DXA-Based Finite Element Analysis Ultra-Distal Radius Predicts Osteoporotic Fracture Independently of BMD and TBS

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INTRODUCTION: Osteoporotic fractures are common, and associated with substantial morbidity, mortality, and economic cost. While bone mineral density (BMD) measured by dual-energy x-ray absorptiometry (DXA) at hip, spine or forearm is the clinical standard for assessing bone quality, substantial overlap exists in BMDs between patients with and without fracture. Subject-specific finite element (FE) models, which include both bone geometry and the distribution of BMDs, have been shown to better predict bone strength and fracture risk compared to BMD when applied to DXA images of the spine and hip [1-5]. Although hip and spine are the preferred sites for DXA imaging, recent studies reporting higher fracture prediction accuracy for the ultra-distal radius (UD) than other sites brought the UD radius in focus [6]. However, the utility of DXA-based FE modeling has not been examined for the forearm. Therefore, the objectives of the present study were to 1) establish the extent to which stiffness and strength obtained from DXA based forearm UD-FE correlate with those from micro-CT FE, and 2) demonstrate the utility of DXA-based UD-FE by comparing postmenopausal women with and without osteoporotic fracture, and examining the extent to which UD-FE discriminates fracture status independently from BMD.

METHODS: All studies were conducted under IRB approval. Ex-vivo studies: In order to develop and validate a DXA-based UD-FE model, 5 cadaveric forearms (age and sex were anonymized) were scanned using (Horizon A, Hologic) and a custom micro-CT system. Pixel by pixel areal BMDs were extracted from DXA images to construct FE models of ultra-distal radius. We assumed UD radius as a truncated ellipse and defined patient specific constant depth, t =2W/3 (where W is the mean width) [7], and volumetric BMDs were calculated to assign elastic modulus to each element [8]. A uniform compressive displacement of 1 mm was simulated for each FE model of UD radius (Figure 1). From FE results, stiffness, and failure strength (corresponding to 2% of total number of elements reached 0.007 strain [9]) were calculated and correlated to those from micro-CT based FE.

In-Vivo studies: 150 postmenopausal women (age ≥50 years) with (n=50) and without (n=100) history of osteoporotic fracture were recruited. DXA scans were performed at the hip, spine and forearm. The present study is limited to females because of higher susceptibility to bone fracture in postmenopausal women. Vertebral fracture assessment was performed for each participant to identify unreported vertebral fractures. Next, DXA-based FE models were constructed and simulated as described for the ex-vivo study. Load to strength ratio (LSR) was calculated as the ratio of the expected impact load from a fall on an outstretch hand to the strength [10], and considered as the primary FE based study variable in subsequent multivariate logistic regression analysis.

Regression was performed to examine the relationship of DXA-based and micro-CT-based FE stiffness and strength. The Fx and NFx groups were compared using t-test or Wilcoxon test based on the normality of data. Multivariate logistic regression was used to examine the extent to which the study variables predict fracture status. All analyses were performed in R and significance was set as $p<0.05$.

RESULTS: Correlation between DXA and micro-CT based stiffness (R^2=0.84) and strength (R^2=0.78) were significant ($p<0.05$) (Figure 1). Age and BMI were not different between the Fx and NFx groups ($p>0.6$). Fx group had significantly lower BMD at all sites (5.8-11.1%, $p<0.001$ to $p<0.04$), lower TBS (5.3%, $p<0.001$), lower strength (18.7%, $p<0.001$) and higher LSR (26.0%, $p<0.001$). In univariate models, all BMDs, TBS, strength and LSR were significantly associated with Fx status, with strength and LSR yielding the highest AUC (Table 1). In multivariate analysis, the best model of Fx status constructed using BMDs and TBS, and yielded the highest AUC (0.72), included hip BMD ($p<0.002$) and TBS ($p<0.02$) (Figure 2). Addition of LSR to this model yielded the highest AUC (0.74), with hip BMD), TBS, and LSR all being significant ($p<0.05$, $p< 0.03$, $p<0.02$, respectively) (Figure 2).

