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Assessing Age-Related Ossification of the Petro-Occipital Fissure: Laying the Foundation for Understanding the Clinicopathologies of the Cranial Base

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Abstract

The petro-occipital fissure (POF) lies within a critical interface of cranial growth and development in the posterior cranial fossa. The relationships between skeletal and soft tissues make this region especially important for examining biomechanical and basic biologic forces that may mold the cranial base and contribute to significant clinicopathologies associated with the structures located near the POF. Therefore, this study investigates the POF in adults in both preserved human cadavers and dried crania in order to determine if developmental changes can be observed and, if so, their value in age assessment as a model system for describing normal morphogenesis of the POF. This study demonstrates that tissue within the POF undergoes characteristic changes in ossification with age, the onset of which is considerably later than that of other synchondroses of the cranial base. Statistically, there is a moderate to strong correlation between age and stage of ossification within the POF. Further, male crania were observed to reach greater degrees of ossification at a younger age than female crania and that individual asymmetry in ossification of the tissue within the POF was not uncommon. An understanding of the basic temporal biological processes of the POF may yield insight into the development of clinicopathologies in this region of the cranial base.

Keywords

human anatomy; cranial base; petro-occipital fissure; petro-occipital synchondrosis; petro-occipital complex; hearing loss; myxoid chondrosarcoma

The petro-occipital fissure (POF) lies within a critical interface of cranial growth and development in the posterior cranial fossa. The relationships between skeletal and soft tissues make this region especially important for examining biomechanical and basic biologic forces that may mold the cranial base and contribute to significant clinicopathologies associated with the structures located within the POF. Although of importance during regional growth and development, little attention has been focused on assessing the normal age-related changes to this complex of hard and soft tissues. Therefore, this study investigates the POF in adults in

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both preserved human cadavers and dried crania in order to determine if developmental changes can be observed and, if so, their value in age assessment as a model system for describing normal morphogenesis of the POF.

Background

Anatomically, the skull base or chondrocranium separates the neurocranium from the viscerocranium and serves as an important interface between the soft and hard tissue of the head and neck (Moss and Greenberg, 1955; Laitman, 1978; Laitman and Reidenberg, 1988; Reidenberg and Laitman, 1991). Phylogenetically, the skull base is one of the oldest skeletal components, sharing features with the skull bases of earlier vertebrate progenitors. Developmentally, the skull base is relatively stable as compared to the rapidly expanding face and calvaria due to the transit of major blood vessels, nerves, and spinal cord into the head (Enlow and Hunter, 1968; Hoyte, 1971).

The POF is clinically important as it is often associated with skeletal myxoid chondrosarcomas of the skull base. While these tumors may be found in various soft tissues throughout the body, 66% of cranial base chondrosarcomas (CS tumors) occur within the POF (Sandberg and Bridge, 2003). CS tumors of the POF can be painless and locally invasive tumors that present particular problems to the patient and treating clinician due to the complex anatomical architecture of this region of the cranial base (Prades et al., 1994). The contiguous petrous apex of the temporal bone may become involved if POF CS tumors become invasive. Histologically, CS tumors lie between the benign chondroma and malignant sarcomas and its prognosis can be correlated with histologic grading (Kveton et al., 1986). Of further clinical interest, our observations suggest that the ossification of the POF may be a factor in a number of clinicopathologies such as age-related conductive hearing loss, malocclusion, upper respiratory dysfunction, and apnea. An understanding of the age-related morphological changes to the POF may further our understanding of basic biological processes underlying important clinicopathologies of the head and neck.

