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THE CORRELATION OF CRANIOFACIAL FORM BETWEEN SIBLINGS

Abstract

by

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The goal of the research pursued in this masters thesis is to investigate aspects of the genetic basis of craniofacial form. It has been argued that certain morphological characters, such as the shape and form of a human face or head, are under the control of two sets of genes. One set dictates the overall appearance or structure of the face or head (i.e., pleiotropic genes underlying the gross morphological structure of the head and face) and one set causes minor deviations from this overall appearance or structure (i.e., polygenes that "fine tune" and individual's facial form). Although it would be difficult to determine the exact role individual genes have in terms of their contribution to either an overall facial plan or minor deviations from that plan, it is important to consider and test the hypothesis that a gene or set of genes actually *does* control an overall facial or head plan. This thesis investigates this hypothesis using a suite of twenty-three craniofacial measures obtained from fourty-four pairs of female siblings whose measures were obtained

at the same age and developmental stage as well as a number of statistical techniques appropriate for testing this hypothesis. The main results suggest that certain facial features such as horizontal measurements of the cranial base and mandible, measurements resulting in mandibular and maxillary projection, and vertical measurements of the overall craniofacial skeletal complex are more strongly inherited than any of the component measurements used to derive the overall feature. Thus, pleiotropy and genetic control of gross morphological features appear to dictate craniofacial development. This result could have an impact on not only the way evolutionary biologists approach the inheritance of related morphological features, but also on the way clinicians and orthodontists must account for and accommodate factors influencing facial form during the assessment of pathologies.

Dedicated to

My parents, Raymond and MaryJo

Lisa Lehky

Dominic, Mother, and all the Bocce Boys

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INTRODUCTION

The importance of estimating the outcome of growth and development of a child prior to orthodontic treatment cannot be over emphasized. The result of this importance has led to numerous clinical analyses by a number of different methods. Any insight that can consistently predict the phenotypic outcome of a child prior to orthodontic treatment would be greatly received. Therefore, studies of familial similarity seem to be a good adjunct to the many clinical analyses present today.

Many studies as well as a number of statistical models have been designed involving parent offspring, sibling-sibling, and monozygotic twins to dizygotic twins to evaluate the genetic influence on facial form. If a practitioner could assess which craniofacial areas are more strongly influenced by genetic causes, the information would be invaluable for prediction of craniofacial form and direction of growth.

The present study is a descriptive approach examining the genetic and environmental determination of craniofacial form by evaluating concordance between sisters utilizing a number of statistical analyses. The present study was undertaken to compliment previous studies of familial

similarity. The present study differs from previous studies in that very strict parameters for sex, skeletal age, and chronologic age, were used in sample selection, as well as the measurements and statistical analysis employed. Results of studies like the present study could provide meaningful and useful information in diagnosis and treatment planning. Such information should prove helpful in prediction of the phenotypic result a younger sibling may exhibit prior to orthodontic treatment via examination of an older sibling.

LITERATURE REVIEW

Brief History of the Study of Heritability

The review of the literature must first begin with Jean-Baptiste Lamarck (1744-1829). Lamarck believed that characteristics are acquired and then inherited by the offspring. For instance, Lamarck suggested that giraffes acquired their long neck by continuously stretching to reach the tender leaves found in the tree tops. The acquired long neck is then passed on to the offspring of the giraffe. Lamarck's theory of acquired characteristics can be disproven by simply cutting off the tail of mice and then observing the tail length of the offspring. (Tamarin 1991) Mice that have had their tail removed surgically have offspring with tails of normal length.

Charles Darwin suggested an alternative view in 1859, termed "evolution by natural selection". Darwin's theory would explain variation in giraffe neck length by suggesting that longer necked animals can take advantage of a food source not accessible to the short necked giraffes. The advantage of a longer neck would allow giraffes to exploit a food niche that was not available to short necked giraffes. Because of this, selection for longer necked giraffes would occur, whereby long-necked giraffes would

have a survival advantage, and whose offspring would have a similar advantage. Gradually the population of giraffes would change. The future generations of giraffes would have longer necks. In the *Origin of the Species*, Darwin also described a number of other examples of such selections. Darwin used the example of pigeon breeding, and the diversity of characteristics obtained in pigeons by selective breeding. Though he considered the inherited characteristics of the pigeons as artificial selection as opposed to "natural" selection, because the characteristics were induced by man.

Darwin, after the celebrated publication of *Origin of Species*, also presented his hypothesis of Pangenesis, which characterized contemporary understanding of the basic mechanics of heredity at the time. A quote from Darwin in 1868 describes this view of heredity:

> "....But besides this means of increase I assume that cells before the conversion into completely passive or "form-material," throw off minute granules or atoms, which circulate freely throughout the system, and when supplied with proper nutriment multiply by self-division, subsequently becoming developed into cells like those from which they were derived. These granules for the sake of distinctiveness may be called cell granules or, as the cellular theory is not fully established, simply gemmules. They are supposed to be transmitted from the parents to the offspring and are generally developed in the generation which immediately succeeds, but often are transmitted in a dormant state during many generations and are then developed. Their development is supposed to depend on their union with other partially developed cells or gemmules which proceed them in the regular course of

> growth. Why I use the term union will be seen when we discuss the direct action of pollen on the tissues of the mother plant. Gemmules are supposed to be thrown off by every cell or unit, not only during the adult state, but during all the stages of development. Lastly, I assume that the gemmules in their dormant state have a mutual affinity for each other, leading to aggregation either into buds or into sexual elements. Hence, strictly, it is not the reproductive elements, nor the buds, which generate new organisms, but the cells themselves throughout the body. These assumptions constitute the provisional hypothesis which I have called Pangenesis."(Nardone 1968)

A cousin of Darwin, Sir Francis Galton published Hereditary Genius in 1869 which complemented Darwin's research. Galton established a research lab where the best pre-Mendelian genetic research was carried out. (Nardone 1968) Galton is considered the pioneer of twin research because he was the first to conduct a scientific analysis of twins. Galton actually qualified the two types of twin pairs; identical (monozygotic) twins and fraternal (dizygotic) twins. Galton concluded that comparison of the two types of twins could establish characteristics that are likely under genetic control (nature) and those that are environmentally influenced or under environmental control (nurture). In 1903 Pearson implied that Galton's data could lay the groundwork for a theory on the mechanics of inheritance. Galton ultimately argued that inheritance resulted from the "blending" of characteristics from mates, which provided much material for statistical and descriptive studies. (Pearson and Lee 1903) Later, Galton

and Pearson led the formation of the study of biometry, or the use of statistical tools of correlation and regression analysis, to study the inheritance of traits that are continuous or quantitative, such as height and weight. (Tamarin 1991)

In 1903 Karl Pearson actually collected a sample of more than four thousand individuals and one thousand families to test the hypothesis consistent with the biometrical and blending theory orientation he and Galton were pursuing. Records of stature and appendage lengths were taken. His data showed that offspring from tall fathers tend to "regress" back to the normal average height values. (Pearson and Lee 1903)

Pearson also made other conclusions from his data. For example, Pearson argued that sons and daughters are equally influenced by both mother and father; however, a change in sex appeared to weaken the hereditary influence. In addition, Pearson felt that the inheritance of all characters is not the same: the more complex the character the greater the intensity of hereditary resemblance. (Pearson and Lee 1903) Pearson formulated the "law of universal regression" from his data, which simply states that offspring tend to regress back toward the mean trait values in relation to their parents.

The major advance in the study of heritable traits was initiated by Gregor Johann Mendel. Mendel, an Austrian

monk, basically discovered the algebraic rules of inheritance which would guide all future genetic research and practice. Mendel crossbreed garden peas that possessed non overlapping characteristics such as wrinkled or round seeds, yellow or green pods, et cetera. He then observed the distribution of the characteristics of the peas over several generations, and noted that predictable ratios were observed in these characteristics.

Although Mendel is credited with developing the modern theory of inheritance many people prior to Mendel contributed similar ideas on the inheritance of characteristics. For instance, in the first century Columella described inheritance patterns in sheep which suggested that traits are transmitted from parents to offspring. In 1588, Tabernaemontanus studied colors of grain found in corn and concluded that this was an act of god. In 1683, Leeuwenhoek observed dominance effects in rabbits. In 1799 Sir Andrew Knight crossed different types of peas and noted that the hybrids appeared different than the parent plants and concluded that a mixing of the parents must be responsible. Most of these observations were considered acts of deity by their contemporaries, and dismissed the possibility that natural, as opposed to divinely guided, mechanical laws could guide trait formation.

Mendel's Laws and Segregating Genes

Mendel's main tenet assumed that "phenotypes" or traits are controlled by genetic elements. Each individual possesses two copies of a specific genetic element or gene. The genes reside at different "loci" along a "genome" forming a string of chromosome pairs. During fertilization organisms receive half the genetic material from a paternal contribution and half the genetic material from a maternal contribution. If both halves of the genetic material contributed by the parents are the same then the offspring are homozygous for that locus. For example, if tall genes are contributed from both parents, the offspring are homozygous for the "tall" gene. If on the other hand the contribution is a tall gene from one parent and a short gene from the other parent, the offspring are heterozygous for the genotype. All genes are not expressed equally. Some genes may display dominance. For instance, if a tall pea plant is crossed with a dwarf pea plant the offspring that have both tall and dwarf genes tend to be tall. Therefore, although the offspring contain a genotype of both tall and dwarf genes the phenotypic expression is tall. Mendel considered tallness as a dominant trait and dwarfism as a recessive trait. If the heterozygous offspring are cross bred the resulting generation will present with both tall and dwarf phenotypes (3 tall : 1

dwarf). Mendel's work resulted in two laws. 1) The law of segregation and 2) The law of independent assortment.

The law of segregation as mentioned above shows that genetic material does not mix but in fact is carried on into the following generation. The law of Independent assortment states that alleles of one gene will segregate independently from the alleles of another gene. Two characteristics will behave independently of each other in accordance with the law of segregation. Therefore, there is not a mixing of genetic material, but in fact the genetic material maintains it's own integrity.

Mendel's work was not well-received by the scientific community at that time. Mendel's views were rather radical and went unnoticed for thirty-five years after the presentation of his discoveries. However, the study of inheritance began to blossom sixteen years after Mendel's death when the importance of his discoveries were finally realized. Mendel's work resulted in the concept of chromosomal inheritance. (Nardone 1968)

Heritability and Polygenic Traits

Heritability characterizes the contribution of genetic factors to a given trait. A trait may have contributions from many loci. Heritability basically describes the proportion of the trait that is influenced by genetic factors. (Kang, Corey et al. 1977) Mendel's work involved examining traits that arise from a single locus.

Therefore, the inheritance patterns mentioned above demonstrate simple ratios. Mendel's pea plants were either dwarf or tall, wrinkled or round. However, many traits demonstrate a spectrum of variation or "continuous variation". The presentation of continuous variation makes it difficult to explain in simple ratios. A distinction between simple and continuous traits became difficult to reconcile with Mendelian algebraic laws of inheritance. As a result two schools of thought arose: Biometrical and Mendelian genetics. Discontinuous variability found in Mendel's experiments was viewed by Biometricians as being different from continuous variation. The two theories where considered two different alternatives. (Osborne and DeGeorge 1959) However, it could be argued that when many loci contribute to the expression of a trait then the different phenotypes might occur in a manner consistent with the segregation of many loci. For instance, if two unlinked-loci contribute to a certain trait then nine genotypes in the ratio of 1:2:1:2:4:2:1:2:1 are produced. According to these genotypic ratios a number of phenotypes would occur if each genotype produced a different phenotype. As an example, Nilsson-Ehle in 1909 crossed two different color wheat strains. One wheat strain produced red grain and the other wheat strain produced white grain. The F1 generation produced a variety of intermediate colors. When the F1 generation was self fertilized, seven

intermediate color variations were found. The phenotypic ratio of intermediate colors displayed was 1:6:15:20:15:6:1. One sixty-fourth of the wheat in the F2 generation displayed pure white or pure red grain. The other colors appeared in proportions consistent with the segregation of alleles at three loci.

Nilsson-Ehle's example demonstrates that the more loci involved in a given trait the more continuous is the intermediate expression of that trait. This is an example of a polygenic or quantitative inheritance pattern. This particular type of polygenic segregation is "additive" because every locus involved contributes in part to the phenotypic expression of the trait. Thus, Mendel's laws are preserved in polygenic inheritance as the law of segregation and the law of independent assortment are operative for the different loci. Mathematically one it can expect that the number of loci for a given trait can be found by 1 divided by 4 to the nth power, where 1 is the total dominant or total recessive display of the trait, and 4 to the nth power is the total number of offspring in the generation. The nth power is the number of loci involved. For example, in Nilsson-Ehle's experiment $1/4^3$ will give us 1/64. Because the phenotypic ratio was 1 plant with pure red grain or 1 plant with pure white grain for every 64 plants produced in the generation, we can expect that three loci are segregating in accordance to the additive model.

With this simple observation it is easy to visualize that the more loci involved for a given trait the more variance might be observed if additive effects are assumed. The amount of variation in phenotypic expression would soon give the appearance of a continuous spectrum where intermediate groups cannot be discerned with the human eye. Additionally, environmental factors may have some effect on the expression of the trait, inducing further variation. (Tamarin 1991) For example in 1909, Johannsen, worked on bean seed weight measurements and found that polygenic traits are controlled by many genes. Johannsen divided bean seeds into different weight classes. He then self bred each bean weight class with itself until each weight class stabilized (i.e., each class showed no variation). Thus Johannsen assumed that all loci were fixed for genes within each weight class, suggesting that any variation exhibited in each weight class was due to environmental influences and not genetics.

After the studies by Nilsson-Ehles and Johannsen it became apparent that discontinuous variability and continuously graded variation could be products of the underlying segregation of individual genes. In addition, it was believed that both genetic and non genetic factors could influence the same trait and cause further variation. However, it was thought to be difficult to distinguish genetic influences from environmental influences. The

Mendelian methods of tracing segregation of individual loci would not work well for characteristics that resulted from more than three loci.

Using the theory of Mendelian inheritance, R. A. Fisher (1918) devised a statistical method of analyzing traits that demonstrate continuous variance. The basis for modern analysis of inheritance stem from Fisher's methods of analyzing multifactorial inheritance. The methods in use today depend principally upon correlation studies between relatives and Fisher's analysis of variance. The major development of Fisher's analysis was primarily to apply genetic principles to animal and plant breeding. However, Fisher's model of analyzing traits did not consider environmental influences. Any positive correlation was considered evidence of a polygenic mechanism of inheritance. (Rice, Cloninger et al. 1980)

Unfortunately, there were flaws in Fisher's notions beyond a lack of environmental effects, since the phenotypic expression of a certain genotype may not be expressed in all individuals as would be predicted. Genes may not be fully "penetrant". For instance, many developmental traits may fail to result despite the presence of an appropriate gene. (Kang, Corey et al. 1977)

An example of varying degrees of penetrance of a gene involves the expression of cleft lip and vitamin D resistant rickets. Some cleft lip and rickets appears to

be genetically determined, but is actually the result of environmental trauma. For example, in dietary deficient rickets, a deficiency of vitamin D can result in rickets that is indistinguishable from the genetically determined vitamin D resistant rickets. Both phenotypes are identical. However, the etiology is very different between dietary deficient and vitamin D resistant rickets. (Tamarin 1991) Another example is found in the expression of cleft lip and palate where mechanical interference of the fusion and merging of the palatal shelves during development may be clinically identical to a recessive genetic predisposition to clefting. (Proffit and White 1991)

Basic Methods for Estimation of Heritability

True heritability is defined in the broad sense and in the narrow sense. In the broad sense heritability is the total phenotypic variation caused by all genetic factors. For example, total phenotypic variation is a result of variation induced by additive polygenes, variation induced by dominant genes, variation induced by epistasis, interacting genes and variation induced by environmental stimuli. Therefore, heritability in the broad sense is the sum of additive genetic variance, dominance and epistasis divided by the total phenotypic variance. On the other hand, heritability in the narrow sense is the amount of phenotypic variation that is caused by additive genetic factors only. Heritability in the narrow sense is only the

additive genetic variance divided by the total phenotypic variance.

On average parent-offspring, dizygotic twins, siblings, and half siblings (which are first cousins that are offspring from monozygotic twins) share 50% of their genetic make up. Whereas monozygotic twins share 100% of their genes and first cousins share on average 12.5% of their genes. From this knowledge a number of models have developed to explore heritability estimation between relatives. For instance, heritability estimates for twins, siblings, half sibs, parent offspring and mid parents (which are the mean values for both parents) have all been explored in previous studies.

Holzinger in 1929 suggested that the evaluation of genetic and nongentic sources of variation for a trait was best done by comparing intraclass correlation coefficients between monozygotic and dizygotic twins. He proposed the equation:

$$h2= tDZ-tMZ/1-tDZ$$

Where h2 is the contribution of the variability due to heredity. The intraclass correlation coefficient tMZ was used for monozygotic twins and tDZ was the intraclass correlation coefficient for dizygotic twins. (Holzinger 1929)

By the end of the 1950's it was apparent that better methods of analysis were needed to help decipher the

problem of assessing heritability. Dobzhansky suggested that the approach of researching heritability may be too simplified in that the effects of single genes preoccupy the research. (Dobzhansky 1959) Dobzhansky made the analogy that you must learn arithmetic before you can do trigonometry.

In the seventies there was a dichotomy that developed in the approach of analyzing twin data. Some authors evaluated heritability estimates while other authors evaluated estimated genetic variance. Various models developed in hopes to develop a more rational system of analysis.

Nance in 1973 suggested a half sib model for estimating heritability and genetic variance. (Kang, Lindemann et al. 1974) The model that Nance suggested utilizes half sibs. Half sibs are offspring of identical twins that are raised in different environments. The half sibs will share on average half of the genetic material like full siblings. Falconer in 1960 expressed the value of utilizing half sib data in the use of plant and animal studies. (Falconer 1960) Analysis of data from full sibs, half sibs, and monozygotic twins should help control the confounding influence of covariance or environmental effect on heritability studies.

Christian, Kang, and Norton in 1974 reviewed the general model and the needed assumptions to estimate

genetic variance in twins. (Christian, Kang et al. 1974) The two assumptions that are required to utilize twin studies for estimating genetic variance are 1) The environmental covariance is equal between monozygotic and dizygotic twins. If the environmental covariance is greater for monozygotic twins than for dizygotic twins then the estimate of genetic contribution is inflated. 2) The other assumption is that the covariance between genetic and environmental effects within the same individual are equal to the covariance between genetic and environmental effects of the other twin in a twin pair.

Two examples of estimating genetic variance that only use within-twin-pair mean squares were proposed by Falconer, Haseman and Elston. (Falconer 1960; Haseman and Elston 1970) These two models will be useful for estimation of genetic only if certain assumptions are met. For instance, unequal partition of cytoplasm or unequal distribution of nutrients in utero, as well as other competitive forces that result in an unequal environmental effect could cause spurious estimates. (Price 1950; Kempthorne and Osborne 1961) Christian suggests that if the environmental influences are believed to be unequal between dizygotic and monozygotic twins, then the arithmetic mean of the sum of the mean squares of within and among twin pairs must be used to estimate genetic variance. (Christian, et al. 1974)

Genetics and Craniofacial Form

Nakata et al., in 1974, applied a multivariate analysis to twin data as was proposed by Vandenberg (1962). The sample was sixty-seven monozygotic twin pairs and twenty-nine dizygotic twin pairs. The sample was not controlled for sex or age and siblings that were both pre and post pubertal were used. Zygosity was determined by serologic testing. Nakata found that there appears to be independent genetic determination of the upper and lower halves of the craniofacial complex. However further studies are needed to verify this finding. He found that the greatest measurement error resulted in the difficulty in locating nasion, basion, sella, gonion, gnathion, menton, PNS, and pogonion. The determinants of mandibular growth seem to involve two genetic and two environmental factors. Two specific areas that environmental factors relate to the mandible are the size of the mandible and the flexion angle. From this study Nakata found nine independently significant components of genetic variation and eleven independently significant factors of environmental variation. Nakata states that a multivariate analysis was useful in evaluating interrelated heritable traits. (Nakata, Yu et al. 1974)

Kang in 1977 presented a method of partitoning estimated genetic variance into additive and dominance variance using Falconer's variance component model. Prior

to Kang the consideration of dominance variance had not been evaluated in twin studies. Kang suggested that further work was needed in future studies to evaluate the extent that dominance variance as well as environmental variance contributes to estimates of heritability. (Kang, Corey et al. 1977)

Heritability and Facial Form

The influence of genetics on facial form and facial features has been documented in many studies. It is thought that family resemblance results from genetic factors. For example, Rubbrecht (1939) studied the well-known Hapsburg jaw of the Royal German family, and suggested that the resemblance of mandibular prognathism through many generations was due to genes. Rubbrecht constructed pedigrees noting not only the presence but the severity that prognathism is displayed in every generation. However, Rubbrecht also thought that mandibular prognathism or maxillary retrognathia can develop by local influences such as habits, thumb sucking, mouth breathing et. (Rubbrecht 1939) Brodie, Brash, Macmillan and others believed, however, that the form of the jaw bones was under genetic control entirely and that environmental influences had little effect. (Macmillian 1928; Brash 1929; Brodie 1948; Brodie 1948)

Development of the Craniofacial Complex

Even though the hard structures of the craniofacial complex are not separate organ systems and are derived from nuerocrest mesenchyme they do follow different pathways of development.

There are basically two types of bone formation: 1) endochondrial bone formation and 2) intramembranous bone formation. Both types of bone formation are found in the craniofacial complex. Endochondrial bone growth is found in the chondrocranium specifically the synchondroses of the cranial base. Interstitial growth in the cartilage of these regions as well as destruction and finally bone replacement of the cartilage is responsible for the development of the cranial base. Whereas the desmocranium, the calvaria and facial skeleton, is developed by intramembranous growth. The sutures and periosteum are responsible for the development of the facial skeleton.

The chondrocranium is developed from a series of cartilage. The basal plate or the parachordal cartilage as well as the occipital somites form the occipital bone. The hypophyseal cartilage and the trabeculae cranii form the body of the sphenoid and the ethmoid bones. (Sadler 1985)

The vicerocranium on the other hand is primarily formed from the first two brachial arches. As far as hard tissues, the first brachial arch is responsible for the formation of the mandibular processes, Meckel's cartilage,

the incus, and malleus. As well as the maxillary processes which give rise to the premaxilla, maxilla, zygomatic bone and portions of the temporal bone. The second pharyngeal arch or Reichert's cartilage gives rise to the stapes. (Sadler 1985)

Therefore, the cranial base is not only formed differently then the facial skeleton but also is derived from different primordia. In addition the maxilla and mandible develop differently. The maxilla and mandible by definition are formed by intramembranous bone. However, unlike the sutural growth of the maxilla, the mandible is unique because the mandible develops utilizing Meckel's cartilage as a framework to lay bone upon. The mandible also demonstrates endochondrial bone development in the condylar region. It would be interesting to statistically evaluate the genetic relationship of size and shape of these areas to each other using more sophisticated variance component models.

It has been suggested by Limborgh that the cartilage of the synchondroses is under strict intrinsic genetic control with little influence from epigenetic (effects from other gene sources controlling or influencing development) or environmental effects. However, the growth of bone is primarily controlled by epigenetic sources and also influenced by environmental factors. (Limborgh 1972) Limborgh suggested that the epigenetic control of the

facial skeleton is generated from the synchondroses of the cranial base. Cartilage is less plastic and is resistant to change. Koski and Ronning mention, in a transplant study, that epiphysis transplants differentiate into normal long bones whereas, condylar cartilage rapidly loses its integrity and fails to promote bone growth. On the other hand, transplanted cranial base synchondroses seem to demonstrate an intermediate display of intrinsic control between condylar and epiphysial cartilage. Koski concluded that there appears to be more intrinsic genetic control in epiphysial cartilage and less in cranial base synchondroses. However, there is greater inherent growth potential in the cranial base synchondroses compared to condylar cartilage. (Koski and Ronning 1970)

If in fact the cranial base is responsible for the control of the facial skeleton via epigenetic determinants then there should be evidence of a pleotropic effect where one gene source is responsible in part for the formation of both the facial skeleton and the cranial base.

Animal Studies of Facial Form

An often cited study was conducted by Stockard and Johnson (1941). Skeletal and occlusal discrepancies were induced by crossbreeding dogs. The resulting malocclusions were primarily from jaw discrepancies and not from tooth size/arch length discrepancies. The results were thought to demonstrate the problems that may occur with interracial

breeding. However, dogs are an inappropriate model for this type of study. Some of the dog breeds possessed a gene for achondroplasia which results in a deficient mid face and short appendages. The use of various dog breeds as separate genetically-determined subgroups of animals did show dramatic malocclusions and skeletal discrepancies. However, most of these discrepancies were the result of the introduction of achondroplasia. (Stockard and Johnson 1941; Harris and Smith 1980; Lundstrom 1984; Harris and Johnson 1991; King, Harris et al. 1993)

Twin Studies on Heritability of Facial Form

Twin studies have been conducted to accommodate and measure environmental effects. Monozygotic twins are in fact two genetically identical individuals. Whereas dizygotic twins are two siblings that shared the same environment in utero. Therefore, dizygotic twins are basically like any other sibling pair in that they share half of the genetic material. (Lundstrom 1954; Hunter 1965; Pelle 1971; Corrucini and Potter 1980)

Goldberg in 1929 did a comparison of fifteen identical twins. He primarily compared individual tooth positions in the maxilla and mandible. His conclusions were that the arch form is primarily inherited and that environmental influences have little effect. Goldberg stated,

> "Therefore, every interference with the general form of the dental arch may depend merely upon the elasticity of Wolff's law, which

> states in effect that the growth of bone depends upon the need for it." (Goldberg 1929)

Following the pioneer work of Broadbent (Broadbent 1931) a new avenue to study heritability became realized. Previous techniques allowed a great potential for error. The standardized control of anode to object distance in lateral and frontal cephalometric x-rays allows consistent evaluation of craniofacial morphology. Many studies following the discovery of Broadbent's technique utilized cephalometrics to quantify craniofacial variation.

The first significant study of heredity using cephalometrics was published by Wylie. Wylie (1944) studied the frontal and lateral cephalograms of 15 families. Twenty eight parents and thirty seven offspring. In the study thirteen families had like sex twins. The zygosity of the twins was not mentioned. Wylie's conclusions were that twins show a similarity in appearance but may have very different craniofacial patterns. All the angular relationships studied were (N-S-Gn, N-S-Go, S-Go-Gn, S-N-SN, S-N-Mx1, S-N-Gn, X-Y axis, cant of occlusal plan, cant of the palate, cant of Go-Gn, N-GN-GO, Gonial angle). Wylie's conclusion was that angular measurements are not precise enough to be predictable. (Wylie 1944)

Snodgrasse in 1948 used cephalometrics to study facial growth in one family of twins. Although his sample was far too small to establish any conclusions, he stated that in

the dentition there seems to be a tendency for hereditary traits from the maternal side to predominate over those from the paternal side. Snodgrasse plotted his standard deviations with the use of Wetzel grids. (Snodgrasse 1948)

Lundstrom conducted two twin studies in 1954, and 1955. The sample contained fifty monozygotic and fifty dizygotic twin pairs. He concluded that genetic factors have a greater influence than environmental factors for occlusion, tooth size, and both linear and angular craniofacial measurements. (Lundstrom 1954; Lundstrom 1955) In addition Lundstrom suggests that the results demonstrate that finger sucking has little effect on overjet. In 40-50% of the twins contained at least one twin that admitted finger sucking at some time in their life. No consistent evidence of habit was found related to overjet. Lundstom stated that one possibility is that there is a stronger hereditary influences on overjet then finger sucking. However, the determination of the presence of finger sucking involved individuals in all ages and stages of growth and development, as well as varing durations of the habit. Interestingly, the monozygotic twin pairs demonstrated finger sucking in both individuals considerably more frequently then the dizygotic twin pairs. Because of this observation, Lundstrom suggested that habit/behavior may be genetically influenced.

Kraus, Wise and Frei in 1959 conducted a study on six sets of monovular triplets. Lateral and frontal cephalograms were evaluated using superimposition for all the triplets. The hope was to estimate the concordance between the twins and to verify the genetic determination of the craniofacial complex. Seventeen bone traits were evaluated. At first, Kraus used a polygon superimposition for the overall craniofacial complex and came to the conclusion that cephalometric studies at that time were not applicable to the study of heritability. However, Kraus et al. then evaluated specific bone traits and found the highest concordance in the mandible (specifically the posterior border of the ramus) profile of the posterior border of the mandibular symphysis, the anterior border of the symphysis, and the frontal view the point of the ramus that intersects the mastoid process to the same point on the contralateral side. Their conclusions were that genetics governs the morphology. However, the environment seems to decide how those bone traits combine to formulate the head and face. (Kraus, Wise et al. 1959)

Twin studies conducted in 1959 by Osborne and DeGeorge emphasized that the polygenic inheritance pattern in man is evident and that the bulk of genetic variation observed is due to a polygenic pattern. Osborne and DeGeorge noted that most of the genetic variability was found in post cranial measurements, parallel with the longitudinal axis

of the body. However, Osborne and DeGeorge also found that head and neck measurements differ from postcranial measurements. Head and neck measurements that are not parallel to the long axis of the body show a more genetic component of variability. These findings are consistent with Howells' findings. The measurements in the head and neck region that show the highest genetic variability are: head breath, upper facial height, bizygomatic breath, and head circumference. (Osborne and DeGeorge 1959)

Horowitz, Osborne and DeGeorge in 1960 studied fifty-six like sexed twins. In the study they concluded that measurements of anterior cranial base, mandibular body length, total facial height, and lower facial height present with highly significant genetic variation. (Horowitz, Osborne et al. 1960)

Vandenberg in 1962 wished to evaluate the stability of heritability estimates by comparing F-ratio statistics in six previously conducted twin studies. The studies evaluated were; Dalhberg 1926, Verschuer 1925, Clark 1956, Vogel and Wendt 1956, Osborne and DeGeorge 1959, and finally Vandenberg and Strandskov 1962. The F ratios used by Vandenberg depended on the excess of variance found in the heritability factors of the other studies. Therefore, Vandenberg used F-ratios even though they are not direct measures of heritability. Vandenberg found that measures of length demonstrated a higher F-ratio than did

measurements of width. Bigonial breadth (Go-Go'), total facial height (Na-Gn) and nose height (N-Nasolabial angle) demonstrated the highest F-ratios. Vandenberg expressed that the growth pattern between twins should also be included as an indication of heritability. Vandenberg also suggested the use of multivariate statistics to evaluate data as this form of analysis may show the influence of heritability more clearly. (Vandenberg 1962)

Hunter in 1965 conducted a twin study that contained a sample of seventy-two like sexed twins. Lateral cephalograms were traced and measured and fourteen depth and twelve height measurements were evaluated. The measurements that demonstrated the highest heritability values were as follows: Ar-Go, Go-Me, Na-Me, S-Na, Ar-Gn. Mandibular measurements showed a less significant level of heritability for male verses female twins. He concluded that mother offspring relationships are stronger than father offspring relationships. (Hunter 1965)

Chung in 1975 studied Hawaiian school children and found high correlations in incisor width and low correlation in buccal occlusion. He hypothesized that the difference in intrafamily correlation is the result of environmental influences on the development of a trait. (Chung and Niswander 1975)

Lundstrom and McWilliam (1988) in a twin study using twenty-eight monozygotic and twenty-seven dizygotic pairs

evaluated a heritability comparison between vertical and horizontal cephalometric size variables as well as variables based on facial form. Lundstrom constructed a horizontal line that was four degrees to the S-Na plane. Lundstrom then measured the distance between points perpendicular to this plane. The highest values of heritability estimated were found for facial height to facial depth. High estimates of heritability were found in the mandibular proportions of Na-Gn/S-Go, Na-Gn/S-Pg, and the lowest heritability values were found to be incisal edge position. (Lundstrom and McWilliam 1988)

In the foregoing study, path analysis was utilized and cultural inheritance did not seem to have an effect on the variables studied. The only area that appeared to be affected was the ratio of upper to lower facial height. It has been reported by Lundstrom (1988) that discordant values for lower facial height may be common in certain families as a result of environmental factors such as mouth breathing. (Linder and Aronson 1970; Lundstrom and McWilliam 1988) In Lundstrom and McWilliam's study, anterior facial height in relationship to posterior facial height demonstrated a high heritability in monozygotic twins compared to dizygotic twins.

