DXA and QCT Geometric Structural Measurements of Proximal Femoral Strength

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Abstract

Introduction:
The worldwide annual incidence of hip fracture is approximately 1.7 million and the projected increase by 2050 is 6.26 million. In the presence BMD measurements have provided the gold standard of assessing the risk of fracture, but this approach does not reflect to bone geometry and clinical risk factors. Proximal femoral strength consists of the distribution of bone mass, diameter, area, length and angle of the femoral neck. Commercial software applications calculate bone distribution variables such as CSMI, CSA, HAL, angle of femoral neck or FSI. They can be either obtained by DXA absorption curves (2D measurement) or by QCT scans (3D measurement).

Patients and Methods:
93 clinic and outpatient individuals (cross sectional, not population based) were consecutively measured with a mean age of 67.6 ± 11.97 years with femur neck BMD between 0.452 to 1.171 g/cm² (mean 0.795 ± 0.126 g/cm²). DXA measurements (Lunar iDXA) were compared with CT scans (Mindways QCT Pro).

Results
The study population showed high correlations for CSMI (r = 0.91), CSA (r = 0.87), and HAL (r = 0.94) between the two measurement systems. After splitting into normal, osteopenic, osteoporotic subgroups the correlations became weaker by decreasing T-score, especially at femoral neck BMD. The coefficient of variance of QCT on cortical thickness, cortical BMD and center of mass was highly significant within the three groups.

Conclusion:
DXA and QCT have very high correlations on parameters of bone strength and biomechanical quality, but they have different approaches of measurement (X-ray absorption curves versus structural measurement).
Also assessment of clinical risk factors must be considered as part of the patient’s individual risk of sustaining an osteoporotic fracture.

Key Words:
Proximal femoral strength, geometric structural measurements, DXA, QCT
Epidemiology of Osteoporotic Fractures

Osteoporosis is considered as a serious public health concern. Currently it is estimated that over 200 million people worldwide suffer from this disease [1]. Approximately 30% of all postmenopausal women have osteoporosis in the United States and in Europe. At least 40% of these women [2] and 15-30% of men [3] will sustain one or more fragility fractures in their remaining lifetime. Ageing of populations worldwide will be responsible for a major increase of the incidence of osteoporosis in postmenopausal women [4].

An initial fracture is a major risk factor for a new fracture. People that have already sustained a fracture [5] have an increased risk of 86% for any fracture. Patients with a history of vertebral fracture have a 2.3-fold increased risk of future hip fracture and a 1.4-fold increase in risk of distal forearm fracture [6].

A hip fracture is associated with serious disability and excess mortality. Women who have sustained a hip fracture have a 10-20% higher mortality compared to aged matched non-osteoporotic individuals [7].

The worldwide annual incidence of hip fracture is approximately 1.7 million [8]. The incidence of hip fracture rates varies between populations. After age adjustment, hip fracture rates are more common in Scandinavian and North America than these observed in southern European, Asian and Latin American countries. There are wide discrepancies between the incidence rate in women and men: the sex ratio F/M is 4/5 and 90% of the hip fractures occur in people over 50 years old with a vast increase at the 7th decade of life [9].

By 2050, the worldwide incidence of hip fracture is projected to increase by 240% in women and 310% in men [10]. The estimated number of hip fractures worldwide will rise from 1.66 million in 1990 to 6.26 million in 2050, even if age-adjusted incidence rates remain stable [9].
Assessment of Risk Factors

For decades bone mineral density (BMD) measurements have provided the gold standard of assessing the risk of fracture, based on the WHO classification of osteoporosis as a bone mineral density 2.5 standard deviations or more below peak bone mass (T-score -2.5) [26]. But this approach captures only a small proportion of these individuals who will suffer a fracture and does not reflect to clinical risk factors, geometry or micro architecture of bone. BMD itself is only one component of bone strength.