The most comprehensive data concerning the age-related changes to the cranial base come from osteological studies in classical physical anthropology, anatomy, forensic anthropology, and radiology (Melsen, 1969; Redfield, 1970; Thilander and Ingervall, 1973; Buikstra and Gordon, 1980; Giles et al., 1981; Delinger and Le Minor, 1993; Okamoto et al., 1996; Hershkovitz et al., 1997; Galera et al., 1998; Baccino et al., 1999; Kahana et al., 2003). Previous work by us and others has demonstrated the importance of changes within the cranial base, both of soft tissue and the underlying hard tissue, in the growth and development of the human upper respiratory system (Crelin, 1973; Wolfson and Laitman, 1990; Reidenberg and Laitman, 1991). The critical interrelatedness between the soft and hard tissues of the upper respiratory system is evident in studies demonstrating severe airway obstruction in patients with syndromic craniosynostosis and premature ossification of the synchondroses of the cranial base (Sirotnak et al., 1995; Lo and Chen, 1999).

Conflicts in Terminology

The topic of this study has been defined variously in the literature as the petro-occipital fissure, the petro-occipital synchondrosis, and the petro-occipital complex (Table 1). Regardless of the nomenclature used, the anatomical position of the structure is described as lying between the petrous portion of the temporal bone and the basilar portion of the occipital bone (Gray, 1858; His, 1895; Hartman and Strauss, 1933; Spalteholz, 1935; Silver et al., 1983; Madeline and Elster, 1995; Singh et al., 1997). The nomenclature used in the literature to describe this region has been largely based on structurally descriptive terminology and not on functional or developmental processes. Nomenclatural definitions may arise from the observed physical state of the structure (i.e., open or ossified), and whether the region is viewed in dried bones,

cadaveric material, or radiographic images, thereby giving a different perspective to the anatomical structures. While the most widespread terminology for this region is petro-occipital fissure, Oettking (1957: p. 31) points out that “the terminology regarding cranial fissures is not entirely unequivocal, since certain authors prefer suture for fissure, and vice versa.”

Classical studies in human anatomy, the clinical surgical literature, and most modern radiological research use the term “petro-occipital fissure” when describing the anatomy of this region of the cranial base (Gray, 1858; His, 1895; Oettking, 1957; Silver et al., 1983; Prades et al., 1994). The use of the petro-occipital fissure nomenclature is a descriptive term of a physical space on the cranial base. For example, Oettking (1957) describes the region as a cleft or groove as it might be observed in a dry skull, and as filled with organic matter (fibrous or cartilaginous) as it appears in a cadaveric specimen. Similarly, the surgical literature describes the region as a physical space important for transcranial approaches to the cranial base during surgery (Mazzoni et al., 1997; Lee et al., 2001). Radiologists, when imaging this region of the cranial base, tend to define the hard tissue boundaries of the fissure much as one would in a dry skull (Weber et al., 1995).

The use of the term petro-occipital synchondrosis is a much less common description of this region of the cranial base. For example, Kreiborg and Bork (1982) described the region as one of many prematurely ossified synchondroses of the chondrocranium in their study of Crouzan syndrome in dry human skulls. Similarly describing ossified sutures, Madeline and Elster (1995) used CT imaging to describe ossification patterns of the human chondrocranium from birth through the early teens, noting that the petro-occipital synchondrosis is largely open in teens. It appears then that the use of petro-occipital synchondrosis is a retrospective application of the term to all synostotic structures of the chondrocranium that are observed or assumed to ossify. The lack of widespread usage of the term “synchondrosis” to describe this region may have to do with the specific mechanism of ossification that is attached to this nomenclature (i.e., ossification from a cartilaginous precursor).

The more recent use of the term “petro-occipital complex” is the most general nomenclature used to define this region of the cranial base (Singh et al., 1997). In their study of the relationship between alterations of the cranial base and malocclusions, Singh et al. (1997) treat the complex interplay between soft and hard tissues in this region of the cranial base systemically, acknowledging the potential for such interactions to influence regional morphology.

