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REVIEW

Advanced Hip Analysis: Simple Geometric Measurements Predict Hip Fracture Beyond Bone Mineral Density

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ABSTRACT

Osteoporosis is a condition that affects both the mineral density and geometry of bone, resulting in an increased susceptibility to fracture. Current dual-energy x-ray absorptiometry (DXA) densitometric measurements of bone mineral density (BMD) are unquestionably linked to osteoporosis and serve as a convenient and cost-effective means to monitor bone loss, diagnose osteoporosis, and assess fracture risk in a recognized population at risk for fragility or osteoporotic fractures. Measures of BMD do not, however, unequivocally measure any known mechanical strength properties. Since the fundamental issues inherent to osteoporosis are reduced bone strength and increased fracture risk, it is critical to establish a means of evaluating bone strength at skeletal sites, with clinical and performance relevance, to predict the likelihood of fracture. Thus, the purpose of this paper is to review the literature on methodologies for quantifying geometric parameters of hip bone developed for the widely applied DXA. Most notably, the calculated femur strength index (FSI) and the measured hip axis length (HAL) were evaluated for the ability to predict hip fracture independently of BMD along with the limitations.
Keywords: Osteoporosis; Bone mineral density; Hip fracture risk.

INTRODUCTION

In the United States, estimates are that 10 million people have osteoporosis and 34 million more have low bone mass [1]. Osteoporosis is a skeletal syndrome of severely reduced bone strength that is characterized by low bone mass and disrupted bone structure. Hip fracture is one of the most catastrophic, life-threatening, and costly types of bone fracture in the elderly [1,2]. Osteoporosis is more often manifested in the elderly because of a lifetime accumulation of risk factors that contribute to a decline in skeletal integrity. Several clinical methods are available to monitor changes in bone health in order to assess fracture risk. One such method is to measure areal bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA). According to the

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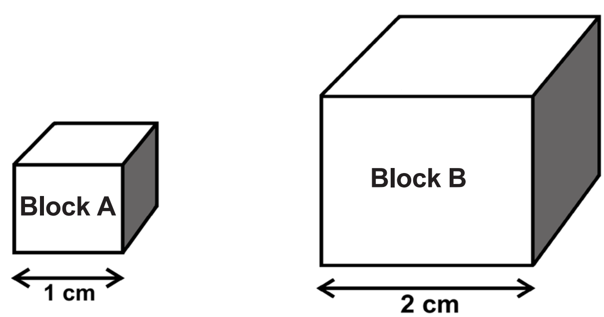
World Health Organization (WHO), one can be diagnosed as osteoporotic when BMD of the hip or spine drops below 2.5 standard deviations from the average BMD of a young, healthy population (ie, T-score of -2.5) [2]. This commonly applied clinical test informs the physician of the relative risk for fracture for an individual known to be at risk for osteoporosis. While these guidelines assist clinical decisions for intervention, they are not useful for identifying who will fracture.

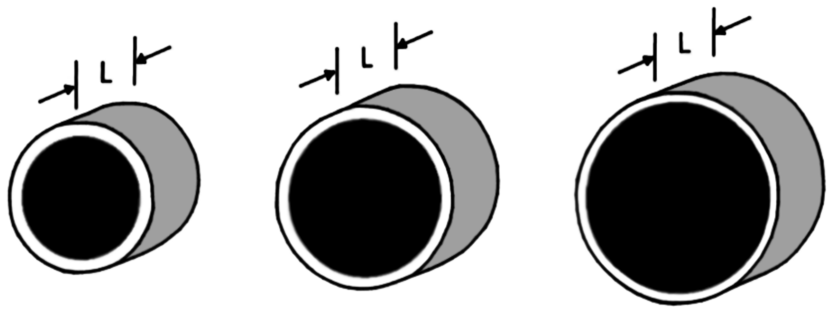
DXA: Strengths and Limitations

DXA technology provides a convenient and cost-effective means of diagnosing and monitoring bone disease with low ionizing radiation. Because of its application to large population studies with fracture outcome, DXA-measured BMD is a widely accepted surrogate of bone strength and a predictor of fracture risk [3]. DXA determines BMD by dividing total bone mineral content (BMC) by bone area. This two-dimensional areal measure of BMD is not, however, without limitations. A person with larger bones will be assessed with a higher areal BMD score than someone with smaller bones of the same volumetric density (Figure 1). In fact, a considerable number of hip fractures occur in patients with high areal BMD [4,5]. It is becoming increasingly evident that fracture risk depends on numerous factors independent of BMD. WHO led the development of the FRAX® fracture risk assessment tool (www.shef.ac.uk/FRAX), which includes several osteoporosis risk factors to predict a patient's 10-year probability of fracture, including BMD, age, sex, body mass index, parental history of hip fracture, glucocorticoid use, prior fragility fracture history, smoking, daily alcohol use, and secondary osteoporosis [6]. In addition to the clinical



	Block A	Block B
Total Material Density (g/cm^3)	1 g/cm^3	1 g/cm^3
Total Material Bone Mineral Content (g)	1 g	8 g
Bone Area (cm^2)	1 cm^2	4 cm^2
Areal Material Density (g/cm^2)	1 g/cm^2	2 g/cm^2

Figure 1. DXA (areal) BMD is highly size dependent. Although blocks A and B are made of the same material, block B is measured to have a higher areal BMD simply because it is larger.



