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# Soft Tissue Facial Asymmetry and Family Resemblance in Normal and Syndrome-Affected Individuals

by

Deborah Jean Shaner 

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Department of Anthropology

Edmonton, Alberta

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## ABSTRACT

The central concern of this physical anthropological research was to compare objectively the soft tissue facial measurements of individuals with syndromes that affected the facial features with those of normal individuals. Since the method chosen for this research was photogrammetry, and no facial measurement norms obtained by this method were available, two studies were conducted that compared measurements taken by photogrammetry, calipers, or a ruler. These studies indicated that there were systematic differences between the data gained from the different methods; therefore, both normative data and data from syndrome-affected individuals would have to be collected by the same method (i.e., photogrammetry). Facial asymmetry in normal and syndrome-affected males and females was investigated next. The statistically significant results from all groups indicated that the right side of the face was dominant for the bilateral measurements and X coordinates of the landmarks, whereas the midline landmarks were mainly deviated to the left side of the face. The syndrome-affected individuals showed no evidence that they had greatly asymmetrical facial features: When the bilateral measurement differences of each syndrome-affected subject were compared to the limits defined by the normal groups, less than 10% of the comparisons for each sex exceeded the norms. The final investigation involved facial feature resemblance among family members with and without syndromes and resemblance among related and unrelated individuals diagnosed with the same syndrome. The highest correlation was found for a pair of sibs with the same syndrome, and all but two correlations for syndrome-affected individuals were positive and statistically significant. For parent-child and sib-sib correlations (regardless of medical status), there was a greater number of significant correlations for sib pairs than for parent-child pairs, and the signs of the significant correlations were mixed in the latter group, but were all positive in the former. It was concluded that some factor, possibly environment, was more influential in the resemblance between sibs than between parents and children. The common factor among subjects with the same syndrome appeared to be the genetic error(s) in the case of most unrelated individuals, to which was added family resemblance in the related individuals.

## ACKNOWLEDGEMENT

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# CHAPTER 1

# INTRODUCTION

The central concerns of anthropology are human biological and cultural evolution and variation. Physical anthropology focuses on the biology and behavior of humans and alloprimates; human variation studies within this subdiscipline are concerned with how and why humans differ biologically. Investigations of biological variation are not confined to medically normal individuals, but also include individuals with abnormalities, such as syndromes (Relethford, 1994). Understanding human variation is also the concern of medical disciplines involved in diagnosing and treating individuals with abnormalities. In the case of some abnormalities, an initial clinical assessment is needed in order to choose the correct laboratory test, if one is available, to confirm the diagnosis. If no test exists, then clinical assessment constitutes the entire investigative procedure. Initial diagnoses are often based on subjective examination of the patient for deviations from normal morphology. The use of objective methods during clinical diagnosis is not consistent in clinics; however, quantification of medically normal physical variation and abnormal variation are areas in which physical anthropologists have made contributions to the medical arts, including those concerned with syndromes (Farkas, 1996; Robinow, 1982).

This dissertation is a physical anthropological study of modern human soft tissue facial feature variation in medically normal and syndrome-affected individuals. The syndrome-affected subjects had syndromes that affected their soft tissue facial features; their clinical diagnosis was based, at least in part, on observation of abnormal facial feature morphology. That syndromes affecting the soft tissue facial features can be detected and identified by characteristic facial signs suggests that syndrome-affected individuals have facial traits that take precedence over family and ethnic characteristics and that the identifying traits are not strongly affected by environment. However, it is not yet clear whether the observations used to identify subjectively the features common to each syndrome are quantifiably outside of the measured range of normal variation or whether the

characteristics are a more subtle combination of mild to severe abnormalities that, taken together, enable clinicians to identify each syndrome. In addition, it has not yet been fully explored whether individuals with the same syndrome, irrespective of ancestral background, are alike in regards to the measurements of those features that are used to identify the syndrome. These issues are investigated here through analysis of soft tissue facial feature asymmetry and family and syndrome resemblance in groups of syndrome-affected and normal individuals.

Photogrammetry was chosen as the method with which to produce the soft tissue facial measurements. Since the available published norms and measurement data on syndromes were obtained by calipers and rulers, it was necessary to investigate the differences between measurements taken by calipers, rulers, and photogrammetry. Chapter 2 presents a study of soft tissue facial feature measurements taken with calipers and a ruler by two anthropometrists with different levels of experience. Each observer repeated the facial measurements on four normal subjects. It was concluded that there was a systematic difference between the data obtained by the two types of instruments because the means, standard deviations, and ranges were often different. Furthermore, the level of experience of the anthropometrist was a factor in the amount of variation in the measurement data. Chapter 3 presents an investigation of the differences between soft tissue facial feature measurements obtained by calipers and photogrammetry. Two observers each repeated the measurements on one normal subject. This study also assessed the effect of marking the landmarks on the subject's face before taking measurements with calipers. This was done because many of the landmarks could not be identified on the images without first marking them on the subject, but there were no studies that researched the effect of marking the landmarks on the variability of facial measurement data. This study indicated that there were systematic differences between measurements gained by calipers and photogrammetry; therefore, measurement data on syndrome-affected individuals and normal subjects would need to be obtained by the same method (i.e., photogrammetry). Chapters 4 and 5 present examinations of two aspects of the soft tissue facial features of individuals with syndromes. The former chapter involves an investigation into soft tissue

facial feature asymmetry in medically normal and syndrome-affected males and females. The latter chapter is concerned with facial resemblance within families where the members were normal or were diagnosed with a syndrome. In addition, facial resemblance in related and unrelated subjects with the same syndrome was also investigated. In the reviews of the pertinent literature in Chapters 2 to 5, the terminology of the original authors describing the sample composition and any measurements taken has been retained.

The facial features present in the syndromes studied and the landmarks used in the investigations have not been described in each chapter as brief descriptions of each are presented in Table 1-1 and Figure 1-1, respectively. The facial features characteristic of the syndromes are based on the comprehensive reviews compiled by Gorlin et al. (1990) and Jones (1997), unless stated otherwise. The landmark information is based on the descriptions given by Farkas (1981, 1994), except gonion (Krogman, 1970) and center of the iris (a new landmark).

Table 1-1. Description of the Syndromes Diagnosed in the Subjects*

| Syndrome | Common Facial Characteristics Used in Diagnosis |
|---|---|
| Achondroplasia [4] | Low nasal bridge and underdeveloped maxilla/midface |
| Cardio-facio-cutaneous [1] | Downslanting eye fissures and low nasal bridge |
| Cohen [1] | Downslanting eye fissures; high nasal bridge; underdeveloped maxilla; short philtrum; open mouth with an arched, everted upper lip; and mild micrognathia |
| Crouzon [1] | Widely spaced eyes with protruding eyeballs; underdeveloped maxilla; and curved nose ("parrot-like") in some cases |
| Deletion of 18q [1] | Deep-set eyes; broad nasal bridge; underdeveloped or retruded maxilla; and "carp-like" mouth |
| Down [1] | Close-set, upward slanting eye fissures; underdeveloped midface with small nose and low bridge; broad, malformed lips; and open mouth |
| Myotonic dystrophy [2] | Triangular-shaped, open mouth |
| Placental anastamoses in monozygotic triplets [3] | Features are unique to each case, depending on the vessel abnormalities |
| Russell-Silver [2] | Triangular face shape; relatively large appearing eyes; and wide appearing mouth with down-turned corners and a thin upper vermilion |
| Spondylometaphyseal dysplasia [1] | There are no typical facial traits for this syndrome; the subject was included due to an unusual facial appearance |
| Stickler [1] | Underdeveloped midface or short maxilla resulting in midfacial flattening; prominent eyes; low nasal bridge; long philtrum; underdeveloped mandible; and small chin. The face may appear normal in up to 25% of patients |
| 3C (cranio-cerebello-cardiac) [1] | Widely spaced eyes with downslanting fissures and depressed nasal bridge (Kosaki et al., 1997) |
| Trisomy 8 (mosaic) [1] | Long face; widely spaced and deep-set eyes; wide nose, often with upturned tip; full lips with lower one sometimes everted; and small mandible |
| Uniparental disomy chromosome 16 (maternal) [1] | No information on the common facial characteristics of this syndrome is available. According to Schneider et al. (1996), the majority of reported cases involve fetal deaths or young infants |
| Velocardiofacial [1] | Long face; narrow palpebral fissures; flattened or deficient zygomatic arches; vertically long maxilla; wide nasal root with narrow alae; long philtrum; thin upper lip and open mouth; and retruded mandible with small chin |
| X-linked Aarskog carrier [1] | Affected individuals show widely spaced eyes with a minor downward slant; underdeveloped maxilla; short, broad nose; wide or long philtrum; and crease or depression under the lower lip. Carriers may exhibit some of the facial features |

* The number of individuals with each syndrome is given in square brackets beside the syndrome name. An additional seven individuals had unknown syndromes, two of which were initially diagnosed with velocardiofacial syndrome and one with occulodentodigital syndrome. The medical status of the individuals with syndromes and their family members participating in this research was ascertained by Dr. J. S. Bamforth, Director of the Medical Genetics Clinic, University of Alberta Hospital, Edmonton, Alberta, Canada. Several additional individuals, who were known to this author or to Dr. Bamforth, were also included as normal individuals without examination by Dr. Bamforth.

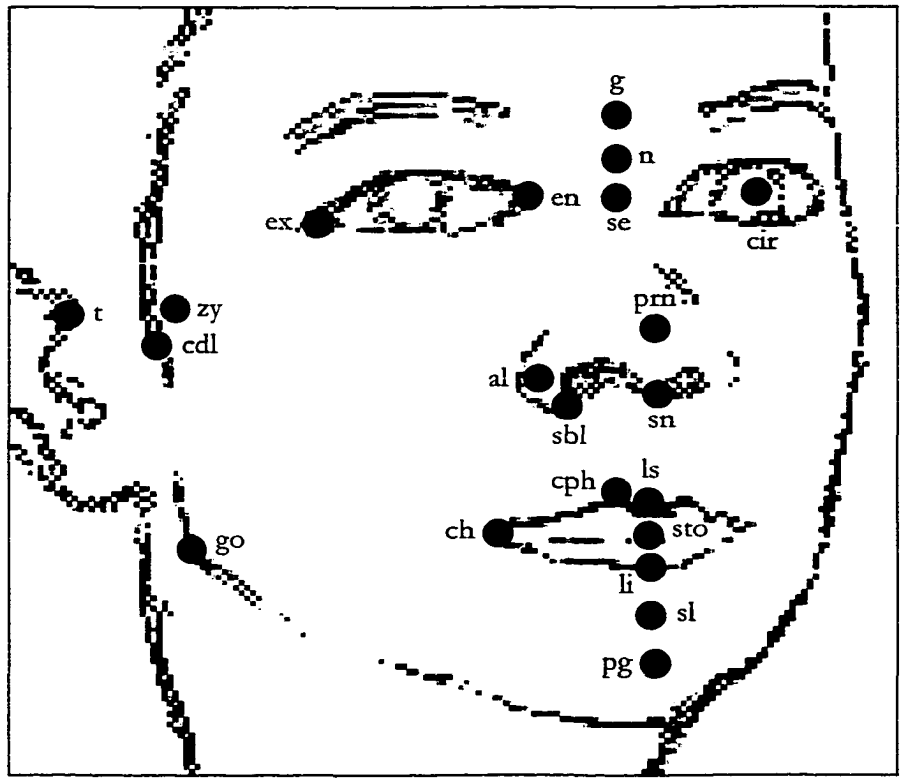


Figure 1-1. The Landmarks Used in the Studies

Paired landmarks are illustrated on one side of the face only. The landmarks were located on each subject's face as follows.

Paired landmarks:

| | | |
|---|---|---|
| al | alare | most lateral point on the nasal ala |
| cdl | condylion laterale | most lateral point on the mandibular condyle. Located when subject's mouth is open and traced back to its position when the mouth is closed |
| ch | cheilion | lateral union of the upper and lower lips |
| cir* | center of the iris | middle of the iris, as identified by the circular cursor during digitization |
| cph | christa philtri | elevated point on the philtrum above the vermilion line of the upper lip |
| en** | endocanthion | medial union of the upper and lower eyelids |
| ex | exocanthion | lateral union of the upper and lower eyelids |
| go | gonion | point at which the posterior border of the mandibular ramus joins the inferior margin of the mandibular body |
| sbl | subalare | where the lower alar base of the nose joins the skin of the upper lip |
| t | tragion | notch on the superior margin of the tragus |
| zy | zygion | most lateral point on the zygomatic arch. Identical to bony zygion |

Unpaired Landmarks:

| | | |
|---|---|---|
| g | glabella | most anterior midline point between the eyebrows (on the frontal bone). Identical to the bony glabella |
| li | labiale inferius | midpoint of the lower vermilion line |
| ls | labiale superius | midpoint of the upper vermilion line |
| n | nasion | the midline point of the bony nasofrontal suture. Identical to the bony nasion |
| pg | pogonion | most anterior midline point of the chin. Identical to the bony pogonion |
| prn | pronasale | most anterior point of the apex of the nose |
| se | sellion | most posterior point of the nasofrontal angle |
| sl | sublabiale | midline point of the mentolabial sulcus between the lip and chin |
| sn | subnasale | midpoint of the angle between the nasal septum and the upper lip |
| sto* | stomion | on the labial fissure at the vertical facial midline when the mouth and teeth are closed |

* These landmarks were never marked on the subjects' faces.

** This landmark could not be marked when an eyeliner pencil was used to mark the landmarks; however, when washable felt pens were used, endocanthion could be marked on the subjects' faces.

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# CHAPTER 2

# COMPARISON OF CALIPER- AND RULER-DERIVED MEASUREMENTS TAKEN BY AN EXPERIENCED AND AN AMATEUR ANTHROPOMETRIST[1]

## INTRODUCTION

Clinical morphology is a specialty that is based on recognition of a pattern of facial traits, allowing for age, sex, and ancestral background of the individuals in question. It is predominantly an art (Winter, 1996), learned through an apprenticeship to an experienced clinical geneticist. While a lack of knowledge on what measurements to take and how to analyze the data may prevent clinicians from performing measurements on their patients (Meaney and Farrer, 1986), diagnostic reference works are available which urge clinicians to objectify their impressions with measurements. These works range greatly in their encouragement from giving basic introductions to some measurements (e.g., Aase, 1990), to providing some previously published normative data with little comment (e.g., Gorlin et al., 1990; Jones, 1997), to presenting original or published normative data and discussing how measurements should be taken (e.g., Farkas, 1994a; Hall et al., 1989). The book by Hall et al. (1989) is a compendium of published norms, designed as a pocket book for the physician to use in clinical practice; however, the instruments recommended by these researchers were not always the same as the instruments used in the original studies. This raised the question of whether measurements obtained by different instruments are identical and if physicians should employ the same instruments as were used to collect the normative data, when utilizing such data to analyze a patient's measurements, as suggested by Farkas and Deutsch (1996). The objectives of this study were to compare the means and variability of repeated measurements taken with a ruler and anthropometric calipers. Two observers with vastly different amounts of experience collected the measurements, thereby allowing comparison of the data obtained by an amateur and an expert

[1] A version of this chapter has been published. Shaner DJ, Peterson AE, Beattie OB, and Bamforth JS (1998) Facial measurements in clinical genetics: How important are the instruments we use? American Journal of Medical Genetics *77*:384-390.

anthropometrist.

## LITERATURE REVIEW

Many of the investigations into measurement error have not explored the instruments as part of the problem of measurement variability (e.g., Chumlea et al., 1984; Gaito and Gifford, 1958; Gavan, 1950; Habicht et al., 1979; Herskovits, 1930; Johnston and Mack, 1985; Kemper and Pieters, 1974; Marks et al., 1989; Marshall, 1937; Martorell et al., 1975; Meredith, 1936; Mueller and Martorell, 1988; Solow, 1966; Spielman et al., 1972). In earlier publications, part of this lack of interest in the instruments may have been due to the conviction that the tools used were standardized, and they, therefore, did not contribute to measurement error (Davenport et al., 1934). As pointed out by Cameron (1986), between 1850 and 1950 anthropometric tools remained essentially unchanged; however, even in 1942 Steggerda indicated that the 11 observers he tested used a variety of different instruments. Lincoln (1930) thought that the use of superior tools would obviate instrument error, although this was not found to be so. Others have mentioned several general aspects of the instruments and how they were used as possibly affecting measurement interpretation and reliability: the overall accuracy of the instruments, said to range from 0.5 mm (Ward and Jamison, 1991) to 5 mm (Todd, 1925); the instruments' ability to conform to the contour being measured (Pérez-Pérez et al., 1990); rounding errors (Harvey et al., 1994; Pérez-Pérez et al., 1990; Ulijaszek and Lourie, 1994); positioning of the instruments (Davenport et al., 1934; Jamison and Zegura, 1974; Malina et al., 1973); and incorrect reading of the scales (Cameron, 1986; Davenport et al., 1934; Malina et al., 1973). Particular tools that were the major cause of landmark location problems have also been discussed (Page, 1976; Utermohle and Zegura, 1982).

More specific investigations into the role of the instruments in measurement error were carried out on measurements of stature (Voss et al., 1990), skinfold thickness (Sloan and Shapiro, 1972), and facial and/or body measurements (Harvey et al., 1994; Malina et al., 1973; Munro et al., 1966). Of these, only Voss et al. (1990) and Sloan and Shapiro (1972) repeated the measurements on

the same subjects with a variety of different instruments. Voss et al. (1990) concluded that the five instruments tested made a very small contribution to the total variability of repeated stature measurements, and a significant difference for reproducibility was found only in the case of one instrument (the pocket stadiometer). In Sloan and Shapiro's (1972) study, the means of repeated measurements obtained with each of three skinfold calipers were said to be very similar, though statistically significant interobserver measurement differences were found between the calipers. The other studies did not replicate the measurements with different instruments, but rather grouped their error statistics by instrument. Although Malina et al. (1973) stated that, for example, spreading and sliding calipers had good replicability, this was specifically ascribed to factors other than the instrument, such as the ease of landmark location. Munro et al. (1966) found significant intraobserver variance in measurements taken with an anthropometer, spreading caliper, and measuring tape and significant interobserver differences in measurements taken with spreading and sliding calipers and a measuring tape. Harvey et al. (1994) investigated the effect of the size of tape measures' divisions (1 mm vs. 5 mm) on the distribution of head circumference measurements and concluded that there was bias in the measurements taken with the tape measure with the larger divisions.

## MATERIALS AND METHODS

The facial measurements used in this study were taken with a sliding or spreading caliper and an ordinary 30 cm long ruler of office quality; all were graduated in millimeters. Two observers with different amounts of experience were involved: Observer 1 had ten years of experience in the use of calipers for taking facial measurements, and Observer 2 had two months of training from Observer 1 prior to this study. Four normal women were the subjects of this investigation. Ten basic facial measurements were taken; the landmark nomenclature and abbreviations were from Farkas (1994b). Observer 1 repeated the measurements on five separate occasions, while Observer 2 replicated the measurements on six separate occasions (except for zygion-zygion from Subject A, which was taken five times with a caliper). To minimize the possibility of the observers remembering the previous

values, the subjects were only measured once per day, and the values were transcribed on a new sheet of paper each time. The dimensions were identified as either Type 1, in which both of the landmarks could be defined by eye, or Type 2, in which at least one landmark was a bony point located by palpation (osteometric landmark). The Type 1 measurements, which were all horizontal distances, were taken between pairs of the landmarks as follows: the endocanthions (en) of both eyes, the exocanthions (ex) of both eyes, the exocanthion and endocanthion of each eye, the cheilions (ch), and the nasal alare (al). The following Type 2 measurements were taken: the vertical distances between nasion (n) and subnasale, subnasale (sn) and pogonion (pg), and stomion (sto) and pogonion, and the horizontal distance between the zygions (zy). The sliding caliper was used for all of these measurements except for zygion-zygion, which was taken by spreading caliper.

When taking measurements with all instruments, the subject's face was positioned approximately in the Frankfort Horizontal Plane. When using the calipers, the osteometric points were identified by palpation and the calipers just touched the skin, but were not pressed down sufficiently to cause indentations. For measurements around the eyes, the instrument was introduced as closely as possible without touching the sensitive areas. The observers did not close either of their eyes during this procedure. Measurements taken with the ruler were performed according to the techniques described by Hall et al. (1989). Keeping both eyes open, the observer held the ruler up to the subject's face. Then, with the non-dominant eye shut, the observer's head was moved about 15 cm away from the face of the subject and directly opposite one landmark (which, if an osteometric landmark, was first palpated with the free hand). After aligning the first mark of the ruler to the landmark, the ruler was held between the thumb and index finger with the remaining fingers resting on the subject's face for stability. The observer's head was then shifted until it was directly opposite the second landmark and the distance was read. All measurements were recorded to the nearest millimeter.

The caliper- and ruler-derived data for the measurements taken by each observer were compared with the paired t-test (two-tailed). The differences in the number of repetitions and the

disparity in their levels of experience did not permit direct statistical comparison between the data from both observers. Global t-tests (paired, two-tailed) were also performed in order to compare the caliper- and ruler-derived measurements and global F-tests were used to investigate the averages of the variances obtained by the different measuring instruments. For each observer, these statistics were carried out by combining the data from all four subjects for each type of measurement.

## RESULTS

### *The Statistical Results Obtained for the Two Observers' Data*

Summaries of the measurement data on the four subjects are in Table 2-1 for Observer 1 and Table 2-2 for Observer 2. The caliper-derived data taken by Observer 1 showed three trends: the means were larger and the standard deviations and ranges were smaller when compared with the ruler-derived data. All of the dimensions had at least one statistically significant result, except for the Type 2 dimensions of subnasale-pogonion and stomion-pogonion. These were also the only dimensions that did not have consistently greater means for the caliper-derived measurements on all subjects, nor were the standard deviations and measurement value ranges consistently lower for the caliper-derived data.

The data gathered by Observer 2 also showed that the means of repeated caliper-derived measurements were often larger than the means of repeated ruler-derived measurements. As was found for the data of Observer 1, the data obtained by Observer 2 showed that the caliper-derived means were usually smaller than the ruler-derived means for subnasale-pogonion and stomion-pogonion. Unlike the findings for the data taken by Observer 1, the ranges between the minimum and maximum measurement values and the standard deviations were usually less in the ruler-derived data than the caliper-derived data obtained by Observer 2. Five dimensions had no statistically significant differences when the results of the t-tests were examined: endocanthion-endocanthion, left exocanthion-endocanthion, alare-alare, subnasale-pogonion, and stomion-pogonion. The differences between this inexperienced observer's data and that of the expert Observer 1 highlighted

the need for an extended period of training with calipers and interobserver testing, if the results of both observers are to be pooled or compared.

*The Results of the Global Testing for the Two Observers' Data*

The t-tests comparing the global means of the caliper- and ruler-derived Type 1 and Type 2 data from both observers were all highly statistically significant, underscoring the differences between measurements taken by these instruments (Table 2-3A). One possible explanation for the significant differences between the caliper- and ruler-derived measurements was that the calibrations for the ruler and sliding caliper were different. This was investigated by taking a variety of measurements from the ruler markings with the sliding caliper, but, in all cases, the values from the caliper were in agreement with those from the ruler. Based on the statistically significant differences between the measurements taken with a ruler and calipers by each observer and the typically larger means in the caliper-derived data, it was concluded that there was a systematic difference between caliper-derived and ruler-derived measurements that could not be explained by differing instrument calibrations.

The only measurements that were not statistically significantly different for both observers and all subjects were subnasale-pogonion and stomion-pogonion. These were also the only measurements for which the landmarks were on the same approximate plane with no rigid facial structures protruding outward between them; therefore, the ruler could easily touch both of the landmarks like the arms of the sliding caliper could. (It should be noted that stomion was located at the sulcus between the lips and, therefore, was not actually touched by the ruler, but was closely approximated on the surface of the lips.) Farkas (1994c) also noted that transparent rulers were still in wide use by "amateur anthropometrists" and stated that rulers might give accurate measurements under the circumstances described above for these two measurements. Interestingly, these were both Type 2 measurements involving palpation of one of the landmarks, suggesting an interplay of both landmark location and instrument in measurement variability: When the landmarks can be located consistently, the data obtained by instruments that can be placed directly on the landmarks can be expected to

have a smaller range of values from repeated measurements than can the data from instruments which must be held at a distance. Both observers were particularly aware of an increase in the variability of the Type 2 measurements when having to locate osteometric landmarks. Comparison of the Type 1 and Type 2 global average variances confirmed this for both observers, regardless of whether a ruler or caliper was used (Table 2-3B). F-tests comparing the caliper- and ruler-derived average variances were statistically significantly different only for the Type 1 and Type 2 data gathered by Observer 1, emphasizing the distinctions between the expert and inexperienced anthropometrists.

