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A comparison of DXA and CT based methods for estimating the strength of the femoral neck in post-menopausal women

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Abstract

Purpose—Simple 2-dimensional (2D) analyses of bone strength can be done with dual energy x-ray absorptiometry (DXA) data and applied to large data sets. We compared 2D analyses to 3-dimensional (3D) finite element analyses (FEA) based on quantitative computed tomography (QCT) data.

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Conflicts of Interest:

Drs. Danielson, Atkinson, Cauley, Greendale, Greenspan, Karlamangla, Ruppert and Vuga and Ms. Khaled and Ms. Lian have no conflicts to report. Dr. Beck is co-founder of Beck Radiological Innovations, Inc., a company that develops software and hardware methods for measuring bone structure as well as other products. His former employer the Johns Hopkins University licensed the HSA software used in this paper to Hologic, Inc. and he receives a share of the royalties. Dr. Keaveny has a financial interest in O.N. Diagnostics, and both he and the company may benefit from the results of this work. Dr. Kopperdahl is employed by O.N. Diagnostics.

Methods—213 women participating in the Study of Women’s Health across the Nation (SWAN) received hip DXA and QCT scans. DXA BMD and femoral neck diameter and axis length were used to estimate geometry for composite bending (BSI) and compressive strength (CSI) indices. These and comparable indices computed by Hip Structure Analysis (HSA) on the same DXA data were compared to indices using QCT geometry. Simple 2D engineering simulations of a fall impacting on the greater trochanter were generated using HSA and QCT femoral neck geometry; these estimates were benchmarked to a 3D FEA of fall impact.

Results—DXA-derived CSI and BSI computed from BMD and by HSA correlated well with each other ($R=0.92$ and 0.70) and with QCT-derived indices ($R=0.83$ – 0.85 and 0.65 – 0.72). The 2D strength estimate using HSA geometry correlated well with that from QCT ($R=0.76$) and with the 3D FEA estimate ($R=0.56$).

Conclusions—Femoral neck geometry computed by HSA from DXA data corresponds well enough to that from QCT for an analysis of load stress in the larger SWAN data set. Geometry derived from BMD data performed nearly as well. Proximal femur breaking strength estimated from 2D DXA data is not as well correlated with that derived by a 3D FEA using QCT data.

Keywords

Hip Structure Analysis; DXA; QCT; Bone Mineral Density; Fracture; Women

Introduction

Hip fracture is a leading cause of morbidity and mortality among older adults [1]. Loss of mechanical strength predisposes the proximal femur to fracture easily under traumatic fall conditions. Modern engineering analysis employs computer simulations of failure conditions incorporating information about an object to accurately predict its strength under a particular loading condition. Engineering methods could be applied to the assessment of proximal femur strength if it were possible to extract the necessary data from the hip in a non-invasive manner. It is difficult to assess the structure of the hip for a number of reasons. The strength of bone tissue can be evaluated only by specialized biopsy methods and the fine structural details of bone require imaging technologies and computational methods that are prohibitively expensive or require an unacceptably high radiation dose. While not yet ideal, it is possible to do a low resolution 3-dimensional (3D) finite element analysis (FEA) using quantitative computed tomography (QCT) data, and FEA has been applied to the proximal femur [2,3]. This QCT-based method requires fairly high radiation doses to acquire the quality images needed for the process and its costs and complexity limit its clinical applicability and its use in large research studies. A more limited engineering analysis can be based on low-dose dual energy x-ray absorptiometry (DXA) data but the analysis is restricted to two dimensions and the resolution of the structural dimensions are equally low [4]. In addition, many more assumptions are required to evaluate strength from 2-dimensional (2D) DXA data and it is not known how well the simpler analyses compare to a more rigorous 3D finite element technique.

The current sub-study is an ancillary project of the Study of Women’s Health Across the Nation (SWAN) which was tasked to evaluate hip strength across the menopausal transition. We obtained both DXA and QCT data on the hip in a sample of SWAN participants and used them to compare 2D DXA-based assessments of femoral neck strength with QCT-based assessments.