Outer diameter, cm	2.5	3.0	3.5
BMD	1.0	1.0	1.0
vBMD	1.20	1.0	0.86
BMC or bCSA	0.83	1.0	1.17
CSMI	0.58	1.0	1.55
Section modulus	0.70	1.0	1.33

Figure 2. Scale drawing of three cylindrical cross-sections. Length (L) and areal bone mineral density (BMD) are equated in each cylinder to demonstrate varying strength properties (CSMI, section modulus) of each. Image from Beck TJ [10].

risk factors included in FRAX®, geometric properties of bone may play a significant role in fracture risk prediction [7]. Various methods of inferring structural properties from two-dimensional densitometry instruments are capable through interactive computer programs such as Hip Structural Analysis (HSA). The HSA interactive computer program was developed by Beck [8] and is used to extract geometric properties from DXA scans and output an estimate of femoral neck strength. HSA software is compatible and available for use with the leading DXA manufacturers.

Hip Structural Analysis

The geometric role of bone strength and fracture risk cannot be overstated. A widespread example of how geometric properties affect bone strength is apparent in femoral neck periosteal apposition. To compensate for bone loss due to aging, femoral neck diameter increases in order to partially maintain the strength and modulus of elasticity of the bone [9]. BMD is only, however, a constituent of strength and may not completely reflect strength changes, especially corresponding to geometric adaptations. Consider three cylindrical tubes in Figure 2. Although areal BMD (g/cm^2) is the same for each tube, the narrowest one has 30% less strength in bending (section modulus) and the widest one is 33% stronger [10]. With recognition of the inherent limitations of BMD, Beck [10] designed the HSA technique to help predict the strength, and ultimately the fracture risk, of bone based on geometrically extracted measures obtained from two-dimensional DXA images. This commercially available software automatically derives proximal femur geometric properties, such as femoral neck cross-sectional moment of inertia (CSMI), bone cross-sectional area (CSA), buckling ratio (BR), and neck-shaft angle (NSA) (Table 1; Figure 3), as supplemental predictors of hip fracture risk [10,11].

Table 1. Terminology and equations of hip structural analysis.

Term	Explanation
CSMI: cross-sectional moment of inertia (cm^4)	Property of a cross-section used to predict its capacity to resist bending (also called second moment of area)
BSA: bone cross-sectional area (cm^2)	Total bone surface area in a cross-section, excluding marrow space and soft tissue, assuming fixed average mineralization
w: total bone length (cm)	Length of bone cross-section after blur correction
x_c: distance to center of mass (cm)	Coordinate of the center of mass of bone cross-section determined from the centroid formula
Z: section modulus (cm^3)	Index of maximum bending strength: $$Z = \frac{CSMI}{d_{max}}$$ where d_{max} = greatest distance from xc to outer bone surface (cm)
CT: mean cortical thickness (cm)	Length of bone cross-section after blur correction
BR: buckling ratio	Index of cortical wall stability; unstable when ratio exceeds a factor of 10: $$BR = \frac{d_{max}}{CT}$$
NSA: neck-shaft angle	Angle formed between neck and shaft axes

To validate hip fracture prediction by HSA, several retrospective analyses have been conducted to compare the predictive strength of HSA parameters versus BMD among patients with osteoporotic hip fracture. Kaptoge et al. tested whether CSMI, NSA CSA, section modulus (Z), buckling ratio (BR), and mean cortical thickness (CT) extracted from DXA images predict hip fracture better than BMD [3]. Although significant correlations were found, no HSA variables measured provided superior hip fracture prediction when compared with BMD [3]. Among the 635 incident hip fractures from the 7,474 women evaluated, BMD, CT, and BR were the strongest predictors while CSMI was the poorest [3]. It is possible, however, that failure loads leading to fracture were out of the scan plane. Thus, the assumption of uniform cross-sectional properties by the simple bending failure model led to overestimation of the bending strength (CSMI) of the bone (Figure 4). A similar re-analysis was conducted using DXA data from 232 elderly women from the EPIDOS study [12]. Among the 232 women,

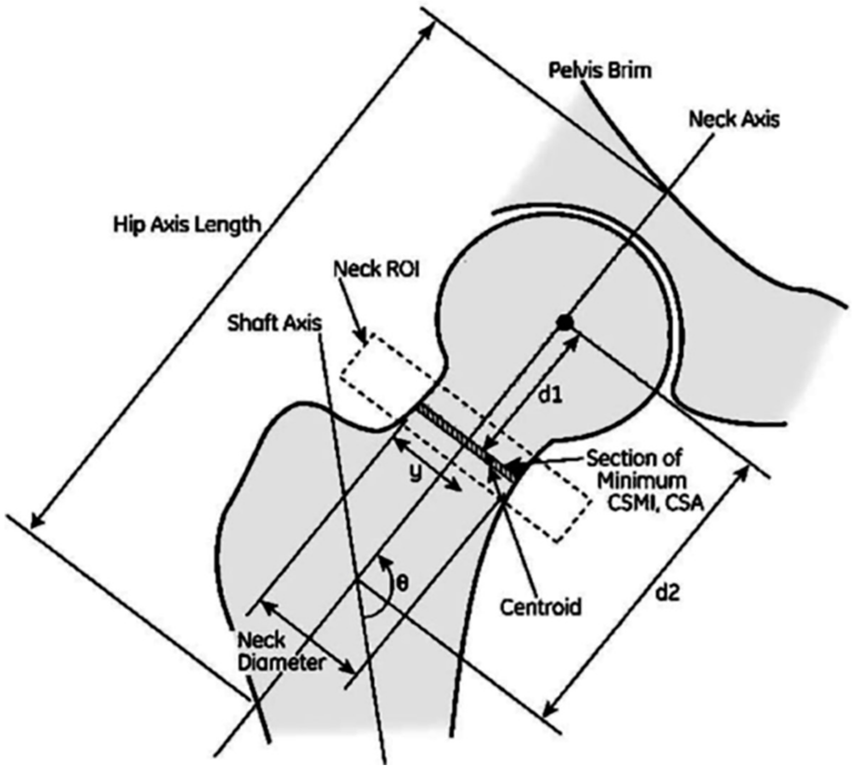


Figure 3. Hip structural analysis (HSA) variables obtained from DXA scans. Reproduced from Faulkner KG et al. [25].