Clinical risk factors act independently of BMD and increase the risk of fracture. They optimize sensitivity (i.e. detection rate) of fracture risk prediction and should be implemented in primary care to identify patients at risk of osteoporotic fracture. The predictive value of clinical risk factors has been studied in a number of large, prospectively studied population-based cohorts. Easily identifiable risk factors shown to improve the prediction of fracture risk include the following:

- age
- previous fracture
- family history of hip fracture
- glucocorticoid (steroid) use
- current smoking
- alcohol use >2 units/day
- rheumatoid arthritis

Individually the presence of these risk factors increases the risk of hip fracture at least 1.5 to 2-fold after adjustment for bone mineral density [11].

Assessment of BMD and Geometric Properties of the Femur

Measurement of BMD with dual energy X-ray absorptiometry (DXA) is the most commonly used technique for diagnosing osteoporosis, estimating fracture risk by reduced BMD [12] or evaluating success of medication. But simple increases in bone
mass do not necessarily increase the bone’s load bearing capacity. Reliance on BMD alone may not provide the best predictive ability to identify individuals with increased risk for hip fracture.

Proximal femoral bone strength is not only a function the spatial distribution of bone mass intrinsic in structural geometric properties. Geometric properties including distribution of bone mass, diameter, area, length and angle of the femoral neck provide further information and can be used in calculations of quality of bone [13]. Fractures occur when mechanical stress on bone exceeds local material strength [14].

Geometric information is contained in the absorption curves generated by DXA. The X-ray absorption curve (pseudo-bone mineral, PBM) provides information not only about the amount of bone mineral such as BMD (g/cm²), bone mineral content (BMC, g) or area (cm²) but also about its distribution. The length of the X-ray path g(x) corresponds to the absorption value, factor $\kappa$ converts PBM into BMC and factor $\rho$ is the assumed physical density of bone (1.85 g/cm³) [15] Fig 1.

According to this commercial manufacturer’s analysis software applications automatically calculate a number bone geometry variables of the femur from the scan image and the bone distribution variables derived from the DXA absorption curves [15,16] Fig 2.

- CSMI (mm⁴), *cross sectional moment of inertia* of the section of minimum CSMI within the neck region of interest (ROI) describes femur geometry and density and its resistance to bending from a biomechanical point of view.
- CSA (mm²), *cross sectional area* of the minimum CSMI within the neck region of interest (ROI)
- $d_1$ (mm), distance from the center of the femoral head to the minimum CSMI
- $y$ (mm), distance from the centroid (center of mass) to the superior neck region of minimum CSMI. The superior neck region is of special interest due to higher bone loss in age compared to the whole femoral neck [17].
\[ \theta \text{ (degrees), angle of femoral neck} \]

\[ \text{HAL (mm), hip axis length, distance measured along the axis of the neck from the base of the trochanter to the inner pelvic rim [15].} \]

These variables can be used to calculate femur strength index (FSI), which is the ratio of estimated compressive yield strength of the femoral neck to the expected compressive stress of a fall on the greater trochanter. The greater the FSI, the lower is the risk for hip fracture from a fall on the great trochanter. Faulkner et al published DXA data of the proximal femur obtained from 2,506 postmenopausal women. 365 of them had a record of prior hip fracture and 2,141 were controls without hip fracture. According to his findings femoral neck BMD was significantly lower in the fracture group. FSI, after adjustment for T-score and HAL, was significantly lower in the fracture group. An increase of HAL equivalent to 1 standard deviation (SD) was associated with a 1.8 fold increase in the risk of hip fracture in women [14]. Other studies have also appeared in support of the predictive power of HAL for hip fracture [13,18,19]. But there are also studies questioning the predictive power of these variables [20, 21].

In the Faulkner study mean CSMI at femoral neck showed no significant difference between the fracture and the control group after adjustment for BMD and HAL. However recent studies investigated the clinical use of this variable in comparison to the morphology of the upper femur and focused on the risk for trochanteric and cercival hip fractures. A longer femoral neck is associated with a higher risk of cervical fractures, but not trochanteric ones.

