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Sexual Determination from Frontal Sinus Analysis in a Subadult Population Using Archival Radiographic Records

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SEXUAL DETERMINATION FROM FRONTAL SINUS ANALYSIS IN A SUBADULT
POPULATION USING ARCHIVAL RADIOGRAPHIC RECORDS

By

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Thesis Submitted in Partial Fulfillment
of the Requirements for the Degree of

Master of Science – Oral Biology

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Thesis Approval

The Graduate College
The University of Nevada, Las Vegas

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This thesis prepared by

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Sexual Determination from Frontal Sinus Analysis in a Subadult Population Using
Archival Radiographic Records

is approved in partial fulfillment of the requirements for the degree of

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Abstract

Sexual Determination from Frontal Sinus Analysis in a Subadult Population Using

Archival Radiographic Records

By

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The goal of this study is to use the improved imaging capability of cone-beam computerized tomography (CBCT) to investigate the development and sexual dimorphism of the frontal sinus and surrounding supraorbital region in the subadult population of urban Southern Nevada. CBCT radiographs were obtained from the UNLV School of Dental Medicine archival dental records. Five hundred and fifty six of these radiographs were reviewed for the study. Two hundred and sixteen patients (92 males, 124 females) between the ages of 7 and 20 years were included based on inclusion/exclusion criteria. Samples were categorized into 3 subadult age groups for analysis: Group 1 (age 7-11), Group 2 (age 12-15), and Group 3 (age 16-20). Cross-sectional slices were obtained of the frontal sinus in coronal and transverse sections. The maximum height, width and anteroposterior length (depth) were measured for the right and left sides of each frontal sinus. A mid-sagittal slice was also taken and the nasofrontal angle was measured. The relationship of the anterior border of the frontal sinus to a vertical reference line drawn from nasion to A-point was also determined.

The incidence of bilateral and unilateral agenesis of the frontal sinus was recorded for the 556 radiographs reviewed. An independent samples t-test was utilized to compare the maximum

height, width, depth and nasofrontal angle between males and females within the three age groups. Statistically significant values ($p < 0.01$) were found between depth of the right and left frontal sinus in Group 3, with females having smaller dimensions. In Groups 2 and 3 nasofrontal angle was larger in females than males at a significant level ($p < 0.05$). No correlation was found between the relationship of the anterior border of the frontal sinus to the NA line in males and females in any age group.

Incidence of bilateral agenesis of the frontal sinus was 9.3% and occurred twice as often in females. Unilateral agenesis of the frontal sinus occurred equally in men and women at a rate 9.5%. Females experienced right sinus agenesis more often while males manifested equal incidence of right and left sinus agenesis. A discriminant function analysis was utilized to assess the forensic identification capability of the frontal sinus dimensions. The model was only a good fit for Group 3 with correct sex allocation observed 79.2% of the time.

Results of this study indicate that the frontal sinus and the surrounding supraorbital region show sexual dimorphism in depth as early as 16 years old, nasofrontal angle as early as 12 years old, and height and width still developing beyond the age of 20. This region is a reliable adjunct for sex determination in subadults greater than 16 years of age. The findings of this radiographic gender determination research are applicable to many biomedical disciplines including physical anthropology, forensic science, head and neck development and medical and dental specialties.

Acknowledgments

I would like to thank my committee chair, Dr. James K. Mah as well as the rest of my committee members, Drs. Cliff Seran, Robert A. Danforth, Edward E. Herschaft and Debra Martin for all their help and support with this project. A special acknowledgment is given to Dr. Marcia Ditmeyer for her assistance with the analysis and comprehension of the statistics. I would also like to thank Narek Akopyan in the DMD class of 2018 for his countless hours in helping me organize my data for statistical analysis.

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Dedication

To my friends and family,

You are my inspiration and motivation.

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Chapter 1: Introduction

Forensic anthropology is one discipline within anthropology that deals with the identification of human remains in a legal context (Krishan et al, 2016). It is an important specialty within the broad area of forensic sciences that encompasses aspects ranging from physiognomy to the complex osteology of the human skeleton. Forensic anthropologists are called upon when extreme causes of death such as multiple fatality incidents, mutilation and decomposition occur (Krishan et al, 2016). It is imperative that unknown individuals are identified for humanitarian as well as medico-legal reasons; especially when the identification of human remains is requested by criminal investigating agencies (Krishan et al, 2016).

Identifying skeletal remains requires an understanding of the biological profile including age, ancestry, stature and sex of the decedent (Krishan et al, 2016). Biological reconstruction of a skeletonized body during the preliminary stages of a forensic investigation relies on stature and age variables which are profoundly dependent on sex determination (Christensen et al, 2014). Sex estimation from skeletal remains is essential in the identification process because, if successful, it eliminates 50% of the population from further consideration and assists in the collection of information for the biological profile of the unknown individual (Christensen et al, 2014).

When faced with the task of sexing an unknown individual, forensic anthropologists rely on various methods to help reach an accurate conclusion. The relative fragility of the soft tissue of a decedent and its postmortem degradation susceptibility often requires the expertise of a forensic anthropologist. Their knowledge of different interpretive techniques contributes to the identification process (Bidmos et al, 2010). The various anthropologic methods can be classified into three categories: non-metric, metric, and molecular (Krishan et al, 2016).

The non-metric method involves a visual assessment of skeletal features that tend to vary between males and females, due particularly to the degree of expression of certain traits (Christensen et al, 2014). Males tend to exhibit larger, more robust features that can be seen throughout the cranial and post-cranial skeleton. Females tend to retain more of the pedomorphic traits throughout development (Krishan et al, 2016). Estimating sex from the morphological difference of the pelvis is the most reliable method of gender determination with an accuracy of up to 96% (Christensen et al., 2014). However, non-metric methods rely heavily on expertise in the field of osteological differences. Thus, these are highly subjective and render considerable intra- and inter-observer errors (Krishan et al, 2016). Visual assessment also depends on the nature of the skeletal remains and gives better results when intact bones are present (Krishan et al, 2016).

The second method utilized for sexual determination employs metric techniques. It is more objective and involves examining various measurements of maximum or minimum skeletal dimensions based on osteological landmarks and subjecting them to different statistical analyses. These include the Student's t-test, discriminant function analysis and logistic regression analysis to compare and determine sex (Christensen et al, 2014). The reliability of these measurements depends on the basic principle that males surpass females in size of the post-cranial skeleton. For this skeletal area measurements are accurate up to 90% (Christensen et al, 2014). Metric methods for sex estimation of the skull are not considered as reliable. However, they are still widely applied and useful in cases where no post-cranial skeleton is present for analysis. They can reach accuracy levels up to 85% (Christensen et al, 2014). Although the accuracy of the metric method varies among regions of the human skeleton it represents an accurate and unbiased way to evaluate sexual dimorphism.

It is also possible to determine the sex of skeletal remains using molecular methods. In order to use these, DNA is amplified using Polymerase Chain Reaction (PCR). Base pairs along the X and Y chromosomes are compared for differences in number. Genes on the sex chromosomes such as the amelogenin gene can be used in determining gender. However, in rare instances, mutations within the amelogenin gene can result in false results (Christensen et al, 2014). Although this technique is highly reliable, it is not as widely used by forensic anthropologists because it is time consuming, complicated, costly, and invasive (Krishan et al, 2016).

The review of various sex determination methods demonstrates that sexual dimorphism is differentially conveyed throughout the skeleton (Christensen et al, 2014). Most of these methods are performed on fully developed adult skeletons that show sexually dimorphic traits. It is generally accepted that sexing subadults is extremely difficult due to the fact that most sexual differences do not appear until the increase in sex hormones during puberty. Therefore, estimations of sex from a skeleton are not advisable prior to age 14 (Christensen et al, 2014). Despite this caveat, an understanding of when development of skeletal structures of subadult populations begin to show sexual dimorphism, may assist forensic anthropologists and others working in related disciplines.

It is more convenient and consistent to determine the sex of an unknown adult skeleton than a subadult skeleton (Scheuer et al (page 1), 2000). Lack of familiarity with subadult remains has led to avoidance of working with this population. This has ultimately resulted in a deficiency of subadult skeletal data regarding sex determination in this population (Scheuer et al (page 1), 2000). Understanding the developmental stages of human growth is imperative to divide the subadult from the adult populations. Adulthood can be considered when there is

fusion of spheno-occipital synchondrosis. Enlow maintains that this occurs around the age of 20 (Enlow et al, 1996). Within the subadult population (20 years of age and younger) there is a further division related to age. Late childhood ranges from 6-12 years and according to Scheuer et al (page 468) puberty can begin as early as 10 years of age in females and 12 years of age in males. It is completed at approximately 14 years of age and 16 years of age in females and males respectively. Studying development of structures within these age ranges allows for insight into when sexual dimorphism occurs and its relationship to puberty. In this study, the following age ranges reflect the milestones in childhood development and will allow for comparison of sexual dimorphism related to these age groupings:

- Pre-pubertal (6-11 years)
- Peri-pubertal (12-15 years)
- Post-pubertal (16-20 years).

Sex estimation has been performed using a variety of skeletal areas with varying degrees of accuracy. Due to the sexual dimorphic nature of the skull, and in particular the supraorbital region (Nowaczewska et al, 2014), this area is the focus for this study. The frontal sinus and surrounding supraorbital regions are very resistant to trauma and are likely to be well-preserved in cremains or dismembered corpses (Akhlaghi et al, 2015).

The purpose of this study is to utilize cone beam computed tomography (CBCT) to assess the sexual dimorphism of the supraorbital region and frontal sinus of subadults within the urban population of Southern Nevada. The techniques assessed include morphometric measurements of the maximum height, width and anteroposterior length (depth) of the right and left frontal sinus areas, inclination of the nasofrontal angle, and anatomical location of the frontal sinus

compared to a vertical Nasion-A point (NA) reference line. Additionally, prevalence of bilateral and unilateral agenesis of the frontal sinus and differences between males and females of the given subadult population are evaluated. Discriminant function analysis utilizing frontal sinus measurements is also assessed for the accuracy of predicting the sex within the given population groups.

Research Questions and Hypothesis

1. Do morphometric measurements of the maximum height of the right and left frontal sinus, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

- Age group 6-11
- Age group 12-15
- Age group 16-20

Hypothesis: Morphometric measurements of the maximum height of the right and left frontal sinus, as measured from a CBCT radiograph, are sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group.

Null Hypothesis: Morphometric measurements of the maximum height of the right and left frontal sinus, as measured from a CBCT radiograph, are not statistically significantly sexually dimorphic for this population.

2. Do morphometric measurements of the maximum width of the right and left frontal sinus, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

- Age group 6-11
- Age group 12-15
- Age group 16-20

Hypothesis: Morphometric measurements of the maximum width and of the right and left frontal sinus, as measured from a CBCT radiograph, are sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group.

Null Hypothesis: Morphometric measurements of the maximum width of the right and left frontal sinus, as measured from a CBCT radiograph, are not statistically significantly sexually dimorphic for this population.

3. Do morphometric measurements of the maximum anteroposterior length of the right and left frontal sinus, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

- Age group 6-11
- Age group 12-15
- Age group 16-20

Hypothesis: Morphometric measurements of the maximum anteroposterior length of the right and left frontal sinus, as measured from a CBCT radiograph, are sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group.

Null Hypothesis: Morphometric measurements of the maximum anteroposterior length of the right and left frontal sinus, as measured from a CBCT radiograph, are not statistically significantly sexually dimorphic for this population.

4. Does the nasofrontal angle, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

- Age group 6-11
- Age group 12-15
- Age group 16-20

Hypothesis: Morphometric measurement of the nasofrontal angle as measured from a CBCT radiograph, is sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group.

Null Hypothesis: Morphometric measurement of the nasofrontal angle as measured from a CBCT radiograph is not statistically significantly sexually dimorphic for this population.

5. Does the distance from the most anterior border of the frontal sinus to a line drawn through (NA), as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?
 - Age group 6-11
 - Age group 12-15
 - Age group 16-20

Hypothesis: The anatomic relationship of the anterior border of the frontal sinus to a line drawn through NA, as measured from a CBCT radiograph, is sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group.

Null Hypothesis: The anatomic relationship of the anterior border of the frontal sinus to a line drawn through NA, as measured from a CBCT radiograph, is not statistically significantly sexually dimorphic for this population.

6. What is the incidence of bilateral absence of the frontal sinus within the given subadult population? Does it occur more in males or females?

Hypothesis: The frequency of bilateral absence of the frontal sinus falls within the range found in the literature (0.73%-43%) and occurs more frequently in females (Danesh-Sani, 2011).

Null Hypothesis: The frequency of bilateral absence of the frontal sinus is not consistent with the range found in literature.

7. What is the incidence of unilateral absence of the frontal sinus within the given subadult population?

Hypothesis: The frequency of unilateral absence of the frontal sinus is consistent with the range found in the literature at 0.8%-7.4% (Danesh-Sani, 2011).

Null Hypothesis: The frequency of unilateral absence of the frontal sinus is not consistent with the range found in the literature.

8. Is unilateral frontal sinus agenesis more common on the right or left side and is this sexually determined?

Hypothesis: The right side of the sinus is more commonly missing in females and there is no difference in right vs left frontal sinus agenesis in males (Danesh-Sani, 2011).

Null Hypothesis: Sexual determination of unilateral agenesis of the frontal sinus will not be consistent with results of previous studies.

9. Can a discriminant function analysis be performed utilizing the frontal sinus measurements for the three defined age groups?

Hypothesis: The frontal sinus dimensions can be utilized in a discriminant function analysis with the highest accuracy in the 16-20 age group.

Null Hypothesis: The frontal sinus dimensions do not show any difference in accuracy among the age groups when utilized in a discriminant function analysis.

Anatomy of the Frontal Sinus

The frontal sinus is a paired lobulated cavity that is located within the frontal bone and each frontal sinus opens via the infundibulum into the middle meatus (Belaldavar et al, 1970). The frontal sinus is divided into right and left sides via the intersinus septum, which usually deviates from the midline, thus causing an asymmetry between right and left sides (Belaldavar et al, 1970). The general shape of the frontal sinus is triangular, with its apex being superior and its base being inferior. Superiorly and laterally the frontal sinus is bordered by the frontal bone. The anterior and posterior borders are the anterior and posterior tables of the frontal bone respectively. The posterior table portion of the frontal bone covers the frontal lobe of the brain with only a thin layer of dura mater separating the structures (Kountakis et al, 2005).

The inferior border represents the superior border of the orbital rim and the medial border is shared with the contralateral frontal sinus (Belaldavar et al, 1970). The general asymmetry of the frontal sinus can be explained through the development, it is believed that the right and left frontal sinuses develop from two independent structures (Gagliardi et al, 2004).

