Euclidean Distance Matrix Analysis of Surgical Changes in Prepubertal Craniofacial Microsomia Patients Treated With an Inverted L Osteotomy

A. D. Hay, B.M.Sc.
A. F. Ayoub, Ph.D.
K. F. Moos, O.B.E.
G. D. Singh, Ph.D.

Objectives: Correction of craniofacial microsomia (CFM) presents several challenges concerning the modality of surgical intervention. The aim of this study was to assess early and late surgical outcome, by undertaking Euclidean distance matrix analysis (EDMA) of CFM patients exhibiting an unilateral mandibular deformity that was surgically corrected by an inverted L osteotomy and autogenous bone graft.

Design: Longitudinal study. Preoperative, ≈1-year postoperative and ≈3-year postoperative assessments of 14 consecutive children (mean age 9 years) with CFM. Posteroanterior cephalographs were scanned and five homologous mandibular landmarks were digitized in triplicate (< 1% digitization error). Average mandibular geometries, scaled to an equivalent size, were generated using a generalized rotational fit program (Procrustes superimposition) and subjected to EDMA.

Results: The mean pre- and both postoperative mandibular configurations differed statistically ($p < .01$). Early postoperative improvements in mandibular form were noted; increases in length arising in the treated mandibular body (≈ 19%) and ramus (≈ 13%). Comparing early and late postoperative configurations, a decrease of ≈ 22% in the late postoperative mandibular body length was evident, but the ramus maintained steady vertical growth (≈ 7%). Comparing the preoperative and late postoperative configurations, the decrease observed in the mandibular body on the treated side was reduced to ≈ 8% while the ramus maintained good growth (≈ 20%) on that side.

Conclusion: Mandibular morphology is improved significantly in CFM patients surgically treated by an inverted L osteotomy, but relapse in the mandibular body is evident after ≈ 3 years. Nevertheless, ramus growth proceeds well after the surgical reconstruction.

KEY WORDS: *Euclidean, hemifacial, microsomia, morphometry, osteotomy*

Craniofacial microsomia (CFM) is the second most common congenital facial abnormality after cleft lip and palate, having an estimated incidence of 1:5,600 live births (Gorlin et al., 1990). Although structures primarily affected are those derived from the first and second branchial arches, a large amount of variation exists between different cases when considering the structures involved and the severity of the abnormalities (Loevy and Shore, 1985; Poole, 1989). Growing evidence implies that the condition is caused by a disturbance of neural crest cell migration into the first and second arches during early embryonic development (Seow et al., 1998). Thalidomide-induced syndromes comparable with CFM have been reproduced in animal models to support this theory (Jacobsson and Granstrom, 1997), and although mutant genes associated with the condition have been localized (Juriloff et al., 1987), genetic inheritance still remains unclear. Thus, large numbers of cases appear to be sporadic, even though autosomal dominant, autosomal recessive, X-linked, and multifactorial hypotheses have been suggested (Burck, 1983; Rollnick and Kaye, 1983; Taysi et al., 1983).

The mandible is substantially important when surgically correcting CFM skeletal imbalances because this is the region in which the largest growth deficiencies occur in many cases (Mathog and Leonard, 1980; Smahel, 1986; Ortiz-Monasterio et al., 1997). Indeed, the earliest signs of skeletal deformity have been localized in the mandible. The abnormal growth patterns appear to be progressive and without surgical intervention skeletal symmetry deteriorates over time (Murray et

---

Mr. Hay is a Predoctoral student, and Dr. Singh is a Clinical Lecturer, Dundee Dental Hospital and School, University of Dundee, Scotland. Dr. Ayoub is a Clinical Lecturer, Department of Oral Surgery, University of Glasgow, Scotland. Dr. Moos is a Consultant Oral and Maxillofacial Surgeon, Canniesburn Hospital, Scotland.

Submitted January 1999; Accepted December 1999.

This study was supported by the Nuffield Foundation (GDS, ADH).