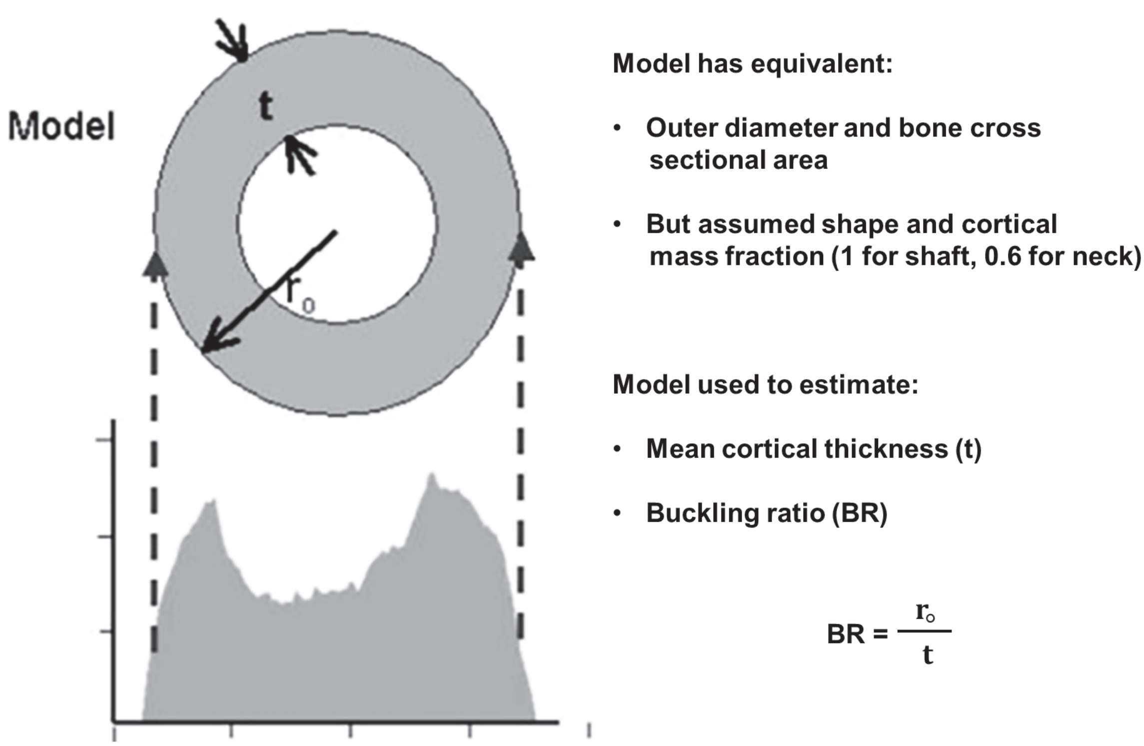


Figure 4. To calculate the buckling ratio (BR), cortical thickness (t) must be constant throughout the annulus. To achieve consistency, CSA is apportioned throughout the cross-section while a constant thickness is maintained. Image from Beck TJ [26].

65 suffered a previous hip fracture. Increases in BR and decreases in CT, CSMI, and Z were predictive of all hip fractures. Statistical significance was lost, however, when there was adjustment for BMD, suggesting a dependence on BMD and not on actual structural properties [12]. Faulkner et al. [7] revealed similar results of CSMI losing significance between fracture and non-fracture groups after adjustment for BMD.

Altogether, the aforementioned HSA estimated structural parameters do not appear to provide information on fracture risk susceptibility beyond the capability of BMD. They do, however, express DXA data in such a way that is more mechanically and structurally interpretable than conventional density measurements. Future investigations on the dimensional effects of aging on bone and the mechanisms leading to bone fragility may be enhanced through the use of HSA variables. Yet there still remains a need to supplement BMD data with structural parameters that contribute to bone strength calculations [13]. To address this issue, the Advanced Hip Assessment (AHA) software was created and is available through high-resolution GE Lunar iDXA densitometer.

Advanced Hip Assessment

Compared with software for structural analyses of the hip available on the Hologic densitometers, there is software on the GE Lunar iDXA absorptiometer that calculates an index of hip strength (femur strength index, FSI) from additional variables of hip structure, namely, CSMI, CSA, distance from femoral head center to minimum CSMI, distance from centroid to superior neck margin for minimum CSMI, and NSA [7]. FSI is defined as the ratio of the compressive yield strength of the femoral neck to the expected compressive stress of a fall to the greater trochanter after adjustment for the age, height, and weight of the patient [7,14]. In other words, FSI estimates a patient's resistance to fracture after a fall to the greater trochanter of hip [15]. Bone fractures occur when stresses acting on the bone (denominator of FSI) surpass the strength of the bone (numerator of FSI). Thus, FSI values less than 1 will theoretically result in a hip fracture. Estimation of bone strength, however, is dependent on several factors, including mechanical properties, loading conditions, and geometry [16]. To address the geometric component of bone strength, hip axis length (HAL) is used and has been shown to be a significant and independent predictor of hip fracture [16,17].

