CTXA Hip - An Extension of Classical DXA Measurements Using QCT

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Abstract

Bone mineral density (BMD) estimates for the proximal femur using DXA are currently considered the standard for making a diagnosis of osteoporosis in an individual patient using BMD alone. We have compared BMD results from a commercial QCT BMD analysis system, CTXA Hip (see Figure 2), which provides clinical data for the proximal femur, to results from DXA. We have also used CTXA Hip to determine cortical and trabecular contributions to total BMD.

Sixty-nine patients were scanned using 3D QCT and DXA. CTXA Hip BMD measurements for Total Hip and Femoral Neck were compared to DXA results. Twenty-two women were scanned at 0,1,2 years and CTXA Hip and DXA results analyzed for long term reproducibility.

Reproducibility was 0.011 g/cm2 for CTXA Total Hip and 0.012 g/cm2 for CTXA Femoral Neck compared to 0.012 g/cm2 and 0.013 g/cm2 respectively for DXA (see Table 1). The correlation of Total Hip BMD CTXA vs. DXA was R=0.97, and for Femoral Neck (see Figure 2) was R=0.95 (SEE 0.044 g/cm2 in both cases). Cortical bone comprised 62 ± 5% (mean ± SD) of total hip bone mass in osteoporotic women.

CTXA Hip provides substantially the same clinical information as conventional DXA, and in addition provides estimates of volume-derived parameters which may be useful in evaluation of bone strength.

Introduction

Bone mineral density (BMD) estimates for the proximal femur using DXA are currently considered the standard for making a diagnosis of osteoporosis in an individual patient using BMD alone (1). Quantitative computed tomography (QCT) BMD estimates have generally been restricted to the spine or peripheral sites, with limited prospective clinical data available to form a context for interpretation of these measurements in terms of fracture risk (2,3). We have compared paired-BMD results from the CTXA Hip bone densitometer (Mindways Software Inc., Austin, TX) with DXA results in order to evaluate the clinical utility of CTXA Hip.

CTXA Hip uses 3D QCT volume data sets to generate bone projection images that visually look like those generated by DXA. CTXA Hip exploits the anatomical detail in the 3D QCT data set to segment bone from surrounding tissues rather than relying on the dual-energy imaging method of DXA. While CTXA Hip and DXA use somewhat different technologies to generate bone projection images of the proximal femur, the projection images from both devices convey the same basic information—total bone mass per projected bone area. This leads to the hypothesis that CTXA Hip BMD estimates can provide the same clinical information as that afforded by DXA.

QCT studies of the proximal femur have shown a strong relationship between bone mass and its distribution and bone strength (4), suggesting that BMD parameters derived from volumetric QCT studies of the hip can provide information useful in assessing bone strength that is not available from conventional DXA. CTXA Hip may provide more information than DXA from a study due to the greater anatomical detail accessible from the 3D QCT volume data set relative to the information present in the planar projection images intrinsic to DXA. We present cortical and trabecular BMD estimates from standard (DXA) hip ROIs derived using CTXA Hip to illustrate this point.

Materials & Methods

Subjects

Precision Study: The precision study group was made up of 22 subjects enrolled as placebo controls in an osteoporosis treatment study at the University of California, San Francisco (UCSF). These subjects were all postmenopausal osteoporotic women, aged 55 to 72 years, receiving hormone replacement therapy, calcium and vitamin D. All the women were identified as osteoporotic based on a spine or hip BMD T-score by DXA. Ten of the 22 women received three hip BMD scans over a two year interval while 12 of the women received four hip BMD scans over a three year interval.

Inter-observer Variability Study: The inter-observer variability for BMD estimates using CTXA was estimated by comparing results obtained independently by two trained operators on the same *in vivo* data set of 28 studies from a single clinical trial site.

CTXA-DXA Comparison

For comparison of CTXA Hip and DXA results, 69 patients aged 20-80 years were recruited from two clinical centers, 30 from the University of Manchester, UK and 39 from Schenectady Radiology/Ellis Hospital, Schenectady, NY. Seven patients were men and 62 were women. All subjects had DXA exams for osteoporosis, and the cohort was predominantly postmenopausal women.

