Allometry of the cranial base in prepubertal Korean subjects with Class III malocclusions: Finite element morphometry

G.D. Singh, BDS, PhD; J.A. McNamara Jr., DDS, PhD; S. Lozanoff, PhD

Abstract: Sphenoethmoidal allometry could be associated with ethnic heterogeneity of the midfacial profile. Thirteen cranial base landmarks were digitized from cephalographs of 69 Korean and 73 European American prepubertal children exhibiting Class III malocclusion. Average geometries were normalized, and a color-coded finite element (FEM) program was used to localize differences in morphology. ANOVA indicated that mean Korean and European American cranial base configurations differed statistically ($p < 0.01$); this was also true for seven age groups tested ($p < 0.001$). For size-change, FEM analysis revealed that in the anterior cranial base, Korean sphenoethmoidal and sella turcica regions were smaller (≈12%). Local increases in size were apparent for the posterior region of the Korean cranial base (≈35%). For shape-change, Korean and European American cranial base configurations were isotropic with minor anisotropy in the sphenoethmoidal and spheno-occipital regions. A sphenoethmoidal mechanism of midfacial retrognathism appears to be implicated in the development of a skeletal Class III morphology.

Key words: Cranial base, Cephalometric, Class III, Craniofacial, Korean, Finite element, Morphometry

A clear understanding of how the cranial base affects the final midfacial profile remains obscure.[1] Theories explaining the anterior translation of the midface include the septal traction model.[2-5] Moss,[6] however, supports the primary role of function in craniofacial growth, acknowledging that genomic instead of epigenetic (functional) factors regulate such growth. But specific cranial base components responsible for midfacial retrognathia have not been delineated. Traditionally, the study of midfacial retrognathia has been performed using cephalometric analysis in human groups, while experimental studies have used extirpation experiments in animals in an attempt to identify craniofacial regions that direct midfacial advancement.[7]

The Brachyrrhine (Br) mouse mutant provides a useful model for studying factors associated with midfacial hypoplasia.[8] Abnormal growth activity in the presphenoidal component of the presumptive anterior cranial base (ACB) has been reported.[9] Indeed, in achondroplastic mice, a reduction in length of the cranial base by ≈25% has been reported,[10] and it was suggested that this reduction was due to diminished growth at the spheno-occipital and mid-sphenoidal synchondroses. In contrast, Cohen et al.[11] found a normal ACB length but a shortened posterior cranial base (PCB) in achondroplastic human subjects. They suggested that growth in length of the ACB takes place primarily at the sphenoethmoidal synchondrosis. Similarly, in a cephalometric study in humans,[12] it was also shown that patients with premature craniosynostosis had shorter cranial bases; it was suggested that inhibited growth affected the ACB and appeared to involve the sphenoethmoidal, intersphenoidal and sphenofrontal synchondroses.

The spheno-occipital complex is closely related to the skeletal facial pattern and contributes to final facial form.[13] But Coben[14] contended that the role of the spheno-occipital synchondrosis has been masked by traditional cephalometric analy-

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Submitted: March 1999, **Revised and accepted:** June 1999
Angle Orthod 1999;69(6):507-514

ses. Furthermore, Coben[14] suggested that superimposition on ACB has led to misinterpretation of the direction of facial growth. Hoyte[15] indicated that the basicranium ossifies in a posteroanterior axis but ceases growth in an anteroposterior sequence. Although the ethmoid was thought to stop elongating early in human postnatal development, Hoyte[16] suggested that it continues to grow for a longer time than was originally thought. Support for this concept comes from Rosenberg et al.,[17] who reported that ACB was significantly shortened in experimental craniofacial synostosis in rabbits.

The aim of this study was to determine the contribution of the cranial base in the heterogeneic expression of human Class III malocclusions, a condition that exhibits midfacial retrognathia in the lateral profile. The hypothesis tested was that there are no morphological differences in the cranial base of diverse human ethnic groups that exhibit Class III malocclusions. Rejection of the null hypothesis would provide support for the view that the cranial base has a role in the final positioning of the midface that could account for part of the diversity in clinical presentation of children with Class III malocclusions.