## DISCUSSION

While some anthropometrists, such as Farkas (1994b), clearly state the importance of using the proper instruments and the correct technique, clinicians may opt for other instruments, especially rulers and tape measures. This is probably due to a lack of training in the use of the specialized anthropometric instruments, dealing with young patients who are not cooperative enough to allow the use of anthropometric instruments, and the cumbersome number of specialized instruments (Hall et al., 1989). However, it has been shown that measurements derived from different instruments are not the same. The presence of large differences in the ranges of the caliper- and ruler-derived zygion-zygion measurements, the landmarks of which were located several centimeters posterior to the front of the face where the ruler was held, served as a caution to using rulers to measure between landmarks so distant from the instrument. Table 2-4 lists the recommended and alternate instruments suggested by Hall et al. (1989) and those actually used by the original researchers for eight of the measurements used in this study. It is interesting to note that many of the charts in Hall et al. (1989) presented data combined from several sources, often with non-overlapping age ranges. These charts may not be appropriate for use in longitudinal growth investigations due to the different instruments used by the original investigators.

In addition to the systematic differences found between caliper- and ruler-derived data, the

problem of taking a single measurement was also highlighted by the data presented here. That is, if only one measurement is taken on each individual (for each of the dimensions), the representation of his or her facial structure might be deceiving. For example, the endocanthion-endocanthion measurements taken by sliding caliper on Subject C by Observer 2 range from -1 to -3 standard deviations from the normal adult population (mean 31.8 mm; standard deviation 2.3 mm) taken with the same type of instrument (Farkas et al., 1994). While the mean indicated that this subject's endocanthion-endocanthion length was mildly abnormally short, a single measurement by itself could indicate that the subject was normal (within ±1 standard deviation), mildly abnormal (greater than ±1 standard deviation, but not more than ±2 standard deviations), or definitely abnormal (±3 or more standard deviations). This was true for both the caliper and ruler data, but the ruler yielded larger ranges of values for most dimensions than did the calipers in the hands of the expert anthropometrist, Observer 1. Therefore, erroneous results may be obtained from a single measurement often, regardless of the instrument used. If measurements are repeated a sufficient number of times, the mean should be a good indicator of the true measurement. The data presented provided evidence that using a ruler to take facial measurements, even when repetitions were made, often yielded values that were statistically different from measurements taken by anthropometric calipers. So, while the inexperienced anthropometrist may favor a ruler for its ease of use and, as was found in this study, may find that the standard deviations and ranges of the measurement values are often lower when a ruler is used, the significant differences between the means of caliper- and ruler-derived measurements prohibit comparison of data taken by different instruments. The sizable ranges of the measurement values taken by both observers also indicated that a portion of the normal range given in normative population studies is due to measurement variability.

It is suggested that clinicians who are interested in taking measurements invest in anthropometric instruments designed for the specific task. The expense of the equipment (which could consist of one sliding and one spreading caliper for basic facial measurements) will be offset by more accurate measurements and will allow comparison to extensive normative data such as that by

Farkas et al. (1994). As well, measurements taken by ruler on an uncooperative patient are likely to be even more variable than caliper-derived measurements taken on the same patient. The differences between the expert and inexperienced observers' data highlight the need for extended practice with calipers. The lower standard deviations and measurement value ranges for the ruler-derived data of Observer 2 are probably more indicative of the ease of using a ruler over calipers when inexperienced, than of the greater reliability of measurements taken by ruler. While compendia are convenient, it is also recommend that clinicians go to the original sources of the normative data for instructions on how to take measurements, what instruments to use for each one, and how to interpret measurements taken in clinical practice. Anthropometrists should also be aware that there is considerable variation in the measurements that are taken.

Table 2-1. Comparison of the Caliper- and Ruler-Derived Measurement Data Gathered by Observer 1, an Experienced Anthropometrist

| Mmt & Type | Subject & (Instrument) | Mean | Range | SD | Sig | Mmt & Type | Subject & (Instrument) | Mean | Range | SD | Sig |
|---|---|---|---|---|---|---|---|---|---|---|---|
| en-en Type 1 | A (Caliper) | 31.0 | 31-31 | 0.0 | ‡‡ | ch-ch Type 1 | A (Caliper) | 49.8 | 48-51 | 1.6 | ‡‡ |
| | A (Ruler) | 29.0 | 28-30 | 0.7 | | | A (Ruler) | 43.2 | 42-45 | 1.6 | |
| | B (Caliper) | 25.2 | 24-27 | 1.3 | | | B (Caliper) | 48.2 | 46-51 | 2.3 | |
| | B (Ruler) | 23.8 | 22-25 | 1.1 | | | B (Ruler) | 43.6 | 41-47 | 2.4 | |
| | C (Caliper) | 29.6 | 29-30 | 0.5 | ‡‡ | | C (Caliper) | 51.8 | 48-54 | 2.3 | |
| | C (Ruler) | 26.2 | 25-28 | 1.1 | | | C (Ruler) | 48.8 | 46-53 | 3.1 | |
| | D (Caliper) | 32.2 | 31-33 | 0.8 | ‡‡ | | D (Caliper) | 49.0 | 45-53 | 2.9 | |
| | D (Ruler) | 30.2 | 30-31 | 0.4 | | | D (Ruler) | 46.6 | 42-49 | 2.8 | |
| ex-ex Type 1 | A (Caliper) | 89.8 | 88-91 | 1.3 | ‡‡ | zy-zy Type 2 | A (Caliper) | 130.6 | 128-132 | 1.7 | |
| | A (Ruler) | 84.2 | 82-88 | 2.7 | | | A (Ruler) | 128.0 | 127-132 | 2.2 | |
| | B (Caliper) | 84.6 | 83-86 | 1.1 | ‡‡ | | B (Caliper) | 137.8 | 136-140 | 1.5 | † |
| | B (Ruler) | 81.2 | 77-84 | 2.7 | | | B (Ruler) | 128.4 | 122-132 | 4.6 | |
| | C (Caliper) | 89.4 | 87-91 | 1.8 | | | C (Caliper) | 129.8 | 126-134 | 3.5 | |
| | C (Ruler) | 86.6 | 83-91 | 3.6 | | | C (Ruler) | 125.8 | 122-131 | 3.6 | |
| | D (Caliper) | 96.2 | 94-97 | 1.3 | ‡‡ | | D (Caliper) | 140.2 | 139-141 | 0.8 | † |
| | D (Ruler) | 90.6 | 89-93 | 1.8 | | | D (Ruler) | 136.0 | 133-139 | 2.2 | |
| ex-en R Type 1 | A (Caliper) | 30.6 | 30-31 | 0.5 | ‡ | n-sn Type 2 | A (Caliper) | 54.0 | 52-55 | 1.2 | |
| | A (Ruler) | 28.2 | 27-29 | 0.8 | | | A (Ruler) | 52.8 | 51-56 | 1.9 | |
| | B (Caliper) | 31.2 | 31-32 | 0.4 | | | B (Caliper) | 44.2 | 43-46 | 1.3 | |
| | B (Ruler) | 29.6 | 26-33 | 2.9 | | | B (Ruler) | 42.8 | 36-46 | 4.1 | |
| | C (Caliper) | 31.2 | 31-32 | 0.4 | | | C (Caliper) | 55.4 | 54-57 | 1.5 | † |
| | C (Ruler) | 30.4 | 28-32 | 1.5 | | | C (Ruler) | 53.2 | 52-56 | 1.6 | |
| | D (Caliper) | 32.8 | 32-34 | 0.8 | | | D (Caliper) | 47.4 | 45-52 | 2.8 | |
| | D (Ruler) | 30.6 | 27-33 | 2.3 | | | D (Ruler) | 45.6 | 44-48 | 1.5 | |
| ex-en L Type 1 | A (Caliper) | 30.8 | 30-31 | 0.4 | † | sn-pg Type 2 | A (Caliper) | 57.0 | 54-59 | 2.0 | |
| | A (Ruler) | 28.8 | 28-31 | 1.3 | | | A (Ruler) | 56.4 | 54-58 | 1.5 | |
| | B (Caliper) | 31.0 | 30-32 | 0.7 | | | B (Caliper) | 58.6 | 56-61 | 2.3 | |
| | B (Ruler) | 29.8 | 27-33 | 2.6 | | | B (Ruler) | 57.0 | 54-59 | 2.0 | |
| | C (Caliper) | 30.8 | 30-31 | 0.4 | | | C (Caliper) | 67.6 | 63-71 | 3.0 | |
| | C (Ruler) | 30.6 | 28-32 | 1.7 | | | C (Ruler) | 68.0 | 65-70 | 1.9 | |
| | D (Caliper) | 32.4 | 31-34 | 1.1 | | | D (Caliper) | 55.0 | 53-56 | 1.2 | |
| | D (Ruler) | 30.0 | 27-31 | 1.7 | | | D (Ruler) | 52.8 | 51-54 | 1.1 | |
| al-al Type 1 | A (Caliper) | 30.4 | 29-32 | 1.1 | | sto-pg Type 2 | A (Caliper) | 39.6 | 38-42 | 1.5 | |
| | A (Ruler) | 28.6 | 27-30 | 1.1 | | | A (Ruler) | 39.6 | 38-42 | 1.8 | |
| | B (Caliper) | 31.2 | 31-32 | 0.4 | ‡‡ | | B (Caliper) | 37.4 | 36-39 | 1.5 | |
| | B (Ruler) | 29.8 | 29-30 | 0.4 | | | B (Ruler) | 38.6 | 37-41 | 1.5 | |
| | C (Caliper) | 34.2 | 31-36 | 1.9 | † | | C (Caliper) | 47.2 | 46-48 | 0.8 | |
| | C (Ruler) | 31.0 | 30-33 | 1.2 | | | C (Ruler) | 45.0 | 43-48 | 2.0 | |
| | D (Caliper) | 35.0 | 34-36 | 0.7 | † | | D (Caliper) | 33.8 | 32-36 | 1.5 | |
| | D (Ruler) | 33.4 | 32-34 | 0.9 | | | D (Ruler) | 34.6 | 34-36 | 0.9 | |

These data were rounded to one decimal place for this table, but the complete values were used in all calculations. All measurements are in millimeters. The number of measurements taken was five in all cases. The Mmt & Type column lists the measurements taken and whether the landmarks were identified visually (Type 1) or by palpation (Type 2). R and L refer to the right and left sides, respectively. The SD column contains the standard deviations. The Sig column indicates significant t-test probabilities of the caliper- and ruler-derived data comparisons as follows: † is $0.01 < P \leq 0.05$; ‡‡ is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$.

Table 2-2. Comparison of the Caliper- and Ruler-Derived Measurement Data Gathered by Observer 2, an Amateur Anthropometrist

| Mmt & Type | Subject & (Instrument) | Mean | Range | SD | Sig | Mmt & Type | Subject & (Instrument) | Mean | Range | SD | Sig |
|---|---|---|---|---|---|---|---|---|---|---|---|
| en-en Type 1 | A (Caliper) | 30.3 | 29-32 | 1.0 | | ch-ch Type 1 | A (Caliper) | 47.2 | 45-50 | 1.7 | |
| | A (Ruler) | 30.7 | 30-32 | 0.8 | | | A (Ruler) | 46.3 | 43-48 | 2.1 | |
| | B (Caliper) | 25.0 | 24-27 | 1.3 | | | B (Caliper) | 47.8 | 45-51 | 2.1 | |
| | B (Ruler) | 24.8 | 24-26 | 1.0 | | | B (Ruler) | 45.7 | 42-49 | 2.8 | |
| | C (Caliper) | 28.3 | 26-30 | 1.6 | | | C (Caliper) | 51.3 | 49-54 | 2.2 | |
| | C (Ruler) | 27.7 | 27-28 | 0.5 | | | C (Ruler) | 46.8 | 45-49 | 1.5 | ‡ |
| | D (Caliper) | 31.0 | 30-33 | 1.1 | | | D (Caliper) | 48.0 | 46-50 | 1.4 | |
| | D (Ruler) | 30.8 | 29-32 | 1.0 | | | D (Ruler) | 47.5 | 46-50 | 1.5 | |
| ex-ex Type 1 | A (Caliper) | 87.8 | 83-92 | 3.3 | | zy-zy Type 2 | A (Caliper) | 125.6 | 123-130 | 2.7 | |
| | A (Ruler) | 84.0 | 82-87 | 2.4 | | | A (Ruler) | 120.7 | 115-127 | 4.7 | |
| | B (Caliper) | 83.3 | 81-87 | 2.2 | | | B (Caliper) | 128.2 | 122-137 | 5.7 | |
| | B (Ruler) | 79.8 | 77-82 | 1.7 | † | | B (Ruler) | 124.2 | 118-128 | 3.9 | |
| | C (Caliper) | 87.0 | 83-91 | 3.0 | | | C (Caliper) | 119.5 | 117-126 | 3.4 | |
| | C (Ruler) | 83.5 | 82-85 | 1.2 | | | C (Ruler) | 121.5 | 110-126 | 6.0 | |
| | D (Caliper) | 88.8 | 86-92 | 2.2 | | | D (Caliper) | 126.5 | 123-133 | 3.6 | |
| | D (Ruler) | 86.8 | 84-91 | 2.3 | | | D (Ruler) | 121.2 | 117-126 | 3.3 | † |
| ex-en R Type 1 | A (Caliper) | 29.8 | 28-32 | 1.5 | | n-sn Type 2 | A (Caliper) | 52.7 | 52-54 | 0.8 | |
| | A (Ruler) | 28.2 | 27-30 | 1.0 | † | | A (Ruler) | 49.7 | 47-52 | 1.6 | † |
| | B (Caliper) | 29.0 | 28-30 | 0.6 | | | B (Caliper) | 44.0 | 41-45 | 1.5 | |
| | B (Ruler) | 28.2 | 27-30 | 1.2 | | | B (Ruler) | 41.2 | 40-42 | 1.0 | † |
| | C (Caliper) | 30.5 | 30-31 | 0.5 | | | C (Caliper) | 53.7 | 52-55 | 1.2 | |
| | C (Ruler) | 29.7 | 29-30 | 0.5 | † | | C (Ruler) | 50.5 | 48-52 | 1.6 | † |
| | D (Caliper) | 30.2 | 30-31 | 0.4 | | | D (Caliper) | 47.5 | 46-50 | 1.5 | |
| | D (Ruler) | 28.2 | 27-29 | 0.8 | †† | | D (Ruler) | 42.5 | 42-44 | 0.8 | ‡ |
| ex-en L Type 1 | A (Caliper) | 28.7 | 27-31 | 1.4 | | sn-pg Type 2 | A (Caliper) | 52.5 | 51-55 | 1.6 | |
| | A (Ruler) | 28.8 | 27-31 | 1.3 | | | A (Ruler) | 53.2 | 51-55 | 1.6 | |
| | B (Caliper) | 28.3 | 27-30 | 1.0 | | | B (Caliper) | 56.8 | 55-58 | 1.2 | |
| | B (Ruler) | 28.8 | 27-30 | 1.2 | | | B (Ruler) | 56.5 | 55-58 | 1.0 | |
| | C (Caliper) | 29.0 | 27-31 | 1.7 | | | C (Caliper) | 61.7 | 60-63 | 1.5 | |
| | C (Ruler) | 29.0 | 28-30 | 0.6 | | | C (Ruler) | 62.0 | 61-63 | 1.1 | |
| | D (Caliper) | 29.3 | 28-31 | 1.0 | | | D (Caliper) | 49.8 | 47-52 | 2.4 | |
| | D (Ruler) | 28.8 | 28-30 | 1.0 | | | D (Ruler) | 51.0 | 50-52 | 0.9 | |
| al-al Type 1 | A (Caliper) | 29.8 | 29-30 | 0.4 | | sto-pg Type 2 | A (Caliper) | 36.0 | 32-39 | 3.0 | |
| | A (Ruler) | 29.7 | 29-30 | 0.5 | | | A (Ruler) | 36.3 | 34-38 | 1.6 | |
| | B (Caliper) | 31.0 | 31-31 | 0.0 | | | B (Caliper) | 36.0 | 35-38 | 1.1 | |
| | B (Ruler) | 31.2 | 28-33 | 1.8 | | | B (Ruler) | 36.0 | 35-38 | 1.3 | |
| | C (Caliper) | 35.8 | 35-39 | 1.6 | | | C (Caliper) | 43.3 | 41-45 | 1.5 | |
| | C (Ruler) | 34.2 | 33-35 | 0.8 | | | C (Ruler) | 43.8 | 42-46 | 1.3 | |
| | D (Caliper) | 35.0 | 34-36 | 0.6 | | | D (Caliper) | 31.8 | 31-33 | 0.8 | |
| | D (Ruler) | 35.0 | 34-36 | 0.9 | | | D (Ruler) | 32.0 | 31-34 | 1.3 | |

These data were rounded to one decimal place for this table, but the complete values were used in all calculations. Al measurements are in millimeters. The number of measurements taken was six, except for the zy-zy series taken by calipe on Subject A where five repetitions were done. The Mmt & Type column lists the measurements taken and whether th landmarks were identified visually (Type 1) or by palpation (Type 2). R and L refer to the right and left sides, respectively The SD column contains the standard deviations. The Sig column indicates significant t-test probabilities of the caliper and ruler-derived data comparisons as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$.

Table 2-3A. Global Statistics for the Caliper- and Ruler-Derived Measurements of Observer 1 (Experienced Anthropometrist) and Observer 2 (Amateur Anthropometrist): T-Test Results

| Mmt Type | Observer | Mean Difference Caliper–Ruler | SEM Diff | Degrees of Freedom | Computed T Value | Sig |
|---|---|---|---|---|---|---|
| Type 1 | 1 | 2.7 | 0.3 | 119 | 10.19 | ‡ |
| Type 2 | 1 | 1.9 | 0.4 | 79 | 4.41 | ‡ |
| Type 1 | 2 | 1.2 | 0.2 | 143 | 5.67 | ‡ |
| Type 2 | 2 | 1.5 | 0.4 | 94 | 3.42 | ‡ |

Table 2-3B. Global Statistics for the Caliper- and Ruler-Derived Measurements of Observer 1 (Experienced Anthropometrist) and Observer 2 (Amateur Anthropometrist): F-Test Results

| Mmt Type | Observer | Average Variance of Caliper Mmts | Average Variance of Ruler Mmts | Degrees of Freedom for Caliper Mmts | Degrees of Freedom for Ruler Mmts | F Ratio | Sig |
|---|---|---|---|---|---|---|---|
| Type 1 | 1 | 1.7 | 3.9 | 96 | 96 | 2.27 | ‡ |
| Type 2 | 1 | 3.6 | 5.7 | 64 | 64 | 1.56 | † |
| Type 1 | 2 | 2.6 | 2.0 | 120 | 120 | 1.32 | |
| Type 2 | 2 | 6.0 | 6.5 | 79 | 80 | 1.08 | |

The data were rounded to one decimal place for the tables, but the complete values were used in all calculations. Mmt(s)=measurement(s). In Table 23A, the SEM Diff column has the standard errors of the mean differences. The Sig columns indicate significant t- and F-test probabilities as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$.

Table 2-4. Comparison of Hall and Others' (1989) Recommended and Alternate Instruments and Those Used by the Original Researchers for Eight Measurements Employed in This Study*

| Mmt | Recommended Instrument(s) | Alternate Instrument(s) | Instrument Used and Reference |
|---|---|---|---|
| en-en | Transparent Ruler | Tape Measure; Blunt Caliper | Sliding Caliper: Feingold and Bossert (1974)[a]<br>Caliper Rule: Laestadius et al. (1969)[a]<br>Caliper or Steel Tape: Merlob et al. (1984) |
| ex-ex | Transparent Ruler | Tape Measure; Blunt Caliper | Sliding Caliper: Feingold and Bossert (1974)[a]<br>Caliper Rule: Laestadius et al. (1969)[a,c]<br>Caliper or Steel Tape: Merlob et al. (1984) |
| ex-en | Transparent Ruler; Blunt Caliper | Tape Measure | Custom Instrument: Chouke (1929)[a]<br>Sliding Caliper: Farkas (1981)[a]<br>Caliper, Plastic Ruler, or Steel Tape: Iosub et al. (1985)<br>Ruler or Steel Tape: Jones et al. (1978)[b]<br>Caliper Rule: Laestadius et al. (1969)[a]<br>Ruler: Méhes and Kitzvéger (1974)[b,d]<br>Caliper or Steel Tape: Merlob et al. (1984)[b]<br>Thomas et al. (1987)[a,e] |
| al-al | Spreading Caliper | Transparent Ruler; Tape Measure | Sliding Caliper: Farkas (1981)[a]<br>Not Stated: Goodman and Gorlin (1977)[a] |
| ch-ch | Spreading Caliper | Transparent Ruler; Tape Measure | Feingold and Bossert (1974)[a,f]<br>Sliding Caliper: Farkas (1981)[a]<br>Caliper or Steel Tape: Merlob et al. (1984) |
| n-sn | Spreading Caliper | Tape Measure | Sliding Caliper: Farkas (1981)[a]<br>Not Stated: Goodman and Gorlin (1977)[a]<br>Roentgencephalometric Measurements: Saksena et al. (1987)[a] |
| zy-zy | Spreading Caliper | Tape Measure | Spreading Caliper: Farkas (1981) |

* Two of the measurements used in the present study, sn-pg and sto-pg, were not covered by Hall et al. (1989). Mmt=measurement. [a,b] References with the same superscript are combined into a single chart for that measurement in Hall et al. (1989). [c] Laestadius et al. (1969) actually presented data on the outer orbital dimensions, which were measured from the lateral edges of the bony orbits, not the distance between the exocanthions. [d] Méhes and Kitzvéger (1974) actually presented data on the inner canthal index, the ratio of the inner canthal distance and head circumference, not measurements for the length between the canthi. [e] These authors used previously published data from Jones et al. (1978) and Chouke (1929). [f] Although listed as a reference for the chart on the distance between the cheilions, Feingold and Bossert (1974) have no such data in this publication.

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# CHAPTER 3

# COMPARISON OF PHOTOGRAMMETRIC AND CALIPER-DERIVED MEASUREMENTS AND THE EFFECT OF MARKING THE LANDMARKS PRIOR TO TAKING MEASUREMENTS[1]

## INTRODUCTION

Allanson et al. (1993) reported that up to 30 minutes were needed to take 21 facial measurements with calipers on cooperative subjects with Down syndrome. Whereas one-half hour might not be impractical when measuring willing subjects, it is a substantial amount of time to require young children to remain motionless. In addition, this length of time might negatively influence participation rates, especially when all members of a family are asked to take part in a study involving soft tissue facial measurements. The method of photogrammetry (by which measurements are extracted from images) should be considered as a practical alternative for collecting facial measurements: While the time needed to obtain the data from the images may be lengthy, it takes only minutes to acquire images of each subject. An investigation was undertaken into the method of photogrammetry and how photogrammetric measurements compared with caliper-derived measurements. While there have been studies comparing facial measurements taken by photogrammetry and calipers, such as that by Farkas et al. (1980), they extracted measurements from single photographs, whereas a stereophotogrammetric method was employed in this study. It was found, however, that most of the landmarks could not be located on the images without being marked on each subject's face prior to the images being taken. This raised the issue of what effect marking the landmarks has on the measurement values. Consequently, while the primary objective of this investigation was to compare photogrammetric measurements with measurements taken by

[1] A version of this chapter has been published. Shaner DJ, Bamforth JS, Peterson AE, and Beattie OB (1998) Technical note: Different techniques, different results—A comparison of photogrammetric and caliper-derived measurements. American Journal of Physical Anthropology *106*:547-552.

caliper with the landmarks marked, the difference between caliper-derived measurements taken with and without the landmarks marked was also studied. The results of this study may interest anthropologists and medical clinicians who take measurements, as well as those who use measurements gathered by others (e.g., normative data) when the exact techniques of data collection are unknown.