HAL can be extracted by software from both HSA and AHA but, when used in combination with FSI, hip fracture prediction power is greatly enhanced. HAL is defined as the distance in millimeters measured along the femoral neck axis beginning at the base of the greater trochanter and ending at the inner rim of the pelvis (Figure 5) [18]. Several explanations of the physical significance of HAL to hip fracture exist. First, HAL can be thought of as the moment arm of the femur (Figure 5) [16]. From an engineering perspective, longer moment arms require less force to produce the same bending moments on a structure. Thus, hip fracture will likely occur in a patient with a longer moment arm (HAL) than a shorter one when subjected to the same magnitude of force (Figure 5). A second interpretation is that a longer HAL creates a larger target area during impact to the greater trochanter [16]. In other words, the authors suggest that higher HALs may cause the greater trochanter to protrude farther away from the

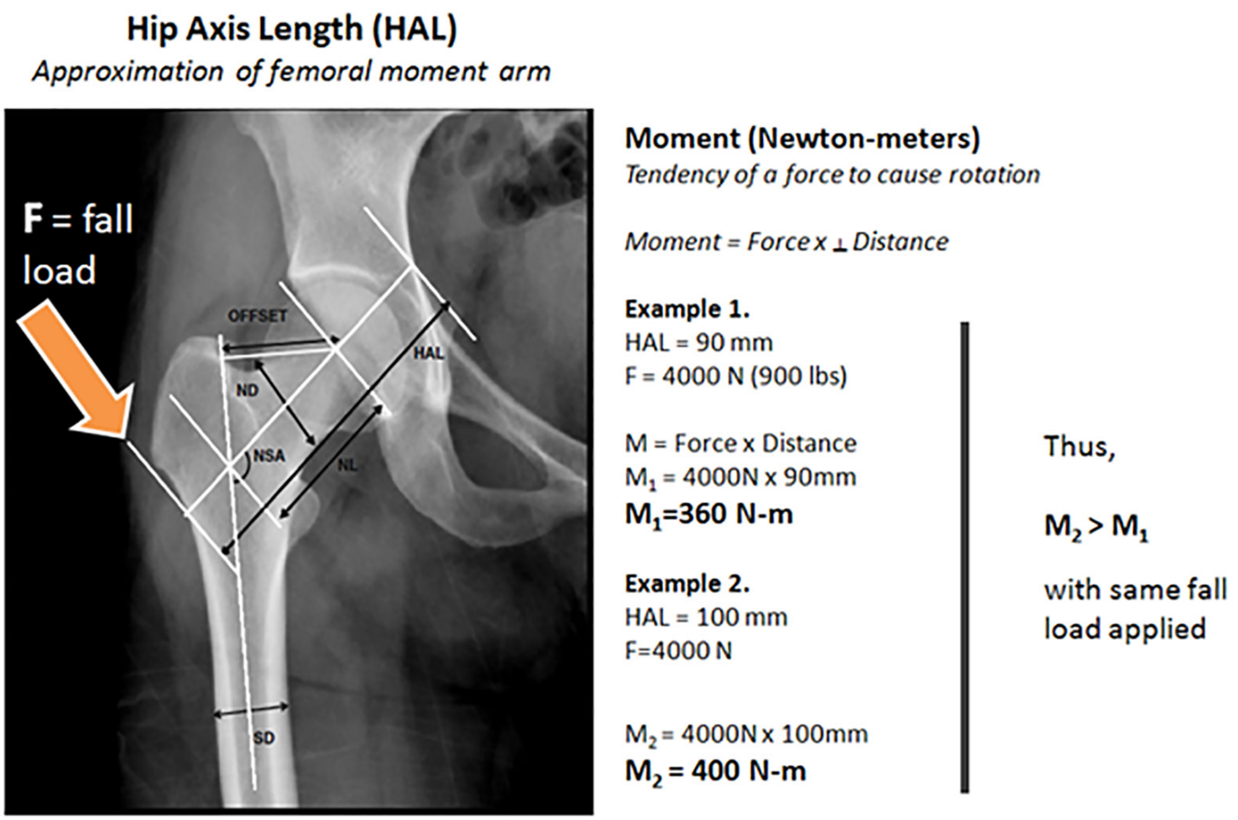


Figure 5. Demonstration of how HAL may serve as an approximation for a femoral moment arm. With the same fall load (F=4000 N) applied to the greater trochanter, example 1 reveals how a shorter HAL (90 mm) results in a lower bending moment (M1=360 Nm) when compared with the bending moment (M2=400 Nm) corresponding to a longer HAL (100 mm) in example 2. X-ray image from Im & Lim [22].

pelvis, creating a target more susceptible to fracture [16]. It is also possible that HAL measurements are capturing a structural property relevant to hip fracture that are not measured in the AHA analysis [16]. Although the manner by which HAL contributes to the prediction of hip fracture remains unknown, HAL and FSI are proving to be useful tools in conjunction with and independent of the fracture prediction capacity of BMD.