Reprint requests: Dr. G. D. Singh, Dundee Dental Hospital and School, University of Dundee, Park Place, Dundee DD1 4HR, Scotland, United Kingdom. E-mail g.d.singh@dundee.ac.uk.

al., 1984; Kaban et al., 1986), although one study has shown that growth on the abnormal side of the mandible paralleled that of the nonaffected side (Polley et al., 1997). It is also suspected that abnormal maxillary growth may have a secondary effect on the displaced mandible. Should the mandibular ramus on the diseased side be elongated early enough, maxillary growth may proceed following a more normal growth pattern. Thus, the need for maxillary correction may be reduced because its primary restriction for normal growth is removed by early mandibular correction (Murray et al., 1984; Kaban et al., 1986).

The mandible is the focus of this current study because its asymmetric morphology has perhaps the most critical influence on overall facial esthetic appearance (Kaban et al., 1981). The primary aim of this study is to carry out geometric morphometric assessments to localize alterations in mandibular form prior to and after surgical correction, using an inverted L osteotomy and an autogenous bone graft procedure. The null hypothesis to be tested is that there are no postoperative differences in mandibular morphology that contribute to improved facial symmetry. A further aim of this study is to indicate preoperative asymmetrical features of the mandible in CFM patients and to localize the regions most responsible for the deformities. Therefore, as well as obtaining a thorough surgical evaluation, further insight into the pathoetiology may be achieved, adding to the knowledge obtained in previous studies (e.g., Smahel, 1986).

MATERIALS AND METHODS

Posteroanterior (PA) cephalographs of 14 consecutive patients (mean age at the time of surgery 9 ± 2.5 years [SD]; range 5 to 14 years) with unilateral features of CFM (Pruzansky type IIa) were retrieved. Each patient had been operated on by the same surgeon using an inverted L mandibular osteotomy and autogenous bone graft. The progress of each patient throughout their surgical treatment plan was represented by three sequential PA cephalographs. The preoperative cephalograph was taken prior to surgery, the mean early postoperative cephalograph 1 ± 1 year after surgery, and the mean late postoperative cephalograph 3 ± 2 years after surgery.

Each PA cephalograph was scanned using a Hewlett-Packard flatbed scanner to provide a digital image. Each image was viewed at a constant brightness and resolution (150 dpi) to provide uniform representations of each individual cephalograph. An appropriate software package was used to identify and digitize five homologous landmarks (Fig. 1). A digitization error of < 1% was allowed for each landmark to be deemed as successfully identified. For mandibular form comparisons, conventional linear measurements were made on the five-noded geometry (Fig. 1). The mean distances among the five landmarks were calculated for the three groups and a Student's *t* test was used to determine whether the observed differences were statistically significant.

To ascertain whether morphological differences existed between pre- and postoperative mandibular forms, it was necessary to compute average forms or consensus configurations of each group using Procrustes (generalized rotational fit) analysis (Gower, 1975; Rohlf and Slice, 1990). Procrustes superimposition (the construction of a two-form superimposition by a least-squares method) was employed to generate an average five-noded geometry for each group. Following this method, every object's coordinates were translated, rotated, and scaled iteratively until the least-squares fit of all configurations was no longer improved. Therefore, all configurations were registered with respect to one another, and as a result of this procedure, geometric mandibular configurations were scaled to equivalent areas, avoiding problems introduced by differences in size. This procedure was undertaken for all three time-dependent groups (preop, postop 1, postop 2).