We have opted in this study to use the term “petro-occipital fissure” for the following reasons. First, it is the most commonly used term in the literature. Second, it most precisely defines a physical hard tissue landmark on the skull while acknowledging the organic tissue component within the fissure during life. While we agree that systematic terminology such as “petro-occipital complex” accurately reflects the important morphological relationships that exist between the cranial base, the upper respiratory system, and the rest of the head and neck, the term lacks the precision necessary to describe specifically the anatomical landmark we are studying in this article. The use of the term “synchondrosis,” a temporary cartilaginous joint that often ossifies in adulthood, is not entirely accurate. As we will show below, the POF is not purely cartilaginous.

MATERIALS AND METHODS

Phase 1

Cadaveric material—Fifteen human cadavers from the University of New Mexico School of Medicine were dissected in order to visualize the soft tissue structures of the cranial base contiguous with the POF. Removal of the crania from the thorax at the level of the axis (C2) was effected in order to facilitate radiographic study of the POF. Human cadavers used in this

study were preserved in accordance with internal protocols at the University of New Mexico School of Medicine; each human cadaver was infused with 9–12 gallons of preservation solution (16 oz of a 70% ethyl-alcohol and 30% formaldehyde solution in one gallon of water).

Radiographs—Plain-film radiographs of the cadaveric skull were taken in the submentovertex position with a film and screen combination of 250 (kVp 70 and mA 100). The central ray was directed perpendicular to the film and the bisected cranial were tilted back so that the orbital-meatal line was parallel to the film. All crania had the mandibles removed to facilitate radiographic analysis. Radiographs were analyzed for the presence or absence of the POF by a radiologist in the Department of Radiology, University of New Mexico School of Medicine.

Histology—Histological samples were obtained from human cadaveric material at the University of New Mexico School of Medicine after dissection and localization of the POF. An approximately 2 cm³ section of tissue was isolated and removed from the POF equidistant between foramen lacerum and jugular foramen. Decalcification of the fixed tissue was performed in a 5% formic acid solution as described by Retzlaff and Mitchel (1987). The excised tissue was stored in a 70% ethyl-alcohol solution prior to decalcification. Decalcification effectiveness was tested for the presence of calcium by the use of white 5% ammonium oxalate in 5 mL formic acid solution. The process of decalcification was determined to be complete when precipitation of calcium was no longer formed. The sample was then washed in running water and sectioned with a rotary microtome with a blade tilt between 45 and 50°. Hematoxylin and eosin (H&E) and Masson's trichrome stains were used to illustrate the cellular structures.

Phase 2

Skeletal analysis—Dry skulls for our observational analysis were identified by the New Mexico Office of the Medical Investigator (OMI) computer database as being contemporary human skeletal remains with a known age at the time of death, sex, race, and ethnicity. All skulls contained in the database were identified by a certified forensic anthropologist as part of a medicolegal investigation. All skulls in our sample were chosen without regard to sex, age, race, or ethnicity (n = 73). All crania used in this study are physically archived in the Maxwell Museum of Anthropology Skeletal Collection at the University of New Mexico in Albuquerque, New Mexico.

Statistical data—Statistics were compiled using SPSS 12.0. The sample (n = 73) comprised males and females from 14 to 91 years of age at the time of death. Cases were staged by the individual examiner at the POF midpoint, i.e., between foramen lacerum and jugular foramen, and were identified as either anatomical right or anatomical left. Testing of the descriptive system for accuracy and for interobserver error was completed on contemporary crania of known age, sex, race, and ethnicity. Crania were chosen randomly and without replacement. All crania were marked with an organizational number randomly generated for this study. Description of the stage of POF ossification was defined numerically from least ossified (stage 1) to complete fissure ossification (stage 6) in whole number increments. Linear regression analysis and correlation between the chronological age of the subject and degree of POF ossification were performed.