Szulc et al published a nested case-control study that was performed in 232 elderly community-dwelling women from the EPIDOS cohort, including 65 women with hip fracture. After adjustment for confounding variables, women who sustained a cervical fracture had lower areal bone mineral density (aBMD), lower cortical thickness and a higher average buckling ratio (highly significant for all values) as well as longer femoral neck (P<0.01) than controls. Women who sustained a trochanteric fracture had significantly lower aBMD, lower cortical thickness and higher buckling ratio than controls or women who sustained a cervical fracture. Their CSMI was significantly
lower in comparison with controls. A decrease in aBMD, cortical thickness, CSMI and section modulus as well as an increase in buckling ratio were predictive of all hip fractures [22]. Also smaller femoral neck diameter (FND) is associated with increased risk for hip fracture in both men and women. Lower CSMI values appear to have the same predictive power for increased risk factors for hip fracture in men and women [23].

The Vienna Hip Study

Introduction

The reproducibility of femoral neck BMD, CSA, CSMI, FSI by DXA measurement have been reported to be between 1% and 5% [15,24]. Still it is under debate to measure a 3 dimensional structure like the femur with proportions of cortical and trabecular structures with an X-ray absorption curve. DXA measurements are projectional and therefore influenced by changes in geometrical configuration. Inconsistency and non-standard femur positioning may result in inaccurate femoral structural dimensions. QCT measurement of hip is also a biomechanical approach for assessment of fracture risk and parameters of hip geometry [25], because QCT may provide improved accuracy due to its ability to locate the correct frontal plane and generate the appropriate projection image, thus eliminating variations and uncertainties in structural measurements due to patient positioning. QCT also distinguishes between cortical and trabecular bone. The aim of our study was the comparison of the individual patient with DXA femoral geometric dimension measurements and similar measurements acquired with QCT.

Methods

93 female and male patients (clinic and outpatient; cross sectional, not population based) were consecutively measured from 37 to 91 years of age (mean 67.6 ± 11.97 years) with femur neck BMD between 0.452 to 1.171 g/cm² (mean 0.795 g/cm² ± 0.126 g/cm²). DXA (Lunar iDXA, software version 11.2, GE Healthcare) measurements were compared with CT (Phillips MX8000 4-slice CT, 3.2 mm slices) measurements. The iDXA automatically measures CSMI as the minimum CSMI in the neck ROI, and CSA of the minimum CSMI line in the neck ROI. These are often
found in the narrowest section of the neck, but may occur further up the neck due to individual variation in location of center of mass. The iDXA also automatically measures HAL, the distance from the lateral aspect of the greater trochanter, along the femoral neck axis, to the inner pelvic brim.

A QCT application (QCT PRO version 4.1, Mindways Software, Inc) that generates measurements of CSMI, CSA, and HAL from cross-sectional images was used. The QCT cross-sectional image was chosen at the narrowest portion of the femoral neck to most closely duplicate the DXA measurement site. During analyses of the DXA and CT scans it was detected that these two measurements might not match exactly. The CSMI generated by both DXA and QCT reflect bone porosity and degree of bone mineralization. The assumed physical density value used by DXA was 1.85 g/cm\(^3\), while the value used in the QCT calculations was 1.05 g/cm\(^3\). Therefore, normalized CSMI and CSA values derived from QCT by the ratio of 1.85/1.05 were calculated. Regression analysis and paired T-tests were used to test for significant differences between DXA and QCT results.

Primary objectives of the study were calculations of the values of femoral bone geometry for the whole study population. Secondary objectives were the partition of the study population into normal, osteopenic and osteoporotic individuals according to WHO-criteria and T-score at femoral neck [26]. 21 individuals were identified as normal, 57 were osteopenic and 15 individuals were considered as osteoporotic at femoral neck.