## LITERATURE REVIEW

Although photogrammetry is a well-established method, having been in use since shortly after the invention of modern photographic methods in 1839 (Wolf, 1983), its use in studying humans is relatively recent. Sheldon's 1940 publication has been credited for bringing this technique to the attention of North American researchers involved in quantifying human morphology (Gavan et al., 1952; Tanner and Weiner, 1949). Sheldon (1927/28) turned to photogrammetry because he wanted a technique which would have small uncertainties and be sensitive to differences in head and facial measurements. He felt that photogrammetry would fulfill these needs because it allowed the observer to take the measurements at his or her convenience. Following Sheldon, many others have used two- and three-dimensional photogrammetric techniques to measure the soft tissues of the face. These investigations ranged from clinical orthodontic studies based on photographs of the lower face (e.g., Neger, 1959; Stoner, 1955; Sushner, 1977); tooth and facial morphology from contour maps (e.g., Savara, 1965); facial abnormalities from single photographs (e.g., Butler et al., 1988; Clarren et al., 1987; Fraser and Pashayan, 1970; Kaiser and Abt, 1996; Sharland et al., 1993; Stengel-Rutkowski et al., 1984) and contour maps (e.g., Burke, 1971, 1983); pre-and post-surgery changes in three-dimensional representations of the face (e.g., Berkowitz and Cuzzi, 1977; Burke et al., 1983; Rasse et al., 1991); and normal facial growth from two-dimensional photographs (e.g., Hautvast, 1971) and from three- dimensional representations (e.g., Burke and Beard, 1979; Burke and Hughes-Lawson, 1989). Other studies were primarily concerned with the theoretical and practical aspects of various photogrammetric systems in the study of the human form (e.g., Adams, 1978; Chadwick, 1992;

Deacon et al., 1991; DiLiberti and Olson, 1991; Gruner et al., 1967; Hertzberg et al., 1957; Hunt and Giles, 1956; MacLeod, 1986; Miskin, 1956), including uncertainty in photogrammetric measurements (e.g., Burke and Beard, 1967; Farkas, 1981, 1994c; Farkas et al., 1980; Gavan et al., 1952; Tanner and Weiner, 1949).

Some researchers reported marking the soft tissues of the face before taking direct or indirect measurements (Burke, 1971, 1983; Burke et al., 1983; Burke and Beard, 1979; Farkas, 1981, 1994a, b, c, d; Farkas et al., 1980; Farkas and Deutsch, 1996; Gavan et al., 1952; Hertzberg et al., 1957; Tanner and Weiner, 1949); however, the purposes of the markings, when specified, were varied. They were described as necessary for aligning the photographs for plotting (Burke, 1971); identifying the landmarks in the photographs (Gavan et al., 1952); comparing photogrammetric and direct anthropometric distances (Hertzberg et al., 1957); uniformly locating landmarks used in multiple measurements (Farkas, 1981, 1994b; Farkas and Deutsch, 1996); diminishing measurement uncertainties (Farkas, 1994d; Farkas and Deutsch, 1996); decreasing the procedure length (Farkas and Deutsch, 1996); and aiding new practitioners (Farkas, 1994a).

The conclusions of previous researchers studying facial measurement uncertainties as to what influenced higher intraobserver uncertainty rates were numerous. The landmarks (Davenport et al., 1934), particularly nasion (Herskovits, 1930; Ward and Jamison, 1991), condylion laterale, and gnathion (Ward and Jamison, 1991), were identified as contributing to measurement uncertainties. Herskovits (1930) also named the nasal width as a difficult measurement to take in children since they might flare their nostrils, and Ward and Jamison (1991) cited the curved form of the face as causing problems. In contrast to the latter, Burke (1971) found that his stereophotogrammetric method overcame the intricate nature of the face, but landmarks on the eyes and mouth were a problem (Burke, 1971, 1983).

While the size of the subject was not found to contribute to the uncertainty in measurements (Dahlberg, 1926), the size of the measurement did have an effect according to several studies. Davenport et al. (1934) concluded that larger dimensions had larger absolute errors, but smaller

measurements had larger coefficients of variation. Ward and Jamison (1991) found that craniofacial measurements with means below 10 cm, and especially those below 6 cm, were prone to the highest degree of uncertainty according to their statistical methods. However, further analysis of their data led them to conclude "measurement size, at least at the small end of the measurement scale, provides a continuous relationship with precision and reliability, not a threshold effect" (Jamison and Ward, 1993: 499). Herskovits (1930) stated that the length of the facial height measurement (nasion to gnathion) contributed to its relatively greater uncertainty.

The measuring instruments, subjects, and conditions under which measurements were taken have been noted to be sources of measurement uncertainty. Davenport et al. (1934) mentioned instrument positioning, and Munro et al. (1966) identified spreading calipers as agents in measurement uncertainties. Ward and Jamison (1991) estimated instrument accuracy to be 0.5 mm generally, thereby adding to measurement uncertainty. Unwilling subjects, combined with taking measurements under field conditions, were implicated by Spielman et al. (1972) as factors in their measurement uncertainty. In contrast, when time is a factor in willingness to participate, photogrammetry has been found to be an advantageous method since images can be taken very quickly (Rasse et al., 1991). The influence of subject age was investigated by Jamison et al. (1989); they found that measurement uncertainties were increased in adults as compared with children. Davenport et al. (1934) also thought that the conditions under which measurements were taken contributed to measurement uncertainty, with poor lighting affecting instrument readings.

A few studies have compared facial measurements taken by direct anthropometry and photogrammetry; all involved extracting measurements from single photographs. Tanner and Weiner (1949) concluded that measurements taken directly and by photogrammetry were very similar in their reliability. Likewise, Fraser and Pashayan (1970) concluded that the two types of measurements were congruent, but the direct measurements were more uniform. Gavan et al. (1952) investigated photogrammetric measurements as a means of verifying data gained from direct measurements and concluded:

> the photographic measurement should always be slightly larger than the caliper one. If the relation is reversed or if the caliper measurement is too much smaller, there has been a mistake in measuring or recording. It is in this way that the photographic measurements can be used to check many of the traditional ones, although the two measures are not precisely the same (Gavan et al., 1952: 341).

Whereas these authors did not specify how much larger photogrammetric measurements might be, others (Farkas, 1981, 1994c; Farkas et al., 1980) employed a cutoff of 1 mm to identify reliable photogrammetric distances. These researchers found that photogrammetric measurements were larger or smaller, or variable between these two, in comparison to direct measurements. DiLiberti and Olson (1991) criticized Farkas' 1981 publication for the lack of data on the uncertainties in the direct measurements and for how reliability was defined. They also pointed out that there might be a systematic difference between the methods.

## MATERIALS AND METHODS

Thirteen facial soft tissue measurements were repeated ten times (or as indicated in Table 3-1) on one adult female (Subject 1) and one adult male (Subject 2), who were also the observers in this study (Observer B and A, respectively). All of the caliper-derived measurements were taken with a sliding caliper (Mitutoyo dial caliper with a smallest division of 0.01 mm), except zygion-zygion, condylion laterale-condylion laterale, and gonion-gonion, which were measured with a spreading caliper (Abaware caliper with 1 mm divisions). The dimensions were identified as being one of two types, depending on whether or not the landmarks were marked: Type 1 measurements were those in which both of the landmarks were marked, and Type 2 measurements were those involving the landmarks endocanthion and stomion, which could not be marked at any time. (The inner corner of the eye was too sensitive to the pressure of the eyeliner pencil, and stomion was at the midline of the fissure between the upper and lower lips.) The Type 1 measurements were taken between the following bilateral landmarks: exocanthion (ex), zygion (zy), alare (al), condylion laterale (cdl),

cheilion (ch), and gonion (go). Two vertical distances were taken and were designated as Type 1: sellion (se) to subnasale (sn) and subnasale to pogonion (pg). The Type 2 measurements were taken between the following landmarks: the bilateral endocanthion (en) landmarks, exocanthion and endocanthion of each eye, sellion and stomion (sto), and stomion and pogonion. The landmarks and their abbreviations were based on the descriptions of Farkas (1981), except for sellion (Farkas, 1994b) and gonion (Krogman, 1970).

The period of data collection spanned 22 days, with a minimum of 24 hours and a maximum of five days between the repeated sets of measurements. All measurements were taken with the same protocol. For the caliper-derived measurements taken without marking the landmarks, the subject sat upright with his or her head held in a natural position while the 13 measurements were taken. These values were covered up before the next stage was begun. All of the landmarks of interest, except for endocanthion and stomion, were marked with a black eyeliner pencil, and the 13 measurements were taken again with the calipers. Without removing the markings, the subject was seated approximately 1.5 meters in front of six Logitech FotoMan Plus cameras arranged for frontal and oblique lateral facial coverage. They were triggered simultaneously after the subject had been properly positioned. Each camera had a fixed focus lens with a focal length equivalent to 64 mm in a 35 mm camera (Logitech Inc., 1993). A x1.5 enlargement Optex telephoto video lens had been added to each camera.

Observer B processed the photographic images after the experiment was completed. A calibration grid was imaged at each session, and the digitized targets were used to determine each camera's perspective center coordinates, angles of rotation (about the three camera axes), and principal distance, as well as the principal point coordinates of the image, one term for radial distortion of the lens, and two terms for the decentering distortion. Next, the facial landmarks were digitized, and a record was kept of the landmarks that were difficult to digitize. This information was used to decrease the weight of the digitized coordinates in a camera view, when warranted by poor conditions such as faint or no markings, an exceptionally oblique view of the marks, or shadows that

obscured the marks. The appropriate camera calibration data were combined with the digitized facial landmark data, and the three-dimensional coordinates of each landmark were determined using the collinearity equations (Wolf, 1983). The program for this procedure automatically flagged, but did not reject, data having large residuals of fit (greater than ±2 standard deviations), which permitted reassessment of the digitized landmarks. A landmark was redigitized only when it was clear that it had been originally digitized incorrectly. Once the coordinates of each landmark had been determined, the distances between specified landmarks (i.e., the same measurements as were taken by calipers) were calculated. This program output the distances to 0.1 mm.

The caliper-derived data were analyzed after removing blunders resulting from measuring from the wrong landmarks or transcription errors. (The instances in which measurement values were removed are listed in Table 3-1). None of the measurement values were eliminated from the photogrammetric data since dissimilar landmarks were flagged and reassessed before calculating distances from them. The means and standard deviations of every dimension taken by each technique were computed. The caliper-derived data taken with the landmarks unmarked and marked for each subject were compared with the paired t-test (two-tailed). The results of the statistical analyses are in Table 3-1.

## RESULTS

### *Comparison of the Photogrammetric and Caliper-Derived (With the Landmarks Marked) Measurements*

The photogrammetric method presented special problems for the unmarked landmarks endocanthion and stomion (Type 2 measurements). For Subject 2, stomion could only be digitized in images from one measurement session, whereas it was digitized in images from all of the ten sessions involving Subject 1. While the endocanthion landmarks were digitized in images of both subjects from nine of the ten measurement sessions, comparison of the photogrammetric and caliper-derived (with the landmarks marked) means of dimensions that included endocanthion revealed that these

landmarks were never digitized correctly. On the other hand, the similarity of the exocanthion-exocanthion means from measurements taken by caliper and photogrammetry indicated that these markings were digitized correctly. Of the remaining measurements, it was expected that the photogrammetric means would be somewhat larger than the caliper-derived means because photogrammetry did not cause the soft tissues to be compressed. This expectation was confirmed in all of the measurements, except for sellion-subnasale and stomion-pogonion from Subject 1.

The standard deviations of the photogrammetric distances (excluding those involving endocanthion) were greater than those from the caliper-derived measurements in the majority of cases for both subjects. The dimensions that showed decreased standard deviations were all Type 1: sellion-subnasale from Subject 1, and exocanthion-exocanthion, sellion-subnasale, condylion laterale-condylion laterale, and gonion-gonion from Subject 2.

*Comparison of the Caliper-Derived Measurements With and Without the Landmarks Marked*

The t-tests of the caliper-derived measurements taken with the landmarks unmarked and marked showed that the data were statistically significantly different in ten cases out of a total of 26. Both Type 1 and 2 dimensions were found to be significantly different, but never in both subjects' data for any one dimension. It was not known whether this was attributable to differences between the two subjects (e.g., male vs. female and varying amounts of physiological change), or the observers (e.g., Observer A had more experience in taking facial measurements than did Observer B). Interestingly, t-tests of the right and left exocanthion-endocanthion measurements indicated that only the left eye measurements from Subject 1 and the right eye measurements from Subject 2 were statistically significantly different. Moreover, the endocanthion-endocanthion measurements from Subject 1 were significantly different although there were no differences in the collection procedures. Non-significant t-test probabilities were noted for both subjects for the Type 1 dimensions of zygion-zygion, alare-alare, and sellion-subnasale.

The standard deviations of the caliper-derived measurements taken with the landmarks

marked showed a relative decrease in magnitude in eight cases for both subjects when compared with the data taken with the landmarks unmarked. Although the majority of the decreases were of the order of 0.5 mm or less, there were some instances where they were more substantial. Relative reductions of between 0.67 and 1.86 mm occurred predominantly in Type 1 measurements (zygion-zygion, subnasale-pogonion, and gonion-gonion from Subject 1, and exocanthion-exocanthion and sellion-subnasale from Subject 2), with only one in the Type 2 category (stomion-pogonion from Subject 1). Except for right exocanthion-endocanthion from Subject 1, relative increases were less than 0.5 mm for the standard deviations of the caliper-derived data taken with marked landmarks as compared with the caliper-derived data taken without the landmarks marked.

## DISCUSSION

### *The Photogrammetric and Caliper-Derived Data*

Comparison of the photogrammetric data with the caliper-derived data taken with the landmarks marked revealed a systematic difference, as was previously described by Gavan et al. (1952) and DiLiberti and Olson (1991), and increased variability, which was also noted by Fraser and Pashayan (1970). The increased variability in the measurements taken by photogrammetry was probably due to three main causes. First, an oblique view of the marks presented a problem because the center of the mark extended over several pixels, and one central pixel could not be consistently digitized. Obliquity was a common problem for the most lateral landmarks of zygion, gonion, and condylion laterale, but affected all of the landmarks in accordance with each camera's position relative to each marking. Second, landmarks that were obscured by shadows were difficult to digitize. Third, when the landmarks were not marked (as in Type 2 measurements), it was hard to locate and digitize them. In addition, it was possible that the standard deviations of the caliper-derived measurements taken with the landmarks marked were decreased in relation to the photogrammetric data because successive values were influenced by previous ones, despite each observer believing that they forgot the results shortly after taking each measurement (Fleiss, 1986). Photogrammetry

essentially eliminated this problem since the distances were produced by computer. The standard deviations calculated from the data gathered by this method probably showed the most realistic amounts of variability in repeated measurements.

The t-test results from the two sets of caliper-derived data suggested two possibilities: there is naturally a great amount of variability in the measurements, or there is a systematic difference between the data gathered by the two techniques. The first interpretation was bolstered by the statistically significant t-test result for the endocanthion-endocanthion data from Subject 1. However, the measurement values taken with the landmarks marked had larger means in ten cases for the data on Subject 1 and eight cases for that on Subject 2, as well as decreased standard deviations in eight cases for the data from both subjects, which strongly suggested that there was a systematic difference between the two techniques.

### *The Effect of Marking the Landmarks*

Marking the landmarks had a positive effect on controlling two sources of variability in the caliper-derived measurements: different amounts of caliper pressure on highly compressible areas and accidental slippage of the calipers off the landmarks. The dimension alare-alare demonstrated the first case. The means of the caliper-derived data taken with the landmarks unmarked and marked were nearly identical for each subject, but the standard deviations of the data taken with the landmarks marked were decreased. Since this was a measurement where both landmarks could be palpated without the observer shifting position, there was no great advantage conferred by marking the landmarks, other than to allow the observer to focus on the amount of pressure exerted on the skin by the calipers. The dimension gonion-gonion demonstrated the second advantage. This was a particularly difficult measurement to take since each landmark could only be viewed and palpated by the observer shifting to each side. With the landmarks marked, any slippage of the calipers could be corrected easily. Neither advantage, however, was able to negate the basic problem of locating troublesome landmarks such as condylion laterale. In addition, this procedure was not beneficial

when the landmarks were highly mobile, as in the case of cheilion.

Marking the landmarks in the sensitive areas of the eyes (i.e., exocanthion) did not appear to improve consistently the observers' ability to measure these features. However, when each subject's means for the right and left exocanthion-endocanthion and endocanthion-endocanthion measurements were added together, the absolute differences between the estimated exocanthion-exocanthion lengths and those actually measured were the greatest when all of the landmarks were unmarked: 2.76 mm (vs. 1.81 mm when exocanthion was marked) for the data from Subject 1 and 1.65 mm (vs. 0.62 mm when exocanthion was marked) for the data from Subject 2. Marking the landmarks before taking the measurements with calipers helped make multiple measurements taken from them uniform, as suggested by Farkas (1981, 1994b) and Farkas and Deutsch (1996). When the same computations were done for the photogrammetric means, the data from Subject 1 showed the lowest difference (1.2 mm), whereas the data from Subject 2 demonstrated the highest difference (1.7 mm).

This investigation found systematic differences between photogrammetric measurements and caliper-derived measurements (with the landmarks marked), as well as between caliper-derived data taken with the landmarks marked and unmarked. Researchers and clinicians relying on measurements to objectify their diagnoses or classifications of subjects should be aware that small (i.e. marking or not marking the landmarks) and large (i.e., taking measurements with calipers or by photogrammetry) differences in measurement techniques may result in statistically significant findings, even in data taken from the same subject.

Table 3-1. The Means and Standard Deviations of the Soft Tissue Facial Measurements Taken by Photogrammetry and by Calipers With the Landmarks Either Unmarked or Marked

| | | Subject 1 | | | | Subject 2 | | | |
|---|---|---|---|---|---|---|---|---|---|
| Type 1 Mmts | Method | N | Mean | SD | Sig | N | Mean | SD | Sig |
| ex-ex | Photogrammetry | 10 | 87.0 | 1.1 | | 10 | 103.7 | 0.9 | |
| | Calipers-Unmarked | 10 | 82.67 | 0.59 | | 10 | 101.52 | 3.06 | |
| | Calipers-Marked | 10 | 87.03 | 0.77 | ‡ | 10 | 102.83 | 2.05 | |
| zy-zy | Photogrammetry | 10 | 135.8 | 2.0 | | 10 | 150.8 | 2.6 | |
| | Calipers-Unmarked | 10 | 128.40 | 1.50 | | 10 | 144.70 | 0.90 | |
| | Calipers-Marked | 10 | 128.80 | 0.40 | | 10 | 143.70 | 1.10 | |
| al-al | Photogrammetry | 10 | 36.3 | 1.0 | | 10 | 41.4 | 2.1 | |
| | Calipers-Unmarked | 10 | 35.08 | 0.69 | | 10 | 39.55 | 0.99 | |
| | Calipers-Marked | 10 | 35.06 | 0.60 | | 10 | 39.54 | 0.62 | |
| cdl-cdl | Photogrammetry | 10 | 133.5 | 2.9 | | 10 | 151.8 | 2.1 | |
| | Calipers-Unmarked | 9 | 119.67 | 1.63 | | 8 | 137.38 | 2.64 | |
| | Calipers-Marked | 5 | 123.20 | 1.47 | ‡ | 8 | 139.63 | 3.16 | |
| ch-ch | Photogrammetry | 10 | 44.4 | 1.7 | | 10 | 55.2 | 1.8 | |
| | Calipers-Unmarked | 10 | 43.89 | 1.61 | | 9[a] | 52.26 | 0.75 | |
| | Calipers-Marked | 9 | 43.43 | 1.72 | | 10 | 53.54 | 1.21 | †† |
| go-go | Photogrammetry | 9 | 104.4 | 2.6 | | 10 | 123.1 | 1.9 | |
| | Calipers-Unmarked | 10 | 93.50 | 2.69 | | 8 | 115.50 | 3.35 | |
| | Calipers-Marked | 4 | 97.25 | 0.83 | † | 8 | 112.88 | 3.18 | |
| se-sn | Photogrammetry | 10 | 48.3 | 1.0 | | 10 | 56.6 | 1.3 | |
| | Calipers-Unmarked | 8 | 47.91 | 1.35 | | 10 | 54.55 | 2.32 | |
| | Calipers-Marked | 9[a] | 48.72 | 1.29 | | 10 | 56.13 | 1.44 | |
| sn-pg | Photogrammetry | 10 | 51.5 | 0.9 | | 10 | 53.1 | 2.8 | |
| | Calipers-Unmarked | 10 | 52.39 | 1.36 | | 9[a] | 52.62 | 1.84 | |
| | Calipers-Marked | 10 | 50.57 | 0.69 | †† | 9[a] | 51.15 | 1.84 | |

| | | Subject 1 | | | | Subject 2 | | | |
|---|---|---|---|---|---|---|---|---|---|
| Type 2 Mmts | Method | N | Mean | SD | Sig | N | Mean | SD | Sig |
| en-en | Photogrammetry | 9 | 39.2 | 1.7 | | 9 | 49.6 | 3.6 | |
| | Calipers-Unmarked | 10 | 30.55 | 0.28 | | 10 | 35.56 | 0.95 | |
| | Calipers-Marked | 10 | 30.89 | 0.33 | †† | 10 | 35.95 | 0.64 | |
| ex-en R | Photogrammetry | 9 | 23.8 | 1.1 | | 9 | 28.7 | 2.5 | |
| | Calipers-Unmarked | 10 | 27.21 | 0.94 | | 10 | 31.92 | 1.29 | |
| | Calipers-Marked | 10 | 28.39 | 1.99 | | 10 | 33.08 | 1.01 | †† |
| ex-en L | Photogrammetry | 9 | 25.2 | 1.4 | | 9 | 27.1 | 1.6 | |
| | Calipers-Unmarked | 10 | 27.67 | 0.82 | | 10 | 32.39 | 1.32 | |
| | Calipers-Marked | 10 | 29.56 | 0.76 | ‡ | 10 | 33.18 | 1.26 | |
| se-sto | Photogrammetry | 10 | 71.0 | 1.3 | | 1 | 80.3 | NA | |
| | Calipers-Unmarked | 10 | 68.80 | 1.12 | | 10 | 74.97 | 1.77 | |
| | Calipers-Marked | 9[a] | 69.08 | 1.23 | | 10 | 76.97 | 1.27 | † |
| sto-pg | Photogrammetry | 10 | 28.3 | 1.4 | | 1 | 32.9 | NA | |
| | Calipers-Unmarked | 10 | 28.93 | 2.41 | | 10 | 33.62 | 2.29 | |
| | Calipers-Marked | 10 | 29.02 | 1.15 | | 10 | 30.63 | 2.60 | †† |

The data were rounded to one or two decimal places for this table, but the complete values were used in all calculations. All data are in millimeters. The measurements (Mmts) are separated by type (Type 1 where both landmarks could be marked and Type 2 where one or both of the landmarks could not be marked). R and L refer to measurements on the right and left sides of the face, respectively. The N column lists the number of measurements taken for each method. [a] One value was removed. The SD column lists the population standard deviations of the repeated measurements, and NA indicates that this statistic is not available. The Sig column indicates the significant t-test probabilities for the comparisons of the caliper-derived measurements as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$.

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# CHAPTER 4

# SOFT TISSUE FACIAL FEATURE ASYMMETRY IN MEDICALLY NORMAL AND SYNDROME-AFFECTED INDIVIDUALS[1]

## INTRODUCTION

Waddington (1957) suggested that some of the variation in adult morphology was the result of developmental noise, or random variation in early prenatal development; under the influence of natural selection, small differences in the environment and genetic constitution of individuals would not tend to affect substantial deviations in the final organism. The process of producing a consistent end-result was termed canalization (or buffering). If this process failed, the result was increased variability and abnormalities above those resulting from developmental noise (Waddington, 1942). Medically normal individuals have most often been the focus of facial asymmetry studies that attempt to quantify the amount of normal variability (i.e., from developmental noise). Much less is known about facial asymmetry in individuals with syndromes, except those conditions that are characterized by obvious lateral differences in the facial features, such as cleft lip with or without cleft palate and hemifacial microsomia. There is some evidence that individuals with medical conditions are more variable bilaterally. Malina and Buschang (1984) reported that asymmetries in the body dimensions of males with mental retardation were greater than those of the normal control males and noted that the males with cerebral palsy had the greatest asymmetries. In measurements of the palate, Shapiro (1975) found that those dimensions that were the most susceptible to environmental influences in normal subjects were -2 or more standard deviations below the norm in individuals with Down syndrome. He suggested that the chromosomal abnormalities in Down syndrome and other trisomy conditions led to decreased canalization.

[1] A version of this chapter has been published. Shaner DJ, Peterson AE, Beattie OB, and Bamforth JS (2000) Assessment of soft tissue facial asymmetry in medically normal and syndrome-affected individuals by analysis of landmarks and measurements. American Journal of Medical Genetics *93:*143-154.

With these studies in mind, an investigation was undertaken into soft tissue facial feature asymmetry in individuals with syndromes and normal individuals. The main purpose was to determine whether there was detectably greater variation in bilateral facial measurements among groups of males and females with syndromes than in normal male and female groups. It was hoped that some facial measurements would be identified as particularly asymmetric in the syndrome-affected groups and that they could be used in routine clinical pre-screening for the possible presence of syndromes in uncertain patients. Whereas direct anthropometry, which has often been employed in facial asymmetry research, provides only one way to view facial asymmetry (i.e., through the measurements), the method of photogrammetry used in this investigation produced three-dimensional information on the landmarks as well as measurements. Therefore, soft tissue facial feature asymmetry was investigated with several sets of data, and the results gained through studying bilateral measurement asymmetry were compared with those obtained from the three-dimensional coordinates of the landmarks.