RESULTS

Phase 1

Morphological changes to the POF were demonstrated in human cadaveric material using plain-film radiographs and histological analysis. Plain-film radiographic analysis of the POF

in cadaveric specimens defined the presence or absence of POF ossification (e.g., 24-year-old vs. 82-year-old). The presence of both hard and soft tissue within the POF made it difficult to fix the anatomical limits of the fissure precisely and the relative degree of POF ossification using plain-film radiographs (Fig. 1).

Decalcified samples of tissue obtained from the POF of cadaveric material were used to analyze the soft tissue within the POF. Histological analysis of decalcified cadaveric tissue taken from the POF showed characteristic traits of dense connective tissue (Fig. 2). The destructive nature of the tissue collection procedure and the low numbers of human cadavers available to us for this study precluded obtaining a statistically large enough sample to determine whether age assessment of POF ossification could be done using histological analysis alone.

Phase 2

This study developed a descriptive staging system outlining the completeness of POF ossification in a large sample of dried human crania. This descriptive staging system demonstrated a statistically significant age-related and progressive POF ossification in human crania. Statistical correlations using the Pearson product-moment correlation coefficient (r), coefficient of determination (r^2), and the ϵ and ϵ^2 measures of association were determined using age as the dependent variable and the stage descriptive measure of POF ossification as the independent variable (Table 2). The correlation between age and stage of POF ossification in a mixed-gender sample range from 0.526 to 0.807 (significant at the 0.01 level). These calculations demonstrate a strong positive correlation between age and stage of POF ossification for one observer (POSTRTE, POSTLTE) and a moderate positive correlation for another observer (POSTRLP, POSTLLP; Fig. 3).

These data showed significant differences when sorted by sex. Male crania were observed to reach greater degrees of fissure ossification at a younger age than female crania in our sample. Male correlations ranged from 0.413 to 0.737, and female correlations ranged from 0.706 to 0.938 (significant at the 0.01 level; Table 3). While all of the recited values are statistically significant, it is worth noting that males represented 71% of the sample ($n = 52$) and females 29% of the sample ($n = 21$), and that asymmetry in POF ossification was noted between male and female crania. Degree of POF ossification could be categorized into general stages from stage 1 (least ossified) through stage 6 (complete ossification of the POF).

Stage 1—The medial and lateral walls of the POF are in close approximation but there is no contact at any point along the length of the fissure. The bony surface along the medial and lateral walls is described as having a textured appearance with high relief due to numerous projections extending into the fissure. The depth of the fissure appears shallow ectocranially to endocranially (Fig. 4a).

Stage 2—The medial and lateral walls of the fissure are in close approximation and block a clear view into the endocranium. There is a marked reduction in the high-relief appearance of the fissure walls. The overall depth of the fissure is increased due to bony deposition (Fig. 4b).

Stage 3—Bony spicules extend across the fissure, giving an appearance of bridging between the lateral and medial walls of the fissure. Note that this bridging trait is more pronounced in males than females. Further, males tend to exhibit greater bony deposition ectocranially to endocranially (Fig. 4c).

Stage 4—The medial and lateral walls of the fissure are abutting, often with large bony protrusions extending up through the fissure space (Fig. 4d).

Stage 5—The medial and lateral walls of the fissure show a nearly complete ossification (Fig. 4e).

Stage 6—The medial and lateral walls of the fissure are completely ossified. There is little gross difference between the POF and the surrounding bony landscape (Fig. 4f). The POF, much like fully ossified cranial sutures, is obliterated.

DISCUSSION

Mechanisms of Ossification

Mechanical interactions between the bony skull base and the muscles, ligaments, and dense connective tissue of the upper respiratory tract are observed to occur within the POF. Accordingly, morphological changes that occur within this complex of hard and soft tissue may be related to the interaction of basic biomechanical and molecular forces during growth. An understanding of the normal morphological processes within the POF may provide important clues to the development of clinicopathologies. Whereas much attention has been focused on the age-related changes that occur in the hard tissue of the cranial base during early growth and development and the soft tissue of the upper respiratory system through early adulthood, the POF itself has not been extensively examined for osseous changes from early adulthood through senescence. As our concern was with elucidating the normal morphological changes to the POF that might portend clinicopathologies of this region in adults, this study undertook an examination of the potential age-related ossification of the POF in adult humans.