In an abstract from the department of anthropology in the university of Wisconsin by L.A.P. Kohn, eighty-nine monozygotic and ninety-one dizygotic twin pairs were

studied for form changes. The sample of twins came from 180 families taken from the Forsyth Longitudinal Twin Study. Lateral cephalometric radiographs were studied. Morphologic form changes from ages six-eleven, eleven-sixteen, and six-sixteen were analyzed annually in hopes of finding differential gene action on craniofacial morphology. They reported two major findings. First, heritability exhibited an irregular pattern from ages six-eleven years. And second, heritability values increased until puberty then stayed stable at the end of the maximum growth period. Kohn suggests that the observed patterns in morphology during growth are spurious. Therefore, the differential effect of gene expression on cranial morphology could not be estimated. (Kohn 1989)

Parent Offspring Studies on Heritability of Facial Form

Iwagaki in 1938 studied Japanese school children with prognathic mandibles and edge to edge bite. He used a questionnaire to determine which family members also demonstrated mandibular prognathism. He was one of the first researchers to attempt a heritability study of the craniofacial complex from a statistical view point. He computed the probability of one parent having a prognathic mandible if their child demonstrated prognathia. His findings after collecting more than two thousand family histories were poor. Iwagaki only stated that the trait appears to be familial and is probably a Mendelian

recessive. Iwagaki expressed the need for further research with detailed tracings of the family members. (Iwagaki 1938)

Morre and Hughes (1942) in summary of the literature at that time implied that there was very little data present to support clinical findings. However, there is a growing understanding of the importance of the hereditary mechanism. In 1942 Moore and Hughes conducted a parent-offspring study with 265 individuals grouped into seventy-eight families 130 children and 135 parents. Moore evaluated resemblance and non-resemblance between parents, between each child and each parent, between each child and both parents. The questions that Moore and Hughes wished to answer were:

1. Does the child resemble the male parent?
2. Does the child resemble the female parent?
3. Is the child intermediate between the two parents?
4. Does the child show a feature that is vaguely present in both parents, or one of the parents?
5. Is the child unlike both parents?

Moore graded each trait small, medium, large and then computed the percentage that the trait was observed in the sample.

Moore found that there is little evidence that demonstrates that a child will resemble one parent more than the other. However, if the parents resemble each

other than there was an 85% chance that the child would resemble the parents. Specific findings in Moore and Hughes work are the following: Children that had parents with asymmetries had a tendency to show asymmetries three to four times as much as children whose parents did not have asymmetries. Analysis of the absolute size of the maxilla was non-conclusive. However, there is a tendency for children to have a medium sized maxilla if the parents have a medium sized maxilla. Absolute size of the mandible shows that there is a tendency for children to present with mandibular deficiency if one or both of the parents present with a deficient mandible. Moore suggests that there is little tendency for mandibular prognathism to be transmitted. However, the evidence suggests that mandibular size is under genetic control. Mandibular ramus height also demonstrated genetic control. Moore also found that mandibular body size as well as the shape of the angle is transmitted to children from their parents. (Moore and Hughes 1942) Moore and Hughes believe that single genes were involved for rotations of teeth. However, there are many factors involved in spacing and crowding of the dentition.

In a study conducted by W.S. Hunter and D.R. Balbach lateral cephalograms were collected from two or more children in twenty-one families. Cephalograms were also collected from the parents of these families. Hunter tried

to determine if several facial dimensions in adult offspring could be predicted by evaluating the same measurements of the parents. The measurements that he used are S-N, Na-Me, Ar-Gn, Ar-Go and Go-Me. The reason that Hunter choose the measurements mentioned is that they proved to show a high correlation and were assumed to be inherited in an earlier twin study that Hunter conducted in 1965.

The sample in Hunter's study consisted of middle class individuals of European decent. Only mature post-pubertal individuals were used so that growth/maturation's impact on heritability could not be observed. Although correlation studies do not imply a cause and effect, Hunter's findings disagree with Moore in that the statistical relationship shows that the correlation of father-offspring is greater than mother-offspring for prediction of growth. Hunter's findings also contradict the findings in his previous study in which mother offspring relationships demonstrated greater significance. Hunter concluded that there is a significant heritable component to facial dimension. However, further study is required prior to making any interpretations about the heritability of facial growth. (Hunter, Balbach et al. 1970) In Hunter's 1970 study the measurements that demonstrated the highest correlations were the mandibular measurements Ar-Go, Ar-Gn, and Go Gn.

Litton (1970) observed families of fifty-one probands demonstrating Class III malocclusion. A proband is the person in which a pedigree is discovered. Litton constructed pedigrees of the family members and observed Class III occurrence in the following generation. Litton's conclusions are that approximately 13% of siblings of the probands exhibited the trait. This is very high when compared to the prevalence of Class III individuals in the population which is less than 4%. Litton found no evidence to suggest that Class III malocclusion is sex linked. Litton suggests that the results did not support an autosomal dominant mode of transmission or a simple autosomal recessive transmission. He concluded that the mode of transmission seems to be consistent with a polygenetic pattern. (Litton, Ackerman et al. 1970)

Harris in 1980 conducted a family study with a sample of twelve hundred. The evaluation of occlusion and arch widths of dental casts were recorded. Harris's results indicate that there is a major effect of genetic variation in arch width and arch length. The highest heritability estimates were found to be mandibular arch length (mesial edge of the central incisor to the distobuccal edge of the first molar), mandibular arch width (buccal surfaces from canine to canine), and mandibular width ratio (canine to canine arch width/first molar to first molar arch width x 100). Harris found that arch width and length are under

more genetic control. However, environmental similarities among families are more important in occlusal variables such as crowding, rotations, overjet, overbite, and molar relationship. (Harris and Smith 1980)

Harris in 1982 conducted a study with over 112 Melanesian families and 761 individuals. Harris studied arch size and occlusion. Harris's conclusion was that there is an interplay between environment and genetics. Some combinations of traits seem to be under a higher genetic influence such as arch length but not arch shape. However, individual occlusal traits seem to be environmentally induced. The question isn't; "are occlusal variables purely genetic or environmental?" but rather "what contribution does genetic and environment factors have on occlusion?". Harris states that the factors most responsible for the similarities between siblings and their parents are more related to environment than genetics. (Harris and Smith 1982)

Nakasimia, Ichinose, Nakata, and Takahama (1982) conducted a cross-sectional study of parents and their offspring. Lateral and frontal cephalograms were taken from ninety-six Class II (thirty-seven boys, fifty-nine girls, mean age of 9.7 years) and 104 Class III (thirty-eight boys, sixty-six girls mean age, of 9.4 years) children. The parents of the children were also studied. Nakasimia's conclusion was that there is a high correlation

between parents and their offspring in Class II and Class III patients. Nakasima suggested that U-I to nasal floor angle, gonial angle, articulare to gonion length and U-Nasion-A point angle are related to environmental factors. Nakasima also suggested that UNA, defined as the angle created by the inferior border of the pituitary fossa (U) to Nasion to A point is influenced by thumb sucking/biting habits in Class II patient. (Nakasimia, Ichinose et al. 1982) Nakasimia's study showed high correlations in the mandible for bigonial width when Class II and Class III patients are compared to the mean of both parents.

Suzuki and Yasuhide in 1991 conducted a parent-offspring study based on the assumption that if the face of an offspring resembles at least one of the parents than it should continue to resemble that parent through adulthood. (Suzuki and Yassuhide 1991) Therefore, if the craniofacial dimensions of a child resemble the dimensions of one of the parents, then the parent who is most like the child can be used to predict the child's future craniofacial form.

Suzuki's study utilized lateral and frontal cephalograms as well as handwrist radiographs. The sample contained 150 families with mature offspring and one hundred families with immature offspring. Principle component analysis was used to summarize eighty-one variables and then cluster analysis was used to classify the craniofacial pattern. Their results demonstrated that

64% of the 13.5 age group studied agreed with at least one of the parents facial growth patterns. (Suzuki and Yassuhide 1991) Whereas 58% of the children at an age of ten years had agreement with at least one parent's facial growth pattern.

Sibling Studies on Heritability of Facial Form

The vast majority of studies conducted have been on twins. However, sibling studies are needed to support previous findings. Similar to dizygotic twins, siblings on average share half of their genes.

Howells in 1949 and 1951 studied male brothers. He found that the head and neck measurements differed in many ways from postcranial measurements. Howells felt that his findings demonstrate that the head and neck is distinctly different from the postcranium. Head length tends to be associated with general head size not brain size. Whereas, head breadth tends to be strongly associated with brain size. (Howells 1951) Howells examined pairs of brothers to see if brothers differ in some body measurements more then others. He compared the measurements to a random male sample of the same population. Howell found that measurements that are parallel with the longitudinal axis of the body tend to demonstrate higher correlation between brothers than the population. Howells found above all that the bones of the facial skeleton, legs and arms demonstrate this pattern. Facial height demonstrated the highest

correlation. However, bigonial breadth failed to produce a very high correlation between brothers. (Howells 1949; Howells 1951)

Stein, Kelly and Wood in 1956 did a clinical and cephalometric study of female college students that had sisters attending the same college. Other family members were also included if possible. One hundred seventy-five subjects in all were interviewed and studied. Stein used angular measurements, correlation coefficients, Fisher Z scores, and family pedigrees, as well as superimposition of tracings to compare similarities between family members. They found the highest correlation in angles were between sister-sister combinations. The least significant correlation was found between mother-daughter and father-son. (Stein, Kelly et al. 1956)

Schreider in 1961 conducted a study on thirty-two adult brother siblings. He found the there were correlations as high $r = 0.72$ for head breadth and as low as $r = 0.16$ for bizygomatic width.

Niswander (1963) studied the effects of heredity and environment on the developing dentition. Niswander examined the result of inbreeding verses non inbred offspring. He found that there is no difference between those siblings in each group. However, Niswander did find that there is more variation between nonsibling pairs. Niswander in 1963 as well as Horowitz in 1963 and Goodman

in 1965 expressed the difficulty of conducting nature-nurture studies. (Horowitz 1963; Niswander 1963; Goodman 1965)

Six Master's thesis projects were conducted at the University of Michigan in 1968, using the same measurements as Hunter. The dentofacial relationships were analyzed for father-son, mother-daughter, mother-son, brother-brother, sister-sister, and brother-sister. The sample studied had a slight predominance of Class II division I individuals. In these studies there was a high degree of variability in correlation coefficients. There was a higher correlation between related pairs than between unrelated pairs with highest correlations found in the anterior cranial base, mandibular morphology, total facial height, lower facial height, and facial depth. (Johnson 1968; Kanter 1968; Leddy 1968; Masty 1968; Roshel 1968; Warren 1968)

In 1971 another similar study was conducted at the University of Michigan. The goal of this study was to use sibling data to establish if a better prediction of growth could be found. The sample used in this study also had a predominance of Class II division 1 malocclusions. However, ANB values greater than eight were excluded from the study. The use of twenty-three sister pairs, twenty-two brother pairs, twenty-one brother probands, and twenty-three sister probands were studied in four separate thesis projects. The findings suggest that comparison of both

proband and sister or brother provide more information than studying the proband alone in Class II division 1 individuals. ANB, A-B difference and Y-axis demonstrated the most firm foundation for growth prediction in Class II division 1 individuals. (Aagesen 1971; Fromhart 1971; Timm 1971)

In 1971 Pelle conducted a study at Case Western Reserve University. Pelle utilized the Bolton Brush Records and collected a sample of siblings which contained twenty-one females and twenty-four males. Linear measurements that showed high genetic variation previously used by Hunter (1970) were employed in this study. Angular measurements taken from Downs, Tweed, as well as SNA, SNB, ANB, were used in this study.

The subjects were analyzed at two points in time. Pelle's findings show a higher correlation between siblings after the majority of growth has taken place. Linear measurements especially appear to be more reliable than angular measurements when comparing two siblings. Greater correlations were observed in linear measurements when compared to angular measurements. This has been observed by several authors. (Howells 1949; Osborne and DeGeorge 1959; Horowitz, Osborne et al. 1960; Hunter 1965) However, angular measurements appear to be reliable when comparing the same individual at two different points in time. The conclusions in Pelle's study are that correlations taken

before and after the peak growth spurt are more significant in the same individual than between siblings. Measures of height and depth show the same degree of genetic variation. Linear measures show greater heritability than do angular measures. The use of a sibs data did not enhance predictions of growth better than the individuals own measurements. (Pelle 1971)

Linear measurements are often from the same bone where angular measures may involve more then one bone or even different components of the craniofacial complex. Limiting measurements to one bone may allow a more precise evaluation of genetic contribution. Measurements that incorporate multiple bones may give erroneous information. Different bony components of the craniofacial complex may not be under the same source of genetic control. (Garn, Cole et al. 1979)

Byard and cohorts in 1984 studied the correlation of sibling's cranial measurements. The study was longitudinal and evaluated sibs at one year intervals. The study suggests that sibling correlations are lowest in the first few years of life and increase with age reaching the highest values as the sibs reach adulthood. This finding is consistent with Pelle's findings. No reliable pattern of growth was found during that time frame. Byard suggests that in the sample studied there is shared environmental

and genetic contribution resulting in similarities of phenotype. (Byard, Lewis et al. 1984)

Harris and Johnson (1991) conducted a longitudinal study with a sample size of thirty sibships taken from participants in the Bolton Brush study. The criteria for the study was that there was at least one same sex sibling pair with annual radiographic records and dental models available for the three ages studied (four years with full primary dentition, fourteen with early permanent dentition, and twenty years of age).

The result of the study suggested that the heritability of craniofacial (skeletal) relationships are significantly high and increase with age. There was a significant increase in heritability estimates in craniofacial variables from ages four to fourteen. Whereas dental characteristics are low and decrease with age. There was a decrease in heritability estimates for arch parameter from ages four to fourteen. There was no significant change in heritability estimates between the ages of fourteen and twenty years which is consistent with Pelle and Byard's findings. (Harris and Johnson 1991) Harris and Johnson's study suggests that environmental influences contribute to the dental variation and that genetic control has more influence on skeletal relationships. Extreme cases were eliminated in Harris and Johnson's study.

King, Harris, and Tolley (1993) used a cross-sectional design to examine the heritability of cephalometric and occlusal variables in siblings that required orthodontic treatment. The sample was from pretreatment records of 104 white sibling pairs. Both siblings required full fixed orthodontic treatment, all four permanent canines were at least partially erupted, and neither sibling had any prior treatment with serial extractions or functional appliances. The members of this sample all had overt malocclusions and were not normal Class I subjects. Previous studies had been conducted by Harris on more normal subjects and found that there is a dichotomy between bone based variables being under genetic control and tooth based variables being under environmental control. The previous studies used subjects that possessed normal Class I skeletal relationship. King's study suggests that a simple dichotomy between bone based structures and occlusal or tooth positions does not exist. In King's study, cephalometric bone based variables in subjects with overt malocclusions do not show a high degree of heritability. Whereas occlusal based variables in overt malocclusions do demonstrate a significantly higher amount of heritability. (King, Harris et al. 1993)

Issues in Assessing the Heritability of Facial Form

The following is meant to provide an overview of the question; "Why are certain traits passed on to future

generations?" as well as some of the confounding variables and draw backs in all heritability studies. The formation of mutifactorial traits involves many factors. In order to correctly dissect out the genetic contribution to a trait. Statistical models must be utilized that simultaneously estimate variance due to common environmental factors, dominant genes, and random environmental factors. (Schork 1993) Hopefully this overview will allow the reader to comprehend that proper heritability studies are at best difficult because the confounding variables cannot always be controlled.

Environmental Factors

Environmental factors easily confound the detection of genetic factors on a trait. (Luigi and Feldman 1973; Susanne 1975; Devor 1987) Family members live in similar environments. Therefore, cohabitation may effect overall phenotypic variation because individuals who live together may share similar but not identical diets, housing, "cultural environment" as well as mimic each other's habits. (Garn, Cole et al. 1979; Lundstrom 1984) Luigi published a paper in 1973 on cultural verses biological inheritance. He stated that it should be expected to see a correlation between biological relatives even if there is no genetic variation. Luigi called this phenomenon "pure cultural transmission", where a physical trait may be affected by cultural or learned behavior. For example, the

composition of diet may be culturally related and in turn the diet may effect the physical trait being observed. (Luigi and Feldman 1973)

In 1979 Garn studied parent offspring, sibling, and adopted parent offspring pairs focusing on serum cholesterol, outer fatness, long term fat changes, vitamin A and C intake, and stature. Garn found that a cohabitational effect is, in part, responsible for great similarities between individuals that are not genetically related. Garn did not deny that genetic factors were in part, responsible for family similarities. However, Garn suggested that family line similarities have much to do with energy intake and energy expenditure. Since meals and activities are often shared in a family, energy intake as well as energy expenditure would be influenced by a cohabitational factors and hence influence serum cholesterol levels. (Garn, Cole et al. 1979)

Lundstrom and others argued that it is important to realize that two types of non genetic influences may affect morphologic features. First, there are those factors that affect the external environment such as diet, housing, socioeconomic factors, habits, etc. Secondly, there is a random or internal environment affect. For instance, hormonal disturbances, endocrine disturbances, disturbances in synchronous development of growing parts, prenatal insult, fetal position, and independent tooth formation,

have all been mentioned as environmental influences that cannot be easily accounted for or controlled. (Price 1950; Corrucini and Potter 1980; Lundstrom 1984) The variation in the internal environment is thus not under clinical control. However, the external environment can be modified. The need to understand and distinguish those environmental factors that can be controlled is obviously very important for helping patients with developing malocclusions. (Lundstrom 1984) For example, understanding the morphologic change due to thumb and finger sucking behavior or lip biting allows clinicians to intervene to stop those habits. Curbing the habit may result in a more favorable growth pattern. (Corrucini and Potter 1980)

Environmental influences on traits can be observed in different ways. For example, in primitive civilizations malocclusions were rarely found. It has been stated by Corruccini, and others that malocclusion is a disease of Western urban populations, in that it is associated with modern habits and environment unique to urban people. Since mastication was important for survival in ancient civilizations, malocclusions that were severe enough in primitive man were likely deleterious to the survival of the individual. Those individuals would likely not contribute their genes to ensuing generations. Thus, natural selection for a well functioning masticatory complex might have occurred. However, modern interventions

can allow individuals with masticatory pathologies to survive and thus contribute their genes to ensuing generations, allowing the trait to be propagated. It is now accepted that environmental influences play a significant role in the development of the craniofacial complex.

Falconer showed that the heritability of traits is decreased if the trait is related to reproductive fitness. (Falconer 1960) Whereas traits that are not involved with reproductive fitness demonstrate higher estimated values of heritability. For example, the heritability of the spotting pattern of a dairy cow is much higher than the heritability of the production of milk. Therefore, traits that demonstrate low heritability are more likely influenced by environmental factors. Such environment sensitivity provides a "plasticity" for a species and allows them to adapt to changing environments. If traits were completely under genetic control, and directly related to reproductive fitness, then organisms would be intolerant of environmental change. Intolerance to an ever changing environment would be deleterious to survival. The observation that heritability relates to reproductive fitness is thus compatible with Darwinian theory. A quote from Moore and Hughes (1942) brings this insight out:

> " It is in error to presume that genetic factors can ever exist independent of environment or to insist that environmental

> influences cannot affect or even seriously modify a structure of genetic origin."

This fact is easily seen in the example of malocclusion in primitive society. Although genetics factors certainly played a role in the lack of malocclusion found in primitive civilizations, the quality of the food was different in primitive civilizations. The processing of foods in primitive civilizations was crude resulting in grit, sand et. being incorporated in the diet. Foods were also naturally more course and fibrous unlike the cultivated and processed foods in modern diets. (Corrucini and Potter 1980) Differences like these must have affected the occlusion and the development of the supporting structures of the dentition. The diets that are available today allow individuals to survive nicely with diminished masticatory function.

Another example of a trait influenced by genetic and non-genetic factors of evolutionary importance is "attrition of the denture" which is much more pronounced in skulls found from ancient civilizations than those of modern man. Attrition of the teeth was not only a result of the diet, since the teeth were also used as tools for softening leather, cutting and tearing materials, as well as processing pigments for painting. (Johanson, Johanson et al. 1994) Attrition reduces the amount of tooth substance in the vertical as well as the mesiodistal dimension of the

dentition. It is believed that the decrease in tooth size from attrition reduces the chance of malocclusion because the teeth are smaller and crowding is less likely to occur. (Watt and Williams 1951; Begg 1977; Corrucini and Potter 1980)

In 1954 Begg, after studying Australian aborigine skulls, found that the occlusion was sound and that malocclusion was for the most part absent in these skulls. He concluded that the lack of malocclusion was due to the natural wearing of the dentition. Begg hypothesized that attrition of the dentition begins immediately following the eruption of teeth. This allowed a reduction of tooth substance resulting in sufficient arch space for the complete dentition. Therefore, in the absence of dental crowding, an "ideal" occlusion can occur. This concept rationalized the idea of extraction in orthodontic treatment using the Begg technique. (Begg 1977) Begg's concept also paints a vivid picture of how environmental influences can effect the outcome of occlusal relationships regardless of the genetic component.

Continuous parafunction of the masticatory complex results in hypertrophy of the muscles of mastication as well as increased density of the bone. Tension stresses promote bone formation and determine the osseous architecture. (Glucksmann 1942) Studies have shown that if the temporalis is freed from it's mandibular insertion or

if atrophy of the temporalis muscle should occur, then the coronoid process of the mandible fails to fully develop. (Washburn 1947; Moss and Rankow 1968) This is an ideal example of how function as well as genetic determination play a role in the development of bony traits. With adequate stimulation due to tension and stress the morphology of the bone changes to meet the functional demand.

In 1951 Watt examined the effects of mandibular development in the rat with two different diet consistencies. The exact chemical composition of the food was maintained. However, the physical character of one diet was hard and the other diet was soft. It appeared that the diet affected the development of the mandible, so Watt concluded that pre existing genetic make up is only partially responsible for the developmental outcome of the mandible in the rat. (Watt and Williams 1951)

Waddington (1972) elaborated on the impact of environmental and genetic factors on a trait by describing an "epigenetic" landscape, where an individual develops down one of many routes depending on which genes he possesses and environmental factors he must meet. This, individual may have a genetic "potential" toward a certain morphologic goal, but will only reach that goal if environmental factors are favorable. Environmental stress will thus affect each individual differently. If the

environmental stress is severe enough then individuals may completely change direction and follow different paths. For instance, allergies may cause an individual to become an obligate mouth breather. As growth occurs the morphology of the individual will change as a result of the behavior caused by airway obstruction. Therefore, the phenotypic expression in each individual should have some apparent differences due to unique environmental stressors. (Waddington 1974; King, Harris et al. 1993)

Secular Change

Craniofacial traits are influenced by secular change. There is a trend toward an increase in size and prominence in the mandible. (Hunter and Garn 1969) Vlastovsky offers an interesting scenario that suggests reasons for such secular changes. He argues that the most important cause of secular trends in the development of humans is the change in living conditions and nutrition, although he does admit that living conditions are not the only cause of secular change in growth and development. For example, the first and second world war led to mass displacement of populations as well as technological progress in developed countries. There was a reduction in inbreeding because the concentration of populations occurred in major cities and not in the country side. (Vlastovsky 1966) Vlastovsky also suggested that once isolated genetic populations began to mix, new genes were incorporated into the melting pot.

Therefore over time morphologic changes occurred because of this genetic mixing.

In a study conducted by Hunter, cephalometric dimensions for skull base, facial height, mandibular length, and ramus height were collected in an attempt to examine secular trends in facial dimensions. Lateral cephalograms from thirty-seven families and eighty-six offspring were analyzed. The findings for cross-generation comparisons of six measurements (Ar-Go, Ar-Gn, Go-Me, Na-Me, S-Na, and S-Ar) suggest that facial height is significantly smaller in daughters than in mothers. Both sexes, however demonstrated an increase in mandibular size and prominence. The only measurement that did not show a significant change consistent with the trend was mandibular ramus length measured as Ar-Go. (Hunter and Garn 1969)

Problems with Zygosity and Twin Studies

There is question in determining if a twin pair is monozygotic or dizygotic (Price 1950; Kraus, Wise et al. 1959; Lundstrom 1984). If zygosity cannot be precisely determined then the conclusions from previous studies must be under suspect. In the past zygosity was determined in many ways such as fetal membrane examination, blood group similarity, sex, dental casts etc. Unfortunately, there are flaws in assuming zygosity from previous methods. Recent authors have suggested that DNA fingerprinting can

and should be used for zygosity determination. (Eufinger, Rand et al. 1993)

Twin studies are confounded with epigenetic influences, even with the correct assessment of zygosity. There are internal uterine environmental factors that may play a role in the future development of monozygotic twins. For example, Price in 1950 discussed some of the problems found in the inutero environment: for twins there are two types of structures that may occur for the absorption of nutritive materials in the uterus. These chorio-placental structures in twins may present as a double (dichorial) or a single (monochorial) placental structure. A mistake often made is the assumption that all dichorial twins are dizygotic. (Price 1950) Monozygotic twins can also present with two separate chorio-placental structures. Therefore, there are three types of twins; dizygotic-dichorial, monozygotic-monochorial, and finally monozygotic-dichorial. Therefore, the determination of zygosity by examination of chorial-placental structures flawed many early twin studies. The results of these studies may be suspect.

Twins may also exhibit lateral inversions or asymmetrical reversals to the extent of situs inversus or visceral inversion. For example, the liver may be found on the left side and the heart on the right in one of the monozygotic twins. Twins may also share circulation

resulting in unequal nutritional distribution. The fetal position will not be identical between twins. The delivery of the twins will not be identical. All of these internal or uncontrollable environmental factors can introduce bias in twin studies. (Price 1950) Differences that occur between twins may be due to prenatal and not post-natal environmental factors. (Kraus, Wise et al. 1959)

Other problems of assessing heritability arise from data collection. Horowitz in 1963 mentions that analytic techniques may affect the interpretation of genetic contribution. He mentions several techniques that are available:

1. Superimposition, such as those used to show growth changes in the Bolton standards, and Kraus, Wise, and Frei's triplet study, (Kraus, Wise et al. 1959)

2. Co-ordinate grid deformation, such as the grid analysis described by Moorrees, (Moorrees 1953)

3. Shape index comparison, as in the analysis of photographs described by Young, (Young 1956)

4. Linear measurements, which are most often used. However, many linear measurements tend to involve more than one bone which lump together many variables.

5. Measurements of single bones or parts of bones, as mentioned by Garns. (Garn 1961) Limiting measurements to one bone may allow a more precise evaluation of genetic contribution to local components.

Horowitz suggests that when evaluating twins several techniques may be needed to confirm the results. (Horowitz 1963) Lundstrom suggests that because of the difficulties

in separating cultural or environmental variance from true genetic variance, family studies are needed to compliment twin studies. (Lundstrom 1984)

The Multivariate Nature of the Parameters

The literature presents varying results on what craniofacial characteristics are, in fact, heritable as well as to the degree they are of genetically controlled. Harris and others argue that there is a dichotomy in the craniofacial complex between heritability values for skeletal and occlusal characteristics. Heritability estimates of skeletal components in the craniofacial complex tend to demonstrate more genetic control then occlusal estimates. This genetic control over skeletal components appears to increases with age, reaching near maximum values following the prepubertal growth spurt. (Pelle 1971; Byard, Lewis et al. 1984; Kohn 1989; Harris and Johnson 1991; Suzuki and Yassuhide 1991)

On the other hand, King has found that overt malocclusions (Class II, Class III) tend to demonstrate lower heritability values for the skeletal components of the craniofacial complex then Class I skeletal relationships. A possible explanation could be that the dentition must compensate for the skeletal discrepancy in a predictable manner. The window of variability is narrow because the dentition is housed in the basal bone. The dentition therefore is dependent on the relationship of the

skeletal members. For example, to obtain a Class II dental relationship in a Class III skeletal relationship would be unlikely. However, a Class I, II, or III relationship is possible when the skeletal members are in a Class I relationship. Nakasima in a parent/offspring study of Class II and Class III individuals found a significantly higher correlation for skeletal components than occlusal components which is not in agreement with King's findings.

It has been noted by many authors that angular measurements tend to demonstrate lower heritability estimates then linear measurements. (Wylie 1944; Howells 1949; Osborne and DeGeorge 1959; Horowitz, Osborne et al. 1960; Hunter 1965) Possibly, the inequality of linear and angular measures can be explained by the fact that angular measures tend to utilize more then one bone or more then one component in the craniofacial complex (cranial base-maxilla-mandible). (Pelle 1971) It has been reported by Garn and Kraus that single bone measurements or parts of single bones tend to demonstrate higher estimates then measurements involving multiple bones. (Kraus, Wise et al. 1959; Garn 1961)

The highest heritability estimates in the majority of the studies appear to be found in linear measurements dealing with the mandible (Ar-Gn, Ar-Me, Ar-Po) (Arya, Savara et al. 1973) as well as anterior cranial base (S-

Na), total facial height (Na-Gn) and upper facial height (Na-ANS).

Howells and others have found that measurements that are longitudinal to the long axis of the body tend to show a higher correlation then measurements that are not longitudinal to the long axis of the body. (Howells 1949; Susanne 1975)

Some authors such as Hunter, Osborne report sexual dimorphism in heritability estimates. While other studies failed to find estimates that demonstrate sexual dimorphism. (Harris and Smith 1980; Harris and Johnson 1991)

Studies conducted by Saunders, Litton and Susanne reported that there is no evidence of suspected sex linkage observed in the morphology of the craniofacial complex. (Litton, Ackerman et al. 1970; Susanne 1975; Saunders, Popovich et al. 1980)

Heritability is population specific, since every population is under a different environmental influence. The genetic contribution to a phenotype will be inversely proportional to the environmental contribution. Lower heritability values are demonstrated in traits related to reproductive fitness. (Falconer 1960) Therefore, environmental change as well as secular change will effect heritability values. As a trait becomes increasingly important or more related to reproductive fitness, then

heritability values should decrease. This could explain why so many studies find heritability values for occlusal relationships so low, often failing to reach significance. Mastication is needed for survival and therefore more closely related to reproductive fitness. Occlusion must be plastic to cope with environmental change. The effects of orthodontics would be impossible if the occlusion was under strict genetic control and not plastic to environmental change.

Feldman, commenting on the contribution of genetic and environmental effect on phenotype, suggested that heritability estimates are meaningless and confuse our understanding of traits. (Feldman and Lewontin 1975) This statement, however, is not true. Heritability studies demonstrate that there is genetic control of some traits, in certain environments. Heritability values can identify what traits in the craniofacial complex that are under genetic influence. The vast number of studies verify that a genetic component is present in areas of the craniofacial complex, consistent with a polygenic pattern. A question thus arises from this: "Is the same genetic source governing control overall the components in the craniofacial complex or is each component under the control of separate genes?"

Pleiotropy is a phenomenon such that more than one phenotype is effected by the same gene or group of genes.

Pleiotropy is usually thought of as one gene or group of genes that effects more then one organ system. An example is osteogenesis imperfecta where a change in one nucleotide in the genes for collagen type I is responsible for spontaneous fractures of bones and cardiac insufficiency. Another example is when an enzyme is affected that is responsible for more then one organ system. In Hurler's syndrome, alpha L-iduronidaze is affected, resulting in accumulation of dermatansulfate affecting both the skeleton, nervous system, spleen and liver et.. (Junqueira, Carneiro et al. 1992) Therefore, pleiotropy is the production of apparently unrelated multiple effects at the phenotypic level from a single gene. (Stedman 1987)

A more inclusive definition of pleiotropy is outlined by Schork et al. in 1994. (Schork, Weder et al. 1994) This definition suggests that pleotropy includes two or more traits that are related by a common biochemical or physiologic pathway influenced by a common genetic locus. This definition encompasses situations where a primary phenotype influences the development of a secondary phenotype.

Although many authors imply that components of the craniofacial complex are probably under individual genetic control, few studies have examined pleiotropy in the craniofacial complex. If individual bones of the craniofacial complex are under unique sources of genetic

control as suggested, then the presence or absence of a pleiotropic effect will give insight into the genetic contribution of skeletal based malocclusions. It has been stated by Proffit that malocclusions from inherited characteristics can result from two major components, the tooth size in relationship to the size of the bone base and the relationship of the size and position of the maxilla and the mandible to each other. The more genetically independent tooth size and bony base characteristics are from each other, the more likely that malocclusions could be inherited. (Proffit 1986)

STATEMENT OF THE THESIS

The objective of this study is to investigate aspects of the genetic basis of craniofacial morphology. The inheritance of craniofacial components is important in the etiology, assessment and treatment of pathologies. In order to achieve the objective a number of statistical techniques appropriate for testing this hypothesis were employed on a sample controlled for sex, age and development. The specific aims of the present study are as follows:

1. Establish, via a number of statistical methods, which measurements or groups of measurements of the craniofacial skeleton correlate highly between related individuals. Compare the correlations of these measures to unrelated individuals to identify which values demonstrate the highest discrepancy between the related and unrelated sample.

2. Statistically investigate the presence of a pleiotropic effect among craniofacial components by evaluating correlations between the various components of the craniofacial complex.

3. Determine the familial aggregation of groups of variables apparently under the control of the same factors.

MATERIALS AND METHODS

Sample Selection

This study employed a cross-sectional design. All records were selected from the Bolton Brush Growth Study (BBGS) at Case Western Reserve University in Cleveland, Ohio. Participants in the BBGS had been chosen because they were well nourished, in good health, and well developed. (Behrents, 1985) The subjects were Caucasian, and tended to be from middle to high socioeconomic status. In addition, most participants have radiographic records from birth to approximately twenty years of age.

Subjects were selected for the following criteria:

1. There was at least one same sex sibling who had participated in the Bolton-Brush study.
2. Records were obtainable for evaluation at ages equal to, or greater than, fourteen years of age.
3. Records at 14-15 years of age contained handwrist radiographs with evidence of adductor sesamoid calcification, and fusion of the distal phalanx of the third finger. (Fishman,1982)
4. Neither sibling had received orthodontic treatment.

There was a normal range of Class I Class II and Class III individuals. However, extreme cases were eliminated if they were not healthy as defined by the Bolton Brush study, or they had received orthodontic treatment, or there was

not evidence of adductor sesamoid calcification. Individual subjects were included in the sample if their age was between 14-20 years and their same-sex sibling was matched with in six months of age. This is reasonable because a number of studies demonstrate that heritability estimates reach the highest values at the prepubertal growth spurt and have an insignificant increase following puberty. Exclusion of poor health and extreme malocclusion as well as orthodontic treatment introduces a potential bias by reducing intra-group variation caused by rare genetic and environmental factors.

Sample Size

From the 4309 individuals enrolled in the BBGS, one hundred female siblings within forty-four sibships fit the above criteria and were included in the analysis.

Cephalometrics

Standardized lateral and frontal cephalometric radiographs were traced onto 8" x 10", 0.003" thick, frosted acetate using a 0.5 mm pentel H lead, mechanical pencil. Using an X-Y coordinate digitizer, Numonics model # 2210-0.30TL.E, all lateral cephalometric landmarks were located and digitized by the same investigator (See Figure 1). Frontal radiographs were measured by hand using a linear digitizer and Geo Calc® software designed by Robert Mensforth to the nearest 0.1 mm, all measurements were made by the same investigator. An IBM® computer model #8508-311

was used to digitize all landmarks found on the lateral radiographs into Dental Facial Planner® (Dentofacial Software Incorporated, P.O.Box 950, Staton A, Toronto, Canada). Midline to the base of the film (ML) on the lateral and center of head to film (P+) on the frontal were used to correct each variable for magnification.

Twenty-three craniofacial measurements were recorded from the digitized cephalograms (See Figures 2-6). All lateral craniofacial linear and angular measurements were computed by Dental Facial Planner®. All frontal craniofacial linear and angular measurements were computed by Geo Calc®.

Reliability for landmark identification and data collection was estimated by retracing and digitizing 10% of the sample. The portion of the sample selected for retracing was determined by the use of a random table. All landmarks were redigitized by the same investigator and Intra-class Correlation Coefficients were computed to test reliability of the measurements.

Data analysis

The analysis of the twenty-three craniofacial measures obtained from the forty-four pairs of female siblings proceeded in nine steps. Step 1 involved assessing the reliability of the individual measures by examining the correlation and agreement between repeated measurements made on the same ten individuals. Step 2 involved assessing

age effects and then ultimately correcting for age effects by regression on the variables over the range of the sample. This was done with one thousand repeated samplings to overcome the non-independence of the sibling pairs. The repeated samplings were carried out by randomly choosing one sibling from each sibpair. Average estimates of correlation and regression parameters were computed and used as the estimates for adjustment purposes. Step 3 involved assessing the degree of correlation between the twenty-three craniofacial measures. Step 4 involved assessing the correlation of the measures between the siblings in an effort to examine the strength of the familial aggregation and possible heritability of the measures. Step 5 involved calculating heritability estimates for each measurement analyzed in step 4. Step 6 involved the assessment of correlations between unrelated individuals. Step 7 involved the assessment of cross-correlations between the measures, this involved correlating a measure on one sibling with a different measure on the second sibling. This analysis gave insight into the general contribution of pleiotropy and sibling-shared environmental factors on pairwise combinations of the traits. Step 8 involved determining the number and definition of gross underlying factors which appeared to influence the twenty-three craniofacial measures. This step was carried out using a principal component analysis.

Step 9 involved assessing the correlation of the principal components obtained in Step 8 between the siblings in an effort to examine the strength of their familial aggregation and possible heritability.

RESULTS

The results will be presented in nine sections. The first section will deal with age effects on the variables and correction by regression. The second section will deal with correlations among variables. The third section will deal with correlations of the variables between siblings. The fourth section will deal with correlations of the variables between unrelated individuals. The fifth section will deal with component analysis of the variables and explained variance in the craniofacial complex. The sixth section will present the results of the principal components analysis. The seventh section will deal with correlations of the principle component scores between siblings. The eighth section will deal with intraclass correlation coefficients to determine reliability of the measures.

I. Control for Changes of the Variables Due to Age Over the Range of the Sample

The criteria for sample selection attempted to minimize the change in the variables due to growth. This was done by selecting only subjects with evidence of fusion of the distal phalange of the third finger and adductor sesamoid calcification. (Fishman 1982) The range in age of the sample was great enough that changes in the variables

due to age were investigated. A regression analysis was performed using one thousand random samplings of one individual in each sib pair (See Table 1).

The results from t-statistics of one thousand resamples support the design and criteria of sample selection. All variables produced t-statistic results rejecting the hypothesis of age effects at the 5% level. Although the overall change in variables due to age effects were not significant, four variables showed significant ($p<0.05$) age effects in 160 of the one thousand simulations. Those variables were ANB, mandibular body length, articulare-pogonion, and AR-AR. Mandibular body length showed significant ($p<0.05$) age effects in 350 out of the one thousand simulations (See Table 1). Although the results depicted in Table 1 suggest that age differences among the sibpairs produced little, if any, effect on the traits studied, each variable was age-adjusted through regression.

II. Correlation between Variables in the Cranialfacial Complex

Following age-adjustment of the measures, pair-wise correlations were then conducted between the variables using an unrelated sample. Again, one individual was randomly chosen from each sibpair for the correlation estimation. This was repeated one thousand times.

Both parametric (Pearson's) and nonparametric (Spearman's) correlation analysis were conducted. Both Pearson correlation and Spearman correlation coefficient values demonstrated comparable results. Therefore, the estimated correlations between variables were robust. All correlations were significant at the 95% confidence level (See Table 2).

III. Correlations of Variables between Siblings

The objective of this analysis stage was to test if correlations exist between siblings for each variable. Both Pearson and Spearman correlations were then performed between siblings for each variable in the present study (See Table 3 and Figures 7-22). The highest correlation between siblings is found in posterior facial height r = 0.579, followed by SNA r = 0.547, and ramus height r = 0.545. Correlations above r = 0.5 were also found in the variables SN-GoGn and anterior cranial base. The lowest correlation is found in the posterior cranial base which demonstrated a slightly negative correlation between siblings at r = -0.013 (See Table 3 and Figures 7-22). Heritability estimates were then calculated for all measures (See Table 4).

IV. Correlations between Unrelated Individuals

The objective of this analysis stage was to examine the strength of correlations between unrelated individuals in the sample. Pearson correlations were performed between

age matched unrelated individuals for each variable in the present study. Most variables demonstrated a very low correlation between unrelated individuals with the exception of Go-Go (r = 0.35), AR-AR (r = 0.33), which correlated slightly higher then the sibling correlation for Go-Go (r = 0.34). The largest discrepancy between the measures of related and unrelated individuals appeared in the variable SNA (See Figures 7-22). Correlations between unrelated individuals represent the degree to which "erroneous" correlations could arise in our sample.

V. Cross-sibling Correlations between Variables

The objective of this analysis stage was to establish if any variables in one sibling demonstrated a high correlation with a different variable in the second sibling. Both Pearson and Spearman correlations were performed between siblings. Each variable was cross correlated for each of the other variables in the other sibling (See Table 5 and Figures 23-24). The highest correlation was found between posterior facial height of one sib and ramus height for the other sib (r = 0.67). Relatively high correlations between sibs (r = 0.47) were found between Ar-Me and Ar-Apt. as well as Ar-Po and Ar-Apt. No correlation was found between anterior facial height and mandibular body length as well as posterior facial height and mandibular body length.

VI. Variance Described by Principle Component Analyses

The objective of this analysis stage was to examine if "clusters" or groups of craniofacial variables could be influenced by common factors, such as a gene or genes. Potentially, it is possible to have as many independent genetic factors as there are variables examined. However, this is very unlikely. The use of component analysis is thus advantageous in that it allows interrelationships of the variables to be examined and ultimately put into components that describe the overall variance observed amoung the variables. Because many of the cephalometric variables used are interrelated, principal component analysis could reveal groups of variables which are influenced together and thus provide basic "plans" for craniofacial morphology.

Principle component analysis grouped the measures used in the present study into eight principal components that describe 93% of the variance observed amoung all craniofacial measurements studied (See Table 6).

VII. Principle Component Loadings of the Variables

Table 7 provides average principle component loadings computed from one thousand random samples of a sibling from each sibling pair. Since loadings that are small suggest that a variable isn't influenced by the same factor as other variables with higher loadings, one can assess groupings of the variables by determining which sets of

variables have high loadings on each factor. In addition, if a particular factor does not explain much variation in the original measures, it can be ignored. The results of the interpretation of the factor loadings suggested eight factors could be abstracted from the original measures. An interpretation of each factor is given below.

Component 1

The first component loads higher on linear variables for mandibular vertical shape (ramus height, Ar-B-pt, Ar-Po, Ar-Me, posterior facial height). Ramus height and posterior facial height were deemed redundant in that the vertical vector including ramus height is incorporated in the measure of posterior facial height. Therefore, the first component was considered to represent size of the mandible and represents 32% of the overall variance observed (See Figures 25 and 26).

Component 2

The highest loadings for the second component are found in measures that represent the projection of the lower 2/3 of the face (SNA, SNB) as well as high negative loading on anterior facial height, lower facial height, and mandibular plane to SN. These measurements are primarily those involved in rotation of the mandible or mandibular projection. Therefore this component was considered to represent mandibular and maxillary projection (See Figures

27 and 28). This second component explained approximately 19% of the overall variance observed.

Component 3

The third component demonstrated highest loadings on both linear and angular measures involved in vertical dimension of the face. The variables with the highest loading in this component were anterior facial height, lower facial height, posterior facial height, and articulare angle. There was negative loading in saddle angle and gonial angle. This component was considered to represent vertical dimension of the face (See Figures 29 and 30). The third component explained approximately 14% of the overall variance.

Component 4

Component four appears to represent linear horizontal measures of the mandible both in the anterior-posterior and transverse dimensions, as well as the cranialbase in the anterior-posterior and transverse dimensions. Highest positive loadings for component four are on bigonial width, mandibular body length, as well as posterior cranial base, and cranial base length. Highest negative loadings on anterior facial height, lower facial height, ramus height and posterior facial height (See Figures 31 and 32). The fourth component explained approximately 9% of the variance observed in the crainofacial complex.

Component 5

All variables in component five have relatively low loadings. The highest positive loading was saddle angle and highest negative loading was gonial angle. Component five is entirely composed of angular measurements (See Figures 33 and 34). The fifth component explained approximately 7% of the overall variance observed.

Component 6

All variables in component six demonstrated low loadings. The highest loadings were found in posterior cranial base, saddle angle, gonial angle, and bigonial width (See Figures 35 and 36). The sixth component can explain approximately 6% of the overall variance observed.

Component 7

All variables in component seven demonstrate low loadings. The highest loadings involved anterior cranial base, cranial base length, and bigonial width (See Figures 37 and 38). The seventh component explained approximately 4% of the overall variance observed.

Component 8

All variables in component eight demonstrated low loadings. The highest loadings involved the lower facial height, anterior cranial base, cranial base length, ANS-PNS, and bigonial width. The eighth through the twenty-third components could collectively explain approximately

10% of the overall variance observed, and were thus considered insignificant.

VIII. Correlation of Principle Component Scores between Siblings

Although the correlation between sibs is much higher for the majority of the variables in comparison to the unrelated sample, the correlation of individual variables was still relatively low between siblings. The correlation of principle component derived factors, however, is high between sibs (See Table 8 and Figure 39). A very high correlation can be seen between components two, three and four, which explains 41% of the variation, in the original measure. Surprisingly, the first component which explains 32% of the overall variation, demonstrated a low correlation between siblings.

IX. Reliability

In order to examine possible measurement error, 11% of the sample was randomly selected, retraced, and remeasured thirty days following the initial data collection of the main sample.

Intraclass correlations were used to the original and re-assessed measurements. The majority of the measures proved to be reliable (See Table 9), with the exception of the linear measure ANS-PNS which demonstrated an r value of 0.68. The low r value for this measurement is most likely due to the difficulty in locating posterior nasal spine in

the lateral cephalogram. The majority of the measures demonstrating r values greater then 0.95.

DISCUSSION

Evaluation of the Sample Criteria

Cephalograms were collected from eighty-eight normal, Caucasian, middle-class, individuals in good health in the Bolton Brush study. Data from the subjects were collected in such a way as to allow control for chronologic age, skeletal age, as well as sex, and had not been previously treated orthodontically. The criteria for sample selection were chosen for a number of reasons. Several studies suggest that heritability values reach peak values following the pubertal growth spurt. Kohn, Suzuki and King report that heritability values of skeletal components increase with age with little significant increase following the growth spurt. (Kohn 1989, Suzuki 1991 and King 1993) Harris found that there is no significant increase in heritability between fourteen and twenty years of age. (Harris 1991) Because of these findings the present study chose subjects under very strict age parameters. Few if any, of the past studies controlled for chronologic age by such strict sample selection.

Handwrist and cephalograms for all subjects in the present study had to be within six months of the chronologic age of the other sibling. This was done by

establishing that adductor sesamoid calcification and fusion of the distal phalanx of the third finger had occurred. This criterion is consistent with Fishman's Skeletal Maturation Index (SMI) #8. (Fishman 1982) Articles written by Fishman demonstrate that this is an accurate measure for predicting that the majority of the circumpubertal growth spurt has occurred. (Fishman 1982) Fishman's Skeletal Maturation Indicators demonstrate that there is a sharp drop off in growth rate following capping of the middle phalanx of the third finger. Fishman deemed this stage of development SMI #7. All subjects in the present study demonstrated a level of development SMI #8 or above which coincides with a sharp drop off in skeletal growth and indicates the end of the circumpubertal growth spurt.

The results from t statistics of one thousand resamples support the design and criteria for the control of age effect in the sample. All variables produced t-statistic results rejecting the null hypothesis at the 95% confidence level. However, the use of a resampling procedure showed that four variables showed minor age effects. These variables included ANB, mandibular body length, articulare-pogonion, and AR-AR'. Mandibular body length showed the strongest age-effects. Changes in the craniofacial complex as a result of growth has been documented throughout life. (Behrents 1985) Therefore, the

insignificant changes found due to growth in the present study are to be expected. Behrents' study demonstrates that a plateau of growth occurs in females between 15-16 years of age. (Behrents 1985)

Twenty-three cephalometric measurements were selected for the present study in accordance with results demonstrating high genetic transmission between siblings in previous studies. These measurements were first verified for reliability, then each measure was subjected to Pearson correlations, and Spearman correlations between each variable. Both Pearson and Spearman correlation values were comparable, indicating robustness of the correlation coefficient estimates. All correlations were significant at the 5% level.

The correlations were performed to evaluate relationships between the measures. Because the correlations of the twenty-three variables were from an averaged individual cephalogram, obvious correlations were present between the measurements. These findings are not surprising, as there are proportional relationships that are to be expected in a Class I skeletal relationship.

Correlation of the Variables between Siblings

Siblings on average share 50% of their genetic make up and are typically raised in the same household and general environment. How an individual responds to environmental stress may be synergistic or antagonistic to the overall

phenotype. Low correlations between unrelated individuals should be evident in that they lack shared genetic and environmental conditions. The results from simple Pearson and Spearman correlation analysis demonstrated relatively high correlations between sisters for approximately half of the measurements. Low correlations were found between unrelated individuals for all the measurements. However, posterior cranialbase, ANS-PNS, ANB and measurements in the transverse (i.e., Go-Go and Ar-Ar) demonstrated comparable correlations between the related and unrelated sample. Therefore, it can be concluded that the results of the present study fail to support a strong role for familial and genetic determinants for posterior cranialbase, ANS-PNS, and transverse measurements.

All other measurement used in the present study were considered reasonable measurements for estimating genetic variance. It should be noted that high correlations between siblings (i.e., $r \geq 0.50$) were found in the following measurements: SNA, ramus height, posterior facial height, SN to GoGn, and anterior cranialbase. SNA and ramus height demonstrated the greatest discrepancy between correlations derived from related and unrelated individuals, followed by posterior facial height, SN to GoGn, and finally anterior cranialbase. All of these measurements were deemed very acceptable for estimated

genetic control because they demonstrated high correlations between siblings and a weak correlations between unrelated individuals in our sample.

Changes in SNA with orthodontic treatment have been documented clinically as well as in the literature. (McNamara and Brudon 1993) However, there is an envelope of change that can realistically be influence with orthodontic treatment. (Proffit, White 1991) There is also a relationship of SNA to the position of Nasion. A more posterior positioned Nasion will demonstrate an increased SNA value. Therefore, the high discrepancy between correlations of the control group and the study sample can be suggestive of phenotypic transmission of the anterior posterior position of the maxilla in relation to the cranialbase.

Heritability Estimates

Heritability is an estimate of the phenotypic variation due to genetic causes. Heritability in the narrow sense was estimated using the classic formula by Falcolner for siblings (Falconer 1960), which is twice the r value. However, in sibling studies heritability estimations fail to partition variance into effects due to dominance, epitasis as well as any concordance due to environmental effects. Therefore, it is common to find inflated heritability estimates that exceed values of h2 > 1.0. In 1979 Garn had termed this phenomenon

"cohabitational effect" and Feldman 1973 called the similarities "cultural transmission". (Garn 1979; Feldman 1960) Heritability estimates were calculated in the present study for a means of comparison to previous studies. The investigator feels that heritability estimates are meaningless in sibling studies because there is no control for dominance, epitasis or environmental effects. Therefore heritability is not an accurate representation of genetic influence. The information gained from heritability estimates is thus comparable to that gained by simple correlation analyses.

Cross Variable Correlations between Siblings

Cross variable correlations were performed to evaluate for the presence of a pleiotropic effect relating measurements between the cranialbase, maxilla, and mandible. Results from cross variable correlations between siblings demonstrate a surprisingly high correlation of posterior facial height of sibling one to ramus height of sibling two ($r = 0.67$). In fact the cross correlation of posterior facial height to ramus height is higher than either measurement relating to itself. Measurements of the cranialbase cross correlate between siblings but fail to demonstrate similar correlations between the other skeletal components measured. On the other hand, mandibular and maxillary measurements did correlate within each other. The results of the present study could suggest that there

is separate genetic control of the cranial base and the lower two-thirds of the face. This finding is in agreement with Nakata's findings in 1974. However, all cross correlations values in the present study are small (i.e., $r < 0.50$), except for the cross correlation between posterior facial height and ramus height ($r = 0.67$). The anterior vertical measurements (i.e., anterior facial height, upper facial height, and lower facial height) did not demonstrate very high cross correlations with any other variables ($r < 0.35$). The results for this section suggest the following:

1. There is greater genetic control over the posterior vertical measurements than anterior vertical measurements.
2. There is separate control over the cranialbase and shared control over the maxilla and mandible.

Principal Component Analysis

Multivariate analysis such as principal component analysis allows the identification of factors which underlie a group of measurements that account for the majority of variation of the original measurements. The measurements of the present study were subjected to principal component analysis in hopes of identifying a trend of familial concordance between components. This was attempted to identify components that are more highly concordant, and components that may be more discordant between sisters. The technique of component analysis revealed four components that describe 73% of the variance

observed. These components could be assessed and interpreted from the strength of the loadings on individual measurements.

Component 1

The first component represents 32% of the overall variance observed and loads higher on linear variables for effective length of the mandibular as well as vertical size (ramus height, Ar-B-pt, Ar-Po, Ar-Me, posterior facial height). Ramus height and posterior facial height were deemed redundant in that the vertical vector including ramus height is incorporated in the measurement of posterior facial height. The measurements Ar-B-pt, Ar-Po, Ar-Me, also demonstrated a vertical as well as a horizontal component. However, mandibular body length demonstrated a low loading score (0.06) for component 1. The first component was considered to represent the overall size of the mandible in the vertical and anterior posterior dimensions. Neither of the transverse measurements demonstrated high loading for component one nor did these measurements prove acceptable in the previous analysis.

Component 2

The second component contained linear and angular measurements that represent the projection of the lower two-thirds of the face (SNA, SNB) as well as high negative loading on anterior facial height, lower facial height, and mandibular plane to SN. The measurements in component two

are involved in rotation of the mandible, or mandibular projection as well as maxillary projection in reference to the cranialbase. Therefore, this component was considered to represent mandibular and maxillary projection and represents 19% of the overall variance observed.

Component 3

The third component demonstrated highest loading on both linear and angular measurements involved in vertical size of the face. The variables with the highest loading in this component were anterior facial height, lower facial height, posterior facial height, and articulare angle. There was negative loading in saddle angle and gonial angle. Because the variables in component three reflect a composite of vertical size across the cranialbase, maxilla and mandible it was considered to represent the vertical size of the overall craniofacial complex. Component three represents 14% of the overall variance observed.

Component 4

The forth component appears to represent linear horizontal measurements of the mandible and cranialbase both in the anterior-posterior and transverse dimensions. Highest positive loadings for component four is on bigonial width and mandibular body length, as well as posterior cranialbase, cranialbase length. Highest negative loading was found on anterior facial height, lower facial height, ramus height and posterior facial height. Component four

was considered to represent horizontal measurements of the mandible body and cranialbase and represents 9% of the overall variance observed.

Components 5-7

In components five, six and seven the measurements failed to reach the arbitrary cut off value of 0.10 for loading except for Articulare-Nasion that participated at the 0.10 level in component seven. Components five, six, and seven demonstrated a composite of relatively equal loadings. Components five and six shared negative loadings on gonial angle. Components five through seven shared positive loadings on saddle angle and combined represent approximately 17% of the variance observed (See Figures 33 through 38). Components five through seven are difficult to explain and have been considered by the investigator as an overall participation of all variables in those components.

Correlations of Principle Components between Sibs

Pearson and Spearman correlation were conducted between siblings for each component. Components two, three and four prove to be highly correlated between sisters. These components include horizontal measurements of the cranialbase and mandibular body, vertical measurements of the overall skeletal complex as well as measurements resulting in mandibular and maxillary projection. The second, third, and fourth components combined explained 42%

of the overall variance. In comparison to components two, three and four, component one demonstrated a low correlation between siblings (r = .46). Component one was considered to represent overall size of the mandible. Below is the percent coefficient of determination for each component.

1. The percent coefficient of determination for component one is 20%.
2. The percent coefficient of determination for component two is 76%.
3. The percent coefficient of determination for component three is 48%.
4. The percent coefficient of determination for component four is 67%.

Component Complexity

Some of the variables loaded on more than one component, and some components demonstrated equally low loading for the majority of the variables. Each component is a composition of the variables used in the present study. While some of the components demonstrated high loading for several of the variables other components appeared to load equally for all the variables. For example, components five, six, seven and eight demonstrated equally low loading for all the variables. It can be assumed that each variable contributed relatively equally to these components. In these components it is difficult to explain exact representation of the variation. (Harris 1982, Hauspie 1985) Several of the principal components

that demonstrated this phenomenon also demonstrated high correlations between siblings. This supports the idea that there is an overall plan or blue print governing the development of the facial skeleton. No one measure demonstrates very high correlations between siblings. However all of the measures in concert do demonstrate high concordance between sibs. For example, mandibular plane angle, cranial base length, anterior facial height and lower facial height all demonstrate correlations below r = 0.52. However, these measurements combined represent component 2 and demonstrate a correlation of r = 0.87 which is a much greater correlation then any of the individual measurements. The remarkable similarity between family members also supports the idea that a shared "blueprint" exists governing the appearance of the face, that is, one that involves a few genes or familial factors that influence a number of craniofacial features simultaneously.

Comparison to Previous Studies

Ever since the publication by Vandenberg in 1960 that suggested using multivariate analysis to assess genetic influences on a trait or traits, many studies have been conducted on head and neck measurements. (Nakata 1974, Lundstom 1984, Hauspie 1985, Suzuki 1991) It is difficult to compare results of these studies because they utilize different statistical methods (i.e., path analysis, factor analysis, principal component analysis, maximum

likelihood), choice of materials (i.e., dry skulls, living material, x-rays) and variables. However, there are some trends that can be discussed.

Hunter's findings in 1964 suggested that vertical variables are more influenced by genetics then horizontal variables. This finding is interesting because environmental effects on lower facial height due to allergies have been documented in the literature. (Linder 1970) Hunter's finding was not confirmed by the present study, although measurements for posterior vertical dimension did demonstrate high simple correlations between siblings in the present study. Principal component analysis in the present study reveals that projection of the lower two-thirds of the face followed by horizontal measurements of the cranialbase and mandibular body. Vertical measurements did demonstrate phenotypic transmission in the present study but must be ranked after horizontal measurements. This is not to imply that horizontal measurements are more genetically influenced. Food consistency and environmental conditions of the sample population as a whole may effect these measurements. Lundstrom, utilizing heritability estimates generated by path analysis, failed to find any difference between genetic transmission of horizontal and vertical measurements. (Lundstrom 1988)

Suzuki in 1991 conducted a similar study to the present study and applied principal component analysis to 81 measurements. The results of Suzuki's study demonstrate a first factor involved in size relationship of the overall craniofacial complex. Size relationship for the first component was found in the present study. However, the loadings were primarily mandibular measurements in the first component rather than cranialbase measurements. Suzuki's second factor demonstrated downward and backward rotation of the mandible which was also found in the present study.

Heritability

Heritability estimates were calculated and compared to previous studies. Harris in 1991 conducted a study that contained ten of the variables used in the present study. Calculated heritability estimates in Harris's study for the fourteen and twenty year age group were evaluated with the results of the present study. Harris's results agree with several of the heritability values calculated in the present study. For instance, both studies suggest that there is high genetic transmission to phenotype found in posterior facial height, anterior cranialbase, articulare-B point and articulare-pogonion. However, Harris argues that heritability estimates for occlusal variables decrease with age. His results show that the measures SNA and SNB demonstrate low additive genetic transmission. This was not

found in the present study. Although the present study focused on skeletal relationships, SNA and SNB were evaluated. In fact, SNA heritability estimates were second only to posterior facial height in the present study. SNA also displayed the highest discrepancy between siblings and unrelated individuals. Harris reports low heritability values for mandibular plane to SN. Again, this was not the finding of the present study.

It has been argued that angular measurements tend to demonstrate smaller heritability estimates then linear measurements. (Horowitz 1960; Howells 1949; Hunter 1965; Osborne 1959; Wylie 1944) In the present study the results do not support these findings. Relatively high correlations were found in both angular and linear measurements. Component two demonstrated the highest correlation between sibs and demonstrated high loadings on both linear and angular measurements.

In the present study most measurements demonstrated relatively high heritability estimates (See Table 4). These results agree with the majority of previous studies if the appropriate age group is evaluated. (Harris 1991; Byard et al. 1984) Saunders demonstrates slightly higher estimations in all comparable measurements then the present study; however, her sample size was 25% larger and like the present study included females fourteen years of age or older. In studies like the present study the larger the

sample size the stronger the power of the study. Ideally The magnitude of the correlation will be greater in a larger sample if a correlation is present. Possibly the increased values found in Saunder's studies are the result of a more adequate sample size then the present study.

There was low heritability found in ANB, posterior cranialbase and ANS-PNS. Leech argued that skeletal morphology is genetically determined on the evaluation of ANB alone and the assessment of one pair of monozygotic twins. It has been concluded in the present study that ANB angle is influenced primarily by an overall genetic plan governing the relationship of all portions of the craniofacial complex as well as environmental factors. It appears that all components work in concert to preserve the mandibular maxillary relationship in a sample that is primarily skeletal Class I.

Correlation coefficients between the measurements of the present study and the control group agree with the findings of Fromhart 1971 who also used an unrelated control. Unlike the present study, which contained primarily skeletal Class I individuals, the Fromhart's sample consisted primarily of Class II division 1 individuals. In the present study, the correlations of Gonial angle, articulare pogonion and articulare gonion and bigonial width did not agree with his findings.

In 1959 Kraus and associates suggested that the measurement deemed AR-AR in the present study is very concordant between siblings. However, their assessment was based on superimposition of individual bones and was not statistically analyzed and no unrelated control sample was used. (Kraus et al. 1959) Other studies conducted by Arya and Savara suggest that bigonial width demonstrated a low genetic component of variability between related individuals this finding is consistent with the present study. (Arya and Savara 1973) It appears that the dimension of bigonial width is predominately influenced by the environment. The masseter and medial pterygoid muscles appear to effect the shape and size of gonion. Such an effect on gonion due to function will result in lower correlations between siblings.

Limitations of the Study

Measurements Used

Measures used in the present study were chosen because they represent specific hard tissue structures and demonstrated high heritability in previous studies. (Arya 1973, Harris 1991, Fromhart 1971) However, There is inherent limitations in using data from a two dimensional source. The complex morphology in the head and neck cannot be adequately represented with linear and angular measurements from a two-dimensional x-ray. Much of the shape information is lost with the x-ray technique employed

by the present study. Each measurement of a particular bone only represents an arbitrary portion of a morphologic unit. In the present study the choice of measurements did not represent all planes of space equally. Therefore, correlation analyses of three-dimensional imaging should be explored.

In addition, certain landmarks prove to be difficult to repeat precisely. The measurement ANS-PNS demonstrated low reliability. Hence any conclusions from ANS-PNS are erroneous. The linear measures ramus height and articulare B-point demonstrated lower but acceptable reliability in the present study.

Environmental Factors

The genetic control of a morphologic structure cannot be simply evaluated based on a sibling model. There is a complex interrelationship of factors (i.e., diet, internal and external environment and/or habit) that cannot be controlled in this type of study model. Additional studies must be conducted using other models such as twins, half sibs, mid-parents, and parent-offspring models.

Study Population

The sample used in this study was composed of Caucasian females from the early portion of this century. Therefore, it is a biased sample. Generalizations cannot be applied to other ethnic populations as they are not represented in the present study.

When investigating phenotypic variation, the parameters of the population limit the investigator. Skeletal Class I, II, and III individuals are represented in this sample. A more homogeneous sub-population such as skeletal Class III individuals would be more suitable to study. Unfortunately, a homogeneous sample that could fit the criteria of the present study would be difficult to obtain.

Effects of secular change cannot be controlled. A Study conducted by Hunter and Garn in 1969 reports an increase in size and projection of the mandible as well as a decrease in facial height in this century. It is the investigator's belief that secular change may result in an increase or decrease in mandibular size depending on what slice of time is examined. One thing is clear and that is there is change in the craniofacial skeleton over generations and the present study sample is from the early portion of this century. Nutrition, environmental, and socioeconomic conditions have changed since the turn of the century. Vlastovsky argues that the most important cause of secular trends is the change in living conditions and nutrition. (Vlastovsky 1966) Therefore, accurate representation of the present day population cannot be certain.

Interpretation of the result of principal component analysis is to some degree subjective. The interpretation

of the variables that load for any one component is influenced by the investigator's judgment. All variables take part in each component to some degree. Equally low loading demonstrates a participation of all variables in that component.

Future Studies

The results of the present study suggest an overall genetic plan or blueprint in the craniofacial complex. Minor changes make each individual unique in a family. Possibly three dimensional morphometric evaluation of monozygotic twins will shed light on what morphology is influenced by environmental stress and more subject to change. Unfortunately, human samples of sufficient size would be difficult to obtain. The most logical option would be correlations of three dimensional, morphometric data of animals. An animal sample could provide a genetic as well as environmental conditions that could be more easily controlled.

The pitfalls of this study and previous studies are that three dimensional structures cannot be represented adequately with two dimensional x-rays. Linear and angular cephalometric measures do not provide enough information to adequately evaluate shared phenotypic variation between siblings. A previous study conducted by Kraus and associates in 1959 attempted to analyze concordance between triplets with cephalometric superimposition. Kraus's study

was in the right direction. Superimposition is not limited to simple measurements. Superimposition of three dimensional images in sibling and twin study models could provide some interesting results on the effects of functional appliances on the craniofacial complex. Studies of phenotypic variation in animal models that are genetically identical but placed in different environmental conditions should present a better understanding of environmental effects on phenotype. Animal studies correlating three dimensional data of a genetically identical sample with a hybridized sample should allow a better understanding of genetic effects on phenotype. With advances in three dimensional imaging techniques, correlations of shape information should allow a better understanding of genetic and environmental effects on phenotype.

Another avenue to take in future studies is genetically linked pathology with profound effects on the face. A number of genetic syndromes present with dentofacial deformity. Stockard's dogs possessed an autosomal dominant gene responsible for achondroplasia. (Stockard and Johnson 1941) Achondroplasia is a defect in cartilage proliferation resulting in short appendages as well as a midface deficiency. The midface fails to translate secondary to abnormal length development of the cranialbase. Wet lab studies locating genetic sources for

phenotypic displays on the face will also facilitate understanding in this area.

Hormonal disturbances with phenotypic effects on the face should be explored thoroughly. The facial changes observed in acromeglia can isolate areas of potential growth in the face. Prospective animal studies involving increased levels of growth hormone administered at different stages of growth and development should provide information on growth potential.

SUMMARY AND CONCLUSIONS

The present study has shown that principal component analysis, if applied with sufficient control can provide a better understanding of the main determinants responsible for the variability in head form. Principal component analysis is a logical approach to decipher data involving a large number of correlated variables. The cross correlations of measurements between and within sibships suggests that there is greater genetic influence over the posterior vertical dimension and projection of the maxilla. Cross-correlations between siblings of these measurements suggests that the upper one-third and the lower two-thirds of the craniofacial skeleton are under separate genetic control.

The present study suggests that an overall craniofacial skeletal plan could exist. Correlations of principle components between siblings suggest that pleiotropy cold play a significant role in governing facial form, and possibly, govern the overall formation of the individual bones in craniofacial skeleton. High correlations of components two, three and four between siblings suggests that the highest genetic variation shared is present in variables responsible for horizontal

measurements of the cranialbase and mandibular body, vertical measurements of the overall skeletal complex as well as measurements resulting in mandibular and maxillary projection.

APPENDIX A

Abbreviations

Cephalometric Landmarks

Variables

ABBREVIATIONS

A pt.	A point
ACB	Anterior Cranial Base
AFH	Anterior Facial Height
ANB	The angle: A point, Nasion, B point
ANS	Anterior Nasal Spine
Ar	Articulare
B pt.	B point
Go	Gonion
GoGn	The constructed line between Gonion and Gnathion
Gn	Gnathion
LFH	Lower Facial Height
Me	Menton
Na	Nasion
PCB	Posterior Cranial Base
PFH	Posterior Facial Height
PNS	Posterior Nasal Spine
Po	Pogonion
S	Sella
SN	The constructed line between Sella and Nasion
SNA	The angle: Sella, Nasion, A point
SNB	The angle: Sella, Nasion, B point
UFH	Upper Facial Height

CEPHALOMETRIC LANDMARKS

1) A Point	The deepest midline point in the curved outline of the base of the maxillary alveolar process. A Point corrisponds with the anthopometric landmark subspinale.
2) ANS	Anterior nasal spine, The point in the median plane that is the tip of the bony anterior nasal spine. ANS is the radiographic analog of the anthopologic landmark acanthion.
3) AR	The radiographic point of intersection of the lateral border of the neck of the condyle and the inferior boarder of the mastoid process. (This point was used by Wise Frey and Moore in 1954).
4) Articulare	A radiographic landmark introduced by Bjork. The intersection of the posterior, dorsal margin of the asending ramus of the mandible and the outer margin of the cranial base.
5) B Point	The most anterior point of the mandibular base. In the median plane it is the most posterior point of the mandibular alveolar contour. B point corresponds with the anthopometric landmark supramentale.
6) Gonion	The intersection of the posterior margin of the ascending ramus and the inferior boarder of the mandible.

7) Gnathion	The constructed radiographic point that is located between the most anterior point of the chin (Pogonion) and the the most inferior point of the chin (Menton).
8) Menton	The most inferior and caudal radiographic point of the outline of the chin. Menton corresponds to the anthopometric landmark gnathion.
9) Nasion	In the median plane nasion is the most anterior point of the nasofrontal suture.
10) PNS	Posterior nasal spine is a constructed radiographic point that is the intersection of the anterior wall of the pterygopalantine fossa and the nasal floor.
11) Pogonion	The most anterior point of the chin in the median plane.
12) Sella	Sella is a radiographic point that is contructed in the median plane representing the midpoint of the hypophysial fossa.

VARIABLES

1) ANB	The angle formed by the radiographic landmarks: A point, Nasion, B-point.
2) ANS-PNS	The linear distance in millimeters between the radiographic landmarks: Anterior Nasal Spine, Posterior Nasal Spine.
3) Anterior cranial base	The linear distance in millimeters between the radiographic landmarks: Nasion, Sella.
4) Anterior facial height	The linear distance in millimeters between the radiographic landmarks: Nasion, Menton.
5) AR-AR'	The linear distance in millimeters between the intersection of the lateral boarder of the neck of the condyle and the mastoid process in the frontal cephalogram.
6) Articulare angle	The angle formed by the radiographic landmarks: Sella, Articulare, Gonion.
7) Articulare A pt.	The linear distance in millimeters between the radiographic landmarks: Articulare, A Point.
8) Articulare B pt.	The linear distance in millimeters between the radiographic landmarks: Articulare, B point.

9) Articulare Menton	The linear distance in millimeters between the radiographic landmarks: Articulare, Menton
10) Articulare Pogonion	The linear distance in millimeters between the radiographic landmarks: Articulare, Pogonion.
11) Body length	The linear distance in millimeters between the radiographic landmarks: Gonion, Menton.
12) Cranial base	The linear distance in millimeters between the radiographic landmarks: Nasion, Articulare.
13) Go-Go'	The linear distance in millimeters between the radiographic landmarks: Gonion, Gonion taken in the frontal cephalogram.
14) Gonial angle	The angle formed by the radiographic landmarks: Articulare, Gonion, Menton.
15) Lower facial height	The linear distance in millimeters between the radiographic landmarks: Anterior Nasal Spine, Menton.
16) Posterior cranial base	The linear distance in millimeters between the radiographic landmarks: Sella, Articulare.
17) Posterior facial height	The linear distance in millimeters between the radiographic landmarks: Sella, Gonion.

18) Ramus height	The linear distance in millimeters between the radiographic landmarks: Articulare, Gonion.
19) Saddle angle	The angle formed by the radiographic landmarks: Nasion, Sella, Articulare.
20) SNA	The angle formed by the radiographic landmarks: Sella, Nasion, A point.
21) SNB	The angle formed by the radiographic landmarks: Sella, Nasion, B point.
22) SN to GoGn	The angle formed by the radiographic planes: Mandibular plane (formed by the radiographic landmarks Gonion, Gnathion), and the reference plane formed by the radiographic landmarks Sella, Nasion.
23) Upper facial height	The linear distance in millimeters between the radiographic landmarks: Nasion, Anterior Nasal Spine.

APPENDIX B

Figures

Tables

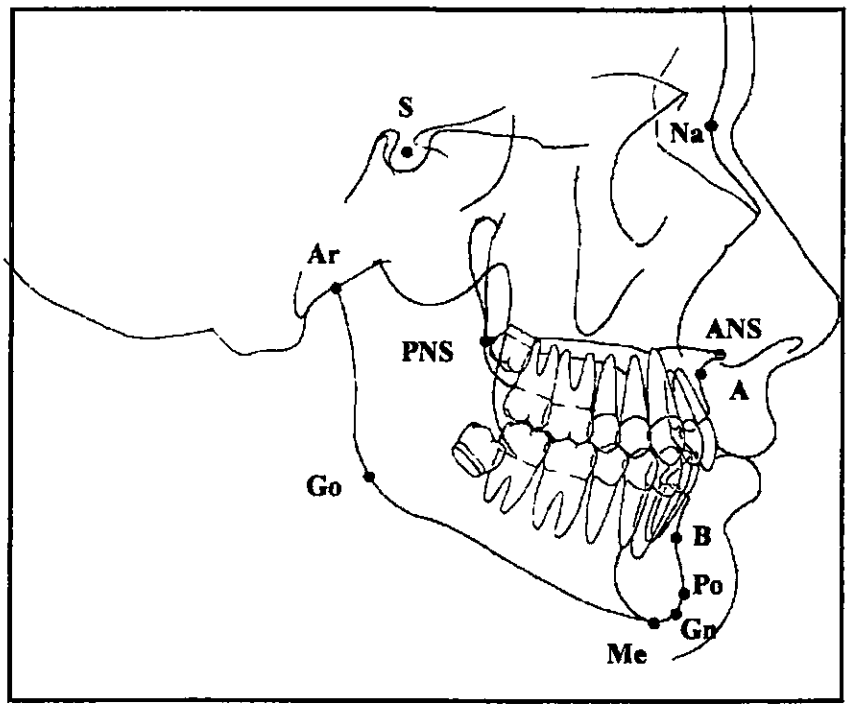


Fig. 1 : Landmarks located on lateral Cephalometric Radiographs

A — A Point, the deepest midline point in the curved outline of the base of the maxillary alveolar process. A Point corresponds with the anthropometric landmark subspinale.

ANS — Anterior nasal spine, the point in the median plane that is the tip of the bony anterior nasal spine. ANS is the radiographic analog of the anthropologic landmark acanthion.

Ar — Articulare, a radiographic landmark introduced by Bjork. The intersection of the posterior, dorsal margin of the ascending ramus of the mandible and the outer margin of the cranial base.

B — B Point, the most anterior point of the mandibular base. In the median plane it is the most posterior point of the mandibular alveolar contour. B point corresponds with the anthropometric landmark supramentale.

Go — Gonion, the intersection of the posterior margin of the ascending ramus and the inferior boarder of the mandible.

Gn — Gnathion, the constructed radiographic point that is located between the most anterior point of the chin (Pogonion) and the most inferior point of the chin (Menton).

Me — Menton, the most inferior and caudal radiographic point of the outline of the chin. Menton corresponds to the anthropometric landmark gnathion.

Na — Nasion, in the median plane nasion is the most anterior point of the nasofrontal suture.

PNS — Posterior nasal spine is a constructed radiographic point that is the intersection of the anterior wall of the pterygopalantine fossa and the nasal floor.

Po — Pogonion, the most anterior point of the chin in the median plane.

S — Sella is a radiographic point that is constructed in the median plane representing the midpoint of the hypophysial fossa.

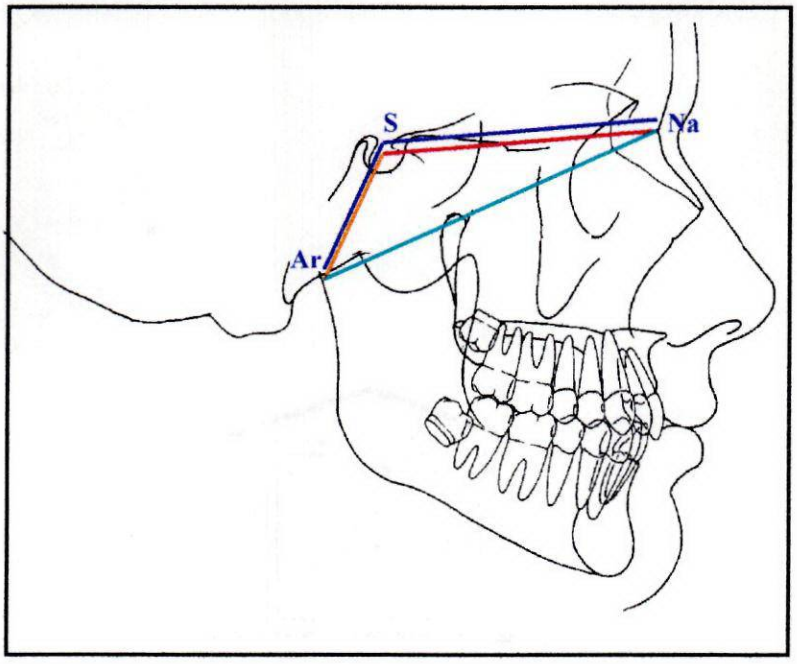


Fig. 2 : Measurements of Cranial Base on lateral Cephalometric Radiographs

S-Na : Anterior Cranial Base
S-Ar : Posterior Cranial Base
Ar-Na : Overall Cranial Base
Na-S-Ar : Saddle angle

Ar Articulare, a radiographic landmark introduced by Bjork. The intersection of the posterior, dorsal margin of the ascending ramus of the mandible and the outer margin of the cranial base.

Na Nasion, in the median plane nasion is the most anterior point of the nasofrontal suture.

S Sella is a radiographic point that is contructed in the median plane representing the midpoint of the hypophysial fossa.

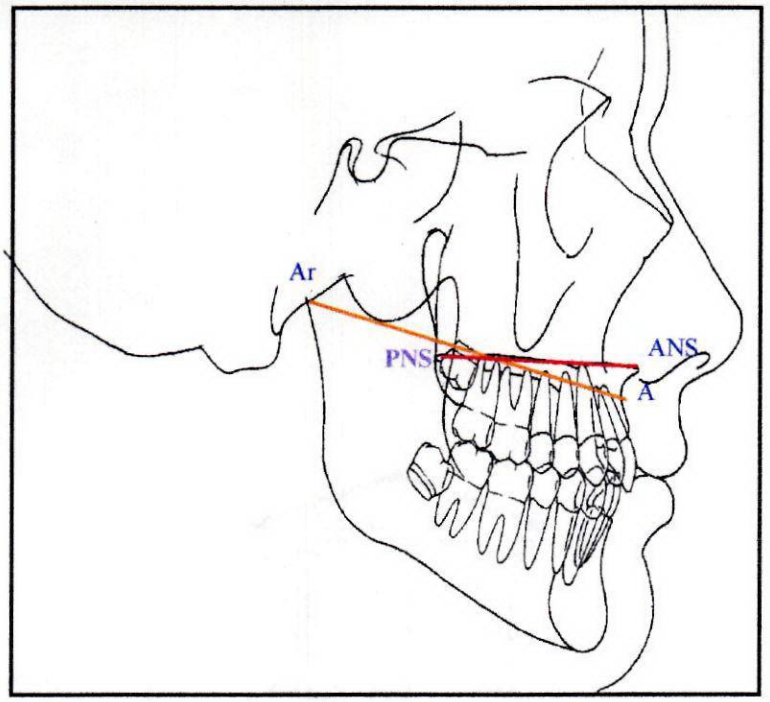


Fig. 3 : Measurements of Maxilla on lateral Cephalometric Radiographs

ANS-PNS : Palatal Length

Ar-A point

A	A Point,the deepest midline point in the curved outline of the base of the maxillary alveolar process. A Point corresponds with the anthopometric landmark subspinale.
ANS	Anterior nasal spine, The point in the median plane that is the tip of the bony anterior nasal spine. ANS is the radiographic analogue of the anthopologic landmark acanthion.
Ar	Articulare, a radiographic landmark introduced by Bjork. The intersection of the posterior, dorsal margin of the ascending ramus of the mandible and the outer margin of the cranial base.
PNS	Posterior nasal spine is a constructed radiographic point that is the intersection of the anterior wall of the pterygopalantine fossa and the nasal floor.

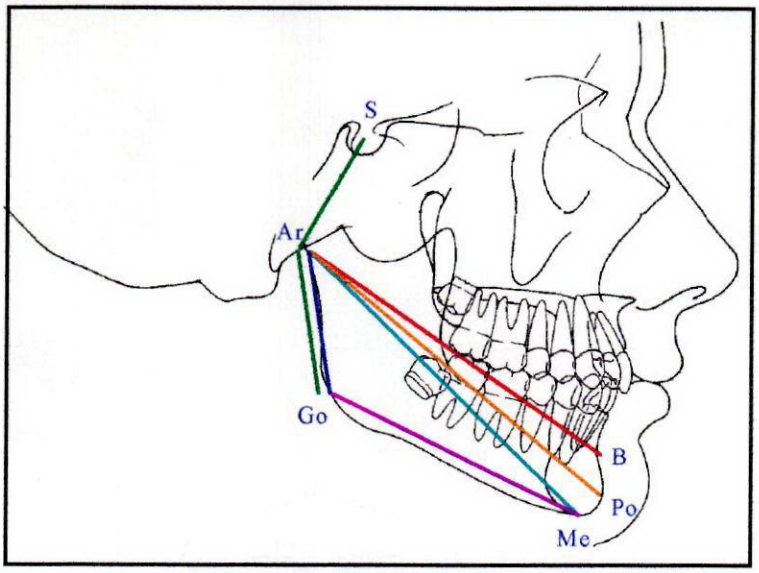


Fig. 4 : Measurements of Mandible on lateral Cephalometric Radiographs

Ar-B point **Ar-Po** **Ar-Me**
Ar-Go : Ramus Height
Go-Me : Mandibular body Length
S-Ar-Go : Ar angle
Ar-Go-Me : Gonial Angle

Ar	Articulare, a radiographic landmark introduced by Bjork. The intersection of the posterior, dorsal margin of the ascending ramus of the mandible and the outer margin of the cranial base.
B	Point, the most anterior point of the mandibular base. In the median plane it is the most posterior point of the mandibular alveolar contour. B point corresponds with the anthopometric landmark supramentale.
Go	Gonion, the intersection of the posterior margin of the ascending ramus and the inferior border of the mandible.
Me	Menton, the most inferior and caudal radiographic point of the outline of the chin. Menton corresponds to the anthopometric landmark gnathion.
Po	Pogonion, the most anterior point of the chin in the median plane.
S	Sella is a radiographic point that is constructed in the median plane representing the midpoint of the hypophysial fossa.

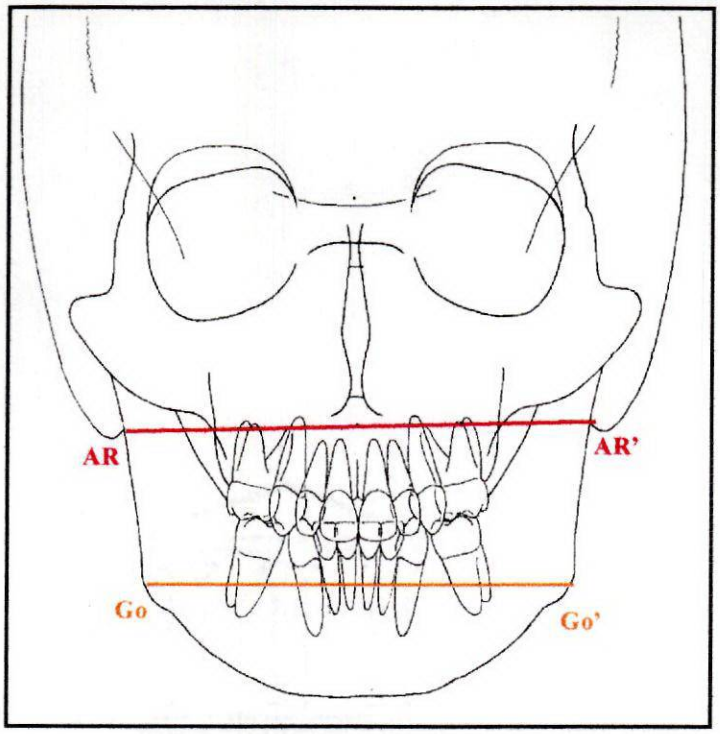


Fig. 5 : Transverse Measurements of Cranial Base and Mandible on P-A Cephalometric Radiographs

AR-AR'

Go-Go'

AR The radiographic point of intersection of the lateral border of the neck of the condyle and the inferior border of the mastoid process. (This point was used by Wise Frey and Moore in 1954).

Go Gonion, the intersection of the posterior margin of the ascending ramus and the inferior border of the mandible.

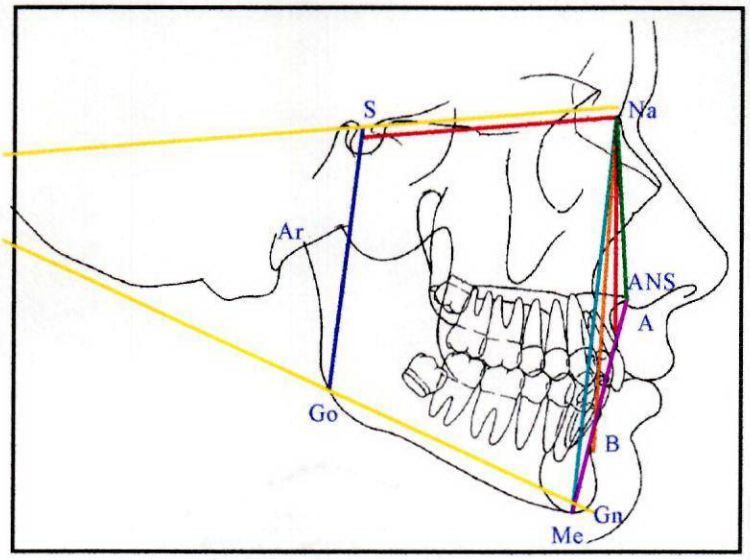


Fig. 6 : Measurements Between the Craniofacial Components on lateral Cephalometric Radiographs

S-Na-A, S-Na-B , ANB
Na-Me: Anterior Facial height
S-Go : Posterior Facial height
Na-ANS : Upper Facial Height
ANS-Me : Lower Facial Height
SN-GoGn

A	A Point, the deepest midline point in the curved outline of the base of the maxillary alveolar process. A Point corresponds with the anthopometric landmark subspinale.
ANS	Anterior nasal spine, the point in the median plane that is the tip of the bony anterior nasal spine. ANS is the radiographic analogue of the anthopologic landmark acanthion.
B	B Point, the most anterior point of the mandibular base. In the median plane it is the most posterior point of the mandibular alveolar contour. B point corresponds with the anthopometric landmark supramentale.
Go	Gonion, the intersection of the posterior margin of the ascending ramus and the inferior border of the mandible.
Me	Menton, the most inferior and caudal radiographic point of the outline of the chin. Menton corresponds to the anthopometric landmark gnathion.
Na	Nasion, in the median plane. Nasion is the most anterior point of the nasofrontal suture.
S	Sella is a radiographic point that is constructed in the median plane representing the midpoint of the hypophysial fossa.

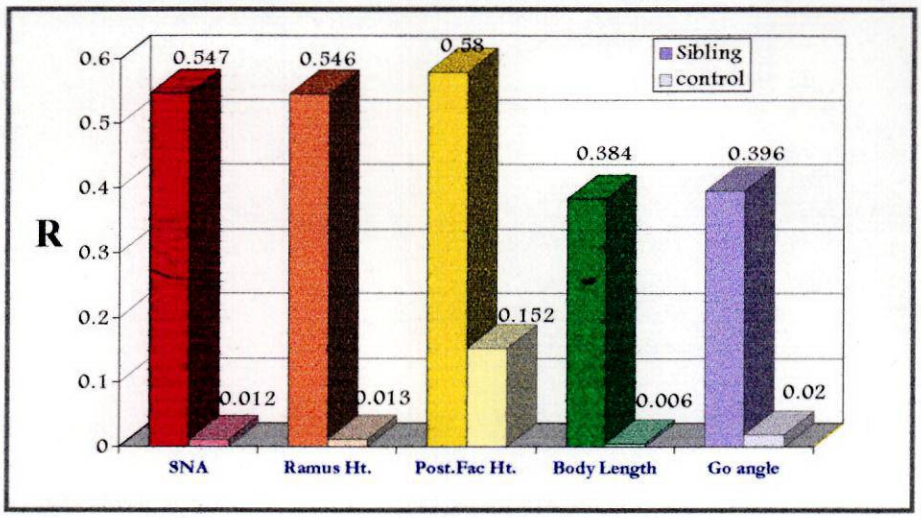


Fig. 7 : Comparison of Pearson Correlations between Siblings and Non-related Control Subjects

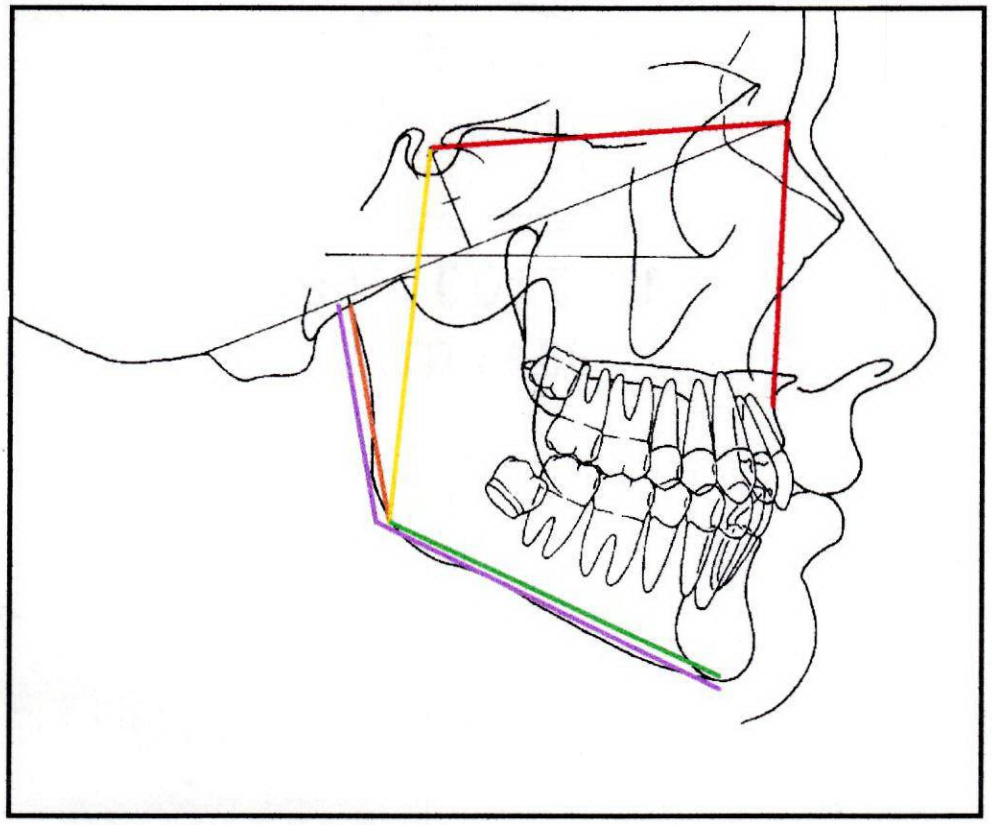


Fig. 8: Cephalometric Demonstration of Fig. 7

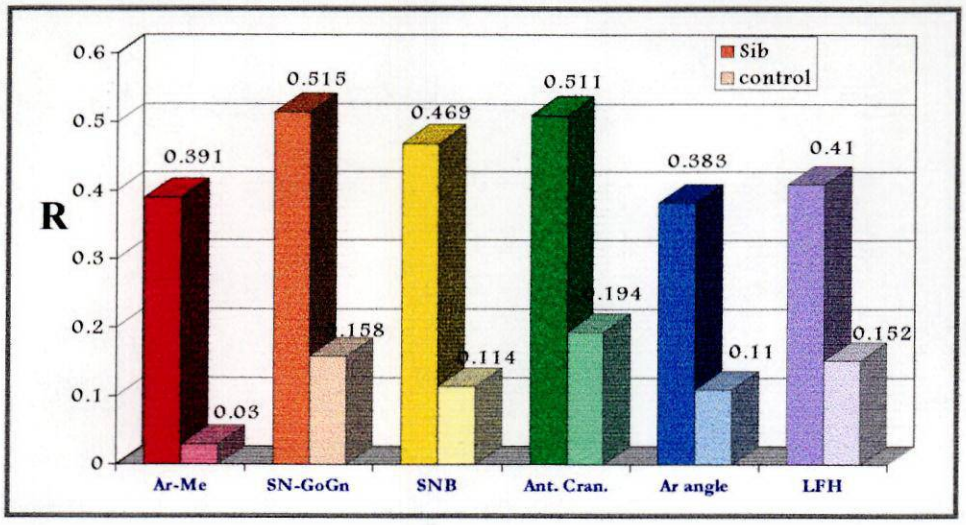


Fig. 9 : Comparison of Pearson Correlations between Siblings and Non-related Control Subjects

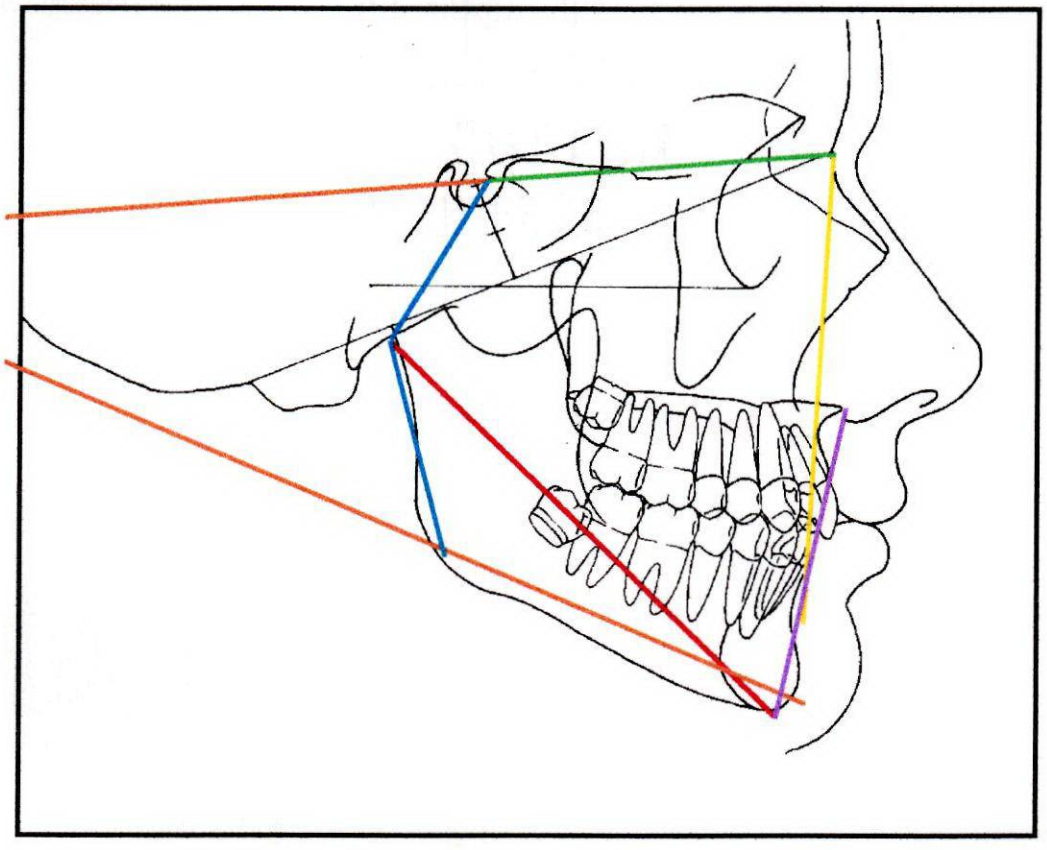


Fig. 10 : Cephalometric Demonstration of Fig. 9

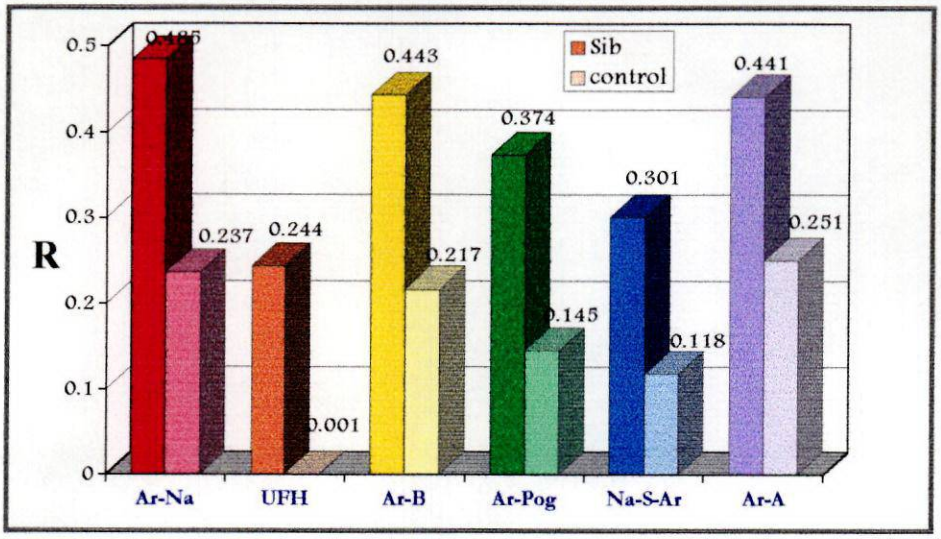


Fig. 11 : Comparison of Pearson Correlations between Siblings and Non-related Control Subjects

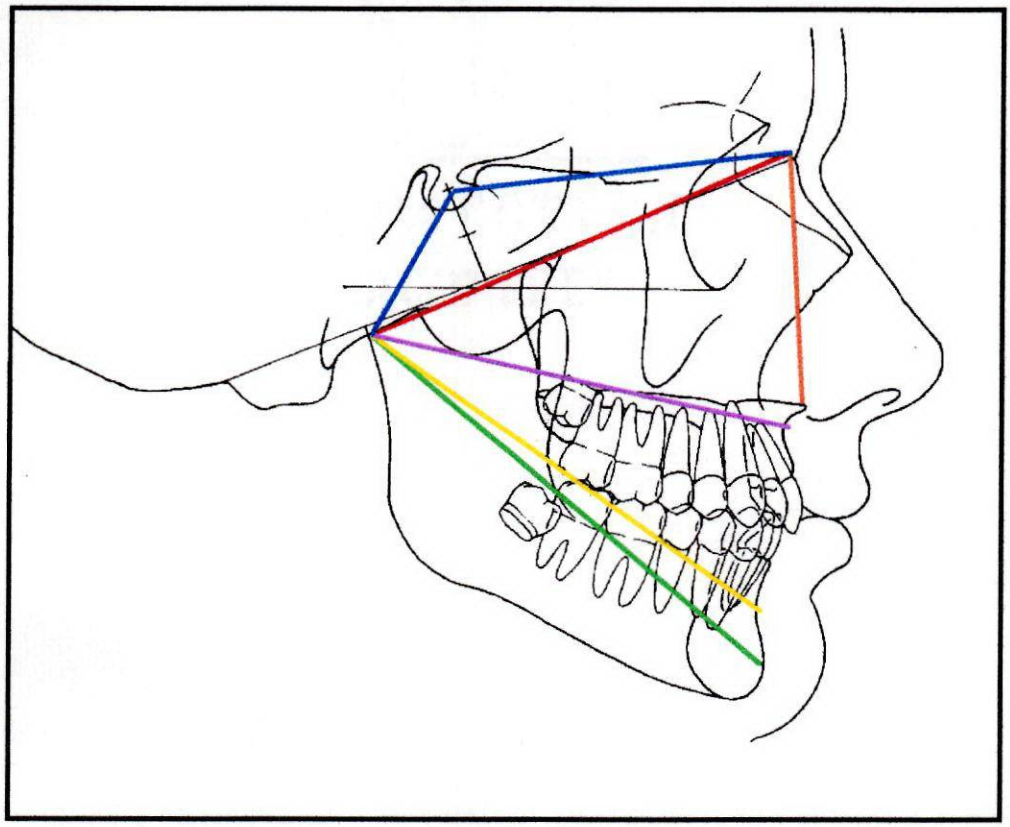


Fig. 12: Cephalometric Demonstration of Fig. 11

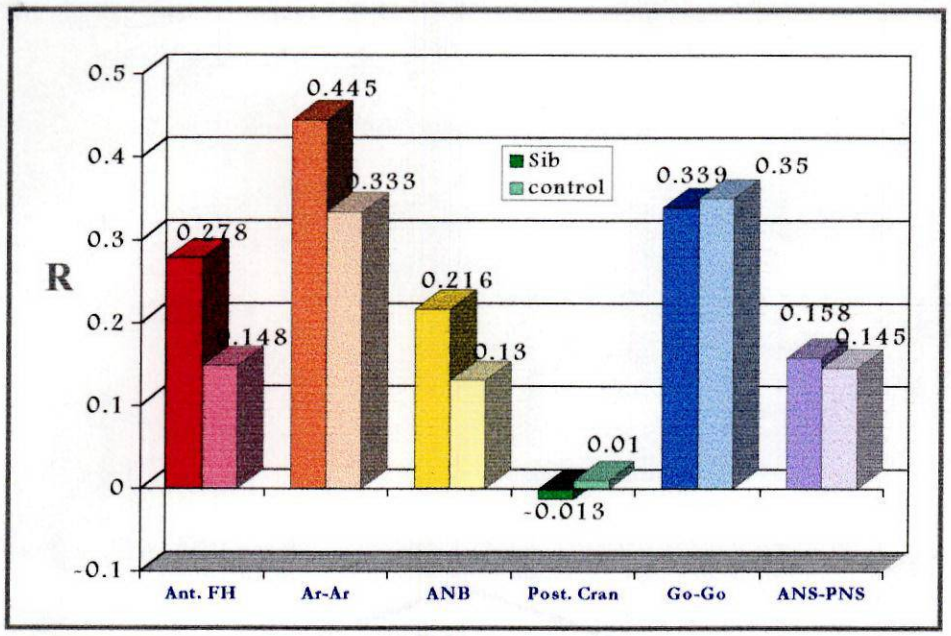


Fig. 13 : Comparison of Pearson Correlations between Siblings and Non-related Control Subjects

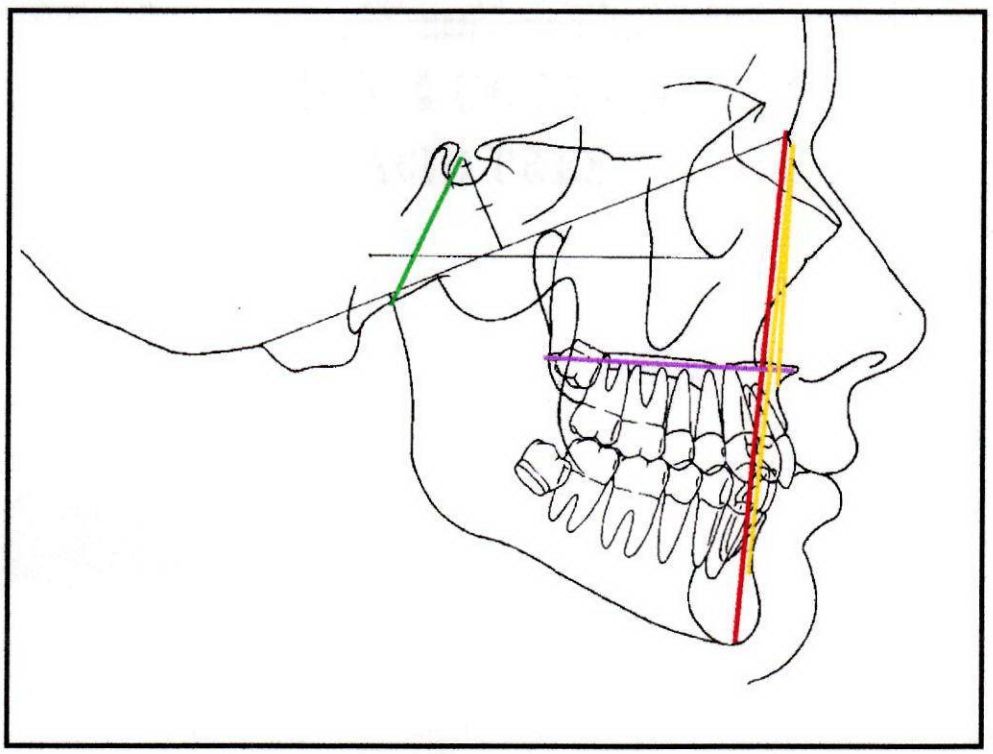


Fig. 14: Cephalometric Demonstration of Fig. 13

Fig.15 : Pearson's Correlation of SNA Angle between Siblings

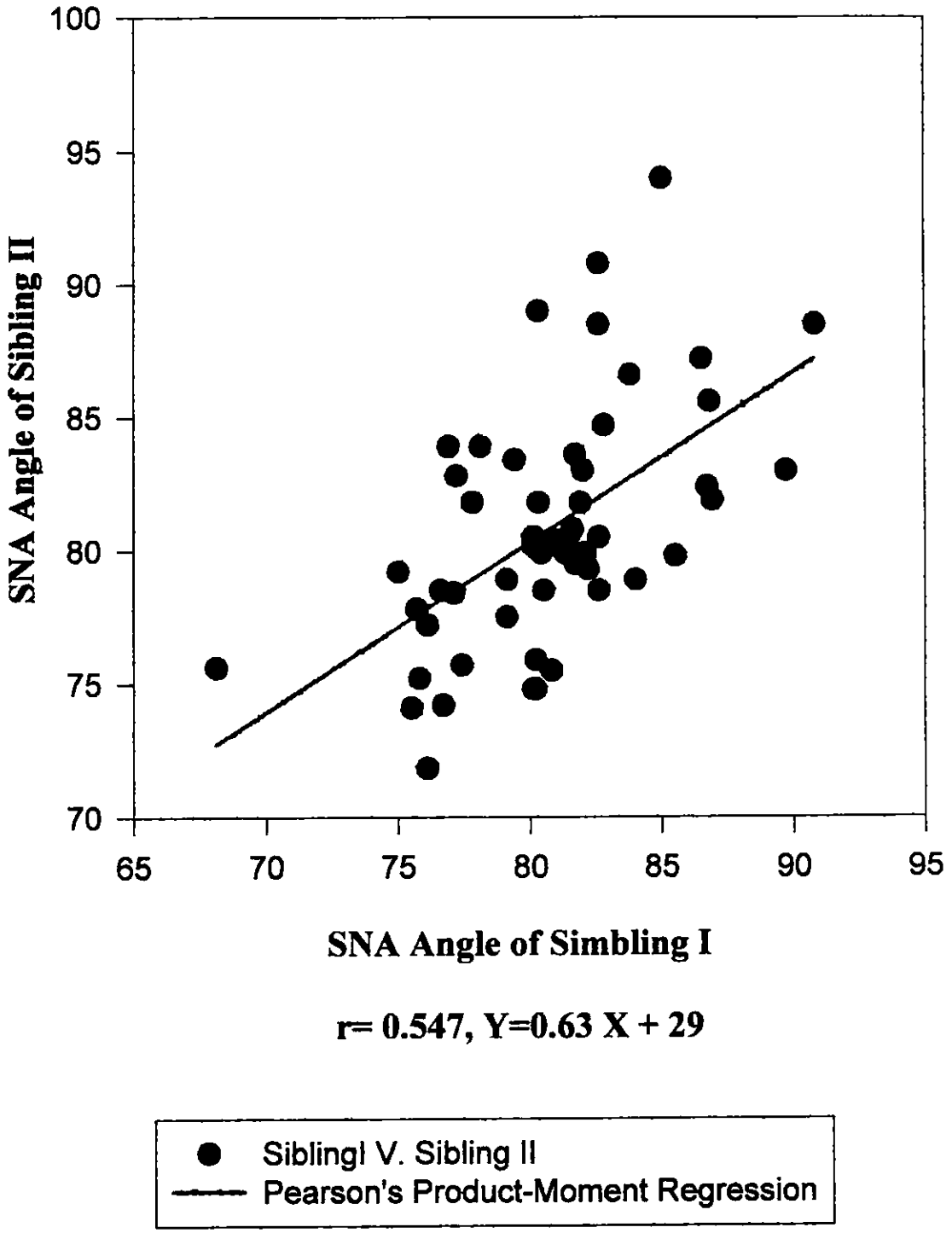


Fig. 16 : Pearson's Correlation of SNA Angle between Non-related Subjects

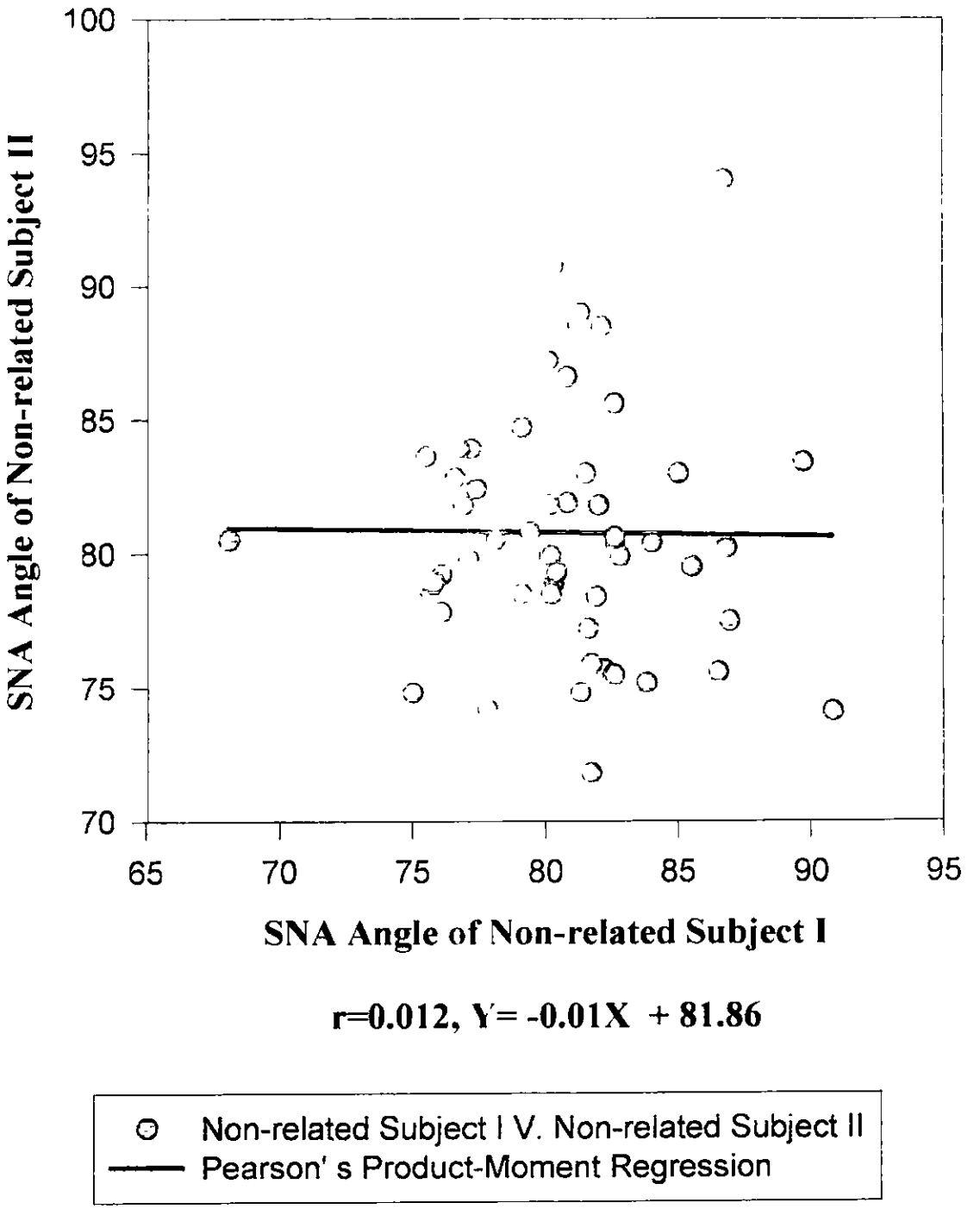


Fig. 17 : Pearson's Correlation of Ramus Height between Siblings

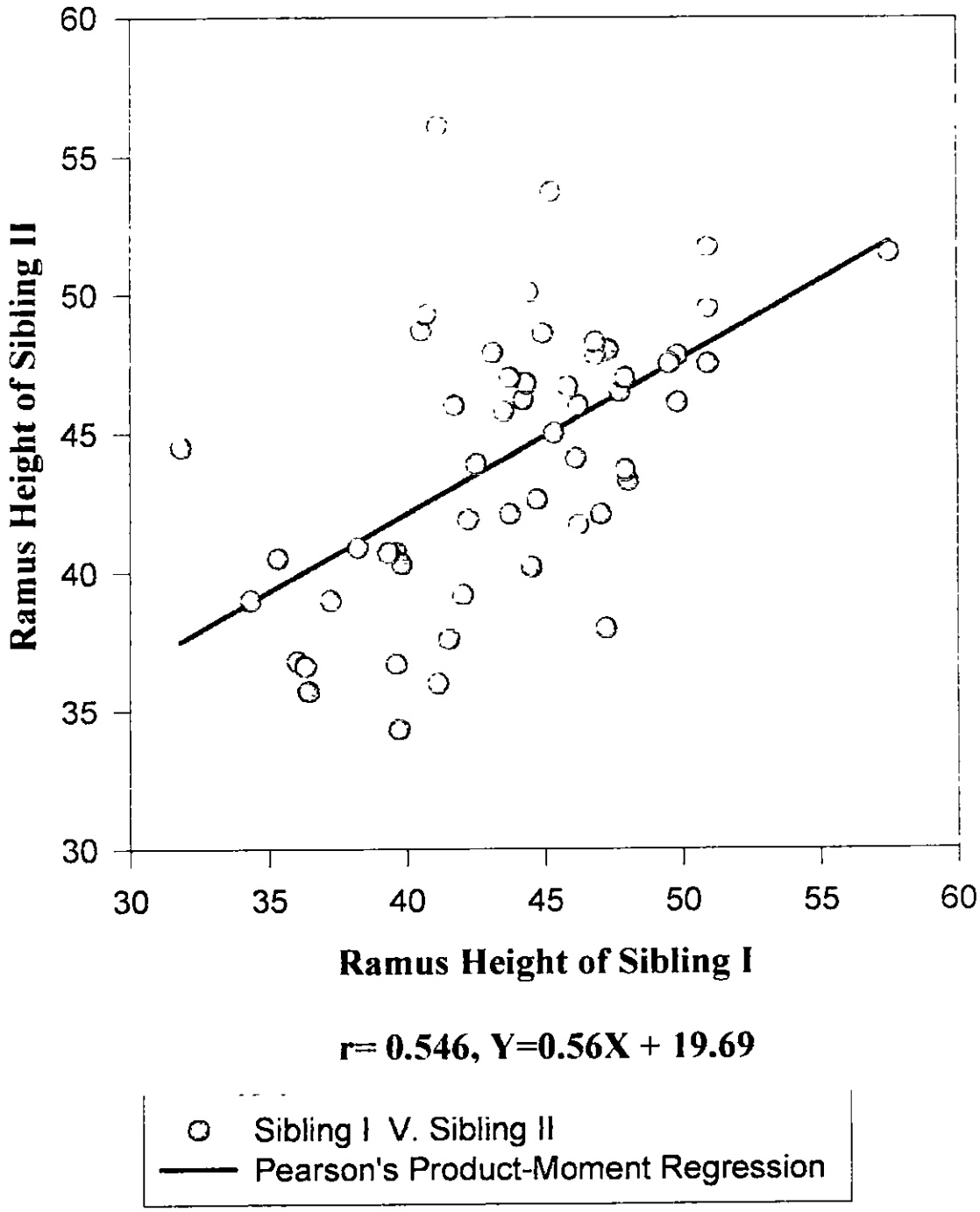


Fig. 18 : Pearson's Correlation of Ramus Height between Non-related Subjects

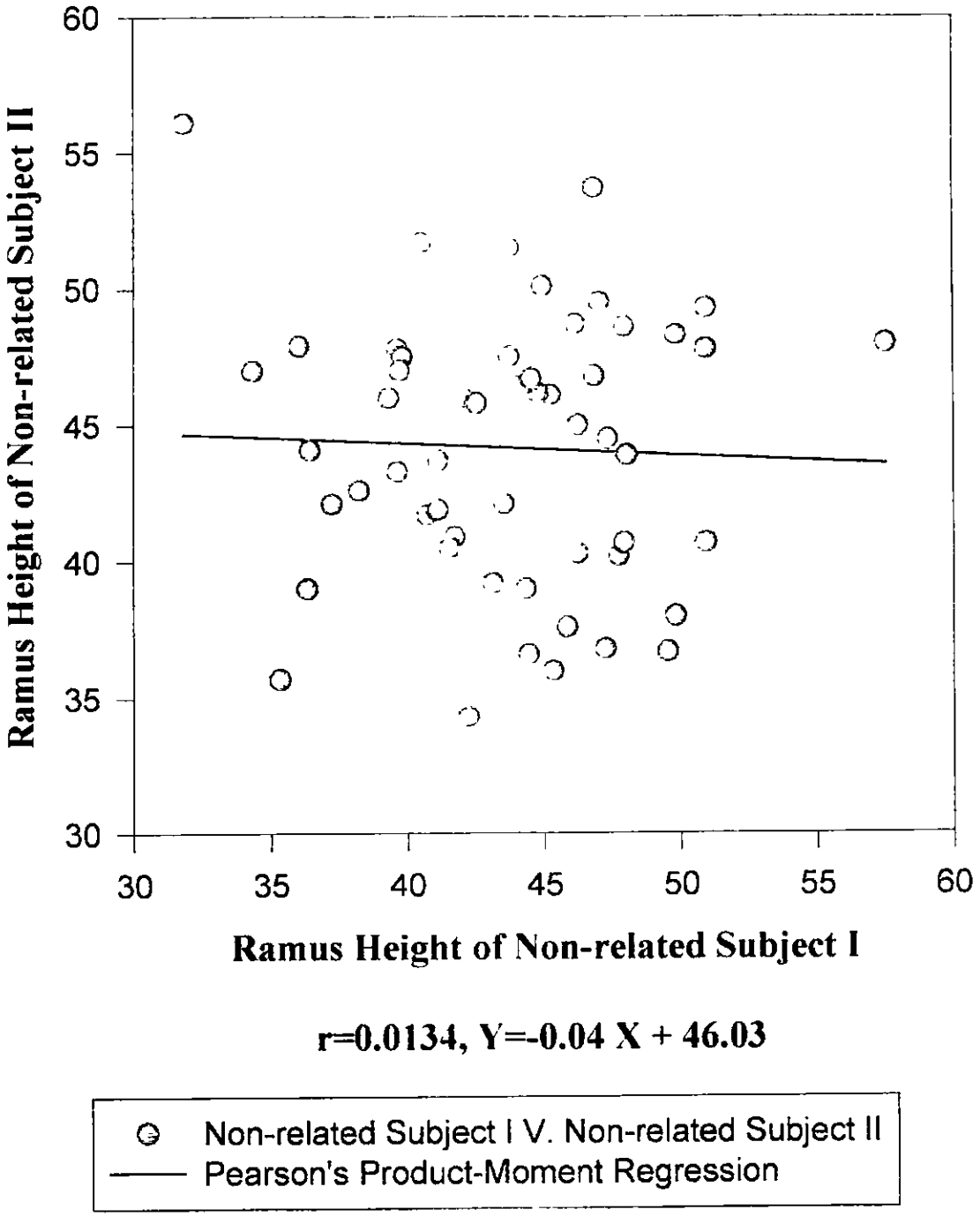


Fig. 19 : Pearson's Correlation of Posterior Cranial Base Length between Siblings

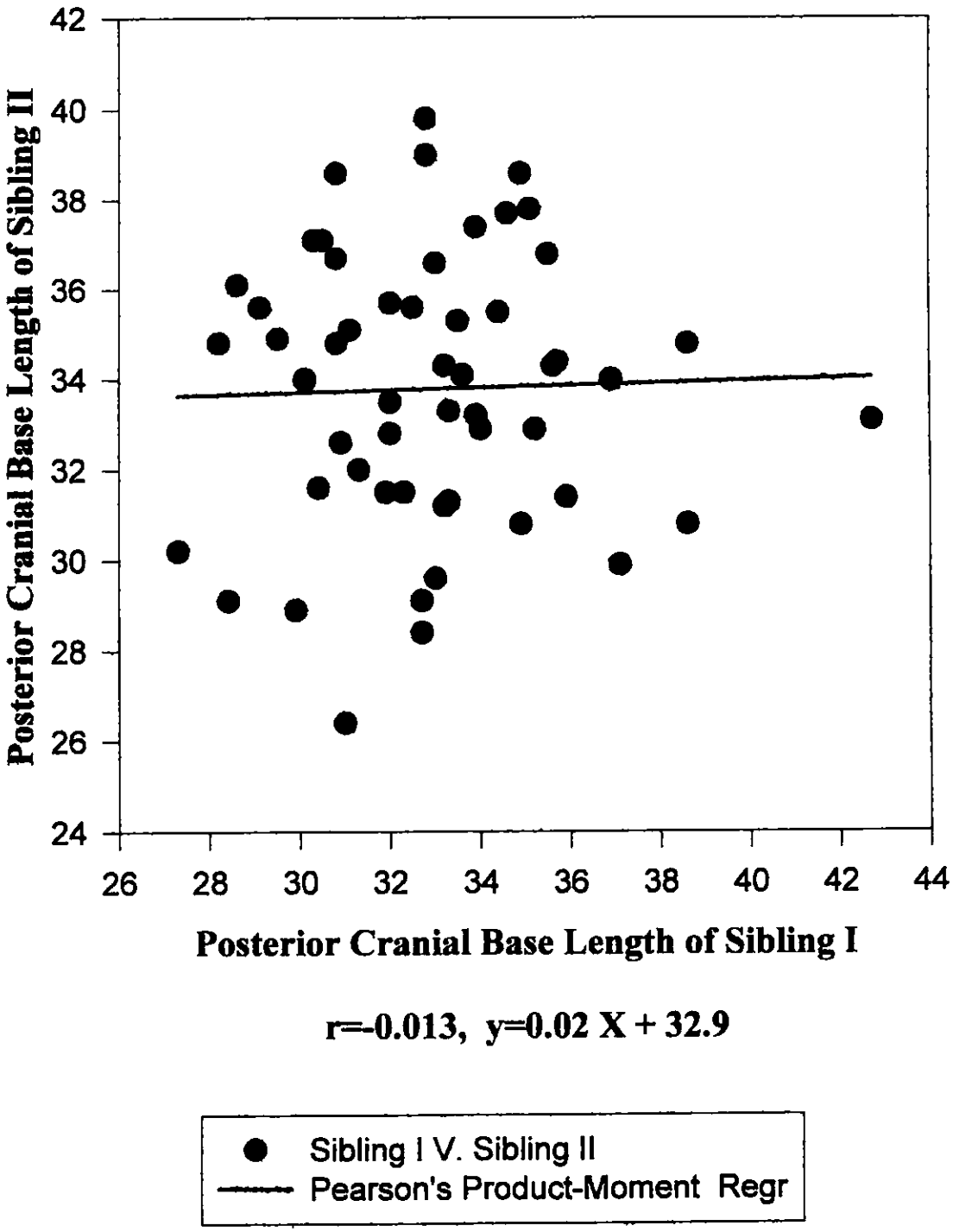


Fig. 20 : Pearson's Correlation of Posterior Cranial Base Length between Non-related Subjects

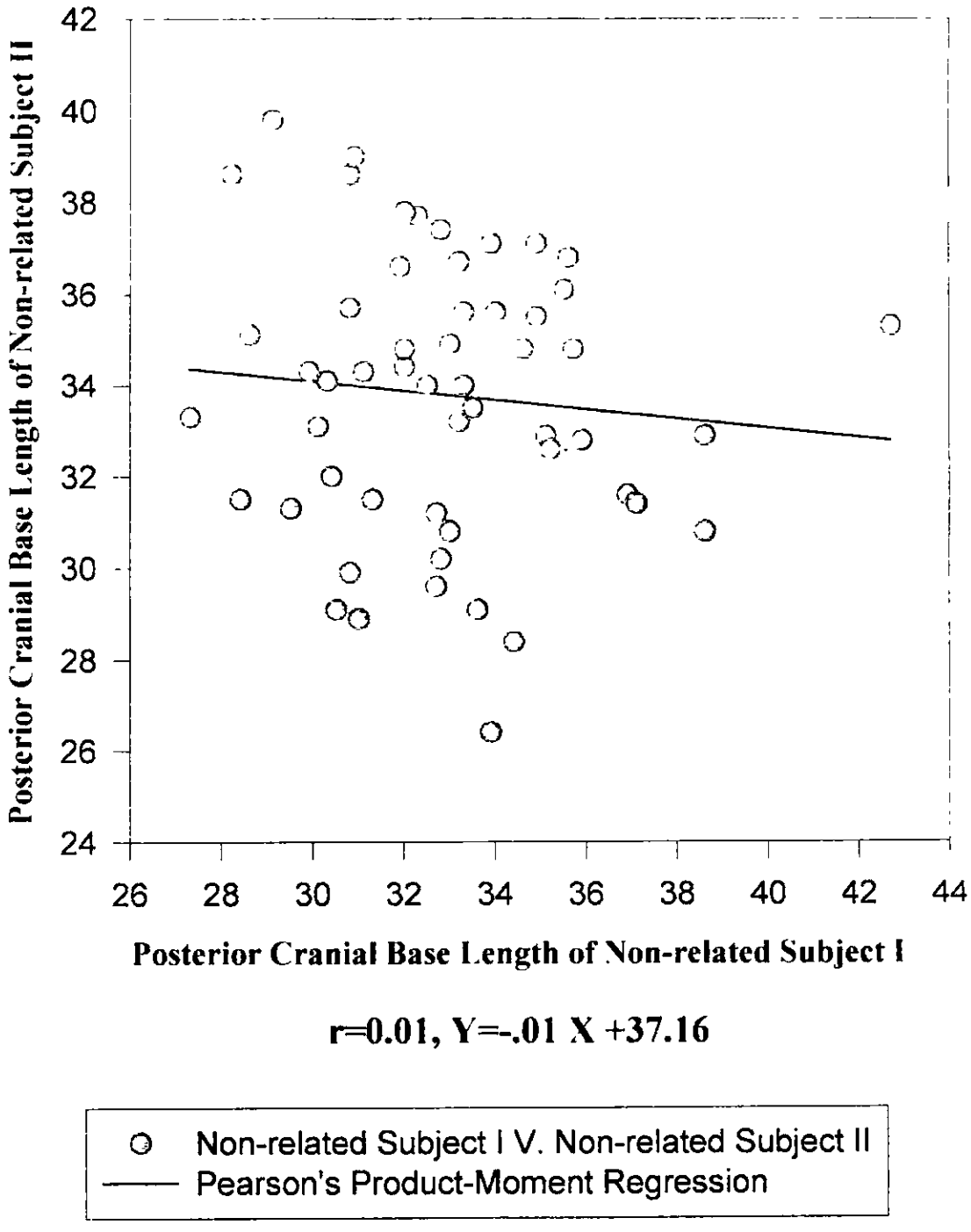


Fig. 21: Pearson's Correlation of Go-Go' Width between Siblings

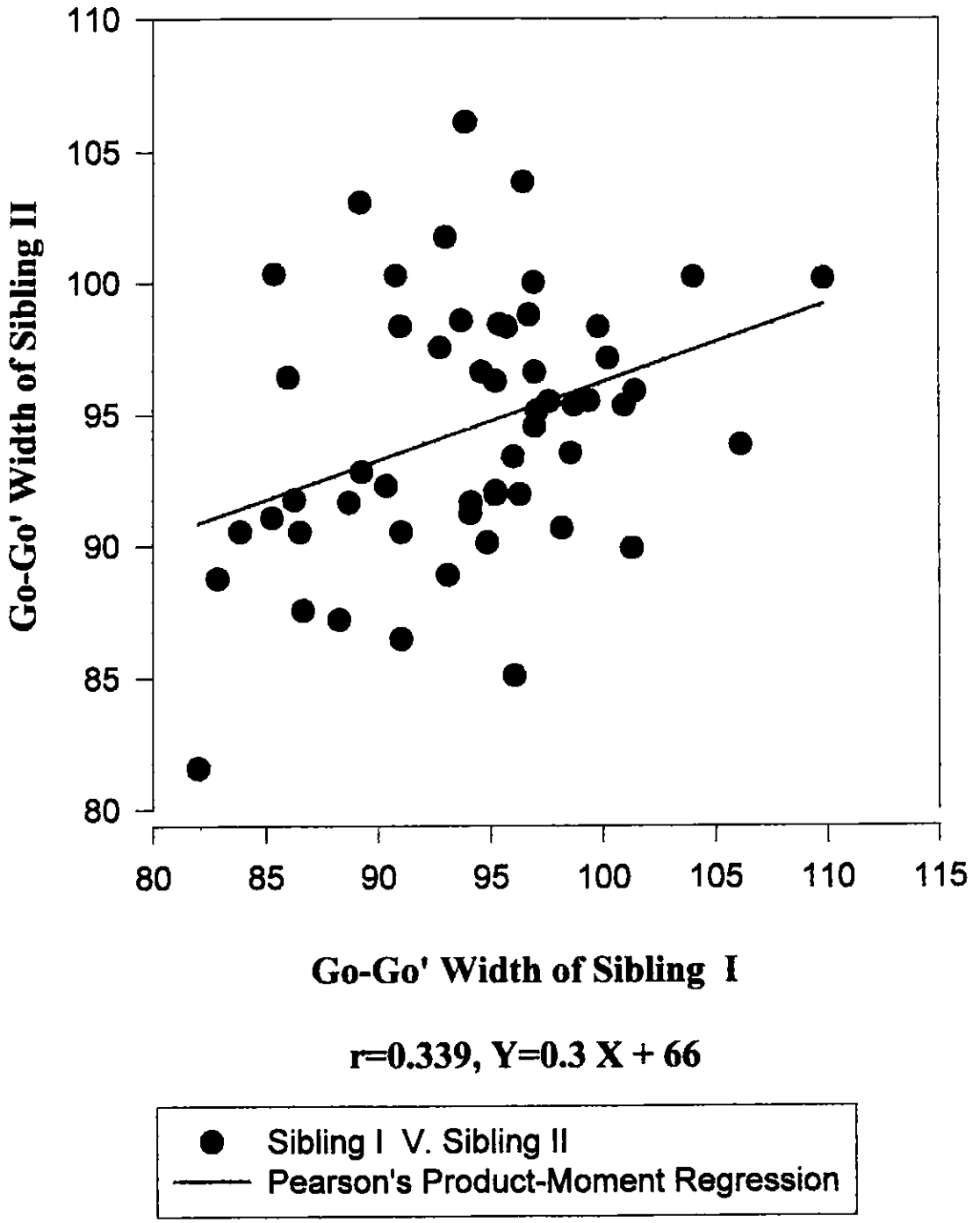
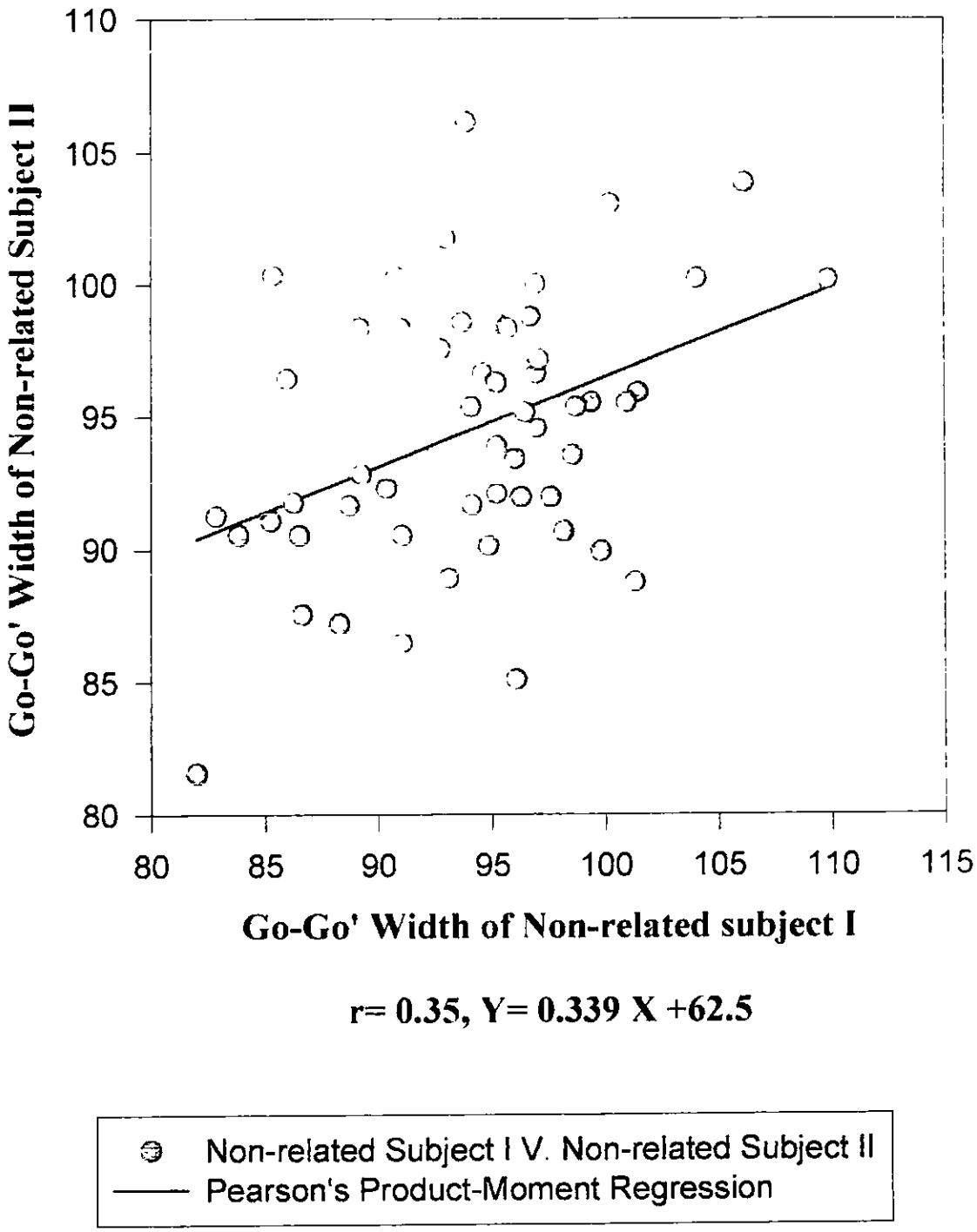


Fig. 22 : Pearson's Correlation of Go-Go' Width between Non-related subjects



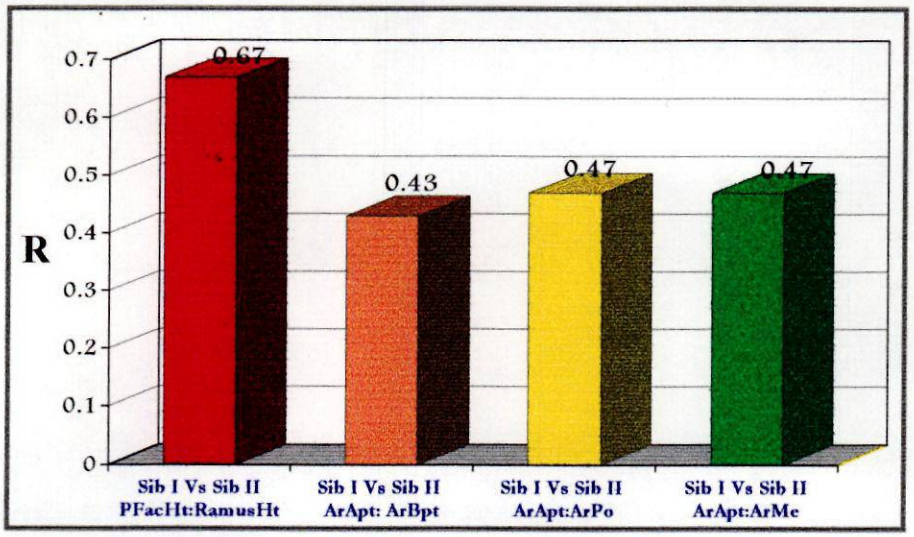


Fig. 23 : High Cross-Siblings Correlations of Measures

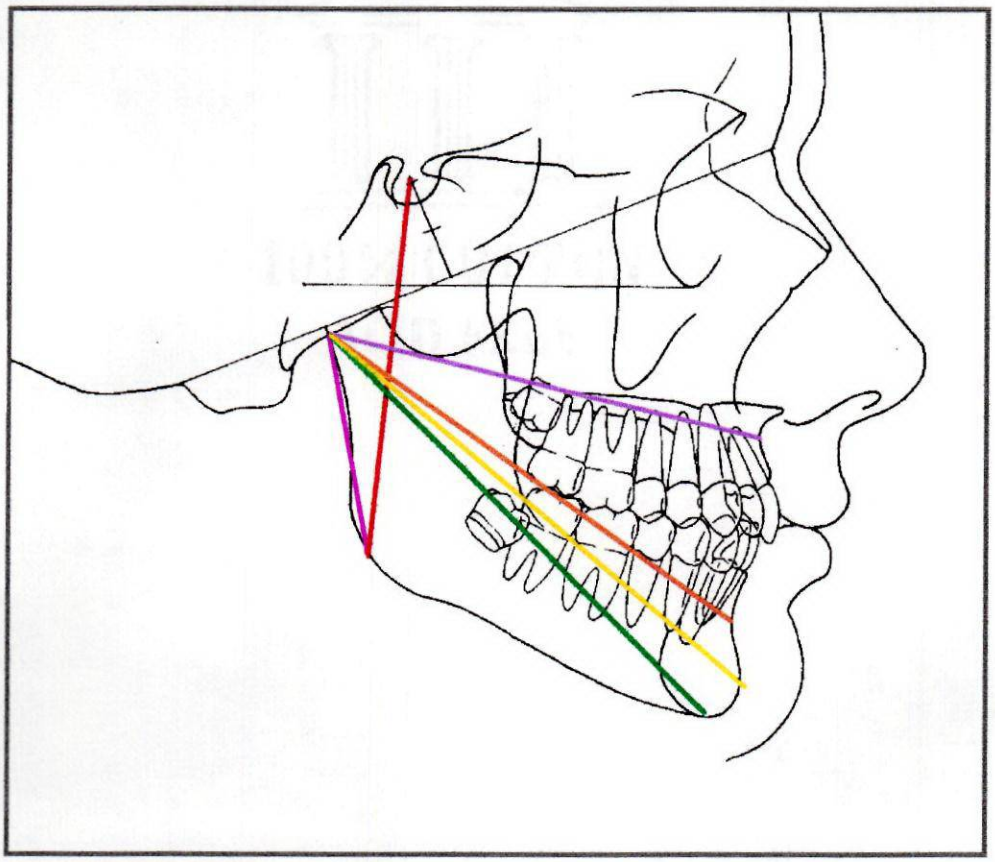


Fig.24 : Cephalometric Demonstration of Fig. 23

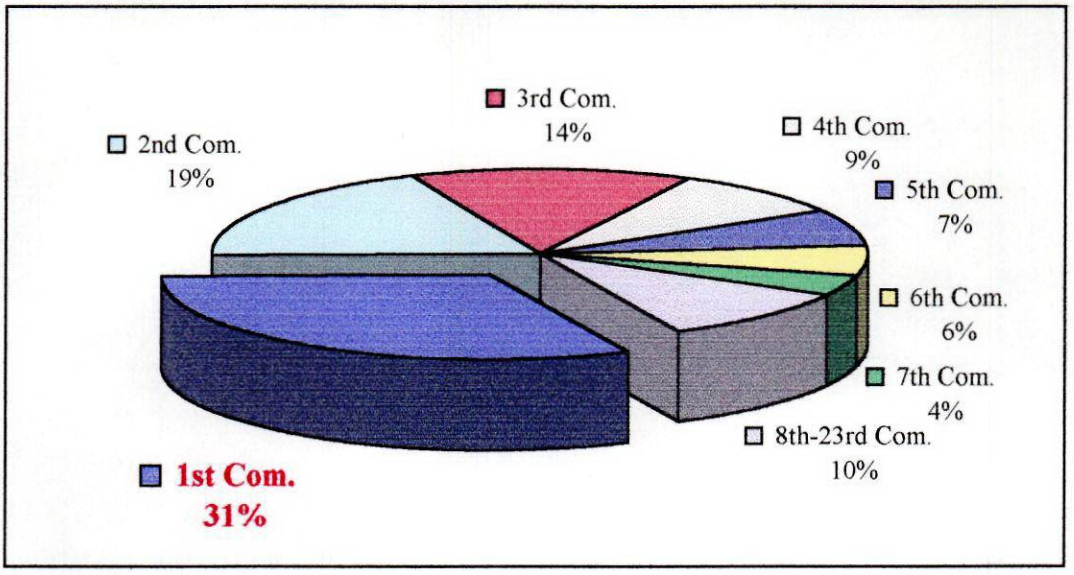


Fig. 25 : Average Principal Loadings of the First Component from 1000 Random Samplings

- Ar-Me : 0.15 •Ar-Pog : 0.15
- Post. Facial Height. : 0.14 •Ar-B : 0.13 •Ramus Height : 0.13

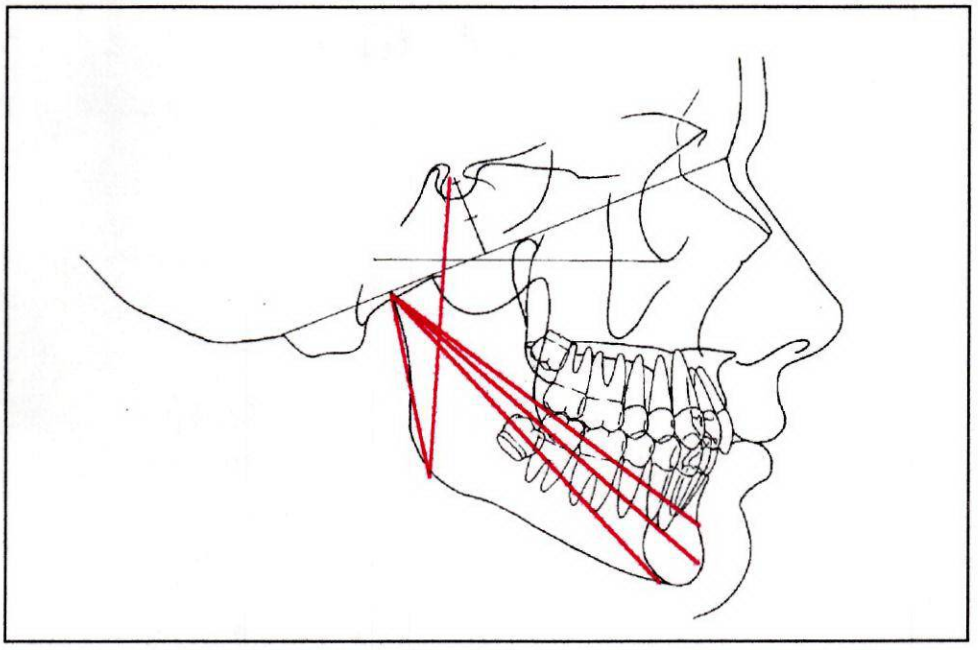


Fig. 26 : Cephalometric Demonstration of Fig.25

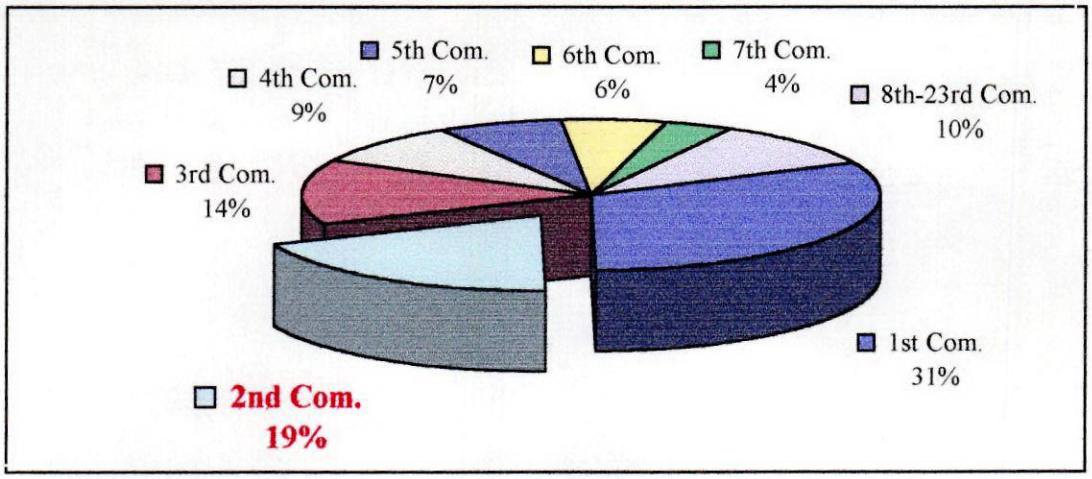


Fig. 27 : Average Principal Loadings of the Second Component from 1000 Random Samplings

- Anterior Facial Ht.: -0.41 • SN-GoGn : -0.32 •Lower Facial Ht.: -0.31
- SNA : 0.27 • SNB : 0.24 • Ar-Na : -0.19 • Ar-Ar : -0.15
- Upper Facial Height : -0.14 • Ant. Cranial Base : -0.14

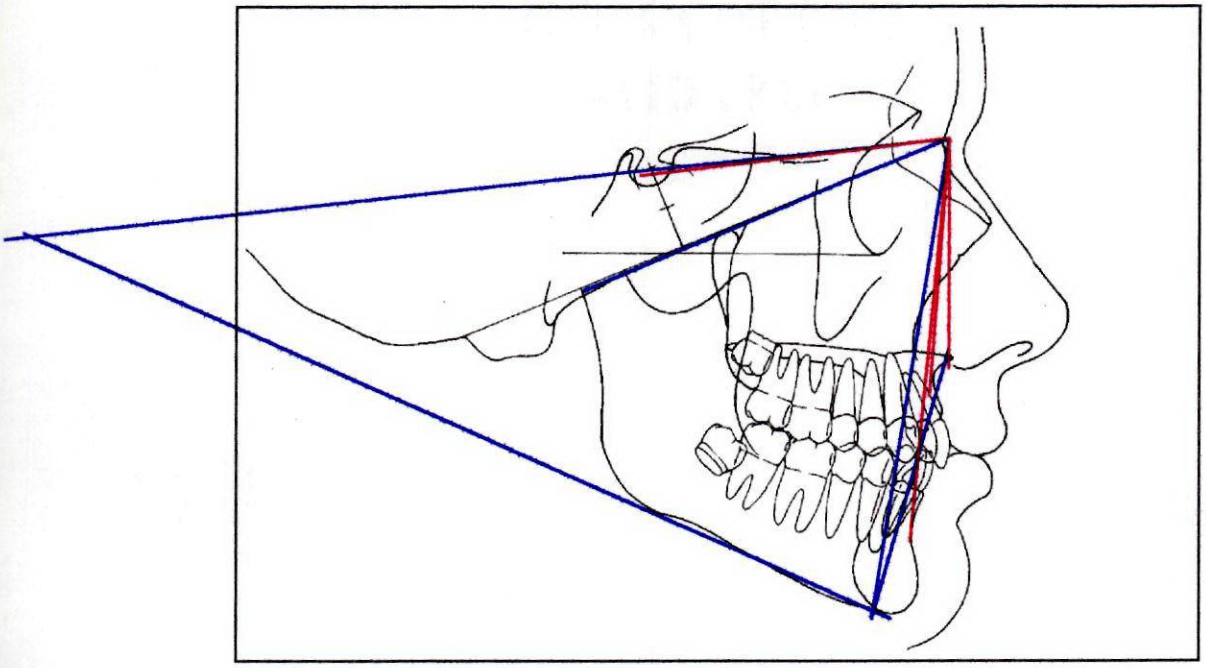


Fig. 28: Cephalometric Demonstration of Fig.27

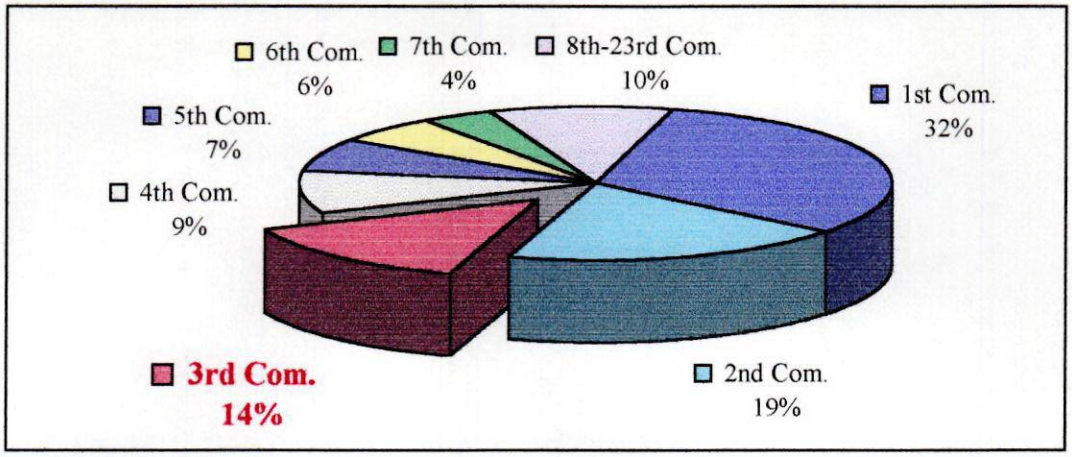


Fig. 29 : Average Principal Loadings of the Third Component from 1000 Random Samplings

- Ar angle : 0.48 • Gonial angle : -0.29 • Ant. Facial Height : 0.22
- Lower Facial Height : 0.21 • Na-S-Ar angle : -0.15
- Posterior Facial Height : 0.11

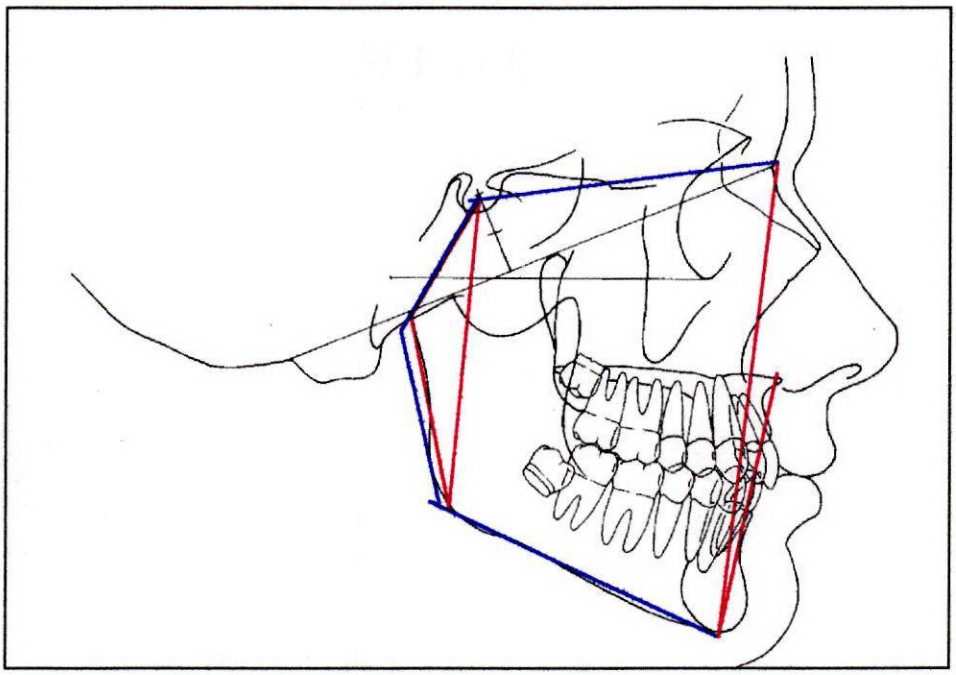


Fig. 30 : Cephalometric Demonstration of Fig. 29

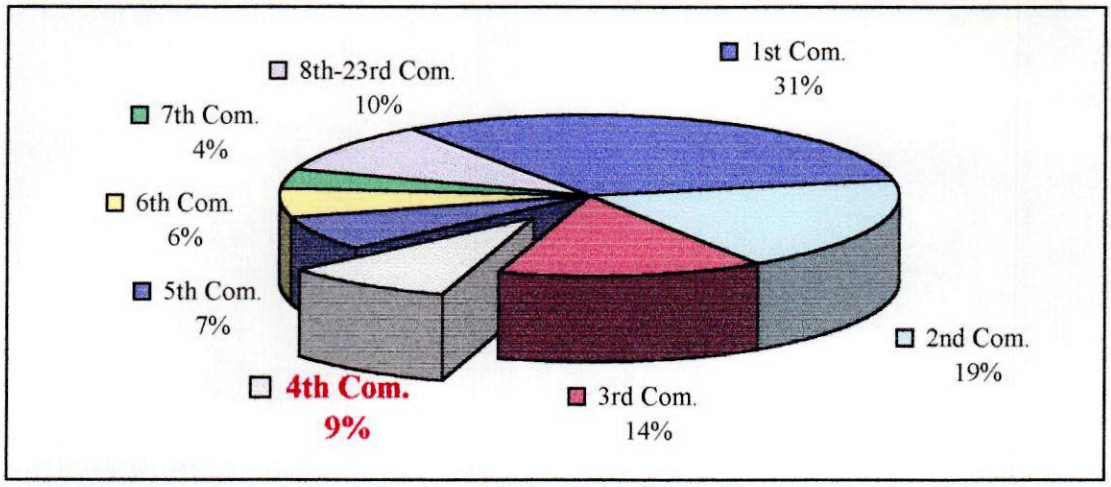


Fig. 31 : Average Principal Loadings of the Fourth Component from 1000 Random Samplings

- Go-Go : 0.40 • Ramus Height : -0.32 • Body Length: 0.21
- Posterior Facial Height : -0.19 • Ant. Facial Height : -0.18
- Ar-Ar : 0.18 • Ar-Nasion : 0.14 • Post. Cranial Base : 0.13

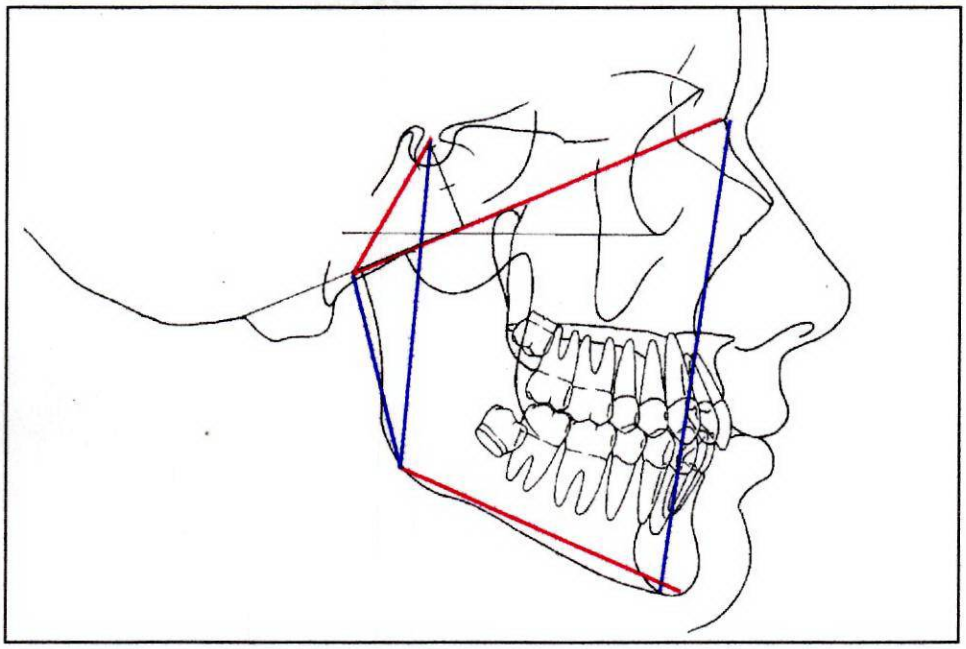


Fig.32 : Cephalometric Demonstration of Fig. 31

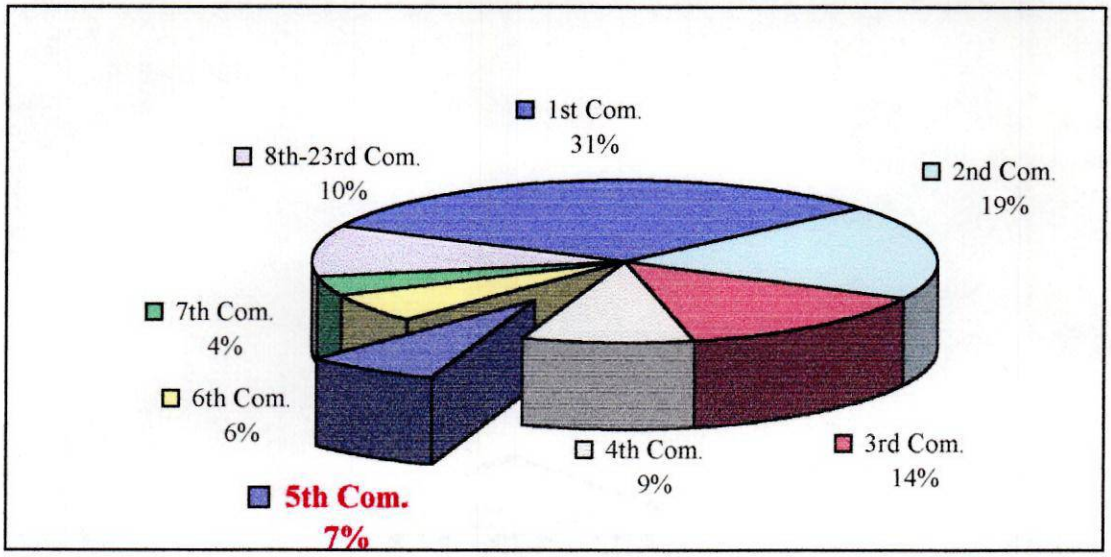


Fig. 33: Average Principal Loadings of the Fifth Component from 1000 Random Samplings

- Nasion-S-Ar : 0.09 • Go Angle : -0.09 • SNA :-0.05

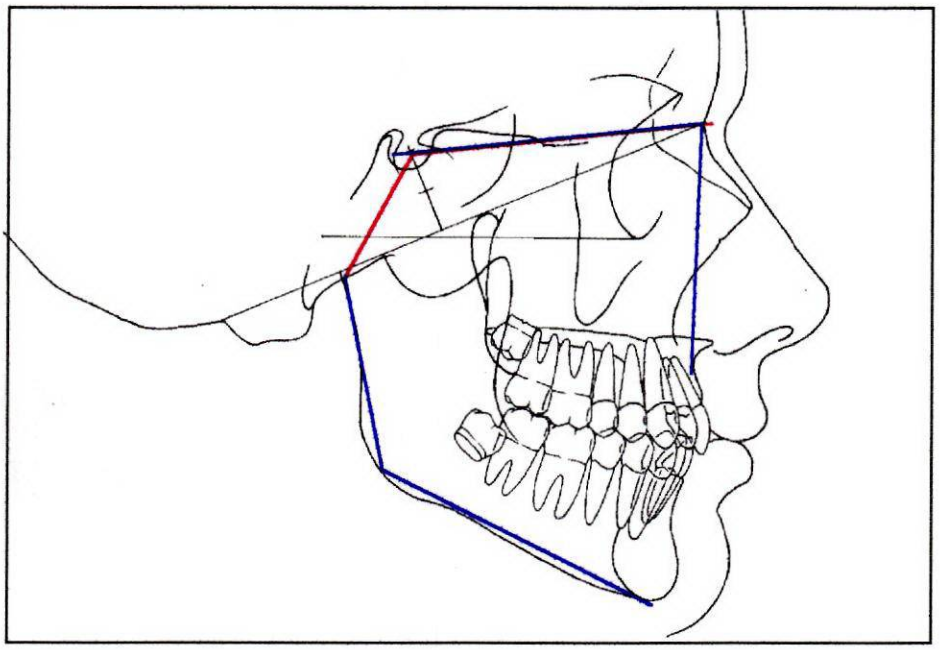


Fig.34 : Cephalometric Demonstration of Fig. 33

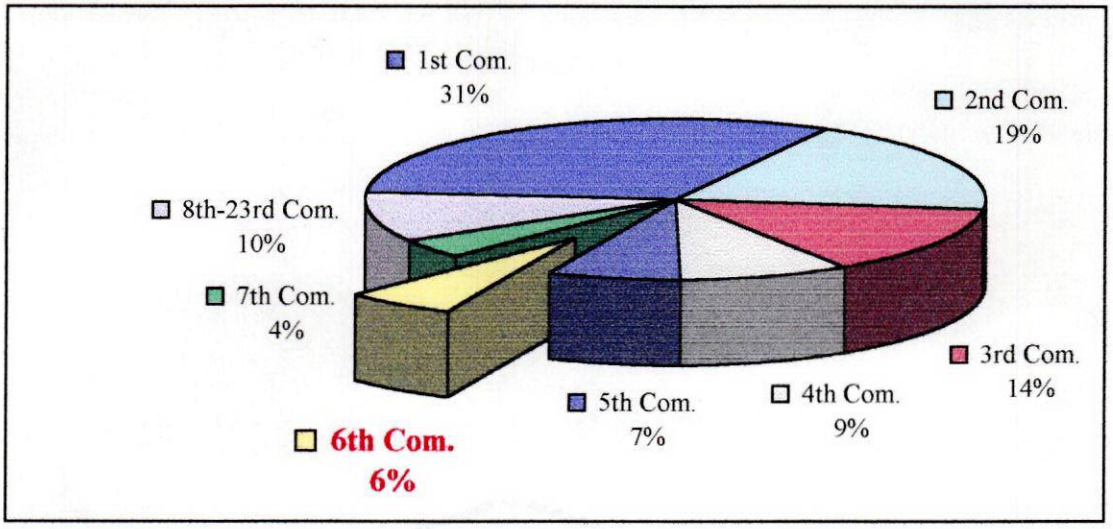


Fig. 35 : Average Principal Loadings of the Sixth Component from 1000 Random Samplings

- Nasion-S-Ar : 0.08
- Post. Cranial Base : -0.05
- Gonial Angle : -0.05
- Ar-Ar : -0.05

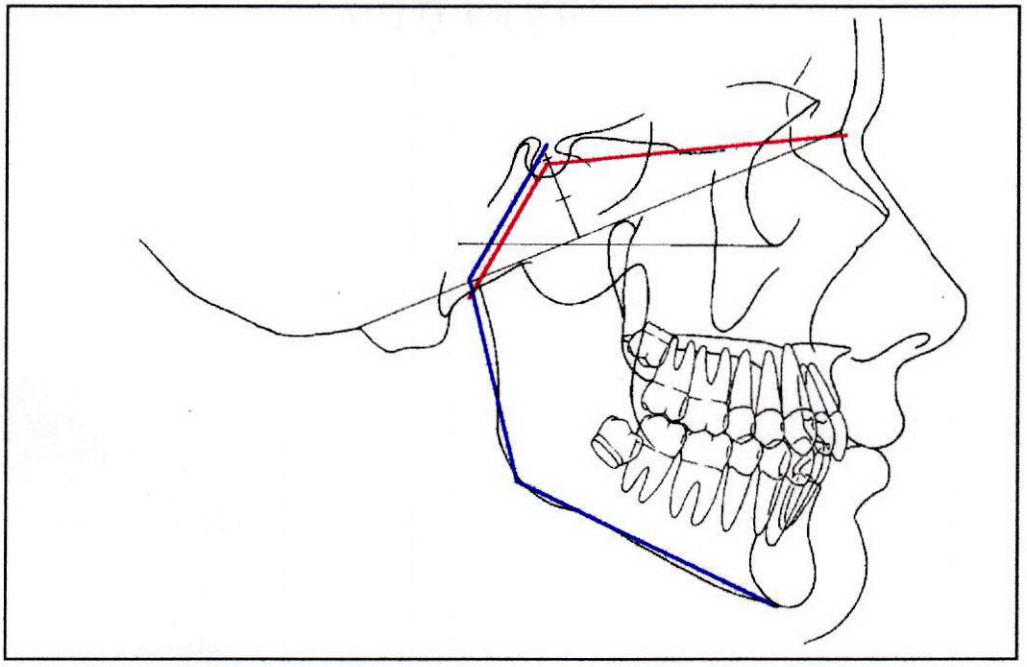


Fig. 36 : Cephalometric Demonstration of Fig. 35

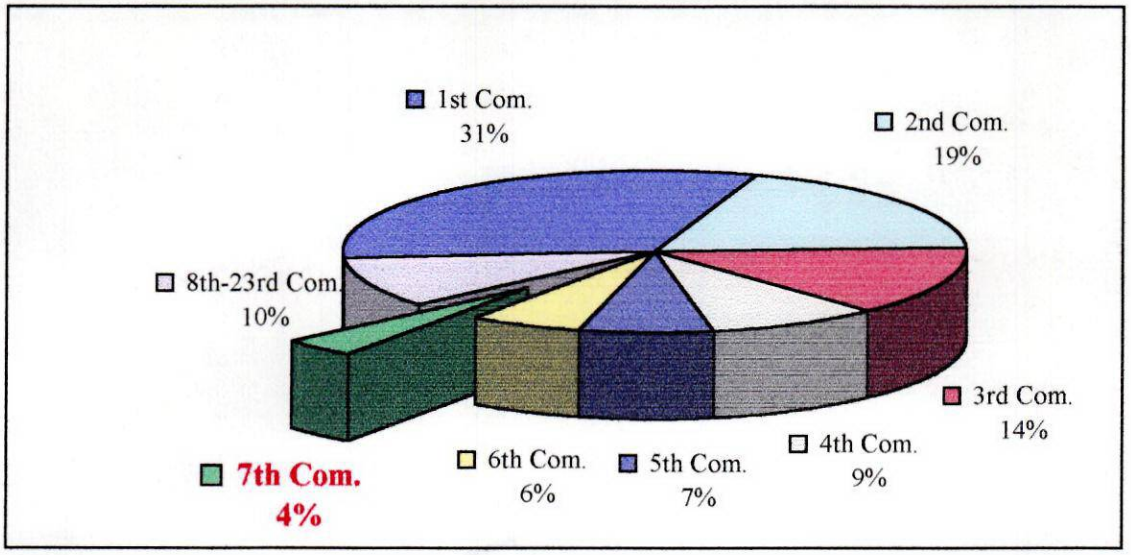


Fig. 37 : Average Principal Loadings of the Seventh Component from 1000 Random Samplings

- Ar-Nasion : -0.10
- Go-Go : 0.09
- Anterior Cranial Base : -0.08

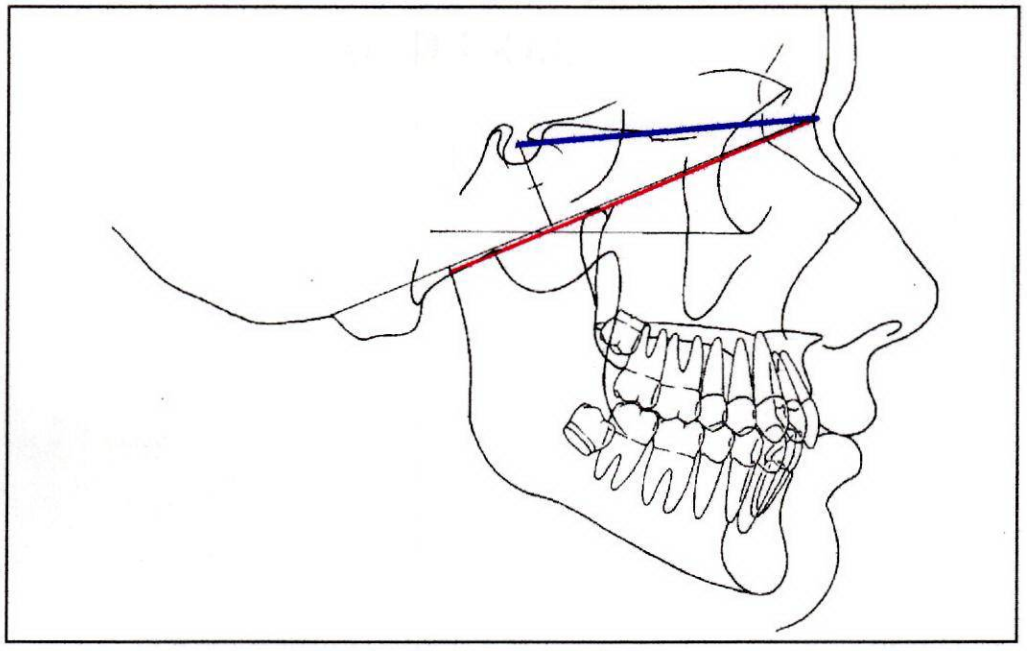


Fig. 38 : Cephalometric Demonstration of Fig. 37

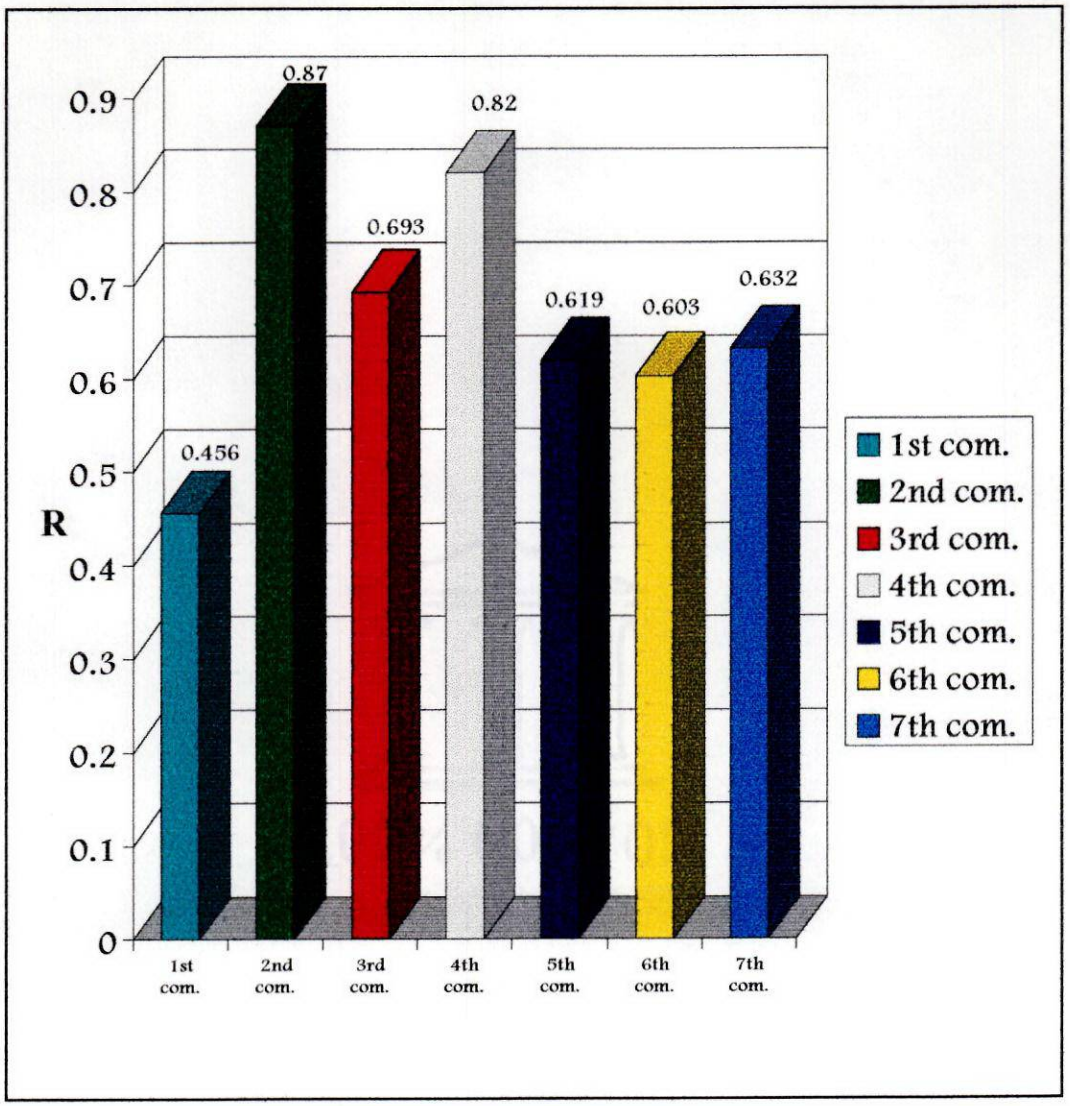


Fig.39 : Sibling Correlations for the Principal Component Scores (n=44 sibpairs)

Table 1.--Regression Analysis Results Investigating Age-Effects on the Measures (n=44)

Measure	Y-intercept	Error	Coefficient	Error	Ave. t-stat	>1.64	<-1.64
ANTFAC	110.52887	8.12741	.01433	.04458	.28569	.09500	.02000
UFH	50.47843	3.23588	.01109	.01742	.42059	.02300	.00000
LFH	59.56104	6.59695	.02105	.03611	.51041	.11400	.00000
POSTFAC	66.13470	5.81350	.03189	.03194	.67250	.09500	.00000
SNA	79.53838	3.42536	.00573	.01830	.15846	.00100	.00000
SNB	81.08548	3.83102	-.01684	.02071	-.46758	.00000	.01100
ANB	-1.52567	2.16602	.02248	.01178	1.14155	.21000	.00000
SNTOGOGN	29.37823	5.89509	.01294	.03226	.22705	.00300	.00000
ANTCRAN	72.86387	4.28731	-.02007	.02346	-.66481	.00000	.12200
POSTCRAN	31.64357	4.59002	.00955	.02511	.32471	.07200	.00400
ARNA	94.33382	3.49117	-.01107	.01866	-.26962	.00000	.00000
NASAR	125.02443	4.21051	-.00209	.02287	-.05541	.00000	.00200
RAMUSHT	37.78670	8.07815	.03116	.04461	.69024	.22400	.00000
BODYLEN	83.14151	4.77602	-.06097	.02596	-1.39231	.00000	.34800
GOANGLE	125.83656	7.82206	.00677	.04306	.11663	.01700	.00300
ARANGLE	140.88577	7.49694	.01008	.04135	.16982	.01100	.00000
ARME	109.17439	7.31612	-.02807	.04024	-.60517	.00000	.15400
ARBPT	98.65761	4.64800	-.02299	.02517	-.56014	.00000	03200
ARPO	112.47677	6.49570	-.04702	.03574	-1.09456	.00000	.29700
ANSPNS	55.49643	5.03846	.00161	.02755	.06137	.03100	.02100
ARAPT	85.14670	4.12213	-.00662	.02205	-.15752	.00000	.00300
ARAR	96.09610	4.10393	.04148	.02242	1.05008	.16300	.00000
GOGO	91.66465	5.36804	.01473	.02933	.28644	.00500	.00000

Note: ***Measure*** . Cranio-facial measure (see text for definitions), ***Ave. t-test*** Average t-statistics associated with the age regression coefficient from the 1000 samples (see text) ; ***>1.64***: fraction of the 1000 samples producing t-statistics greater than 1 64, ***<1.64***: fraction of the 1000 samples producing t-statistics less than 1 64.

Table 2.-- Pair-Wise Correlations Between the Measurements

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1	1.00	.53	.78	.34	-.44	-.42	.08	.44	.37	.14	.38	.10	.22	.16	.07	.24	.36	.20	.38	.11	.00	.32	.10
	.00	.07	.04	.10	.10	.10	.08	.10	.08	.10	.05	.09	.10	.10	.12	.08	.09	.11	.08	.07	.12	.09	.09
2	.40	1.00	.02	.21	-.26	.33	.10	.20	.27	-.01	.28	.25	.23	.05	-.02	.02	.21	.16	.25	.11	.20	.22	.12
	.09	.00	.09	.10	.11	.11	.11	.11	.09	.11	.08	.13	.10	.10	.12	.11	.09	.09	.09	.09	.11	.11	.09
3	.79	-.03	1.00	.16	-.36	-.40	.01	.51	.23	.18	.26	-.03	.05	.00	.18	.31	.12	.08	.11	.10	-.14	.24	.01
	.05	.10	.00	.10	.09	.08	.10	.07	.09	.10	.07	.08	.08	.09	.09	.07	.08	.09	.09	.08	.10	.07	.08
4	.33	.17	.15	1.00	.27	.30	-.02	-.60	.33	.39	.39	-.16	.85	-.02	-.36	-.10	.53	.50	.50	.22	.48	.35	.02
	.09	.10	.10	.00	.09	.09	.09	.06	.07	.08	.07	.09	.03	.09	.07	.12	.08	.07	.08	.09	.07	.08	.10
5	-.41	-.18	-.35	.24	1.00	.86	.38	-.64	-.23	.19	-.24	-.48	.20	.15	-.15	-.09	.25	.40	.17	.08	.48	-.11	-.18
	.08	.10	.08	.07	.00	.03	.10	.07	.08	.11	.07	.09	.09	.07	.09	.08	.07	.07	.07	.08	.07	.11	.09
6	-.40	-.25	-.42	.25	.84	1.00	-.13	-.71	-.16	.19	-.19	-.46	.25	.33	-.13	-.19	.46	.55	.40	-.02	.40	-.05	-.04
	.08	.10	.07	.07	.04	.00	.13	.05	.09	.12	.08	.09	.09	.07	.08	.10	.07	.05	.08	.11	.09	.11	.11
7	-.12	.08	.00	-.01	.37	-.08	1.00	.04	-.15	.01	-.13	-.08	-.05	-.31	-.06	.17	-.35	-.21	-.40	.20	.24	-.13	-.29
	.09	.10	.10	.09	.11	.11	.00	.12	.08	.10	.09	.12	.09	.11	.10	.10	.10	.12	.10	.11	.11	.09	.09
8	.42	.19	.50	-.57	-.55	.65	.09	1.00	-.15	-.30	-.19	.21	-.52	-.23	.55	.23	-.39	-.42	-.35	-.20	-.59	-.15	.02
	.08	.10	.06	.06	.07	.06	.11	.00	.08	.09	.07	.09	.06	.07	.07	.10	.09	.09	.09	.09	.08	.10	.11
9	.33	.24	.27	.26	.23	.17	-.09	-.08	1.00	.18	.82	-.03	.26	.30	.07	-.06	.46	.40	.50	.29	.55	.53	.32
	.08	.09	.08	.08	.08	.08	.09	.09	.00	.10	.03	.08	.08	.09	.06	.08	.07	.07	.06	.08	.06	.07	.07
10	.17	.02	.21	.34	.19	.17	.02	-.25	.14	1.00	.58	-.23	-.06	.24	-.04	-.08	.15	.17	.16	.15	.35	.33	.19
	.09	.11	.10	.09	.11	.11	.10	.10	.10	.00	.07	.09	.09	.09	.09	.09	.11	.11	.10	.11	.09	.09	.09
11	.33	.22	.29	.31	-.22	-.17	-.11	-.13	.71	.57	1.00	.23	.20	.31	-.05	-.28	.43	.40	.49	.34	.64	.56	.38
	.08	.09	.09	.08	.09	.08	.10	.08	.06	.08	.00	.08	.09	.09	.08	.08	.07	.07	.07	.08	.04	.07	.08
12	.03	.25	.07	-.13	.40	-.36	-.13	.17	-.03	-.20	.25	1.00	.11	-.08	.05	-.53	.04	.04	.09	.14	.10	-.01	.12
	.10	.10	.09	.08	.09	.09	.10	.08	.10	.10	.09	.00	.09	.10	.08	.07	.09	.10	.09	.10	.11	.11	.09
13	.20	.19	.03	.85	.16	.20	.03	.48	.25	-.07	.15	.11	1.00	.16	.27	-.28	.57	.55	.52	.17	.44	.24	-.04
	.09	.10	.09	.04	.08	.09	.09	.07	.08	.09	.09	.09	.00	.09	.08	.10	.08	.07	.09	.09	.08	.09	.11

Table 2.--Continued

14	13	00	01	01	.17	31	-.24	-.22	.21	.25	.26	-02	-.15	1.00	-.37	.17	.59	.39	.60	16	.34	.23	.10
	10	09	09	09	.07	09	.10	.08	.08	.10	.09	.10	09	.00	07	09	.07	.09	.07	10	.07	.09	.09
15	05	01	.14	-37	-09	-08	-.04	53	-.02	-.08	-.03	03	-.30	-.37	1.00	-.46	-.08	-.02	-.07	-.19	-.17	-.10	.22
	09	11	.07	08	.08	08	.10	.07	.08	.09	09	.09	.09	.08	00	.07	.08	.09	.08	.08	.10	.11	.08
16	30	01	35	-07	-.10	-21	.13	.21	-.05	-.03	-.26	-.52	-.24	.18	-.43	1.00	-.33	-.38	-.33	-.08	-.43	-.03	-.27
	09	10	08	10	.09	09	.10	.08	10	.09	.09	.07	.09	.09	.08	.00	.10	.08	.10	.11	.08	.11	.09
17	.33	17	13	51	.20	38	-.32	-.32	.41	.13	.37	.09	.52	.53	-10	-.29	1.00	.83	.97	.22	.61	.35	.17
	.09	.08	.09	08	09	.08	.09	.09	.08	.11	.09	.10	.08	.08	.09	.08	.00	.03	.01	.11	.05	.10	.11
18	.17	.14	.10	48	38	.50	-.15	-34	.40	.19	.36	06	.51	.31	00	-.35	.76	1.00	.82	23	.72	.26	.14
	09	10	.09	06	08	.06	.11	.09	09	.10	.09	.09	.08	.10	.09	.08	05	.00	.03	.10	.05	.10	.10
19	.32	18	13	48	16	.36	-.33	-.31	.47	.13	43	.13	.50	.51	-08	-.30	.95	.77	1.00	.23	.62	.32	.22
	09	08	10	08	.10	08	.09	.09	07	.09	.08	.09	.09	.08	08	.08	.01	.05	.00	.11	.05	.08	.09
20	.06	.08	12	13	.08	-01	.25	-.14	29	.11	.28	.12	.12	.13	-20	-.04	.17	.20	.20	1.00	43	.19	.14
	09	10	.09	09	.09	.10	.10	.10	.08	.11	.09	.10	.08	.11	09	.11	09	.09	10	.00	09	.09	.10
21	07	20	14	44	.44	36	25	-50	.54	32	.59	13	.42	.32	-.16	41	55	68	57	38	1.00	35	.18
	10	.08	10	08	08	.07	10	08	07	10	06	.11	.08	.08	10	08	06	07	.06	09	.00	.09	10
22	32	19	.25	.29	.14	-.11	11	-.11	51	.36	50	.00	.19	.21	-.13	-.03	.30	.23	28	.16	34	1.00	44
	09	.11	08	08	09	10	10	.10	.08	.09	.09	.10	.09	.10	11	10	.10	.10	.09	.09	10	.00	.09
23	13	11	06	-03	-15	-03	-.21	.01	.35	20	36	09	-.07	.05	21	-.24	.11	.08	.15	.12	.16	.49	1.00
	10	10	09	09	.09	.10	.10	10	09	.09	.10	10	.10	.10	10	.09	.10	.10	.10	.11	.10	.09	.00

Note: All measures have been age-adjusted (see text); The upper entry is the correlation, the lower entry is the standard error of the correlation based on 1000 repeated samples; ***The upper diagonal entries are Pearson's correlations, the lower diagonal entries are Spearman's non-parametric correlations***, 1=ANTFAC; 2=UFH; 3=LFH; 4=POSTFAC; 5=SNA, 6=SNB, 7=ANB; 8=SN-GOGN, 9=ANTCRAN; 10=POSTCRAN, 11=ARNA; 12=NASAR; 13=RAMUSHT; 14=BODYLEN; 15=GOANGLE, 16=ARANGLE; 17=ARME, 18=ARBPT; 19=ARPO, 20=ANSPNS; 21=ARAPT; 22=ARAR; 23=GOGO

Table 3.--Sibling Correlations for the Measures (n=44)

Measure	Pearson's R	Ave. t-stat.	Spearman's R	Ave. t-stat.
ANTFAC	.27759	1.91233	.28927	1.99747
UFH	.24401	1.67059	.22358	1.52558
LFH	.41023	2.92399	.43087	3.09228
POSTFAC	.57902	4.43404	.62527	4.92123
SNA	.54748	4.12408	.57211	4.36473
SNB	.46917	3.41452	.47657	3.47841
ANB	.21647	1.47545	.14625	.98813
SNTOGOGN	.51528	3.82295	.56200	4.26475
ANTCRAN	.51113	3.78512	.36840	2.59318
POSTCRAN	-.01316	-.08830	-.02888	-.19376
ARNA	.48547	3.55610	.33920	2.36923
NASAR	.30123	2.08538	.35976	2.52636
RAMUSHT	.54590	4.10888	.55221	4.16956
BODYLEN	.38378	2.71335	.40302	2.86606
GOANGLE	.39612	2.81099	.39329	2.78852
ARANGLE	.38377	2.71329	.36546	2.57038
ARME	.39092	2.76975	.34224	2.39229
ARBPT	.44281	3.19120	.36226	2.54570
ARPO	.37353	2.63312	.34674	2.42659
ANSPNS	.15761	1.06616	.10671	.71856
ARAPT	.44086	3.17501	.39380	2.79257
ARAR	.44492	3.20886	.44453	3.20559
GOGO	.33905	2.36813	.27139	1.86729

Note: All measures have been age-adjusted ***Measure*** : Cranio-facial measure (see text for definitions)

TABLE 4.-- HERITABILITY ESTIMATES

Heritability Estimates Calculated for all Measurements

h2 = r obs. / r exp.

N = 44 with 1000 resampling (see text)

Measurement		h2 value
1.	Anterior Facial Height	0.55
2.	Upper Facial Height	0.49
3.	Lower Facial Height	0.82
4.	Posterior Facial Height	1.16
5.	SNA	1.09
6.	SNB	0.94
7.	ANB	0.43
8.	SN to GoGn	1.03
9.	Anterior Cranial Base	1.02
10.	Posterior Cranial Base	0.03
11.	Articulare-Nasion	0.97
12.	Nasion-Sella-Articulare	0.50
13.	Ramus Height	1.09
14.	Mandibular Body length	0.77
15.	Gonial Angle	0.79
16.	Articulare Angle	0.77
17.	Articulare-Menton	0.78
18.	Articulare-B pt.	0.88
19.	Articulare-Pogonion	0.74
20.	ANS-PNS	0.30
21.	Articulare-A point	0.88
22.	AR-AR	0.89
23.	Gonion-Gonion	0.68

Table 5.--Pair-Wise Cross-Sibling Correlations for the Measures (n=44)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1	00	15	26	.05	-.28	- 23	- 09	.15	.33	-.02	.27	.12	.10	.00	.11	-.06	.13	.04	.18	-.02	.05	.35	.11
2	07	00	17	- 05	- 25	-.17	- 17	.06	.25	-.24	10	.15	.06	- 01	.04	-.09	.07	.00	.15	.20	.00	10	.12
3	.35	18	.00	- 03	-.18	-.22	09	.27	.13	-.04	.08	.01	.01	-.13	.17	.07	-.05	-.07	-.03	-.17	-.09	.21	.00
4	.10	04	03	.00	.11	.15	- 06	-.37	.23	.04	.21	.09	.67	.00	-.32	-.12	.43	.47	.42	.07	.35	.20	-.18
5	- 30	- 23	- 15	.12	.00	.42	.28	-.36	-.17	.03	-.22	-.32	.39	-.01	-.23	.11	.22	27	.13	.08	.22	-.18	-.32
6	-.14	-.11	.11	.16	.37	.00	.17	-.49	-.15	.18	-.10	-.23	.43	.05	-.31	.02	.26	.36	.17	.06	.31	-.06	-.26
7	-.11	-.22	.14	-.09	.25	.13	.00	.12	-.08	-.22	-.24	-.21	.01	-.09	.09	.15	-.02	-.09	-.03	.05	-.10	.22	-.14
8	13	-.02	20	-.39	- 30	-.44	-.03	.00	.02	-.13	-.03	.03	-.39	-.17	.44	.05	-.30	-.39	-.25	-.09	-.34	.08	.25
9	30	.23	.21	.22	-.15	-.22	-.08	-.01	.00	.22	.48	-.02	-.02	.21	-.08	-.11	.15	20	.19	-.01	.31	.39	.21
10	-.10	-.20	.06	-.06	.08	.25	-.21	-.20	.06	.00	.15	.03	.27	.22	-.37	.31	.26	.26	.32	.12	.12	.17	-.14
11	.20	-.02	.12	.13	-.20	-.08	-.29	-.08	.25	.15	.00	.13	.12	.27	-.21	-.05	.26	.29	.34	.13	.32	.40	.14
12	.11	05	-.03	.16	-.31	-.19	-.24	.00	.04	-.02	.13	.00	-.03	-.04	.13	-.34	.00	-.02	.03	.20	.05	.01	.16
13	.13	.09	.02	.73	.34	.38	.04	-.42	-.02	.18	.09	.07	.00	-.17	-.09	-.36	.28	.36	.24	.04	.30	.09	-.11
14	04	-.02	-.03	.01	.06	.08	-.03	-.13	.07	.29	.27	-.03	-.13	.00	-.34	.04	.22	.17	.23	.02	.26	.08	-.10
15	- 02	-.04	.03	-.42	-.15	-.21	.01	.37	-.02	-.33	-.23	.00	-.11	-.40	.00	-.11	-.10	-.08	-.10	.08	-.05	.19	.29
16	00	-.08	.15	-.16	.11	-.08	.19	.17	-.17	29	-.02	-.41	-.44	.06	.00	.00	-.20	-.27	-.18	-.30	-.30	-.12	-.15
17	.17	.03	02	.48	.16	.21	-.04	-.32	.17	.28	.33	-.01	.36	.27	-.17	-.11	.00	.43	.36	.10	.47	.25	-.03
18	06	- 03	- 02	.50	.25	.31	-.03	-.44	.23	.26	.33	-.04	.42	.19	-.12	-.21	.33	.00	.27	.15	.43	.16	-.10
19	.17	.12	- 04	.47	.12	.18	- 02	-.32	.21	.34	.38	.03	.35	.24	-.21	-.10	.32	.25	.00	.14	.47	.23	.04
20	-.07	.23	- 11	.00	.08	.03	.02	.01	.04	.05	.21	.22	-.02	.04	.12	-.25	.18	.15	.19	.00	.07	-.08	-.04
21	-.01	-.04	-.03	.35	.24	.30	-.05	-.45	.18	.13	.27	.05	.26	.30	-.18	-.17	.32	.30	.31	.05	.00	.14	-.08
22	37	17	.28	.23	-.20	-.15	-.20	.05	.38	.18	.35	.07	.06	.07	.17	-.13	.21	.12	.18	-.12	.08	.00	.14
23	.15	.15	03	-.21	-.33	-.22	-.15	.28	.30	-.18	.15	.10	-.11	-.09	.26	-.11	.04	-.08	.16	-.07	-.11	.17	.00

Note: All measures have been age-adjusted (see text); ***The upper diagonal entries are Pearson's correlations, the lower diagonal entries are Spearman's non-parametric correlations***, 1=ANTFAC; 2=UFH; 3=LFH; 4=POSTFAC; 5=SNA; 6=SNB, 7=ANB, 8=SN-GOGN, 9=ANTCRAN; 10=POSTCRAN; 11=ARNA, 12=NASAR; 13=RAMUSHT, 14=BODYLEN; 15=GOANGLE, 16=ARANGLE, 17=ARME, 18=ARBPT; 19=ARPO, 20=ANSPNS; 21=ARAPT; 22=ARAR; 23=GOGO

Table 6.--Average Principal Component Statistics from the 1000 Random Samplings from the 44 Female Sibling pairs

Component	Eigenvalue	Variance	Cumulative	Ave. Chi-square	D.F.
1	153.9936	.3169	.3169	2370.0878	275.0000
2	90.0482	.1858	.5027	2160.6964	252.0000
3	66.5190	.1373	.6401	2010.3090	230.0000
4	43.7577	.0905	.7306	1866.4360	209.0000
5	34.6960	.0717	.8022	1753.5490	189.0000
6	28.3838	.0587	.8609	1638.6656	170.0000
7	18.2257	.0378	.8987	1510.2277	152.0000
8	13.3058	.0276	.9263	1411.3226	135.0000
9	10.5849	.0218	.9481	1321.9347	119.0000
10	8.3943	.0174	.9655	1226.9188	104.0000
11	6.7477	.0139	.9794	1119.2195	90.0000
12	5.1269	.0106	.9900	980.9468	77.0000
13	2.9036	.0060	.9960	781.3532	65.0000
14	.8123	.0017	.9977	535.5381	54.0000
15	.5767	.0012	.9989	436.5263	44.0000
16	.2330	.0005	.9994	307.1891	35.0000
17	.1613	.0003	.9997	236.1034	27.0000
18	.0546	.0001	.9998	147.9988	20.0000
19	.0404	.0001	.9999	121.6912	14.0000
20	.0284	.0001	1.0000	91.9516	9.0000
21	.0127	.0000	1.0000	51.0455	5.0000
22	.0048	.0000	1.0000	20.8342	2.0000
23	.0010	.0000	1.0000	.0000	.0000

Note : All statistics computed on age-adjusted measures; ***Component*** Principal component, ***Variance*** Fraction of variance explained by the component, ***Cumulative***. fraction of variance explained; ***Ave. Chi-square*** Average chi-square associated with the principal component; ***D.F.*** · degree of freedom for the chi-square statistics

Table 7.--Average Principal Component Loadings Computed from 1000 Random Samplings from the 44 Female Sibling Pairs

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1	07	.03	02	14	01	.04	-.02	-.09	.07	.03	.10	.03	.13	.06	-.02	-.11	.15	.13	.15	.04	.11	.06	.08
2	41	- 14	31	-.05	27	.24	.03	-.32	-.14	-.01	-.19	-.12	- 03	-.03	-.12	-.07	-.09	- 03	-.11	.04	.03	-.15	- 13
3	22	.02	.21	11	- 08	-.07	00	04	.08	.02	.04	-.15	01	.15	-.29	.48	.02	-.05	00	.04	- 07	.13	-.07
4	18	- 07	- 12	19	.02	.05	-.03	-.09	.08	.13	.14	-.10	- 32	.21	-.03	.04	-.07	-.06	-.04	03	.07	.18	.40
5	.03	.00	-.04	-.01	-.05	-.04	.00	-.03	.00	-.03	.02	.09	.02	-.01	-.09	-.03	-.02	-.01	-.01	.03	.01	.01	.02
6	00	.01	-.02	-.02	-.02	-.01	-.01	.00	-.01	- 05	- 02	08	03	.02	-.05	-.02	.02	.00	.04	-.01	.00	-.05	.00
7	04	-.01	.01	.01	.00	.01	-.02	.02	-.08	-.05	-.10	.06	.05	.03	-.05	.01	.05	.01	.03	- 02	-.06	.03	.09
8	02	.08	10	-.01	.07	.05	02	.02	- 17	-.07	-.18	.08	.04	.02	-.08	.04	.02	.00	.00	.27	-.06	-.04	.23
9	00	15	-.16	-.03	.00	-.03	.03	.02	.13	-.11	.00	-.10	.02	-.04	.07	.06	.01	.01	.02	.05	.05	-.04	.02
10	02	15	15	00	05	06	.00	-.01	- 16	.05	-.07	.12	-.02	.03	-.06	-.06	.00	.00	-.05	-.08	-.03	.18	.01
11	01	-.04	07	-.03	.06	.02	.04	.03	-.01	-.04	-.01	.07	.00	-.04	-.07	.03	-.06	.11	-.05	-.17	.09	.05	.05
12	.10	- 14	10	- 04	-.03	.03	-.06	.00	.01	-.07	-.02	.06	04	-.05	-.06	.00	-.03	.14	-.01	.00	-.01	.04	.02
13	07	- 02	- 01	.05	.03	-.04	.07	-.02	-.02	.02	-.01	00	-.01	.05	.01	-.05	.04	-.16	.00	-.04	.02	-.03	.02
14	07	.04	.03	-.02	.00	.00	.00	.04	-.04	.05	.01	00	.01	-.03	-.01	.02	-.03	-.01	.12	.03	-.01	-.01	-.01
15	- 12	- 02	.01	.02	.00	-.07	.06	.08	-.03	.06	.01	-.02	.06	.01	-.01	.02	.02	-.03	.09	- 01	- 01	-.01	.01
16	.06	-.13	-.13	.11	-.01	-.10	.08	.15	-.02	.08	-.02	-.03	.04	.07	.00	.00	.05	.09	-.05	.01	-.03	.02	.00
17	.02	-.05	-.05	.03	.05	.13	-.09	.22	.05	.03	.03	.00	06	-.02	-.07	-.01	-.01	-.08	-.01	.01	.06	.00	-.01
18	.04	.04	.07	.07	- 06	-.03	-.04	- 02	-.01	-.06	-.08	-.04	-.05	.05	.00	-.04	-.05	00	-.01	-.01	.09	.00	.00
19	.01	02	.05	.04	-.17	-.10	-.07	04	-.11	-.02	-.16	-.19	- 05	.03	-.08	-.12	-.03	.03	.00	-.01	.24	.00	.00
20	- 03	.04	.01	.04	15	.03	.06	- 03	.13	-.02	.07	.13	08	.13	.09	03	-.10	.00	-.02	.01	- 23	.00	.00
21	09	- 03	-.04	.15	.00	04	.03	01	- 02	-.05	.07	.15	-.12	-.06	.09	.14	.15	.00	-.02	.00	-.03	.00	.00
22	- 02	.01	01	.01	.04	-.03	-.03	.00	.01	.00	.00	.01	-.01	-.01	.01	.01	.01	.00	.01	.00	-.01	.00	.00
23	.01	.01	00	.01	.01	.00	.00	.00	.03	.02	-.02	.01	.00	.00	.00	.00	.00	.00	.00	.00	-.01	.00	.00

Note: The principal component analysis was carried out on age-adjusted measures ***The numbers in the left-most column and the upper-most row indicate the principal component (in order of decreasing significance as in Table 6) and the measures, respectively*** For the measures, 1=ANTFAC; 2=UFH, 3=LFH, 4=POSTFAC; 5=SNA; 6=SNB; 7=ANB; 8=SN-GOGN; 9=ANTCRAN, 10=POSTCRAN; 11=ARNA; 12=NASAR, 13=RAMUSHT, 14=BODYLEN; 15=GOANGLE; 16=ARANGLE, 17=ARME; 18=ARBPT, 19=ARPO; 20=ANSPNS, 21=ARAPT; 22=ARAR, 23=GOGO

Table 8.--Sibling Correlations for the Principal Component Scores (n=44)

Component	Pearson's R	Ave. t-stat.	Spearman's R	Ave. t-stat.
1	.45582	3.30061	.42607	3.05284
2	.86969	8.93394	.87679	9.13469
3	.69350	5.73324	.67933	5.55353
4	.81922	7.74427	.80710	7.50414
5	.61899	4.85246	.58022	4.44617
6	.60277	4.67886	.59835	4.63250
7	.63195	4.99532	.68823	5.66568
8	.40347	2.86970	.48155	3.52177
9	.89588	9.73336	.73882	6.35853
10	.80161	7.39984	.56882	4.33203
11	.39281	2.78469	.29364	2.02952
12	.86811	8.89071	.82186	7.79849
13	.78449	7.09012	.80102	7.38877
14	.86327	8.76114	.87885	9.19500
15	.89527	9.71247	.88482	9.37515
16	.82716	7.90944	.78691	7.13257
17	.70475	5.88093	.68964	5.68370
18	.68684	5.64792	.64807	5.17847
19	.43818	3.15266	.40632	2.89253
20	.56121	4.25701	.43954	3.16396
21	.53198	3.97732	.52030	3.86896
22	.85112	8.45377	.83446	8.06749
23	.67411	5.48888	.63667	5.04828

Note: The principal component analysis was carried out on age-adjusted measures ***Component***: Principal component, ***Ave. t-test***: Average t-statistics associated with the age regression coefficient from the 1000 samples (see text).

