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Biological sex variation in bone mineral density in the cranium and femur

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ABSTRACT

Objectives: Sex and age trends in bone mineral density (BMD) play an important role in the estimation of age-at-death (AAD) of unidentified human remains. Current methodologies lack the ability to precisely estimate age in older individuals. In this study, BMD of the cranium and femur measured by DXA were examined to establish their applicability for age estimation in older adults. BMD as measured by DXA, is most commonly used clinically for prediction of osteoporotic fracture risk. We hypothesized that weight-bearing and non-weight-bearing bones, the femur and cranium, respectively, would provide valuable insights for aging.

Methods: The sample consists of 32 sets of excised cranial fragments from the Regional Forensic Center, Johnson City, Tennessee and 41 associated crania and femora from the North Carolina Office of the Chief Medical Examiner. All crania and femora were scanned using a Hologic (R) DXA scanner and data were analyzed using Student *t*-tests, Loess regression, and ANOVA.

Results: Student *t*-tests indicate a significant relationship between the sexes and cranial BMD and a significant relationship between age cohorts and femoral neck BMD. The Loess regression showed different aging patterns in the cranium for females and males older than 55. And the ANOVA showed changes in femoral neck after age 55.

Conclusions: These results indicate age and sex dependent changes in BMD especially for individuals over the age of 55, which offers improvement from current aging methods for older individuals. Further research using a larger sample size could improve the predictive capabilities of the model.

1. Introduction

Age-at-death (AAD) plays a crucial role in estimating a biological profile for unidentified decedents [1–3]. Currently, most skeletal biologists use phase methods, which focus on gross morphological degenerative changes of skeletal elements such as the sternal rib ends, *os coxa*, vertebrae, and others [3,5–7]. These aging methods are more variable than subadult aging methods as degenerative changes are due in part to environmental factors (e.g. nutrition, activity, etc.) not correlated to chronological age [1,4–7]. Consequently, adult age estimation methods have greater error and less precision than subadult age estimation with error increasing with chronological age [1]. Currently, many aging methodologies lump all adults over the age of 50–60 into a single age cohort [3–7]. As such, a void exists for accurate (includes the individuals age in the estimate although the range maybe very large) and precise (estimate is close to the actual age) estimation of age in the older adult population [1].

As we age, the rate of periosteal apposition significantly declines and is surpassed by the rate of periosteal resorption; resulting in a permanent deficit of bone loss and development of senile osteoporosis or "a deficiency of bone tissue relative to the volume of anatomic bone [8]." Osteoporosis was quantitatively defined in 1994 by the World Health Organization (WHO) according to the young adult mean bone mineral density (BMD) as measured by dual energy X-ray absorptiometry (DXA). According to this definition, normal BMD is defined as higher than one standard deviation (SD) above the mean, osteopenia as between 1 and 2.5 SD below the mean, and osteoporosis as 2.5 SD below the mean [9]. BMD is clinically measured using DXA for estimation of osteoporotic fracture risk.

DXA measures bone mineral content (BMC) based on attenuation of photons. A fan beam of photons passes through the material and is projected into a 2D coronal plane. The absorptiometry is measured based on the change in intensity:

$$\Delta I = -\mu L \cdot I \Delta x \quad (1)$$

Where ΔI represents change in intensity, μL represents the attenuation coefficient, I represents intensity, and Δx represents the thickness of the material [10]. The attenuation coefficient is dependent on both the energy of the x-rays and the properties of the material. While the attenuation coefficient is normally measured per unit of length, the equation can be modified to be mass based:

$$I = I0 \cdot e\text{^}(-\mu M x) \quad (2)$$

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Where I0 represents initial intensity measured at an arbitrary point, and μM represents the mass based attenuation coefficient calculated as

$$\mu M = \mu L/\rho \quad (3)$$

Where ρ represents the density of the material. The change in intensity is representative of the absorbance of the x-rays [10]. Higher x-ray attenuation is indicative of a higher material density. Bone mineral density (BMD) measured through DXA represents BMC/cm^2. As a function of area, unlike BMC, BMD corrects for discrepancies in size within the sample.

From a forensic perspective, age-at-death estimates based on quantitatively measured properties of skeletal elements are especially useful as bone is one of the longest surviving elements of the human body [11]. BMD based age estimations has been previously examined using micro CT for the development of regression equations [12–13]. However, these models were limited in their applicability, with an error range of ± 18 years at 75% confidence [12–13]. The poor performance of these models is reflective of the numerous interacting factors that determine an individual's peak bone mass [8]. In addition to age and sex related changes, BMD is also affected by ancestry, genetic predisposition, physical activity levels, body composition, consumption of alcohol and nicotine, and use of contraceptives [12]. Therefore, Altman and Aaron [10] proposed that multifactorial analysis of DXA through the incorporation of multiple skeletal elements could result in improved DXA based age estimations.