Four previously published engineering analysis methods were used on the data in order of increasing complexity that include:

- *DXA areal BMD-based Analysis (DBA)*: This method uses conventional areal bone mineral density (BMD) at the femoral neck with femoral neck width and hip axis length measurements from the DXA image to estimate strength indices under pure axial compression and pure bending [5]. This is the simplest method since most of the information is derived from the conventional analysis with the least additional effort. It uses the areal BMD from the conventional analysis and makes the assumption that the mineral in the cross-section is confined to an annular cortical region. The original report describes strength indices scaled to body size [5]. For the purposes of comparison with the other 3 methods, we computed the strength estimates without reference to body size since we are comparing the same individuals across methods.
- *DXA Hip Structure Analysis (HSA)*: Hip Structure Analysis (HSA) uses principles first described by Martin and Burr [6] to derive geometric properties of femur cross-sections. Unlike the simpler areal BMD-based method, it uses the distribution of bone mineral across the width of the femoral neck to assess strength of the cross-section. It is somewhat more complex since it requires a separate analysis of the DXA scan data. Both DXA-based methods rely on assumptions regarding bone mineral distribution in the third dimension. Historically, HSA was mainly used to compute geometry of specific cross-sections without deriving strength estimates. For comparison with other methods, we computed simple strength indices at the femoral neck under pure compression and pure bending as well as a more complex strength estimate employing a 2D engineering analysis in a simulation of a fall impacting on the greater trochanter (Fig. 1).
- *QCT-based Analysis of Femoral Neck Cross-sections (QCA)*: This analysis derives geometric properties of femoral neck cross-sections from a series of reformatted computed tomography (CT) cross-sections [7]. For comparison with DXA based DBA and HSA methods, strength indices under pure axial compression and bending were computed for the femoral neck cross section. Unlike DXA-based methods, this approach uses the distribution of bone mineral over both dimensions of the cross-section (width and depth). Although amenable to a 3D beam analysis, the 2D loading condition used in the HSA method (i.e., in frontal plane only) was combined with CT femoral neck geometry for a fall mode strength estimate for comparison with the FEA method.
- *3D Finite Element Analysis (FEA)*: This method uses QCT images of the proximal femur to develop a full 3-dimensional finite element analysis (FEA) simulating a fall impacting on the greater trochanter. This approach has been validated for estimation of femoral strength via mechanical testing of cadaver bones [8] and has been shown to be a good predictor of fracture risk in the MrOs study of elderly men, though not superior to DXA areal BMD [9]. In the present study we have neither hip fractures cases nor a “gold standard” method for determining femoral neck strength to benchmark the methods we compare. We therefore used the FEA method as the comparison reference because it is 3-dimensional and the most sophisticated of methods (see Discussion).

For brevity the four methods are abbreviated as DBA, HSA, QCA, and FEA, respectively, in the remainder of the paper.

METHODS

Study Sample

The Study of Women's Health Across the Nation (SWAN) is a multi-center, multi-ethnic longitudinal study designed to characterize changes that occur during the menopausal transition in a community-based sample of 3302 women. Enrolled women were 42–52 years of age, had experienced at least one menstrual cycle in the 3 months prior to screening, were not using hormone contraceptives or hormone therapy at baseline, and self-identified as a member of one of five eligible racial/ethnic groups. Details of eligibility and recruitment are published elsewhere [10]. Of the 3302 women participating, 1550 were Caucasian, 935 African-American, 286 Hispanic, 250 Chinese, and 281 Japanese. Women completed their baseline clinic visit during 1996–1997.

A Bone Density Sub-Study was conducted at five of the seven SWAN centers including Boston, MA; Detroit area, MI; Los Angeles, CA; Oakland, CA; and Pittsburgh, PA. Areal BMD of the proximal femur was measured by DXA (QDR 4500, Hologic Inc. Waltham, MA). In addition, QCT scans of the proximal femur were acquired on a subset ($n=213$, 91%) of women attending the Visit 11 (2007–2009) assessment at the University of Pittsburgh. Height (cm) and weight (kg) measurements, used in calculating various strength indices, were recorded at the clinic visit without shoes and in light clothing. Written informed consent was obtained from all participants and the study protocol was approved by each center's Institutional Review Board.

Data Acquisition

DXA Scanning—DXA scans of the proximal femur were acquired using Hologic QDR 4500 scanners. A standard quality control program included daily measurement of a Hologic anthropomorphic spine phantom, cross-site calibration with a single anthropomorphic spine phantom, local review of scan images, as well as monthly and quarterly reviews of QC scans plus all problem scans by Synarc, Inc. (Waltham, MA). Duplicate scans of the proximal femur and spine, with complete repositioning, conducted on five women (ages 42–52 years) at each site yielded short-term *in vivo* standard deviation values of 0.014 g/cm² (1.4%) and 0.016 g/cm² (2.2%), respectively. Details of the QC program are published elsewhere [11]. Scan images were then transferred to analysis centers at UCLA and Johns Hopkins University for further analyses.