## LITERATURE REVIEW

Van Valen (1962) distinguished three types of asymmetry: antisymmetry, directional asymmetry, and fluctuating asymmetry. In antisymmetry, either side could be dominant, as in handedness. The directional type was asymmetry that was consistently dominant (i.e., larger, in the case of measurements) on one side. Van Valen considered these two types to be normal. By contrast, fluctuating asymmetry was considered to be a measure of canalization and developmental noise, since it was the result of "the inability of organisms to develop in precisely determined paths" (Van Valen, 1962: 126). Many studies have focused on the results of abnormal environmental stressors on symmetrical development. Dental and post-cranial asymmetry have been studied in insects and animals under the influence of stressors such as the incubation temperature and salt level in the growth medium of fruit flies (Waddington, 1959); audiogenic stress in rodents (Siegel and Doyle, 1975b; Siegel and Smookler, 1973; Smookler et al., 1973); cold stress in rodents (Siegel and Doyle,

1975a, b); modification of environment so that climbing was prohibited or forced in rodents (Siegel and Doyle, 1975b); and prenatal chemical treatment in mice (Brown et al., 1989). Studies of the types of facial asymmetry in humans (and non-human primates) have been less common and have often involved dental analyses (e.g., Adams and Niswander, 1967; Kieser et al., 1986; Kohn and Bennett, 1986; Noss et al., 1983). The studies by Skvarilova (1993, 1994) were exceptions. Skvarilova (1993) investigated soft tissue facial asymmetry in children age six to 18 years old. Of the 12 direct measurements, only gonion-exocanthion and tragion-exocanthion clearly showed statistically significant directional asymmetry to the right; the remainder exhibited non-statistically significant fluctuating asymmetry. Sex- and age-related differences were not found. Subsequently, Skvarilova (1994) investigated asymmetry in adult males by means of radiographic images. Bilateral landmark positions were evaluated by their distances to the median line and to a horizontal line through the orbits. Fluctuating asymmetry was identified in 39 of the 42 comparisons; no consistent side of dominance was identified for the three bilateral comparisons that were of the directional asymmetry type. The greatest standard deviations of the bilateral differences were found in the regions of the lateral cranial vault and mandible.

The focus of the majority of facial asymmetry research has been the identification of the facial side of greatest magnitude. Several studies reported dominance of the left side of the face in normal individuals. Vig and Hewitt (1975) studied seven area measurements from radiograph tracings of children and found that the cranial base, upper maxillary, and lateral maxillary regions were significantly larger on the left side. Burke (1971) investigated facial soft tissue asymmetry in 12 pairs of male twins and 12 pairs of female twins (age seven to 19 years). He concluded that the left side of the maxillary area was generally larger and that age was not a factor in asymmetry. The right side of the face has also been identified as having larger measurements in normal subjects. Shah and Joshi (1978) used a method similar to that of Vig and Hewitt (1975) on a group of 18- to 25-year-old subjects and concluded that the lateral maxillary area was significantly larger on the right side. They considered their subjects to have completed growth and cited the young ages of the subjects in other

studies as one possible cause of the differences between the side of dominance findings in the literature. Figalova (1969) studied the soft tissue facial structures of six- and 16-year-old children by direct anthropometry. Measurements on the right side were larger in most cases and it was concluded that age did not affect asymmetry. Farkas and Cheung (1981) defined asymmetry as a difference of 2 mm (or degrees) or greater. They stated that measurements on the right side of the face were typically longer in Canadian Caucasian subjects six, 12, and 18 years old. The proportions of males and females with asymmetries were not statistically different with age, and only one measurement had a statistically greater proportion of either sex with asymmetries (nasion-tragion in 18-year-old males). In a later study, Farkas (1994a) reduced the cutoff point for measurement symmetry to less than 1 mm. In his group of normal subjects age one to 18 years old, the proportions of males and females with facial measurement asymmetries were all non-significant, except for one surface arc (tragion-subnasale, which had a higher frequency in males).

Not all studies found that dominance was confined to one side of the face. Halperin (1931) stated, without quantification, that in people with no medical abnormalities the left side of the face was larger, but the eye and ear were placed higher on the right side of the face. Although Woo (1930/31) concluded that the right side of the skull was dominant in a sample of 800 Egyptian skulls, he also noted that the left zygomatic bone was significantly larger and that two measurements of the maxilla showed opposite dominance in side. Woo (1937) also investigated the zygomatic bone in skulls representing 14 ancestral backgrounds. Eight of the groups showed significant differences between the sides, but not consistently for one side and not for all of the measurements.

A few studies have reported no significant differences in measurements taken between the right and left sides of the face. Cleaver (1937) investigated the mandible in skeletal material from four groups. Citing three measurements from native Australian mandibles, he concluded that there was no significant asymmetry in this bone. Peck et al. (1991) investigated skeletal asymmetry in living subjects. Measurements taken from radiographs of adolescents and adults who were public figures widely recognized for their beauty were non-significantly larger on the right side.

Several studies have reported on asymmetry in the three-dimensional coordinates of soft tissue facial landmarks. In a group of white adults, Ferrario et al. (1994) found differences between the sexes: landmarks on the right side of the male face were wider laterally and situated more cranially and anteriorly, whereas the female face also had landmarks that were wider on the right side, but they were more caudally and posteriorly placed on this side. Furthermore, in males the midline landmarks were deviated to the left, but they were deviated to the right in females. In later research on a sample of adult Caucasian males and females, Ferrario et al. (1995) investigated the lateral halves of the face as units with Euclidean distance matrix analysis. They found that both sexes had statistically significant differences in shape between the facial halves. Comparisons of size were not statistically different, although measurements from the right side of the face were often largest in both sexes. While investigating soft tissue facial landmark asymmetry in children with unilateral cleft lip and palate, Ras et al. (1994) made observations on the three-dimensional nature of the landmarks from a control group of 80 normal children. When the landmarks were investigated in the horizontal, vertical, and sagittal planes, the left side was dominant horizontally and the right side was dominant sagittally. No side was dominant for the vertical direction of the landmarks. The midline landmarks were deviated to the left side. In a later mixed longitudinal study, these researchers found that the pattern of dominance did not change in children between the ages of four and 12 years. In addition, sex did not have a significant effect on bilateral landmark asymmetry (Ras et al., 1995).

Midline deviation was also noted by other researchers. Ferris (1927) identified the facial midline, along with the corners of the eyes and mouth, as asymmetric. Using a qualitative method, Sutton (1968) reported an increase in the deviation of subnasale with age and a bimodal increase in the deviation of pogonion over time in Australians of European ancestry and Polynesians. Vig and Hewitt (1975) compared midlines of the maxillary and mandibular regions from roentgenograms and stated that the former deviated to the left of the mandibular axis by an average of 1.9 degrees.

Theories as to the causes of asymmetry have been put forth based on the observations of researchers investigating this phenomenon. Schultz (1923) found that asymmetry could be measured

in human fetuses by the fourth month and concluded that post-natal behaviors and environmental influences were not the major cause of asymmetry in children and adults (Schultz, 1926). Bartelmez and Evans (1926) found marked asymmetry in the neural folds, vascular system, and pharynx of embryos. They furthermore noted that no side was consistently dominant. Additional evidence that environment had a negligible effect on asymmetry was provided by Chierici et al. (1970). They created unilateral clefts in 30 *Macaca mulatta* monkeys and observed that there was no asymmetry introduced into the zygoma by this procedure. In contrast, Kohn and Bennett (1986) concluded that prenatal environment was a significant factor in the fluctuating asymmetry found between bilateral mandibular dental measurements taken in fetal rhesus monkeys exposed to prenatal stress in the form of diabetic mothers, as compared with fetuses from normal mothers.

Others found evidence that postnatal factors influenced asymmetry in the facial skeleton and soft tissues. In a study of identical and fraternal triplets, Mulick (1965) did not find statistically significant differences in the amount of asymmetry between the classifications of triplets and concluded that heredity was not the cause of normal asymmetry. Sutton (1968) determined that asymmetry in the landmark subnasale increased with age, and therefore it was the result of factors after birth. Earlier, Sutton (1963) found a significant relationship between the side of the face to which subnasale was deviated and the hand most preferred for performing actions: both occurred on the same side. Vig and Hewitt (1975) suggested that the mandibular and dental regions were more symmetric than the maxilla in normal individuals because of the functional needs of mastication. Shah and Joshi (1978) concluded that the soft tissues compensated for any underlying skeletal asymmetry and that stronger mastication on one side led to increased skeletal development on that side. However, Pirttiniemi (1998) pointed out that mandibular asymmetries might be the end-result of a chain of asymmetries starting with the brain, to the neurocranium, and on to the mandible by way of the mandibular joint. Similarly, in their study of facial asymmetry in adult males and females (age 21 to 35 years old) from Eastern Turkey, Keles et al. (1997) concluded that cerebral lateralization was a factor in facial asymmetry. In investigating the interactions between facial asymmetry (as

measured by triangular areas on posteroanterior radiographs), sex, and handedness, these researchers found that hand preference was a significant factor in facial asymmetry: male and female right-handed subjects showed significantly greater areas on the left side of the face. This was thought to result from the greater size of the structures on the left side of the brain. However, when left-handed subjects were investigated, there were few significant differences between the facial sides, which was attributed to inconsistent cerebral lateralization. This research also indicated that the sex of the subjects played a role in facial asymmetry, since males had significantly larger facial areas than did females. It was also noted that left-handed males were less frequently asymmetric than were left-handed females. The conclusion of these authors was that sex hormones might be a factor in cerebral lateralization and, therefore, in facial asymmetry.

## MATERIALS AND METHODS

The control subjects in this study consisted of 32 normal males age 1.6 years to adulthood and 38 normal females age 1.7 years to adulthood. Some of the adults declined to give their birth years, but the oldest recorded age was 63.1 years for normal males and 60.3 years for normal females. There were also 30 syndrome-affected individuals: 13 males age 2.0 to 20.4 years and 17 females age 4.4 to 28.6 years old. The syndromes diagnosed in the subjects were ones in which the facial features were affected, but were not known to be characterized by facial asymmetry. Many of the subjects were related, and the relationships between the syndrome-affected individuals are noted in Table 4-1 along with the diagnosed syndromes. As an option, subjects were asked to identify their ancestral background. Seventy-nine answered European, ten were a mixed heritage of European and Native American, two were full Native American, one was Korean, one had a Lebanese heritage, two answered Chinese, and five were Spanish and African American and/or Mayan.

Photogrammetry was used to obtain the three-dimensional coordinates of the landmarks, from which the measurements were made, with a method described previously (Shaner et al., 1998). It should be noted that initially there were six cameras with which to image the subjects, but one

camera failed during the period of data collection. The remaining five cameras were repositioned for full frontal and oblique lateral coverage of the subjects' faces. The following lateral landmarks were marked on both sides of the subjects' faces: tragion (t), zygion (zy), gonion (go), exocanthion (ex), endocanthion (en), alare (al), subalare (sbl), cheilion (ch), and christa philtri (cph). Center of the iris (cir) was the only landmark that was not marked on the face, but was produced by setting the custom circular computer cursor (with central cross hairs) on the outer edge of the iris and digitizing the center. The pupil was not specifically digitized with this procedure. The following midline landmarks were also marked: glabella (g), sellion (se), pronasale (prn), subnasale (sn), labiale superius (ls), labiale inferius (li), sublabiale (sl), and pogonion (pg). The descriptions of the landmarks as explained by Farkas (1981) were used, except for sellion and sublabiale (Farkas, 1994b), gonion (Krogman, 1970), and center of the iris (a new landmark). Not all landmarks were marked on every subject, usually due to poor cooperation in children, the subject's stated desire not to have certain markings, such as endocanthion and exocanthion, or the presence of facial hair in adult males.

The subjects could not be posed in a standard position for imaging; therefore, for each subject, the three-dimensional coordinates were mathematically transformed into the same orientation by a three-dimensional conformal coordinate transformation with no change in scale (Wolf, 1983). The landmarks were initially oriented by means of a plane defined by the right and left tragion and pronasale, but some subjects' images lacked the tragion or pronasale landmarks. In these cases, the three-dimensional coordinates of the landmarks were transformed by modeling them against an average of already-transformed data from subjects of the same age and sex. A second transformation was carried out on all of the subjects' data to ensure that the differences in procedure did not affect the outcome. The three-dimensional coordinates of one subject (a 16-year-old girl whose coordinates were all present and nearly symmetrical) were averaged between each side, and all midline X coordinates were set to zero. This file was then used as the model to transform all of the facial data into the final orientation. The following midline and paired lateral landmarks were used in the procedure: zygion, exocanthion, endocanthion, glabella, sellion, pronasale, subnasale, alare, labiale

superius, labiale inferius, sublabiale, and pogonion. All other landmarks were passively oriented at the same time. The origin of the three-dimensional coordinate system was approximately at the center of the head so that the Z coordinates, which represented the anterior-posterior positioning of the landmarks, were always positive. The positive and negative Y axes divided each face into lateral halves, and the Y coordinates depicted the relative cranial-caudal direction of the landmarks. The X axes divided each face into upper and lower sections, and the X coordinates described the lateral positioning of the landmarks.

All data were grouped by the sex and medical status (normal or syndrome-affected) of the subjects. The measurements investigated were of three types: distances between two landmarks, angles made between two landmarks and the horizontal plane (referred to as "angles" in the tables), and depths. Differences between measurements from the lateral halves of the subjects' faces were examined with the paired t-test (two-tailed). Further investigations of the right and left sides of the face were carried out on the three-dimensional coordinates of the landmarks and the coordinate direction angles of the landmarks with the same statistical test. The coordinate direction angles, $\alpha$ (alpha), $\beta$ (beta), and $\gamma$ (gamma), were the angles between the vectors (from the origin of the coordinate system to the landmarks) and the positive X, Y, and Z axes, respectively (Figure 4-1). Each was calculated as the inverse cosine of the ratio of the X, Y, or Z coordinate value to the magnitude of the landmark vector (Hibbeler, 1995). Since the $\alpha$ angles from the right side of the face were in reference to the positive X axis, these angles were much larger than the angles from the left side of the face that were on the same side as the positive X axis. The right $\alpha$ angles were therefore transformed into the equivalent angle from the negative X axis. The X coordinates of the midline landmarks were investigated for midline asymmetry with the one-sample t-test (two-tailed) against the hypothesized test value of zero. Assessment of every measurement from all syndrome-affected individuals was also carried out. Based on the description given in Smith et al. (1982), the limits of normal asymmetry for each measurement were defined by the standard deviations of the paired differences (also referred to as the root mean square asymmetry measure). Positive and negative

signs, respectively, were added to identify the upper and lower limits. As suggested by Skvarilova (1993), the magnitude of the normal groups' standard deviations was doubled, so as to reflect the variability of 95% of the normal sample.

## RESULTS

### *Measurement and Landmark Asymmetry in All Groups*

Significant asymmetries between paired measurements (Table 4-2) were most common in normal males (seven in total) and least frequent in males and females with syndromes (four significant differences in each group). Normal females had six significantly asymmetrical bilateral measurements. No single measurement was statistically significantly different in all four groups. For the distance measurements, four showed no significant differences in any of the groups: tragion-exocanthion, tragion-subnasale, tragion-cheilion, and subalare-subnasale. For the remainder of the measurements (angles and depths), only the depth difference between endocanthion-exocanthion was not statistically significantly different in all four groups. The right side of the face was dominant for the statistically different measurements, excluding the angle between the horizontal plane and endocanthion-exocanthion in normal females, exocanthion-endocanthion length in females with syndromes, and the depth difference between sellion-endocanthion in males with syndromes. No measurements were found that were significantly asymmetric in both syndrome-affected groups and non-significantly different in the normal groups.

The coordinate direction angles of the paired landmarks gave an initial impression as to the positioning of the landmarks on the right and left sides and whether there were significant differences in the placement of the paired landmarks relative to the coordinate system (Table 4-3– note that only the significant differences are reported here). A pattern was found to the dominant angles that was consistent in all four groups: of the statistically significant results, all $\alpha$ angles were greater on the left side of the face, and all $\gamma$ angles were larger on the right side. The $\beta$ angles were larger on the right side of the face, apart from zygion in normal females and males with syndromes.

In contrast, when the statistically different positions of the three-dimensional coordinates were assessed (Table 4-4—note that only the significant differences are reported here), only the X coordinates were all greater on the right side of the face, indicating that these landmarks were more laterally placed on this side in all groups. There were fewer numbers of Y and Z coordinates to consider, but from those available, no side consistently exhibited a greater cranial or caudal placement of the Y coordinates or a more anterior or posterior position of the Z coordinates.

The statistical results for the position of the X coordinates in relation to the facial midline were mixed (Table 4-5). Males and females with syndromes had the least number of significant deviations. In all four groups, pronasale and labiale superius were not significantly deviated from the midline. Apart from subnasale, which was significantly deviated in both normal groups, all statistically different midline landmarks were deviated to the left side of the face.

### *Asymmetry in the Syndrome-Affected Individuals*

In their study of soft tissue facial traits in a group of children with over 30 different syndromes, Stengel-Rutkowski et al. (1984) demonstrated that facial measurement ratios often fell within the normal range of variation. However, for the present syndrome-affected groups, it was recognized that inclusion of many conditions might mask those subjects with excessive soft tissue facial asymmetry. Therefore, asymmetry was also investigated on an individual basis. The differences between the paired measurements for each individual with a syndrome were evaluated against the limits of asymmetry in normal males and females (as described in the Materials and Methods section). Thirteen of the 170 (7.6%) differences investigated in the males with syndromes exceeded the normal male limits of bilateral asymmetry; for females with syndromes, eight out of 181 (4.4%) paired differences were greater than those obtained for the normal females group (Table 4-6).

# DISCUSSION

## *Facial Measurement Asymmetry in All Groups*

This study has indicated that, for the statistically significant measurements, the means from the right side of the face usually had the greatest values in all four groups. Variations from this pattern were isolated to one comparison in three of the groups, and all involved the landmark endocanthion. This appeared to be a coincidence, since no other measurements involving endocanthion were statistically significantly larger on the left side. It was not known why there was a lack of consistency in which measurements were statistically significantly different between the sexes and between the medically normal and syndrome-affected groups. The bilateral absolute mean differences, when compared between groups by sex (e.g., normal females vs. syndrome-affected females) and medical status (e.g., syndrome-affected males vs. syndrome-affected females), were typically within 1 mm. Exocanthion-gonion and gonion-pogonion were the consistent exceptions, demonstrating high absolute differences in all comparisons.

Figalova (1969) estimated that normal asymmetry should not exceed 2.45 mm, although this researcher noted that differences of 10 and 20 mm occurred in normal individuals. A wider limit to the range of normal variation, between 4 to 5 mm for lateral facial dimensions, was recommended by Skvarilova (1993), based on the average standard deviations of the differences in males and females from different age groups. However, the data supplied by this researcher indicated that the upper-most limit of normal variation was closer to 6 mm for some measurements, particularly those involving the landmark tragion. Data from the present samples of normal males and females suggested that an even greater amount of variability was normal (although there are cautions to consider as described in the following section). Using twice the value of the standard deviation of the paired measurement differences, it was noted that the normal female group had a greater range of normal variation than did the males: females ranged from ±3.2 mm to ±16.6 mm, whereas males ranged from ±2.6 mm to ±8.8 mm. Both groups had the greatest range for gonion-pogonion and the

lowest for subalare-subnasale. As a general rule, in the majority of normal males and females, the normal limits of asymmetry in the measurements taken from the upper and central regions of the face (involving the landmarks of the eyes and nose, plus tragion and glabella) did not exceed 5 mm (or degrees) in males and 6 mm (or degrees) in females. Measurements that involved one or two landmarks from the mouth region and below had a much higher normal variability, with bilateral differences of 6 mm or greater. However, tragion-pogonion was an exception in both normal males and females, with differences of 5 to 6 mm, as in the upper facial regions.

### *Canalization and Asymmetry*

Differences in the amount of fluctuating asymmetry have been used to detect discrepancies in the buffering capacity, or canalization, of two or more groups. However, some statistical techniques have been shown to be compromised in dental studies by two factors: the size of the structure being measured, because asymmetry is a function of size; and the size of the sample. When use of the F-test was investigated, a combined sample size of 100 or more was needed to accurately detect small, but significant, differences in the variances of two groups. In the case of the root mean square asymmetry statistic (i.e., the standard deviation of the paired differences), the greatest ranges of estimates were found for small sample sizes; only sample sizes of 600 or more observations presented reasonably small ranges of estimates (Smith et al., 1982). Fields et al. (1995) also demonstrated that anthropometric traits had relatively low reliability due to measurement error, which confounded the bilateral differences.

With these cautions in mind, the syndrome-affected subjects were investigated on an individual basis. The small number of abnormally large bilateral differences suggested that the individuals with syndromes did not show highly consistent deviations from the norms in measurements characterized by directional or fluctuating asymmetry in the normal groups. Most of the measurements that were abnormally asymmetric were those in the upper and central regions of the face, which were noted earlier to have relatively lower limits of normal asymmetry of 5 to 6 mm

(or degrees). While this might tend to imply that these areas were more prone to stressors in some subjects, overall there was little evidence that the soft tissues of the face were more poorly canalized in the syndrome-affected subjects. That is, there were fewer dimensions with significant asymmetries in the syndrome-affected groups as compared with the normal groups and only a small number of abnormally large bilateral differences in the individuals with syndromes, when asymmetry in each individual was compared to the normal limits of asymmetry. One additional consideration was that the samples used in this investigation had individuals who were related. Livshits et al. (1988) found increased fluctuating asymmetry in parents of children who were born prematurely when they were compared with parents of normal-term children. It is possible that, in the present sample of subjects, the medically normal parents and sibs of the individuals with syndromes had a greater degree of variability in their bilateral measurements, thereby inflating the normal limits of the measurement asymmetries.

### *The Role of the Landmarks in Facial Asymmetry*

It is not always straightforward to determine which of the landmarks might be the cause of significant bilateral measurement differences. With the current photogrammetric method, landmarks, such as the right and left tragion, that were used in multiple measurements were exactly the same for every measurement. Therefore, it was possible to evaluate the role of the landmarks in facial asymmetry. In contrast, direct anthropometry requires that the instrument be repositioned on the landmarks for every measurement taken.

Peck et al. (1991) suggested that asymmetry increased in the facial skeleton as measurements were taken in the caudal direction. For measurements taken from the lateral regions of the face, Farkas (1994a) also found that the frequency of asymmetry increased as the measurements were taken lower on the face. The three-dimensional coordinate results from the two normal groups in the current investigation did not support these observations. Normal females showed three-dimensional coordinate asymmetries for the landmarks of the eyes, and both normal groups had asymmetries for

upper facial measurements, such as endocanthion-sellion. However, the variability of the bilateral measurements did appear to increase in the lower regions of the face, as already described. Peck and Peck (1970: 300) reported that asymmetry might "characterize and individualize" a pleasing face. Farkas and Cheung (1981) noted the equilibrium of the normal face, as demonstrated through a general lack of significant correlations between measurements, thus rendering the asymmetries unnoticeable. Mulick (1965) asserted that the amounts of asymmetry differed in each region of the face; asymmetry in individual bones was diminished by the surrounding tissues. The current investigation has also showed that the distribution of landmark asymmetries was throughout the face, generally without any specific area of concentration, which might disguise the asymmetries from visual detection.

Farkas (1994a) reported that the measurements that located the ear (which included the landmark tragion) were the most frequently asymmetric. Others have also implicated the asymmetric positions of the right and left tragions as a cause of side differences (Farkas and Cheung, 1981; Ferrario et al., 1995; Ferrario et al., 1994). On the other hand, deviation of the midline landmarks has been noted (Ferris, 1927; Sutton, 1968). In the present study, there was no evidence that the tragion landmarks had significantly different positions on the right and left sides, but the midline and other paired lateral landmarks were often statistically significantly different. The statistical results from the X coordinates of the paired lateral landmarks agreed with the findings of Ferrario et al. (1994) that the right side of the face was dominant in the horizontal direction, but the sex-related differences in the vertical and sagittal directions described by these authors were not detected in the current investigation. Unlike Ferrario et al. (1994), there was no evidence of sex-related differences for the side to which the midline landmarks deviated in the present data, nor were all of the midline landmarks deviated to the left as described by Ras et al. (1994).