Previous studies of sexd dimorphism of skeletal apposition and reabsorption have indicated that males demonstrate increased apposition in the appendicular skeleton, while females demonstrate an increased rate of trabecular reabsorption [14–15]. Therefore, sexual differences in BMD could be apparent in elements of both the axial and appendicular skeleton, with females overall demonstrating a more dramatic loss of bone mineralization in the appendicular skeleton [16]. Moreover, according to Wolff's law, the microscopic structure of bone is determined in response to the mechanical stresses of compression and tension experienced during weight-bearing activity [17] with confirmation of a positive correlation between BMC/BMD and body weight from multiple studies [18–19]. In contrast to the appendicular skeleton, Turner et al. [20] found that the skull was not influenced by body weight and remained a reliable estimate of total body BMD.

Thus, the aim of this study is to provide a more accurate and precise AAD estimate, particularly for the older adult population using a multifactorial DXA analysis of BMD of the human cranium and proximal end of the femur.

2. Materials

2.1. Sample

The sample consists of excised cranial fragments, crania, and femora from identified skeletal collections. The cranial fragments from 32 individuals from the Ross et al. [21] study were collected during autopsy at the Regional Forensic Center, Johnson City, Tennessee. Each sample consists of four fragments representing bilateral frontal and parietal segments. The parietal fragments were excised measuring 4 cm posterolaterally from bregma and the frontal fragments were excised 4 cm anterio-laterally from bregma [21]. The excision location was chosen due to the minimal effect of muscle attachments. In addition, a sample consisting of 41 crania and associated femora, 25 from the North Carolina Office of the Chief Medical Examiner and 16 from identified forensic skeletal remains housed at North Carolina State University were included. All skeletal elements scanned were free of visible pathology and trauma and included individuals of European, African, and Hispanic Americans. Table 1 presents the age and sex distribution of the sample.

Table 1
Age distribution of sample.

	Skeletal remains		Cranial fragments	
Age	Male	Female	Male	Female
≤ 19	–	1	2	–
20–30	4	–	4	1
31–40	7	1	7	–
41–50	8	2	6	3
51–60	6	1	5	1
61–70	4	2	–	–
71–80	4	–	2	–
81–90	–	1	1	–
Totals	33	8	27	5

3. Methods

3.1. Dual energy X-ray absorptiometry

The DXA scans were performed on a Hologic® QDR Discovery 4500 W scanner. Prior to scanning, the machine was calibrated through radiological uniformity tests using a spine phantom. The scanner uses a constant x-ray source with an effective dose of 5 μSv. According to the manufacturer, the expected coefficient of variation for BMD measurement is 0.5%. Due to the use of excised bone, a soft-tissue proxy is required for accurate BMD measurement. In this study, rice served as the soft-tissue proxy to compensate for the absence of soft tissue [22].

3.2. Scan procedures

3.2.1. Cranial fragments

The cranial fragments were placed in a shallow plastic container and covered with rice. The fragments were scanned using the whole body scan with a shortened scan length of approximately twenty inches. After completion of the original scan, small sub-regions were positioned around each fragment to increase accuracy (Fig. 1).

3.2.2. Crania

Each cranium was scanned in three orientations: anterior, lateral, and superior (Fig. 2). The anterior position was especially important because it is the least affected by attachment sites of the craniofacial muscles and is not impacted by artifacts such as dental amalgams [23]. The skull was placed in a clear acrylic cube, which was filled with rice to simulate soft-tissue. Again, the whole body scan was used with a scan length of 20.1 in. After completion of the first scan, the skull was isolated in a sub-region for higher precision.

3.2.3. Femora

The right and left femora were each scanned using their respective hip scan (Fig. 3). Each femur was placed in rice and positioned so that the lesser trochanter was barely visible [9]. While the positioning of the femur is important for longitudinal studies, the error rates caused by rotation between 0 and 27 degrees are comparable to the standard error rates when the leg was placed in the standard anatomical position [24]. In addition to the date of the scan, age was included in the scan. To allow for automatic classification of BMD according to WHO standards, ancestry was also included. In addition to total BMD, the BMD of the femoral neck, trochanter, intertrochanteric region, and Ward's Triangle were reported. Ward's triangle is positioned at the location of minimum density in an area of 1 cm^2, a location not standard between scans. Therefore, due to its higher error rates and low reproducibility, Ward's triangle was not used for calculation purposes [25]. Furthermore, due to comparable correlation values, the ROIs (region of interest) from Prevrhal [25] for the separation of trabecular and cortical bone were not utilized.