QCT Scanning—Computed tomography scans were acquired on a single scanner, a GE Hi-Speed ZXi CT (Milwaukee WI) at settings of 120 KVp, 170–200 mAs, and 1-mm slice thickness. Scan extents ranged from 2 cm above the femoral head to 2 cm below the base of the lesser trochanter. A solid calibration phantom with known bone mineral concentrations (Image Analysis, Inc., Columbia, KY) included in each participant scan was used to convert pixel values to bone mineral densities, and an Image Analysis torso phantom was used to adjust for field non-uniformity. A bolus bag (gel-filled, water equivalent) was also placed between the participant and the phantom to prevent air gaps. O.N. Diagnostics (Berkeley, CA) provided a standard scan acquisition protocol and reviewed scans for image artifacts and adherence to the protocol. Scan images were then exported and shipped to the reading centers (O.N. Diagnostics and Mayo Clinic) for strength and structural analyses.

Structure/Strength Analysis

To facilitate comparisons, all measurement units were converted to a consistent format. Linear and surface dimensions were converted to meters (m) and all forces to Newtons (N). In effect, the strength indices were expressed in reciprocal units of stress (m²/N) and the strength estimates in N. Areal (DXA) BMD was converted into linear thickness in cm by

dividing g/cm² by the average mineral density of bone ($\rho_m = 1.053 \text{ g/cm}^3$), as in HSA. Although differing from original publications, these scalar adjustments should have no bearing on correlations but should permit easier comparisons across methods.

Simple Strength Indices—Two simple strength indices were computed using 3 of the 4 methods. In a fall mode the femoral neck will be subjected to a complex combination of axial compressive and bending stresses. Very simple indices of strength in pure axial compression (CSI) and pure bending (BSI) can be computed as:

$$CSI = \frac{A}{F}$$

$$BSI = \frac{Z}{M}$$

Where A and Z are the bone surface area and section modulus, respectively of that surface in the femoral neck cross-section, F is the axial force and M is the bending moment. For simple indices F was assumed to be body weight (BW) converted to Newtons (N) by multiplying by the acceleration due to gravity (9.8 m/s^2). The bending moment M was taken to be BW (N) x femoral neck axis length (FNAL) in m. FNAL is the distance along the femoral neck axis from the lateral margin of the base of the greater trochanter to the apex of the femoral head as measured by the DBA method. The geometric parameters A and Z are computed individually by the three methods; hence any difference between CSI and BSI is due only to those differences.

DXA-Derived Methods

DBA Method: The two strength indices were calculated for the femoral neck using femoral neck region areal BMD derived by the DXA scanner software to estimate A and Z [5]. For Compressive Strength Index (CSI_{DBA}) the bone surface area (A in m²) was estimated as $(BMD * FNW) / (\rho_m * 10^4)$, where ρ_m is the mineral density of adult cortical bone (1.053 gm/cm^3). For Bending Strength Index (BSI_{DBA}) the section modulus (Z in m³) was estimated as $(BMD * FNW^2) / (\rho_m * 10^7)$. Femoral neck width (FNW) was measured as the smallest diameter of the femoral neck along any line perpendicular to the femoral neck axis in the DXA image. Measurements of FNAL and FNW were each performed using the scanner manufacturer's region of interest (ROI) window, which was repositioned and resized by the operator so that a side of the ROI window spanned the geometric measure of interest. Pixel coordinates of relevant window corners were recorded and used with the manufacturer's pixel spacing to calculate the relevant distances along the desired vector.