Although the precise molecular mechanisms for POF ossification are not completely understood, there is strong evidence in the literature regarding the ossification of cranial sutures via molecular signaling from the dura (Levine et al., 1998; Rice et al., 2003; Ogle et al., 2004). In cranial sutures, the dura mater is believed to regulate suture fusion through multiple pathways, including signaling by transforming growth factor β_1 and fibroblast growth factor 2 (FGF2) (Opperman et al., 1997; Greenwald, 2000). Identifying the molecular pathways involved in suture ossification has proven an important step in identifying the genesis of the human Apert and Crouzon syndromes, a syndromic craniosynostoses involving Fgfr2 gain-of-function mutations (Warren, 2001).

The POF shares structural similarities to cranial sutures in so far as both are comprised of fibrous connective tissue that ossifies during adulthood. Accordingly, these structural similarities and the intimate connection between the underlying dura and the POF may indicate a similar molecular mechanism for its ossification. While it is clear that the POF is prematurely ossified in Crouzon syndrome from Fgfr-mediated craniosynostoses via the inappropriate downregulation of noggin expression, it is currently unclear why the POF remains relatively unossified in the nonpathological state until late in adulthood (Warren, 2001). Attempts to discern whether biomechanical forces in fact play a role in cranial base ossification belong to an area of research that is both active and contentious (Levine et al., 1998; Ogle et al., 2004).

Most of the data currently available regarding suture growth and fusion in relation to major mechanical loads from soft tissue-hard tissue interactions come from studies of the cranial vault sutures (Moss, 1957; Bradley et al., 1996; Herring and Teng, 2000; Opperman, 2000; Borke et al., 2003). Specifically, Opperman (2000) and Herring and Teng (2000) found that as growth sites, cranial vault sutures respond readily to epigenetic factors such as static loads from brain expansion and dynamic loads from masticatory strain. These data suggest a possible role for mechanical loads from the soft tissue of the upper respiratory tract in directing POF ossification and shaping cranial base morphology. We believe that basic biomechanical factors may affect ossification of the POF by altering the cellular environment and gene expression

possibly via Fgfr-mediated pathways. Further research will determine whether this is in fact the case.

Statistical Analysis

The statistical data demonstrate a correlation between age and our stage descriptive measure of ossification of the POF. When our skeletal sample is evaluated by sex, differences in POF ossification between the male and female subpopulations were observed. Specifically, the correlation between age and stage of POF ossification was stronger for the female sample than for the male sample. Of particular note is that the very oldest males classified as stage 6 exhibited an almost complete obliteration of the POF, while the stage 6 female crania that had a fully ossified POF were not obliterated. In other words, none of the female crania reached the same ultimate degree of POF ossification at stage 6 as the male crania. In addition, females described as having stage 5 ossification of the POF were chronologically older than corresponding stage 5 males.

The difference in assignment of stage to a particular POF between observers is the measure of interobserver error. While all of our observations were shown to be statistically significant, there are differences between observers. This type of error is frequently observed in subjective descriptive systems and may be related to experience levels of the observers regarding the staging system or the amount of experience each observer has handling the material being studied. Indeed, the observers in this study had very different relative levels of experience handling skeletal material. Further analysis would have to be undertaken to confirm that this is the cause of the interobserver error in this study.

Even for the less-skilled observer, the statistical relationship between age and stage of ossification is clear. Particularly noteworthy is that while 40% of the dried human skulls were derived from people over the age of 60, they included only 3 out of 27 of the gradings less than or equal to 3 (Fig. 5).