Materials and methods

Pretreatment lateral cephalographs of 73 European American subjects between 5 to 11 years of age, with Angle Class III molar malocclusion were retrieved.[18] A further 69 cephalographs of untreated Korean subjects with a similar Class III molar relationship were obtained from a Korean orthodontic practice. The total sample included an approximately equal number of age-matched males and females with negative history of airway problems and no obvious vertical skeletal problems. It was presumed that all radiographs were taken from subjects exhibiting left-right symmetry and that the central X-ray passed along the transmeatal axis when the teeth were in occlusion. The magnification of each film was standardized to 8%. The chronological age was assumed to match the developmental age in this study, as carpal ages were unavailable.

Each lateral cephalograph was traced on frosted acetate film (0.03" thick) and checked by one investigator (GDS). Digitization of landmark coordinates from cephalographs taped to a light box of uniform brightness was achieved using appropriate software and a digitizing tablet (Numonics Inc, Montgomeryville, Pa). Thirteen homologous landmarks were identified and digitized (Figure 1). These landmarks encompassed the lateral profile of the cranial base and permitted the construction of the cranial base configurations to be studied. Although a digitizing error study was not included, all films were digitized twice, and any x, y landmark coordinates that showed a discrepancy of >1% on duplicate digitization were deemed to be identified unreliably and were excluded from the final analyses.

For statistical analysis, Procrustes analysis was employed to compare geometric configurations comprising the cephalometric landmarks representing each subject. (In Greek mythology, Procrustes was an innkeeper who would stretch victims, or shorten them by cutting off limbs, to fit his only bed.) This numerical analysis is now used in the context of superimposition methods. Following this method, every object's coordinates were translated, rotated, and scaled repeatedly until the least-squares fit of all configurations was no longer improved. Once the intercephalometric landmark distances were minimized in this fashion, an overall average form was calculated for each group. Then, the groups' average forms were compared, in much the same way as analysis of variance is performed on linear cephalometric measures. The Procrustes routine was implemented on an Amiga 3000 computer, and an average 13-noded geometry for each age group was determined using a generalized orthogonal Procrustes analysis.[19] Therefore, all configurations were registered with respect to one another, and as a result of this procedure, geometric cranial base configurations were scaled to equivalent areas, avoiding prob-

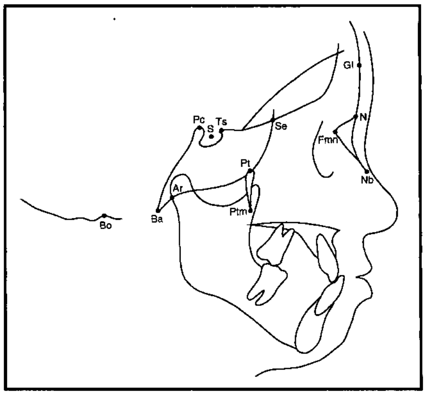

Figure 1
Cranial landmarks
Ba: Basion (lowest point on anterior border of foramen magnum)
Bo: Bolton point (highest point behind occipital condyle)
Fmn: Frontonasomaxillary suture
Gl: Glabella (most prominent point on frontal bone)
Pc: Posterior clinoid process (most superior point on clinoid process
N: Nasion (most anterior point on frontonasal suture)
Ptm: Pterygo-maxillare (most inferior point of pterygomaxillary fissure)
S: Sella (center of sella turcica)
Se: Sphenoidale (intersection of greater wings of the sphenoid and anterior cranial base)
Ts: Tuberculum sellae (most anterior point of sella turcica)
Nb: Rhinion (tip of nasal bone)
Pt: Pterygoid point (superiormost point on lateral outline of pterygoid fissure)
Ar: Articulare (intersection of dorsal contour of condylar head and posterior cranial base)

Table 1
Procrustes analysis of mean cranial base configurations of European American and Korean Class III subjects

Age (yrs)	5	6	7	8	9	10	11	Total
Residual	0.0041	0.0028	0.0055	0.0031	0.0048	0.0041	0.0039	0.0027
F-value	3.97	3.31	6.71	4.83	7.33	4.54	2.56	7.89
p <	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.005

When the total sample is decomposed into seven age groups, most groups maintain statistical significance.

Table 2
FEM analysis comparing Korean and European American Class III cranial base nodal values for size- and shape-change

	Ba	Bo	Pc	S	Ts	Se	Fmn	N	Gl	Nb	Pt	Ptm	Ar
Size	1.56	1.481	0.98	0.95	0.96	1.01	1.02	1.07	1.18	1.07	1.14	1.08	1.18
Shape	1.010	1.004	1.011	1.009	1.009	1.006	1.008	1.011	1.021	1.008	1.003	1.009	1.007

lems introduced by differences in size. To determine whether cranial base landmark configurations differed between ethnic types and at each age interval, each European American group mean geometry was compared statistically with the age-matched Korean group average geometry using an analysis of variance, ANOVA.[19] In each instance, the null hypothesis was that the European American mean was not significantly different from the Korean average. Residuals and corresponding *F*-values were computed, tabulated, and compared.

In order to visualize sources of heterogeneic cranial base morphology, finite-element (FEM) analysis was undertaken that incorporated a spline interpolation function.[20] FEM analysis consists of deforming one geometric configuration into a second geometry and then calculating the local strains within the first configuration as it is deformed. These strains can be expressed as a color scale and mapped within the geometry indicating local areas of strain. Additional equations can be used to partition the strains into size- or shape-change.[21,22] The FEM software was written in "C" and implemented on an Amiga 3000 computer. The overall mean European American configuration was taken as the initial geometry, and this configuration was compared with the overall Korean mean. Size-change variables were computed as the product of the principal extensions, while shape-change measures were calculated as the ratio of the greater divided by the lesser principal extension.[23] The mean geometries at each age interval also were compared (≈10 subjects per group; ≈5 males, ≈5 females). Therefore, eight comparisons were generated in total, and deformation values were computed for at least 2000 points per geometry for graphical display. A log-linear interpolation of the size- and shape-values was used to generate a color map. These form-change measures then were color-mapped into each European American configuration to provide graphical displays of geometrical change for the overall and each agewise comparison.

Results

The terms used in this section are in accord with the NATO ASI Series.[24]

Table 1 shows the residuals from the overall Procrustes analysis and those at each age when compared using an *F*-distribution. Statistically significant differences between the European American and Korean cranial base configurations occurred at $p < 0.01$ for the total sample. When the total sample was decomposed over seven age intervals, the comparisons showed statistical significance at $p < 0.001$ for all age groups tested.

Table 2 summarizes nodal values for size- and shape-change using FEM to compare European American and Korean cranial base configurations. Size-change variables indicated little change at nodes in the anterior and midcranial base regions, e.g., Se, Fmn, Ts. For the PCB regions, increases in size at nodes were notable, e.g., Bo, Ba, with increased values within regions encompassed by the PCB. Shape-change variables, however, indicated little heterogeneity.

Given the conditions of parsimony, the FEM color maps showed a high degree of correspondence. The FEM program optimizes the color range so that the scale bar varies in color for different configurations. The degree of size- or shape-change, however, can be estimated by comparing the color of the region in the configuration with that on the scale bar and reading the value assigned at that level of size- or shape-change. Comparing the European American and Korean cranial base configurations for

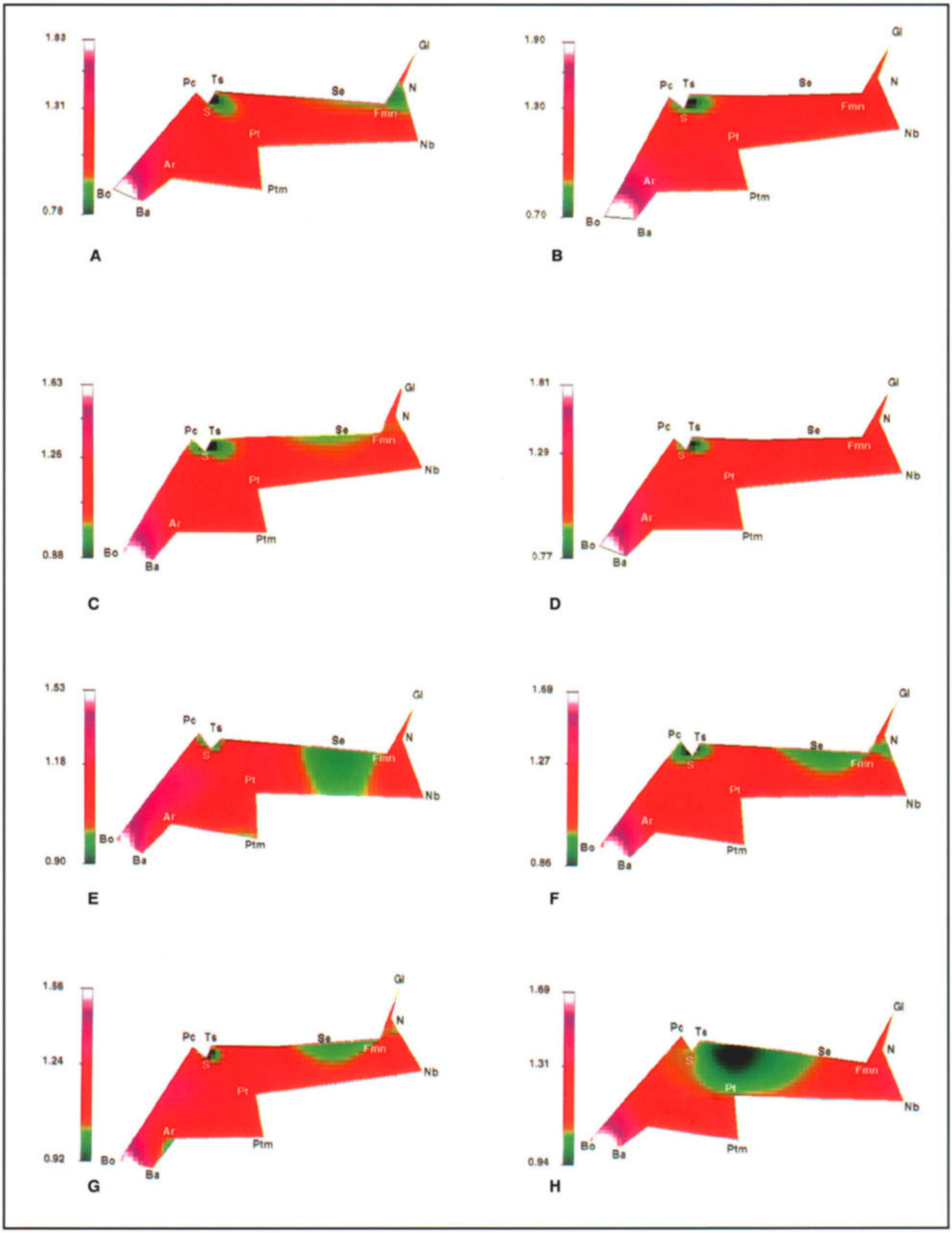
1.83
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Figure 2

Figure 2
Comparison of European American and Korean cranial base configurations for size-change.
A: Overall comparison. Between Bo and Ba, an increase in size of ≈60% is evident. Around sella turcica, ≈10% decrease in size is visible and a decrease in size in regions encompassing the sphenoethmoidal synchondroses is discernible.
B: Age 5 years. Between Bo and Ba, an increase in size of ≈70% is evident. The sella turcica region shows ≈25% decrease in size, but anterior cranial base is predominantly isometric.
C: Age 6 years. Between Bo and Ba, an increase in size of ≈80% is seen. The anterior aspect of the sella turcica region shows ≈20% decrease in size. While anterior cranial base is largely isometric, its anteriormost region shows a ≈20% decrease in size.
D: Age 7 years. Between Bo and Ba, an increase in size of ≈80% is seen. The anterior aspect of the sella turcica region shows a decrease in size (≈10%) but the anterior cranial base is predominantly isometric.
E. Age 8 years. Between Bo and Ba, an increase in size of ≈50% is seen, while the sella turcica region shows small, localized decreases in size (≈10%). In contrast, the anterior cranial base now shows negative allometry (≈10% decrease in size) in the middle of anterior cranial base.
F. Age 9 years. Between Bo and Ba, an increase in size of ≈65% is seen while the sella turcica region shows localized decreases in size (≈12%). In contrast, the anterior cranial base now shows negative allometry (≈10% decrease in size) in the middle and anteriormost regions of anterior cranial base.
G. Age 10 years. Between Bo and Ba, an increase in size of ≈50% is seen while the anterior aspect of the sella turcica region shows small, localized decreases in size (≈10%). In contrast, the anterior cranial base now shows negative allometry (≈10% decrease in size) with its epicenter around sphenoidale.
H. Age 11 years. Between Bo and Ba, an increase in size of ≈65% is seen while the sella turcica region shows a decrease in size (≈5%) extending through the anterior cranial base up to sphenoidale.

size-change graphically, FEM revealed that overall decreases in size in regions encompassing sella turcica and the sphenoethmoidal synchondroses were discernible. Conspicuously, there was a localized (light green) area of negative allometry (size-related shape change) between the frontonasomaxillary suture and sella turcica, with an epicenter based around the region of the sphenoethmoidal synchondroses (Se: Figure 2A; ≈10% decrease in size). In contrast, between Bo and Ba, a white area showing an increase in size of ≈60% was evident (Figure 2A).

Decomposition of the sample into the seven age- and sex-matched groups revealed that at age 5 to 7 years, an interesting pattern of size-change emerged (Figure 2B-D). Invariably, the sella turcica region showed a (black-green) decrease in size (≈10-30%), while ACB was largely red and isometric (invariant with respect to local size change) at these ages. In contrast, the posteriormost region of the cranial base showed a white area of positive allometry (≈60-90% increase in size) in these age groups.

Similarly, for the 8- to 11-year-old groups (Figures 2E-H), the posteriormost cranial base region exhibited a (white) area of positive allometry (≈50-60% increase in size) and the sella turcica region showed a (black-green) decrease in size (≈10%) as in the younger age groups. In contrast to the earlier findings reported above, the regions of the sphenoethmoidal synchondroses exhibited a (green) region of negative allometry (a decrease in size of ≈5-10%) contrary to the (red) isometry in the younger age groups.

For shape-change, the Class III cranial base nodal mesh was predominantly isotropic (uniform with respect to local shape-change; Figure 3A). Shape-changes in the 5- to 11-year-old age groups were similar (Figures 3B-H). The majority of the configurations were isotropic, with evidence of anisotropy (non-uniform local shape-change) restricted to small, localized areas in the sella turcica region.

Therefore, it appears that a combination of reduction in size in the sella turcica region and increase in size in the PCB region distinguish the Korean Class III cranial nodal mesh from the European American. Moreover, the early pattern of ACB isometry is not maintained in the later postnatal stages, suggesting that cranial foundations for the Korean Class III child are laid down in early childhood but are manifest in the older child. That these morphological differences are localized in the region of the sphenoethmoidal synchondroses may have a bearing on the final positioning of the midfacial complex, associated concomitantly with midfacial retrognathia and a Class III malocclusion.

Discussion

Localization of form differences is an important concept in quantitative morphoanalysis. Superimposition-based techniques presume to recreate vectors that depict the form change, commonly using the Procrustes distance[25,26] as a measure of proximity of landmarks. But Lele[27] notes that there are many different measures of proximity and corresponding superimposition methods, and holds the opinion[28] that superimposition techniques and transformation grids cannot recreate the true form change, even under conditions of parsimony. Mardia[29] supports the view that Procrustes-based approaches can be justified through isotropic models. Lele[28] believes that the description of form change using form difference matrices (Euclidean distance matrix analysis; EDMA) satisfies invariance requirements and is useful for draw-

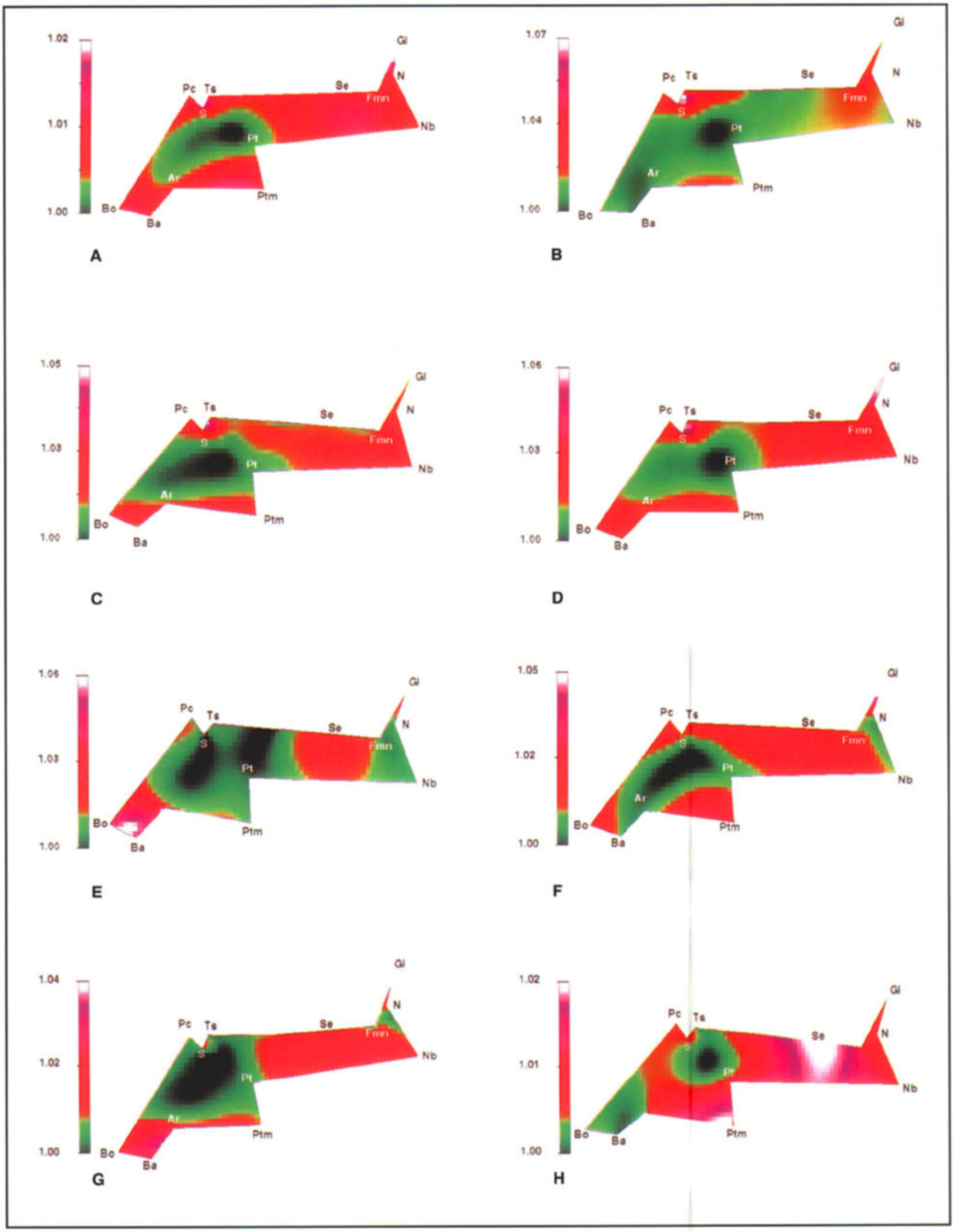
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Figure 3

Figure 3
Comparison of European American and Korean cranial base configurations for shape-change.
A: Overall comparison. The vast majority of the configuration is isotropic, with low levels of anisotropy in the anterior cranial base.
B: Age 5 years. Anisotropy is restricted to small, localized areas of the sella turcica region. Although low levels of anisotropy are discernible in the anterior cranial base, the vast majority of the configuration is isotropic.
C: Age 6 years. Anisotropy is restricted to a small, localized area of the sella turcica region. Low levels of anisotropy are discernible in the anterior cranial base, and the body of the configuration is isotropic.
D: Age 7 years. Anisotropy is restricted to a small, localized area of the sella turcica region. Very low levels of anisotropy are discernible in the anterior cranial base, but the vast majority of the configuration is isotropic.
E. Age 8 years. Some anisotropy is evident for the posterior cranial base, and low levels are discernible in the middle of the anterior cranial base. However, the remainder of the configuration is isotropic.
F. Age 9 years. Low levels of anisotropy are discernible in the anterior cranial base, but the configuration is predominantly isotropic.
G. Age 10 years. Some anisotropy is discernible in the anterior cranial base, but the majority of the configuration is isotropic.
H. Age 11 years. Although low levels of anisotropy are discernible in the anterior cranial base and pterygoid regions, the vast majority of the configuration is isotropic.