DISCUSSION: FE-derived stiffness and strength were strongly correlated between micro-CT and DXA. These correlations are within the range of those between micro-CT and other modalities such as high-resolution peripheral quantitative CT (HR-pQCT) and micro-MRI (R^2 = 0.73–0.95) [11-13], suggesting that DXA FE captures the stiffness and strength information for UD radius. In-Vivo analysis revealed that women with fracture had lower strength and higher load to strength ratio, and the ability of the FE variables from UD radius to discriminate fracture status was comparable to or greater than standard BMD and TBS measurements. Moreover, multiple logistic regression analysis revealed that LSR was associated with fracture status independently from BMD and TBS, and moderately improved fracture prediction. These findings suggest that forearm FE provides information complementary to BMD and TBS, and would be clinically valuable in situations where hip or spine DXA cannot be utilized.

The AUC values from models of "any" osteoporotic fracture constructed using DXA UD-FE are similar to those from HRpQCT based UD-FE (AUC: 0.63-0.74) [14-15], but higher than those from models with bone strain index (BSI) – a FE variable derived from DXA images of the spine (0.60-0.62) [4]. Future studies should investigate the efficacy of UD-FE for predicting fractures of a single type such as hip and spine, as well as the utility of the UD-FE in men.

SIGNIFICANCE/CLINICAL RELEVANCE: Load to strength ratio obtained from DXA-FE discriminates fracture status independently from all standard BMDs and TBS, and provides biomechanical information that complements standard DXA measures. These data further support the use of forearm DXA as an alternative site, of particular benefit to patients for whom DXA images cannot be acquired at a central site.

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IMAGES AND TABLES

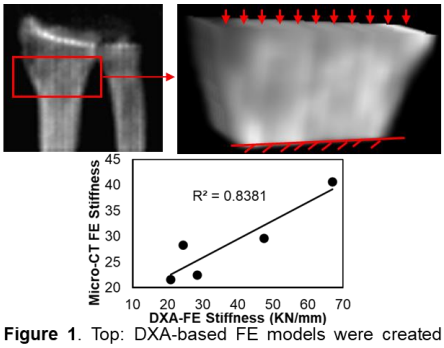

Figure 1. Top: DXA-based FE models were created from DXA images of the ultra-distal radius. Bottom: Stiffness derived from DXA FE models was well correlated with reference values from micro-CT FE.

Table 1. Descriptive data for Fx and NFx groups, along with AUC values from models of fracture status. Results show larger % differences between Fx and NFx groups for strength and LSR than for standard DXA variables. AUC values from models of fracture status are also comparable to or higher for strength and LSR than for standard DXA variables.

Variable	Fx	NFx	%Diff	AUC
BMD_{NECK} (g/cm2)	0.610±0.076	0.684±0.128	10.9*	0.67*
BMD_{HIP} (g/cm2)	0.726±0.101	0.812±0.131	10.6*	0.68*
BMD_{SPINE} (g/cm2)	0.820±0.152	0.922±0.188	11.1#	0.64*
BMD_{UD} (g/cm2)	0.342±0.068	0.383±0.075	10.5#	0.64#
BMD_{MID} (g/cm2)	0.499±0.078	0.538±0.080	7.2#	0.63#
BMD_{THIRD} (g/cm2)	0.585±0.080	0.621±0.086	5.8$	0.61$
TBS	1.208±0.107	1.276±0.108	5.3*	0.67*
Strength (kN)	4.336±1.233	5.333±1.515	18.7*	0.69*
LSR	0.561±0.199	0.445±0.120	26.0*	0.69*

*: $p<0.001$, #: $p<0.01$, $: $p<0.05$

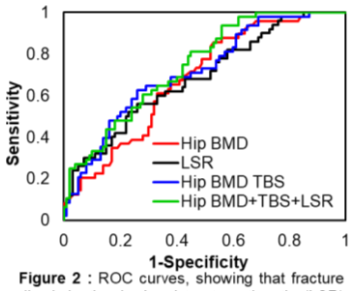

Figure 2 : ROC curves, showing that fracture discrimination by Load to strength ratio (LSR) alone is similar to hip BMD. