midsagittal plane had an average image parallax error of 1.87 degrees in 85% of a sample population (Spolyar, 1987). A 2.3 degree error occurred with a portable cephalostat (Spolyar, 1988). With anatomic landmarks in the midsagittal plane unaffected by parallax distortions, serial errors were found to be insignificant (Midtgard et al., 1974).

Reliability of measurements and methods to check implant stability were not discussed in well-known longitudinal implant studies (Björk, 1955, 1963, 1968; Shaw, 1978; Mathews and Payne, 1980; Williams and Melsen, 1982). Implant instability and image parallax of implanted structures lying outside the midsagittal plane caused problems with bone marker analysis discussed by Friede et al. (1977), Shaw (1978), and Rune et al. (1980). However, in numerous three-dimensional studies reviewed by Selvik (1990), these commonly cited problems were controlled. Radiograph stereophotogrammetric analysis was used for evaluating movement between bones ascertained without using a standardized cephalometric technique (Selvik, 1974).

Other three-dimensional techniques use only anatomic landmarks extracted from coplanar imaging (Baumrind et al., 1983a,b), and biplanar imaging (Grayson et al., 1988; Bookstein et al., 1991). These methods have inherent dimensional errors because anatomy is ambiguous or impossible to find in both film views, landmarks are not discrete points, and technique sensitive factors are constant (Baumrind et al., 1983b). Furthermore, anatomic landmarks are subject to spatial relocation by both displacement and remodelling growth processes. Such anatomic landmarks represent composite change in form without rigorously revealing growth processes, i.e., remodelling or displacement. It is possible to describe both processes with serial cephalometry when bone markers are used and distortion errors are eliminated (Björk, 1955).

## METHODS AND MATERIALS

**Implant Placement and Imaging.** In each skeletal component to be studied, two or more implants were placed in cortical bone as in the maxilla and mandible with three on each side, the single occipital and frontal bones with two or three on each side, and each temporal squama with two implants. After the bone markers were placed, cephalometric radiographs were taken initially and at subsequent periods. For the size scale to be constant, the lateral films were taken with standardized source to image-receptor distance (SID) and object (midsagittal) to film distance (OFD). Frontal surveys were taken with known SID and

OFD. Taken at essentially 90 degrees to each other, the surveys were effectively biplanar.

**Basic Concept: The Reference Body.** Because it was essential for the implants to remain in a constant position to each other, a rigid or single bone is necessary to be used as a reference body. Three or more bone markers remained stable within the reference bone and had the widest possible separation, side to side. Bones that best met the criteria were the frontal and occipital or with completed growth, maxilla and temporal bone extracranial surfaces. A reference body was used as a rigorously controlled region of three-dimensional space with constant points represented within by metallic implants. These implants then projected a unique image array in each film exposure. The difference in array uniqueness (distortion) between serial views defined a coordinate vector. The coordinate vector provided for a mathematical solution to reconstruct implant images to an individual subject array or a referenced image parallax (RIP).

**Film Tracing and Processing.** To be used as the RIP, one set of lateral and frontal tracings was defined as the "referenced" set (Figs. 1A and 1B). The referenced set had a stable head position during both film exposures taken at a 90 degree angle to each other. All other tracings were designated "corrected" sets. Anatomic outlines were traced, and all implant locations including machine porion were defined by "points" (centered dots). In each film set, the landmarks and implant images were identified by side and bone component in each film series.

**Referenced Frontal Film.** A line constructed parallel to machine porion was used as the coordinate horizontal (CH) axis (see Fig. 1A). The midsagittal plane was constructed perpendicular to the CH axis at approximately a midorbital position so as to lie on the machine midsagittal plane.

**Referenced Lateral Film.** By convention, the Frankfort plane (FH) was used as the CH plane. Another plane was constructed horizontally to best represent the central ray (focal line) of the frontal film. Another line, the extracranial reference plane (ERP), was constructed perpendicular to this focal line, either anterior or posterior to all lateral tracing landmarks (see Fig. 1B). It was used to assist in computing the OFD of each point in the frontal view.

**Corrected Frontal Film.** Here, the plane constructions applied only to configuring implants for ICCA use in reconstructing lateral film implant points. The CH was constructed so the implants had an identical relative position as with the "referenced" frontal film CH. The midsagittal plane, which may not be parallel to the machine midsagittal plane, was constructed perpendicular to CH and midorbital in position.

**Corrected Film Parallax Vector.** In this example, the occipital bone was chosen as the reference body. The reference body bone marker points were manually transferred from the "referenced tracing" to the "corrected tracing" (Fig. 2). At the discretion of the operator, these points were defined by side, as registration (preferably

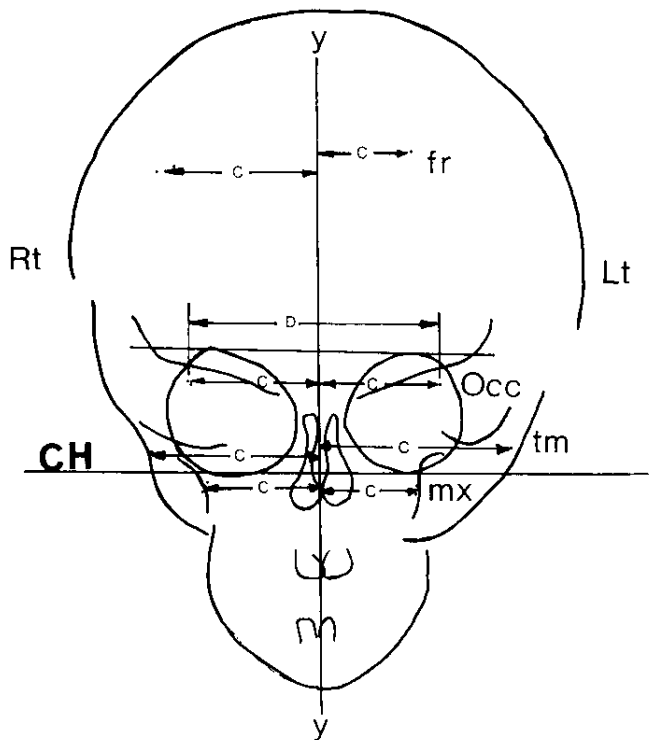


FIGURE 1A Patient C record "referenced tracing" of frontal cephalogram. Midsagittal plane, y-y is perpendicular to CH, coordinate horizontal. D, left to right side transverse distance of reference body implants (occipital squama). C, the colateral distance of each implant to the midsagittal plane. Skeletal components with bone markers on each side: frontal (fr), occipital (Occ), temporal (tm), and maxilla (mx).

double) and orientation (preferably single) points. If only one registration point was used, then both FH planes or reference bone composite outlines, such as the occipital squamae, were oriented to be parallel.

**Registration Points.** These points were precisely superimposed over each other, "corrected" on "referenced." Orientation points: with two registration points superimposed, the opposite side orientation points became separated from each other. The separated "orientation points" defined a "parallax vector" (PV) line (see Fig. 2).

**Corrected Lateral Film.** This film tracing was constructed like the "referenced" tracing. The FH was constructed to have the same angle with the S-N plane as in the referenced tracing. The PV line was drawn, and another line was drawn over machine porion and at the same time constructed perpendicular to PV. This latter line defined the "focal" rotation axis (RA) (Fig. 3). The shortest distance from each implant to the RA line defined the implant midsagittal distance.

**Data Acquisition and Precision Testing.** Data points were recorded in a coordinate grid using a Houston Instrument model 7024 digitizer,\* set for 0.025 mm resolution and minimal 0.125 mm accuracy of the tablet specifica-

\*Houston Instrument, P.O. Box 15720, Austin, TX 7876.