ing biological conclusions. On the other hand, Mardia[29] notes that EDMA is sensitive to outliers, and that using different loss functions in EDMA will lead to different results. In contrast, FEM attempts to describe form differences in terms of deformation of the space in the vicinity of a reference specimen into that of a target specimen. The principal strains that arise in deforming the elements between reference and target can be calculated at equivalent points within the elements. Importantly, increasing experience in the application of morphometric techniques indicates that these methodologies are robust in terms of the biological conclusions.[30]

In humans, the ACB undergoes extensive growth during the late embryonic and early fetal period.[31] Due to its dramatic growth activity during the prenatal and early postnatal periods, the ACB is thought to play an important role in the emergence of normal midfacial form. Recently[32] it was demonstrated that the murine cranial base displays two distinct growth zones, one located posteriorly (the presumptive sphenoethmoidal region) and the other anteriorly (presumptive nasal septal region). The results showed that the posterior region is associated with midfacial retrognathia.[32] That the sphenoethmoidal region is expected to display cellular growth deficiency was supported by an autoradiographic follow-up study.[33] Thus, the sphenoethmoidal region appears significant for the final positioning of the midface; deficient growth at the sphenoethmoidal synchondroses could be expected to prevent anterior translation of the midface. If the sphenoethmoidal region fails to develop normally, a short ACB is expected and midfacial retrognathia is likely to ensue.

In this study, it emerges that Koreans with Class III malocclusions have a smaller ACB compared with their European American counterparts. This finding parallels that of Chan,[34] who suggested that a significantly shorter sella-nasion length accounts for the high incidence of Class III malocclusions in the Cantonese, and concords with earlier work.[35] In contrast, further posteriorly, it is likely that growth activities persist longer in the PCB in prepubertal Korean children, as this region showed an increase in local size compared with European American children. Our study reflects the report of Masaki,[36] who noted a longer PCB but shorter ACB in Japanese boys and girls compared with Caucasians. Melsen[37] found that growth activity persists in the sphenoethmoidal synchondrosis up to 8 years of age, but growth in the spheno-occipital synchondrosis normally continues until 12 to 18 years.[38] In the present study, the decrease in size of the ACB in Korean children leads us to hypothesize that deficient growth or premature closure of the sphenoethmoidal synchondroses arise from early cessation of growth activities.

In European Americans, the cranial base appears to show less orthocephalization, i.e., deficient flattening in the anteroposterior plane[21] and, allied with deficient growth or earlier closure of the Korean sphenoethmoidal synchondroses, may be one factor leading to morphologic heterogeneity of the cranial base. In the clinical presentation of children with Class III malocclusion, differences in cranial base morphology may become apparent in the lateral profile when the facial appearance of European Americans and Koreans with Class III malocclusion are compared. Ostensibly, the Korean children display a more pronounced midfacial retrognathia, and this retrusion may be exacerbated by differential allometry of the PCB.

Conclusions

Reduction in size or alteration in shape of the ACB may cause a retrognathic midfacial profile associated with Class III malocclusions. However, the morphometry of the midfacial and mandibular complexes has not been undertaken in this study, and further analyses are warranted. Such studies would test the hypothesis that the spheno-ethmoidal model of midfacial retrognathia in isolation can account for the increased prevalence and heightened severity of the Class III condition in the Southeast Asian child. The genes thought to be associated with the Class III condition also require identification.

Acknowledgments

This study was supported by a Tattersall Scholarship (UK), the Wellcome Trust (UK), and the Medical Research Council (Canada). The authors would like to thank Dr. Y.G. Choi for supplying the lateral cephalographs of Korean children used in this study.

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