Implications for Understanding Clinicopathologies of Head and Neck

The cranial base is a critical anatomical juncture between soft and hard tissues responsible for vocalization, hearing, breathing, and deglutition and is the major transit point for critical nerves and blood vessels into and out of the head. This study has demonstrated an age-related pattern of ossification of the POF. We believe that this age-related ossification may contribute to age-related conductive hearing loss in adult humans by altering the bony landscape surrounding the POF and the associated cochlear aqueducts. In addition, 66% of CS tumors of the cranial base are located within the POF and an understanding of the morphological changes to this region may provide important insights into the underlying biological mechanisms of this type of tumor.

Forces are transmitted through the vertebral column to the occipital condyles and occipital bone. The connective tissue within the POF may act to dampen the transmission of these forces from the more lateral structures of the basicranium, thereby acting as a protective device of the cochlear apparatus in the young. We posit that the dampening affect of the soft tissue is lost when the POF ossifies, and the resulting undampened mechanical forces that impact the inner and middle ear and may be a factor in age-related hearing loss.

A recent longitudinal study of the incidence of age-related hearing loss demonstrated that 21% of adults aged 48–59 and 90% of adults over 80 had hearing loss (Cruikshanks et al., 2003). In addition, regardless of age or occupation, data seem to indicate that men are more likely than women to develop hearing loss (Monocodocicki et al., 1985; Reis, 1994; Cruikshanks et al., 1998, 2003). Conductive hearing loss (CHL), described in humans, is a disorder

characterized by a loss of sensitivity to sound due to nonair conductive hearing pathways. While often due to mechanical blockage of the middle ear, conductive hearing loss may also be associated with changes to the bones of the inner ear, mechanical vibration, obstruction of the cochlear aqueducts, and with the use of some drugs (Manninen, 1983). This type of hearing loss is in contrast to deficits to the sensory elements of the cochlea and changes to the neural components of hearing (Jimenez et al., 1999). Of particular relevance to POF ossification is the studies in both humans and animals that have demonstrated a conductive hearing loss due to the effect of increasing mechanical vibration on the loss of high-frequency sensitivity to sound (Manninen, 1983). It is noteworthy that the POF is comprised of dense connective tissue and cartilage that physically isolates the petrous portion of the temporal bone from the basicranium. Complete POF ossification is primarily observed only in humans older than 60 years of age. We believe that ossification of the POF and the resultant alteration of the bony landscape of the cranial base may alter CSF flow around the cochlear aqueduct and reduce vibrational dampening of the petrous portion of the temporal bone, thereby exacerbating high-frequency hearing loss in older adults.

Our examination of the POF has identified an age-related ossification that is temporally unlike other ossifying regions of the cranial base. While other studies involving the cranial dura in suture ossification strongly implicate Fgfr-mediated ossification pathways, theories of a potential role for biomechanical forces transmitted to the dura via the soft tissue of the upper respiratory system should be revisited. A case for an interrelated biomechanical and biochemical role in POF ossification can be made in light of experimental data demonstrating that extrinsic tension applied to a dura/suture complex in vivo results in FGF-2 release, membrane permeability change, and intracellular Ca^{++} increase in immature cranial sutures (Yu et al., 2001). Given the hard tissue-soft tissue interface within the POF, we believe that both biomechanical and biochemical forces influence the mechanism and timing of POF ossification in adult humans. Further studies will have to be undertaken to determine whether perturbations in either biomechanical or biochemical pathways underlie the significant clinicopathologies of the POF. It is hoped that this study of the POF has laid a template on which a more complete understanding of normal postnatal development, and, in turn, of the development of human disease involving this region of the upper respiratory tract, can be built. Indeed, the melding of molecular developmental pathways with an understanding of basic biomechanical studies will allow further insight into the normal and pathological changes that underlie this complex region of the cranial base.

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Fig. 1. Plain-film radiographs of the cranial base of a 24-year-old male (a) and an 82-year-old male (b). The POF of the 24-year-old male appears to be free of ossification and is distinguishable from the POF of the 82-year-old male.