**Results**

Results of the whole study population showed high correlations for CSMI (r = 0.91), CSA (r = 0.87), HAL (r = 0.94) and femoral neck BMD (r = 0.91 between the two measurement systems, but DXA and QCT values were significantly different in all cases (Table 1, Figures 2-5). The intercept for CSA and HAL was not significantly different from zero, and the HAL slope was not significantly different from identity. Femur neck BMD by DXA was highly correlated with QCT results (r = 0.91) Table 1, Figures 3 - 6.

After splitting into the three subgroups according to the valid WHO classification [26] (normal, osteopenic, osteoporotic) the correlations became weaker by decreasing T-score, especially at femoral neck BMD (range of correlation 0.76 – 0.38) and CSA.
Correlations of CSMI (range 0.93 – 0.66) and at HAL (range 0.95 – 0.85) sustained at high level [27].

The coefficient of variance of QCT on cortical thickness, cortical BMD and center of mass was highly significant within the three groups Figures 7-8. The comparison of the coefficient of variance on CSMI measured by DXA and QCT showed almost equal, but significant high values in all three groups and at both techniques. Figures 9-10.

**Discussion**

Very good agreements were detected between DXA and QCT measurements of several structural variables of the femur that are related to bone strength and fracture risk. The correlations between the measurement for CSMI, CSA, and HAL are 0.91, 0.87, and 0.94 respectively. Although the measured values of HAL showed a small but significant offset difference between DXA and QCT measurements, the slope and intercept were not significantly different from identity and zero, respectively. Somewhat larger differences were shown for the structural variables (cortical thickness, cortical BMD) derived from DXA absorption curves and QCT cross-sectional images.

A 4 slice CT-scanner (scan thickness 3.2 mm) was used. From a technical point of view a scanner with higher resolution (e.g. 16 or 64 slices CT scanner) is considered to have no statistical influence on the quality and quantity of the hip measurement results.

Additional measurement differences between DXA and QCT may be due to difficulties in positioning of femur DXA scans. These scans are completed with the leg rotated internally about 25° to eliminate femoral head anteversion, a normal situation where the axis of the femoral shaft is positioned posterior to the femoral head and the femoral neck is not parallel to the table surface. If anteversion is not corrected, a cross-sectional slice taken through the bone occurs at an oblique rather than a right angle to the bone. As a consequence the cross-sectional image used in deriving structural measurements (CSMI, CSA) will be distorted. Also, individuals differ in the degree of femur anteversion, and standard femur rotation prior to DXA scanning may not adequately compensate for these differences among different subjects [28].
There is a high correlation between DXA and 3D QCT measurements of femur neck BMD ($r = 0.91$). The HAL offset apparent in Figure 5 may in part be related to differences in positioning of the measurement site between DXA and QCT. DXA measurement algorithms for femur neck BMD locate the cross section along the neck with the lowest BMD. This measurement position is often - but not always - located at the narrowest part of the femoral neck.

The QCT measurement is always taken at the narrowest part of the femoral neck in a cross sectional image, so differences in measurement location could contribute to the BMD differences seen between DXA and QCT in this study. Furthermore QCT splits the cross sectional image of the narrowest part of the femoral cervix into 16 sectors and differentiates between the outer margin, the corticalis, the center of mass and the geometric center. Statistically significant differences in the coefficient of variance over the 16 sectors could indicate an increased inhomogeneity of osteoporotic bone in comparison to healthy or osteopenic bone. The diverse variance of the subgroups (normal, osteopenic, osteoporotic) could also have a statistical or in the broader sense spurious influence on parameters of correlation.

DXA is an area measurement [15]. As people are aging their bones grow larger, and the structural changes are caused by internal bone loss and increased outer diameter. An apparent stable density which is being measured can actually be a larger, compensating quantity of bone when in fact density is decreasing. BMD alone seems to be the wrong parameter being measured and used for description of mechanical quality of bone or effects of osteoporotic treatment. As it is evident the femoral cervix consists of about 70% cortical structure, but only 30% are trabecular structure. Effects of medication or distortion of micro architecture should not only be investigated at trabecular sites but also on cortical sites.