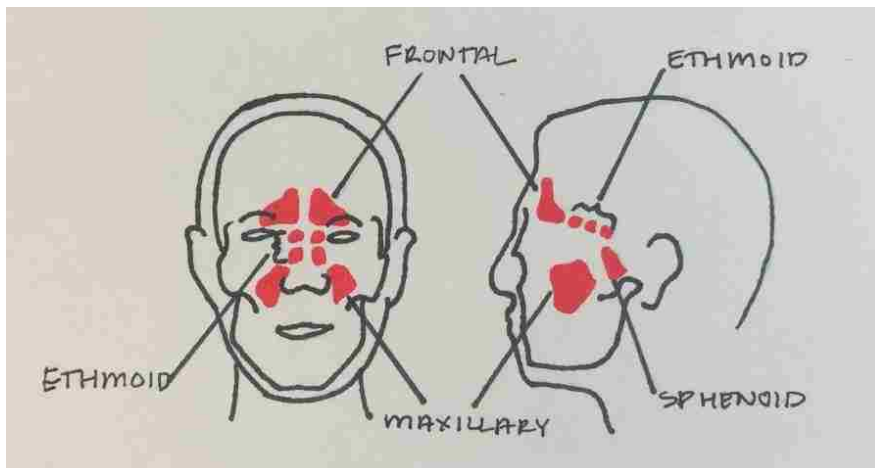


Figure 2.1 *Paranasal sinuses from frontal and sagittal view*

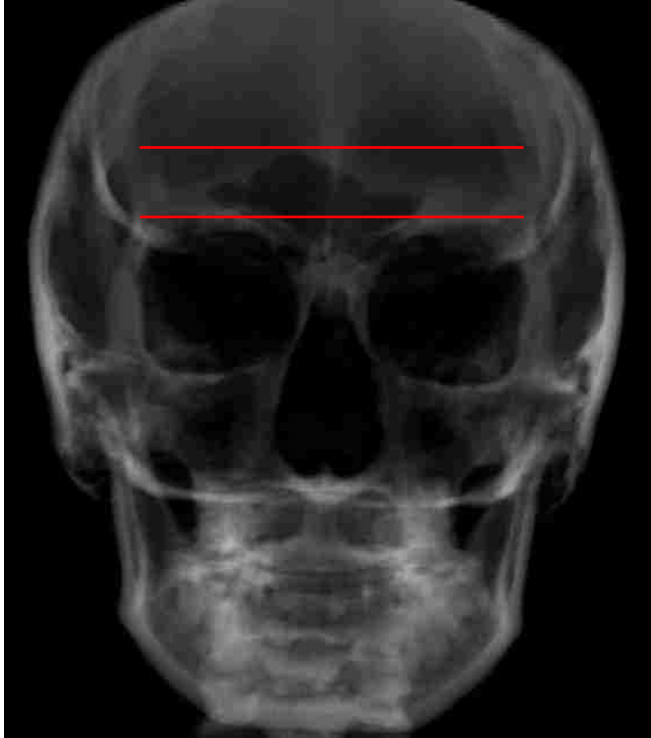


Figure 2.2 Superior and inferior borders of the frontal sinus from a frontal view (PA radiograph derived from CBCT using Invivo 5.3 Software)

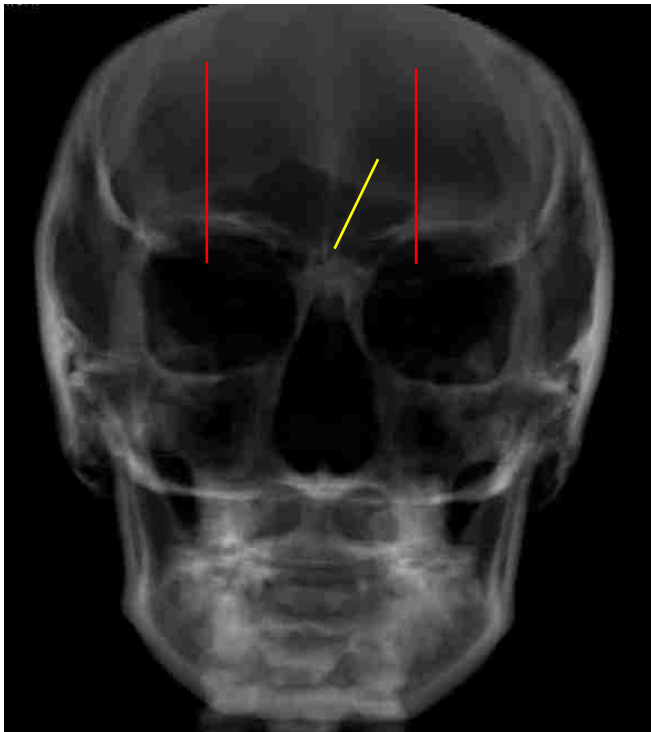


Figure 2.3 Medial (intersinus septum in yellow) and lateral borders of the frontal sinus from a frontal view (PA radiograph derived from CBCT using Invivo 5.3 Software)

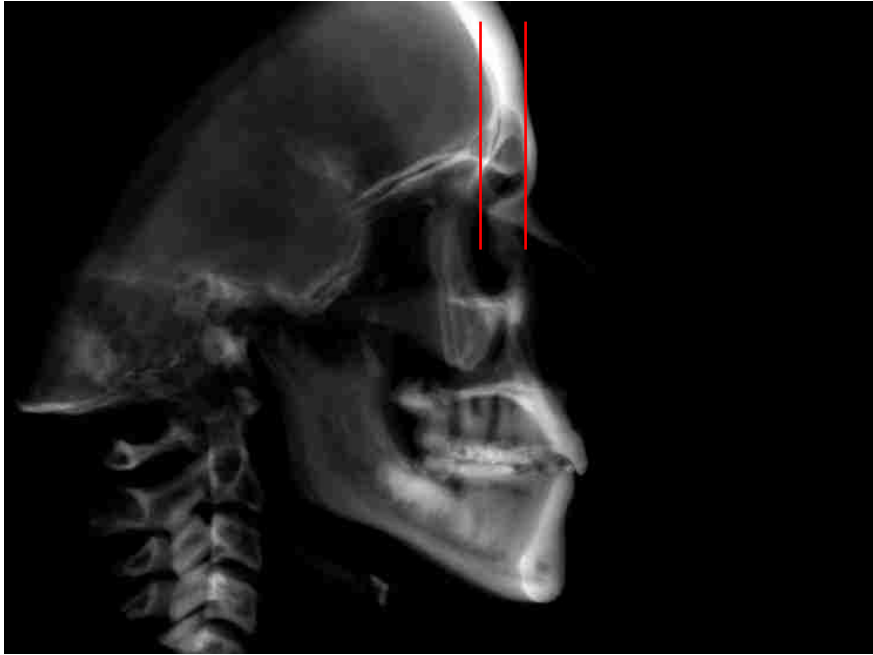


Figure 2.4 Anterior and posterior borders of the frontal sinus from a sagittal view (Cephalogram derived from CBCT using Invivo 5.3 Software)

Development of the Frontal Sinus

The paranasal sinus cavities begin initially as small outpouchings that eventually develop into the frontal, ethmoid, maxillary and sphenoid sinuses (Gagliardi et al, 2004). From an embryologic and anatomical standpoint the frontal sinus is generally considered with the anterior ethmoid air cells because of their close proximity. This unit is called the frontoethmoidal complex and begins development in the third month in utero along with the development of the nasal cavity (Fatu et al, 2006).

Prenatally the frontal sinus has been described as having two methods of development, a direct mode and an indirect mode (Gagliardi et al, 2004). The direct mode of growth refers to the outgrowth of an initial-sinus into the frontal bone whereas the indirect mode of growth involves the extension of the ethmoid air cells in the frontal bone (Gagliardi et al, 2004).

At birth the direct mode of growth is evident, but the anterior ethmoid air cells do not start their migration towards the frontal sinus until the end of the first year of life (Ruf et al, 1996). The migration of the ethmoid air cells marks the first evidence of pneumatization. This pneumatization begins in the horizontal plate of the frontal bone during the first year of life, followed by pneumatization of the vertical plate in the latter half of the second year of life (Shapiro et al, 1980). The frontal sinus may not be radiographically evident until further pneumatization which may take up to the eighth year of life (Ruf et al, 1996).

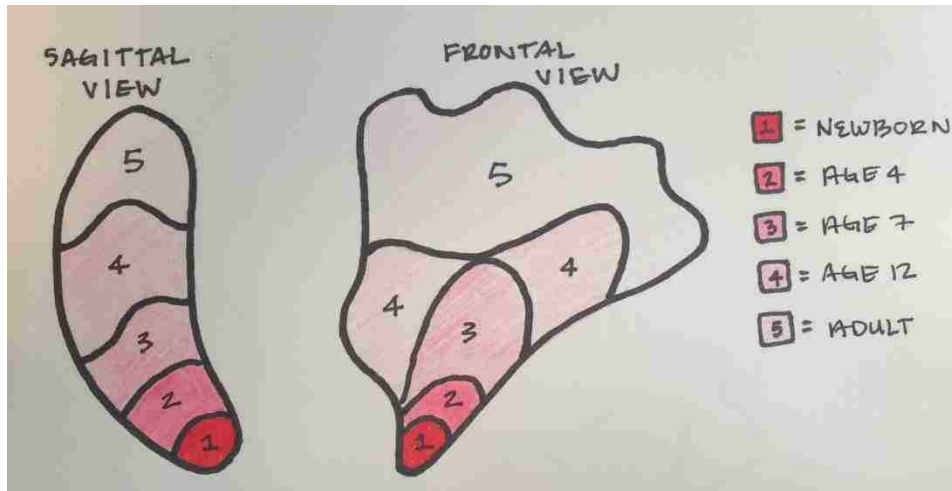


Figure 2.5 showing development of the frontal sinus in different stages

According to two studies, the frontal sinus follows a growth pattern similar to adolescent development with peak sinus growth occurring after the ultimate height velocity (Gagliardi et al, 2004, Ruf et al, 1996). The first of these studies evaluated frontal sinus development on lateral head films compared to hand-wrist radiographic development and stature recordings on Aboriginal Australians ages 7-18 (Gagliardi et al, 2004). It was found that females attain peak sinus height velocity earlier than males and peak sinus depth velocity concurrently with males. Results indicated that frontal sinus growth exhibits an adolescent growth spurt which tends to occur after statural velocity has peaked. The latter study was performed using the same methods by assessing lateral head films, hand wrist radiographs and body height growth curves on male Europeans age 9-22 years (Ruf et al, 1996). Conclusions were similar to the previous study in that enlargement of the frontal sinus displayed a similar pattern with a well-defined peak occurring on average 1.4 years after body height peak.

A third report investigated the development of the paranasal sinuses observed on computed tomography (CT) scans of individuals from birth to age 25 (Spaeth et al 1997). No further expansion of the frontal sinus was observed at age 16 for females and 18 for males.

However, there were statistically different sizes of the sinus noted between the two sexes (Spaeth et al 1997). It was concluded that female frontal sinuses are on average 13.4-17.1% smaller than males (Spaeth et al, 1997). A CT study examined volumes of paranasal sinuses in subjects 5-55 years old (Karakas et al, 2005). It was demonstrated that frontal sinus volume reaches maximum dimension in females between the ages of 16-20 and males between ages 21-25 (Karakas et al, 2005). A final paper investigated frontal sinus dimensions in patients 20-83 years of age and showed that these features increased in those greater than 20 years old (Tatlisumak et al, 2008).

When evaluating frontal sinus expansion it is important to understand why the frontal sinus increases in size throughout childhood. There are three important factors that influence frontal sinus pneumatization:

1. Craniofacial configuration
2. Thickness of the frontal bone
3. Hormonal growth factors (Shapiro et al, 1980).

Primarily, when considering craniofacial configuration, congenital abnormalities including developmental diseases may effect frontal sinus pneumatization. Along with congenital abnormalities, heredity factors (ethnic or genetic) may also impact the extent of pneumatization (Shapiro et al, 1980).

There are considerable ethnic variations in the size and shape of the human calvarium and face. Individuals having long, narrow heads and faces are considered *dolicocephalic*. Their frontal bones tend to protrude leaving a spatial gap; which allows the frontal sinus to pneumatize into this region (Spaeth et al, 1980). Conversely, individuals with short, wide heads are considered *brachycephalic*. The frontal bones do not extend in these individuals resulting in a

smaller frontal sinus (Spaeth et al, 1980). Most individuals are characterized and *mesocephalic* and lie somewhere in between the two extremes.

The second consideration in evaluation of frontal sinus pneumatization is the thickness of the frontal bone. The ability of the developing mucosal lining of the sinus to penetrate into bone is related to thickness of cortical bone (Spaeth et al, 1980). Thick cortical bone will resist pneumatization while thin cortical bone will not.

Since hormonal factors may influence cortical bone thickness as well, a third category to consider in frontal sinus pneumatization is the role of hormonal growth factors such as growth hormone (GH) (Spaeth et al, 1980). An increase in GH (e.g. gigantism and acromegaly) may cause an increase in frontal sinus pneumatization; whereas a deficiency in growth hormone (e.g. pituitary dwarfism) may cause an absence or hypoplasia of the frontal sinus (Spaeth et al, 1980).

Frontal sinus agenesis is uncommon but can be influenced by the aforementioned conditions. An analysis of frontal sinus agenesis in 565 patients aged 15-88 found that bilateral agenesis was seen in 8.32% of cases and unilateral absence of the frontal sinus was observed in 5.66% of patients (Danesh-Sani et al, 2011). This study noted a range for bilateral frontal sinus agenesis from 0.73% in Turkish populations to 43% in Canadian Eskimos (Danesh-Sani et al, 2011). Although the cause of bilateral frontal sinus agenesis is not well documented its occurrence is not uncommon within some populations. As previously discussed, the role of craniofacial configuration, frontal bone anatomy and hormonal influences could influence frontal sinus agenesis (Spaeth et al, 1980). Additionally, environmental conditions (e.g. climate), local osseous inflammation and mechanical masticatory stress could be factors (Danesh-Sani et al,

2011). Additionally, this study reported that bilateral agenesis of the frontal sinus is more common in females.

Unilateral agenesis of the frontal sinus has also been noted. This is partially due to the fact that the left and right sides of the frontal sinus develop separately from one another (Gagliardi et al, 2004). According to another study on frontal sinus agenesis, the range reported for unilateral agenesis for several populations is 0.8%-7.4% (Danesh-Sani et al, 2011). When unilateral absence of the frontal sinus occurs, it is more common in females and is usually present on the right side. In male patients, however, there is no difference between the frequencies of frontal sinus agenesis on either side (Danesh-Sani et al, 2011).

Statistical Evaluation in Forensic Science

Metric studies have employed numerous statistical approaches regarding the sexing of skeletal material. These include simple proportions, sectioning points, demarking points, identification points, logistic regression analysis and discriminant function analysis for assigning sex (Krishan et al, 2016). Currently, discriminant function analysis (DFA) remains the most widely utilized statistical test for sexing skeletal material (Krishan et al, 2016). A recent study performed at UNLV SDM utilized cephalometric radiographs for sex determination evaluated by discriminant function analysis (Sprowl, 2013). Twenty-five variables found on lateral cephalograms of pre- and post-adolescent Hispanic individuals were evaluated. Results indicated an average overall accuracy of 74.6% for establishing sex allocation with a distribution of 100% accuracy for 6.5-8.5 age groups; 83.3% for 8.6-10.5 age groups; 71.7% for 10.6-12.5 age groups; 78.3% for 12.6-14.5 age groups; 94.7% for 14.6-17.9 age groups..