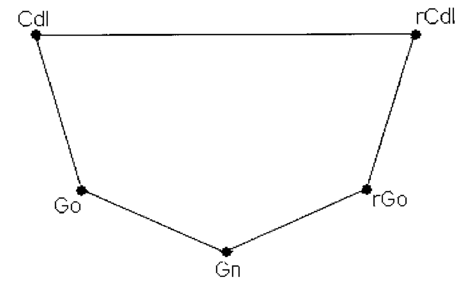

FIGURE 1 Homologous landmarks used for construction of the five-noded mandibular geometries. Cdl (condylion laterale) = most lateral point on the concylar head; Go (gonion) = most lateral point of the mandibular angle; Gn (gnathion) = notch in the center of the convexity of the mandibular symphysis; rGo (gonion) = most lateral point of the mandibular angle; rCdl (condylion laterale) = most lateral point on the condylar head. Landmarks having the prefix "r" indicate equivalent landmarks on the mandible, which are on the treated side.

After obtaining mean consensus configurations, Euclidean distance matrix analysis (EDMA) was employed (Lele and Richtsmeier, 1991) to compare the mandibular form of the three groups (preop, postop 1, postop 2). EDMA is a coordinate-free, statistical procedure that compares two forms using all the possible linear distances between homologous landmarks. For each form, a form matrix is produced and the matrices are compared to identify the linear distances that are most and least different. Corresponding linear distance differences are expressed as ratios in the form difference matrix (Lele and Cole, 1996). For example, if no difference exists between two landmarks, the relevant form difference matrix value would be 1.00. Consequently, values of > 1 or < 1 indicate that distances between landmarks differ in size. For example, a value of 1.13 indicates that the numerator configuration distance is 13% longer than that of the denominator configuration. For EDMA, mandibular form comparisons were undertaken that employed the five-landmark geometry shown in Figure 1. The statistical method used to test the result was a nonparametric bootstrap method (Lele and Richtsmeier, 1991), and the *p* values obtained relate to the likelihood of no morphological difference existing between the two consensus configurations.

Therefore, three mandibular form comparisons were undertaken: Comparison 1 considers the preop and postop 1 groups;

TABLE 1 Conventional Linear Analysis of the Total Mandibular Form Shows the Mean Linear Distances Between Landmarks ± Standard Deviation for the Three Time-Dependent Groups. The Probabilities that the Observed Differences are the Same for the Group Comparisons are Shown. Statistically Significant ($p < .05$) Comparisons are Indicated in Bold Face

							p *values*		
Landmark Pair	*Mean (mm)*	*Preop SD*	*Mean (mm)*	*Postop 1 SD*	*Mean (mm)*	*Postop 2 SD*	*Pre-Post 1*	*Post 1-Post 2*	*Pre-Post 2*
Cdl rCdl	112	9	115	7	115	8	0.29	0.92	0.27
Cdl rGo	112	9	117	6	116	8	0.11	0.69	0.26
Cdl Gn	104	12	113	8	106	11	**0.03**	0.06	0.71
Cdl Go	58	8	60	7	62	9	0.52	0.48	0.23
rCdl rGo	45	9	50	9	52	11	0.15	0.56	0.07
rCdl Gn	82	9	94	11	87	11	**0.01**	0.11	0.21
rCdl Go	105	9	113	8	113	9	**0.02**	0.97	**0.03**
rGo Gn	41	8	48	10	40	9	0.06	**0.04**	0.75
rGo Go	83	8	89	7	85	10	**0.04**	0.27	0.45
Gn Go	57	7	64	5	57	9	**0.01**	**0.03**	0.90

comparison 2 considers the postop 1 and postop 2 groups; and comparison 3 considers the preop and postop 2 groups.

Results

For the five mandibular landmarks utilized, digitization errors did not exceed 0.4%. Therefore, all landmarks included in the analysis were deemed to be reliably identified. Results from the linear analysis appear first (Table 1), followed by EDMA analyses of the consensus configurations. The EDMA results are presented as the form difference matrices of the preop, postop 1, and postop 2 groups.

Linear Measurements

Comparison 1 (preop, postop 1) indicated a mediolateral condylar-symphyseal width (rCdl Gn) increase of 12 mm on the treated side of the mandible and 9 mm on the untreated side (Cdl Gn). The mediolateral mandibular width (rCdl Go) showed an 8-mm postoperative increase, and the bigonial width (rGo Go) showed a similar 6-mm improvement. After ≈ 1 year, the untreated mandibular body length (Gn Go) showed a mean elongation of 7 mm.