It was clear from comparison of the statistically significant landmark and measurement results that different conclusions regarding asymmetry could be made, depending on which method was used to analyze asymmetry. It was found that measurements identified differences in facial feature

size, but not necessarily differences in landmark position, as was also suggested by Farkas (1994a) in his study of soft tissue facial measurements. For example, the right and left palpebral fissure distances (exocanthion-endocanthion) were not significantly larger on either side of the face except in the females with syndromes group. Yet, analysis of the three-dimensional coordinates of these landmarks indicated that one or two coordinates were asymmetric for either or both landmarks in three of the groups (all but normal males). While significant differences in landmark position might be inferred from multiple measurements taken between the landmarks of interest and other facial landmarks, different measurements designed to investigate the positions of a landmark in one direction could present dissimilar results. For instance, to detect differences in the anterior-posterior position of the landmarks along the Z axis, depth measurements were taken. In the present groups, only males with syndromes had a significantly more anterior position of the right Z coordinate of endocanthion, and this was accurately reflected in the significantly greater depth difference between sellion-endocanthion on the left side of the face. On the other hand, when the depth difference between endocanthion-exocanthion was tested in this same group, the right and left measurements were symmetrical.

It was also found that significant differences in the position of one landmark might be compensated for by the second landmark: A measurement between two landmarks could be statistically symmetrical even though one of the landmarks exhibited significant asymmetry in one or more of the three-dimensional coordinates. For instance, the distance between tragion-subnasale was never statistically significantly different in any of the groups, but subnasale was significantly deviated in both normal groups. Interestingly, this was the only midline landmark that deviated significantly to the right. This suggested that the average position of the X, Y, and Z coordinates of tragion were (non-significantly) greater on the same side of the face, counteracting the deviation of subnasale.

Ferrario et al. (1994) asserted that the variations in the literature on the findings of facial asymmetry were the result of the wide varieties of subjects, measurements, and techniques employed. In particular, they cited the use of two-dimensional methods in the study of facial asymmetry. In

accordance with the results of this study, the following factors should also be included: variations in the types of data analyzed (e.g., measurements or landmarks); the use of non-statistically significant side differences to identify the side of facial dominance; and differences in treatment of the data, such as pooling the data or investigating each landmark or measurement separately. Another factor that should be considered is fluctuating asymmetry. This type of asymmetry may be a plausible explanation for the many conflicting results in the literature on bilateral facial differences (Skvarilova, 1993). In addition, Keles et al. (1997) have suggested that failure to take into account the hand preference of the subjects under investigation might be a factor in the variable findings on the side of facial dominance in the literature.

Figalova (1969) felt that the maximum limit of normal asymmetry and the minimum limit of abnormal asymmetry were equal. The present research suggested that asymmetries in individuals with syndromes not known to be characterized by facial asymmetry were usually within the normal boundaries. Whatever the causes were of the syndromes investigated in this study, there was little evidence for a greater influence of genes or environment on soft tissue facial asymmetry in the syndrome-affected groups as compared to the normal groups; that is, measurements from the normal and syndrome-affected groups indicated that all were equally canalized and presumably were similarly affected by developmental noise. Despite that no specific measurements were identified for routine screening of patients with uncertain medical status, clinicians should still be encouraged to take facial measurements of patients. As knowledge of normal facial variation increases, measurement data will provide a permanent record of each patient's development over time and could be compared at any time to the published normative data.

Table 4-1. The Syndromes Diagnosed in the Subjects

| Syndrome | Males | Females |
|---|---|---|
| Achondroplasia | 1 | 3[a] |
| Cardio-facio-cutaneous | 0 | 1 |
| Cohen | 0 | 1 |
| Crouzon | 1 | 0 |
| Deletion of 18q | 0 | 1 |
| Down | 1 | 0 |
| Myotonic dystrophy | 1[b] | 1[b] |
| Placental anastamoses in monozygotic triplets | 0 | 3[c] |
| Russell-Silver | 1[d] | 1[d] |
| Spondylometaphyseal dysplasia | 1 | 0 |
| Stickler | 0 | 1 |
| 3C (cranio-cerebellar-cardiac) | 1 | 0 |
| Trisomy 8 (mosaic) | 1 | 0 |
| Uniparental disomy chromosome 16 (maternal) | 0 | 1 |
| Velocardiofacial | 1 | 0 |
| X-linked Aarskog carrier | 0 | 1 |
| Unknown | 4 | 3 |

[a] Two subjects are sisters. [b] Brother and sister. [c] Sisters. [d] Mother and son.

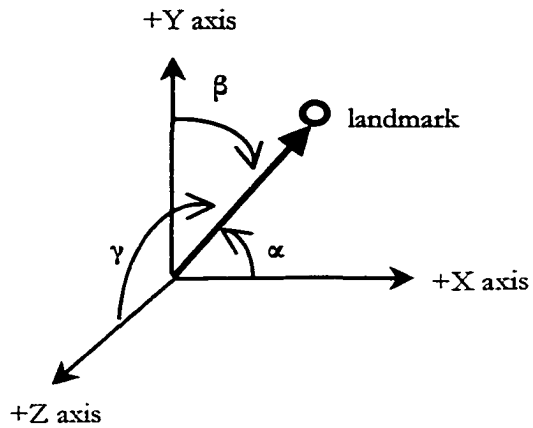


Figure 4-1. Diagrammatic Representation of the Coordinate Direction Angles

The angles alpha (α), beta (β), and gamma (γ) were measured between the vectors (from the origin of the axes to the landmarks) and the positive X, Y, and Z axes, respectively.

Table 4-2. Comparison of the Right and Left Measurements in All Groups

| Normal Males | | | | | | Normal Females | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mmt | Side | Mean of Sides | N | Mean Diff | SD | Mmt | Side | Mean of Sides | N | Mean Diff | SD |
| t-g | R | 116.8 | 25 | 0.9 † | 2.0 | t-g | R | 115.3 | 28 | 0.6 | 3.4 |
| | L | 115.9 | | | | | L | 114.7 | | | |
| t-se | R | 112.9 | 26 | 1.0 †† | 1.8 | t-se | R | 112.2 | 28 | 0.9 | 3.2 |
| | L | 111.8 | | | | | L | 111.3 | | | |
| t-ex | R | 71.7 | 26 | 0.5 | 2.9 | t-ex | R | 72.9 | 25 | 0.7 | 5.1 |
| | L | 71.2 | | | | | L | 72.2 | | | |
| t-sn | R | 115.3 | 24 | 0.2 | 2.2 | t-sn | R | 116.9 | 27 | 0.1 | 3.1 |
| | L | 115.1 | | | | | L | 116.8 | | | |
| t-ch | R | 100.7 | 26 | -0.5 | 2.9 | t-ch | R | 100.2 | 28 | 0.4 | 3.3 |
| | L | 101.2 | | | | | L | 99.7 | | | |
| t-pg | R | 130.3 | 26 | 1.1 † | 2.4 | t-pg | R | 132.0 | 28 | 1.5 †† | 2.7 |
| | L | 129.2 | | | | | L | 130.5 | | | |
| ex-en | R | 31.6 | 26 | -0.1 | 1.8 | ex-en | R | 31.7 | 34 | -0.3 | 1.7 |
| | L | 31.7 | | | | | L | 31.9 | | | |
| en-se | R | 21.3 | 26 | 1.2 †† | 1.8 | en-se | R | 20.5 | 35 | 1.4 ‡ | 2.1 |
| | L | 20.1 | | | | | L | 19.1 | | | |
| cir-se | R | 32.7 | 30 | 1.3 †† | 2.4 | cir-se | R | 32.6 | 35 | 1.5 †† | 3.1 |
| | L | 31.4 | | | | | L | 31.2 | | | |
| ex-go | R | 86.9 | 9 | 0.9 | 3.4 | ex-go | R | 89.3 | 9 | 3.2 †† | 3.2 |
| | L | 86.0 | | | | | L | 86.1 | | | |
| ex-g | R | 54.2 | 30 | 0.9 † | 2.1 | ex-g | R | 52.8 | 35 | 0.9 †† | 2.1 |
| | L | 53.3 | | | | | L | 51.9 | | | |
| sbl-sn | R | 10.8 | 27 | -0.3 | 1.3 | sbl-sn | R | 11.2 | 35 | -0.4 | 1.6 |
| | L | 11.1 | | | | | L | 11.6 | | | |
| go-pg | R | 92.5 | 9 | 4.8 †† | 4.4 | go-pg | R | 87.7 | 12 | 1.9 | 8.3 |
| | L | 87.7 | | | | | L | 85.9 | | | |
| en-ex angle | R | -1.1 | 26 | 0.8 | 2.9 | en-ex angle | R | -0.2 | 34 | 1.9 ‡ | 2.9 |
| | L | -1.9 | | | | | L | -2.1 | | | |
| al-prn angle | R | 14.9 | 32 | 0.2 | 3.5 | al-prn angle | R | 13.4 | 37 | 0.8 | 4.0 |
| | L | 14.7 | | | | | L | 12.6 | | | |
| se-en depth | R | 10.3 | 26 | 0.4 | 1.5 | se-en depth | R | 9.3 | 35 | -0.2 | 2.0 |
| | L | 9.9 | | | | | L | 9.5 | | | |
| en-ex depth | R | 10.0 | 26 | -0.2 | 1.8 | en-ex depth | R | 8.8 | 34 | -0.5 | 2.9 |
| | L | 10.1 | | | | | L | 9.3 | | | |

| Males With Syndromes | | | | | | Females With Syndromes | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mmt | Side | Mean of Sides | N | Mean Diff | SD | Mmt | Side | Mean of Sides | N | Mean Diff | SD |
| t-g | R | 111.5 | 10 | -0.3 | 1.3 | t-g | R | 112.5 | 7 | 1.5 | 2.0 |
| | L | 111.7 | | | | | L | 111.0 | | | |
| t-se | R | 107.2 | 10 | -0.3 | 1.8 | t-se | R | 108.6 | 7 | 1.4 | 1.6 |
| | L | 107.5 | | | | | L | 107.2 | | | |
| t-ex | R | 70.5 | 9 | -0.2 | 3.0 | t-ex | R | 67.1 | 6 | 1.0 | 1.8 |
| | L | 70.7 | | | | | L | 66.1 | | | |
| t-sn | R | 107.4 | 9 | -1.2 | 2.3 | t-sn | R | 108.4 | 6 | 0.8 | 1.1 |
| | L | 108.6 | | | | | L | 107.6 | | | |
| t-ch | R | 96.2 | 10 | 0.0 | 3.6 | t-ch | R | 94.8 | 7 | -0.1 | 1.7 |
| | L | 96.2 | | | | | L | 94.9 | | | |
| t-pg | R | 120.5 | 10 | -0.2 | 3.1 | t-pg | R | 120.2 | 6 | 1.6 † | 1.3 |
| | L | 120.6 | | | | | L | 118.7 | | | |

Table 4-2 Continued

| Males With Syndromes | | | | | | Females With Syndromes | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mmt | Side | Mean of Sides | N | Mean Diff | SD | Mmt | Side | Mean of Sides | N | Mean Diff | SD |
| ex-en | R | 30.5 | 11 | -0.5 | 1.6 | ex-en | R | 29.0 | 14 | -1.1 † | 1.9 |
| | L | 31.0 | | | | | L | 30.1 | | | |
| en-se | R | 20.8 | 11 | 0.7 | 1.3 | en-se | R | 20.2 | 14 | 2.1 ‡ | 1.7 |
| | L | 20.1 | | | | | L | 18.1 | | | |
| cir-se | R | 31.7 | 12 | 1.2 | 3.4 | cir-se | R | 31.3 | 17 | 2.0 †† | 2.8 |
| | L | 30.5 | | | | | L | 29.3 | | | |
| ex-go | R | 82.7 | 4 | 4.9 †† | 1.0 | ex-go | R | 80.6 | 5 | 0.6 | 4.4 |
| | L | 77.9 | | | | | L | 80.1 | | | |
| ex-g | R | 53.0 | 12 | 0.6 | 1.6 | ex-g | R | 50.2 | 14 | 0.5 | 1.9 |
| | L | 52.5 | | | | | L | 49.7 | | | |
| sbl-sn | R | 11.6 | 12 | 0.1 | 1.4 | sbl-sn | R | 11.0 | 14 | -0.1 | 1.2 |
| | L | 11.5 | | | | | L | 11.1 | | | |
| go-pg | R | 86.1 | 4 | 7.9 †† | 1.6 | go-pg | R | 83.8 | 5 | 3.2 | 4.6 |
| | L | 78.2 | | | | | L | 80.6 | | | |
| en-ex angle | R | -2.8 | 11 | 0.4 | 3.8 | en-ex angle | R | -2.1 | 14 | 1.4 | 3.5 |
| | L | -3.2 | | | | | L | -3.5 | | | |
| al-prn angle | R | 16.8 | 13 | 3.1 † | 4.2 | al-prn angle | R | 13.9 | 17 | 1.5 | 3.8 |
| | L | 13.8 | | | | | L | 12.3 | | | |
| se-en depth | R | 9.7 | 11 | -1.0 ‡ | 0.5 | se-en depth | R | 8.5 | 14 | -0.1 | 1.6 |
| | L | 10.8 | | | | | L | 8.7 | | | |
| en-ex depth | R | 8.6 | 11 | 0.4 | 2.8 | en-ex depth | R | 9.7 | 14 | 1.2 | 2.2 |
| | L | 8.2 | | | | | L | 8.5 | | | |

The data were rounded to one decimal place for this table, but the complete values were used in all calculations. All data are in millimeters, except the angles, which are in degrees. The Mmt column lists the measurements investigated. For the Side column, R is the right side and L is the left side of the face. The Mean of Sides column has the averages of each measurement for the right and left sides of the face, as indicated by the Side column. The N column lists the numbers of pairs of right and left measurements. The Mean Diff column has the differences between the means of the right and left measurements and the probabilities associated with the t-test. The probabilities are indicated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. The SD column has the standard deviations of the paired differences.

Table 4-3. The Statistically Significant Findings for the Comparisons of the Right and Left Coordinate Direction Angles in All Groups

**Normal Males**

| Angle | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al α | R | 79.7 | 32 | -0.5 †† | 0.9 |
| | L | 80.2 | | | |
| al γ | R | 11.4 | 32 | 0.5 †† | 0.9 |
| | L | 10.8 | | | |
| ch α | R | 75.7 | 30 | -0.8 ‡ | 0.9 |
| | L | 76.5 | | | |
| ch γ | R | 27.5 | 30 | 0.5 † | 1.2 |
| | L | 27.0 | | | |
| cph α | R | 86.8 | 31 | -0.6 ‡ | 0.9 |
| | L | 87.5 | | | |
| cph β | R | 105.7 | 31 | 0.2 †† | 0.4 |
| | L | 105.5 | | | |
| cph γ | R | 16.1 | 31 | 0.3 ‡ | 0.5 |
| | L | 15.7 | | | |
| ex γ | R | 37.2 | 31 | 0.4 † | 1.0 |
| | L | 36.8 | | | |
| go γ | R | 73.0 | 9 | 2.5 † | 3.2 |
| | L | 70.5 | | | |

**Normal Females**

| Angle | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al α | R | 79.7 | 37 | -0.6 ‡ | 1.0 |
| | L | 80.2 | | | |
| al γ | R | 11.3 | 37 | 0.6 ‡ | 0.7 |
| | L | 10.7 | | | |
| ch α | R | 74.9 | 38 | -0.4 †† | 0.9 |
| | L | 75.3 | | | |
| ch β | R | 113.1 | 38 | 0.5 † | 1.3 |
| | L | 112.7 | | | |
| ch γ | R | 28.2 | 38 | 0.6 ‡ | 0.9 |
| | L | 27.6 | | | |
| cph α | R | 86.8 | 38 | -0.5 ‡ | 1.0 |
| | L | 87.3 | | | |
| cph γ | R | 16.1 | 38 | 0.2 †† | 0.5 |
| | L | 15.9 | | | |
| en α | R | 79.1 | 35 | -0.5 †† | 1.0 |
| | L | 79.6 | | | |
| en β | R | 75.0 | 35 | 0.4 ‡ | 0.7 |
| | L | 74.6 | | | |
| zy β | R | 88.6 | 35 | -0.9 ‡ | 1.4 |
| | L | 89.5 | | | |

**Males With Syndromes**

| Angle | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al β | R | 93.7 | 13 | 0.7 †† | 0.7 |
| | L | 93.0 | | | |
| cir β | R | 74.1 | 12 | 0.6 †† | 0.6 |
| | L | 73.5 | | | |
| en α | R | 78.8 | 11 | -0.7 † | 0.8 |
| | L | 79.5 | | | |
| go β | R | 132.2 | 4 | 2.2 † | 1.0 |
| | L | 130.1 | | | |
| go γ | R | 70.4 | 4 | 5.5 ‡ | 0.6 |
| | L | 64.9 | | | |
| zy β | R | 90.7 | 11 | -1.6 †† | 1.3 |
| | L | 92.3 | | | |

**Females With Syndromes**

| Angle | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al β | R | 93.9 | 17 | 0.4 † | 0.7 |
| | L | 93.5 | | | |
| al γ | R | 10.1 | 17 | 0.5 † | 1.0 |
| | L | 9.6 | | | |
| ch α | R | 76.5 | 17 | -0.6 † | 1.1 |
| | L | 77.2 | | | |
| cir α | R | 69.9 | 17 | -1.0 † | 1.7 |
| | L | 71.0 | | | |
| cir γ | R | 25.8 | 17 | 1.1 †† | 1.3 |
| | L | 24.7 | | | |
| cph α | R | 86.8 | 17 | -0.5 † | 1.1 |
| | L | 87.4 | | | |
| en α | R | 78.9 | 14 | -1.1 †† | 0.8 |
| | L | 80.0 | | | |
| en β | R | 76.1 | 14 | 0.5 † | 0.8 |
| | L | 75.6 | | | |
| ex γ | R | 35.0 | 14 | 0.5 † | 0.9 |
| | L | 34.5 | | | |
| sbl γ | R | 10.7 | 15 | 0.4 † | 0.6 |
| | L | 10.3 | | | |

These data were rounded to one decimal place for this table, but the complete values were used in all calculations. All measurements are in degrees. The Angle column lists the coordinate direction angles that were statistically significantly different between the right and left sides of the face. For the Side column, R is the right side and L is the left side of the face. The Mean of Sides column has the averages of each angle for the right and left sides of the face, as indicated by the Side column. The N column lists the numbers of pairs of right and left angles. The Mean Diff column has the differences between the means of the right and left angles and the probabilities associated with the t-test. The probabilities are indicated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. The SD column has the standard deviations of the paired differences.

Table 4-4. The Statistically Significant Findings for the Comparisons of the Right and Left Three-Dimensional Coordinates in All Groups

**Normal Males**

| Coord | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al X | R | 16.9 | 32 | 0.8 †† | 1.5 |
| | L | 16.1 | | | |
| ch X | R | 24.0 | 30 | 1.2 ‡ | 1.5 |
| | L | 22.8 | | | |
| cph X | R | 5.7 | 31 | 1.1 ‡ | 1.6 |
| | L | 4.6 | | | |
| cph Y | R | -28.1 | 31 | -0.3 † | 0.7 |
| | L | -27.8 | | | |
| cph Z | R | 99.6 | 31 | -0.4 ‡ | 0.6 |
| | L | 100.0 | | | |
| go Z | R | 23.1 | 9 | -3.9 † | 5.2 |
| | L | 27.0 | | | |

**Normal Females**

| Coord | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al X | R | 17.0 | 37 | 1.0 †† | 1.8 |
| | L | 16.0 | | | |
| ch X | R | 25.1 | 38 | 0.6 † | 1.8 |
| | L | 24.5 | | | |
| ch Y | R | -37.9 | 38 | -0.6 † | 1.6 |
| | L | -37.3 | | | |
| cir X | R | 29.9 | 35 | 1.0 † | 2.6 |
| | L | 28.9 | | | |
| cph X | R | 5.9 | 38 | 1.0 ‡ | 1.7 |
| | L | 4.9 | | | |
| en X | R | 15.0 | 35 | 0.7 †† | 1.4 |
| | L | 14.3 | | | |
| en Y | R | 20.5 | 35 | -0.6 †† | 1.1 |
| | L | 21.1 | | | |
| ex X | R | 45.3 | 35 | 0.5 †† | 1.1 |
| | L | 44.8 | | | |
| ex Y | R | 20.5 | 35 | 0.5 †† | 1.2 |
| | L | 20.0 | | | |
| zy Y | R | 1.8 | 35 | 1.2 ‡ | 1.9 |
| | L | 0.7 | | | |

**Males With Syndromes**

| Coord | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al Y | R | -6.1 | 13 | -1.1 †† | 1.2 |
| | L | -5.0 | | | |
| cir Y | R | 22.7 | 12 | -0.8 † | 1.2 |
| | L | 23.6 | | | |
| cph Y | R | -26.0 | 12 | -0.3 † | 0.5 |
| | L | -25.7 | | | |
| en X | R | 15.5 | 11 | 1.1 †† | 1.2 |
| | L | 14.4 | | | |
| en Z | R | 75.3 | 11 | 1.0 ‡ | 0.5 |
| | L | 74.3 | | | |
| go Z | R | 25.2 | 4 | -8.5 †† | 1.6 |
| | L | 33.7 | | | |
| sbl X | R | 11.0 | 13 | 0.8 † | 1.3 |
| | L | 10.2 | | | |
| zy Y | R | -0.9 | 11 | 2.1 †† | 1.6 |
| | L | -3.0 | | | |

**Females With Syndromes**

| Coord | Side | Mean of Sides | N | Mean Diff | SD |
|---|---|---|---|---|---|
| al Y | R | -6.3 | 17 | -0.6 † | 1.1 |
| | L | -5.6 | | | |
| ch X | R | 22.4 | 17 | 1.1 † | 2.1 |
| | L | 21.3 | | | |
| cir Y | R | 21.8 | 17 | 0.6 † | 1.1 |
| | L | 21.2 | | | |
| cph X | R | 5.6 | 17 | 1.0 † | 1.9 |
| | L | 4.7 | | | |
| en X | R | 15.3 | 14 | 1.5 ‡ | 1.1 |
| | L | 13.8 | | | |
| ex Z | R | 66.1 | 14 | -1.0 † | 1.7 |
| | L | 67.1 | | | |
| go X | R | 51.4 | 5 | 2.6 †† | 1.4 |
| | L | 48.7 | | | |
| sbl X | R | 10.5 | 15 | 0.9 † | 1.7 |
| | L | 9.6 | | | |

These data were rounded to one decimal place for this table, but the complete values were used in all calculations. All measurements are in millimeters. The Coord column lists the X, Y, and Z coordinates that were statistically significantly different between the right and left sides of the face. For the Side column, R is the right side and L is the left side of the face. The Mean of Sides column has the averages of each coordinate for the right and left sides of the face, as indicated by the Side column. The N column lists the numbers of pairs of right and left coordinates. The Mean Diff column has the differences between the means of the right and left sides and the probabilities associated with the t-test. The probabilities are indicated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. The SD column has the standard deviations of the paired differences.

Table 4-5. Comparison of the Positions of the Midline Landmarks Against the Hypothesized Test Value of Zero

| **Normal Males** | | | | **Normal Females** | | | |
|---|---|---|---|---|---|---|---|
| X Coord | N | Mean | SD | X Coord | N | Mean | SD |
| g | 31 | 0.4 †† | 0.8 | g | 38 | 0.4 † | 0.9 |
| li | 31 | 0.2 | 1.0 | li | 38 | 0.3 | 1.0 |
| ls | 29 | -0.2 | 0.8 | ls | 36 | -0.3 | 1.0 |
| pg | 31 | 0.5 †† | 1.0 | pg | 38 | 0.9 ‡ | 1.1 |
| prn | 32 | -0.3 | 1.0 | prn | 38 | 0.0 | 1.1 |
| se | 32 | 0.5 ‡ | 0.8 | se | 38 | 0.5 ‡ | 0.8 |
| sl | 30 | 0.4 †† | 0.9 | sl | 38 | 0.4 † | 1.0 |
| sn | 27 | -0.4 †† | 0.7 | sn | 36 | -0.3 † | 0.8 |
| **Males With Syndromes** | | | | **Females With Syndromes** | | | |
| X Coord | N | Mean | SD | X Coord | N | Mean | SD |
| g | 13 | 0.2 | 0.8 | g | 17 | 0.2 | 1.1 |
| li | 9 | 0.7 † | 0.8 | li | 15 | 0.1 | 0.8 |
| ls | 13 | 0.1 | 1.4 | ls | 16 | -0.2 | 1.0 |
| pg | 13 | 0.5 | 1.4 | pg | 16 | 0.7 † | 1.1 |
| prn | 13 | -0.4 | 1.3 | prn | 17 | -0.1 | 1.2 |
| se | 13 | 0.4 | 0.8 | se | 17 | 0.4 | 0.8 |
| sl | 13 | 0.6 †† | 0.6 | sl | 16 | 0.4 † | 0.7 |
| sn | 12 | -0.1 | 0.5 | sn | 15 | -0.4 | 0.9 |

These data were rounded to one decimal place for this table, but the complete values were used in all calculations. All measurements are in millimeters. The X Coord column lists the midline landmarks for which the positions of the X coordinates were tested. The N column lists the numbers of X coordinates. The Mean column has the mean X coordinate positions, and a negative sign on the mean indicates deviation to the right side of the face. This column also indicates the probabilities associated with the t-test as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. The SD column has the standard deviations.