FSI and HAL: Geometric Measurements to Predict Hip Fracture

Numerous studies have been conducted to compare hip fracture prediction by the geometric indices FSI and HAL, and to determine whether the variables provide information independent of BMD [17-22]. Perhaps the most notable of these studies was performed by Faulkner et al. in 2006 [7]. Analyses of 2,506 women 50 years old or older, 365 of which suffered a prior hip fracture, were used to determine whether FSI and HAL could be considered significant independent predictors of hip fracture. The relative frequency distributions plot of FSI in Figure 6 suggests that individuals with low FSI values are at a heightened risk for hip fracture compared with non-fracture controls [7]. FSI values below 1 can be physically translated as loading forces to the hip exceeding the ultimate strength of the bone. Thus, it is not surprising that lower FSI values appear

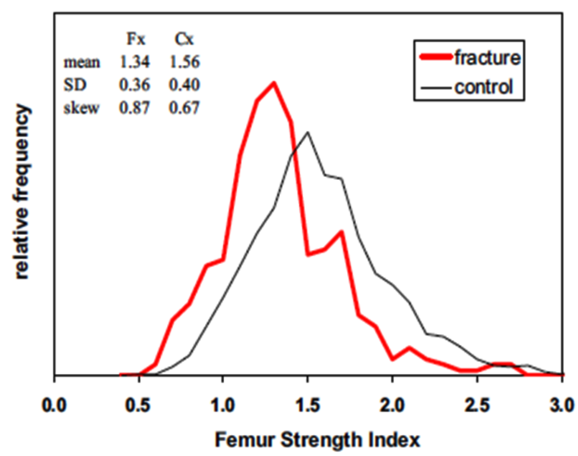


Figure 6. Relative frequency distributions of femur strength index (FSI) values for fracture and control groups suggesting that FSI is a significant predictor of hip fracture. Reproduced from Faulkner KG et al. [7].

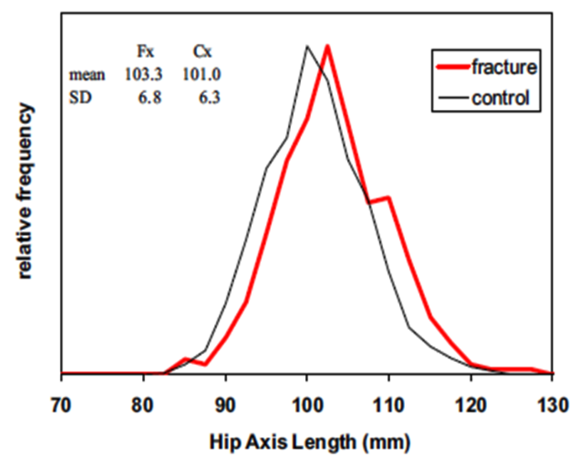


Figure 7. Relative frequency distributions of hip axis length (HAL) values for fracture and control groups suggesting that longer HALs correspond to higher incidences of hip fracture. Reproduced from Faulkner KG et al. [7].

well correlated to increased fracture incidences. Even after adjustment for BMD and HAL, FSI remains a significant predictor of hip fracture [7, 23]. Similarly, HAL has been shown to be a predictor of hip fracture independent of BMD, age, height, and weight. Figure 7 shows a higher incidence of hip fractures in patients with longer HAL measurements [7]. In fact, for every standard deviation increase in HAL, the odds of experiencing a hip fracture double [16].

FSI and HAL are also reported to change as a result of age. Zhang et al. performed the first study investigating the aging trends of hip geometry [23]. After adjustment for height and weight, HAL was shown in this cross-sectional study to increase with age while FSI tended to decrease (Figures 8 and 9) [23]. These unfavorable age-related geometric changes correspond to the increased fracture occurrences in the elderly, increasing exponentially in both men and women after 50 years of age. Although it is well established that aging leads to significant decreases in femoral neck BMD, geometric indices such as FSI and HAL may be able to reveal hip fracture risk before density measurements would conventionally define a patient as at risk. According to clinically accepted guidelines, a person can be diagnosed as osteoporotic when his or her T-score falls below 2.5 standard deviations (T-score <-2.5) from young adults at peak bone density. T-scores between -1 and -2.5 correspond to low bone mass (osteopenia) and values above -1 are considered normal. Figure 10 shows that over half of the female patients assessed (n=471) had an FSI<1 despite T-scores falling in the normal BMD range [18], suggesting a disconnect between FSI and BMD for assessing hip integrity. Wendlová suggested that any discrepancies between FSI and BMD fracture risk assessment are likely due to the insufficiency of BMD as a sole surrogate of bone strength [18]. Bone quality could be perceived as a multifaceted biomechanical property that integrates geometric, material, and densitometric variables. Thus, FSI and HAL, in conjunction with BMD, may be a way to discover a higher percentage of patients who are at risk for hip fracture beyond T-scores alone. Faulkner et al. showed that combining HAL and BMD measurements dramatically increased prediction of fracture risk (Figure 11) [16]. Given new insight into the contributions of simple geometry measurements on bone health, as well as the ability of AHA variables to predict hip fractures independently of BMD, FSI and HAL may serve as new criteria for the initiation of therapeutic countermeasures in normal and osteopenic patients who may be at risk for a fracture of the hip.