TABLE 9.-- RELIABILITY OF CEPHALOMETRIC MEASUREMENTS

Intraclass Correlation Coefficients for Repeated Cephalometric Measurements

$$r = MSB - MSW / MSB + MSW$$

VARIABLE r

Measurement		r value
1.	Anterior Facial Height	0.91
2.	Upper Facial Height	0.95
3.	Lower Facial Height	0.95
4.	Posterior Facial Height	0.86
5.	SNA	0.97
6.	SNB	0.95
7.	ANB	0.84
8.	SN to GoGn	0.98
9.	Anterior Cranial Base	0.98
10.	Posterior Cranial Base	0.83
11.	Articulare-Nasion	0.84
12.	Nasion-Sella-Articulare	0.99
13.	Ramus Height	0.81
14.	Mandibular Body length	0.85
15.	Gonial Angle	0.98
16.	Articulare Angle	0.96
17.	Articulare-Menton	0.97
18.	Articulare-B pt.	0.82
19.	Articulare-Pogonion	0.94
20.	ANS-PNS	0.68
21.	Articulare-A pt.	0.96
22.	AR-AR	0.96
23.	Gonion-Gonion	0.99

APPENDIX C

Data

Pt. #	Age	AFH Na-Me	UFH Na-ANS	LFH ANS-Me	PFH S-Go	SNA	SNB	ANB	SN-GoGn	ACB S-Na	PCB S-Ar	Ar-Na
AA1	15-0	106.2	52.8	55.3	65.2	81.3	79.5	1.8	30.1	68	31.9	91
AA2	15-0	111.1	51.9	56.5	72.1	79.9	76.6	3.3	28.7	68.2	31.5	90
AA2	15-0	106.6	53.1	61.2	65.8	81.4	79.6	1.7	30.1	67.6	35.5	93.7
AB1	15-0	111.6	50.3	63.4	72.7	80.3	76.4	3.9	29.2	68.3	33	92.2
AB2	14-11	108.9	50.5	60.1	73.4	89	84.8	4.2	25.8	63.7	36.6	89.4
AC1	14-0	119.5	53.6	66.7	73	76.6	75.8	0.8	36.2	69.6	31.3	92.9
AC1	14-0	119.4	52.3	68.4	70.7	77.2	76.2	1	37.3	69.5	31.1	92.5
AC2	16-8	117.9	54.5	65.4	80.7	83.4	82.4	1	30	69.3	33.3	90.9
AC3	14-0	118	53.6	65.2	74.6	78.5	77.7	0.8	36	68.1	32	90.4
AD1	14-4	112.1	56.8	57.4	71.3	80.3	77.6	2.8	30.5	71.5	28.2	90.7
AD2	16-1	107.5	56.7	51	70.6	81.8	81.9	-0.1	27.2	68.7	34.8	93.3
AE1	15-0	116.6	61.3	58.4	66.9	74.8	72.4	2.4	41.2	68.8	29.1	93.4
AE2	14-11	110.6	56.4	58.9	72.3	80.1	75.6	4.4	32.8	69.5	32.7	93.4
AE3	14-11	109.3	53.2	57.7	65.1	80.2	77.3	2.9	35.3	69.3	28.4	89.7
AF1	20-0	113.4	53	61.6	78	85.5	82.5	3	27.9	64.7	42.7	93.6
AF2	20-1	129.3	58.7	73.4	85.3	79.8	75.6	4.2	32.2	73.4	33.1	96.6
AG1	14-1	108.9	52.7	58	83.4	90.8	83.9	7	19.6	69.5	38.6	92.9
AG1	14-1	108.9	53	57.7	83.3	90.3	83.4	6.8	19	69.8	38.4	93
AG2	14-4	110.9	50.4	61	72.4	88.5	90.2	-1.7	24.9	66.6	30.8	87.9
AG3	14-1	118.3	52	68.1	81.6	82.6	78.1	4.5	28.4	67.8	34.9	91.5
AH1	15-0	107.1	51	57.3	70.4	84	80.1	3.8	27.8	66	29.5	85.7
AH2	15-0	115	56.6	61.9	73.7	78.9	76.8	2.2	32.2	67.6	34.9	93.8
AI1	17-11	112.5	53.8	61.1	79.6	80.1	76.1	4	26.4	71.2	27.3	90.9
AI2	17-11	112.8	53.6	61.1	76.9	80.5	76.8	3.7	27.9	71.2	30.2	92.6
AJ1	19-0	107.2	53.2	56.9	73.5	81.9	79.7	2.2	27.2	66.5	33.3	90.9
AJ2	18-11	116.8	54.8	65.1	76.6	81.8	78.5	3.3	31.9	67.3	33.3	89.5
AK1	15-0	117.3	50.8	68	77.2	80.8	78.2	2.6	29.4	70.8	33.3	93.6
AK2	15-0	113.6	50.3	65.1	71.4	80.4	80.8	-0.4	28.6	69.8	31.3	93.6
AL1	15-0	110.3	51.4	60.9	69.6	86.9	83.5	3.5	30.2	68.3	29.1	87.1
AL2	15-0	112.8	52	63.9	69.4	81.9	78.3	3.6	35.1	69.3	35.6	93.7
AM1	15-0	112.5	54.1	60.1	73.8	79.1	75.7	3.3	28.7	69.1	32.8	93.4
AM1	15-0	110.5	53.5	60	73.4	78.1	75.2	2.9	27.6	70.4	32.7	94.5
AM2	15-0	113.7	51.1	64.4	81.3	77.5	79	-1.5	24.2	73.7	39.8	100.1
AN1	15-0	111.8	53.7	64.4	69.9	82.8	77.8	5	34.5	73.2	33.9	95.8
AN2	15-0	110.9	51.7	61.6	71	84.7	83.9	0.8	27.8	67.4	37.4	90.6
AO1	15-11	106.4	53.4	55	66.5	81.5	79.5	2	29.9	68.5	32	91.7
AO2	16-6	111.5	51.8	61.9	71.9	80.6	77.2	3.4	30.1	67.6	35.7	93.3
AP1	14-7	106.6	51.3	57.5	72.8	82.8	80.5	2.3	26.6	69	32.3	92.2
AP2	14-1	118.9	56.3	65.2	70.6	77.2	76.7	0.5	35.8	70.6	31.5	93.5
AQ1	16-0	114.5	53	64	72.1	77.8	75.6	2.1	34.2	68.2	35.2	93.8
AQ2	16-1	112.5	55.9	61.8	72.9	81.8	78.2	3.6	29.6	71.9	32.9	90.9

Pt. #	Age	AFH Na-Me	UFH Na-ANS	LFH ANS-Me	PFH S-Go	SNA	SNB	ANB	SN-GoGn	ACB S-Na	PCB S-Ar	Ar-Na
AR1	15-0	103.5	48.6	58.5	61.7	80.4	78.6	1.8	33.8	61.2	31	82.1
AR2	15-0	108.1	49.9	63.2	62.8	79.9	77.5	2.4	39.5	60	26.4	78
AS1	14-0	104.7	48.3	58.1	68.9	75.5	75.6	-0.1	29.2	67.2	34	91.1
AS2	14-9	107.7	47	63.6	63.4	74.1	71.2	2.9	36.5	67.1	32.9	92.7
AS2	14-9	107.8	47.4	63	65.8	74.4	71.4	3	34.8	66.9	33.1	92.3
AT1	15-0	109.7	52.3	62.7	64.4	82.2	75.4	6.9	36.7	67.1	29.9	85.8
AT2	15-0	113.2	51.6	66.8	61.5	79.3	75.2	4.1	40.7	69.6	28.9	88.5
AU1	15-1	108.9	53.3	60.8	73.5	86.5	79.3	7.1	27.5	69.3	33.2	92.2
AU2	15-1	109	55.3	59.8	73.8	87.2	81.3	5.9	28.9	70.3	31.2	89.9
AV1	14-0	112.8	50.3	63.7	74.5	81.7	79.7	2.1	28.9	67.5	32.5	89
AV2	14-0	120.2	54.5	69.1	78.2	83.6	78.3	5.4	31	68.3	35.6	94.3
AW1	15-0	116.1	55.2	67	76.7	77.4	73.4	4	32	77.7	35.6	101.9
AW2	15-0	116.2	50.9	68.2	73.4	75.7	75.1	0.6	31.3	75.9	34.3	99.5
AX1	17-4	120	58.3	67.6	72.7	74.2	75.1	-1	43.2	69.2	32.6	91.2
AX2	16-10	110.3	52.9	66.6	67.9	76.7	72.1	4.7	37.5	68.8	30.9	92
AY1	15-2	125.9	60.4	69	75.7	80.8	75.3	5.5	36.2	69.2	37.1	97.5
AY2	15-2	122.7	57.5	66.2	74.6	75.5	71.8	3.8	36.7	73	29.9	95.1
AZ1	14-9	113.1	53.1	63.5	68.5	82.1	78.6	3.4	35.7	64.9	33	87.1
AZ2	14-9	113.2	54.2	60.5	66.2	79.9	77.2	2.7	37.3	65.2	29.6	86
BA1	15-6	110.2	52.3	59.8	70.8	81.7	77.2	4.5	29.6	68.8	33.5	94
BA2	15-6	111.1	52.1	61.5	72.1	79.5	77.6	2	26.1	70.7	35.3	95.4
BB1	17-5	107.4	48.5	60.5	68.6	78.1	77	1.1	31	68	32.8	93.4
BB2	17-2	114.5	49.5	67.4	73.8	83.9	80.3	3.6	29.8	68.3	39	96.6
BB2	17-2	114.6	49.2	68.5	75.2	85.4	80.9	4.4	28.7	68.1	38.1	95
BC1	15-2	116.7	49.6	76.2	72.9	83.8	78.7	5.2	40.9	62.1	35.9	87.4
BC1	15-2	116.4	49.6	76.3	73.6	82.6	78.1	4.5	40.9	62.3	33.8	86.1
BC2	16-4	112.9	50	66	76.1	86.6	81.9	4.7	34	59.9	31.4	81.4
BD1	15-0	109.8	45.7	64.7	73.1	86.7	88.7	-2	26.4	66.9	35.5	86.4
BD2	15-0	116	56.4	63	81.5	82.4	78.1	4.3	24.4	71.1	36.8	96.1
BE1	15-0	112.5	51.3	61.3	73.9	85	86.9	-1.9	26.6	70.3	28.6	89.7
BE2	15-0	105	46.7	60.1	81.2	94	90	4	14	69.9	36.1	92.2
BF1	15-3	119.2	52	71.2	75.8	80.5	76.5	4.1	32.3	72.3	38.6	99.9
BF2	15-9	118.6	55.4	64.3	75.5	78.5	76	2.5	32.7	70.2	34.8	96.8
BF3	15-2	112.8	48.2	66.7	74.5	82.6	80.1	2.6	27.5	68.5	30.8	90.6
BG1	15-0	107.1	46.6	61.8	74.6	89.7	86.6	3.1	22.7	75.5	31.1	94.7
BG2	15-0	113.9	54	62.5	78.7	83	80.1	2.9	27.8	68.5	35.1	91.6
BG2	15-0	113.6	53.2	63.8	74.6	83	79.4	3.6	30.1	68.2	35.4	91.8
BH1	15-11	109.1	48.9	61.8	76.7	82	81.5	0.5	26	69.3	35.1	93.2
BH2	15-8	113.2	54.3	63.5	71.8	83	80.5	2.5	31.3	69.9	37.8	98.5
BI1	15-0	112.8	51.1	63.2	74.3	79.4	80.5	-1	24.7	77	33.2	99.5
BI2	15-4	106.4	51.3	56.8	65.5	83.4	80.4	3	28.4	70.3	34.3	95.2

Pt. #	Age	AFH Na-Me	UFH Na-ANS	LFH ANS-Me	PFH S-Go	SNA	SNB	ANB	SN-GoGn	ACB S-Na	PCB S-Ar	Ar-Na
BJ1	14-11	111.9	53	60.5	73	86.8	80.9	5.9	28.2	67.4	34.4	88.3
BJ2	15-0	111.1	51.7	60.5	80.4	85.6	83.2	2.4	22.3	69.2	35.5	92.1
BK1	15-0	104.8	52.9	55.3	61.1	81.6	78.7	2.9	30.8	64.9	33.9	91
BK2	15-0	111.3	51.8	62.8	65.1	80.8	78.4	2.4	33.5	66.2	33.2	91.3
BL1	15-2	115.7	50	68.9	65.3	75.8	74.3	1.5	41.2	70.3	32	90.4
BL2	14-11	113	51.5	66.1	64.8	75.2	72.1	3.1	39.4	71.8	32.8	94.1
BM1	15-8	114.5	50.1	68	68.4	80.2	75.5	4.7	37.5	68.8	32	89.4
BM2	15-4	118.2	53.8	68.4	64.5	75.9	71.4	4.5	43.6	67.4	33.5	90.7
BN1	15-2	115.1	52.9	63.5	67.3	79.1	75.2	3.9	34.8	70.5	35.7	94.5
BN2	15-8	119.1	57.1	63.7	69.2	78.9	77.4	1.5	35.3	72.5	34.4	96.1
BO1	14-5	109.8	53	58.4	65.5	81.3	78.8	2.5	34.4	67.2	30.5	88.3
BO2	14-7	112.2	51.2	65.8	72.3	80.4	77.1	3.3	29.3	74.7	37.1	98.9
BP1	19-8	114.1	50.4	69.1	73.5	78.4	75.3	3.1	31.4	69.3	34	92
BP1	19-8	114.5	49.6	69.1	76	75.8	75.2	0.6	30.3	69.1	32.5	91.1
BP2	19-0	111.9	49.1	67	60.2	77.1	70.1	7	45.9	65.3	30.1	84.8
BQ1	15-1	129.8	55.3	77.2	68.2	68.1	67.1	0.9	51	71.6	30.8	94.1
BQ2	15-1	111.7	53.7	64	65.2	75.6	71.8	3.9	38.2	72.6	36.7	99.5
BR1	15-0	114.8	51.8	64.4	68.6	76.1	77.3	-1.2	38	68.6	30.3	90.6
BR2	15-0	112.7	51.9	64.1	79.1	77.2	75.5	1.7	28	66.9	37.1	94.1
BR2	15-0	111.5	52.4	63.4	77.7	76.9	74.9	2	28.2	67.2	37.1	94.5
BS1	14-0	119.4	51.3	72.4	76.5	76.1	75.6	0.5	32.4	73.4	36.9	99.2
BS2	14-0	120.3	56.3	67.5	81.3	71.8	71.8	-0.1	29.9	75.9	34	101.5
BT1	14-1	117.1	50.5	69.3	67.7	76.9	75.7	1.2	39.6	68.3	34.6	91.8
BT2	14-10	123	55.1	69.9	72.9	83.9	81.7	2.2	34.1	74.8	37.7	98.2
BU1	15-0	115.7	53.3	62.5	72.6	75	76.9	-1.9	33.7	70.8	33.6	91.9
BU2	15-0	114.2	50	64.3	69.1	79.2	83.6	-4.4	30.9	70.4	34.1	93.5
BV1	14-0	116.7	57.8	60.2	77	75.7	75.9	-0.2	30.3	67.7	30.4	89.3
BV2	14-11	114.1	53.8	62	73.1	77.8	75.9	1.9	31.5	65.8	31.6	89.4

Pt. #	Na-S-Ar Saddle <	Ramus Ht Ar-Go	Body len Go-Me	Gonial < Ar-Go-Me	Ar < Go-Ar-S	Ar-Me	Ar-Bpt	Ar-Po	ANS-PNS	Ar-Apt	AR-AR' Frontal	Go-Go' Frontal
AA1	127.5	38.2	77.4	126.3	138.3	104.6	93.7	104.2	58	84.4	99.53	93.86
AA2	126.6	40.9	69.3	125.6	141	98.9	91.2	100.1	60.38	83.5	98.19	106.11
AA2	126.3	39	73.7	127.2	139.4	102.1	92.9	103.6	59.54	83.4	98.93	107.3
AB1	127.5	44.7	73.1	122.9	141.3	104.4	91.3	105.1	55.96	85	104.99	98.13
AB2	123.9	42.6	75.4	124.4	140	105.5	97.9	104.3	54.28	86.7	98.82	90.68
AC1	130.2	46.8	71.9	130.7	137.6	108.4	96.6	109.7	51.16	82.9	104.07	90.97
AC1	129.8	44.7	74.5	130.8	139	109.1	97.4	107.5	54.64	83.6	104.78	91.42
AC2	120.7	52.4	71	128.4	142.5	111.4	101.1	110.5	54.08	84.9	108.17	96.63
AC3	125.3	48.3	67.1	136.5	136.1	107.4	94.1	106	57.89	81.2	104.29	98.35
AD1	125.3	47	69.9	126.2	142.7	104.8	96.9	104	58.13	85.3	106.48	95.35
AD2	125.5	42.1	72.2	131.4	133.4	104.8	96.6	107.5	52.82	85.9	103.65	98.43
AE1	141.7	46	68.7	134.8	126.7	106.2	99.7	103.7	54.35	87	105.37	96.62
AE2	128.6	46.2	62.6	133.1	134.6	100	95	100.1	52.55	86.3	103.14	96.93
AE3	128.3	41.7	69.7	133.2	136	102.8	95.5	103	58.87	84.3	101.45	94.56
AF1	119.9	41.1	69.3	132.3	138.2	101.6	93	99.5	52.52	83.6	107.62	94.07
AF2	125.9	56.1	76.1	117.7	150.8	113.6	101	111.5	57.77	88.8	111.71	91.24
AG1	115.5	49.5	69	123.9	142.1	105	94.4	104.1	56.96	89.3	105.37	86.48
AG1	115.4	49.5	69.2	123.5	142.7	105	93.7	104	54.4	89	105.55	87.09
AG2	124.7	47.5	82.9	126.5	136.6	117.5	106.1	118.9	57.15	87.6	104.85	90.53
AG3	122.7	50.9	69.6	124.1	144.3	106.8	94.4	107.8	62.91	84.2	102.15	91.01
AH1	122.8	44.2	72.2	121.3	146.2	102.4	91.4	102.1	56.45	82.2	100.65	88.67
AH2	129.7	46.2	72.2	128.9	136.1	107.4	96.6	105.4	54.05	84.9	98.06	91.66
AI1	129.1	57.5	63.8	123.2	136.9	106.7	93.5	103.8	59.18	86.9	111.38	99.78
AI2	127	51.5	68	124.2	139.1	105.9	93	103.5	54.08	86.7	111.88	98.34
AJ1	127.8	47.3	66.8	128.7	133.4	103.3	93.8	101.9	57.94	84.5	107.01	101.27
AJ2	121.8	48	69.8	128.6	144.5	106.6	96	105.4	56.55	82.2	101.01	89.92
AK1	124.2	47.7	73.1	123.1	145.1	106.8	95.6	107	57.53	85.6	101.08	89.24
AK2	131.7	46.5	80.4	120.2	139.7	111.3	103.8	112	61.66	87.3	104.2	92.82
AL1	121.4	44.5	76.4	125.4	145.2	108.5	98.8	107.9	58.54	85.7	103.83	86.23
AL2	123.2	40.2	69.7	140.5	134.4	103.9	95.4	103	54.59	85.5	101.28	91.76
AM1	129.5	45.8	71.6	120.7	141.7	102.8	92.4	103	57.85	85	101.91	90.77
AM1	128.9	45.7	71.7	119.5	142	102.3	92.8	102.4	55.26	84.8	102.23	90.51
AM2	120.8	46.7	70.4	124.1	141.9	104	96.7	106.1	61.97	84.4	106.26	100.29
AN1	122.6	41.5	68.9	134.7	140	102.5	99	104.1	59.62	89.4	108.5	109.81
AN2	116.6	37.6	77.9	121.7	152.6	102.7	93.7	102.2	60.6	82.1	107.75	100.17
AO1	127.6	39.6	76.5	126.4	137.4	105	93.8	105	60.38	85.2	98.19	106.11
AO2	126.3	40.7	69.3	127.1	140.2	99.3	91.5	101.2	58	83.7	99.53	93.86
AP1	127.2	46.8	69.3	125.5	136.1	103.7	96.6	105.9	54.23	86.7	97.97	92.09
AP2	128.4	44.3	76.5	126.2	143.8	108.6	100.5	108.7	55.63	84	101.58	95.18
AQ1	127.3	42.5	69.8	129	140	102	91.8	101	54.46	82.3	104.4	97.03
AQ2	115.3	43.9	74.8	118.9	158.1	103.4	93	102.4	52.64	83.2	111.03	95.15

Pt. #	Na-S-Ar Saddle <	Ramus Ht Ar-Go	Body len Go-Me	Gonial < Ar-Go-Me	Ar < Go-Ar-S	Ar-Me	Ar-Bpt	Ar-Po	ANS-PNS	Ar-Apt	AR-AR' Frontal	Go-Go' Frontal
AR1	122.4	35.3	68.9	126.9	148	94.4	85.1	94.7	50.02	73.8	96.05	85.24
AR2	124.3	40.5	66.4	129.5	148.8	97.4	87.6	95.6	55.29	72.5	96.96	91.07
AS1	125.1	39.6	69.4	123.6	141.7	97.1	86.4	98.4	55.63	77.4	100.09	86.62
AS2	133.2	36.7	68.3	128.6	136.9	95.6	85.9	94.7	54.26	79.9	101.69	87.55
AS2	132	38.6	66.2	128.7	136.8	95.2	85.8	93.8	52.29	79.5	101.67	88.79
AT1	119.1	36.4	66.5	126.1	155.3	92.7	88.6	94.5	59.71	79.9	97.73	85.95
AT2	122.4	35.7	72.3	132.3	149.2	99.9	90	97.9	59.37	81.2	101.6	96.42
AU1	124.3	45.3	66.7	127	139.7	100.6	96.5	100.6	57.46	89.3	97.27	81.98
AU2	119.6	46.8	65.5	130.2	142.1	102.2	98	102	60.15	88.5	97.57	81.55
AV1	121.8	45	73.8	118.9	150.3	103.3	94.1	103.1	53.42	80.9	97.85	83.83
AV2	127.5	47.8	73.7	122.9	143.9	107.4	100.7	106.7	58.29	89.1	96.95	90.54
AW1	123.7	46.1	68.9	124	146	102.1	97.9	102.1	55.87	89.2	106.44	95.98
AW2	124.6	44.1	75.3	125	144.4	106.9	96.4	107.3	52.93	85.6	107.7	93.4
AX1	123	45.8	65.9	143.6	139.6	106.3	96	105.9	52.71	77.2	109.38	97.15
AX2	130.7	43.5	62.9	128	142.5	96	92.8	96.8	60.15	82.6	104.5	100.21
AY1	130.9	44.9	79.4	125.5	142.4	111.7	99.1	111.3	59.8	91	111.14	93.07
AY2	130.3	48.6	74.1	124.7	143.2	109.3	94.5	109.2	59.62	85.4	101.24	88.9
AZ1	122.3	39.8	69.1	131.7	145.6	100.1	91.6	100.5	48.21	79.7	103.67	98.52
AZ2	125.9	40.3	70.5	130.3	144.3	101.3	91.9	101.2	50.29	79.4	100.52	93.54
BA1	130.2	42.2	71.6	123	139.3	100.9	93.1	101.7	53.86	87.7	105.18	100.92
BA2	124.9	41.9	76.9	115.7	149.7	102.3	92	103.2	55.89	84.9	104.08	95.36
BB1	132.9	43.7	69	131.1	129.3	103.1	94.4	104.4	52.94	84	94.95	89.17
BB2	126	42.1	76.4	130.1	136.1	108.3	96.3	107.7	62.97	88.8	103.09	103.06
BB2	124.4	43.6	76.2	128.3	138.3	108.8	96.8	108.2	63.98	88.9	103.2	101.45
BC1	124	44.4	66	135.3	143.4	102.4	99.6	102.3	56.47	80.4	101	94.82
BC1	124.7	46.7	63.5	135.3	143.3	102.1	93.2	101.1	55.63	79.1	101.01	94.65
BC2	123	50.1	60.3	135.9	138.2	102.4	92.4	101.8	51.63	79	95.12	90.12
BD1	111.2	40.5	77.8	124.6	152.3	106.2	96.7	103.5	49.67	79.1	99.84	88.24
BD2	122.6	48.7	73.3	113.2	151.8	102.7	94.7	103	58.37	87.9	107.72	87.2
BE1	124.5	50.9	77.5	130.6	134.7	117.2	105.8	115.9	50.35	87.3	102.96	96.03
BE2	117.2	51.7	76.1	123.1	137.8	112.9	103.5	107.1	57.76	91.9	111.12	85.1
BF1	125.7	43.7	75.1	130.2	138.9	108.5	96.5	108.4	60.84	89.6	111.13	96.27
BF2	131.5	47	74.6	127.4	135.5	109.8	98.6	107	54.65	87.6	109.33	91.97
BF3	127.3	47.9	73.2	119.2	144.7	105.3	99.3	104.5	57.17	84.8	112.74	95.18
BG1	119.2	49.8	71.3	134	133.3	111.8	101.9	110.3	54.68	93.2	100.8	99.35
BG2	121	47.8	67.9	124.5	145	102.8	95.2	101.1	51.34	84.2	102.45	95.54
BG2	121.3	43.1	71.5	123.7	147.5	102	94.3	100.1	54.3	83.9	102.67	95.2
BH1	123.1	48	65.1	131.7	134.3	103.5	96.8	103.9	55.13	84.6	105.31	96.43
BH2	129.8	43.3	74	133.4	130.8	108.4	103.2	107.9	55.62	91.9	109.06	103.84
BI1	124.3	47.2	82.3	124.4	139.2	115.7	101.6	116.3	60.68	89.7	110.52	98.67
BI2	127.4	38	79	127.9	135.8	106.6	96	106.9	55.11	89	102.58	95.36

Pt. #	Na-S-Ar Saddle <	Ramus Ht Ar-Go	Body len Go-Me	Gonial < Ar-Go-Me	Ar < Go-Ar-S	Ar-Me	Ar-Bpt	Ar-Po	ANS-PNS	Ar-Apt	AR-AR' Frontal	Go-Go' Frontal
BJ1	116.4	40.7	76.3	118.7	155.6	102.3	89.7	102.6	55.33	83.6	101.54	92.97
BJ2	119.6	49.3	72.8	121.2	144	107.1	95.2	106.2	51.35	86.1	108.22	101.75
BK1	131.5	36	77	127.6	135.5	103	92.1	100.1	54.74	84.9	103.45	94.09
BK2	130.3	36.8	77.9	122.3	143.8	102.4	93.9	101.9	56.88	84.2	106.18	91.67
BL1	119.2	36.3	70.9	136	148.3	100.2	89.6	99.9	48.78	77.2	102.22	95.68
BL2	123.7	36.6	70	132.9	145.7	98.6	88.8	99.2	46.44	80.2	103.48	98.33
BM1	120.5	39.7	65.6	135.9	145	98.1	89.2	97.2	55.75	80.3	105.17	97.57
BM2	124.7	34.3	72.4	129	151.8	97.7	84.8	96.6	56	78.4	103.82	95.51
BN1	122.2	34.3	77.7	122.8	152.3	100.5	89.7	101.7	57.01	82.8	108.56	101.41
BN2	124	39	80	129.3	144.6	109	97.6	109.6	55.82	85.9	108.19	95.91
BO1	125	39.3	73.7	128.1	143.3	102.7	92	102.9	49.98	82	97.85	85.34
BO2	120.5	40.7	76.8	124.6	146.4	105.4	92.6	105.1	62.03	87.3	106.87	100.34
BP1	121.9	44.5	71.2	118.2	154.5	100.2	89.7	98.2	58.38	80.7	104.14	88.76
BP1	123.3	48.2	69	117.3	152.9	100.7	91.6	99.7	51.68	78	103.9	90.4
BP2	120.8	31.8	65.1	124.8	162.4	87.2	83.4	87.7	49.06	73.8	97.75	82.83
BQ1	129.2	41.1	69.2	140.2	144.5	104.2	90.5	104	58.38	75.9	101.67	92.73
BQ2	127.7	36	69.4	139.9	133.8	99.7	89.1	101.4	58.42	85.3	109.94	97.54
BR1	128.5	43.1	69.5	132.5	138.7	103.6	96.7	104.7	52.03	80.3	104.32	96.9
BR2	127.3	47.9	61.5	124.8	139.5	97.2	89	97.5	55.65	81.1	108.98	100.01
BR2	127.7	47.2	62.7	124.4	139.5	97.5	89.4	96.5	56.39	81.3	108.69	100.15
BS1	124.8	45.2	72.7	125.7	145	105.6	96.7	105.9	56.46	84.6	108.6	96.69
BS2	131.1	53.7	69	122.4	139.2	107.8	97.6	107.3	56.35	85.4	109.38	98.79
BT1	122.8	37.2	72	133	146.2	101	88.7	101.7	52.46	78.4	110.62	93.68
BT2	117.8	39	83.6	130.9	147.8	113.1	101	113.5	55.18	90.2	105.15	98.57
BU1	119	42	73.8	128.3	147.5	105.1	90.8	103.8	52.01	76.7	104.64	104.03
BU2	123.1	39.2	85.2	125.2	144	112.5	100.6	113.7	57.06	82.5	102.7	100.23
BV1	126.6	49.8	73.9	116.5	149.1	105.9	92.2	106.2	53.3	78.5	99.71	90.33
BV2	129.9	46.1	71.9	119.3	145	102.7	91.7	102.2	52.83	80.5	102.63	92.29

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