Discriminant function analysis is population specific, simple to use without prior experience, and eliminates subjective criteria for sex estimation. DFA is used to evaluate sex based on a series of cranial or postcranial measurements which are then applied to discriminant function equations (Christensen et al, 2005). The result is a percentage which defines the correct allocation to a specific group. A minimum threshold of 95% accuracy for sex estimation is acceptable in the forensic setting. This is dependent on the condition of skeletal remains available for examination (Krishan et al, 2016). Below the 95% threshold there are varying degrees of reliability (Table 2.1).

Table 2.1
Reliability of Sex Determination (Novotný et al., 1993)

Reliability	Percent of Correct Sex Assignments (%)	Percent of Incorrect Sex Assignments (%)
Very Reliable	>60%	<10%
Reliable	>50%	<15%
Low Reliability	50%	
Unreliable	<50%	>20%

Frontal Sinus in Forensic Science

Schuller in 1921 was the first author to note that frontal sinuses are unique, even in monozygotic twins (Belaldvar et al, 2014 & Ribeiro, 2000) and the individuality of frontal sinus patterns is analogous to individual patterns used in forensic fingerprint analysis (Harris et al, 1987). In 1927, Culbert and Law made the first human identification using frontal sinus patterns in a court of law. Subsequent case reports have been filed with similar findings (Ribeiro, 2000). Based on these reports the unique pattern of the frontal sinus has been a valid aid to

identification (Ribeiro, 201). However, when evaluation of sexual determination is required, can it be relied upon to provide valuable information about sexual dimorphism?

When looking at the frontal sinus from a forensic standpoint there are two areas of study:

1. Morphology - which involves visual observation of a given structure (Bidmos et al, 2005)
2. Morphometry - defined as measurement of external form (Meriam-Webster, 1828).

Morphology is useful when comparing the unique patterns of frontal sinus dimensions between individuals. Morphometry of frontal sinuses has been employed for evaluation of sexual dimorphism between individuals.

Imaging Techniques for the Frontal Sinus

Imaging of the frontal sinus has been performed with a variety of technologies including lateral and posteroanterior cephalometrics, CT, cone-beam computed tomography (CBCT) and magnetic resonance imaging (MRI). Cephalometric methods are limited not only by their two dimensional nature but also by inherent magnification, distortion and superimposition resulting in potentially inaccurate measurements (Mah et al, 2012).

CT overcomes many of the limitations of cephalometry and offers high resolution images. However, drawbacks of this methodology include expense and increase radiation exposure. CT scanners place the patient at the center of a mounted on a rotating frame which holds a radiation source and detector. As the cylindrical scanner assembly rotates around the patient the detector recognizes a series of x-rays that have passed through the patient (Sukovic et

al, 2003). A fan shaped x-ray beam from the radiation source acquires a series of axial plane slices that are subsequently stacked to create a three-dimensional reconstruction (Figure 2).

This design was based on the work of Radon, who in 1917 established that a 3 dimensional object can be reconstructed from an infinite set of two dimensional projections taken at varying angles around the object (Sukovic et al, 2003). Because of these multiple axial radiographs the radiation dose to the patient is greater than that of more recent technology associated with CBCT.

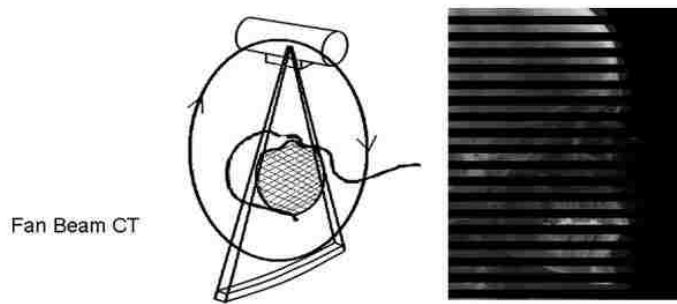


Figure 2.6 *Fan beam CT* (Farman et al, 2009)

CBCT technology was first developed at the Mayo Clinic in 1982 and although the technology has existed for over a quarter of a century it has only recently gained popularity in the dental field (Farman et al, 2009). CBCT scanners utilize a cone shaped beam and a two-dimensional detector (Figure 3) allowing for a single rotation of the x-ray source on a rotating frame (gantry). During this rotation a scan of the entire head is generated. This is in contrast to conventional CT scanners in which multiple “slices” must be stacked in order to complete an image (Sukovic et al, 2003). Another advantage of CBCT is higher resolution and image accuracy allowing for excellent visualization of many structures within the skull, including air-filled spaces like the frontal sinus.

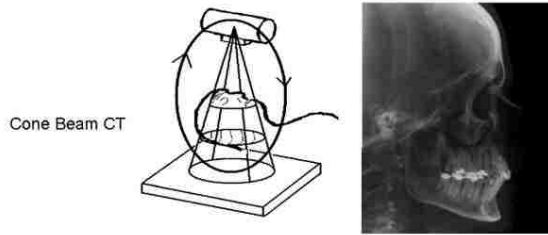


Figure 2.7 *Cone Beam CT* (Farman et al, 2009)

Volumetric imaging with both CT and CBCT produce volume elements or volume cells which are termed voxels. Voxels are small three dimensional cuboidal structures that represent the volumetric data. Voxel sizes are related to image resolution with smaller voxel sizes generally producing higher resolution images. In conventional CT, the voxels are *anisotropic* rectangular cubes. Image dimensions may not be accurate in earlier CT machines due to small gaps between slices. Although the computer compensates for these gaps, and accounts for them using complex algorithms, they still accumulate and create a sizable margin of error (Scarfe et al, 2006).

Conversely, CBCT devices provide *isotropic* voxels that are equal in all three dimensions and represent a cube. This permits precise measurements to be obtained in all planes. CBCT voxel size often exceeds most high grade multi-slice CT capabilities in spatial resolution; with voxel dimensions measuring from 0.4 mm to 0.07 mm (Carestream product brochure for the 9000C 3D).

With the advancement of CBCT technology, more dental education facilities and clinics are utilizing this radiological technique. The orthodontic clinic at University of Nevada - Las Vegas, School of Dental Medicine (UNLV SDM) includes a CBCT evaluation on every patient

undergoing comprehensive diagnosis and treatment. With the wealth of CBCT data, multiple research projects have been performed on the head and neck region in the UNLV clinic. One of these projects assessed airway volume in comparison to different malocclusion and facial types on CBCT images (Huynh, 2013).

A second project was performed by a class of 2014 resident and dedicated to making precise measurements of the lateral canal of the external auditory meatus located within the petrous portion of the temporal bone. Sexual dimorphism was assessed in this temporal region of subadults with significant dimorphic characteristics discovered (Benson, 2014). While the lateral angle of the temporal bone and did not reveal differences between the genders, significant differences were found with the cross-sectional area of the external auditory meatus; those being groups 2, 4 and 5 from the groupings of: Group 1 (age 6-10), Group 2 (age 11-13), Group 3 (age 14-16), Group 4 (age 17-19), and Group 5 (age 20-24)

Although the popularity of CBCT research is increasing and many projects are assessing different regions of the head and neck, CBCT studies of the readily captured frontal sinus have been overlooked in the subadult population.

Only two projects have been reported utilizing CBCT for the analysis of the frontal sinus. The first compares CBCT to conventional radiographs when evaluating the frontal sinus and reveals that CBCT is superior to extra-oral radiographs (Soares et al, 2015). This superiority can be attributed to the ease of measurements of landmarks with CBCT program tools rather than the digital calipers used for radiographic images (Soares et al, 2015). This study confirmed that CBCT is a reliable radiographic resource for frontal sinus analysis. However, it does not provide

insight into sexual dimorphic features of the frontal sinus that may be evaluated on CBCT imagery.

The subsequent study used CBCT to evaluate frontal sinus morphology for individual identification (Gianguido et al, 2015). This research evaluated frontal sinuses of 150 individuals 15-78 years old to determine if volume rendering could help in individual identification (Gianguido et al, 2015). Results indicated that volumetric evaluation could be used as an additional method in the identification process. However, no comparisons were made between males and females regarding possible sexual variations in frontal sinus dimensions.

With continual improvement in CBCT image quality and accompanying advances in development of software measurement tools, more reliable and accurate measurements of the frontal sinus are obtainable. Increased adoption and utilization of CBCT technology to evaluate the frontal sinus will provide a wealth of adjunctive data which can be applied to forensic investigations requiring identification of unknown individuals.

Morphological Approach to Human Identification

A review of the literature revealed a group of articles that utilized various imaging techniques to analyze the morphology of the frontal sinus for forensic identification of unknown individuals. These articles can be divided into 3 categories based on the visualization method:

1. Conventional radiographs
2. CT scans
3. CBCT.

A study of thirty five Japan skulls radiographed from an anteroposterior (AP) position and introduced a classification plan to establish a systematic method of personal identification by the pattern generated for the frontal sinus (Yoshino et al, 1987). The septum of the frontal sinus was divided on the AP radiographs to determine the *asymmetry index* which incorporated areas of both sides of the sinus. An index value of “0” indicated unilateral absence of the sinus and a value of “100” indicated its complete bilateral symmetry. Males and females showed moderate asymmetry in the analysis.

Unilateral superiority was also recorded in this AP study. When the left side of the sinus was superior to the right a value of “1” was assigned. A value of “2” represented the opposing possibility. The configuration of the upper border of the frontal sinus was also recorded according to the following categories:

- 0: absent
- 1: smooth
- 2: scalloped with 2 arcades
- 3: scalloped with 3 arcades
- 4: scalloped with 4 arcades
- 5: scalloped with above 5 arcades.

No sexual differentiation was found between males and females for the upper border of the frontal sinus.

There was no significant sexual dimorphism regarding the presence or absence of partial septa and supraorbital cells in the frontal sinus. Each of the individual criteria exhibited no sexual differentiation. However, combining these criteria into a coded classification system

could be useful in determining the identification of an unknown decedent (Yoshino et al, 1987). Yet, no morphometric measurements of the frontal sinus were used which could have helped improve the results.

A study utilizing occipito-mental radiographs of frontal sinuses of 32 randomly selected patients from the same racial group were analyzed and compared. Based on the results it was concluded that no two frontal sinuses are similar (Harris et al, 1987). Additionally, it was determined that the frontal sinus may be a suitable means of identification when skull orientation in the postmortem radiograph duplicated that of the antemortem radiograph (Harris et al, 1987). Although this report described the value of differences among frontal sinus shapes, it identified limitations in the reliance on frontal sinus morphology as the sole means of identification. Principal among these weaknesses is that antemortem radiographs which include the frontal sinus are often inaccessible. However, when they are, comparative postmortem radiographs still need to represent the same density and angulation for proper comparison (Harris et al, 1987).

Radiographic superimposition has been used to study frontal sinus morphology. Antemortem and postmortem frontal sinus radiographic images were traced and overlaid for comparison and found that the frontal sinus is an excellent distinguishing feature (Quatrehomme et al, 1996). Limitations of this study were the small sample size (two cases) and the fact that radiographs were not standardized for magnification, imaging angle and orientation of the skull.

A computer based data bank has been created to store patterns of 500 frontal sinuses based on a series of nine measurements obtained from plain radiographs (Ribeiro, 2000). Correct identification of an individual frontal sinus pattern among the 500 randomized radiographs was extremely accurate based on the computer program used (Ribeiro, 2000). Although this method

seems reliable the data bank that would need to be created for it to be employed for the general population is unfeasible.

Retrospective antemortem and postmortem Water's view radiographs of 39 individuals between the ages of 28-80 were compared using metric and morphologic approaches (Kirk et al, 2002). It was noted that although morphologic pattern matching was extremely accurate metric matching was not. The authors attributed the inaccuracies of the metric technique to measurement errors or positioning errors between the two successive radiographs (Kirk et al, 2002). By utilizing a three dimensional imaging approach, errors in metric measurements can be avoided.

A study performed in 2005 tested the reliability of analyzing the frontal sinus for positive identification using Elliptical Fourier Analysis (EFA) (Christensen, 2005). EFA analysis methodology quantifies the probability of obtaining a correct identification match of a specific individual versus the probability of an identification match from a general population. Employing this method it was concluded that the probability of establishing either a correct or incorrect identification was 96% (Christensen, 2005).

As described in previous studies the methods used to compare frontal sinus radiographs are highly dependent on accuracy and availability of antemortem and postmortem data. This can prove to be an impediment to the identification process when not available (Christensen, 2005). Additionally, limitations related to imaging three dimensional skeletal structures using two dimensional radiographic techniques poses a problem due to superimposition of overlapping structures (Christensen, 2005).

A final radiographic study explored the accuracy of frontal sinus superimpositions (Hashim et al, 2015). By utilizing three separate methods, it was concluded that comparison of antemortem and postmortem frontal sinus radiographs can only be accomplished when they are superimposed with the skull captured in the antemortem radiograph in the same posture and orientation as in the postmortem radiograph. Subsequent exposures of frontal sinuses of dry skulls taken one minute apart could not be superimposed accurately. Thus, conclusions of this report indicate that relying solely on frontal sinus superimpositions is not advised (Hashim et al, 2015).

CT technology has been used to develop a simple system for the identification of a decedent by features of the frontal sinus (Tatlisumak, 2006). The system was named the FSS system which included presence or absence of the frontal sinus (F), intersinus and intrasinus septum (S), and scalloping (S). Additional measurements which increased accuracy of identification included:

- Width
- Height
- Anteroposterior length
- Total width of the two sinuses
- Distance between the highest points of the two sinuses
- Distance of each sinus to its maximum lateral limit.

In this study resultant FSS system measurements for each case were converted into a coding system and compared among the 100 subjects (Tatlisumak, 2006). For a given case 93% of the codes could be used to eliminate subjects for identification purposes. Thus, among the 100

individuals requiring identification the field could be narrowed so that only seven CT scans required evaluation using pattern matching. It was concluded that the basic FSS formula along with linear measurements are useful tools in discrimination of unknown individuals. This study provided invaluable linear measurements of the frontal sinus for both males and females. These can be employed in future sexual determination studies.

Research utilizing CBCT methodology for individual identification was performed using 150 patients aged 15-78 years old (Gianguido et al, 2015). The technique used CBCT to render a 3D reconstruction of the frontal sinus for comparison. The authors concluded that CBCT can be used as an additional method in the identification process because of its reliability. The limitations of this study are consistent with the morphological problems described in other reports. A reliable method for comparison of images requires the availability of antemortem radiographs and is deemed unusable if such images do not exist.

Frontal Sinus in Sex Determination Utilizing Conventional Radiographs

Standardized posterior-anterior skull radiographs of 60 adult patients were utilized to determine gender and ethnic differences in a study performed in 1987 (Harris et al, 1987). The features assessed included sinus height, sinus width, perimeter, number of edge loculations, interorbital distance and sinus area. It was concluded that male frontal sinuses were significantly greater in both superio-inferior and mediolateral dimensions. It was also concluded that the differences between racial groups and sexes were insignificant. The age of subjects was not mentioned in this article. Additionally, there are inherent technical limitations related to the small sample size of the study and assessment of three dimensional skeletal structural measurements from a two dimensional posterior/anterior radiograph.