**Conclusion**

Parameters such as CSMI, CSA, HAL and FSI describe the structural strength of the bone and its ability to withstand a fall. Therefore these parameters must be taken into account for further and future studies to understand the structure and strength of the femur. DXA and QCT have very high correlations on these parameters of bone
strength and biomechanical quality, but they have different approaches of measurement (X-ray absorption versus structural measurement). Also clinical risk factors such as age, previous fracture, family history or steroid use must be considered as part of the patient’s individual risk of sustaining an osteoporotic hip fracture.
Table 1. Regressions of DXA and QCT Proximal Femur Structural Measurement and BMD. Graphs are shown in figs 3-6

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Regression Equation</th>
<th>SEE</th>
<th>r</th>
<th>P (slope=1)</th>
<th>P (intercept=0)</th>
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<tr>
<td>CSMI (cm$^3$)</td>
<td>CSMI$^\text{QCT}$ = 0.7955 CSMI$^\text{DXA}$ + 0.1343</td>
<td>0.1414</td>
<td>0.91</td>
<td>0.000</td>
<td>0.000</td>
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<tr>
<td>CSA (cm$^2$)</td>
<td>CSA$^\text{QCT}$ = 0.8032 CSA$^\text{DXA}$ + 0.0790</td>
<td>0.1210</td>
<td>0.87</td>
<td>0.000</td>
<td>0.233</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>HAL$^\text{QCT}$ = 0.9957 HAL$^\text{DXA}$ + 4.1492</td>
<td>2.8522</td>
<td>0.94</td>
<td>0.912</td>
<td>0.328</td>
</tr>
<tr>
<td>Femur Neck BMD (g/cm$^2$)</td>
<td>BMD$^\text{QCT}$ = 0.8551 BMD$^\text{DXA}$ - 0.0837</td>
<td>0.0486</td>
<td>0.91</td>
<td>0.000</td>
<td>0.004</td>
</tr>
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Fig 1 X-ray absorption curve generated by DXA (PBM = pseudo bone mineral, $g(x) =$ length of X-ray path through bone [15]
Fig 2 Bone geometry variables of the femur measured by DXA [14]

Fig 3 Comparison of CSMI (DXA vs. QCT)

\[ y = 0.7955x + 0.1343 \]

\[ R^2 = 0.8288 \]
**Fig 4 Comparison of CSA (DXA vs. QCT)**

- Equation: $y = 0.8032x + 0.079$
- $R^2 = 0.75$

**Fig 5 Comparison of HAL (DXA vs. QCT)**

- Equation: $y = 0.9957x + 4.1492$
- $R^2 = 0.8897$
Fig 6 Comparison of femur neck BMD (DXA vs. QCT)

\[ y = 0.8551x - 0.0837 \]

\[ R^2 = 0.8332 \]
<table>
<thead>
<tr>
<th>Level</th>
<th>Number</th>
<th>Mean</th>
<th>Std Error</th>
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<td>0.924375</td>
<td>0.05677</td>
<td>0.81158 – 1.0372</td>
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Fig 7  Coefficient of variance – cortical thickness QCT (P<0.001)
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<tr>
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<th>Number</th>
<th>Mean</th>
<th>Std Error</th>
<th>95%CI</th>
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<td>15</td>
<td>0.452032</td>
<td>0.03671</td>
<td>0.37910 – 0.52497</td>
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Fig 8  Coefficient of variance – cortical BMD QCT (P<0.001)
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<td>1.34534</td>
<td>0.14374</td>
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Fig 9 Coefficient of variance – CSMI QCT (P<0.001)
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<td>0.08084</td>
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<td>0.78348</td>
<td>0.09565</td>
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Fig 10 Coefficient of variance – CSMI DXA (P<0.005)
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