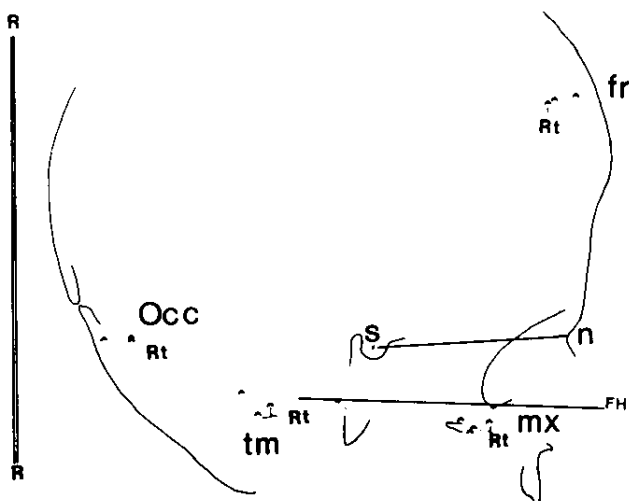


FIGURE 1B C record lateral film "referenced tracing." Note implant pattern differences from tracing in Figure 3. The constructed planes used in ICCA method are: FH, Frankfort horizontal; sn, anterior cranial base; and RR, a plane to compute object-film distances in the frontal view.

tion area. All tracings were positioned on the tablet with the CH of the tracing and tablet parallel.

In a precision test for intra- and interoperator reliability of coordinate point identity, a mean coordinate error of .06 mm (SD = 0.05) was found. There were no statistically significant intra- or interoperator differences at the 0.05 level in a two-tailed T-test. This test was comprised of ten sets of films each with ten points for two-hundred potential coordinate position errors for each operator. At two sittings each operator digitized two separate sets of five films.

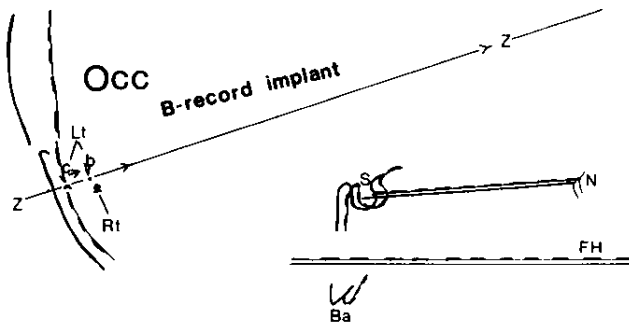


FIGURE 2 "Registration points" were superimposed on the right side occipital bone implant image points. Accurate registration over the two implants resulted in parallel FH and SN planes, and the separation of the opposite side "orientation points." In the B record, the left implant image (b) was shifted 6.4 mm ahead of c, the left implant image of the C record. Along Z-Z, the precise amount and direction of image parallax was measured in relation to FH, which is, as well, the lateral film CH. In use, this vector is transformed by parallax trigonometry to a radian vector R, the angle of rotation, given by  $R = 2 \sin(S/2D)$ ; where S is the measured shift Z-Z, and D is the transverse distance from orientation to registration points. D is taken from the biplanar frontal film as in Figure 1A and adjusted to the size scale of S.

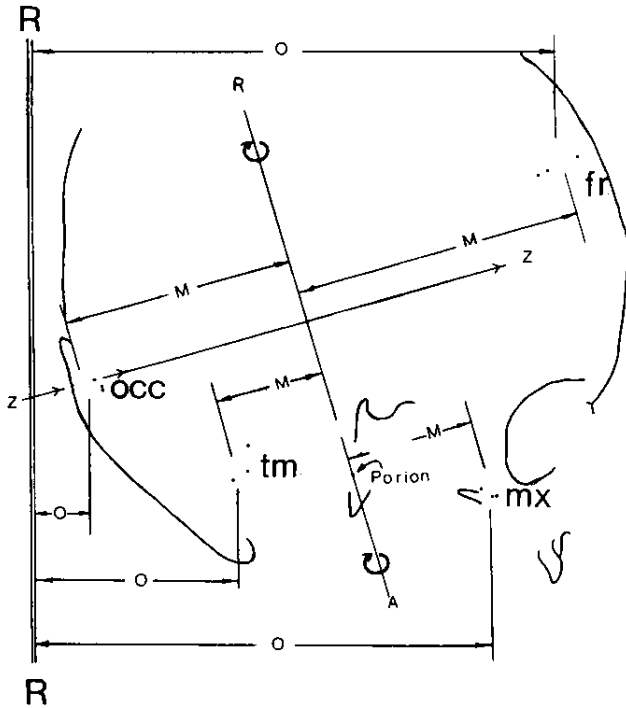


FIGURE 3 Patient B record "corrected tracing." The defined axis of rotation (RA) is constructed to pass through machine porion and perpendicular to Z-Z. Machine porion is assumed to be the focal point on the cephalometric film image. The shortest distance from each implant to RA is M, the implant midsagittal distance. The shortest distance from each component implant to R-R is O, a parameter used to compute the OFD of each implant in the frontal survey. In this illustration, the C record was used as the reference and the B record as the corrected cephalograms. The head image movement is defined by a clockwise rotation, looking down RA.

**Data Processing.** Using Cephmaster software<sup>†</sup> and Zenith PC hardware<sup>‡</sup> data files were created to record implant point transverse distances in the frontal film, midsagittal (rotation axis) distances, extracranial reference plane (ERP) distances, and conventional cephalometer distances defining the SID and OFD for the lateral and frontal films. These files were then used in a file management and ICCA processing program (Landmark software<sup>§</sup>) to reconstruct the corrected lateral film images to the RIP by integral three-dimensional simulation to extract parallax error (Fig. 4).

**Checking Implant Stability.** After the reformatting procedure, implants were checked by measuring their relative intracomponent positions and carefully observing their orientation. Because implants were rectangular (.5 x 1.5 mm), any disorientation seen in serial views were indications of position instability.

<sup>†</sup>Cephmaster, 15894 Northville Rd., Plymouth, MI 48170.  
<sup>‡</sup>Zenith Data Systems Corporation, St Joseph, MI 49085.  
<sup>§</sup>Diamond Head Scientifics, Sterling Heights, MI 48312.

The accuracy of reconstructing implant film images to appear as they would in the absence of parallax error, was the subject of the following studies.

**Manikin Study: A Preliminary Test of the Method.** An implanted skull manikin was used because implant stability, component relationships, and head position within the cephalostat are static. Three lateral surveys were taken, one with the cephalostat hub in normal position, then rotated 2.4 and 5.4 degrees to introduce a known parallax error in the horizontal plane of the last two surveys. A paired frontal film was taken in the normal hub position. The normal position films were used as the "referenced" set, and the others as the "corrected" sets.

Image parallax shift was defined by bilateral markers in the reference body, occipital squama. The ICCA predicted image movements of paired bilateral bone markers in each "corrected" lateral cephalogram were compared to the measured movements, taken from each lateral film set to directly determine the movement of paired bilateral markers.

**Patient Study.** To define the accuracy of the ICCA method using the protocol for the manikin study, five patients were used where no significant time or treatment intervened the subsequent portable cephalometric surveys. From the five patients 20 sets of bilateral implant pairs were studied.

**RESULTS**

The results of the manikin study are shown in Table 1. The average error between predicted and measured movements was 0.199 mm per implant pair and 0.10 mm per

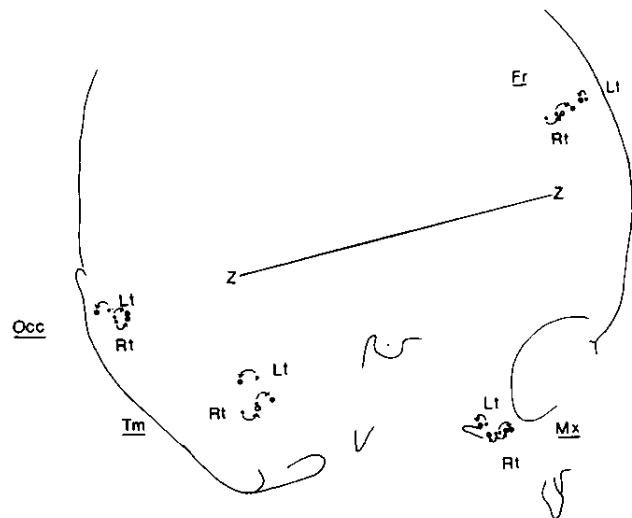


FIGURE 4 Reformating is simulated in the "corrected tracing" for each implant image along vector (Z-Z). Reformating direction is related to implant side and to rotational movement of the head image. The algorithm for computing the reformatting distance of each implant is:  $\{[(2 \sin R/2) (C)] \pm [(1 - \cos R) (M)]\} (MC)$ , where R = parallax angle of rotation, C = implant colateral distance, M = implant midsagittal distance, and MC = magnification coefficient for each implant.

implant. The range was from 0 mm for the occipital "referenced" markers at both hub settings to 0.41 mm per implant pair for the temporal markers at the 5.4 degrees hub setting.