Table 4-6. The Bilateral Differences in Males and Females With Syndromes That Exceeded the Normal Limits

| Males With Syndromes | | | Females With Syndromes | | |
|---|---|---|---|---|---|
| Subjects | Mmt | Diff | Subjects | Mmt | Diff |
| Subject 1 | cir-se | 6.3 | Subject 1 | ex-go | -6.5 |
| Subject 2 | sbl-sn | 2.7 | Subject 2 | en-se | 5.0 |
| | al-prn angle | 8.3 | Subject 3 | se-en depth | -4.1 |
| | en-ex depth | -4.0 | Subject 4 | ex-en | -3.5 |
| Subject 3 | t-pg | 5.0 | | en-ex angle | 6.9 |
| | al-prn angle | 8.3 | Subject 5 | ex-en | -3.8 |
| Subject 4 | t-ex | -6.6 | | en-se | 4.8 |
| | al-prn angle | 7.9 | Subject 6 | en-ex depth | 6.0 |
| | en-ex depth | 5.1 | | | |
| Subject 5 | cir-se | -5.3 | | | |
| | en-ex depth | -3.9 | | | |
| Subject 6 | cir-se | 4.8 | | | |
| Subject 7 | go-pg | 9.2 | | | |

These data were rounded to one decimal place for this table, but the complete values were used in all calculations. All measurements are in millimeters, except the angles, which are in degrees. The Mmt column lists the measurements, by Subject, that exceeded twice the standard deviation of the paired differences (see text for a full explanation). The Diff column has the actual differences for each measurement listed.

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# CHAPTER 5

# RESEMBLANCE BETWEEN INDIVIDUALS WITH SYNDROMES AND NORMAL AND SYNDROME-AFFECTED FAMILY MEMBERS[1]

## INTRODUCTION

Syndromes of the face can be recognized clinically because each syndrome is represented by a set of features not commonly found together in the normal population. This ability to recognize not only abnormal facial features, but to pinpoint the actual syndrome, indicates that there is consistency in the morphological expression of syndromes between unrelated individuals. However, the relative contributions of family resemblance and syndrome resemblance have not been well explored. Therefore, an investigation was undertaken in which the soft tissue facial feature measurements were compared, using the correlation coefficient, between related and unrelated individuals with the same syndrome and between family members with and without syndromes. It was thought that individuals with syndromes would have greater facial measurement correlations with each other than with their normal family members. Since it was common for at least one relative to accompany the patient to the clinic where the data was collected, comparative normal facial measurement data was obtained in many cases from family members. It was hoped that measurement correlations might present a practical and cost-effective method to screen for syndromes in two ways: (1) if the presence of a syndrome was uncertain, facial measurements of the patient and his or her normal relatives could be compared to determine if there was a lack of resemblance, thereby indicating that a syndrome might be present; and (2) if a specific syndrome appeared to be present, correlation coefficients could be used to compare measurements from the person in question to measurements from already diagnosed individuals, with significant positive correlations indicative that the syndrome was

[1] A version of this chapter has been submitted for publication. Shaner DJ, Peterson AE, Beattie OB, and Bamforth JS. Soft tissue facial resemblance in families and syndrome-affected individuals. American Journal of Medical Genetics.

correctly identified.

## LITERATURE REVIEW

Measurements can be used as a method to study the resemblance of genetically related individuals. Both common genes and common environment contribute to family resemblance and tend to increase the differences between unrelated families (Falconer, 1989). Fisher and earlier workers, such as Galton, recognized that both genes and environment contributed to variation between parents and offspring and between sibs (Fisher, 1918). In Dahlberg's (1926) study of Swedish monozygotic and dizygotic twins, the influences of heredity, environment, sex-related differences, and measurement error were recognized. Subsequent analyses have investigated family resemblance through such methods as correlation coefficients, heritability estimates (which estimate the proportion of the variance of a trait due to genetic influence), comparison of variance, factor analysis, and path analysis (which estimates transmissibility, the genetic and environmental influences on the phenotype of offspring).

Some studies using correlations to detail the similarities among family members have indicated that longitudinal measurements had greater correlations than did transverse measurements. This was found to be the case in male sibs (Howells, 1948, 1949, 1953). Product-moment and intraclass correlations ranged from approximately 0.2 for nose breadth to 0.7 for facial height (Howells, 1953). In studying mixed-sex sibs from a homogeneous population, Howells (1966) again reported that intraclass correlation coefficients were highest for "linear" measurements, such as nose height, than for breadth measurements. Furthermore, measurements of fatty tissues had the lowest correlations. Paginini-Hill et al. (1981) studied extended families from the S-leut, a communal-living isolate. Correlations between the categories of parent-child and sib-sib were typically lower than the expected value of 0.50 for most variables (they ranged from approximately 0.2 to 0.5 for four facial measurements). They were, however, statistically significantly different from zero, and, with no evidence for significant marital correlations, the authors concluded that there was a hereditary

component to the traits studied. There were no indications in the facial measurements for either maternal effects or X-linkage. Among the facial variables, only total face height was identified as having very high genetic effects and minimal environmental effects. Using factor analysis, bizygomatic and bigonial widths were grouped with head lengths and diameters; another factor included nose height and length with ear dimensions. While not referring specifically to the facial measurements, these authors concluded that linear bone measurements had the greatest genetic determination, followed by circumference and breadth measurements (combined bone, muscle, and fat), and, lastly, skinfold (fat) measurements.

Other methods of analysis have produced results indicating differences between the length and breadth measurements of the face. Using factor analysis to study traits from adult brothers, Howells (1951) identified two facial factors: lateral facial-cranial factor and facial length. Further investigation of the factors indicated that the facial length and long bone length factors were highly correlated between brothers; analysis of variance showed that the proportion of the variance between the families was far greater than that within the families for both factors. He concluded that some unknown thing was contributing more to the differences between families than to the resemblance within families for these factors. This was not the case for the lateral facial-cranial factor, for which the greatest proportion of the variance was found within families (Howells, 1953). Byard et al. (1985a) used principal components analysis and path analysis to investigate craniofacial resemblance within Indian families. Eight components were identified: cranial size, craniofacial breadth, nasal height, upper facial breadth, lower facial breadth, lower facial height, upper facial height, and ear dimensions. Common sibling environment, marital resemblance, and cultural inheritance had an effect on three of the six components involving the facial measurements (craniofacial breadth, nasal height, and upper facial height), while polygenic inheritance alone was implicated for the remaining three facial components (upper and lower facial breadth and lower facial height). The craniofacial height components had larger transmissibility estimates than did the breadth components. Clark (1956) used measurements from same-sex monozygotic and dizygotic twins to develop heritability

estimates. The estimates of nine transverse and vertical facial traits were 0.60 or higher, except bipalpebral breadth, which was 0.41. Nose height had the greatest heritability estimate of 0.76. While this author did not discuss the heritability estimates for the face, the data in Table I (Clark, 1956: 50) showed that the vertical measurements had the highest heritability estimates, followed by the transverse measurements.

One study concluded that breadth measurements had greater family resemblance than did longitudinal measurements. Osborne and De George (1959) studied adult Caucasian monozygotic and dizygotic twins. They investigated the contributions of genes and environment to head and body measurements by studying the variances in the two groups. As a general rule, they concluded that craniofacial breadths and circumferences showed higher genetic influence than did longitudinal measurements, which was opposite to what they concluded for body measurements. However, upper facial height and nose height were included with head breadth, head circumference, and bigonial breadth as the craniofacial measurements that showed the highest degree of genetic variability. Sex differences were noted as to whether genes or environment had greater influence: in females, a greater genetic influence was found for the bizygomatic and nose breadths, but these traits were more greatly influenced by environment in males.

Other investigations of family resemblance have presented differing conclusions as to whether longitudinal and breadth measurements were clearly separated and which type exhibited the greatest family resemblance. In addition, sophisticated techniques, such as path analysis, have often produced different findings for the modes of facial trait transmission. Susanne (1977) found that bigonial breadth had the highest heritability coefficient (0.662) of the facial measurements compared between parents and children. Nose height had the lowest value (0.391) of all body and facial measurements, which was attributed to measurement error. This author did not note a clear separation of facial longitudinal and breadth measurements. In an earlier comparison of Belgian families, Susanne (1975) also reported that facial longitudinal and breadth measurements were not clearly separated. All facial correlations were below the expected value of 0.50 for polygenic traits in parent-child and sib-sib

comparisons (but were still statistically significantly different from zero). The typically lower parent-child correlations, as compared with the higher sib-sib correlations, were attributed to greater environmental differences between the generations. In a few instances, a factor other than environment was also implicated in the lower than expected correlations: dominance was identified for bizygomatic breadth and external biocular breadth, and error in locating the landmark nasion was implicated in the results obtained for nasion-gnathion, nasion-stomion, and nose height. This researcher concluded that facial measurements of the mouth and nose had low degrees of genetic determination.

Devor et al. (1986a) investigated family resemblance in Mennonite children and adults. Father-child, mother-child, and sib-sib correlations for all six facial measurements were statistically significant, although the correlations were no greater than approximately 0.4. Using factor analysis, two craniofacial factors were identified: one included the facial measurements of bigonial diameter and bizygomatic diameter along with cranial breadths, circumferences, and lengths, and the other consisted of upper facial height, nose height, and morphological face height. Nose breadth could not be assigned to one specific factor. They noted that the craniofacial factors were different from the body factors: the latter were clearly separated into length and bulk measures, whereas the former were not. They suggested that there were morphological fields that had varying amounts of genetic and non-genetic determination and coined the term "functional multifactorial complex" to refer to both influences on the fields. Devor et al. (1986b) subsequently investigated the same group by path analysis. For the facial traits of siblings, there was no evidence for non-transmissible factors (i.e., factors that affected the siblings, but were not passed on from the parents). Significant family resemblance and vertical transmissibility of the facial traits were found; estimates of the latter were intermediate between linear body traits and the transverse and fat measurements.

Susanne et al. (1983) investigated adult monozygotic and same-sex dizygotic twins in order to estimate the presence of significant genetic variance in the measurements taken. They found significant sex-related differences: while all facial measurements from males showed the presence of a

genetic component, three measurements from females did not (nasion-gnathion, nasion-stomion, and lips height). The authors attributed these differences to the continued growth of males, but not females, past the age of 18 years. They noted that this phenomenon led to greater similarity in male monozygotic twins. Another study of Belgian twins by Hauspie et al. (1985) that investigated the presence of a genetic component in the variance also indicated sex-related differences. No genetic component in the variance was found for mouth breadth in males and for bizygomatic breadth, nasion-stomion, and lips height in females. The facial trait with the highest F ratio (calculated by the ratio of the within-mean squares of dizygotic to monozygotic twins) was also different in each sex: in males, it was external biocular breadth, while it was internal biocular breadth in females. The five factors obtained by principal components analysis were somewhat different in each sex. In males the factors were face height, facial breadth I, facial breadth II, ear size, and lips height. In females, the factors were breadth I, face height, ear size, breadth II, and lips height. The measurements grouped as factors were generally the same in both sexes, except for the facial breadths. Breadth I was composed of the same eye measurements and bizygomatic breadth in both sexes, but it also included nose breadth in males and the frontal and bigonial breadths in females. Breadth II included the mouth breadth for both males and females and also the frontal, bizygomatic, and bigonial breadths in males, but nose breadth was highly correlated with mouth breadth in females. These researchers were unable to determine whether the sex differences in the breadths were an accurate reflection of true differences or whether they were the result of a poor selection of breadth measurements. A significant genetic component to the variance was found for all of the factors.

Poosha et al. (1984) studied family resemblance in a group of endogamous Velanti Brahmin nuclear families. For the six facial measurements, only the father-daughter correlation (obtained by the maximum likelihood method) for nasal depth was not significant. They noted that the correlations from same-sex family members were typically higher than the opposite-sex pair correlations. Further statistical testing for heterogeneity of the correlations between the four categories of parent-child pairs (i.e., father-son, mother-son, father-daughter, mother-daughter) and

the four categories of sib-sib pairs revealed significant findings only for the facial variables of nose height and depth for parent-child correlations and for nasal breadth in sib-sib correlations. However, since different observers measured the male and female subjects, these researchers also considered interobserver measurement error as a possible factor in the sex differences found. Using path analysis, they concluded that bigonial breadth was the only facial trait that indicated polygenic inheritance with no influence from marital resemblance or common sibling environment. All other facial measurements (bizygomatic breadth, total facial height, and nasal height, depth, and breadth) were influenced by common sibling environment, cultural inheritance, marital resemblance, and measurement error. Byard et al. (1985b) studied the same families as Poosha et al. (1984), but included twin sibs in their analysis. This investigation indicated that all of the measurements showed family resemblance. Although significant sex differences in transmissibility were found for some cranial variables (males had greater transmissibility for head circumference, minimum frontal breadth, and ear height, whereas females had greater transmissibility for ear breadth), none were indicated for the facial variables. Testing for interobserver measurement error showed that this was a factor only for the bigonial and nose breadths; however, these researchers felt that different levels of replicability between the two observers could have affected the transmissibility estimates and decreased the magnitude of the correlations between husband-wife, opposite sex parent-child, siblings, and dizygotic twins. Polygenic inheritance was indicated for bigonial breadth, total facial height, and nasal depth and breadth, whereas bizygomatic breadth and nose height showed evidence for cultural transmission also.

Sharma et al. (1984) investigated resemblance among Punjabi families, some of which had monozygotic and dizygotic twin sibs. For the facial variables, there was no substantial evidence for sex-based differences when heterogeneity tests were carried out on the correlations calculated between parents and children by sex and siblings by sex. Correlations (obtained by the maximum likelihood method) were typically higher between parent-child pairs than non-twin sib pairs, which these researchers ascribed to either no common sib environment or a masking of the common sib

environment. Further investigation of the same group with path analysis by Byard et al. (1984) showed that all measurements demonstrated significant family resemblance. These researchers noted that the body and cranial measurements (minimum frontal diameter) that showed a maternal effect were all bony breadths; no facial traits were significant for maternal effect. Facial length and jaw height were transmissible by cultural and genetic means, and the remaining facial measurements (bizygomatic breadth, bigonial breadth, nasal height, nasal breadth, and nasal depth) showed only polygenic inheritance. Of all facial and body measurements, nasal height had the highest transmissibility estimate; all others were scattered among the body measurements.

While the results of these diverse methods cannot be compared directly, there are some common findings as noted above. According to Falconer (1989), heritability estimates, which assess the proportion of the variance of a trait due to genetic influence, are only applicable to the population from which they were derived, under the environmental conditions that prevailed at the time of study. This caution would also seem to apply to all statistics used to study family resemblance.

## MATERIALS AND METHODS

Facial measurements from individuals representing 30 families were used in this study. Each family consisted of two or more first-degree relatives (sibs and/or parents); those with three generations were subdivided into nuclear families. The members of each family could be medically normal or have a facial syndrome. Subjects with syndromes not characterized by distinctive facial features were not included in this study. The age range of the subjects was 1.6 years to adulthood (not all subjects gave their ages, but the oldest recorded was 63.1 years). The ancestral background of the majority of the families was mainly European, but three families reported their ancestry as Chinese, Native American, or a mix of Spanish and African American and/or Mayan. The following landmarks were marked on the subjects' faces: glabella (g), sellion (se), pronasale (prn), subnasale (sn), labiale superius (ls), labiale inferius (li), sublabiale (sl), pogonion (pg), tragion (t), zygion (zy),

gonion (go), exocanthion (ex), endocanthion (en), alare (al), subalare (sbl), cheilion (ch), and christa philtri (cph). Center of the iris (cir) was not marked on the face, but was produced by setting the custom circular computer cursor on the outer edge of the iris and digitizing the center. The descriptions of the landmarks as presented by Farkas (1981) were used, except for sellion and sublabiale (Farkas, 1994), gonion (Krogman, 1970), and center of the iris (a new landmark). Not all landmarks were marked on every subject, usually due to poor cooperation in children, the subject's stated desire not to have certain markings done, or the presence of facial hair in adult males. The right and left gonion landmarks were not imaged in enough subjects for statistical analysis, so the data from the landmarks and measurements involving gonion have not been reported here.

The measurement and three-dimensional coordinate data were obtained with a previously described method of photogrammetry (Shaner et al., 1998), and the landmark coordinates were transformed into a standard position as detailed earlier (Shaner et al., 2000). It should be noted that initially there were six cameras with which to image the subjects, but one camera failed during the period of data collection. The remaining five cameras were repositioned for full frontal and oblique lateral coverage of the subjects' faces. In order to eliminate the size variation between subjects due to age- and sex-related differences, the measurement data and three-dimensional landmark coordinates were scaled. The model used was the average of all three-dimensional coordinates from the normal individuals in the total sample, and a custom-written program was used to scale each subject's three-dimensional coordinates. Landmarks of the mouth and mandible (cheilion, christa philtri, labiale superius, labiale inferius, sublabiale, pogonion, and gonion) were not used in the scaling process because some subjects had open or smiling mouths. These were passively scaled along with the remaining landmarks. The facial measurements had already been calculated (from the unscaled three-dimensional coordinates), so the scale factors obtained from the landmark transformations were applied to the appropriate sets of facial measurements.

Prior to the statistical testing, the data were viewed as scatter plots by family. There was no evidence for a relationship other than linear for the three-dimensional coordinates and the facial

measurements. The scaled three-dimensional coordinates and single measurements were analyzed statistically without any further treatment. However, when specific pairs of family members were compared based on all available measurements, consistently high positive correlations were obtained. Therefore, for each measurement, the average was calculated from the entire database of measurements from all available normal individuals of European ancestry (omitting eight individuals who reported their ancestry as primarily non-European), and each average measurement was then subtracted from the appropriate measurement of every subject. These residuals (referred to as "measurements" in the following text and tables) were then used in the comparison of all available measurements (i.e., residuals) between pairs, as described below. Product-moment correlation coefficients (r) were calculated for groups of normal parent-normal child pairs and normal sib pairs for the three-dimensional coordinates and single measurements. All possible combinations of first-degree relatives were used to obtain the correlations. Correlation coefficients were also calculated between paired family members (normal and syndrome-affected) and paired subjects with one of four facial syndromes using all measurements that were present in both subjects. All correlations were tested against the null hypothesis that the population correlation coefficient was equal to zero (using a two-tailed test).

## RESULTS

### *Correlations for the Three-Dimensional Coordinates and Single Measurements in Normal Individuals*

The number of significant three-dimensional coordinate correlations for sibs was more than twice the number found for parent-child comparisons (Table 5-1). There was little patterning in the correlations between the latter, such that only for the landmark zygion were two of the three coordinates significantly correlated for both the right and left sides of the face. For sib pairs, significant correlations were typically found on both the right and left sides of the face for bilateral landmarks, although not necessarily for the same three-dimensional coordinates. Significant correlations for the parent-child pairs were mixed as to sign and ranged from -0.47 to 0.61, whereas

significant correlations for the sib pairs were all positive and ranged from 0.40 to 0.77. Measurement correlations showed the same trends as were found for the three-dimensional coordinates: there was a greater number of significant correlations for the sib pairs than for the parent-child pairs, and the signs of the significant correlations were mixed in the latter group, but were all positive in the former (Table 5-2). The most striking finding for the paired sib correlations was that the midline distances were all significant.

*Correlations Between Family Members and Syndrome-Affected Individuals*

Correlations between family members and syndrome-affected individuals were carried out on all available measurements for each pair, with a maximum of 36 measurements available for use. Based on the results of the correlations of the single measurements and three-dimensional coordinates for normal parent-normal child pairs and normal sib pairs, it was postulated that sib pairs would tend to resemble each other more than would parent-child pairs when all available measurements were used to obtain correlation coefficients. The correlations (Table 5-3) supported this hypothesis: nine out of 27 (33%) correlations in the normal parent-normal child category were significant, and three of these were negative correlations, whereas 12 out of 25 (48%) correlations for normal sibs were significant, and all were positive. The total range of correlations for the normal parent-normal child group was nearly equally negative and positive (-0.62 to 0.63), while those from the normal sibs group were more heavily weighted to positive correlations (-0.26 to 0.80). The numbers of subject pairs in the normal parent-child with a facial syndrome and normal sib-sib with a facial syndrome groups were less than for the comparisons between normal family members, but the percentages of significant correlations were very similar: 33% for the parent-child comparisons and 43% for the sib pairs. As was found for all other comparisons, significant correlations between parents and children were mixed as to sign, but were positive when sibs were evaluated.

Measurement data from individuals with four syndromes were compared by syndrome (Table 5-4). Although not completely consistent, the significant positive correlations obtained indicated that

there was a high degree of resemblance among individuals with the same syndrome. In two cases, a related pair of individuals with Russell-Silver syndrome and one pair of unrelated subjects with achondroplasia, the correlations were not statistically significant.

## DISCUSSION

### *Normal Relatives*

Expected measurement correlations between parent-child and sib pairs are 0.50 for autosomal polygenic traits, with no dominance effects or X-linkage (Susanne, 1975). Using this estimate for the present data, four out of the 78 (5%) three-dimensional coordinate correlations were 0.50 or greater in normal parent-normal child comparisons, and 12 (15%) were at this level or greater for normal sibs. Similarly, none of 36 single measurement correlations were 0.50 or greater in the parent-child comparisons, and eight out of 36 (22%) reached or exceeded this level when correlations between the normal sibs were calculated. Others, (e.g., Howells, 1948, 1953, 1966; Susanne, 1975) also indicated that many correlations did not reach 0.50. In Susanne's (1975) study, lower than expected correlations for measurements involving nasion were attributed to error in locating this landmark. Low correlations for external biocular breadth and bizygomatic breadth were ascribed to the effect of dominance; in the present data, these correlations were also below 0.50, except for zygion-zygion in sibs. This researcher also pointed out that environmental differences were greater between parents and children than between sibs, which could result in low parent-child correlations. Howells (1948) simply stated that his sample of brothers showed varying degrees of likeness for different measurements. The greater number of significant positive correlations for normal sibs as compared with normal parent-normal child correlations in the data presented here also suggested that there was a factor, possibly environment, which contributed more to the resemblance between sibs than to the similarity between parents and children.

As discussed earlier, differences in family resemblance for craniofacial longitudinal and breadth measurements have been reported in the literature. The statistically significant positive

correlations found between normal sibs in the current sample indicated that there was family resemblance for the midline vertical measurements. Several transverse (zygion-zygion and cheilion-cheilion) and lateral (right and left tragion-pogonion and right tragion-subnasale) measurements also demonstrated significant positive correlations. In contrast, the significant parent-child correlations showed no discernible pattern.

*Syndrome-Affected Individuals and Their Family Members*

Although small in number, the correlations obtained from the paired syndrome-affected individuals for all available measurements demonstrated that individuals with syndromes resembled each other in the majority of cases. With the exception of the related individuals with Russell-Silver syndrome, all of these pairs were composed of children (age 3.9 to 13.8 years old). The highest significant correlations were found for related individuals, ranging from 0.72 to 0.83. Unrelated individuals with achondroplasia showed statistically significant correlations ranging from 0.35 to 0.65. The range of significant normal parent-normal child correlations, based on all available measurements, was -0.62 to 0.63, and the range was -0.44 to 0.45 for the normal parent-child with a facial syndrome category. Normal sibs had a range of significant correlations from 0.39 to 0.80, whereas the normal sib-sib with a facial syndrome group had a range from 0.43 to 0.76. Since the ranges of significant correlations overlapped in the normal sibs group and the related syndrome-affected individuals group, it was not possible to identify a definitive cutoff value that separated normal sib resemblance (i.e., family resemblance) from syndrome-based resemblance. That the sib pairs with mixed medical status also had some overlap in range with the related syndrome-affected individuals group indicated that family resemblance could be an important factor, even when one sib was normal and the other had a syndrome.