Fig. 2. Masson's H&E staining of POF tissue from a 24-year-old male (**a** and **b**) and 68-year-old male (**c** and **d**). Red, ossified tissue; blue, nonossified tissue.

Fig. 3. Box plots of age (y-axis) and stage of ossification (x-axis) by observer (**a** and **c**: POSTLTE, POSTRTE; **b** and **d**: POSTLLP, POSTRLP). The statistical mean is represented by the black bar and the high/low range of observed values by the bars.

Fig. 4.
a-f: Inferior view of the POF in human skeletal material illustrating the degree of POF ossification for a given stage (1-6).

Fig. 5.
Individual datum plots of age (y-axis) and stage of ossification (x-axis) by observer (**a** and **c**: POSTLTE, POSTRTE; **b** and **d**: POSTLLP, POSTRLP).

TABLE 1

Comparative terminology describing the POF

Exocranium	Endocranium	Study type	Studies
Fissura petro-occipitalis	Fissura petro-occipitalis	Human/anatomical	Gray (1858)
Synchondrosis petro-occipitalis			
Fissura petro-occipitalis	Fissura petro-occipitalis	Human/anatomical	His (1895)
Petro-occipital fissure	Petro-occipital sulcus	Macaca mulatta/anatomical	Sullivan (1933)
	Inferior petrosal sulcus		
Fissura petro-occipitalis	Fissura petro-occipitalis	Human/anatomical	Spalteholz (1935)
Synchondrosis petro-occipitalis			
Fissura petro-occipitalis	Fissura petro-occipitalis	Human/anatomical	Oetteking, (1957)
Sutura petro-occipitalis			
Synchondrosis petro-occipitalis			
Petro-occipital synchondrosis	Not described	Human/Crouzan syndrome in dry skull	Kreiborg and Bjork (1982)
Petro-occipital fissure	Petro-occipital fissure	Human/clinical radiology	Silver et al. (1983)
Petro-occipital fissure	Not described	Human/clinical surgery	Prades et al. (1994)
Petro-occipital synchondrosis	Petro-occipital synchondrosis	Human/clinical radiology	Madeline and Elster (1995)
Petro-occipital fissure	Not described	Human/clinical radiology	Weber et al. (1995)
Petro-occipital complex	Not described	Human/clinical dental	Singh et al. (1997)
Petro-occipital fissure	Not described	Human/clinical surgical	Mazzoni et al. (1997)
Petro-occipital fissure	Not described	Human/clinical surgical	Lee et al. (2001)

TABLE 2

Measures of association between age of individual crania and observed stage of POF ossification *

	r	r²	e	e²
POSTRTE	0.807	0.651	0.939	0.881
POSTLTE	0.801	0.642	0.930	0.865
POSTRLP	0.535	0.286	0.929	0.862
POSTLLP	0.526	0.277	0.937	0.878

* n = 73. Mixed male/female population. Dependent variable: age. Independent variables: observer 1, right POF (POSTRTE); observer 1, left POF (POSTLTE); observer 2, right POF (POSTRLP); observer 2, left POF (POSTLLP). Correlation is significant at the $\alpha = 0.01$ level (two-tailed).

TABLE 3
Pearson product-moment correlation coefficient (r) by sex^{*}

	Age, male (n = 52)	Age, female (n = 21)
POSTRTE	0.737	0.938
POSTLTE	0.732	0.928
POSTRLP	0.433	0.708
POSTLLP	0.413	0.706

^{*} Measure of association (r) between age of individual crania by sex and observed stage of POF ossification. Dependent variable: Age. Independent variables: observer 1, right POF (POSTRTE); observer 1, left POF (POSTLTE); observer 2, right POF (POSTRLP); observer 2, left POF (POSTLLP). Correlation is significant at the $\alpha = 0.01$ level (two-tailed).