Table 2 shows the results from the study of five subjects comprising 20 pairs of bilateral bone markers. The average difference between predicted and measured movement was 0.23 mm (SD 0.2) for each pair of bone markers. Individual implant average error of the method was .12 mm (SD 0.1) per implant.

**DEMONSTRATION**

Using x/y coordinate analysis, two cases demonstrated the use of ICCA for bone marker tracking. By definition, the horizontal x-axis aligned with the sella-nasion (SN) plane, and the vertical y-axis, perpendicular to the SN plane. Component bone marker displacements were described by translations along the x-axis from a vertical plane through S or along the y-axis from the SN plane.

**Case One**

At age 6 months (mo) the patient was operated for a left unilateral coronal stenosis, plagiocephaly. The left orbit was advanced and stabilized by an interpositional calvarial bone graft, and a frontal craniotomy was performed. Fixation was with wire. Bone contrast implants were placed intraoperatively in the "to be mobilized" left orbit and left frontal bone flap, in the "nonmobilized" right orbit, and right frontal, left temporal, right temporal, and left and right occipital squamae extracranial bone surfaces (Fig. 5A). Frontal and lateral cephalometric surveys were taken preoperatively, then postoperatively at 1 week, 3 mo, 10 mo, 24 mo, and 70 mo. Using the occipital bone markers as the reference body, ICCA was performed for each postoperative survey using the preoperative lateral

**TABLE 1 Manikin Study of Predicted Implant Image Shift Compared to Actual Measured Shift in Four Sets of Implants at Two Different Cephalostat Hub Settings**

Component	Parallax Error (degrees)	ICCA Predicted Movement (mm)	Directly Measured Movement (mm)	Absolute Difference Column (2-3) (mm)
Occipital	2.4	3.25	3.25	0
	5.4	8.20	8.20	0
Temporal	2.4	5.16	4.85	.31
	5.4	12.81	4.85	.41
Maxilla (anterior)	2.4	1.16	1.0	.16
	5.4	2.89	3.0	.11
Maxilla (posterior)	2.4	3.88	4.25	.37
	5.4	9.17	9.4	.23
(2 implant) Set average				0.199
Combined individual average				0.10

The hub was rotated to two different positions that caused image parallax shifts of approximately 2.4 and 5.4 degrees, respectively. Measurements are in millimeters.

**TABLE 2 Predicted and Measured Implant Image Shifts Were Compared between Successive Cephalometric Surveys in Five Subjects Comprising 20 Sets of Paired Bilateral Markers**

Component Bone	Subject ID	Parallax Error (degree)	Predicted Movement (mm)	Measured Movement (mm)	Absolute Difference Column (3-4) (mm)
Occipital	D	1.77	3.57	3.2	0.37
	D	1.77	3.06	3.4	0.34
	E	10.42	12.27	12.4	0.13
Temporal	A	0.79	1.67	1.8	0.13
	B	4.12	8.30	8.7	0.40
	E	10.42	23.00	23.3	0.30
Frontal	B	4.12	4.31	4.6	0.20
	C	4.33	5.05	5.4	0.35
	D	1.77	2.57	2.5	0.07
	E	10.42	8.84	8.4	0.44
	E	10.42	10.20	10.7	0.50
Maxillary	E	10.42	12.00	12.8	0.80
	A	0.79	0.95	1.0	0.05
	A	0.79	1.17	1.2	0.03
	A	0.79	1.30	1.3	0.00
	B	4.12	2.61	2.4	0.21
	B	4.12	4.52	4.6	0.08
	C	4.33	1.89	1.9	0.01
	C	4.33	4.96	5.0	0.04
D	1.77	1.67	1.5	0.17	

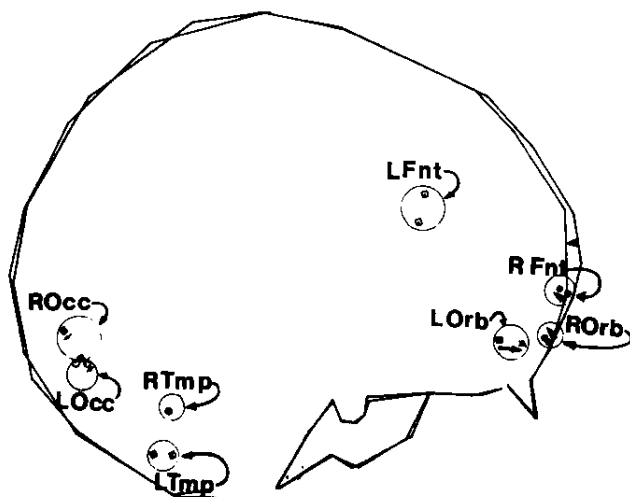
(2 implant) Set average = 0.23  
Standard deviation = 0.20  
(1 implant) Individual average error = 0.12

No significant time interval occurred between paired surveys. The image parallax difference (error) between surveys for subjects A to E were 0.79, 4.12, 4.33, 1.77, and 10.42 degrees, respectively. Measurements are in millimeters.

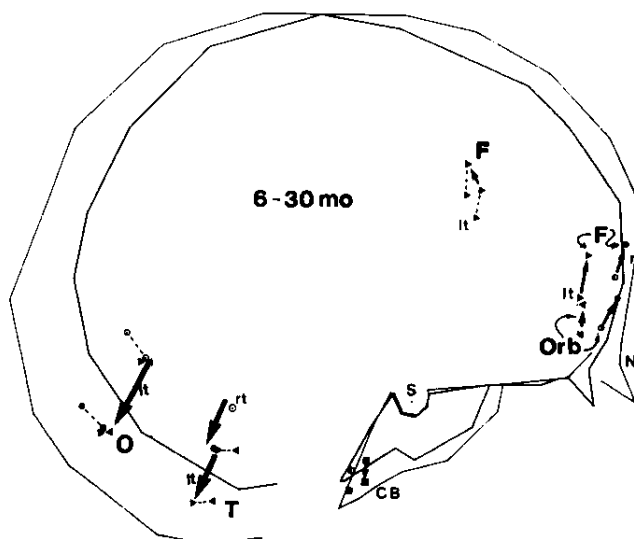
survey as the RIP prior to a quantitative x/y coordinate analysis of bone marker movements between the time points (Table 3).

In observing the reference body, the right and left sides of the single occipital squama appeared to grow symmetrically (see Table 3). Therefore, the two sides were averaged into a single measurement. For comparative self referencing, nasion (N) translation was used to define the patient's "normal" neural growth curve.

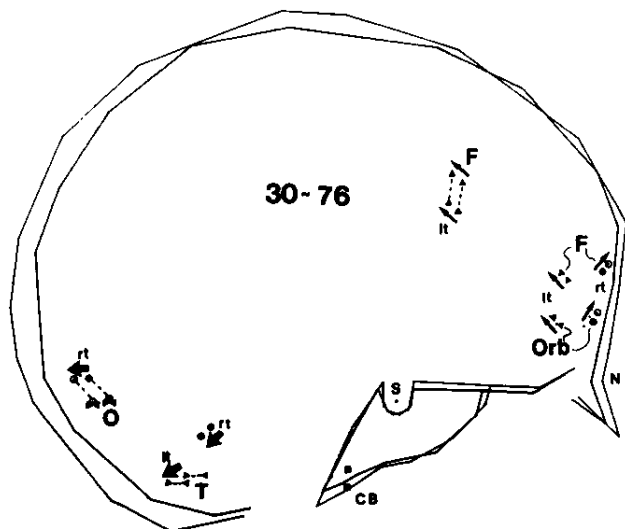
**Orbit Analysis.** Showing the operative change (6-6.1 mo), the left orbit relocated 7 mm forward, and the opposite frontal and orbital components relocated upward and backward to a lesser extent, occurring with the release of the cranial stenosis-deformation (Figs. 5A and 6). Up to age 30 mo, similarity in the patterns of translation were seen for left and right orbits and nasion, but the left orbit compared to the right had a reduced rate of upward and forward displacement growth (see Figs. 5B and 6). From 30 to 76 mo, the right orbit, like nasion, displaced forward 2 mm, but the left orbit displaced backward 2 mm. At age 76 mo, the relative position of the left and right orbits was about the same as was present preoperatively at age 6 mo (Figs. 5C and 6). Throughout the entire postoperative period, the vertical translations of both orbits were nearly alike (Fig. 7).