Scanning Protocols

CTXA Examinations: QCT studies were performed using the QCT PRO calibration phantom and software system with the CTXA Hip analysis module. An anterior-posterior computed radiograph "scout view" was obtained by the scanner from the iliac crest to mid-thigh. Using this, the top of the femoral head to approximately 1 cm below the inferior extent of the lesser trochanter was defined graphically to define the scanning region. A contiguous series of scans was obtained, 3mm thick every 3mm, with a 40 cm display field-of-view (0.781 mm pixel size), and a standard abdomen reconstruction algorithm. Typically 40 images were obtained, with the time to acquire this image set approximately 3.5 minutes on the GE9800 and 1 minute on the Philips and ProSpeed scanners. All subject and QA data were sent to Mindways where analysis was centralized.

DXA Examinations: DXA image data were acquired and analyzed at each site according to standard procedures used at those sites, including daily calibrations for quality control. A single individual at each site was responsible for all DXA analyses. At UCSF, DXA data were acquired using a Hologic QDR1000 (Hologic, Inc., Waltham, MA) scanner, while at the other two sites Hologic QDR4500 scanners were used.

Data Analysis

CT image data were analyzed in a standardized fashion with the CTXA Hip software. A square box region of interest was centered over the femoral neck as identified on the axial images, and a volumetric region of interest containing the proximal femur was extracted from the CT image data set for analysis. Segmentation of bone from surrounding non-bone tissue was performed using an adaptive algorithm. The result of the segmentation process is a set of voxels identified as "bone" all contained within the outer cortex of the proximal femur. This 3D data set of bone voxels was then rotated such that the femoral shaft was vertical in the coronal and sagittal planes and the femoral neck was horizontal in the axial plane (Figure 1).

The CTXA Hip software generates a 2-dimensional image similar to a DXA image from the rotated 3D data set by summing all the bone voxels along lines perpendicular to the coronal plane. Each pixel of the resulting image represented the mass of mineral summed along that line. Regions of interest representing the common ROIs used for DXA analysis (Total Hip, Femoral Neck, Trochanter, Intertrochanter) were identified automatically on the projected image by the software (Figure 2).

Compartmental analysis of the ROIs was performed for the group of 22 women recruited for the precision study as a homogeneous population of postmenopausal women identified as osteoporotic by DXA.

Statistical Analysis

The precision of areal BMD measurements derived with the CTXA Hip was estimated by examining the dispersion of patient measurements acquired at approximately yearly intervals. The mean and standard deviation for the measurements for each patient were calculated. Long-term precision was then estimated by calculating the average of the set of standard deviation estimates for the group of patients. This method provides a conservative estimate of precision. For inter-observer variability, significance of difference of means was tested using a two-tailed t-test.

The accuracy of the CTXA Hip BMD estimates relative to Hologic QDR DXA BMD estimates for the Total Hip and Femoral Neck ROIs was characterized by comparing CTXA Hip and DXA results from the same subject from the two sites using Hologic QDR4500 scanners. No significant differences in the sample mean comparison were found either for the total hip or femoral neck data at the 95% confidence level.

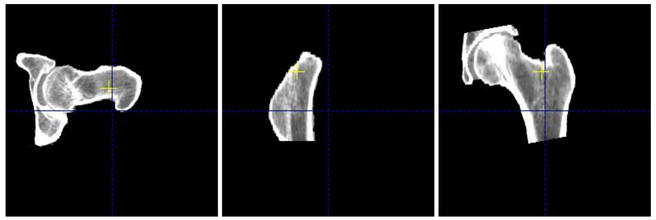

Figure 1. Axial (left), sagittal (middle) and coronal (right) images of segmented bone in proximal femur, rotated into a standard projection.

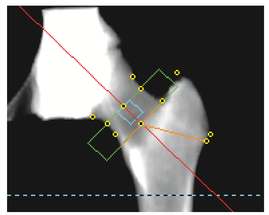

Figure 2. CTXA projected image with standard regions of interest used for BMD calculations (femoral neck, trochanter, intertrochanter, and Total Hip as sum of these three regions). Position of femoral neck box and intertrochanter limit line at base of lesser trochanter, and rotation of femoral neck axis, are adjustable by user.