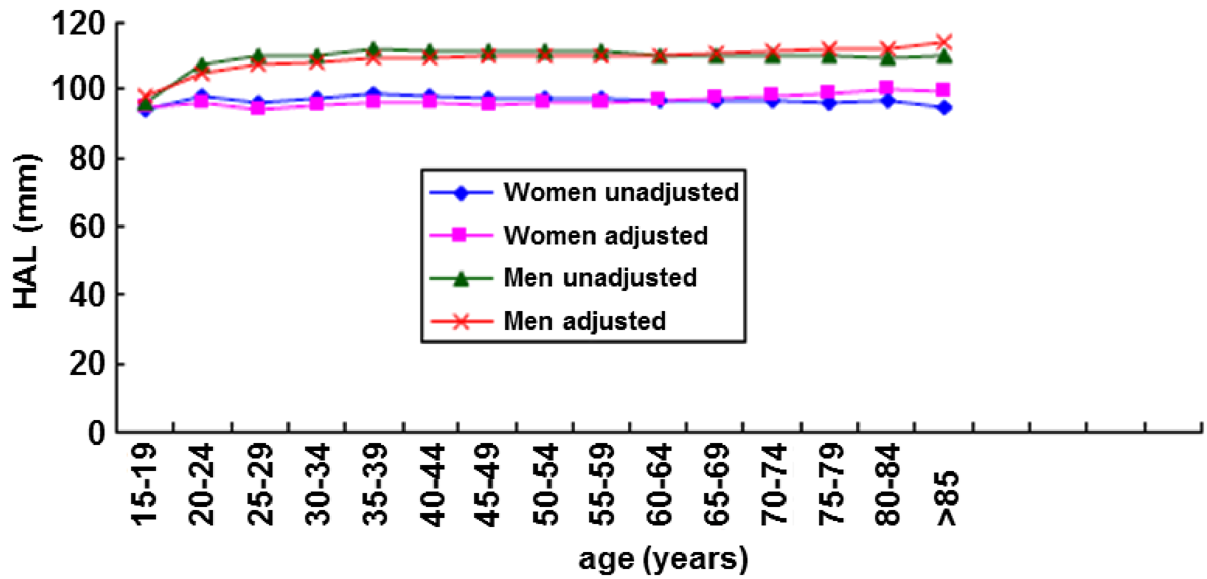


Figure 8. Adjusted (height and weight) and unadjusted HAL changes for women and men with age. HAL increases with age, corresponding to an increased hip fracture risk in the elderly. Graph from Zhang H et al. [23].

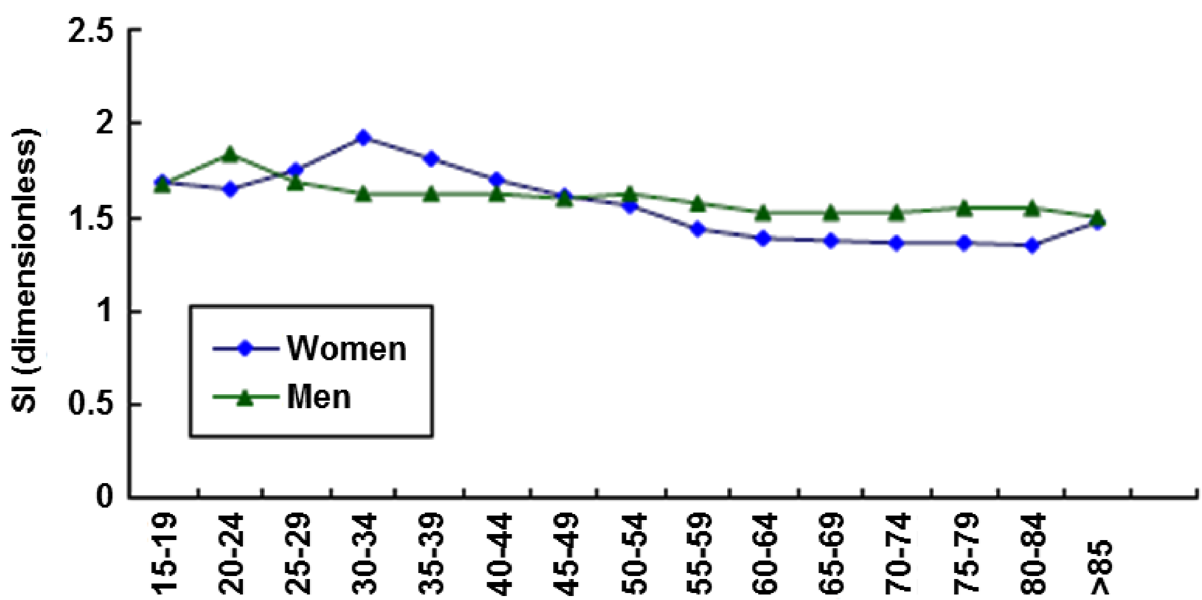


Figure 9. SI (referred here as femoral SI) decreases with age in both women and men although the relationship is more pronounced in women. Graph from Zhang H et al. [23].