Lateral cephalograms of 100 adult skulls were utilized in a report regarding Taiwanese males and females (Hsiao et al, 1996). This project employed a discriminant function analysis of 18 cephalometric variables including frontal sinus height and width. The mean differences for all measurements were statistically significant at $p < 0.05$. The skulls were classified into two sexual groups using the 18 established variables with 100% accuracy. It was possible to determine the sex of the subjects with 98% accuracy using only three variables including frontal sinus width. Although this study seems promising in regard to determining the sex of adults, in actual forensic situations an intact skull may not be available for use. Since only skeletal fragments may remain these findings may be difficult to incorporate into a real-life scenario.

Paranasal sinus radiographs have been used in attempts to identify gender (Goyal et al, 2013). This type of radiograph was used to evaluate the:

- Number of scallops
- Number of partial septa
- Presence or absence of partial septa
- Presence or absence of supraorbital cells within the frontal sinus.

Although advanced statistical methods of logistic regression analysis were used to quantify the variable of sex determination there were no correlations found. This study was limited to the general radiographic morphology of the frontal sinus. Inherent distortion, magnification and other imaging artefacts limited the ability to obtain accurate measurements. In view of the prior work involving 3-dimensional measurements it was not surprising that statistically significant results were not found.

Research was undertaken using posteroanterior (PA) digital radiographs of 300 Indian adults age 25-30 using measurements of right and left frontal sinus height, width, and area (Belaldavar et al, 2014). This project used descriptive statistics as well as logistic regression analysis to analyze the data. The mean value for all variables was consistently higher in males. There were consistently higher values for in right side of the frontal sinus for both males and females. It was determined in a stepwise regression analysis that the left height and the left area were the most suited for sex determination with an accuracy rate of 64.6% and 63.2% respectively.

When all variables were used the predicted value increased to 65.5%. Thus, it was concluded that this was an average level of accuracy in sex determination in an Indian population. As previously stated, the limitation to this study was the nature of a two dimensional radiograph being used to evaluate a three dimensional skull. By utilizing a three dimensional view more measurements can be assessed in this dimension, thus adding value to the study.

Subsequent research using Caldwell digital radiographs of 50 males and 50 females of South Indian heritage who were greater than 20 years old obtained the same basic measurements of right and left frontal sinus height, width, and area (Saumya et al, 2014). However, unlike the previous study not all measurements were recorded as being statistically significant for males and females. The mean areas were deemed significantly higher in males and were used in a logistic regression analysis with a correct prediction of gender of 61%. This result is lower than the previous study.

Based on these findings it was concluded that logistic regression analysis was unreliable to determine sex based on frontal sinus calculations in adult individuals. The differences in the

results of these two studies may be attributed to the different radiographic techniques employed. A posteroanterior radiograph and a Caldwell radiograph are different images with different measuring capabilities which may account for these studies having diverse conclusions. By taking a three dimensional radiograph (e.g.: CBCT) measuring error can be eliminated.

The maximum height (MH) and the maximum width (MW) of the frontal sinus on 216 lateral cephalometric radiographs of adults were studied for gender identification (Kiran et al, 2014). The ratio of the MH and MW called the “sinus index” was taken in addition to highest and lowest points of the sinus. Data showed that the mean height and width of the frontal sinus were significantly higher in males than in females but the “sinus index” was higher in females. Measures of the frontal sinus were useful in correctly identifying sex in 67.59% using a discriminant function analysis and it was concluded that this method is a reliable tool in sexual determination.

The most recent study utilizing conventional PA radiographs was performed on 200 Indian subjects greater than 14 years of age (Soman et al, 2016). Metric and morphological measurements were taken and compared based on gender. Height, width and area of right and left frontal sinus were measured as well as Yoshino’s frontal sinus parameters listed previously (pages 23-24). All metric measurements were larger in males. There was a statistically significant difference of left width and left area which are most suitable for most suitable for gender determination. Morphological characteristics did not show statistically significant differences between age and gender.

With the exception of one radiological study (Saumya et al, 2014); most authors agree that the frontal sinus is a helpful tool in sex determination. As mentioned previously, however,

the limitations of those studies which employed conventional two dimensional radiographs are inherent, and include magnification, distortion and superimposition which prevent accurate measurements. By utilizing the third dimension a more accurate study can be performed. Additionally, age groups of the radiologic studies reported in the literature were principally performed on adults. Because the frontal sinus is fully developed in this age group it can be justified that it is sensible to measure this structure in this population. However, it is imperative that the younger population be studied as well.

Frontal Sinus in Sex Determination Utilizing Computed Tomography

A study utilizing paranasal CT scans evaluated the axial and coronal planes of 300 cases ranging from 20-83 years old (Tatlisumak et al, 2008). Measurements of the width, height and anteroposterior length on both sides of the frontal sinus were compared and sex determination assessed. All measurements were larger in males. Additionally, all measurements were larger on the left side which is inconsistent with other literature. Significant differences were noted in the anteroposterior lengths in males and females, and height for males and width for females. However, no logistic regressions analysis was performed to determine if these measurements were accurate predictors of sex.

A subsequent report used spiral CT, the FSS basic morphological and metric features to study and measure frontal sinus width, height, and AP length. However, additional measurements were also performed (Uthman et al, 2010). These were taken to compare the bilateral asymmetries of the sinuses and included skull measurements. The investigators found that without the skull measurements gender identity was 76.9% and with the skull measurements the accuracy was increased to 85.9%. This study suggests that a CT scan can provide valuable

and precise measurements. Unfortunately, this technology remains costly and not readily available.

CT scans on 150 subjects were evaluated for sexual differences and their effects on frontal cranioplasty (Lee et al, 2010). Based on this project it was decided to include the measurement of the nasofrontal angle in the current study. By using the axial, coronal and sagittal planes of the CT scan the frontal sinus was measured in intervals at 10mm, 20mm and 30mm in each direction from the midline. No significant measurements were found 30mm from the midline although sinus height differences between genders were noted 10mm from midline.

It has been documented that the supraorbital ridge shows sexual dimorphism (Graw et al, 1999 & Nowaczewska et al, 2014). Since the nasofrontal angle is a component of the supraorbital ridge which measures its inclination; it is another measurement of interest. The nasofrontal angle was found to be more acute in males (119.9°) as compared to females (135.5°). This value is at a statistically significant level. This research shows promising results and confirms the idea that the supraorbital region may be a key factor in determining sexual dimorphism. This variable is investigated further in the current study.

A study performed on 119 Korean cadavers between 21-72 years of age, using CT images of the frontal sinus measured morphological and metric variables (Kim et al, 2012). A 10-digit code was formulated based on metric and nonmetric measurements to correctly identify individuals. Based on the metric measurements most of the mean values were greater for males with total volume showing a statistically significant difference between the sexes. These metric values are helpful in understanding the differences between male and female skull architecture.

However, the need for an antemortem CT scan is crucial for the validity of this study to be useful as a morphometric means of human identification.

A subsequent CT study on 100 adults aged 20-70 was performed measuring height, width and anteroposterior length in coronal and axial cross-sections (Hamed et al, 2014). All measurements were found to be statistically significantly higher in males. A multiple regression analysis of the findings determined that among all frontal sinus measurements the right anteroposterior length was the best discriminant variable to determine sex with an overall accuracy of 67%. Thus, the frontal sinus dimensions were valuable in studying sexual dimorphism. Although this study showed promising results regarding sexual dimorphism of the frontal sinus, limitations related to cost and availability of CT scans continues to be a drawback to general use of this modality.

A retrospective study using 69 CT scans of patients aged 16-83 evaluated frontal sinus volumes (Michel et al, 2015). It was found that there was no correlation between right and left frontal sinus volumes or between age and frontal sinus volumes. However, sexual dimorphism in the total frontal sinus volume was noted. It was also possible to predict sex with 72.5% accuracy. While total frontal sinus volume seems to be an accurate method of sex determination it is only valuable if the entire frontal sinus is intact. By utilizing linear measurements of both the right and left frontal sinus to determine sexual dimorphism it may be possible to determine sex of an unknown individual with only part of the frontal sinus intact.

The most recent study using CT scans was performed on 200 Persian adults aged 20 to greater than 55 (Akhlaghi et al, 2016). Metric as well as morphological considerations were evaluated for the different age groups. Conclusions stated that the highest predictor of sex

determination was maximum height (61%); a level that is not practically useful. Other frontal sinus parameters had even lower predictive value as sex determinants. One limitation to this paper was the method in which the metric variables were measured. The anatomic borders of the frontal sinus were not utilized. Specifically, this included the inferior border which is defined as the supraorbital rim. This omission may have created errors in measurements of height and AP length which could have impacted the outcome of the study.

Chapter 3: Methodology

The following protocol, #790432-1, entitled “Sexual Determination from Frontal Sinus Analysis in a Subadult Population Using Archival Radiographic Records” was reviewed by the Office of Research Integrity at UNLV, and deemed excluded from IRB review (Appendix A).

Sampling Protocol

A total sample of 556 anonymized CBCT radiographs from UNLV SDM database were utilized for this study. These CBCT scans were made between August, 2006 and June, 2014 on pre-orthodontic patients from urban Southern Nevada. All CBCT scans were made by trained radiology technicians in the technique and operation of the CBCT machine (CB Mercuray, Hitachi Medical Corp). Scans were made with a matrix of 512 x 512, 193 mm FOV, 100 kV, 15 mA, and exposure time of 10 seconds. The data was sent directly to a UNLV School of Dental Medicine computer with password protected access and stored in Digital Imaging and Communications in Medicine format (DICOM). Volumetric renderings of CBCT scans of the subjects were evaluated with InvivoDental version 5.4.1 software (Anatomage, San Jose, CA).

All 556 anonymized CBCT scans were reviewed for unilateral or bilateral agenesis of the frontal sinus. This could be seen even if the entire frontal sinus was not in the field of view. Measurements were recorded to evaluate the prevalence of unilateral and bilateral agenesis. From the 556 CBCT radiographs, 216 (92 males and 114 females) were chosen for inclusion in the study. These represented subjects between the ages of 6-20. CBCT scans were included only if they were of good image quality and absent of any movement artifact. Radiographs of individuals with bilateral complete frontal sinus development were measured.

Radiographs of patients with pathology (e.g.: mucous retention within the frontal sinus, syndromic cranial variations, or diseases that could affect craniofacial development) were

excluded from the study. CBCT radiographs of persons <6 years old are not readily available in the orthodontic clinic because they are not routinely screened for orthodontic treatment. The upper limit of inclusion was age 20 based on the age of transition into adulthood associated with fusion of the spheno-occipital synostosis described by Enlow. Radiographs of those subjects included in the study were further divided into 3 age groups based on developmental periods (pre-pubertal, peri-pubertal and post-pubertal) reflected in the following:

- Group 1: Age 6-11
- Group 2: Age 12-15
- Group 3: Age 16-20

CBCT scans were anonymized and adjusted for orientation, brightness and contrast. Measurements of the frontal sinus of each of the 216 chosen scans included determination of its maximum height, width, and right and left anteroposterior lengths. The inclination of the nasofrontal angle and the anatomical location of the frontal sinus compared to a vertical reference line drawn through NA were also evaluated. Age and sex for each individual were recorded independently and only made available for this project upon the completion of data collection.

Maximum Height, Width and AP Length Measurements of the Frontal Sinus

The arch section tab of InVivoDental™ was utilized to create the platform on which to measure the frontal sinus. By adjusting the range and orientation, the inferior border of the frontal sinus was created using the superior rim of the orbit. Custom sections were produced at a width of 80mm and a slice thickness of 1mm in order to view the entirety of the frontal sinus for measuring.

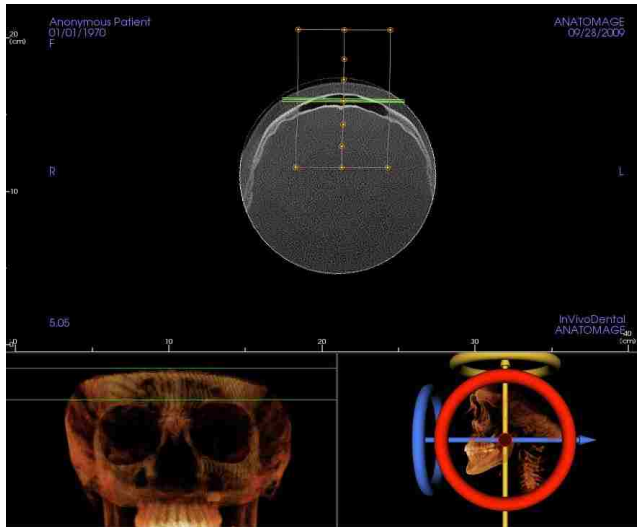


Figure 3.1 Shows cross-sectioning and delineation of inferior border of the frontal sinus

For measuring the maximum *height* of the right and left sides of the frontal sinus the intersinus septum was identified to demarcate right versus left frontal sinus. Custom slices (Figure 3.2 & 3.3) in the *axial view* were measured *perpendicular* to the *inferior border* using the linear measuring tool in InVivoDental™ in millimeters.

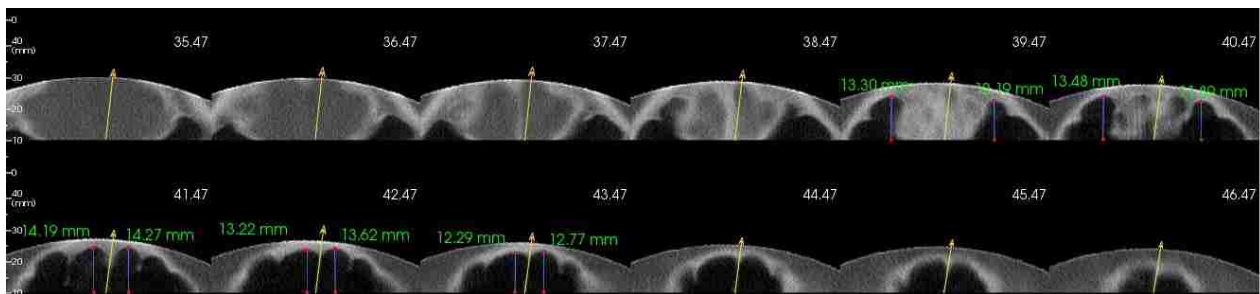


Figure 3.2 Custom sections for measuring maximum height for right and left frontal sinus

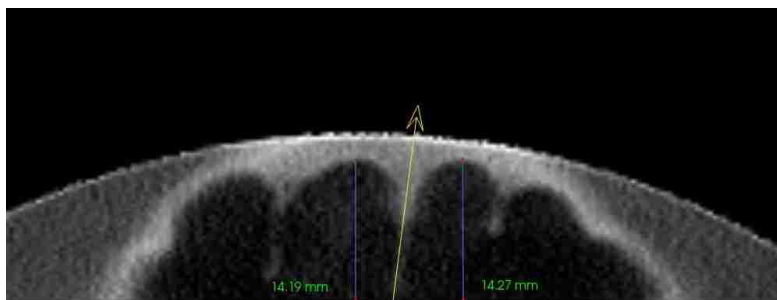


Figure 3.3 Maximum height of right and left frontal sinus

For measuring the maximum *width* of the right and left sides of the frontal sinus the intersinus septum was identified to demarcate right versus left frontal sinus. Custom slices (Figure 3.4 & 3.5) in the *axial view* were measured *parallel* to the *inferior border* using the linear measuring tool in InVivoDental™ in millimeters.