	Total Hip		Femoral Neck	
	CTXA	DXA	CTXA	DXA
Areal Density (g/cm²)	0.645	0.700	0.551	0.598
Precision (g/cm²)	0.011	0.012	0.012	0.013
CV (%)	1.7	1.7	2.1	2.1

Table 1: Summary of Long-Term In Vivo Precision, CTXA vs. DXA, in Osteoporotic Subjects

	Observer 1	Observer 2	Δ O. 2 – O. 1
Total Hip BMD (mean ± SD)	0.668 ± 0.142	0.675 ± 0.146	0.007 ± 0.004 (1.0%)
Femoral Neck BMD (mean ± SD)	0.585 ± 0.121	0.578 ± 0.118	-0.007 ± -0.003 (1.2%)

Table 2. Interobserver Comparison of CTXA BMD Estimates (g/cm²)

Femoral Neck	CTXA BMD	DXA BMD	Slope	Intercept	R	SEE
Site 1 N=30	0.564 ± 0.117	0.645 ± 0.123	0.876	-0.001	0.92	0.047
Site 2 N=34	0.638 ± 0.150	0.713 ± 0.156	0.883	0.004	0.96	0.043
Site 1+2 N=64	0.606 ± 0.141	0.681 ± 0.145	0.888	-0.004	0.95	0.044
Total Hip	**CTXA BMD**	**DXA BMD**	**Slope**	**Intercept**	**R**	**SEE**
Site 1 N=30	0.657 ± 0.143	0.766 ± 0.138	0.988	-0.100	0.95	0.046
Site 2 N=39	0.755 ± 0.175	0.851 ± 0.170	0.999	-0.094	0.97	0.043
Site 1+2 N=69	0.712 ± 0.168	0.814 ± 0.161	1.006	-0.106	0.97	0.044

Table 3. Correlation of CTXA Hip and DXA BMD results (Site 1, Manchester; Site 2, Schenectady)

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Results

The results of the long term in vivo precision studies are given in Table 1, both for precision in terms of the BMD value (g/cm²) and as the coefficient of variation (CV,%), based on the distribution of the individual patient values. The mean BMD values by CTXA Hip and DXA are also given. There were no significant differences in precision between the CTXA Hip and the DXA results obtained in this study.

Inter-observer variability results for CTXA Hip are given in Table 2. The difference in total hip mean BMD estimates was not significant between the two observers at the 95% confidence level (p=0.055), while the femoral neck difference was significant between the two observers at the 95% confidence level (p=0.026). Even though statistically significant, the 1% difference between observers is similar to the 0.9-2.6% obtained using DXA (6,7).

The correlation between BMD estimates made with CTXA Hip and DXA for total hip and femoral neck regions of interest are given in Table 3, for the two clinical sites independently and for pooled results. Figures 3 and 4 show the correlations for total hip and femoral neck graphically. Correlation coefficients of 0.92-0.97 were obtained for femoral neck and total hip ROIs, with Standard Error of the Estimates of 0.043-0.047 g/cm².

The segmentation of total bone in the hip into compartments representing "cortical" and "trabecular" bone in DXA-like ROIs is unique to the CTXA Hip analysis. For the study population, the total hip region of interest was found to contain 62.3% ± 4.8% (mean ± SD) "cortical" bone with the remaining 37.7% ± 4.8% bone belonging to the "trabecular" bone compartment defined by CTXA Hip. For the femoral neck the proportions were 57.7% ± 9.5% and 42.3% ± 9.5%, respectively.

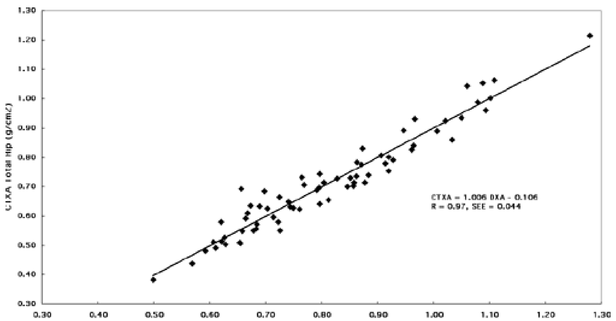

Figure 3. Correlation of area BMD for CTXA and DXA for total hip region of interest.