TABLE 2 EDMA of the Total Mandibular Form. Paired Landmarks are Sorted for Each Comparison Relating to the Size of the Form Differences. Values <1 Depict Decreases in Size of the Numerator Form. Conversely, Values >1 Depict Increases in Size of the Numerator Form. Comparisons 1, 2, and 3 are Separate Analyses and Each One is Considered Individually in the Discussion.

Form Difference Matrix (Sorted)					
(i) Comparison 1		*(ii) Comparison 2*		*(iii) Comparison 3*	
Numerator: postop 1 Denominator: preop		*Numerator: postop 2 Denominator: postop 1*		*Numerator: postop 2 Denominator: preop*	
Cdl Go	1.027	Cdl Go	1.047	Cdl Go	1.076
rCdl rGo	1.128	rCdl rGo	1.067	rCdl rGo	1.203
Gn Go	1.141	Gn Go	0.911	Gn Go	1.040
rGo Gn	1.188	rGo Gn	0.771	rGo Gn	0.917
Cdl Gn	1.104	Cdl Gn	0.924	Cdl Gn	1.020
rCdl Gn	1.170	rCdl Gn	0.901	rCdl Gn	1.054
Cdl rGo	1.041	Cdl rGo	0.994	Cdl rGo	1.035
rCdl Go	1.062	rCdl Go	1.021	rCdl Go	1.084
Cdl rCdl	1.023	Cdl rCdl	1.012	Cdl rCdl	1.035
rGo Go	1.065	rGo Go	0.974	rGo Go	1.037
$p < 0.01$		$p < 0.01$		$p < 0.01$	

Comparison 2 (postop 1, postop 2) showed a mean 8-mm decrease in mandibular body length (rGo Gn) on the treated side and an apparent 7-mm decrease on the untreated side. The majority of the results, however, did not give any clear indication of form differences between the postop 1 and postop 2 groups.

Comparison 3 (preop, postop 2) maintained the mean 8-mm postoperative increase in transmandibular width (rCdl Go), but the majority of the results do not give any clear indication of form differences between the preop, postop 2 groups.

EDMA

Using the nonparametric bootstrap method the five-noded consensus configurations of the mean preop, postop 1, and postop 2 forms showed statistical difference ($p < .01$) in all three comparisons. The form difference matrices for the three comparisons are shown in Table 2i-iii.

Comparison 1 (preop, postop 1) showed that differences were evident throughout the form matrix, but the most significant differences in morphology were seen to occur on the treated side. For example, increases of 19% in the mandibular body (rGo Gn), 17% in the mediolateral condylar-symphyseal width (rCdl Gn), and 13% in ramus length were seen on the treated side, while the untreated mandibular body (Gn Go) revealed an increase of 14%.

In comparison 2 (postop 1, postop 2), increases were located in the mandibular ramus on both the treated (rCdl rGo; 7%) and nontreated (Cdl Go; 5%) sides. Somewhat surprisingly, however, apparent length decreases of 23% were observed in the treated mandibular body (rGo Gn), and 10% in the mediolateral condylar-symphyseal width (rCdl Gn). Also noticeable were apparent decreases in mandibular body length on the untreated side (Gn Go) and mediolateral condylar-symphyseal width (Cdl Gn), demonstrating decreases of 8%, respectively.

Comparison 3 (preop, postop 2) showed that the preop consensus mandibular form undergoes elongations to produce the postop 2 consensus form. The length increases evident within the treated side were consistently greater than the length increases apparent on the nontreated side. The ramus length on the treated side (rCdl rGo) was seen to increase by 20% while the nontreated side ramus (Cdl Go) showed only an 8% increase. The transmandibular width (rCdl Go) also showed an 8% increase while the mediolateral condylar-symphyseal width (rCdl Gn) indicated an increase of 5%. The mandibular body on the treated side, however, showed a reduction is size of 8%.