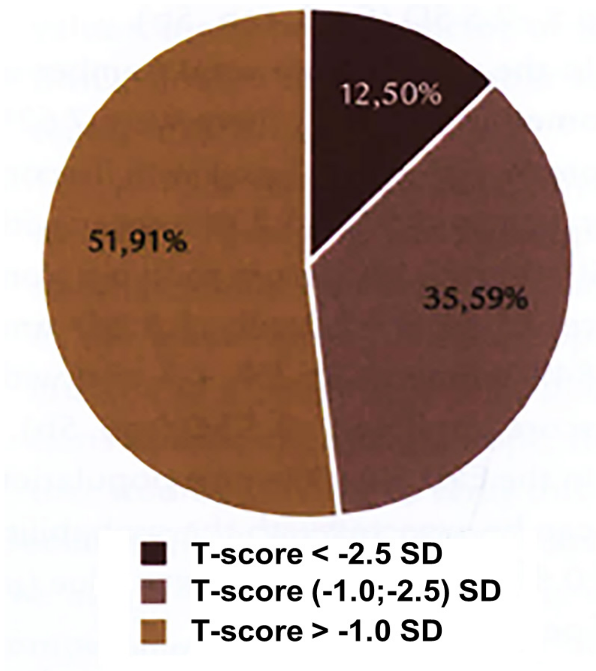


Figure 10. Distribution of women (n=471) with FSI<1. Over half of the women observed (51.91%) had normal T-scores (T-score >-1.0 SD) yet were suggested by FSI to be at risk for hip fracture. Image obtained from Wendlová J [18].

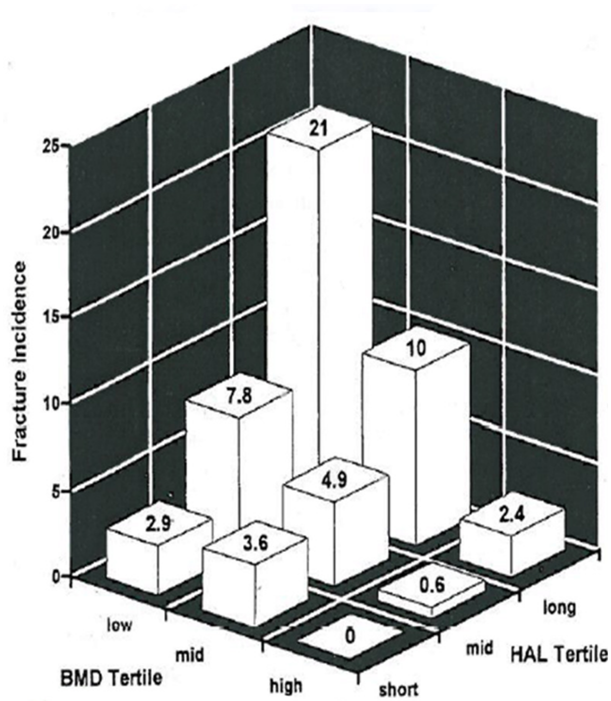


Figure 11. The prediction of hip fracture was greatly enhanced when BMD and HAL measurements were used in combination. Image obtained from Faulkner KG et al. [16].

Limitations

While DXA technology is continuously advancing, both HSA and AHA technologies are not without limitations. DXA scanners were designed to measure density, not geometry. Small differences in pixel value and spacing translate to profound alterations in calculated strength. Furthermore, in order to calculate various geometric parameters, certain assumptions must be made. CSMI, for example, the measure of bone's resistance to bending, is used in the calculation of FSI and operates under the assumption of uniform cortical thickness and axial symmetry. Since bone is inherently asymmetric and unequally distributed throughout a cross-section (Figure 12), these assumptions may be an oversimplification of the mechanical strength of bone. Since DXA images are two-dimensional, CSMI calculations are relevant only for bending in the plane of the image and cannot be used to estimate bending in other directions. Another generalization of HSA and AHA is the assumption that bone is fully and consistently mineralized. The extent to which variations in cross-sectional mineralization have on bone geometry is yet to be elucidated. Magnification error is potentially another notable limitation to DXA technology. To address this issue, narrower fan beams have been introduced that may minimize error from magnification. Furthermore, Young et al. have shown that by using a simple linear model, fan beam DXA technology can predict HAL with a high degree of accuracy when compared with pencil-beam scans [24]. Finally, and perhaps the most critical limitation of these technologies, is inconsistent and inaccurate positioning of the femur. Femoral neck anteversion is a major source of hip positioning imprecision (Figure 13). Careful consideration should be given by the technician to ensure as much consistency among scans as possible. Although beyond the scope of this paper, it would be interesting to determine whether or not body mass is positively related to fracture risk, especially in the overweight population whose body mass is above the general population mean.