**FIGURE 5A** Case one, plagiocephaly surgical treatment effects analyzed by bone marker displacements in tracing superimpositions. Registration is on sella with orientation to nasion on all analyses. Overlay tracings show cranial bone marker locations: LOcc, left occipital; ROcc, right occipital; LTmp, left temporal; RTmp, right temporal; LFnt, left frontal; RFnt, right frontal; LOrb, left orbital; and ROrb, right orbital. Note, LOrb gross anterior movement, and ROrb and RFnt posterior movements over 1 week pre- to postoperative period.



**Figure 5B** From age 6 to 30 months, the bilateral referenced occipital markers translated symmetrically. Left and right temporal markers moved in the same direction but different in extent of translation. Anteriorly, the LFnt frontal bone flap had an obviously different course than the other more anterior frontal and orbital bone markers.



**FIGURE 5C** From age 30 to 76 months, displacement translations of LOrb and LFnt were alike in amount but opposite in horizontal direction from ROrb and RFnt. Posteriorly, the left temporal bone translation was similar to the occipital squama. Both moved together, as the implants had virtually the same relative intrainplant positional distances from age 30 to 76 mo. This suggested that the left lambdoid suture was tensed. Cranial components anterior and posterior to the coronal ring displaced independently, as did the basiocciput (posterior cranial base) in respect to the posterior fossa implants (LROcc, LTmp, RTmp). The right lambdoid suture appeared to be functioning normally because the RTmp implants displaced independently from the LROcc implants.

**Frontal Bone Analysis.** After age 16 months, the right frontal and left frontal bone horizontal translations were clearly divergent (see Figs. 5B, 5C, and 6). During the 6-year postoperative phase, the right frontal implant, like nasion, translated forward about 6 mm, but the left frontal displaced backward about the same amount. Remarkably, a 12 mm anteroposterior separation occurred between the left and right sides of the frontal bone over this time (see Figs. 5B, 5C, and 6). For 10 months following the operation, the upward displacement of the left frontal bone was less than on the right side, and thereafter the pattern was reversed (see Fig. 7).

**Cranium Analysis.** For the duration of the study, the right frontal bone and orbit grew in an apparently normal pattern with virtually similar curves to N (Fig. 8). Yet, in clearly an abnormal horizontal pattern beginning at age 15 mo and certainly after age 30 mo, the left frontal bone and orbit grew like the cranial bones posterior to the coronal ring (see Figs. 6 and 8). Similarly, as early as age 15 mo, left temporal growth reflected an occipital pattern of displacement unlike the right temporal bone (see Fig. 8). In the y-axis, the right frontal and orbit curves were correctly opposite in direction to the downward displacing temporal and occipital squamae (see Fig. 7); as in the horizontal graphs, the left temporal growth curve was more like the occipital than the right temporal curve. This is perhaps *prima facie* evidence of left lambdoid suture stenosis.

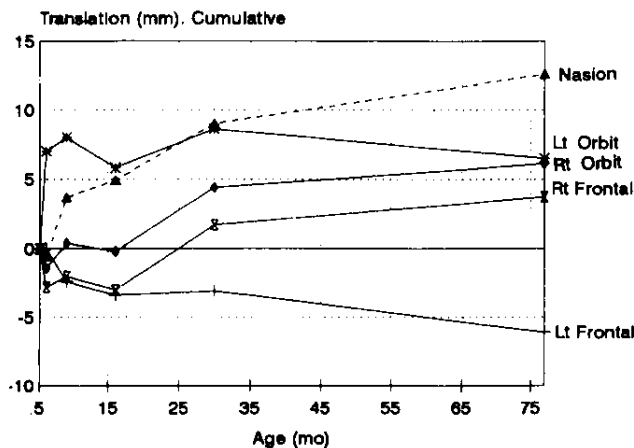
**Summary.** In summary, the operative advancement of the left orbit was stable, but displacement growth in the

**TABLE 3 Case One Coordinate Analysis of Bone Marker Movements. Plagiocephalic Growth: Operative and Postoperative Change**

Parameters	Age in Months				
	6-6.1 Mo	6.1-9 Mo	9-16 Mo	16-30 Mo	30-77 Mo
<b>Horizontal</b>					
Lt Orb	7	1	-2.2	2.8	-2.1
Rt Orb	-1.4	1.8	-0.8	4.6	1.7
Lt Fnt	-	-2.4	-1	0.3	-3
Rt Fnt	-2.5	0.8	-1	4.7	2
LT Tmp	-0.3	-2.4	-2.4	-6.2	-6.2
RT Tmp	-0.4	-1.9	-1.0	-4.7	-3.9
LT Occ	-0.9	-4.9	-4.1	-7.1	-5.8
RT Occ	-0.8	-5.2	-4.3	-7.8	-5.5
LR Occ	-0.9	-5.1	-4.2	-7.5	-5.7
SN	-0.5	4.2	1.2	4.1	3.6
<b>Vertical</b>					
Lt Orb	-2.1	2.9	2.3	2.3	2.6
Rt Orb	1.4	2.9	2	1.8	2.6
Lt Fnt	-	2.1	2	3.2	3.2
Rt Fnt	2	3.6	3	2.1	2.1
LT Tmp	-0.1	-6.2	-5.4	-1.2	-1.8
RT Tmp	-0.1	-5.3	-0.4	-0.1	-2.7
LT Occ	-0.4	-8.3	-7.3	-1.2	-0.2
RT Occ	-0.4	-8.4	-7.8	-1	-0.3
LR Occ	-0.4	-8.4	-7.6	-1.1	-0.2

Translations were measured from SN for vertical "y-axis" translations and from a line perpendicular to SN at S for horizontal x-axis translations. negative (-) notation indicates x-axis posterior movement and y-axis caudad movement. Orbit (Orb), frontal (Fnt), temporal squama (Tmp), occipital squama (Occ), and anterior cranial base (SN) were the measured parameters. Bone marker movements (mm). (-) = posterior or caudad movement.

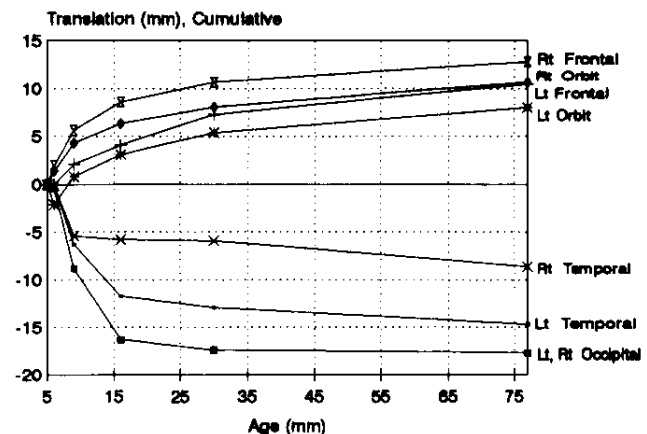
horizontal plane was clearly abnormal after 30 months. The left frontal and left temporal bones were the earliest to behave abnormally displacing like the occipital bone. Disturbance of the displacement growth process caused, in measurable part, a clinically evident return of the fronto-orbital asymmetry found in infancy. The apparent occurrence of a left lambdoid stenosis perhaps represents a progression of a field defect which, before the age of 6 mo, appeared only as isolated unilateral coronal stenosis.



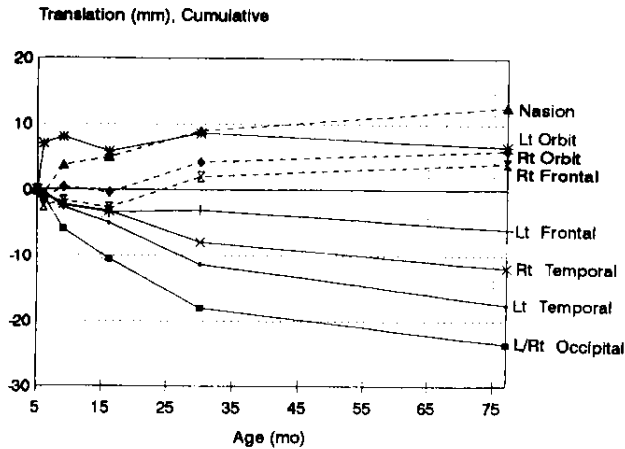
**FIGURE 6** Horizontal cranial bone movements. Comparison between nasal capsule growth (N) with the left and right orbits showed the left orbit to be different from the right after age 30 mo. At age 76 mo, the same relative horizontal positioning of left and right orbits was present at age 6 mo. Nasion and the right frontal and orbit bones have a similar growth curve pattern. The left frontal growth has a much different pattern than the right frontal bone, which occurred after age 16 months, a similar but earlier pattern than that found for the left orbit.