The current results revealed an early improvement in the surgically treated mandibular form with some evidence of relapse or failure of growth over the time span studied.

Discussion

There is considerable debate in the literature concerning the timing of surgical correction of CFM. Those who advocate early reconstruction prior to skeletal maturation do so believing that early surgery may help prevent secondary growth deformities (Munro, 1980; Mulliken et al., 1989). Others feel that skeletal deformity in CFM is not progressive (Obwegeser, 1974; Rune et al., 1981). In this study a limited number of appropriate CFM subjects were available. In all our cases, the decision to carry out surgical correction at this age was due to difficulties experienced by the children and significant pressure from parents to improve facial appearance. It was therefore difficult to construct a homogenous group of patients, but all were treated by the same method, using an inverted L osteotomy procedure. With a larger sample, it might have been possible to match age, sex, and the side displaying the unilateral deformity. Another problem was the difference in time after surgery evident in the postop 2 cephalographs. An indication of mandibular development immediately before, immediately after, and a constant postoperative period subsequent to surgery would have been preferable. In this study, however, the mean time after surgery for the postop 2 cephalographs available varied (3 $\pm$ 2 years), which meant that postoperative findings included some patients that had surpassed the prepubertal stage. Not surprisingly perhaps, very few statistically significant results from linear measurement analyses were found in the preop, postop 2 comparison; presumably the high level of heterogeneity of the sample masked shape and size differences.

To overcome sample heterogeneity, the mandibular forms were scaled to an equivalent size for each stage of the analysis. The EDMA results illustrated the advantages of such techniques because all the form differences rendered statistical significance ($p < .01$) when size variation was removed. Conventional linear measurements, however, have the advantage of being relatively easy to comprehend, returning absolute measures (millimeters). Such methods also avoid the complex and recently developed mathematical techniques employed in the EDMA procedures, which can obfuscate interpretation. Justification for the use of the morphometric techniques comes from their growing use in the scientific literature (Bookstein, 1991b; Lele and Richtsmeier, 1991; Ayoub et al., 1994, 1995; Boes et al., 1994; Singh et al., 1997a, b, c, 1998). In addition, the admittedly scarce number of significant linear measurements corroborated the EDMA findings.

From the preop, postop 1 comparison, the most striking differences were increases in the mandibular body length on the treated side, and consequently the mediolateral condylar-symphyseal width (Table 2). This change can be explained by lateral displacement of the treated side of the mandible during the surgical procedure to the nonaffected side. Also evident from the EDMA was ramus elongation on the treated side. These changes demonstrated the largest overall improvements in appearance when comparing both sides of the mandible. In general, the form differences produced by the surgery were associated with an improvement in mandibular form in the early postoperative phase.

The most obvious changes in the postop 1, postop 2 comparison related to the treated mandibular body and mediolateral condylar-symphyseal width. EDMA presents these changes as length decreases between mandibular body landmarks (rGo Gn; rCdl Gn; Gn Go; Cdl Gn) that can be seen in Table 2. In reality, it is highly unlikely that both sides of the mandibular body would sustain a length decrease in such a manner. The decrease in length observed in the analysis presumably relates to the drawbacks of representing a three-dimensional structure in two dimensions. The mandibular body length incorporates an anteroposterior component as well as a superoinferior component. Therefore, analyses of lateral cephalographs would also be required to more fully depict mandibular body length changes. The current analysis, however, reflects downward and forward mandibular growth that appears to reduce the distance between the mandibular angles and symphysis in a vertical plane. The important feature of these changes is that they are similar on both the treated and nontreated sides. The bilateral decrease in the body length seen in Table 2 occurs to a greater extent on the treated side than the nontreated side, however, suggesting the difference is associated with relapse, local remodeling at rGo or failure of growth of the mandibular body. Therefore, it is likely that postsurgical improvements in overall form appear to deteriorate over the time interval tested. Nevertheless, the ability to achieve bilateral growth in CFM patients after surgery was a primary objective of the operative procedure to overcome the relapse problems observed by Farrell and Kent (1977). To confirm the success of the procedure, mandibular ramus growth on the surgically treated side was found to at least match that of the nontreated side. Interestingly, EDMA indicated slightly more growth on the treated side (Table 2; rCdl rGo). The EDMA results suggest that the treated ramus grew by about 7% and the untreated ramus by about 5% over the time span tested.