Several of the individuals with syndromes represented in Table 5-4 had normal family members represented in Table 5-3. Family 2 included the normal father of the adult woman with Russell-Silver syndrome, and Family 3 compared this same woman to her normal son (age 1.6 years)

and her son with Russell-Silver syndrome (age 3.9 years) to his normal brother. Non-significant correlations were found between father-daughter and between the sibs. However, there was a significant negative correlation between the mother with Russell-Silver syndrome and her normal son (-0.44). All of the individuals with achondroplasia also had one normal parent for comparison (Families 4, 6, and 10). The correlations between them were not statistically significant, except in the case of Family 4. This exception is discussed below.

In this research, a non-significant correlation was found for two unrelated females with achondroplasia. This was an interesting result since the two subjects were the same age, but reported different ancestral backgrounds (Subject 1 was mainly European with distant Native American origins and Subject 2 had a full Native American ancestry). While the difference in ancestry seemed to be an obvious factor in the non-significant correlation, this could not have been the case based on the following observations: Subject 1 and her sister both had achondroplasia, and their high correlation coefficient (0.72) indicated that they resembled each other; the sister (of Subject 1) had a significant correlation of 0.41 with Subject 2; and Subject 2 had a significant correlation (0.45) with a four-year-old boy of Western European ancestry. Environmental differences were also ruled out as the basis for the non-significant correlation because of these observations. The lack of significant correlation between the unrelated individuals with achondroplasia could not be explained.

The other non-significant result was obtained for a mother-son pair with Russell-Silver syndrome. There were no other syndrome-affected parent-child pairs for comparison. However, within the paired family data only seven of the 36 (19%) correlations of all parent-child pairs were significantly positively correlated, compared with 15 of 32 (47%) correlations between sibs (regardless of medical status), which indicated that large age differences and/or different childhood environments could have resulted in the poor correlation between this mother-son pair. This result led to an investigation of the effect of age differences between paired individuals.

Several studies have investigated the effect of age differences on estimates of heritability or correlation coefficients. Vandenberg (1962) reanalyzed twin data from six previously published

studies in order to determine whether the differing age ranges of the subjects in the studies had an effect on the heritability estimates (F ratios calculated by the ratio of dizygotic and monozygotic twin within pair variances) for craniofacial and body measurements. The studies chosen had subjects with age differences ranging from six to 77 years between the youngest and oldest twin pairs. He concluded that the F ratios from all studies were similar, with some exceptions for body measurements, head length, and head height. The author noted that the F ratios did not increase with age, and that the one study in which the subjects were all adults often had lower F ratios than the other studies involving only children or both children and adults. These results suggested that environment did not clearly have a differing role during the various stages of development; it was not known if this was applicable to the mother-son pair with Russell-Silver syndrome (i.e., that different childhood environments might explain their correlation), since Vandenberg studied twins.

Mueller (1977) studied correlations in body measurements of child (seven to 12 years old) and adult (27 to 62 years old) sib pairs. He concluded that the correlations gained from the children were larger than the correlations from adult sibs (although only three measurements were reported as being statistically significantly different between the two groups). Mueller postulated that the similarity in age between the young sib pairs might have meant that their environments were much the same and that similar genes for growth were active in the sib pairs, thus leading to the relatively higher correlations found for them. Furthermore, the correlations from the young sibs showed no patterning, other than that the skinfold coefficients were low. In contrast, the correlations for the adult sibs were distinctive: the highest correlations were found for bone, followed by weight, circumferences, and skinfold measurements. Additional investigation of body measurements from adult sibs that were divided into groups based on an age difference of less than seven years or seven years and more indicated that bony measurement correlations were not typically different in the two groups. On the other hand, weight, muscle, and fat measurements that were typically found not to be significantly correlated between the sibs with the greatest age difference were often significantly correlated for the sibs closer in age (Mueller, 1978). Although these studies did not investigate facial

measurements in parent-child pairs, they suggested that the age span between paired subjects could be an important factor in family resemblance.

In the current study, it was noted that comparisons of parents and children age four and under, regardless of medical status, were most likely to produce significant negative correlations (Families 3, 4, 11, 22, and 27). Family 3 has already been detailed above. Family 4 was a normal mother and a 4.1-year-old son with achondroplasia; they were significantly negatively correlated. Family 11 was two parents with a normal 4.4-year-old son and a two-year-old son with Down syndrome. In this case, only the father was significantly negatively correlated with the normal son, while the mother was significantly positively correlated with the same child. Both parents were non-significantly negatively correlated with the syndrome-affected child, while the sibs had a correlation of 0.00. At least in the case of the correlation between the father and syndrome-affected son, the very small number of measurement pairs (i.e., eight) probably resulted in the correlation of -0.58 not reaching statistical significance. Family 27 was two parents and two normal daughters age 6.3 and 3.7 years. The correlation between the father and the younger daughter was the only one that was significantly negatively correlated. As in the case of Family 11, the small number of paired measurements may have resulted in non-significant correlations within this family. Family 22 was an exception to the finding that correlations between very young children and adults were likely to be significantly negative. This was a mother and three children age 10.2, 12.9, and 15.2 years old. The correlation between the mother and the youngest child was significant and negative; this result could not be explained. There were no significant negative correlations in the normal sib and normal sib-sib with a facial syndrome categories, regardless of whether one of the sibs was age four or under. This suggested that it was not necessarily the actual age difference between the two individuals that was important, but rather the combination of a very young person with an adult.

The son in the mother-son pair with Russell-Silver syndrome was under the age of four years, but the finding that pairing young children with adults produced significant negative correlations did not apply in this case. According to Gorlin et al. (1990) and Jones (1997), individuals with Russell-

Silver syndrome have improved appearance with age. The lack of significant correlation between these two could be the result of the young son's abnormal appearance in comparison with the mother's more normal facial features. A similar explanation might also partly account for the non-significant correlations in Family 11 between the parents and their two-year-old son with Down syndrome. Jones (1997) reported that skeletal growth and maturation in children with Down syndrome normalized with age. Farkas et al. (1991) also reported age-related soft tissue facial changes in subjects age four months to 31 years: increased normalcy occurred for the facial and mandibular vertical lengths and measurements of the eyes, but other features became more abnormal (eye inclination, nasal root depth, and mouth width). For the Russell-Silver pair, it is likely that the correlation could become significantly positive as the child matured. In the case of the Down syndrome child, it was not known whether the syndrome-based facial abnormalities would lead to significant negative correlations with his family members over time, or if family resemblance would eventually play a greater role in his appearance.

### *Syndrome-Affected Individuals and Their Correlations in the Literature*

Correlations between normal and syndrome-affected family members have been obtained most commonly with z-scores (standard deviation units) as examples of the utility of using z-scores to compare individuals of different sexes and ages. In monozygotic twins studied by craniofacial radiographs, Garn et al. (1984) reported correlations of 0.64 for a pair with oto-palato-digital syndrome, 0.92 for a pair with Pierre Robin syndrome, and 0.90 for 12 pairs of twins who were each discordant for cleft lip/palate. These authors recommended their z-score based method as a diagnostic aid for individuals with unknown syndromes. Brown et al. (1993) compared craniofacial morphology in adult males with Klinefelter (47 XXY) syndrome with their normal parents and sibs using roentgenographic measurements. The average correlation coefficients estimated from the measurements were 0.61 for male-male comparisons and 0.44 for male-female pairs. Sibs with Robinow syndrome (two boys and one girl) were investigated by Israel and Johnson (1988).

Craniofacial angles were measured from radiographs, and correlations between the children were 0.80, 0.83, and 0.87. Saksena et al. (1989) computed the correlation between a mother and son using roentgenographic craniofacial measurements. The mother and son were initially believed to have different syndromes due to their dissimilar facial morphology, but the correlation between them was 0.76. The mother's normal brother was used as a control subject; the correlation between him and the adult female was 0.46, and the correlation between him and the boy was 0.31. The son was originally thought to have Stickler syndrome, but the correlations between known Stickler syndrome patients and both the mother and son were low, ranging from 0.03 to 0.30. Ward (1989) calculated craniofacial correlation coefficients from individuals diagnosed with hypohidrotic ectodermal dysplasia, normal relatives, and related carriers. A correlation of 0.77 was found for the affected and carrier groups, whereas the coefficient between carriers and normal relatives was 0.58 and that between syndrome-affected and normal relatives was 0.52.

These findings suggested, at first glance, that correlations (based on z-scores) were not necessarily very discriminating since syndrome-affected individuals had high correlations with normal relatives. An example was the correlation of 0.90 for twin pairs discordant for cleft lip/palate reported by Garn et al. (1984). As noted by these researchers, however, this high correlation showed that the facial morphology of the normal twins was affected in a manner similar to that of the twins with the visible cleft. Further comparisons of both affected and unaffected twins with normal individuals from families with no history of facial clefting might have made clearer the point that correlations can be useful in syndrome diagnosis. In addition, Saksena et al. (1989) noted that the correlation between a syndrome-affected sister and her normal brother (0.46) was close to the expected correlation of 0.50 for normal sibs under the assumption of polygenic inheritance. Unable to explain this result, the authors stated that it was not clear how to separate the genetic and environmental components of family resemblance. Environment might be a much stronger force in morphological resemblance than is currently recognized. The cohabitational effect has been well documented by Garn et al. (1979) for biologically related and unrelated individuals living together,

including for anthropometric traits (fatfold measurements, stature, and weight). More recently, Devor (1987) noted that many studies of family resemblance estimated high genetic heritability for craniofacial traits under the model that genetic factors were responsible for the level of the correlations. However, using path analysis, this author found not only that transmissibility of craniofacial dimensions was similar in the four populations reanalyzed from published accounts, but also that environment was roughly equivalent to genes in influencing craniofacial resemblance. Furthermore, this researcher postulated that environment had a greater role than genes for the craniofacial soft tissue features.

The correlations obtained in this study for specific pairs of family members (normal and syndrome-affected) based on all available measurements could not be used to establish a definitive cutoff point at which the presence of a syndrome was clearly indicated in one of the individuals of a pair. However, the correlations calculated between pairs of syndrome-affected subjects showed that individuals with the same syndrome resembled each other. The highest correlations were found among related pairs of sibs with the same syndrome, indicating that the shared genes (both normal and abnormal genes) and common environment could both be factors in the resemblance between them. It was inferred that common genes (i.e., genetic errors in the syndromes investigated, other than the case of placental anastamoses) were the main cause of the resemblance between unrelated individuals with the same syndrome for two reasons: first, unrelated individuals with the same syndrome were significantly positively correlated in most cases; and second, there were definite environmental differences between several subjects with the same syndromes, yet their correlations were still significant and positive. There was some evidence that individuals with syndromes resembled each other more than they did their own family members; however, the small numbers of normal family members for comparison, plus the finding that significant negative correlations were often the result of pairing young children and adults, did not allow for a definitive conclusion in this matter. Comparison of measurements between individuals with unknown syndromes and individuals with confirmed syndromes could be a practical method for syndrome identification. Age-specific

data would be necessary for those syndromes characterized by significant changes in facial morphology over time, and more than one comparison would need to be made, since it has been shown here that there is a chance for a non-significant correlation between two people with the same syndrome. Taking facial measurements of patients with syndromes and their normal family members should be a part of the normal clinical routine; in this way, a database of measurements for specific syndromes and normative values could be built up and used to diagnose future uncertain cases.

Table 5-1. Correlations for Normal Parents and Their Normal Children and for Normal Sibs: Three-Dimensional Coordinates

| | Parent-Child | | Sibs | | | Parent-Child | | Sibs | |
|---|---|---|---|---|---|---|---|---|---|
| Coord | r | N | r | N | Coord | R | N | r | N |
| al R X | 0.14 | 27 | 0.33 | 24 | li X | 0.09 | 27 | -0.04 | 24 |
| al R Y | 0.11 | 27 | 0.64 ‡ | 24 | li Y | 0.19 | 27 | -0.02 | 24 |
| al R Z | 0.27 | 27 | -0.03 | 24 | li Z | 0.09 | 27 | 0.40 † | 24 |
| al L X | 0.16 | 24 | 0.18 | 24 | ls X | -0.14 | 23 | 0.47 † | 20 |
| al L Y | -0.05 | 24 | 0.58 †† | 24 | ls Y | 0.26 | 23 | 0.66 †† | 20 |
| al L Z | 0.14 | 24 | -0.04 | 24 | ls Z | 0.36 | 23 | -0.01 | 20 |
| ch R X | 0.35 | 26 | 0.41 † | 24 | pg X | 0.11 | 27 | 0.21 | 24 |
| ch R Y | 0.16 | 26 | 0.44 † | 24 | pg Y | -0.19 | 27 | 0.33 | 24 |
| ch R Z | 0.00 | 26 | 0.30 | 24 | pg Z | 0.61 ‡ | 27 | 0.44 † | 24 |
| ch L X | 0.33 | 26 | 0.45 † | 24 | pm X | -0.08 | 27 | -0.05 | 24 |
| ch L Y | 0.00 | 26 | 0.47 † | 24 | pm Y | 0.13 | 27 | 0.37 | 24 |
| ch L Z | 0.03 | 26 | -0.16 | 24 | pm Z | 0.12 | 27 | 0.52 †† | 24 |
| cir R X | -0.47 † | 21 | 0.39 | 19 | sbl R X | -0.13 | 23 | 0.03 | 24 |
| cir R Y | 0.17 | 21 | 0.60 †† | 19 | sbl R Y | -0.30 | 23 | 0.62 ‡ | 24 |
| cir R Z | -0.06 | 21 | 0.47 † | 19 | sbl R Z | 0.36 | 23 | 0.18 | 24 |
| cir L X | -0.06 | 19 | -0.01 | 19 | sbl L X | 0.03 | 23 | 0.33 | 24 |
| cir L Y | 0.32 | 19 | 0.57 †† | 19 | sbl L Y | -0.47 † | 23 | 0.57 †† | 24 |
| cir L Z | 0.19 | 19 | 0.13 | 19 | sbl L Z | 0.22 | 23 | 0.10 | 24 |
| cph R X | 0.25 | 26 | 0.21 | 24 | se X | 0.01 | 27 | 0.16 | 24 |
| cph R Y | 0.24 | 26 | 0.63 ‡ | 24 | se Y | 0.30 | 27 | 0.33 | 24 |
| cph R Z | 0.49 †† | 26 | 0.32 | 24 | se Z | 0.42 † | 27 | 0.13 | 24 |
| cph L X | 0.08 | 26 | 0.42 † | 24 | sl X | 0.37 | 27 | 0.41 † | 24 |
| cph L Y | 0.24 | 26 | 0.71 ‡ | 24 | sl Y | -0.16 | 27 | 0.27 | 24 |
| cph L Z | 0.34 | 26 | 0.22 | 24 | sl Z | 0.52 †† | 27 | 0.31 | 24 |
| en R X | 0.33 | 24 | -0.07 | 21 | sn X | -0.31 | 20 | 0.01 | 24 |
| en R Y | 0.28 | 24 | 0.12 | 21 | sn Y | -0.04 | 20 | 0.77 ‡ | 24 |
| en R Z | 0.00 | 24 | 0.41 | 21 | sn Z | 0.21 | 20 | 0.16 | 24 |
| en L X | -0.02 | 23 | -0.31 | 21 | t R X | 0.38 | 23 | 0.16 | 21 |
| en L Y | -0.13 | 23 | -0.09 | 21 | t R Y | -0.26 | 23 | 0.10 | 21 |
| en L Z | -0.08 | 23 | 0.04 | 21 | t R Z | -0.43 † | 23 | 0.44 † | 21 |
| ex R X | 0.07 | 25 | -0.20 | 22 | t L X | -0.24 | 21 | 0.26 | 17 |
| ex R Y | 0.13 | 25 | -0.06 | 22 | t L Y | -0.30 | 21 | 0.26 | 17 |
| ex R Z | -0.02 | 25 | 0.28 | 22 | t L Z | 0.04 | 21 | 0.20 | 17 |
| ex L X | 0.43 † | 25 | -0.01 | 22 | zy R X | 0.14 | 27 | 0.28 | 24 |
| ex L Y | 0.14 | 25 | -0.22 | 22 | zy R Y | 0.48 †† | 27 | 0.46 † | 24 |
| ex L Z | -0.10 | 25 | 0.43 † | 22 | zy R Z | 0.57 †† | 27 | 0.29 | 24 |
| g X | -0.02 | 27 | 0.12 | 24 | zy L X | -0.09 | 25 | 0.59 †† | 23 |
| g Y | 0.08 | 27 | 0.46 † | 24 | zy L Y | 0.51 †† | 25 | 0.35 | 23 |
| g Z | 0.30 | 27 | 0.36 | 24 | zy L Z | 0.42 † | 25 | 0.18 | 23 |

These data were rounded to two decimal places for this table, but the complete values were used in all calculations. The Coord column lists the three-dimensional coordinates; R and L refer to the right and left sides, respectively. The r column has the correlation coefficients and their significances, designated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. N is the number of pairs of individuals.

Table 5-2. Correlations for Normal Parents and Their Normal Children and for Normal Sibs: Single Measurements

| | Parent-Child | | Sibs | | | Parent-Child | | Sibs | |
|---|---|---|---|---|---|---|---|---|---|
| Mmt | r | N | r | N | Mmt | R | N | r | N |
| t-g R | -0.34 | 23 | 0.30 | 21 | ex-g R | 0.04 | 25 | -0.07 | 22 |
| t-g L | -0.05 | 21 | 0.19 | 17 | ex-g L | 0.31 | 25 | 0.17 | 22 |
| t-se R | -0.56 †† | 23 | 0.30 | 21 | sbl-sn R | 0.47 † | 20 | 0.39 | 24 |
| t-se L | 0.00 | 21 | -0.11 | 17 | sbl-sn L | 0.35 | 20 | 0.05 | 24 |
| t-ex R | -0.50 † | 22 | 0.26 | 19 | t-t | 0.16 | 20 | 0.42 | 16 |
| t-ex L | -0.47 † | 20 | 0.06 | 16 | zy-zy | 0.08 | 25 | 0.64 ‡ | 23 |
| t-sn R | -0.13 | 19 | 0.53 †† | 21 | al-al | 0.35 | 24 | 0.21 | 24 |
| t-sn L | 0.13 | 17 | 0.28 | 17 | sbl-sbl | 0.08 | 23 | 0.10 | 24 |
| t-ch R | 0.13 | 23 | 0.32 | 21 | en-en | 0.19 | 22 | -0.22 | 21 |
| t-ch L | 0.46 † | 20 | 0.12 | 17 | ex-ex | 0.27 | 25 | -0.04 | 22 |
| t-pg R | 0.15 | 23 | 0.58 †† | 21 | cph-cph | 0.32 | 26 | 0.35 | 24 |
| t-pg L | 0.33 | 21 | 0.54 † | 17 | ch-ch | 0.40 † | 26 | 0.49 †† | 24 |
| ex-en R | 0.18 | 24 | -0.26 | 20 | g-sn | 0.08 | 20 | 0.66 ‡ | 24 |
| ex-en L | 0.24 | 23 | 0.08 | 20 | se-prn | 0.24 | 27 | 0.57 †† | 24 |
| en-se R | 0.23 | 24 | 0.14 | 21 | prn-sn | 0.34 | 20 | 0.44 † | 24 |
| en-se L | 0.00 | 23 | 0.16 | 21 | se-sn | 0.16 | 20 | 0.62 ‡ | 24 |
| cir-se R | -0.08 | 21 | 0.41 | 19 | sn-ls | 0.14 | 19 | 0.44 † | 20 |
| cir-se L | 0.15 | 19 | 0.15 | 19 | li-sl | -0.28 | 27 | 0.63 ‡ | 24 |

These data were rounded to two decimal places for this table, but the complete values were used in all calculations. The Mmt column lists the measurements; R and L refer to measurements from the right and left sides, respectively. The r column has the correlation coefficients and their significances, designated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. N is the number of pairs of individuals.

Table 5-3. Correlations for Parents and Their Children and for Sibs, Based on all Available Measurements

| | Normal Parent-Normal Child | | Normal Sibs | | Normal Parent-Child With Syndrome | | Normal Sib-Sib With Syndrome | |
|---|---|---|---|---|---|---|---|---|
| Family | r | N | r | N | r | N | r | N |
| 1 | | | | | | | 0.65[c] †† | 18 |
| 2 | | | | | 0.34[d] | 11 | | |
| 3[a] | | | | | -0.44[d] † | 20 | 0.17[d] | 19 |
| 4 | | | | | -0.41[e] †† | 36 | | |
| 5 | | | | | | | 0.76[c] ‡ | 28 |
| 6 | | | | | 0.18[e] | 16 | | |
| 7 | | | | | | | 0.35[f] | 15 |
| 8 | -0.01 | 35 | | | 0.45[g] †† | 29 | 0.43[g] † | 28 |
| 9 | | | | | | | 0.20[c] | 36 |
| 10 | | | | | -0.09[e] | 23 | | |
| | | | | | -0.24[e] | 23 | | |
| 11 | -0.52 † | 18 | | | -0.58[h] | 8 | 0.00[h] | 25 |
| | 0.39 † | 36 | | | -0.16[h] | 25 | | |
| 12 | | | 0.63 †† | 16 | | | | |
| 13 | | | 0.43 †† | 36 | | | | |
| 14 | | | 0.25 | 22 | | | | |
| 15 | 0.01 | 36 | | | | | | |
| 16 | | | 0.19 | 23 | | | | |
| 17 | 0.26 | 19 | | | | | | |
| 18 | 0.09 | 36 | 0.48 †† | 35 | | | | |
| | 0.22 | 35 | | | | | | |
| 19 | 0.50 †† | 25 | | | | | | |
| | 0.63 ‡ | 34 | | | | | | |
| 20 | 0.28 | 33 | | | | | | |
| | 0.00 | 36 | | | | | | |
| 21 | -0.14 | 34 | | | | | | |
| | -0.20 | 34 | | | | | | |
| 22 | -0.18 | 36 | -0.04 | 36 | | | | |
| | -0.45 †† | 36 | 0.11 | 36 | | | | |
| | 0.13 | 36 | -0.26 | 36 | | | | |

Table 5-3 Continued

| Family | Normal Parent-Normal Child r | N | Normal Sibs r | N | Normal Parent-Child With Syndrome r | N | Normal Sib-Sib With Syndrome r | N |
|---|---|---|---|---|---|---|---|---|
| 23 | 0.42 | 21 | 0.80 ‡ | 29 | | | | |
| | 0.38 † | 28 | 0.18 | 22 | | | | |
| | 0.28 | 28 | 0.39 † | 28 | | | | |
| 24 | | | 0.11 | 36 | | | | |
| | | | 0.04 | 36 | | | | |
| | | | 0.27 | 36 | | | | |
| 25[b] | | | 0.27 | 34 | | | | |
| | | | 0.34 | 31 | | | | |
| | | | 0.10 | 29 | | | | |
| 26 | 0.44 †† | 34 | 0.51 ‡ | 36 | | | | |
| | 0.23 | 36 | | | | | | |
| | 0.55 ‡ | 34 | | | | | | |
| | 0.08 | 36 | | | | | | |
| 27 | -0.55 | 8 | 0.64 ‡ | 25 | | | | |
| | -0.39 | 16 | | | | | | |
| | 0.23 | 17 | | | | | | |
| | -0.62 ‡ | 24 | | | | | | |
| 28 | | | 0.46 †† | 36 | | | | |
| | | | 0.49 †† | 27 | | | | |
| | | | 0.77 ‡ | 34 | | | | |
| | | | 0.34 | 29 | | | | |
| | | | 0.47 †† | 34 | | | | |
| | | | 0.52 †† | 29 | | | | |

These data were rounded to two decimal places for this table, but the complete values were used in all calculations. The Family column lists the families by number. [a] The parent has a facial syndrome, and the child is medically normal. [b] The first correlation is between dizygotic twins. The r column has the correlation coefficients and their significances, designated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. N is the number of measurement pairs used in each instance. For the categories that include a child with a syndrome, the syndromes diagnosed are as follows: [c] unknown, [d] Russell-Silver, [e] achondroplasia, [f] deletion of 18q, [g] uniparental disomy of chromosome 16 (maternal), [h] Down.

Table 5-4. Correlations for Related and Unrelated Individuals with Facial Syndromes, Based on All Available Measurements

| | Related Individuals | | Unrelated Individuals | |
|---|---|---|---|---|
| Syndrome | r | N | r | N |
| Russell-Silver | -0.34 | 28 | | |
| Myotonic dystrophy | 0.73 ‡ | 23 | | |
| Achondroplasia | 0.72 ‡ | 36 | 0.28 | 29 |
| | | | 0.41 † | 29 |
| | | | 0.35 † | 36 |
| | | | 0.65 ‡ | 36 |
| | | | 0.45 †† | 29 |
| Placental | 0.73 † | 10 | | |
| anastamoses in | 0.75 †† | 10 | | |
| monozygotic triplets | 0.83 ‡ | 20 | | |

These data were rounded to two decimal places for this table, but the complete values were used in all calculations. The Syndrome column identifies the syndromes studied. The r column has the correlation coefficients and their significances, designated as follows: † is $0.01 < P \leq 0.05$; †† is $0.001 < P \leq 0.01$; and ‡ is $P \leq 0.001$. N is the number of measurement pairs used in each instance.