HSA method: The HSA program uses the distribution of mineral mass in a line of pixels across the bone to measure geometric properties of cross-sections in cut planes traversing the bone at that location [12,13]. Measurements for five parallel mineral mass profiles spaced ~1 mm apart along the bone axis were averaged, effectively corresponding to a ~5-mm section thickness. Although three regions are analyzed, only the narrow neck (NN) cross-section across the narrowest point of the femoral neck was used here. Bone cross-sectional area (A , m²) and cross-sectional moment of inertia (I_x , m⁴) were measured directly from mineral mass integrals using algorithms detailed elsewhere [13]. Section modulus (Z_x in m³) was then computed as I_x / d_{max} where d_{max} is the maximum distance from the section center of mass to the medial or lateral cortical surface in the image plane. Neck-shaft angle (α) and neck length (NL) were measured by HSA as was the distance from the center of the femoral head to the narrow-neck cross-section. CSI_{HSA} and BSI_{HSA} were computed using A and Z computed by HSA. For STR_{HSA} , the strength estimate was computed using an engineering analysis restricted to the frontal plane due to limitations of 2D DXA. The method is described in abbreviated detail in the Appendix.

QCT Derived Methods

QCA Method: Software developed at Mayo Clinic (Rochester, MN) was used to reformat and segment a cross-section through the femoral neck as described previously [7]. The program first defines the orientation of the proximal end such that the nearly flat anterior surface of the femur in the trochanteric region is horizontal in the transverse view, and the shaft of the femur is vertical in the sagittal and coronal views. This puts the axis of the neck of the femur into the frontal plane, allowing the neck angle to be directly measured, and the oblique neck cross section to be specified in an orthogonal plane. A single mid-level cross-section of the femoral neck is extracted in a plane orthogonal to the neck axis at mid neck length using 3D cubic spline interpolation. This is repeated for a total of 5 parallel sections along the neck spaced at ~ 1mm intervals, i.e., two additional sections on either side of the initial section. All measurements are averaged over the 5 sections to improve precision. Image voxels are linearly scaled to calibration phantom values scanned with the patient so that an image of mineral content in mg/cm³ is formed. This image is used for segmentation and for mineral density measures.

Whole bone cortical and trabecular compartments are segmented from the mineral content image by separate thresholds employing full-width half maximum arguments to define the outer cortical and endocortical boundaries [7]. All area, mineral density and biomechanical measurements are made using these segmentation schemes. The cortical region from both segmentations is used first to compute the cortical area, then the cortical bending moment of inertia about the image x axis:

$$I_x = \sum_{i=1}^N \frac{wh^3}{12} + whd_i^2$$

Where w and h are the width and height of an image pixel (out of scan plane pixels are not necessarily square), respectively and d_i is the distance of the pixel from the neutral axis. I_x corresponds to bending in the frontal plane, comparable to that computed from 2D DXA data. Section modulus in that plane is computed by dividing I_x by the maximum distance from the center of mass of the cross-section to the medial or lateral outer cortex. Note that since only cortical area, which bears most of the load, was used in section modulus (Z) and area (A), these values are somewhat smaller than those computed by HSA which integrates both cortical and trabecular components. The STR_{QCA} used the same 2D beam analysis method described in the Appendix, although using the (cortical) surface properties (A and Z) from QCT.

FEA Method: Finite element models were constructed of the left proximal femur using custom software (O.N. Diagnostics, Berkeley, CA) [2,9,14]. A uniform threshold was used to segment the proximal femur from each CT image and the analyst semi-manually filled any discontinuous edges. The images were re-sampled into 1.5 mm cubic voxels, and the finite element mesh was constructed by converting each voxel into a cube shaped, 8-noded brick element. Boundary conditions were applied to simulate a severe, unprotected fall to the side of the hip, assuming that the diaphysis was angled 10° to the ground surface with 15° of internal rotation. To ensure consistent orientation, each bone was registered to a reference bone in the fall orientation. The cortical and trabecular bone regions in these models were distinguished from each other on the basis of apparent density (cut point of 1.0 g/cm³) and to account for partial volume effects element-specific isotropic material properties were derived from calibrated volumetric BMD values using empirically derived formulas, with different formulas for cortical and trabecular bone regions [15–17].

After creation of the finite element models, nonlinear stress analyses were performed using a custom finite element program to estimate femoral strength. Femoral strength in the fall configuration was calculated from the resulting nonlinear force-deformation curve and defined as the force needed to produce a 4% deformation of the femoral head with respect to the impact point on the greater trochanter.