The preop, postop 2 comparison demonstrates that some improvements in mandibular form were maintained over about 3 years. Table 2 shows that, by far, the largest differences are seen in the ramus, with the treated and nontreated sides displaying increases in length of about 20% and 8% respectively (Table 2; rCdl rGo; Cdl Go). In the postop 2 configuration, the treated side body length (rGo Gn) is 8% shorter than it was in the preop configuration. The nontreated side (Gn Go) appeared to undergo an increase in length of 4%. It can be concluded that the initial, surgically induced ramus elongations (Table 2) are in part maintained over 3 years, but the mandibular body shows some evidence of relapse or differential growth relative to the nontreated side. Smahel (1986) localized skeletal abnormalities in CFM patients, employing conventional cephalometry. When results were compared between asymmetrical and ''normal'' facial appearances, it was shown that hypoplasia was most severe in the lower face. In addition, anterior-posterior dimensions were noted to have the greatest reductions, with chin retrusion and an increased frequency of bite disorders also evident. In this present study, the mandibular EDMA comparisons reinforce the observations made by Smahel (1986) on severe lower-face hypoplasia. It also gives a detailed morphometric indication of the mandibular regions that most contributed to the asymmetry.

Although the mandibular body displayed an improvement after surgery, it was this region, however, that demonstrated evidence of relapse later. Skeletal reconstruction to elongate the mandibular body is difficult because of the location of the inferior alveolar nerve. The asymmetrical mandibular body may benefit more from subcutaneous implants, situated superficial to the skeletal structure. To obtain optimal results, the use of microvascular free-flap soft tissue reconstruction in conjunction with skeletal osteotomies has been recommended (Siebert et al., 1996). Distraction osteogenesis has also been employed recently as a method for surgical correction.

For the mandibular form comparisons, the greatest overall improvements were seen in the ramus. In the postop 2 configuration, the difference was 20%. This is a marked improvement and shows that over 3 years surgical improvements made to correct the ramus imbalance are maintained. Should the hypothesis stating that abnormal growth patterns in CFM are progressive be correct (Kaban et al., 1986; Murray et al., 1984), then the inverted L osteotomy appears to overcome this problem and allows ramus growth to occur. At 2 years following surgery, there were no statistically significant differences between the treated and normal side. These findings demonstrate that the growth rate of the affected side was similar to that of the nonaffected side. This supports the concept that CFM is not progressive in nature. When Farrell and Kent (1977) studied the postoperative stability of inverted L osteotomies, it was found that posterior facial height lost 8% of its correction over a period of 6 to 12 months. Evidence for such postoperative relapse was not found in this study. In fact, the mandibular form comparisons revealed ramus growth on both treated and nontreated sides after surgery.

In this study, surgical correction was restricted to the mandible, and esthetic achievements were judged only by consideration of its skeletal form from the frontal aspect. Thus, the influence of soft tissues on the superficial appearance of the patients was not examined. The skeletal structures, however, provide a primary basis for achieving a good postoperative result. Also, the full evaluation of a surgical procedure involves many other factors such as the resultant mandibular function ability (including dental occlusion). Such evaluations have been undertaken for some surgical techniques (e.g., Naples et al., 1994) and the potential for expansion of this study remains. With a full knowledge of the benefits and flaws of all the procedures, the most appropriate surgical treatment plans for specific cases could be better decided. It is generally accepted that, due to the wide spectrum of malformations associated with the CFM condition, multidisciplinary management is most often necessary (Caldarelli et al., 1980).

In summary, the capabilities of the inverted ''L'' osteotomy procedure analyzed in this study have been demonstrated. Information from this study can also be used to complement previous inverted ''L,'' sagittal split and ''C'' osteotomy evaluations (Farrell and Kent, 1977; Naples et al., 1994). It should be stressed, however, that the results illustrated in this study represent structural observations in only two dimensions, when in reality the structures are three-dimensional. This is particularly important when analyzing the morphometric changes that occur in the mandibular body, because form changes in the anterior-posterior dimension are best discernible from the lateral aspect. Therefore, a further study will be undertaken to include lateral cephalographs to give a fuller indication of the mandibular morphometric changes. Further studies could also investigate maxillary morphology and show how mandibular surgery affects its form. This analysis would test whether maxillary abnormalities are partly the result of secondary deformation caused by the abnormal mandibular location (Murray et al., 1984). This information would be helpful in deciding whether maxillary reconstruction is required, because the likely amount of maxillary growth that would occur after a ramus reconstruction would be estimable.

Acknowledgments. This study was supported by the Nuffield Foundation (GDS, ADH).

References

Ayoub AF, Stirrups DR, Moos KF. Assessment of chin surgery by a co-ordinate free method. *Int J Oral Maxillofac Surg.* 1994;23:6–10.

Ayoub AF, Stirrups DR, Moos KF. Stability of sagittal split advancement osteotomy: Single- versus double-jaw surgery. *Int J Adult Orthognath Surg.* 1995;3:181–192.

Boes JL, Bland PH, Weymouth TE, Quint LE, Bookstein FL, Meyer CR. Generating a normalised geometric liver model using warping. *Invest Radiol.* 1994;29:281–286.

Bookstein FL. Thin-plate splines and the atlas problem for biomedical images. *Lect Notes Comp Sci.* 1991;511:326–342.

Burck U. Genetic aspects of hemifacial microsomia. *Hum Genet.* 1983;64:291–296.

Caldarelli DD, Hutchinson JC Jr, Gould HJ. Hemifacial microsomia: priorities and sequence of comprehensive otologic management. *Cleft Palate J.* 1980;17:111–115.

Farrell CD, Kent JN. Evaluation of the surgical stability of 20 cases of inverted-L and C osteotomies. *J Oral Surg.* 1977;35:239–245.

Gorlin RJ, Cohen MM, Levin LS. Branchial arch and oroacral disorders. In: *Syndromes of the Head and Neck.* New York: Oxford University Press; 1990:641–652.

Gower JC. Generalised Procrustes analysis. *Psychometrika.* 1975;40:33–51.

Jacobsson C, Granstrom G. Clinical appearance of spontaneous and induced first and second branchial arch syndromes. *Scand J Plast Reconstr Surg Hand Surg.* 1997;31:125–136.

Juriloff DM, Harris MJ, Froster-Iskenius U. Hemifacial deficiency induced by a shift in dominance of the mouse mutation far: a possible genetic model for hemifacial microsomia. *J Craniofac Genet Dev Biol.* 1987;7:27–44.

Kaban LB, Moses MH, Mulliken JB. Correction of hemifacial microsomia in the growing child: a follow-up study. *Cleft Palate J.* 1986;23:50–52.

Kaban LB, Mulliken JB, Murray JE. Three-dimensional approach to analysis and treatment of hemifacial microsomia. *Cleft Palate J.* 1981;18:90–99.

Lele S, Cole TM. A new test for shape differences when variance-covariance matrices are unequal. *J Human Evol.* 1996;31:193–212.

Lele S, Richtsmeier JT. Euclidean distance matrix analysis: a co-ordinate free approach for comparing biological shapes using landmark data. *Am J Phys Anthropol.* 1991;86:415–427.