**Case Two**

At age 3.1 years, this patient with left hemifacial microsomia was operated on to place a costochondral rib graft. Bone contrast implants were placed intraoperatively at 4.1 years of age to monitor facial growth with special emphasis on the mandible. Bone contrast implants were placed posteriorly and anteriorly in the left and right mandible, bilaterally in the malar strut regions of the maxilla, left and right temporal squamae, and in two bilateral positions of the occipital squama. Frontal and lateral cepha-



**FIGURE 7** Vertical cranial bone movements. The left temporal bone movement was like the occipital bone, which perhaps reflects a left lambdoid suture stenosis. Vertical orbital displacements were rather symmetric bilaterally throughout the 70 months postoperative period. However the left frontal vertical translation was less than the right frontal up to age 30 mo, and thereafter greater.



**FIGURE 8** Horizontal comparison of the left frontal bone and left orbit with the temporal and occipital skull component displacements. After 30 months similarity of the curve slopes are seen for these components, unlike the right frontal and orbit bones that followed the neural growth curve.

lometric surveys were taken initially at 4.1 yr and then at 4.7, 5.9, 7.1, 7.8, and 8.1 years. Using the initial survey as the RIP and the occipital bone and bone contrast markers as the reference body, ICCA analysis was performed for each subsequent survey in order to extract the implant coordinate values between the time points (Table 4).

**Growth Monitoring Movements.** In a comparison of left and right side mandibular body displacements, both vertical (Fig. 9) and horizontal (Fig. 10), translations of posterior and anterior implants are shown. Same side displacement curves are similar but differ in height due to complex rotational displacements of the mandible. For example, the left posterior implants translated more than at the anterior. Remarkable for the rapid and excessive growth in height from age 4.1 to 7.8 yr, the left side rib

graft displaced downward more than 25 mm but, also, backward more than 12 mm (see Figs. 9 and 10). Opposite in pattern to the left side, the right side implants at the anterior region displaced more than at the posterior region over the same time period, downward 8 mm and forward 7 mm (Figs. 9, 10, and 11).

**Postsurgical Movements.** With a severe asymmetric deformity caused by the excessive rib growth, surgical intervention was necessary at age 7.8 years. A portion of the rib was resected, and on the right side, a sagittal split osteotomy was performed. Intermaxillary fixation was used for a period of approximately 8 weeks. From the time of surgery at 7.8 years until 8.1 years, for the most part, the changes were caused by the surgical intervention (Fig. 12). The left mandibular body elevated approximately 14 mm in the anterior region and 12 mm in the posterior region (see Fig. 9). The left corpus also translated forward approximately 7 mm in the posterior region and 4 mm in the anterior region (see Fig. 10). The reduced anterior displacement was due to rotational movement of the entire mandible to the left. Contrarily, the right mandibular corpus translated backward about 2 mm and downward about 2 mm in the posterior region, but upward 2 mm in the anterior region (see Figs. 9, 10, and 12).

The maxillary growth was asymmetric during these observations. The right maxilla displaced downward nearly 2 mm more than the left from 4.1 to 8.1 yr (see Fig. 9). In the horizontal plane, the left side translations were mostly backward.

**Summary.** The costochondral rib graft grew at a rate more than three times the "normal" right side from age 4.1 to 7.8 years. At age 7.8 years, remedial surgery introduced gross corrective changes to compensate for the discordant and exuberant growth of the costochondral rib graft. Maxillary displacement growth appeared to be impeded and asymmetric throughout the ICCA study.

**TABLE 4** Case Two Coordinate Analysis of Bone Marker Movements Measured in the Same Way as Case One. Hemifacial Growth: Maxilla and Mandible

Parameter	4.1-4.7 Yr 7 Mo	4.7-5.9 Yr 13 Mo	5.9-7.1 Yr 13 Mo	7.1-7.8 Yr 11 Mo	7.8-8.1 Yr 4 Mo
<b>Horizontal</b>					
Lt Max-128-p	-1.1	-1.1	0.4	-0.4	0.6
Rt Max-131-p	-0.5	0.3	0.4	-0.9	1.1
Lt Mnd-136-p	-2	-7.5	-3.3	-1.5	7.5
Lt Mnd-137-a	-0.7	-2	-0.6	-1.5	4.2
Rt Mnd-138-p	1.7	2.8	1.3	-2	-2.9
Rt Mnd-140-a	3.6	3.4	2.0	-2	-1.8
<b>Vertical</b>					
Lt Max-128-p	1.5	0.4	0.1	0.6	0.2
Rt Max-131-p	1.7	0.9	0.8	1.1	0
Lt Mnd-136-p	5.4	12.9	12.2	1.8	-12.5
Lt Mnd-137-a	4.7	10	9.9	4.3	-14.4
Rt Mnd-138-p	0	2.5	4.5	0.9	2.5
Rt Mnd-140-a	0	3	4.1	1.3	-1.8

Negative (-) notation indicates x-axis posterior movement and y-axis cephalad movement. The implant side (Lt/Rt), bone (Max = maxilla and Mnd = Mandible), implant #, and position (a = anterior and p = posterior) are given for each parameter. Five observation periods were measured over a 2-year duration.  
 Bone marker movement (mm), (-) = posterior or cephalad movement.  
 Parameter: side, jaw, implant #, a = anterior and p = posterior location.



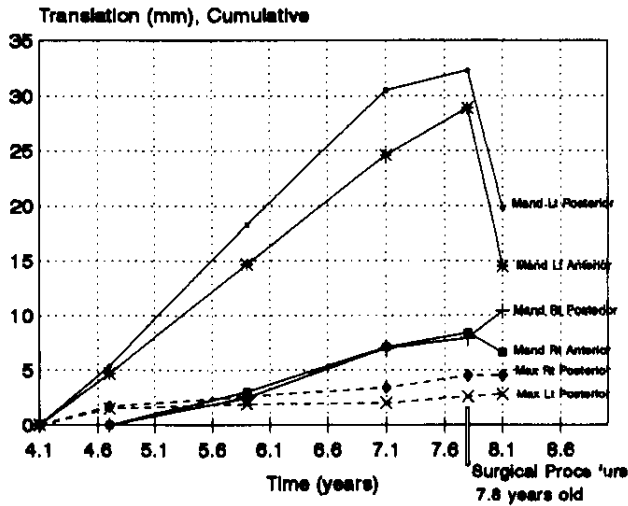


FIGURE 9 Case two, vertical mandibular and maxillary displacement growth translations show excessive left mandibular rib graft height achievement and reduced left maxillary height achievement up to the time of surgery which, in part, reversed the growth history.

DISCUSSION

Using just the left and right orbit and temporal bones to illustrate the effect of serial parallax error on observations, the implant displacements before and after applying ICCA are shown in Table 5. Figures 13A and 13B illustrate horizontal and vertical graph plots of the observed orbit and temporal bone displacements between the time points before and after applying ICCA. Using the initial radiographs as the RIP, the parallax errors between the RIP and the second to sixth time points were 3.24, 3.35,

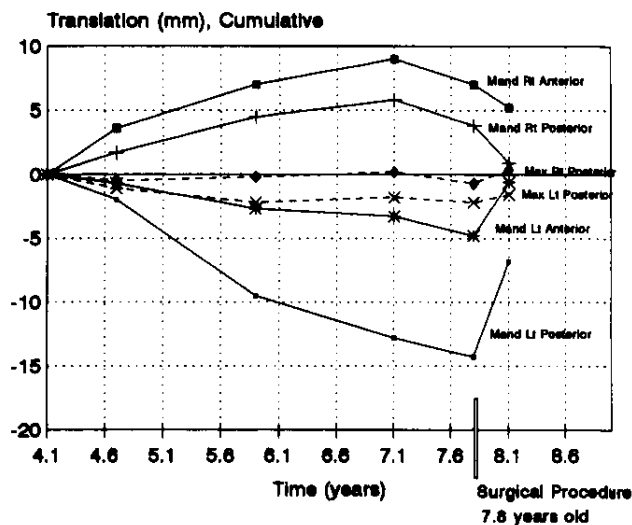


FIGURE 10 Case two, horizontal translations of the mandible and maxilla. Up to the surgery date, left mandibular rib graft grew posteriorly. The right "normal side" showed declining anterior growth up to age 7.1 years, thereafter displacing posteriorly, more so after surgery.

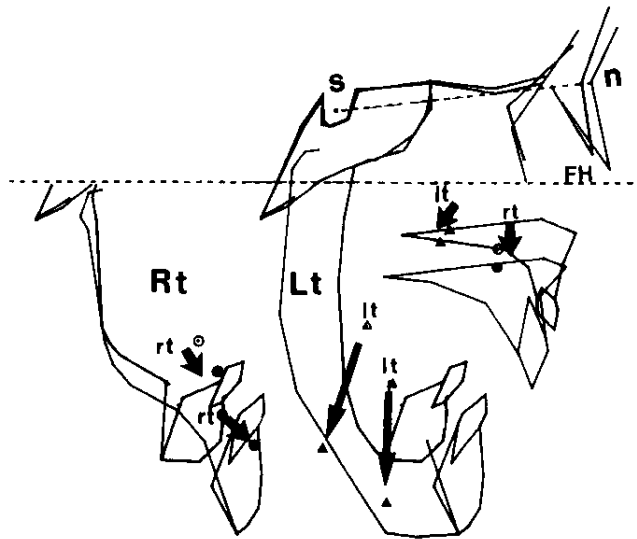


FIGURE 11 Tracing superimpositions demonstrate left and right side bone marker displacements in the mandible and maxilla. Note exorbitant rib growth on left side. Right and left mandible were separated to enhance appreciation of the collateral analysis.

12.00, 4.2, and 7.4 degrees, respectively, and likewise, the direction of parallax shifts were 120, 165, 134, 18, and 101 degrees off the coordinate horizontal. Clearly, no reasonable interpretation of the severely disparate left to right side differences in each bilateral anatomic component is possible from the graph plots before applying ICCA, where the disparity correlates with the direction of parallax shift (see Figs. 13A and 13B). Furthermore, such growth curves would not correlate with assessments of a

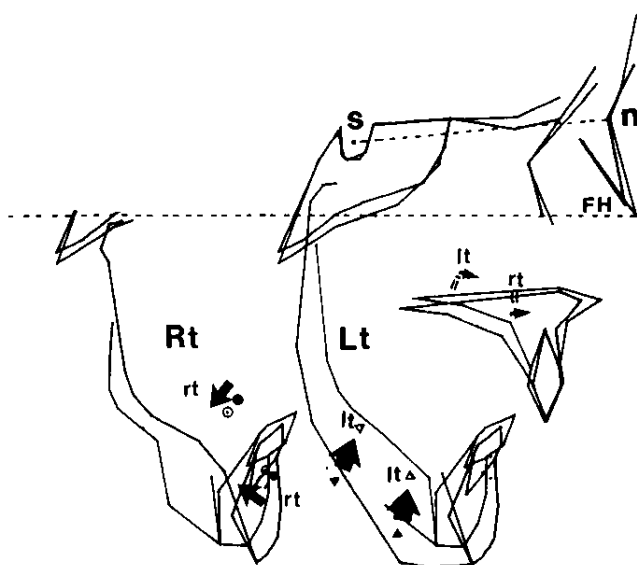


FIGURE 12 Documented effects of surgery to modify the extensive overgrowth of the rib. The surgery successfully removed the excessive growth.

**TABLE 5** Temporal (Tmp) and Orbital (Orb) Bone Marker Movements Before and After Applying ICCA in Case One

Parameters	Age in Months				
	6-6.1 Mo	6.1-9 Mo	9-16 Mo	16-30 Mo	30-77 Mo
<b>Horizontal</b>					
Lt Orb	7 (6)	1 (-.9)	-2.2 (-6.6)	2.8 (4.8)	-2.1 (-2.8)
Rt Orb	-1.4 (-.4)	1.8 (3.3)	-0.8 (4.7)	4.6 (-2.1)	1.7 (2.6)
LT Tmp	-0.3 (-1.8)	-2.4 (-5.3)	-2.4 (-7.9)	-6.2 (-2.3)	-6.2 (-7.5)
RT Tmp	-0.4 (1)	-1.9 (.4)	-1.0 (5.6)	-4.7 (-7.8)	-3.9 (-2.8)
<b>Vertical</b>					
Lt Orb	-2.1 (-.8)	2.9 (2.4)	2.3 (6.9)	2.3 (3)	2.6 (6.2)
Rt Orb	1.4 (.1)	2.9 (3.3)	2 (-3.6)	1.8 (1)	2.6 (-2.1)
LT Tmp	-.1 (1.8)	-6.2 (-7)	-5.4 (2.3)	-1.2 (.1)	-1.8 (5.3)
RT Tmp	-0.1 (-1.9)	-5.3 (-4.7)	-0.4 (-7.2)	-0.1 (-1.1)	-2.7 (-8.3)

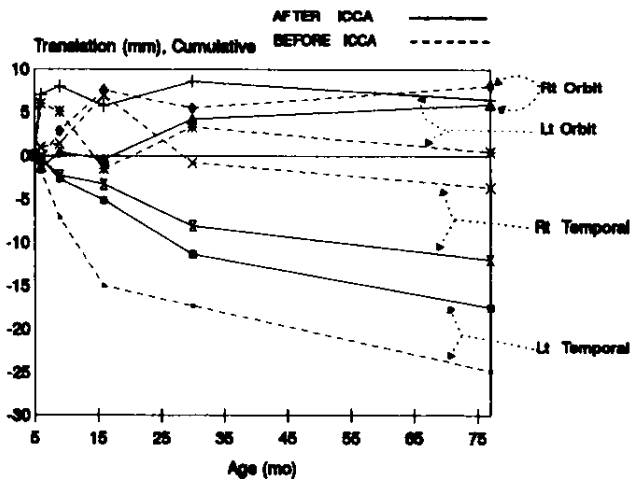
Bone marker movements (mm), (-) = posterior (horiz) or anterior (vert).

patient's clinically apparent physical condition, which was, however, well represented in graph plots after applying ICCA in the two demonstration cases. For an individual serial analysis, there can be little confidence in the reliability of any bone marker movements outside the midsagittal plane without first removing serial image parallax distortion.

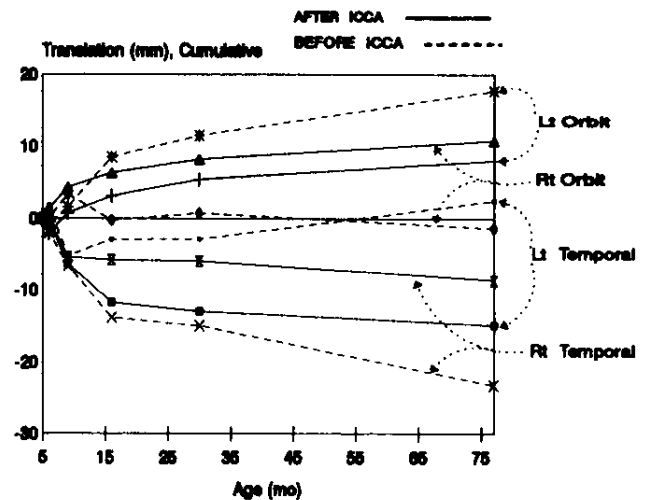
Using the ICCA method for a single subject serial study, it is unlikely that bone marker movement in excess of 0.3 mm (3 times the SD of the gross mean error) is an artifact or perturbation of the method (see Table 2). Given the precision for implant points found in the present study of 0.08 mm (total error) and the mean gross error of the ICCA method of 0.12 mm, the difference 0.04 mm per implant, perhaps best represents the net error of the method. With the 0.10 mm mean gross error found in the manikin study, where virtual control of the focal spot, head positioning, and assembly constraints were possible, net error (.02 mm) is reasonably less than for the patient

study (.04 mm). In comparison to the Roentgen Stereometric Method developed by Selvik (1974) with a mean gross error of 0.09 mm (Jacobsson et al., 1977), ICCA has only a scant .03 mm larger mean error. The smaller mean error of the Roentgen Stereometric Method is perhaps due to a calibration cage used in the method to accurately define the focal spot, head positioning, and assembly constraints needed to scale the image (Selvik, 1974).

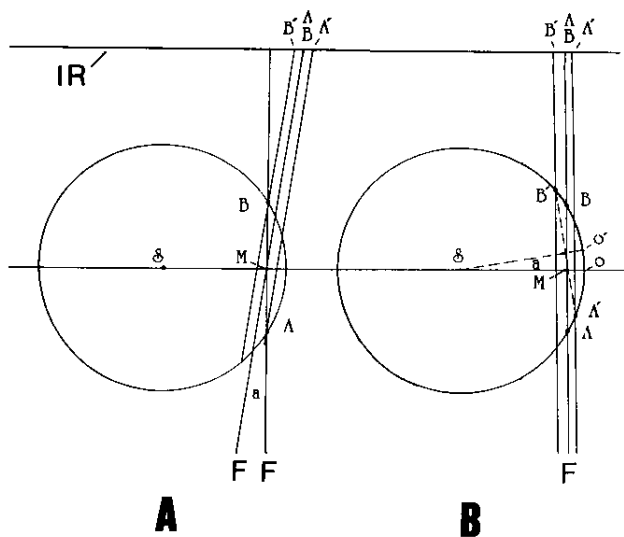
In defining the accuracy of the method, the ICCA mean gross error does include the cumulative effect of variables not virtually controlled in the method. These variables are routinely well controlled, but, in part, contribute to image and data acquisition distortions between serial surveys. The accuracy of the method is, therefore, accordingly reduced in proportion to unaccountable or unquantifiably small variations between serial surveys in SID, OFD, focal spot, exposure technique and film processing, implant point precision, digitizer accuracy, and to algorithm assumptions of the ICCA method.



**FIGURE 13A** Graph of serial horizontal movements of temporal and orbital bone markers before (-----) and after (——) applying ICCA. The difference in the plot lines for each component documents the difference caused by parallax error.



**FIGURE 13B** Graph of serial vertical movements of temporal and orbital bone markers before (-----) and after (——) applying ICCA. The difference in the plot lines for each component documents the difference caused by parallax error.



**FIGURE 14** With the focal point at infinity, identical initial conditions are shown in Figures A and B with bilateral object “implant points” A and B at equal distances from the midobject reference plane M, which is parallel to the image receptor (IR). Figure A, for a given shift in the focal spot (F to F’), each “image point” of the object moves in direct proportion to the distance from the “point” object to the IR. A focal shift from location F to F’ results in equal image separation of bilateral implants in opposite directions from the midobject reference plane. That is, a focal shift equal to angle  $\alpha$  manifests on the image receptor (IR) in equal and opposite separations of implant images from an initially superimposed position (A,B) to one of parallax (A’,B’). Therefore, on (IR):  $A-A' = (AM \tan \alpha)$ , and  $B-B' = (BM \tan \alpha)$ . Figure B, for a given shift in the object position, each “image point” of the object moves in direct proportion to the distance from the “point” object to the IR and proportional to the “phase” change in object position. An object shift from location O to O’ results in unequal image separation of bilateral implants in opposite directions from the midobject reference plane. That is, an object shift equal to angle  $\alpha$  manifests on the image receptor (IR) in opposite, but unequal, separation of implant images from an initially superimposed position (A,B) to one of parallax (A’,B’). Therefore, on (IR):  $A-A' = [(AM \sin \alpha)] - [(SM)(1-\cos \alpha)]$ , and  $B-B' = [(BM \sin \alpha)] + [(SM)(1-\cos \alpha)]$ . Hence,  $A-A'$  (focal)  $\neq$   $A-A'$  (object), and  $B-B'$  (focal)  $\neq$   $B-B'$  (object). But, essentially up to 10 degrees:  $\tan \alpha = \sin \alpha = \text{rad } \alpha$ . Yet,  $\pm SM(1-\cos \alpha) \neq 0$ . However,  $\alpha$  is routinely less than 2.5 degrees as a focal position error. Therefore, by using only the algorithm for object rotation for scaling image parallax shift, the effect of  $(1-\cos \alpha)$  is negligible in causing an image scaling perturbation. Even with serial focal position differences up to 3 inches with conventional cephalometry, in practicality:  $A-A'$  (focal)  $= A-A'$  (object), and  $B-B'$  (focal)  $= B-B'$  (object). That is, if serial focal position shifts are confined within a circle of diameter 7.4 cm, then perturbation of present method is less than .1 mm (assuming SID is 165 cm and the midsagittal distance is 100 mm or less). That is, when  $100(1-\cos \alpha) = .1$ , then  $\cos \alpha = .999$  or .0447 R. Hence,  $(165 \times .0447) = 7.4$  cm. In the present method, scaling image parallax shift is substantially determined by the algorithm for object shift. In conventional cephalometry, image parallax error between serial surveys is caused, for the most part, by object shifts (head positioning differences), and in some part, by focal spot shifts (anode positioning differences) which are, in the ICCA method, assumed to be confined within a common circle of diameter 7.4 cm or about 3 in. In conventional cephalometry, anode positioning differences are observed between serial surveys as inconstant positioning of machine porion to anatomic porion.

In the ICCA method, practical limitations to extract out parallax error can be well identified, but not easily quantified. First, in serial lateral films, focal points are rarely identical, hence, a small error can occur between reformatted points. The error occurs because observed image parallax error, which is due to undifferentiated movements of both object or focal point shift, is removed by applying only the mathematical operation for object rotation (shift) in cone-shaped space. However, with the average focal point shift of about 1 degree in the cephalometric technique used (Spolyar, 1988), the error is very small, indeed, even up to focal point shifts of 3 degrees. The practical limits and effects of focal position error are reviewed in Figure 13. Secondly, caused by inconsistent head positioning, magnification change adds insignificant error, which was estimated to be in the “hundredths” of a millimeter.

Also, in clinical use, consideration must be given to compounding inaccuracy caused by composite superimposition or landmark “reliability” (Baumrind and Frantz, 1971; Baumrind et al., 1976). Compared to implant precision (SD for total error = 0.07 mm), anatomic landmark precision suffers nearly a ten-fold decrease in reliability for the most reproducible point, sella (SD for total error = 0.64 mm) (Baumrind and Frantz, 1971). In an individual assessment, measurement accuracy is necessarily reduced when implants are referenced to anatomic landmarks used in conventional cephalometric analyses.

In conclusion, using ICCA and conventional serial cephalometric films, an accurate analysis of displacement growth is possible. Displacement translations are clearly distinguished and separated from associated border relocations of a changing composite growth form. The two case reports demonstrated precise monitoring of craniofacial growth and surgical treatment effects. From a lateral cephalometric view, the treatment and growth processes were revealed by displacement translations in a numeric and graphic coordinated axis analyses and overlay superimpositional analyses. By using ICCA in the reported cases, bone displacements were described in a manner that would be generally unobtainable by using other conventional composite imaging methods.

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## Commentary

This paper seems to me an ambitious attempt to overcome the problem of distortion errors in serial cephalometric studies. By using implants ad modum Björk combined with a sophisticated analysis of lateral and frontal cephalograms the authors claim they can "accurately identify bony component movements . . . clearly distinguished and separated from associated border relocations of a changing composite growth form." If this should be the case, this paper would bring the profession forward by a major step. However, the study has flaws. In general, I have found the paper difficult reading and small inconsistencies do not help (e.g., why is negative translation along the y-axis caudal in case one and cephalad in case two?)

In terms of data processing I assume the ICCA is correct. Unfortunately, I have to admit that I lack the necessary knowledge to be able to fully appreciate this aspect of the study. However, in view of the extensive technical manipulations and the claimed high degree of precision and accuracy of the ICCA, I am surprised to find statements such as "The referenced set should have a stable head position during both film exposures." This is a critical point and it should have been verified. Indeed, this very probable source of error, especially when small children are examined, could have been eliminated simply by simultaneous exposure. Similarly, the construction of elaborate planes e.g., "at approximately a midorbital position" or "to best represent the central ray," in combination with manually transferring between tracings, makes me

question the validity of the calculated high precision and accuracy in the results.

The authors are very much aware of the many sources of error and limitations of serial cephalometric studies and the use of metallic implants, as stated in the discussion. They admit that these "practical limitations can be well identified, but not easily quantified: and all the same proceed to claim that "using ICCA . . . an accurate analysis of displacement growth is possible." I would have been happy to agree. Unfortunately, the authors have not been able to ensure the single absolutely essential prerequisite for implant studies: the stability of the implants in their original positions in the bone.

In the study implant stability was monitored "by measuring their relative intracomponent positions and carefully observing their orientation." This is an entirely inadequate method to ensure implant stability. First, measurement of implant distances in three dimensions can not be accurately performed in a series of paired two-dimensional cephalograms not simultaneously exposed. And second, implant stability can not be excluded even though no disorientation is observed. Besides, two implants may keep their distance between them and still move in the bone. A minimum of three implants must be inserted in each single bone and their distances and angles maintained if implant stability is to be claimed. It should be mentioned that some confusion exists as to the number of implants placed in each bone in the cases presented. Ac-

ording to "Methods and Materials" three implants are placed in the maxilla on each side, in Figure 1A two implants are indicated on each side, and in Table 2 three sets of paired implants in the maxilla are indicated for only one subject out of four. From my own experience I know that implants, especially when placed in the slim bones of small children, tend to migrate. It seems likely to me that implant migration would have occurred even in the present study, a complication that has not been addressed by the authors. As a curiosity, I would like to mention that identification of each implant in a series of cephalograms has presented a major difficulty to me—at times an insurmountable obstacle to conclude a two-dimensional implant study. I wonder whether the authors have had the same experience and have chosen not to mention it?

## Author's Response to Commentary

With strikingly biased view, the commentator has spun a web of tortuous arguments in discrediting the ICCA method and, perhaps, to obscure the admitted lack of "necessary knowledge to . . . appreciate the study." Made with flat imperatives, misquotes, and bad logic such a divisive commentary only detracted from its few germane or correct criticisms of this paper.

Any difficulty reading this article is perhaps mostly the fault of the senior author. The inconsistent y-axes relate to conventions with the anatomic regions targeted in the case reports. Increasing cranial height (cephalad movement) and facial height (caudad movement) are best displayed as positive in graphs.

Alas! In paragraph two, commentator's critical point is correct. Indeed, eliminating head movement between paired exposures is *necessary* for the referenced set, as it was only implied in methods. If not, I mistakenly thought it would be understood as unacceptable. Of interest, according to the commentator, head movement is eliminated "simply by simultaneous exposure." Overlooked by commentator, there is yet another way; it was used on the subjects in the accuracy study and the case reports, and it is routine on all of our patients. Verified to eliminate head movement, cephalometric paired surveys are taken intraoperatively (meaning the patient is asleep) after bone markers are inserted. Wrongly, the commentator makes another misrepresentation in alleging that head motion was a "very probable source of error," meaning, I assume, in the reported accuracy study and case reports.

As a comment, I might ask commentator, "simply by simultaneous exposure" of what? Paired cephalometric exposure? Is the technique easily integrated with routines of patient care in hospitals and offices? Are special x-ray

In conclusion, I am forced to admit that I cannot find the authors have eliminated the problem of parallax error in serial cephalometric surveys. To do this they would need to identify and eliminate from the study migrating implants—and go on from there. In the mean time asymmetric displacement growth can be reliably monitored with the use of metallic implants and roentgen stereometry while three-dimensional bone surface changes may best be observed using computerized roentgen tomography.

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equipment arrangements necessary? Fitting into hospital and office practice and documentation routines was a main objective in the development of the ICCA method. Commentator obviously endorses roentgen stereometry with surveys made by simultaneous exposure in a *separate facility*. How often are films retaken? "Especially when small children are examined" without a cephalostat used with simultaneous exposure extreme *orientation and position differences* surely occur between the subject and machine coordinate axes. As in the case reports, another advantage of ICCA is that displacement movements can be referenced to the cranial base for classical interpretation. Displacement movements can also be related to the reference body implants. With roentgen stereometry, classical interpretation is, at best, difficult. Without using standardized cephalometric films for serial composite study, the difficulty is in not knowing how the reference body displaced in respect to the cranial base, information neither provided nor possible with roentgen stereometry.

The commentator's "modus operandi" became clear by the second paragraph. What seems to make the commentator "question the validity of the calculated high precision and accuracy in the results" are several clearly out of context quotes. Like the statement, "at approximately a midorbital position," commentator truncated the important phrase, "so as to lie on the machine midsagittal plane." Commentator is *remiss* in not recognizing this important and proper "construct." For it defines, at the same time, the vertical and transverse coordinate axes of the referenced survey and the machine.

Another out of context quotation is, "to best represent the central ray." With careful reading, the commentator would have appreciated that constructed planes are pre-

cisely determined in the films. Construction is aided in the films, either by machine parts (porion and machine midsagittal points), film edges (bottom or top edges of lateral surveys virtually and "best represents the central ray" of frontal biplanar exposures), or anatomy (SN plane referenced for the coordinate horizontal). Misrepresenting ICCA, the commentator again relies on phrases out of context, "practical limitations can be well identified, but not easily quantified." This phrase was taken from the same paragraph that thoroughly explained the "limitations" of the variables that contribute very minor errors to the accuracy of the ICCA method. The commentator misses the point, these accuracy depreciators are factored into the numeric definition of ICCA accuracy.

In summary, the commentator has brought three levels of testing into question and has missed at least two points. Precision testing has no bearing on the cited constructions or point transfers, and secondly, these variables along with the "practical limitations" are accounted for in the numeric definition of ICCA accuracy. Furthermore, it should be made clear, with zero-time periods between sequential surveys in the accuracy studies, that unstable implants can not possibly contribute to the defined error of the ICCA method.

Finally, the commentator dismisses ICCA as an accurate analysis of displacement growth, "not able to ensure . . . the stability of the implants in their original positions in the bone" is the central criticism and violates "the single absolutely essential prerequisite for implant studies." Should we now discard the classic studies of Björk where reformatting was not used, only unilateral implants studied, and certainly, the commentators conditions not met? Furthermore, not measuring same bone implant distances as a test of stability has nothing to do with the operational accuracy of ICCA or, for that matter, the Björk studies.

No technique can ensure against implant instability, and no technique is useful if all markers are unstable. In fact, intracomponent three-dimensional measurements can be done between ICCA referenced and sequential paired surveys that are virtually biplanar or between reformatted paired surveys being sure of reference body implant stability. Theoretically, three-dimensional measurement of same bone implants would be most beneficial, I admit, for short studies over one time period.

There is no one absolute answer or solution to implant instability. In my experience, after multiple sequential views most implants are virtually stable, some are lost, and a few remain unstable, which are easily distinguished and eliminated from study. Certainly, concerted time and effort, experience, and good judgment are important in assessing bone markers in individual studies. The level of assurance one can have in bone market stability is related to the following factors:

1. Tantalum implants are inert and osseointegrate with time.
2. Operator experience, instrumentation in placement, and an intraoperative cephalostat for paired biplanar surveys.
3. Constant orientations and relative positions of multiple intracomponent implants go together. With implants oblong, serial disorientation alerts one to instability. This heuristic principle has been most useful.
4. Observing similar movement patterns of like anatomy not affected by treatment or the infirmity confirms correctness of reformats. As in the plagiocephaly case, trackings were similar for right orbit and frontal bones and the anterior cranial base.
5. With multiple observations as in the case reports, a consistent or stereotypic pattern of marker displacement emerges. As another heuristic principle, a stereotypic pattern of performance is a test of the competency of a system and its underlying common denominators. To suggest, as the commentator has, that bone marker instability is a constant problem, which may even be masked by movements that occur in unison violate, at least, the validity of the cited heuristic principles. It leads to a contradiction, that the sequential orientation of unstable implants may not change, and that perturbations in the sequential tracking of unstable implants would mysteriously emerge in consistent and stereotypic displacement patterns within the same individual or between many individuals of like kind. This is beyond all logic, and highly contradictory. Furthermore, even three-dimensional distance measurements of three intracomponent bone markers would not be an effective test to ensure stability in the commentator's theoretic condition where "two implants keep their distance between them and still move in the bone." Here then, some heuristic principle as with disorientation, tracking perturbation, or dissimilarity observations would clearly reveal the two "misfit" implants that kept their distance as distinct from the one that remained truly stable!
6. Lastly, with the application of the ICCA method for clinical documentation, observations between ICCA and clinical findings will be both consistent and revealing.

Thank you for the opportunity to respond to the commentary.

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