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# CHAPTER 6

# GENERAL DISCUSSION AND CONCLUSIONS

## *Syndrome-Affected Individuals as Compared With Normal Individuals*

Two general areas regarding the nature of syndromes that needed further research were noted in Chapter 1, and these can be posed as the following questions: are the facial features of individuals with syndromes quantifiably outside of the range of normal variation; and do individuals with the same syndrome resemble each other, irrespective of ancestral origins? Several findings of this research strongly suggested that, in the case of soft tissue facial feature asymmetry, syndrome-affected individuals were not identifiable based on grossly abnormal asymmetry. The number of significantly asymmetric measurements was greatest in the normal males group and least in both the males and females with syndromes groups. When the bilateral measurement differences calculated for each syndrome-affected individual were compared to the limits of normal asymmetry obtained from the normal groups, there was little evidence that the soft tissue facial features of individuals with syndromes were very abnormal. Seven male subjects and six female subjects with syndromes were found to have one to three bilateral asymmetries that exceeded the normal limits, usually from the upper areas of the face. Asymmetry in measurements from the upper and central facial regions of normal individuals generally did not exceed 5 to 6 mm (or degrees), whereas measurements involving landmarks from the lower areas of the face had asymmetries that were 6 mm or greater. In all groups, analysis of the three-dimensional landmark coordinates indicated that the significant asymmetries occurred throughout the face without any area of specific concentration. With few exceptions, the right side of the face was dominant in all groups for both the measurements and the X coordinates of the bilateral landmarks, as based on the statistically significant results. The X coordinates of the midline landmarks were significantly deviated mainly to the left side of the face.

The finding that measurements involving the gonion landmarks (exocanthion-gonion and gonion-pogonion) were prone to large bilateral differences in all groups was of interest. While

studying caliper-derived and photogrammetric measurements, gonion (in the measurement gonion-gonion) was identified as a difficult landmark to palpate and to maintain on it a fixed placement of the caliper tip. This was thought to be due to the posterior position of this landmark, which did not allow the observer to view the landmark and caliper placement on it while positioned in front of the subject. With the photogrammetric method, the gonion markings were often imaged from an oblique angle, thereby creating some problems in their digitization. The greater amount of asymmetry in measurements that included the gonion landmarks could have been the result of measurement uncertainty caused by the described difficulties. However, the standard deviations from the replicated measurements of gonion-gonion for Observer 2 (who was the individual that obtained the data for the asymmetry and family resemblance studies) were the lowest for the photogrammetry data as compared to the caliper-derived data. Although the presence of measurement uncertainty for the exocanthion-gonion and gonion-pogonion distances could not completely ruled out, the amount of uncertainty was decreased with the photogrammetric method.

The study of resemblance in family members with and without syndromes also indicated that, overall, syndrome-affected individuals did not consistently have abnormal facial features in comparison with their normal family members. This study also provided some evidence as to whether or not syndrome-affected individuals resembled each other. Of those families with normal and syndrome-affected individuals, there were six statistically significant correlations out of a total of 16 comparisons. Two of these were negative. That there were four significantly positive correlations between syndrome-affected individuals and their normal family members showed that related individuals with differing medical statuses did resemble each other in some cases. The non-significant correlations between syndrome-affected individuals and normal family members were not atypical when compared with the data obtained from pairs of normal relatives, since not all correlations were significant in these groups. Further investigation into all of the significant negative correlations indicated that these were typically obtained when adults were paired with very young children, regardless of medical status.

Although there was only one syndrome-affected individual who reported a predominantly non-European ancestry in the study of family resemblance, examination of the correlation coefficients for this individual and the other subjects with the same syndrome (achondroplasia) provided some information as to whether individuals with the same syndrome, but from different ancestral backgrounds, had similar facial measurements. Within this group of subjects with achondroplasia, the correlations indicated that most of these individuals resembled each other. Two same-sex sibs with this syndrome had a correlation of 0.72, while the unrelated individuals had correlations that ranged from 0.28 (which was not statistically significant) to 0.65. The non-significant correlation involved a female with a non-European ancestry. It was not known why this one correlation was not significant, but it did not appear to be the result of facial differences based on ancestry, since her correlations with the other two unrelated individuals (of European ancestry) were positive and statistically significant.

### *The Advantages of the Photogrammetric Method*

Small variations in measuring technique (such as whether or not the landmarks are marked before taking caliper-derived measurements) and the use of different instruments to take facial measurements (e.g., rulers, calipers, and photogrammetry) resulted in systematic differences. For these reasons, the published normative soft tissue facial feature data taken with calipers and rulers could not be used for comparison with the photogrammetric measurement data. While data collection with calipers would appear to be expedient, photogrammetry was a superior method because it was (1) rapid: in most cases the subjects had their landmarks marked and images taken in 15 minutes or less; (2) not harmful: no reactions to the marking materials were ever reported and there were no concerns about injury from the sharp tips of the sliding caliper; (3) novel: parents and children were often interested in the process of extracting measurements from images and enjoyed posing for the cameras; and (4) versatile: besides being able to analyze the three-dimensional coordinates of the landmarks, any distances, angles, depth measurements, and so on could be made

as desired from the marked landmarks (as well as the center of the iris, which was unmarked). Further measurements could be obtained as the need arose, as long as the three-dimensional coordinates were available, or the landmark could be digitized from the images. Overall, the method of photogrammetry was very convenient for both the person collecting data and the subjects. The subjects had only to make a short time commitment, which was particularly important when the participants had difficulty remaining motionless, and the data gained from the images were completely anonymous. Moreover, the images could be deleted at any time to preserve further the confidentiality of the subjects, in compliance with the ethics review for this project. The observer could perform the work needed to obtain the three-dimensional landmark coordinates and the measurements at any time, and others were able to confirm the accuracy of the data reduction process by viewing the files output by the computer programs or by repeating the work beginning with digitizing the images.

On the other hand, this photogrammetric method requires imaging equipment, a computer, and specialized computer programs. It may not be possible for every clinic that has patients with syndromes to carry out measurements in this fashion. One solution might be to take measurements from single photographs (with an indicator of scale in the picture), since photographs are often taken of patients at clinics to document their facial appearance. While this technique would have some of the advantages of the three-dimensional method, it has the same disadvantage as other two-dimensional methods: the only objective data obtained are measurements. Although there are extensive norms available for ruler- and caliper-derived measurements, and clinicians are encouraged to take facial measurements of their patients with syndromes, it is not a common practice. Photogrammetry, however, could be a practical solution to the difficulties encountered by clinicians in evaluating the soft tissue facial features of individuals with, or suspected to have, a syndrome and to convey objectively the facial features present in these individuals to a wider audience of professionals.

## *Applications of Soft Tissue Facial Measurements to Physical Anthropology*

Human variation studies within physical anthropology are concerned with investigating how and why humans differ biologically. While medically normal individuals are most often the focus of variation studies, individuals with syndromes are also an important group to study because they comprise a part of the modern human population and, therefore, represent a facet of modern human biological variation. The previous chapters have contributed knowledge to the study of human biological variation within the subdiscipline of physical anthropology in the areas of measurement methods, soft tissue facial feature asymmetry, and family and syndrome facial feature resemblance. The systematic differences found between ruler-derived, caliper-derived (with and without the landmarks marked), and photogrammetric measurements provide important information for physical anthropological studies of human variation and other specialties, such as paleopathology and forensic anthropology, since measurement methods are commonly used to identify the age, sex, ancestry, and medical status of individuals. These specialties might also benefit from the information presented in the previous chapters regarding facial feature asymmetry and family resemblance: the overall conclusion suggested by these studies was that syndrome-affected individuals were not identifiable based on grossly abnormal asymmetry nor did they consistently have abnormal facial features in comparison with their normal family members. For paleopathology, if the hard tissues are altered to the same degree as found here for the soft tissues, detection of syndromes in past populations would probably be difficult without accurate depictions of normal and abnormal variation. Fragmentary remains would further compound the problems of investigating normal and abnormal variation in past populations. For forensic anthropology, the normative data obtained in the present investigations might be useful in identifying unknown human remains. For example, abnormal asymmetry in one or more areas of the face might be used as an individualizing trait that could lead to identification of the individual.

The research results described in previous chapters are also important to the area of applied physical anthropology, which undertakes investigations for the purpose of providing solutions to

modern problems. In the case of the present research, it has been demonstrated that the photogrammetric method used is appropriate and convenient for investigations into facial feature variation in individuals who may not have the ability to remain motionless for the time needed to take measurements with calipers or a ruler. The investigations into facial asymmetry and family and syndrome resemblance have indicated that more research into modern facial feature variation in normal and syndrome-affected subjects could make significant contributions to the understanding of what is normal variation and how syndromes can be objectively described and diagnosed. In particular, norms organized by age, sex, and ancestral background are needed, since none currently exist for photogrammetric measurements. Collection of family data should also be emphasized, although it is important to ask each family whether their history includes any individuals with syndromes. It is possible that syndromes cause greater variation during prenatal development, which could be reflected in greater measurement variability in apparently normal individuals. Comparison of families with a history of syndromes with families with no known abnormalities would clarify this issue. In addition, while measurements from every person with a syndrome are important for objective clinical evaluation, concentrated collection of facial feature measurements from many individuals with the same syndrome is particularly important if the natural progression of each syndrome is to be understood.

# APPENDIX

## THE PHOTOGRAMMETRIC METHOD

The photogrammetric method used in the studies is based on the collinearity condition, in which the camera (exposure station), a point on an object, and the image of that point all lie on a straight line (Wolf, 1983). The collinearity condition equations (see Wolf, 1983) were used to obtain the calibration parameters from images of a calibration grid. The calibration parameters were the camera constant, principal point coordinates, two radial and two decentering distortion parameters, camera coordinates, and the angles of rotation, omega, phi, and kappa (Figure A-1). Once these data were known, the collinearity condition equations were used to transform the subjects' image coordinates to the object space coordinate system (Figure A-2). The origin of this coordinate system was one meter to the right, behind, and below the calibration mark located on the lower right side. Definition of the object space coordinate system origin in this manner ensured that all landmark coordinates of the subjects were positive.

The sequence of the programs used (all were in-house programs developed in the Department of Civil and Environmental Engineering, University of Alberta, Edmonton, Alberta, Canada) is as follows (Figure A-3). The images of the calibration grid and subjects were downloaded from the cameras in JPEG format, using the software provided by the camera manufacturer. (Details of the cameras and their setup are in Chapter 3.) IMAGE was the program with which the images of the calibration grid target pegs and subjects' landmarks were digitized. The coordinates output by this program were two-dimensional, i.e., x and y, and they were in the image space coordinate system, with a maximum x coordinate value of 360 pixels and a maximum y coordinate value of 496 pixels. While all six (or five, after one camera failed and was removed) images of the calibration grid or subjects could be digitized at the same time with this program, the view presented by opening two or three images at one time was optimal. Therefore, two or three images were typically opened at once in the program and digitized. This program output a text file containing the coordinates of all images

that had been digitized at one time. These text files were next put into the program ASPECTC to adjust for the aspect ratio of the cameras. The scale of the x coordinates was modified by a ratio of 1.02057. It also split the data for each image into separate files.

The calibration grid files output by ASPECTC were then used in the program NDLT, which was based on the direct linear transformation method (McGlone et al., 1989). NDLT made initial estimates of the unknown calibration parameters, except the two terms for decentering distortion. The data file from each calibration grid image was put into this program, along with a file of the three-dimensional coordinates of the calibration grid target pegs. The coordinates in the latter file were obtained by surveying the pegs and converting the coordinates to the desired object space coordinate system. The collinearity condition equations were solved for the unknown calibration data, and the resulting estimates were copied back into the data file from ASPECTC. The program TRIPLET, based on the collinearity condition with self-calibration (Fryer, 1989), took three of these data files at one time and refined the parameters output by NDLT, plus provided two terms for decentering distortion. In addition to the three data files, two other files were used by this program for its calculations: the file of surveyed calibration grid target peg coordinates in the object space coordinate system and a file in which constraints could be applied as needed. Constraints of 0.5 mm for the X and Y coordinates and 0.2 mm for the Z coordinates of the surveyed calibration grid target pegs were specified in all cases. The parameters of the cameras were put into a location file.

The data files of each subject's soft tissue facial feature landmarks that were obtained from ASPECTC were put through ITOSPA. This program arranged all of the landmark data, by camera, into a single file. SPACO was then used to acquire the three-dimensional coordinates of the landmarks in the object space coordinate system, using the collinearity condition equations. The appropriate camera location data from TRIPLET and the data file from ITOSPA were put into SPACO, and a standard deviation of 0.5 mm for the digitized data was specified. Along with the landmark coordinates, this program output estimates of the standard deviations of the landmarks. Standard deviations that were greater than twice the specified amount were labelled as "bad," while

those standard deviations at or below this threshold had an "ok" indicated. Landmarks labelled as "bad" were reassessed to determine whether incorrect digitization had caused the problem and were redigitized if required.

Three other programs were used to transform the landmark coordinates from the object space coordinate system to other systems as necessary for the asymmetry and family resemblance studies. The FRANK, NSIM3D, and ROTSCALE programs performed three-dimensional conformal coordinate transformations that rotated, scaled, and translated the three-dimensional coordinates from the original object space coordinate system to other coordinate systems (Wolf, 1983). FRANK was a program that was used to orient the three-dimensional coordinates of all subjects to a plane defined by the right and left tragions and pronasale. All three landmarks were required for this program; if any were missing, this transformation could not be carried out. Since this was the case for some subjects, NSIM3D was used to transform their landmarks to the same orientation as a model set of coordinates. As described in Chapter 4, the model used was an average of already-transformed data from subjects of the same age and sex. This program was also used to transform the coordinates of every subject to a coordinate system with the origin in the center of the head. When using NSIM3D, landmarks could be omitted from the calculation process and oriented passively; more details are given in Chapter 4. In using both FRANK and NSIM3D, there was no change in the scale of the coordinates. (Scaling could be performed with NSIM3D, but was not.) For the family resemblance study, NSIM3D was modified to ROTSCALE so that the scale of the subjects' coordinates could be altered to that of a model set of coordinates, without further rotations occurring. (Rotations could be performed with this program, but were not.) As in the case of NSIM3D, specific landmarks could be omitted from the calculations and passively scaled. Further details are in Chapter 5.

The desired distances were calculated by FADIST, using the data files output by SPACO, FRANK, NSIM3D, or ROTSCALE. Microsoft Excel was used to calculate all other types of measurements used in the studies.

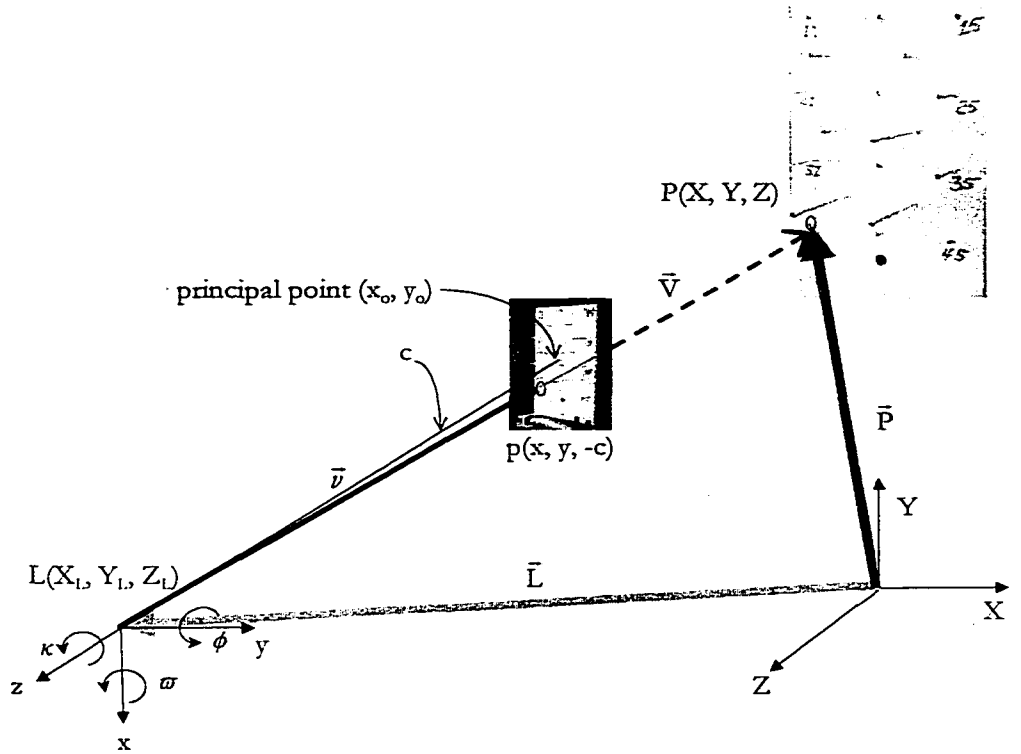


Figure A-1. The Collinearity Condition as Used for Camera Calibration

The collinearity condition is depicted, whereby the camera, L, a point on an image, p, and the corresponding point on the object (in this case the calibration grid), P, are all on a straight line. Using the collinearity condition equations, $\bar{v}$, the vector from the camera to the point on the image in the image space coordinate system, is transformed to $\bar{V}$, the vector from the camera to the point on the object in the object space coordinate system. The known data for the collinearity condition equations are the x and y coordinates of p and the X, Y, and Z coordinates of P. $\bar{P}$ is the vector from the origin of the object space coordinate system to the point on the object. $\bar{L}$ is the vector from the object space origin to the camera. Calibration of the cameras provides the camera constant, c; principal point coordinates, $x_o$ and $y_o$; radial and decentering parameters (not depicted); camera coordinates, $X_L$, $Y_L$, and $Z_L$; and the angles of rotation, omega, $\varpi$, phi, $\phi$, and kappa, $\kappa$.

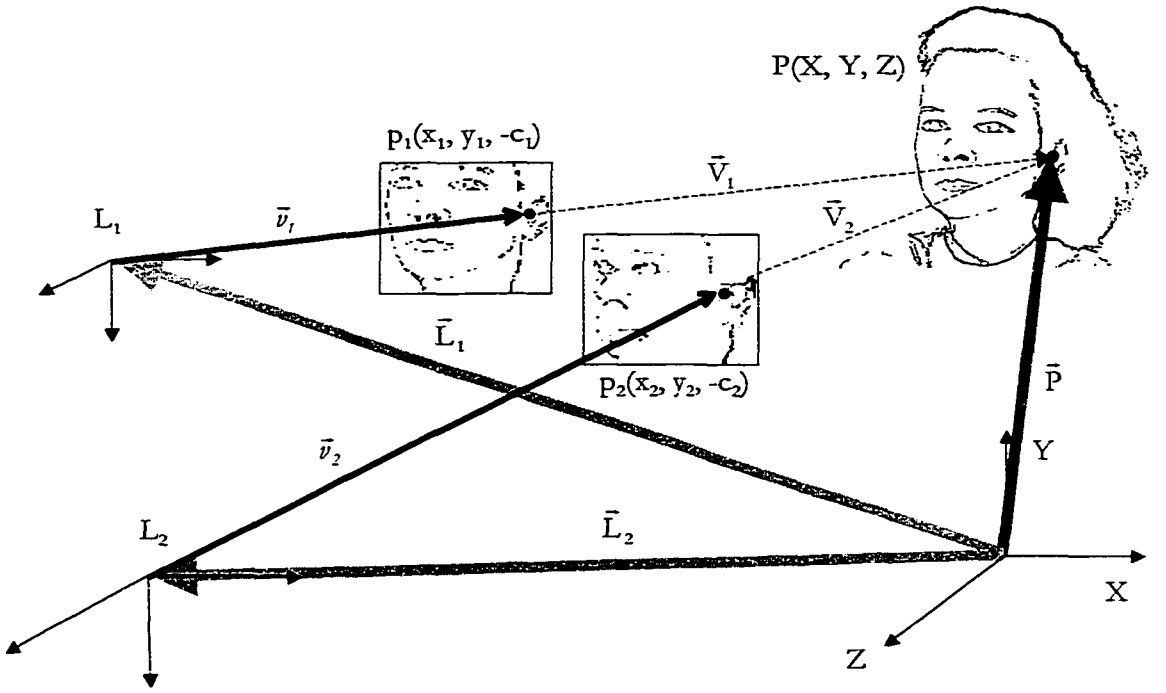


Figure A-2. Obtaining the Three-Dimensional Coordinates of the Soft Tissue Facial Landmarks

The collinearity condition is used in acquiring the three-dimensional coordinates of the soft tissue facial feature landmarks in the object space coordinate system. A landmark (such as the left tragion represented here) must be digitized in two images, $p_1$ and $p_2$, in order to obtain the three-dimensional coordinates of the landmark in object space, P. The digitized landmark coordinates and the camera calibration data (see Figure A-1) are used in the collinearity condition equations to solve for the unknown X, Y, and Z coordinates of each landmark. This involves transforming the vectors $\vec{v}_1$ and $\vec{v}_2$ to $\vec{V}_1$ and $\vec{V}_2$, respectively. $\vec{L}_1$ and $\vec{L}_2$ are the known vectors from the object space origin to the corresponding $L_1$ and $L_2$ cameras. $\vec{P}$ is the vector from the object space origin to the left tragion landmark on the subject.

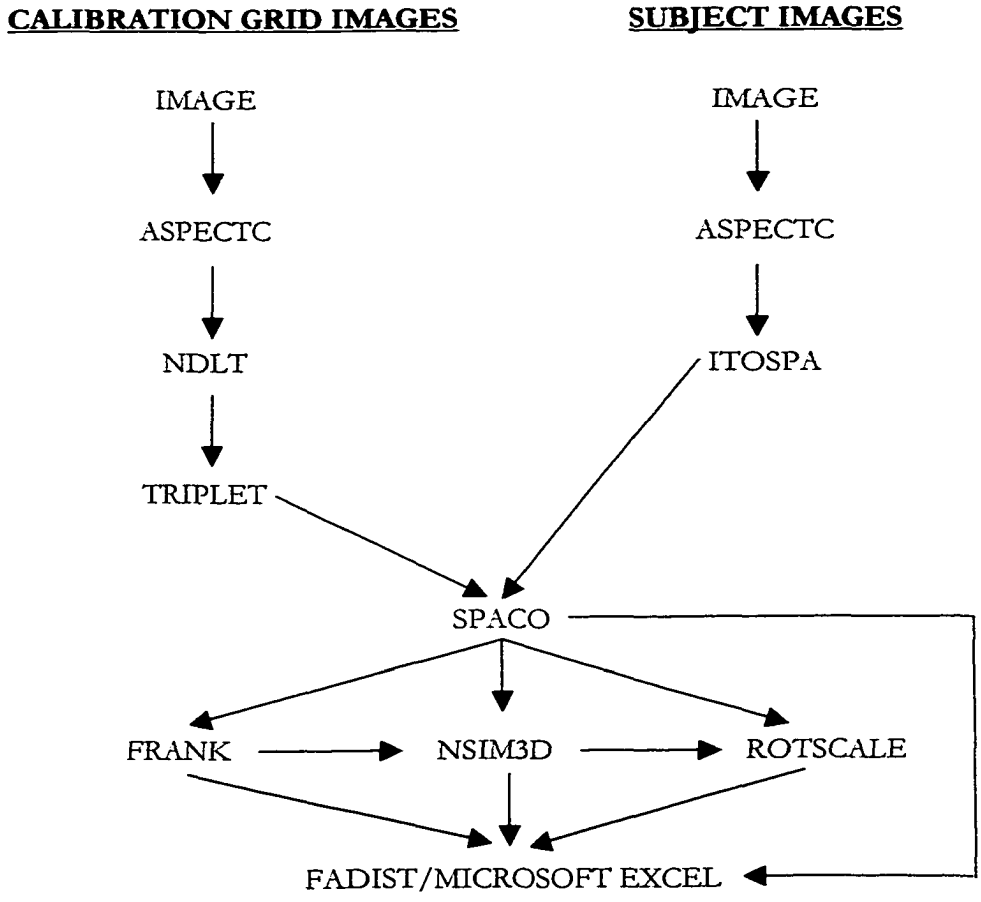


Figure A-3. The Programs Used in the Photogrammetric Method

The programs used for calibrating the cameras and obtaining the three-dimensional coordinates of the soft tissue facial feature landmarks are shown. Details of the programs and the files output by them are provided in the text.

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