Loevy HT, Shore SW. Dental maturation in hemifacial microsomia. *J Craniofac Genet Dev Biol.* 1985;1:267–272.

Mathog RH, Leonard MS. Surgical correction of Goldenhar's syndrome. *Laryngoscope.* 1980;90:1137–1147.

Mulliken JB, Ferraro NF, Vento AR. A retrospective analysis of growth of the corrected ramus in children with hemifacial microsomia. *Cleft Palate J.* 1989;26:312.

Munro IR. One stage reconstruction of temporomandibular joint in hemifacial microsomia. *Plast Reconstr Surg.* 1980;66:699.

Murray JE, Kaban LB, Mulliken JB. Analysis and treatment of hemifacial microsomia. *Plast Reconstr Surg.* 1984;74:186–199.

Naples RJ, Van Sickels JE, Jones DL. Long-term neurosensory deficits associated with bilateral sagittal split osteotomy versus inverted ''L'' osteotomy. *Oral Surg Oral Med Oral Pathol.* 1994;77:318–321.

Obwegeser HL. Correction of the skeletal anomalies of oto-mandibular dysostosis. *J Maxillofac Surg.* 1974;2:73–92

Ortiz-Monasterio F, Molina F, Andrade L, Rodriguez C, Sainz Arregui J. Simultaneous mandibular and maxillary distraction in hemifacial microsomia in adults: avoiding occlusal disasters. *Plast Reconstr Surg.* 1997;100:852–861.

Polley JW, Figueroa AA, Liou EJ, Cohen M. Longitudinal analysis of mandibular asymmetry in hemifacial microsomia. *Plast Reconstr Surg.* 1997;99:328–339.

Poole MD. A composite flap for early treatment of hemifacial microsomia. *Br J Plast Surg.* 1989;42:163–172.

Rohlf FJ, Slice D. Extensions of the Procrustes method for the optimal superimposition of landmarks. *Syst Zool.* 1990;39:40–59.

Rollnick BR, Kaye CI. Hemifacial microsomia and variants: pedigree data. *Am J Med Genet.* 1983;15:233–253.

Rune B, Selvik G, Sarnas KV, Jacobsson S. Growth in hemifacial microsomia studied with the aid of roentgen stereophotogrammetry and metallic implants. *Cleft Palate J.* 1981;18:128–146.

Seow WK, Urban S, Vafaie N, Shusterman S. Morphometric analysis of the primary and permanent dentitions in hemifacial microsomia: a controlled study. *J Dent Res.* 1998;77:27–38.

Siebert JW, Anson G, Longaker MT. Microsurgical correction of facial asymmetry in 60 consecutive cases. *Plast Reconstr Surg.* 1996;97:354–363.

Singh GD, McNamara JA Jr, Lozanoff S. Finite element morphometry of the midfacial complex in subjects with Angle's Class III malocclusions. *J Craniofac Genet Dev Biol.* 1997a;17:112–120.

Singh GD, McNamara JA Jr, Lozanoff S. Localisation of deformations of the midfacial complex in subjects with Class III malocclusions employing thin-plate spline analysis. *J Anat.* 1997b;191:595–602.

Singh GD, McNamara JA Jr, Lozanoff S. Morphometry of the cranial base in subjects with Class III malocclusion. *J Dent Res.* 1997c;76:694–703.

Singh GD, McNamara JA Jr, Lozanoff S. Morphometry of the midfacial complex in subjects with Class III malocclusions: Procrustes, Euclidean and cephalometric analyses. *Clin Anat.* 1998;11:162–170.

Smahel Z. Craniofacial changes in hemifacial microsomia. *J Craniofac Genet Dev Biol.* 1986;6:151–170.

Taysi K, Marsh JL, Wise DM. Familial hemifacial microsomia. *Cleft Palate J.* 1983;20:47–53.

Thompson DW. *On Growth and Form.* Cambridge: Cambridge University Press; 1917.