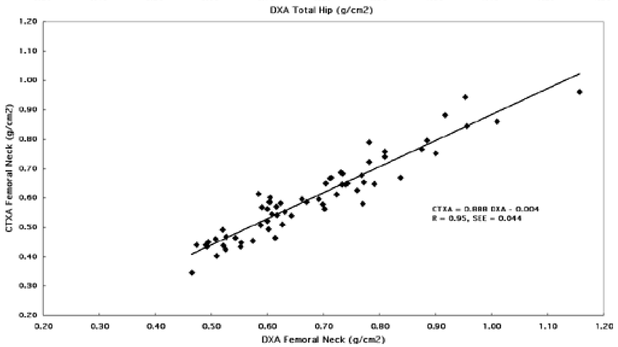

Figure 4. Correlation of area BMD for CTXA and DXA for femoral neck region of interest.

Discussion

The focus on measurements of bone density at the proximal femur as a standard reference (1) has meant DXA has become the gold standard technology used to make these measurements. QCT can produce a BMD estimate at the hip in two dimensions that has characteristics similar to DXA and give a BMD estimate that is highly correlated with a DXA result. The results of our study show that 2D projected BMD results obtained using the CTXA Hip software correlated highly (R=0.95-0.97) with results obtained from a common DXA device (QDR4500), with a SEE on the order of 0.045 g/cm². The results obtained in our study are similar to the relationship seen between DXA systems from Hologic and Lunar, where a correlation of R=0.92 and SEE of 0.051 for the Femoral Neck ROI over the same BMD range in a similar population has been reported (8,9). Long term in vivo precision is an important parameter for clinical practice, and we obtained results for CTXA Hip essentially identical to those from a Hologic QDR1000 system for osteoporotic patients studied under controlled conditions over a 2-3 year period. Our long-term precision of 1.7-2.2% in osteoporotic subjects is similar to short-term precision of 2.1-2.9% obtained by other researchers using DXA in similar populations (6,10), indicating that when properly performed QCT methods are just as precise as DXA.

We observed statistically significant differences in the slope and/or intercept of BMD results from CTXA Hip compared to Hologic DXA. In particular, CTXA Hip BMD estimates for the Total Hip ROI were found to be approximately 0.11 g/cm² lower than QDR 4500 results for the same population. This bias is well modeled by an additive (negative) bias term as shown in Figure 3 where the observed slope in the linear regression analysis was found to be not significantly different from unity. CTXA Hip BMD estimates for the Femoral Neck were also found to be less than the corresponding QDR 4500 results with an average bias of about 0.06 g/cm². In this case, however, linear regression analysis indicated the bias was better explained by a model slope significantly different than unity with an additive offset not significantly different from zero. As can be seen in Table 1, we also observed statistically significant bias in CTXA Hip and QDR 1000 BMD estimates, with an average bias of about 0.05 g/cm2 at both measurement sites reported here for the osteoporotic patient population comprising our precision study group.

Well-established biases in BMD estimates from different devices are currently handled in clinical densitometry practice by reporting normalized BMD estimates and interpreting normalized proximal-femur BMD scores from all DXA units using the same guidelines. The use of T-scores is the prevalent normalization method in use today (1), although alternative methods for generating "standardized" BMD estimates have been proposed (8,9).

We hypothesized that CTXA Hip BMD estimates provide the same clinical utility as that afforded by DXA. High correlation of results from various combinations of DXA devices, along with consistency in measurement precision as characterized by SEE, inter-observer variability, and assessment of long-term and short-term measurement precision have been accepted as a basis for using proximal femur results from all commercial DXA devices for clinical decision making within the context of any of numerous national and international clinical densitometry guidelines. We have subjected CTXA Hip to the same types of comparative tests as have been used with DXA, and we have found that CTXA Hip performs in a manner substantially the same as other DXA devices.