Statistical Analysis

In our comparisons we distinguish between strength indices and strength estimates. The former provide a value that should correlate with force necessary to cause structural failure while the latter estimates the force directly. We benchmark the simple compressive and bending strength indices against the QCA method where cortical geometry of femoral neck cross-sections are measured from 3D QCT data. The strength estimates were benchmarked with the FEA analysis which employs the fewest approximations in geometry and uses the most realistic 3D loading condition to simulate the fall impact. Spearman correlation coefficients were computed to compare corresponding strength indices from DXA and QCT derived by the different methods. These correlation coefficients are a measure of how similarly the various indices rank participants in the sample. We chose to use correlations rather than to conduct a Bland-Altman analysis because the strength indices from the different methods are not cross-calibrated. Due to exclusions for metal implants, incomplete scan acquisition and participant motion, the final data available for analysis included DBA (n=213), HSA (n=210), QCA (n=209) and FEA (n=195).

RESULTS

The demographic characteristics of the mainly Caucasian women in the QCT sub-set of the Hip Strength Across the Menopausal Transition ancillary study are listed in Table 1. The mean and coefficient of variation (CV; $100 \times \text{SD}/\text{mean}$) values of the femoral neck conventional areal BMD, strength indices, and strength estimates are shown in Table 2 and in a correlation matrix in Table 3; non-significant correlations are not shown. Note that CSI values correspond well between the three methods with R values between 0.83 and 0.92, with best correlations between the two DXA-based methods. To better illustrate the scatter patterns of relationships, the DBA and HSA compressive strength indices (CSI) are plotted in Figure 2a with QCA value plotted on the horizontal axis. Bending strength indices (BSI) are similarly plotted in Figure 2b, again as a function of the benchmark QCA value. Correlations between methods are somewhat worse than with CSI although still relatively good, ranging from 0.65 to 0.72. In Figure 2c the HSA estimate of fall mode strength is plotted with the reference FEA method on the horizontal axis. Note that while the HSA strength estimate correlates significantly with FEA, the correlation is modest.

In clinical practice areal BMD is used in fracture prediction. It is also viewed as a surrogate indicator of bone strength. The three different strength estimates are plotted as a function of BMD in Figure 2d. All are significantly correlated with BMD, though with similar underlying mathematics the correlations (Table 3) are poorer with HSA and QCA methods. BMD correlated better with the strength estimate from the most complex FEA estimate and less well with those using the 2D loading model employed in the HSA and QCA methods.

DISCUSSION

Bones fail when external forces generate internal stresses (force concentrations) that exceed material stress limits. It is impossible to measure that force without actually breaking the bone. Engineering simulations are commonly used to predict the strength of objects where it is impractical to test them to failure. An accurate simulation requires information about the structural geometry (dimensions) and the loading conditions (applied forces and their

directions) to compute stresses within the model. We generated strength estimates using engineering simulations as well as ‘strength indices’. The latter are simple parameters that should correlate with strength whereas the former should approximate the force necessary to cause failure. Our main goals were to evaluate 1) how well simple DXA-derived strength indices compare with those using QCT and 2) how well estimates of strength to failure using a 2D proximal femur model compares with a more sophisticated 3D FEA simulation. We compared two different strength indices computed by three different methods as well as two methods for acquiring a strength estimate from an engineering model.

The strongest correlations across methods were obtained for the simplest CSI and BSI strength indices rather than for the more complex estimates of bone strength. CSI and BSI basically rely on measurements or reasonable estimates of bone cross-sectional area and section modulus in the plane of bending, respectively. The simple estimation of bone cross-sectional area (A) using BMD and outer diameter by the DBA method correlated well ($R=0.92$) with the HSA method calculated from the mineral profile integral. Both methods also correlated well with the QCA CT-based method (Fig 2a). One could conclude that if pure axial compression were a likely failure mode for the femoral neck, CSI computed by the simplest DBA method should provide a good index of femoral neck strength. BSI derived using body weight $\times$ hip axis length as the bending moment also agreed well between DBA and HSA methods ($R=0.70$) and both correlated reasonably well with the benchmark QCA method ($R=0.65$ and 0.72 , respectively). Unlike bone cross-sectional area (A), however, section modulus (Z) requires information about the distribution of bone mass in the cross-section. The DBA method uses an outer diameter squared term to approximate the nonlinear weighting of areal distance from the center of mass in the image plane while HSA measures the distribution weighting directly. Since CSI and BSI differ only in the method for generating the important parameters A and Z , one can conclude that the parameters are reasonably well computed by HSA and even by the approximations used in the DBA method. These results are consistent with a more comprehensive *in vivo* study that compared HSA geometry to QCT [18]. Greater effort was expended in that study to ensure correspondence between HSA and QCT cross-section locations and orientations than was done in the present work; hence their correlations were somewhat better than ours. Investigators in that study effectively eliminated femur positioning error, the main source of imprecision in HSA [19]. Given valid geometry from DXA data, we can conclude that femur stresses generated with 2D engineering models used here should be adequate for computing femur stresses in the larger SWAN study.

Extending those 2D stress estimates to estimate strength to failure in the osteoporotic femur is more problematic. The 2D models used with the femoral neck geometry by DXA and QCT were significantly correlated with 3D FEA models but the modest R values do not support the conclusion that they are equivalent. As we do not have fracture cases or a true gold standard, we cannot conclude which model better predicts future fracture in this relatively young, early post-menopausal cohort. There are a number of important differences between the 2D and 3D models that may help to explain disparate results: 1) The 2D model constrains forces to the frontal plane, while the FEA model more realistically oriented the impact force 15 degrees out of this plane; 2) The FEA method evaluates the entire proximal femur rather than just a single femoral neck cross-section that may not include the weakest point; and 3) Failure load is estimated in 2D models as the force necessary to cause stress in the femoral neck cross-section to exceed a literature value of bone compressive strength. The FEA model computes the force necessary to cause a 4% deformation of the model; these failure criteria are probably not equivalent. Strength estimates using 2D models were consistently higher than with FEA in this study.

These issues may help to explain method differences in strength estimates. Beyond the limitation (to all methods) that material strength is unknown, there were further limitations regarding the modeling of cortices in both methods. Reasonably accurate cortical models may be important in evaluating femoral fragility because fall impacts tend to concentrate high compressive stresses on the superior-lateral cortex especially in the osteoporotic femoral neck [20]. These cortices tend to thin with age and become poorly supported by sparse internal trabeculae [21]. High speed video imaging under experimental fall simulations on osteoporotic femora indicates that failure initiates at the thinned cortex, possibly by local buckling [22]. This is an important observation since tubular objects under combined bending and axial compression should fail in tension unless local buckling occurs. If local buckling is responsible for failure, specialized engineering analyses are needed to evaluate it since the process causes rapid changes in geometry as failure progresses [23,24].

It may be possible to further improve QCT based FEA models with accurate cortical simulations so that local buckling may be assessed. A recent study reported that de-convolution methods can accurately recover cortical thicknesses from current generation QCT scans even in very osteoporotic bones [25]. This brings up the possibility that specialized local buckling analyses could be incorporated into future *in vivo* QCT based engineering methods as done by Lee and colleagues on cadaveric material [24].

The correlations between femoral neck BMD data and the strength estimates (Figure 2d) are worthy of comment. While BMD is not itself a property of bone that determines strength, there is considerable evidence that BMD measurements tend to correlate with bone strength and with fracture risk. The correlation between BMD and the three strength estimates was strongest with the FEA method. This may suggest that the two methods better capture similar aspects of femur strength.

This study had a number of limitations. First, our sample size was confined to a sub-set of mainly Caucasian early post-menopausal women enrolled at the Pittsburgh study site thus limiting our ability to generalize the results to the larger population of women or to men. However, correlations were not significantly different when the analysis was limited to Caucasians. Second, the methods used to calculate proximal femur strength and structure are inherently different and have unique limitations. DXA methods measure geometry reasonably well and could be useful in estimating stresses under certain loading conditions in research studies where the limited precision of 2D methods can be overcome with statistical power. It is clear however that failure of the complex 3-dimensional hip is not likely to be accurately depicted by a 2D method. On the other hand, the QCA analysis restricted the geometry to the cortical shell of the femoral neck. This may be responsible for the (weak) negative correlations between BMD and other parameters with some QCA method results.

We cannot assume that the strength of the baseline, cross-sectional correlations between DXA and QCT methods will remain when examining longitudinal change; i.e. if differential changes in cortical and trabecular bone occur over time they would be detected by QCT methods but not necessarily by DXA methods. Finally, because this is a cross-sectional study, we were unable to compare the ability of the various DXA- and QCT-based measures of bone strength and structure to predict fracture, the ultimate insult of osteoporosis.

Our study has a number of strengths as well. This was perhaps the first study to directly compare several validated DXA- and QCT-based methods of assessing proximal femur strength and structure in a sample of women. Although inherent differences existed between the methodologies, an attempt was made to make them more comparable by use of consistent measurement units. While we were not able to compare the ability of DXA- and

QCT-derived measures to predict hip fracture, we will be able to examine the predictive capability of HSA and the DBA indices since we obtained DXA scans of the proximal femur and collected incident fracture data on the larger study cohort.

In conclusion, we observed significant correlations between DXA- and QCT-derived femoral neck geometry on a subset of women from the Study of Hip Strength Across the Menopausal Transition. Results showed good correlations between simple strength indices indicating that the geometry of femoral neck cross-sections is reasonably well characterized by DXA methods. These results indicate that geometry based stress analyses are valid and that simple indices generated from conventional BMD also have value [5]. While we did find significant correlations between proximal strength estimates by 3D FEA and 2D HSA based analyses, the correlations were poorer and did not suggest equivalence. We conclude that the simulation of femoral failure is best handled in a 3D engineering model. The wider availability of DXA scanners and the lower radiation exposure in a DXA scan make the DXA-based methods attractive for clinical research applications.

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APPENDIX: 2D beam analysis used for strength estimates by HSA and QCA methods

The free-body diagram of the femur simulating a fall impact is depicted in Figure 1a. F_I is the ground reaction force assumed to be equal to body weight (W), F_H is the force acting through the center of the femoral head force assumed to be approximately equal to 5/6 of the body weight, and F_S is femoral shaft force assumed to be equal to 1/6 of the body weight [26]. The shaft axis was assumed to be inclined 10° to the ground surface at impact (θ). Forces and moments were balanced to achieve static equilibrium, where l_1 and l_2 were derived as:

$$l_1 = NL \cdot \cos(\theta(180 - \alpha - \theta))$$

$$l_2 = 5 \cdot NL \cdot \cos(\theta(180 - \alpha - \theta))$$

Internal Forces in the neck resulting from external forces F_F , F_H and F_S are shown in Figure 1b, where M_F , P_F and V are bending moment, axial load and shear force, respectively, on the cross-section.

The small shear forces were neglected.

$$M_F = F_{H2} = \frac{5}{6} W \cdot d \cdot \sin(\alpha + \theta - 90^\circ)$$

$$P_F = F_{H1} = \frac{5}{6} W \cos(\alpha + \theta - 90^\circ)$$

Using engineering beam theory, axial stresses on the medial and lateral surface of the femoral neck are computed:

$$\sigma = \pm \frac{M_F \cdot y}{I_x} + \frac{P_F}{A}$$

Where M_F and P_F are the bending moment and axial load on the cortical cross-section, and y is the perpendicular distance from the neutral axis of bending (from HSA). By convention stresses on the lateral surface, in compression are positive while at the medial surface, the bending moment produces negative tensile stress. Strength estimates were then derived as:

$$F_s = F_i \frac{\sigma_y}{\sigma}$$

Where σ_y = ultimate yield stress in compression for cortical bone tissue [27]. Note that strength was also evaluated in tension on the medial surface in both HSA and QCA models but without exception, values were smaller on the compressive surface hence only the latter were used.

Fig 1a

Fig 1b

Figure 1.

Figures 1a and 1b: Free body diagram of femur used in 2D beam analysis in simulation of a fall impacting the greater trochanter. This configuration was used with femoral neck geometry derived from DXA by HSA as well as that extracted by QCT using the QCA method (see Appendix).

Fig 2a

Fig 2b

Fig 2c

Fig 2d

Figure 2.

Figure 2a: Compressive strength indices (CSI) computed from DXA data using DBA and HSA methods compared to those using QCA algorithms from QCT scan data. Note that CSI estimates only differ by measurement of bone cross-sectional area. R values are listed in Table 3.

Figure 2b: Bending strength indices (BSI) computed from DXA data using DBA and HSA methods compared to those computed using QCA algorithms for deriving frontal plane femoral neck cortical section modulus from QCT scan data. BSI estimates only differ by measurement of section modulus. R values are listed in Table 3.

Figure 2c: Strength estimates computed using 2D beam models employing femoral neck geometry from HSA and QCA methods as a function of the 3D FEA estimate. R values are listed in Table 3.

Figure 2d: Strength estimates computed using 2D beam models employing femoral neck geometry from DXA and QCT using HSA, QCA methods, and FEA methods as a function of conventional DXA femoral neck BMD. R values are listed in Table 3.

Table 1Demographic characteristics^a of women in the SWAN QCT sub-set

	n=213
Age (yr)	57 (2.5)
Caucasian Race/Ethnicity (n, %)	143 (67.1)
Height (cm)	161.6 (6.2)
Weight (kg)	79.1 (17.4)
Post-Menopause ^b (n, %)	194 (91.1)

^aData are presented as mean $\pm$ SD unless specified otherwise;^bLate peri-menopause (n=5), early peri-menopause (n=5), and missing (n=4).

Table 2

Mean and percent coefficient of variation (CV, $100 \times SD^a/\text{mean}$) of conventional femoral neck areal BMD, strength indices^b and strength estimates^c

Variable	Mean	% CV
Areal BMD (g/cm ²)	0.823	18
CSI _{DBA} (m ² /N)	3.24E-07	15
CSI _{HSA} (m ² /N)	2.89E-07	20
CSI _{QCA} (m ² /N)	3.48E-07	21
BSI _{DBA} (m ² /N)	8.97E-09	18
BSI _{HSA} (m ² /N)	1.78E-08	21
BSI _{QCA} (m ² /N)	2.43E-08	21
STR _{HSA} (kN)	16.2	20
STR _{QCA} (kN)	12.5	23
STR _{FEA} (kN)	4.43	25

^aSD=standard deviation.

^bBSI_{dba}=Bending Strength Index using DXA areal BMD-based analysis, BSI_{HSA}=Bending

Strength Index using Hip Structure Analysis, BSI_{QCA}=Bending Strength Index using QCT-based analysis of femoral neck cross sections, BSI_{FEA}=Bending Strength Index using 3D Finite Element Analysis, CSI_{dba}=Composite Strength Index using DXA areal BMD-based analysis, CSI_{HSA}=Composite Strength Index using Hip Structure Analysis, CSI_{QCA}=Composite Strength Index using QCT-based analysis, CSI_{FEA}=Composite Strength Index using Finite Element Analysis

^cSTR_{hsa}= Strength estimate using Hip Structure Analysis; STR_{QCA}=Strength estimate using QCT-based analysis; STR_{FEA}=Strength estimate using Finite Element Analysis.

Table 3

Spearman correlation coefficients between conventional femoral neck areal BMD, strength indices^a, and strength estimates^b

	BMD _{DXA}	CSI _{DBA}	BSI _{DBA}	CSI _{HSA}	BSI _{HSA}	STR _{HSA}	CSI _{QCA}	BSI _{QCA}	STR _{QCA}	STR _{FEA}
BMD _{DXA}	1.000	(NS)	0.31	(NS)	(NS)	0.41	-0.22**	-0.31	0.31	0.62
CSI _{DBA}		1.00	0.76	0.92	0.85	(NS)	0.85	0.70	-0.22**	0.36
BSI _{DBA}			1.00	0.69	0.70	(NS)	0.68	0.65	(NS)	0.34
CSI _{HSA}				1.00	0.92	(NS)	0.83	0.67	-0.26	0.33
BSI _{HSA}					1.00	0.21	0.77	0.72	-0.14*	0.35
STR _{HSA}						1.00	(NS)	(NS)	0.76	0.56
CSI _{QCA}							1.00	0.86	-0.20**	(NS)
BSI _{QCA}								1.00	(NS)	(NS)
STR _{QCA}									1.00	0.35
STR _{FEA}										1.00

^aBSI_{DBA}=Bending Strength Index using DXA areal BMD-based analysis, BSI_{HSA}=Bending Strength Index using Hip Structure Analysis, BSI_{QCA}=Bending Strength Index using QCT-based analysis of femoral neck cross sections, BSI_{FEA}=Bending Strength Index using 3D Finite Element Analysis, CSI_{DBA}=Composite Strength Index using DXA areal BMD-based analysis, CSI_{HSA}=Composite Strength Index using Hip Structure Analysis, CSI_{QCA}=Composite Strength Index using QCT-based analysis, CSI_{FEA}=Composite Strength Index using Finite Element Analysis

^bSTR_{HSA}= Strength estimate using Hip Structure Analysis, STR_{QCA}=Strength estimate using QCT-based analysis, STR_{FEA}=Strength estimate using Finite Element Analysis.

P<0.001 except where noted;

* p<0.05;

** p<0.005; NS=not significant.