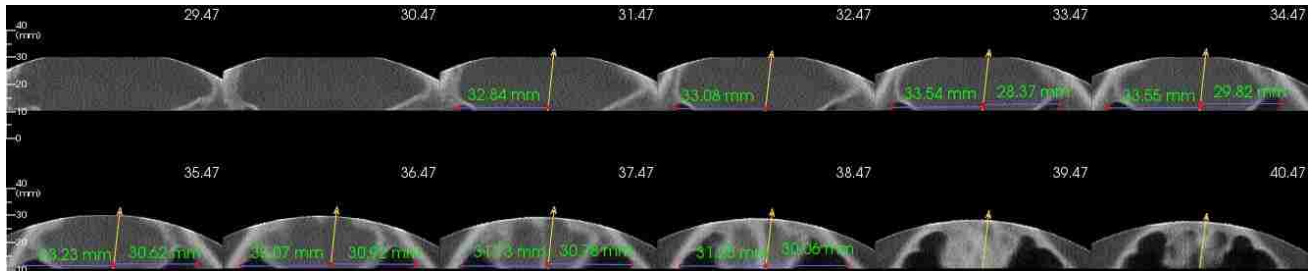


Figure 3.4 Custom sections for measuring maximum width for right and left frontal sinus

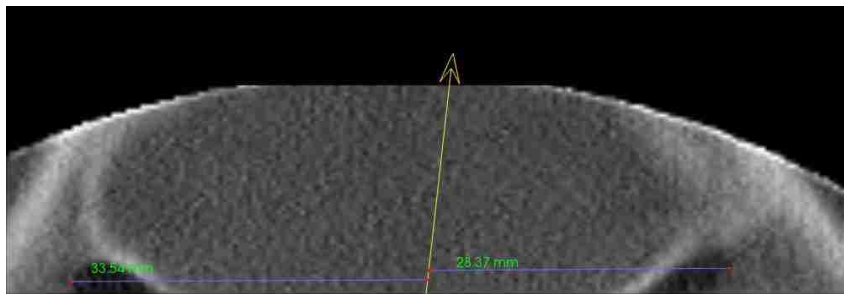


Figure 3.5 Maximum width of right and left frontal sinus

In order to measure the maximum *anteroposterior length* of the right and left sides of the frontal sinus the intersinus septum was identified to demarcate right versus left frontal sinus. Custom slices (Figures 3.6 & 3.7) in the *coronal view* were measured *parallel* to the *mid-sagittal plane* using the linear measuring tool in InVivoDental™ in millimeters.

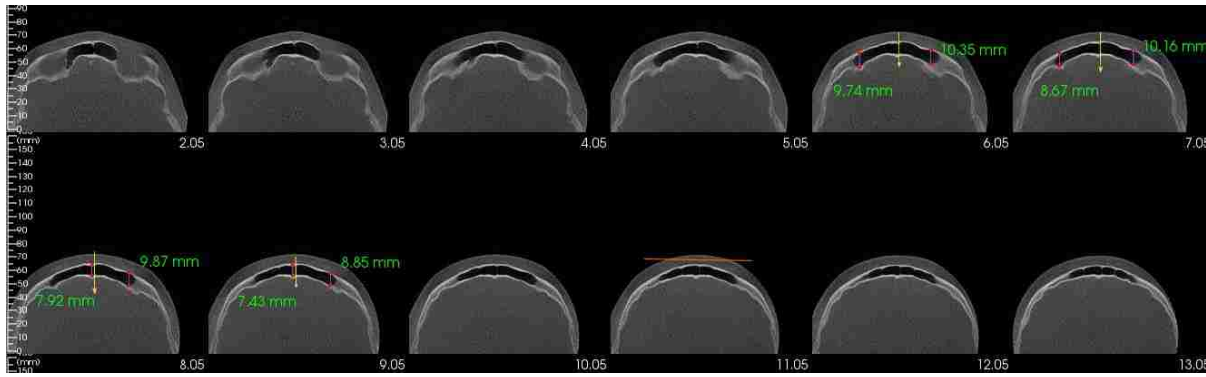


Figure 3.6 Custom sections for measuring maximum AP length of the right and left frontal sinus

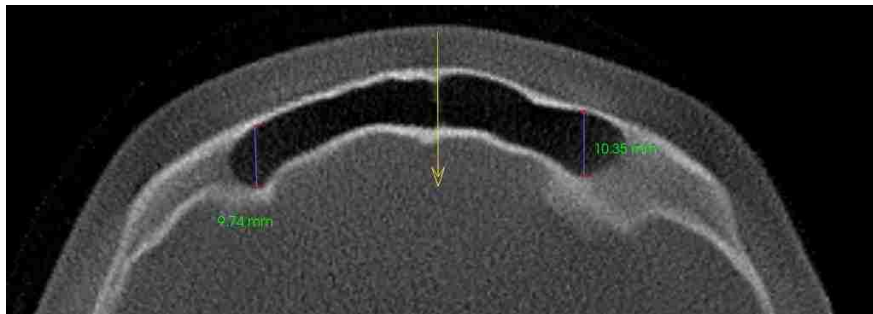


Figure 3.7 Maximum AP length of right and left frontal sinus

Measuring the Nasofrontal Angle

A midsagittal section was taken to measure the nasofrontal angle as reported in a previous study by Lee et al, 2010. This angle is formed between the glabellar prominence and the nasal bone (Figure 3.8). By utilizing the angle measuring tool in InVivoDental™ the apex of the angle terminated at nasion and extended superiorly along the glabellar prominence and inferiorly along the nasal bone (Figure 3.9).

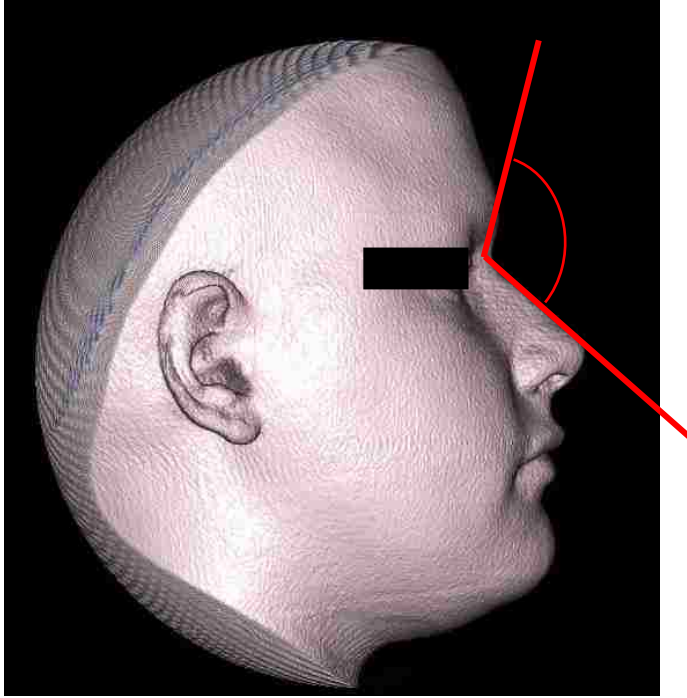


Figure 3.8 *Nasofrontal angle (derived CBCT using Invivo 5.3 Software)*

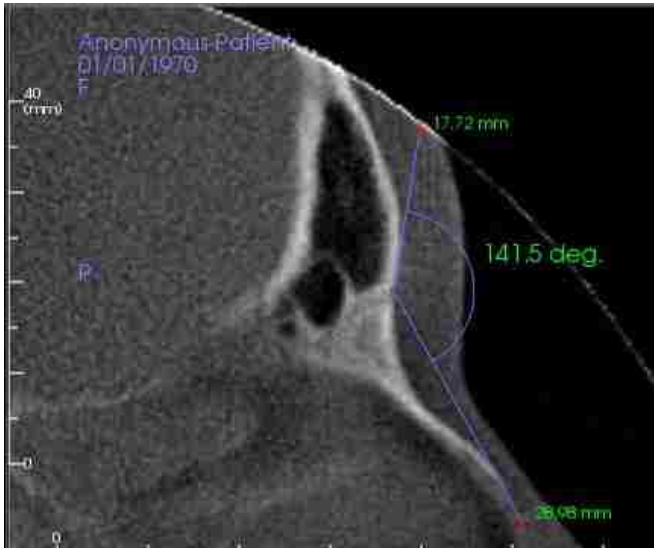


Figure 3.9 *Nasofrontal angle measured from CBCT*

Relationship of Frontal Sinus to a Vertical Reference Line

In the midsagittal section a vertical reference line was established using nasion and A-point (NA line). This line was extended superiorly to evaluate its relationship to the most anterior border of the frontal sinus. This measurement was recorded based on the frontal sinus being behind the line, at the line or in front of the line as depicted in Figure 3.10.



Figure 3.10 *Relationship of the most anterior border of the frontal sinus to the vertical reference line (Nasion-A point); anterior border of the frontal sinus falls at the vertical reference line in this case.*

Statistics

Intra-operator error rate was obtained by repeating measurements on 10 randomly selected subjects four months after initial measurement. CBCT data was opened in its anonymized .INV format without operator knowledge of the true age and sex of the individuals. All of the procedures outlined above were repeated and degree of reliability was determined using a two-way mixed intra-class correlation coefficient.

Data from Excel was transferred into the Statistical Package for the Social Sciences (SPSS) version 22.0 for statistical analysis. Descriptive statistics were calculated to evaluate the measurement variables between males and females of different age groups. The results of each measurement were compared against sex classification within the given age groups using an independent samples t-test with a significance level of $p < 0.05$.

A Pearson's Correlation was performed to evaluate the relationship of the frontal sinus to the NA line against sex classification within the age groups. Descriptive statistics were also performed to evaluate the frequency of unilateral and bilateral agenesis of the frontal sinus between males and females. Finally, a discriminant function analysis was completed to predict the probability of correct sex allocation in the three different age groups.

Chapter 4: Results

Age Distribution

The age distribution of the 216 individuals evaluated for this study ranged from 6-20 years. Table 4.1 shows the distribution of the age groups:

- Group 1: age group 6-11 (20 males and 34 females)
- Group 2: age group 12-15 (50 males and 59 females)
- Group 3: age group 16-20 (22 males and 31 females).

The frequency of males and females within each age group can be observed in Figures 4.1 and 4.2.

Table 4.1
Sample Distribution of Each Age Group

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	6-11	54	25.0	25.0	25.0
	12-15	109	50.5	50.5	75.5
	16-20	53	24.5	24.5	100.0
	Total	216	100.0	100.0	

Figure 4.1
Histogram of Distribution of Males within Each Age Group

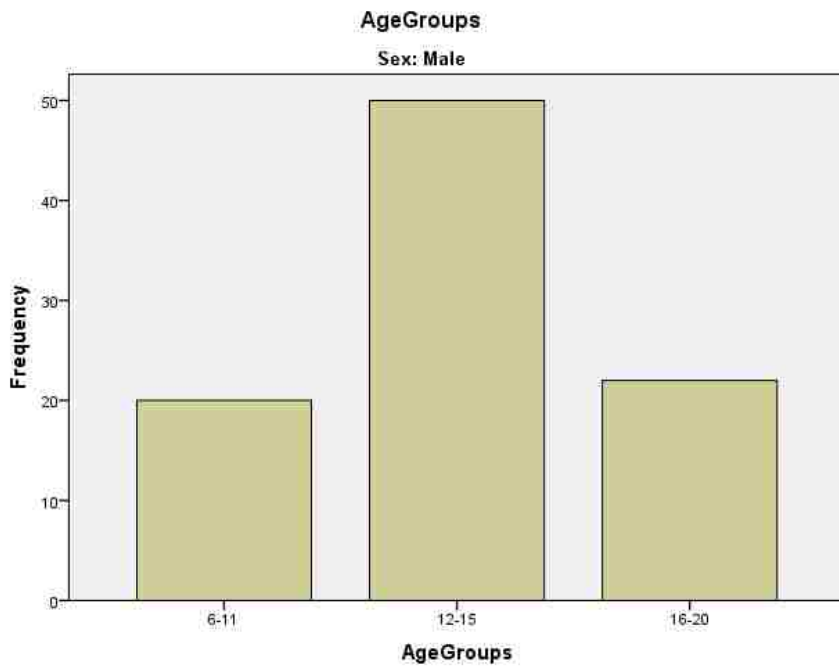
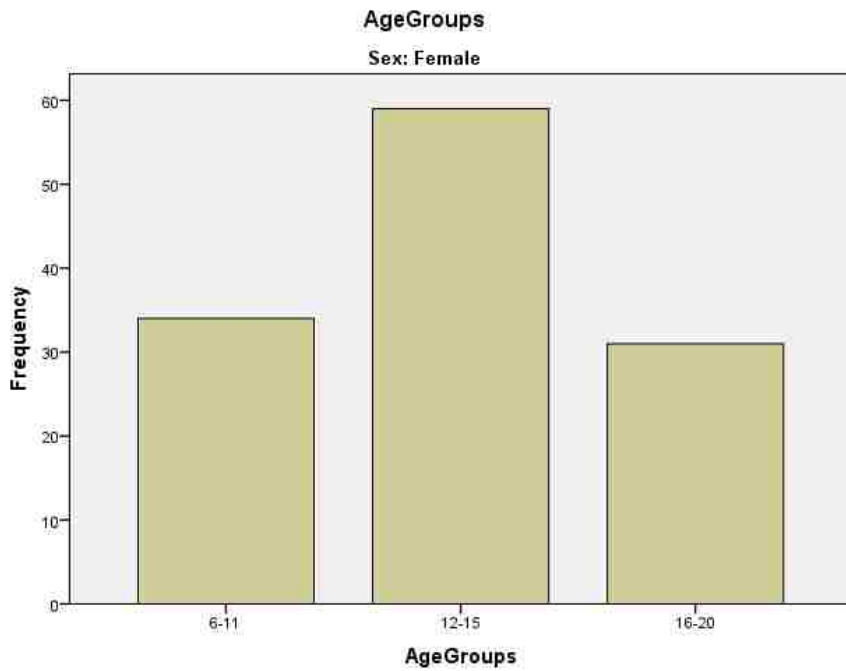


Figure 4.2
Histogram of Distribution of Females within Each Age Group



Intraobserver Error Rate

In order to test the degree of reliability for the methods used in this study, intraobserver error testing was carried out on 10 (6 females, 4 males) randomly selected individuals four months after initial measurements were taken. A two-way mixed intra-class correlation coefficient was carried out to compare the results of the original and secondary measurements for each of the measurements made (Table 4.2). A score of 1 indicated a perfect correlation, whereas 0 indicated no correlation at all. The single measures intra-class correlation score of the 10 subjects was 0.998, which indicates excellent repeatability using the InVivo 5.4.1 software with a single examiner.

Table 4.2
Intra-class Correlation Coefficient

	Intraclass Correlation ^b	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.998 ^a	.992	1.000	953.719	9	9	.000
Average Measures	.999 ^c	.996	1.000	953.719	9	9	.000

Research Question 1

Do morphometric measurements of the maximum height of the right and left frontal sinus, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

Hypothesis: Morphometric measurements of the maximum height of the right and left frontal sinus, as measured from a CBCT radiograph, are sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group (Age Group 3).

Null Hypothesis: Morphometric measurements of the maximum height of the right and left frontal sinus, as measured from a CBCT, are not significantly sexually dimorphic for this population. *The null hypothesis was accepted.* An independent samples t-test was performed and no level of significance was noted in the maximum height of the right and left frontal sinus. Therefore, this dimension of the frontal sinus shows no sexual dimorphism at any age.

Tables 4.3 and 4.4 show the descriptive statistics for maximum height of right and left sides of the frontal sinus in males and females for given age groups. Tables 4.5 and 4.6 summarize the results of the independent samples t-test for the maximum height of the right and left sides of the frontal sinus.

Table 4.3

Descriptive Statistics for Maximum Height of the Right Frontal Sinus

Age Groups	Sex	N	Mean	Std. Deviation	Std. Error Mean
6-11 Max Height Right Sinus (MHRS)	Male	20	9.7510	5.33131	1.19212
	Female	34	8.3882	3.84464	.65935
12-15 Max Height Right Sinus (MHRS)	Male	50	11.6770	5.75588	.81400
	Female	59	10.7163	5.95632	.77545
16-20 Max Height Right Sinus (MHRS)	Male	22	14.1695	6.99080	1.49044
	Female	31	11.4594	5.58384	1.00289

Table 4.4

Descriptive Statistics for Maximum Height of the Left Frontal Sinus

Age Groups	Sex	N	Mean	Std. Deviation	Std. Error Mean
6-11 Max Height Left Sinus (MHLS)	Male	20	9.7805	7.13477	1.59538
	Female	34	8.8409	5.07634	.87059
12-15 Max Height Left Sinus (MHLS)	Male	50	12.9260	6.45337	.91264
	Female	59	12.0439	5.71652	.74423
16-20 Max Height Left Sinus (MHLS)	Male	22	14.1509	6.36701	1.35745
	Female	31	11.9932	6.13892	1.10258

Table 4.5
Independent Samples Test for Maximum Height of Right Frontal Sinus

Age Groups			Levene's Test for Equality of Variances		t-test for Equality of Means						
			F	Sig.	T	df	Sig. (2- tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
										Lower	Upper
6- 11	Max Height Right Sinus (MHRs)	Equal variances assumed	2.667	.108	1.088	52	.282	1.36276	1.25285	-	3.87679
		Equal variances not assumed			1.000					30.746	
12- 15	Max Height Right Sinus (MHRs)	Equal variances assumed	.006	.938	.852	107	.396	.96073	1.12745	-	3.19577
		Equal variances not assumed			.855					105.138	
16- 20	Max Height Right Sinus (MHRs)	Equal variances assumed	1.479	.230	1.568	51	.123	2.71019	1.72892	-	6.18113
		Equal variances not assumed			1.509					38.759	

Table 4.6
Independent Samples Test for Maximum Height of Left Frontal Sinus

Age Groups			Levene's Test for Equality of Variances		t-test for Equality of Means						
			F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
										Lower	Upper
6-11	Max Height Left Sinus (MHLS)	Equal variances assumed	2.864	.097	.564	52	.575	.93962	1.66605	-2.40355	4.28279
		Equal variances not assumed			.517	30.446	.609	.93962	1.81746	-2.76986	4.64909
12-15	Max Height Left Sinus (MHLS)	Equal variances assumed	1.015	.316	.757	107	.451	.88210	1.16584	-1.42904	3.19324
		Equal variances not assumed			.749	98.892	.456	.88210	1.17762	-1.45459	3.21879
16-20	Max Height Left Sinus (MHLS)	Equal variances assumed	.001	.978	1.242	51	.220	2.15768	1.73781	-1.33111	5.64648
		Equal variances not assumed			1.234	44.340	.224	2.15768	1.74882	-1.36606	5.68143

Research Question 2

Do morphometric measurements of the maximum width of the right and left frontal sinus, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

Hypothesis: Morphometric measurements of the maximum width of the right and left frontal sinus, as measured from a CBCT radiograph, are sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group (Age Group 3).

Null Hypothesis: Morphometric measurements of the maximum width of the right and left frontal sinus, as measured from a CBCT radiograph, are not significantly sexually dimorphic for this population. *The null hypothesis was accepted.* An independent samples t-test was performed and no level of significance was noted in the maximum width of the right and left frontal sinus. Therefore this dimension of the frontal sinus manifests no sexual dimorphism among any of the age groups. Tables 4.7 and 4.8 show descriptive statistics for the maximum right and left frontal sinus widths in both sexes and for each age group. Tables 4.9 and 4.10 highlight the results of the independent samples t-test for the maximum width of the right and left frontal sinus.

Table 4.7

Descriptive Statistics for Maximum Width of the Right Frontal Sinus

Age Groups		Sex	N	Mean	Std. Deviation	Std. Error Mean
6-11	Max Width Right Sinus (MWRS)	Male	20	21.7795	6.51057	1.45581
		Female	34	20.3306	6.93748	1.18977
12-15	Max Width Right Sinus (MWRS)	Male	50	24.3452	6.45061	.91225
		Female	59	23.0469	7.86505	1.02394
16-20	Max Width Right Sinus (MWRS)	Male	22	25.7223	8.08661	1.72407
		Female	31	22.8410	6.12639	1.10033

Table 4.8

Descriptive Statistics for Maximum Width of the Left Frontal Sinus

Age Groups		Sex	N	Mean	Std. Deviation	Std. Error Mean
6-11	Max Width Left Sinus (MWLS)	Male	20	20.5170	8.73489	1.95318
		Female	34	21.6371	6.75771	1.15894
12-15	Max Width Left Sinus (MWLS)	Male	50	24.8254	6.72238	.95069
		Female	59	25.6876	7.08502	.92239
16-20	Max Width Left Sinus (MWLS)	Male	22	25.9350	7.26261	1.54839
		Female	31	23.4258	6.92077	1.24301

Table 4.9
Independent Samples Test for Maximum Width of Right Frontal Sinus

Age Groups			Levene's Test for Equality of Variances		t-test for Equality of Means						
			F	Sig.	T	df	Sig. (2- tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
										Lower	Upper
6- 11	Max Width Right Sinus (MWRs)	Equal variances assumed Equal variances not assumed	.000	.996	.758	52	.452	1.44891	1.91191	- 2.38761	5.28544
				.771	42.055	.445	1.44891	1.88014	- 2.34522	5.24304	
12- 15	Max Width Right Sinus (MWRs)	Equal variances assumed Equal variances not assumed	2.088	.151	.931	107	.354	1.29825	1.39392	- 1.46504	4.06154
				.947	106.897	.346	1.29825	1.37137	- 1.42037	4.01687	
16- 20	Max Width Right Sinus (MWRs)	Equal variances assumed Equal variances not assumed	2.463	.123	1.476	51	.146	2.88130	1.95148	- 1.03646	6.79907
				1.409	37.264	.167	2.88130	2.04527	- 1.26183	7.02444	

Table 4.10
Independent Samples Test for Maximum Width of Left Frontal Sinus

Age Groups			Levene's Test for Equality of Variances		t-test for Equality of Means						
			F	Sig.	t	df	Sig. (2- tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
										Lower	Upper
6- 11	Max Width Left Sinus (MWLS)	Equal variances assumed	1.740	.193	-.527	52	.600	-1.12006	2.12492	-	3.14390
		Equal variances not assumed			-.493					32.420	
12- 15	Max Width Left Sinus (MWLS)	Equal variances assumed	.209	.648	-.648	107	.518	-.86223	1.33043	-	1.77519
		Equal variances not assumed			-.651					105.610	
16- 20	Max Width Left Sinus (MWLS)	Equal variances assumed	.129	.721	1.274	51	.208	2.50919	1.96910	-	6.46233
		Equal variances not assumed			1.264					43.997	

Research Question 3

Do morphometric measurements of the maximum anteroposterior length of the right and left frontal sinus, as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

Hypothesis: Morphometric measurements of the maximum anteroposterior length of the right and left frontal sinus, as measured from a CBCT radiograph, are sexually dimorphic and statistically significant ($p < 0.05$) in the 16-20 age group (Age Group 3).

Null Hypothesis: Morphometric measurements of the maximum anteroposterior length of the right and left frontal sinus, as measured from a CBCT radiograph, are not statistically significantly sexually dimorphic for this population. *The null hypothesis was rejected.* An independent samples t-test was performed and statistically significant values ($p < 0.01$) for maximum AP length of the right and left frontal sinus in Age Group 3 were observed. Tables 4.11 and 4.12 present the descriptive statistics for the maximum AP length of right and left frontal sinuses between males and females within the given age groups. Tables 4.13 and 4.14 highlight the results of the independent samples t-test for the maximum AP length of the right and left frontal sinus.

Table 4.11

Descriptive Statistics for Maximum AP Length of the Right Frontal Sinus

Age Groups	Sex	N	Mean	Std. Deviation	Std. Error Mean
6-11 Max AP Length Right Sinus (MAPRS)	Male	20	7.8720	4.46495	.99839
	Female	34	6.5247	2.21536	.37993
12-15 Max AP Length Right Sinus (MAPRS)	Male	50	9.2338	2.93093	.41450
	Female	59	8.5488	4.27118	.55606
16-20 Max AP Length Right Sinus (MAPRS)	Male	22	10.9327	3.73422	.79614
	Female	31	7.9974	2.63141	.47262

Table 4.12

Descriptive Statistics for Maximum AP Length of the Left Frontal Sinus

Age Groups	Sex	N	Mean	Std. Deviation	Std. Error Mean
6-11 Max AP Length Left Sinus (MAPLS)	Male	20	8.0050	4.42983	.99054
	Female	34	7.1109	3.05429	.52381
12-15 Max AP Length Left Sinus (MAPLS)	Male	50	9.5588	2.94627	.41667
	Female	59	9.3722	3.68503	.47975
16-20 Max AP Length Left Sinus (MAPLS)	Male	22	11.2055	3.68352	.78533
	Female	31	8.0016	2.26138	.40616

Table 4.13
Independent Samples Test for Maximum AP Length of the Right Frontal Sinus

Age Groups			Levene's Test for Equality of Variances		t-test for Equality of Means						
			F	Sig.	T	df	Sig. (2- tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
										Lower	Upper
6- 11	Max AP Length Right Sinus (MAPRS)	Equal variances assumed Equal variances not assumed	6.157	.016	1.483	52	.144	1.34729	.90873	-47620	3.17079
					1.261	24.604	.219	1.34729	1.06824	-.85458	3.54917
12- 15	Max AP Length Right Sinus (MAPRS)	Equal variances assumed Equal variances not assumed	4.342	.040	.958	107	.340	.68499	.71466	-.73174	2.10171
					.988	102.795	.326	.68499	.69355	-.69054	2.06051
16- 20	Max AP Length Right Sinus (MAPRS)	Equal variances assumed Equal variances not assumed	4.492	.039	3.361	51	.001	2.93531	.87335	1.18198	4.68864
					3.170	35.337	.003	2.93531	.92585	1.05637	4.81425

Table 4.14

Independent Samples Test for Maximum AP Length of the Left Frontal Sinus

Age Groups			Levene's Test for Equality of Variances		t-test for Equality of Means						
			F	Sig.	t	df	Sig. (2- tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
										Lower	Upper
6- 11	Max AP Length Left Sinus (MAPLS)	Equal variances assumed Equal variances not assumed	.102	.750	.877	52	.385	.89412	1.01957	- 1.15179	2.94003
				.798	29.772	.431	.89412	1.12051		- 1.39500	3.18324
12- 15	Max AP Length Left Sinus (MAPLS)	Equal variances assumed Equal variances not assumed	1.402	.239	.288	107	.774	.18660	.64719	- 1.09638	1.46958
				.294	106.664	.770	.18660	.63543		- 1.07311	1.44631
16- 20	Max AP Length Left Sinus (MAPLS)	Equal variances assumed Equal variances not assumed	13.881	.000	3.920	51	.000	3.20384	.81728	1.56308	4.84460
				3.624	32.127	.001	3.20384	.88414		1.40319	5.00450

Research Question 4

Does the nasofrontal angle, as measured from a CBCT, show sexual dimorphism? If so, in which age group does it appear?

Hypothesis: Morphometric measurement of the nasofrontal angle measured from a CBCT radiograph, is sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group (Age Group 3).

Null Hypothesis: Morphometric measurement of the nasofrontal angle measured from a CBCT radiograph is not statistically significantly sexually dimorphic for this population. *The null hypothesis was rejected.* An independent samples t-test was performed and statistically significant values for the nasofrontal angle in Age Group 2 ($p < 0.05$) & Age Group 3 ($p < 0.01$) were observed. Table 4.15 shows the descriptive statistics for the nasofrontal angle between males and females within the given age groups. Table 4.16 highlights the results of the independent samples t-test for the nasofrontal angle.

Table 4.15
Descriptive Statistics for the Nasofrontal Angle

Age Groups	Sex	N	Mean	Std. Deviation	Std. Error Mean	
6-11	Nasofrontal Angle	Male	20	140.7200	6.05532	1.35401
		Female	34	140.9412	7.98685	1.36973
12-15	Nasofrontal Angle	Male	50	133.9360	10.03375	1.41899
		Female	59	137.7119	6.31097	.82162
16-20	Nasofrontal Angle	Male	22	124.4773	10.99147	2.34339
		Female	31	134.9323	7.78269	1.39781

Table 4.16
Independent Samples Test for the Nasofrontal Angle

Age Groups	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Lower	Upper
6-11 Nasofrontal Angle	.629	.431	-.107	52	.915	-.22118	2.06849	-4.37191	3.92956
			-.115	48.526	.909	-.22118	1.92601	-4.09260	3.65024
12-15 Nasofrontal Angle	9.696	.002	-	107	.019	-3.77586	1.58152	-6.91104	-.64068
			2.387	-	79.787	.024	-3.77586	1.63969	-7.03908
16-20 Nasofrontal Angle	4.050	.049	-	51	.000	-10.45499	2.57581	-	-
			4.059	-	35.460	.000	-10.45499	2.72862	15.62613
			-					-	-
			3.832					15.99180	4.91817

Research Question 5

Does the distance from the most anterior border of the frontal sinus to a line drawn through Nasion-A point (NA), as measured from a CBCT radiograph, show sexual dimorphism? If so, in which age group does it appear?

Hypothesis: The anatomic relationship of the anterior border of the frontal sinus to a line drawn through NA, as measured from a CBCT radiograph, is sexually dimorphic and statistically significant ($P < 0.05$) in the 16-20 age group.

Null Hypothesis: The anatomic relationship of the anterior border of the frontal sinus to a line drawn through NA, as measured from a CBCT radiograph, is not statistically significantly sexually dimorphic for this population. *The null hypothesis was accepted.* No correlation was found between the relationship of the anterior border of the frontal sinus and sex within the different age groups when using a Pearson's Correlation test. Table 4.18 exhibits the results of the Pearson Correlation test.

Table 4.17
Correlation Between Sex and Anatomic Location of the Frontal Sinus

Age Groups			Relationship to Nasion	Sex
6-11	Relationship to Nasion	Pearson Correlation	1	-.051
		Sig. (2-tailed)		.714
		N	54	54
	Sex	Pearson Correlation	-.051	1
		Sig. (2-tailed)	.714	
		N	54	54
12-15	Relationship to Nasion	Pearson Correlation	1	-.144
		Sig. (2-tailed)		.134
		N	109	109
	Sex	Pearson Correlation	-.144	1
		Sig. (2-tailed)	.134	
		N	109	109
16-20	Relationship to Nasion	Pearson Correlation	1	.066
		Sig. (2-tailed)		.637
		N	53	53
	Sex	Pearson Correlation	.066	1
		Sig. (2-tailed)	.637	
		N	53	53

Research Question 6

What is the frequency of bilateral absence of the frontal sinus among the given subadult populations? In which sex does it occur more commonly?

Hypothesis: The frequency of bilateral absence of the frontal sinus falls within the range found in previous studies (0.73%-43%) and occurs more frequently in females (Danesh-Sani, 2011).

Null Hypothesis: The frequency of bilateral absence of the frontal sinus will not be consistent with the values found in previous studies. *The null hypothesis was rejected.* As seen in Table 4.19 the incidence of bilateral agenesis of the frontal sinus occurred in 52 individuals (17 males and 35 females). With a total of 556 CBCT radiographs reviewed, 9.3% of the total population experienced bilateral agenesis of the frontal sinus. Females were twice as likely to demonstrate bilateral agenesis of the frontal sinus.

Table 4.18
Frequency of Bilaterally Missing Frontal Sinus in Males and Females

Sex	Frequency
Male Bilaterally Missing	17
Female Bilaterally Missing	35

Research Question 7

What is the frequency of unilateral absence of the frontal sinus within the given subadult populations?

Hypothesis: The frequency of unilateral absence of the frontal sinus is consistent with results of previous studies at 0.8%-7.4% (Danesh-Sani, 2011).

Null Hypothesis: The frequency of unilateral absence of the frontal sinus will not be consistent with results of previous studies. *The null hypothesis was accepted.* This hypothesis was accepted because the frequency of unilateral agenesis of the frontal sinus occurred in 53 individuals (26 males and 27 females) (Table 4.20). This represents 9.5% of the 556 subadult CBCT radiographs reviewed. This percentage is greater than the 7.4% upper limit observed previously.

Table 4.19
Frequency of Unilateral Agenesis of the Frontal Sinus in Males and Females

Sex			Frequency
Male	Valid	Right Sinus Missing	14
		Left Sinus Missing	12
		Total	26
Female	Valid	Right Sinus Missing	17
		Left Sinus Missing	10
		Total	27

Research Question 8

Is unilateral frontal sinus agenesis more common on the right or left side and is this sexually determined?

Hypothesis: The right side of the sinus is more commonly missing in females and there is no difference in right vs left frontal sinus agenesis in males (Danesh-Sani, 2011).

Null Hypothesis: Sexual determination of unilateral agenesis of the frontal sinus will not be consistent with results of previous studies. *The null hypothesis was rejected.* Table 4.20 shows that females experienced a greater incidence of right sinus agenesis (N=17) than left sinus agenesis (N=10). Males experienced almost equal incidence of right (N=14) and left (N=12) sinus agenesis. This is consistent with results found in previous reports.

Research Question 9

Can a discriminant function analysis be performed utilizing frontal sinus measurements for the three subadult age groups studied?

Hypothesis: The frontal sinus dimensions utilized in a discriminant function analysis will result in the highest accuracy observed in the 16-20 age-group.

Null Hypothesis: Frontal sinus dimensions will not express any difference in accuracy among the subadult age groups when utilized in a discriminant function analysis. *The null hypothesis was rejected.* A discriminant function analysis was performed for each of the three subadult populations using all measurements obtained from the frontal sinus. Table 4.21 describes how well the prediction model fits each age group. There is significance in the prediction model fit for only Group 3 and Table 4.22 shows the discriminant function variables for this group. Among the variables analyzed nasion angle and maximum height of the right sinus were the best predictors of sex allocation. Table 4.23 and the following list show the percentages of correctly classified males or females in each subadult population in the study:

- Age group 6-11 - correctly classified 64.8%
- Age group 12-15 - correctly classified 57.8%
- Age group 16-20 - correctly classified 79.2%.

Table 4.20
Wilks' Lambda and Prediction of Model Fit

Age Groups	Test of Function(s)	Wilks' Lambda	Chi-square	df	Sig.
6-11	1	.905	4.809	8	.778
12-15	1	.913	9.407	8	.309
16-20	1	.642	20.793	8	.008

Table 4.21
Standardized Canonical Discriminant Function Coefficients

16-20	Max Height Right Sinus (MHRS)	.695
	Max Height Left Sinus (MHLS)	-.769
	Max Width Right Sinus (MWRS)	-.054
	Max Width Left Sinus (MWLS)	.174
	Max AP Length Right Sinus (MAPRS)	-.329
	Max AP Length Left Sinus (MAPLS)	-.412
	Nasion Angle	.676
	Relationship to Nasion	.291

Table 4.22
Result of the Discriminant Function Analysis for All Three Age Groups

Age Groups		Sex	Predicted Group Membership		Total	
			Male	Female		
6-11	Original	Count	Male	6	14	20
			Female	5	29	34
	%	Male	30.0	70.0	100.0	
		Female	14.7	85.3	100.0	
	Cross-validated ^b	Count	Male	5	15	20
			Female	9	25	34
%		Male	25.0	75.0	100.0	
		Female	26.5	73.5	100.0	
12-15	Original	Count	Male	22	28	50
			Female	18	41	59
	%	Male	44.0	56.0	100.0	
		Female	30.5	69.5	100.0	
	Cross-validated ^b	Count	Male	21	29	50
			Female	22	37	59
%		Male	42.0	58.0	100.0	
		Female	37.3	62.7	100.0	
16-20	Original	Count	Male	15	7	22
			Female	4	27	31
	%	Male	68.2	31.8	100.0	
		Female	12.9	87.1	100.0	
	Cross-validated ^b	Count	Male	12	10	22
			Female	7	24	31
%		Male	54.5	45.5	100.0	
		Female	22.6	77.4	100.0	

- a. For split file Age Groups=6-11, 64.8% of original grouped cases correctly classified.
- b. For split file Age Groups=12-15, 57.8% of original grouped cases correctly classified.
- c. For split file Age Groups=16-20, 79.2% of original grouped cases correctly classified.

Chapter 5: Discussion

The primary goal of this study was to utilize CBCT radiographs to assess the sexual dimorphism of the supraorbital region and frontal sinus of subadults within the urban population of Southern Nevada. Principal areas of interest were frontal sinus height, width, anteroposterior length, nasofrontal angle and anatomic location of the sinus compared to a vertical reference line drawn through NA. Other areas of note were related to prevalence of frontal sinus unilateral and bilateral agenesis as well as reliability of correct sex allocation within the various subadult age groups evaluated. Overall, statistically significant values were found within the anterior-posterior length (Age Group 3) and the nasofrontal angle (Age Groups 2 and 3). The prevalence of bilateral and unilateral agenesis of the frontal sinus was generally consistent with results of previous studies and the outcome of a discriminant function analysis showed high levels of sex allocation in the Age Group 3.

Intraobserver Error Rate

Intraobserver error rate was calculated to assess whether the image-based measurements developed for this study could be reliably reproduced. Four months after initial data collection, 10 randomly chosen CBCT's (6 females and 4 males) were evaluated using an intra-class correlation coefficient. The test revealed a significant correlation (0.998) between initial and repeat measurements. It can be concluded that the methods utilized for this study could be reproduced reliably by the same researcher.

Morphometric Assessment of Maximum Height of the Frontal Sinus

The first area of interest was determination of the maximum *height* of the right and left sides of the frontal sinus in each CBCT image. Values were compared between males and females within the three *subadult* age groups:

- Group 1: 6-11
- Group 2: 12-15
- Group 3: 16-20.

The mean *height* measurements between males and females in the three groups were higher in males. Additionally, mean difference in *height* measurements between the right and left sides of the frontal sinus reached a maximum in the Group 3 population without statistical significance ($p>0.05$). Therefore, development of the frontal sinus may not be complete in the superior-inferior dimension by age 20 in the populations studied.

These results are in contrast to three studies performed using CT scans of *adult* populations (Uthman et al, 2010, Hamed et al, 2014, Akhlaghi et al, 2016). In these reports statistically significant differences were found regarding the maximum *height* of the right and left sides of frontal sinuses in males and females.

A 2004 developmental study by Gagliardi et al, indicated that on average, females attained peak velocity in frontal sinus *height* earlier than males. This suggests that further development of the frontal sinus can be anticipated in the superior-inferior dimension in males >20 years old.

Morphometric Assessment of Maximum Width of the Frontal Sinus

A second area of interest in this study was the maximum *width* of the right and left sides of the frontal sinus. Values in this dimension were compared between males and females within

the subadult age groups analyzed. There was a higher mean dimension in the maximum *width* of the *right* frontal sinus within the three subadult age groups examined. The largest difference was observed in Group 3. The maximum *width* of the *left* frontal sinus demonstrated a different pattern; with mean differences higher in the females of Groups 1 and 2 but lower when compared in Group 3. However, differences were not statistically significant ($p>0.05$).

Results are inconsistent with three studies performed using CT scans on *adult* populations (Uthman et al, 2010, Hamed et al, 2014, Akhlaghi et al, 2016). In these reports a statistically significant difference was found among the maximum *width* of right and left frontal sinuses in males and females.

The findings indicate that the development of the frontal sinus may not be complete in the medio-lateral dimension by the age of 20 in the subadult population studied. In other frontal sinus developmental studies it has been concluded that females reach maximum frontal sinus dimensions earlier than males (Ruf et al, 1996, Prossinger et al, 2001, Gagliardi et al, 2004). As the development of the frontal sinus continues a larger difference between males and females could be expected in the medio-lateral dimension due to the delayed nature of male development.

Morphometric Assessment of Maximum Anteroposterior Length of the Frontal Sinus

Determination of the maximum *anteroposterior length (depth)* of the right and left sides of the frontal sinus observed in each CBCT radiograph was also investigated. These values were compared between males and females within the three subadult age groups. All mean values for right and left frontal sinus were found to be greater in males in all groups with statistically significant values in Group 3. The right frontal sinus *depth* was significantly larger in males with a p-value < 0.01 . The left frontal sinus *depth* was also significantly larger in males with a p-value < 0.01 . These results are consistent with those of previous studies using CT scans where

the *depth* of the frontal sinus was significantly larger in males (Uthman et al, 2010, Hamed et al, 2014, Akhlaghi et al, 2016). Other research indicates that females and males attain peak velocity in sinus *depth* at a similar age (Prossinger et al, 2001). This study supports and is consistent with these findings. It can be concluded that the *depth* of the frontal sinus shows sexual dimorphism in subadults age 16-20, and this can be attributed to the developmental sequence of the dimensions of the frontal sinus.

This dimension may prove useful in the field of forensics. Since sexual dimorphism is evident in both right and left frontal sinuses as early as age 16, it may be able to be utilized in the field for sex determination in a post-pubertal subadult.

Overview of Morphometric Measurements

The current study delivers insight into the three dimensional development of the frontal sinus region. Numerous previous projects have evaluated this area using two dimensional radiographic imaging; limiting the capacity to which frontal sinus development can be assessed (Ruf et al, 1996, Prossinger et al, 2001, Gagliardi et al, 2004, Fatu et al, 2005). The only study that has evaluated paranasal sinus development in the third dimension was performed using CT technology. Since this research involved assessment of all cranial sinuses it provided only limited information regarding the frontal sinus area (Spaeth et al, 1996).

The conclusion of most previous research indicates that the frontal sinus reaches its maximum dimensions by 19-20 years old. According to the findings of this project the anteroposterior dimension of the frontal sinus is the only dimension that has completed growth in both males and females by age 20. According to Uthman et al, 2010, Hamed et al, 2014 and Akhlaghi et al, 2016 the frontal sinus should show sexual dimorphism in height and width in adulthood, but this study failed to corroborate that conclusion. In the male population, which

develops at a later age, it would be expected that more growth would be observed in height and width of the frontal sinus beyond the age of 20.

This has implications for understanding the development of males and females in the frontal area and can show that development of the craniofacial complex is still changing well after puberty and into adulthood. It may enable therapists and physicians to interpret pathological processes in this region at any stage of development. It may also have implications for determining cessation of growth, especially in the male population, when orthognathic surgery is a treatment modality.

Because orthognathic surgery is ideal to perform when craniofacial growth is complete, this study could be beneficial in helping to determine when the best time to intervene in cases like these. According to Enlow in 1996, the dimensions of the craniofacial complex complete growth at different times in development. The transverse dimension finishes growing first, followed by the anteroposterior dimension and then finally the vertical dimension. This study demonstrates that the frontal sinus may not show this same pattern, with the anteroposterior dimension finishing development first.

Assessment of the Nasofrontal Angle

Statistically significant differences were found between two of the age groups in regards to the nasofrontal angle [Group 2 ($p < 0.05$) and Group 3 ($p < 0.01$)]. Findings for Group 1 were of interest due to the close proximity of values between males and females. Males tended to exhibit larger, more robust features that can be seen throughout the cranial and post-cranial skeleton. Females, however, tended to retain more pedomorphic traits throughout development (Krishan et al, 2016).

As a child develops the contours of the frontal bone increasingly change with age. The nasofrontal angle is obtuse in the pediatric population. Through the pubertal and post-pubertal growth phases both sexes experience a decrease in the nasofrontal angle. Nasofrontal angles in males become increasingly acute while females retain more of the obtuse pedomorphic form.

Lee et al in 2010 studied an adult population with average nasofrontal angles of 119.9° and 133.5° for males and females respectively. The current project found values of 124.4° for males and 134.9° for females in Group 3. These results indicate a larger discrepancy between male values than those found by Lee et al. This suggests that this region may undergo more development in males beyond the age of 20.

The findings of this study also demonstrate that sexual dimorphism can be observed as early as 12 years of age for this region. This may have positive implications for the forensic anthropologist attempting to determine the sex of an unknown subadult individual. In addition to aiding in sex allocation this feature may help to determine the age of an unknown victim. An obtuse nasofrontal angle measuring significantly above the female norm may indicate that the individual is younger than expected and has not undergone major development in the supraorbital region.

The nasofrontal angle is of concern when looking at gender differences for purposes of feminizing male foreheads as a component of gender re-assignment surgery (Lee et al, 2010). One of the procedures performed as a component of gender re-assignment surgery is frontal cranioplasty to ensure that nasofrontal angle appears more obtuse. Measurements taken in this study contribute to an understanding of the age and sex related changes of this region and may help to guide frontal cranioplasty procedures in the future. Surgeons may utilize standard measurements of the nasofrontal angle for males and females to facilitate an esthetic outcome. If

gender re-assignment surgery is being considered for a 20 year old male, it may be beneficial to wait until full development of this region is completed to perform a frontal cranioplasty.

Assessment of Anatomic Location of the Frontal Sinus

No previous studies have evaluated the location of the frontal sinus in relation to an NA vertical reference line to determine its prominence in the sagittal plane. This measurement was evaluated in the current investigation to determine if development of the male supraorbital region is more robust due to the pneumatization of the frontal sinus (Hypothesis #5). The vertical reference line NA is a common landmark in orthodontics. Its proximity to the supraorbital and frontal sinuses was a determinant for choosing this measurement in this study. A correlation analysis was completed on the three subadult age groups to compare sex assignment with the relationship of the frontal sinus to the NA line. There were no significant findings in this regard. Since this was the first time that this relationship was studied no comparisons could be made to previous research.

The more robust supraorbital region in males cannot be related to the anteroposterior pneumatization of the frontal sinus. No sexual dimorphism is evident in the anterior border of the frontal sinus. The current research indicates that additional studies should be performed utilizing different anatomical landmarks to assess sexual dimorphism and supraorbital age variations. A future study measuring the distance of the frontal sinus to the NA line may provide more useful information regarding these issues.

Overview of Bilateral and Unilateral Agenesis of the Frontal Sinus

Bilateral frontal sinus agenesis varies among different populations (Danesh-Sani et al, 2011). It has been reported that this can range from 0.73% in a Turkish population to 43% in Canadian Eskimos (Danesh-Sani et al, 2011). In the current study, incidence of bilateral frontal

sinus agenesis was 9.3%. This figure falls toward the lower region of the documented range described previously. This difference can be attributed to population variances between the two investigations. Additional research has documented that individuals living in colder climates have a higher incidence of agenesis of the frontal sinus. The reason is still under investigation but it can be speculated that conservation of heat and insulation are contributory factors for frontal sinus agenesis in these environments (Marquez et al, 2016 {page 33}, Koertvelyessy, 1972).

Southern Nevada, located within the Mojave Desert, is considered one of the hottest regions in the United States. Average annual temperature is 69.3°F with average summer temperatures well above 100°F and occasionally exceeding 120°F (www.usclimatedata.com). This extreme heat may be the environmental etiology leading to a lower incidence of frontal sinus agenesis observed in this study than in those reports regarding populations from colder climates. Without a need for insulation and conservation of heat in the Nevada desert; this may be a developmental advantage to coping with the hot, dry climate of this region.

The results of the study also determined that females are twice as likely to have bilateral agenesis of the frontal sinus. This is consistent with previous investigations. Although the reasons for male and female variation in frontal sinus agenesis are not well documented; they could be attributed to the following factors:

- Craniofacial development
- Growth hormone levels
- Thickness of the frontal bone (Danesh-Sani et al, 2011).

Further research is warranted to determine if there are additional contributory biological features that influence gender differences in frontal sinus agenesis.

As well as bilateral frontal sinus agenesis, unilateral frontal sinus agenesis can also occur. Either the right or the left side of the sinus can be missing and this varies among populations. Unilateral frontal sinus agenesis has been reported in 0.8%-7.4% of several populations (Danesh-Sani et al, 2011). In the current report a prevalence of 9.5% was found. This is higher than the range found in previous investigations of the issue.

Methods employed to measure frontal sinus agenesis varied among previous studies because each evaluated different landmarks. In the current analysis the inferior border of the frontal sinus, which is also the superior border of the orbit, may have contributed to a higher occurrence of agenesis in both sexes. The frontal sinus was considered radiographically absent if it was not evident above the superior orbital rim. Other studies, which evaluated different borders regarding frontal sinus agenesis led to the variation described.

Patterns of absence of the frontal sinus are consistent with results of other studies. It was concluded that males and females had the same incidence of unilateral agenesis with N=26 and N=27 respectively. Females had a higher incidence of right sinus agenesis whereas males had little difference between right and left side agenesis. Other research reporting on unilateral frontal sinus agenesis does not indicate frequency of this condition among males and females making it difficult to compare the current outcomes with these earlier reports.

The importance of knowing frequencies of frontal sinus agenesis permits one to understand why these variations occur. If patterns can be tracked among populations a potential cause can be identified. Many theories have been proposed but no definitive conclusions have been made to date. By performing longitudinal studies of different subadult populations the roles of *nurture* (environment) and *nature* (heredity) regarding age and sex determination from frontal sinus analysis may become more evident.

Individuals raised in warmer climates may exhibit fewer cases of frontal sinus agenesis. Since frontal sinus agenesis is sexual dimorphic as well, there could potentially be related sexual dimorphism in development of the other paranasal sinuses. Another important practical consideration regarding frontal sinus agenesis is related to pre-operative planning for frontal craniofacial surgeries. An understanding of frontal sinus agenesis and its related sexual dimorphism may help the surgeon to determine the form of frontal craniofacial surgery best suited for a patient and allow for more aggressive procedures with resultant increased esthetic outcomes.

In some instances the frontal sinus has been thought of as a “*crumple zone*” for patients with head trauma (Yu et al, 2014). The size of the frontal sinus can be related to the extent of brain damage; with individuals having larger frontal sinuses suffering fewer brain contusions than those with smaller ones (Yu et al, 2014). Knowledge of populations with increased incidences of frontal sinus agenesis is important since these individuals may be more prone to brain damage following trauma to the frontal region. Conversely, populations with fewer incidences of frontal sinus agenesis may be less prone to brain injuries following trauma to the frontal craniofacial area.

The differences between male and female frontal sinus agenesis may be attributed to an evolutionary difference in behavior. Historically, males (hunters) are more commonly placed in harm’s way to provide for the females (gatherers) and children of the troupe. It is plausible that from an evolutionary standpoint, females may have a higher incidence of frontal sinus agenesis as a result of being sheltered from cranial trauma associated with hunting. In the opinion of the author, males may have been naturally selected through evolutionary processes to develop the

frontal sinus, thus protecting the brain when put in dangerous situations which could result in cranial trauma.

Discriminant Function Analysis

Discriminant function analysis is the most widely utilized statistical test employed to determine the sex of evaluated skeletal material (Krishan et al, 2016). Thus, this statistical approach was used in the current study to compare sex variables among the three different assessed subadult age groups with the following results:

- Group 1 (7-11 years old): 64.8% correct sex allocation
- Group 2 (12-15 years old): 57.8% correct sex allocation
- Group 3 (16-20 years old): 79.2% correct sex allocation.

Comparing these values with previous related work revealed that four of seven studies of sex allocation based on frontal sinus measurements used a discriminant function analysis for correct assessment (Uthman et al, 2010, Kiran et al, 2014, Michel et al, 2014 & Akhlaghi et al, 2016). Three used a logistic regression analysis. Correct sex allocation among studies using discriminant function analysis ranged from 52.3%-85.9% (Uthman et al, 2010, Kiran et al, 2014, Michel et al, 2014 & Akhlaghi et al, 2016). This wide range of values can be attributed to different measuring techniques and different sample sizes used in each investigation.

The value of 85.9% found in the work of Uthman et al in 2014 included other measurements of the skull than just the frontal sinus. By combining frontal sinus measurements with other skull measurements the accuracy of gender determination was significantly improved. In the current study correct sex allocation in Group 3 was 79.2% using discriminant function analysis. This value is significantly higher than in other reports utilizing discriminant function analysis to assess frontal sinus measurements regarding sex determination. This difference can

be attributed to the evaluation of the nasofrontal angle in establishing an accurate skeletal sex allocation in this study. Other reports have not calculated the nasofrontal angle in this regard.

Studies using logistic regression analysis have correctly evaluated sex allocation in a range from 55.2%-79.7% (Goyal et al, 2012, Hamed et al, 2014, Verma et al, 2014 & Belaldavar et al, 2014). This spread is similar to results that employed discriminant function analysis. However, it is difficult to compare the results of previous works with those of the current study due to lack of compatibility between the two statistical tests.

Groups 1 and 2 in the current study have a lower precision for sex determination due to the lack of sexual dimorphism within the frontal sinus region in these subadult age groups. According to Novotný et al, 1993, correct sex allocation above 60% is considered very reliable. With the current value for correct sex allocation of 79.2% in Group 3 it can be concluded that the systems in place for this study are very reliable for post-adolescent subadults.

However, since this value falls below the minimum threshold of 95% accuracy in forensic practice (Krishan et al, 2016); its use in forensics may be limited unless combined with other methods (e.g.: FSS and volumetric measurements). The FSS classification system developed by Yoshino et al in 1987 and volumetric measurements studied by Gianguido in 2015 may increase the accuracy of discriminant function analysis to threshold levels and be more useful in the field of forensic science.

Limitations and Future Studies

A principal limitation to this study was the extensive difference regarding frontal sinus outline shapes among individuals. These variations in shape proved difficult to measure consistently due to irregular lobulations and asymmetric intersinus septa. In some instances it was challenging to localize the intersinus septum and differentiate its outline pattern from

associated bifurcations and intersinus air cells. Thus, the importance of determining an intraobserver error rate became obvious as a means of establishing the potential for tracing error associated with the numerous differences observed among the radiographs of the 216 subjects in the study.

Many of the anonymized CBCT radiographs originally considered for inclusion in the study had to be rejected because they presented a limited field of view. This became another limitation to the project because, in these limited field of view radiographs, the superior border of the frontal sinus was not captured rendering them unusable for the study. The sample size for the frontal sinus measurements would have been larger if a full field of view was captured in every CBCT radiograph.

The current sample size in the study was larger in Group 2 (12-15 years old) reflecting the fact that this is a popular age group seeking orthodontic care. Groups 1 and 3 were underrepresented which is consistent with the nature of the age of patient populations seeking orthodontic treatment.

It is also acknowledged that the study lacked a focus on a specific ethnic representation. The anonymized orthodontic clinic CBCT radiographs were pooled from the general orthodontic clinic population. The latter group reflected the demographics of those residing in urban Southern Nevada. Therefore, individuals from numerous ethnic and cultural backgrounds are represented in this study. Morphometric measurements of the frontal sinus can vary among these groups and the study is not demonstrative of calculations from a single ethnic population (e.g. African heritage individuals or Hispanics). Future studies could be dedicated to investigation of sexual dimorphism of the frontal sinus within specific ethnic populations, especially Hispanics and those of African heritage.

Volumetric assessment of craniofacial structures is becoming increasingly available due to the acceptance of 3D radiology (e.g.: CBCT technology). Currently, Invivo 5.3 software is capable of automatically calculating the nasopharyngeal airway volume (Chen et al, 2016). Prospective research could apply the results of the current study regarding subadult populations, to create a new algorithm for automatic assessment of frontal sinus volume.

Excluding Group 2 results related to the nasofrontal angle most statistically significant values in this project were found in Group 3. This is most likely associated with the onset of puberty occurring in Group 2 and sexually dimorphic characteristics of the frontal sinus not evident in this subpopulation. Regarding Group 3, height and width of the frontal sinus were not significantly sexually dimorphic although AP values were. This is most likely related to the fact that this study restricted the subadult age groups to periods of growth before sexual dimorphism was possible to observe in height and width dimensions. Therefore, future studies regarding frontal sinus sexual dimorphism should include subadults and adults to show this characteristic of the development of the frontal sinus into the third decade of life.

A final limitation to this study was the exclusive use of morphometric variables to determine sexual dimorphism and age. It has been proven previously that the morphology of the frontal sinus can also be a key factor in forensic identification (Quatrehomme et al, 1996). By combining morphometric measurements with morphologic classification systems utilizing lobulations and scalloping of the frontal sinus, potential use of accurate frontal sinus analysis in forensic identification cases requiring subadult age and sex determination may be improved.

Conclusions

This study used the improved imaging capability of CBCT technology to evaluate the development of the frontal sinus in a subadult orthodontic population derived from the general population of urban Southern Nevada. The potential for sex determination in this population and its application to forensic science issues was also evaluated. Results indicated that the following frontal sinus parameters were statistically significant among the three subgroups evaluated in the study:

- Group 2 (12-15 years old)
 - o Nasofrontal angle showed sexual dimorphism
- Group 3 (16-20 years old)
 - o Nasofrontal angle showed sexual dimorphism
 - o Maximum anteroposterior length of right and left sides of the frontal sinus.

The prevalence of bilateral agenesis of the frontal sinus was 9.3%. Females were twice as likely to experience this finding. However, unilateral agenesis of the frontal sinus occurred equally in males and females at 9.5%. Females demonstrated right frontal sinus agenesis more frequently although males experienced equal frequency of right and left frontal sinus agenesis. A discriminant function analysis was a good fit for only Group 3 with a correct sex allocation of 79.2%.

These findings provide insight into the development of the frontal sinus and surrounding supraorbital areas. The frontal sinus region is difficult to study because of the extreme variations of its size and shape among individuals. The conclusions drawn from this study more definitively

define the course of frontal sinus development in a subadult population. Additionally, they have potential bearing on orthognathic and frontal cranioplastic surgical work up and evaluation.

The sexual dimorphic characteristics of the frontal sinus, especially in the older population of subadults (Group 3), may have implications in the field of forensic anthropology and aid in forensic identification of unknowns. This study could also have implications with regards to head trauma and the link between frontal sinus agenesis and the extent of brain injuries. The findings of this research are extensive and can contribute to the disciplines of anthropology, forensic science, head and neck development and medical and dental specialties.

Appendix: UNLV Institutional Review Board Approval



**UNLV Biomedical IRB - Administrative Review
Notice of Excluded Activity**

DATE: December 18, 2015
TO: James Mah, DDS, MSC, DMSC
FROM: UNLV Biomedical IRB
PROTOCOL TITLE: [790432-1] Sexual Determination from Frontal Sinus Analysis Using Archival Radiographic Records
SUBMISSION TYPE: New Project
ACTION: EXCLUDED - NOT HUMAN SUBJECTS RESEARCH
REVIEW DATE: December 18, 2015
REVIEW TYPE: Administrative Review

Thank you for your submission of New Project materials for this protocol. This memorandum is notification that the protocol referenced above has been reviewed as indicated in Federal regulatory statutes 45CFR46.

The UNLV Biomedical IRB has determined this protocol does not meet the definition of human subjects research under the purview of the IRB according to federal regulations. It is not in need of further review or approval by the IRB.

We will retain a copy of this correspondence with our records.

Any changes to the excluded activity may cause this protocol to require a different level of IRB review. Should any changes need to be made, please submit a Modification Form.

If you have questions, please contact the Office of Research Integrity - Human Subjects at IRB@unlv.edu or call 702-895-2794. Please include your protocol title and IRBNet ID in all correspondence.

Office of Research Integrity - Human Subjects
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