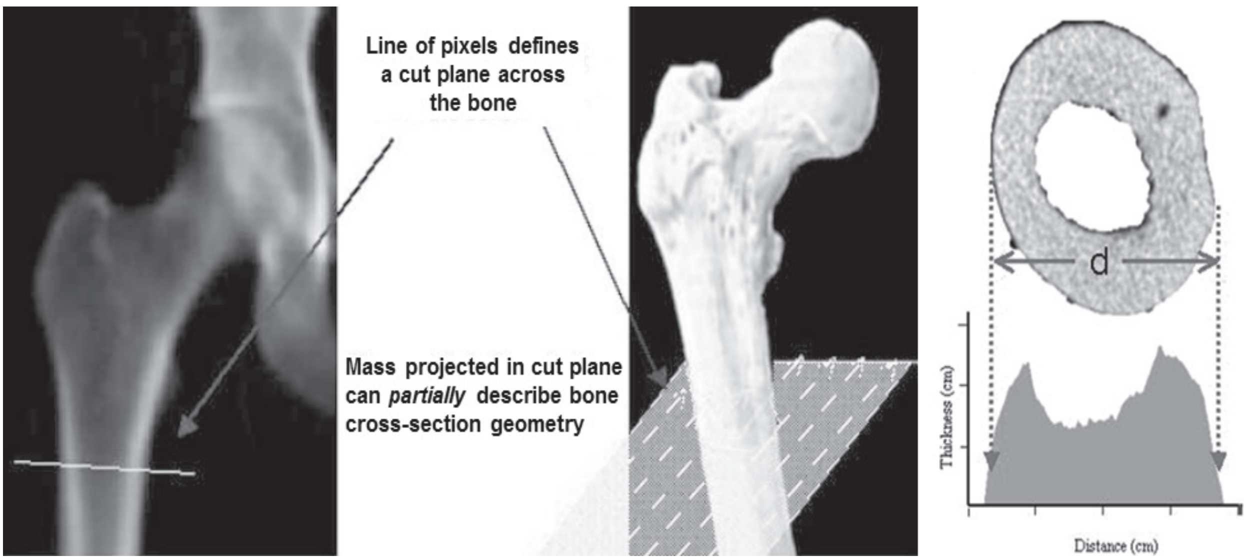


Figure 12. Cortical bone cross-section at midshaft femur obtained from DXA scanner revealing a non-uniform cortical thickness profile. Image adapted from Beck TJ [26].

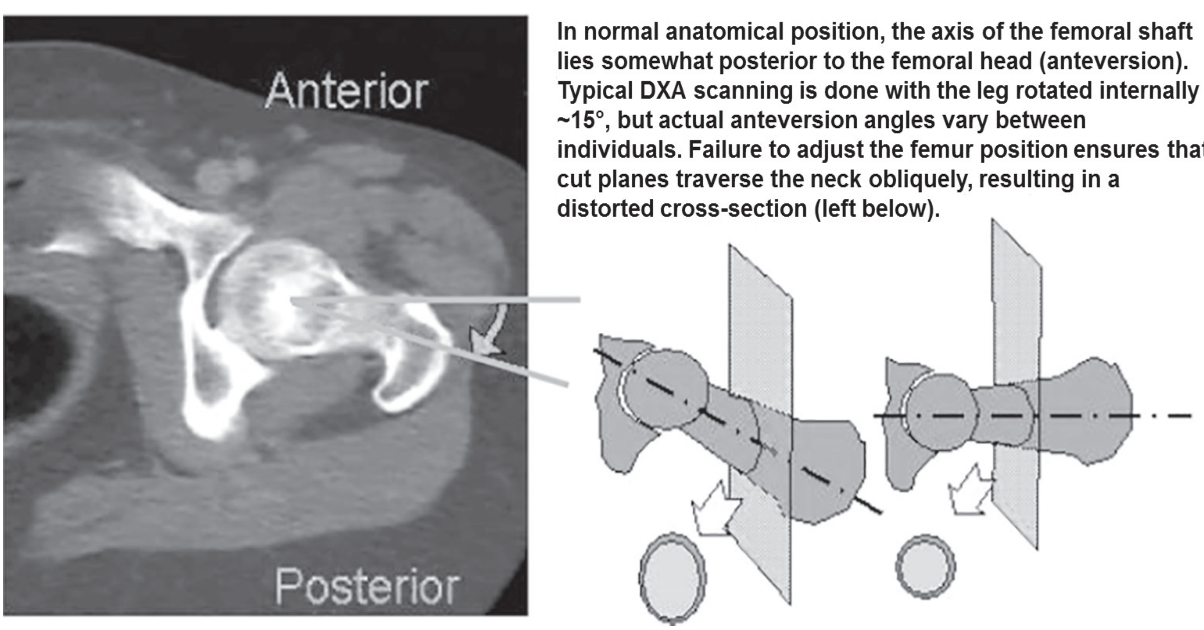


Figure 13. Image demonstrates the importance of positioning. The technician must rotate the femur internally so that the plane of the femoral neck is parallel to the image plane. Failure to do so results in an oblique cross-section that will distort the dimensional analysis. AHA is highly dependent on femur positioning. Image obtained from Beck TJ [26].

CONCLUSIONS

DXA technology remains a valuable tool to help assess bone loss and fracture risk due to osteoporosis. Although not the designed intent of densitometers, hip structural parameters, obtained from two-dimensional DXA scans, may provide a low-risk method of relating the mechanical competence of the hip bone beyond BMD. Initial studies evaluating FSI and HAL have demonstrated the predictive ability of these variables in retrospective, cross-sectional studies, but future work is needed to confirm and expand on these results, especially regarding their utility in predicting fracture risk in more controlled, prospective studies. This potential fracture risk capability, however, is not so apparent for CSMI, CSA, BR, CT, and NSA, which lose predictive capability when adjusted for BMD. When FSI and HAL are used together, hip fracture prediction may be enhanced and perhaps of utility for the primary care physician evaluating fracture risk in the typical clinical patient for osteoporosis (type I postmenopausal or type II senile osteoporosis). However, there are no evidence-based guidelines associated with using these DXA-based indices of hip structure in clinical practice, only personal opinion. Furthermore, astronauts represent a complicated target population for evaluating bone loss and osteoporosis because astronauts are younger, predominantly male, and exposed to environmental risk factors that are not well studied here on Earth (weightlessness, radiation exposure, dietary constraints, reduced physical activity). There is limited baseline knowledge for understanding these effects on skeletal tissue and mineral metabolism. Hence, NASA should continue to pursue the recommendations obtained from a clinical advisory panel (Bone Summit 2010) to use QCT (quantitative computed tomography) as a surveillance tool to evaluate the effect of space flight on fracture risk and early onset osteoporosis.

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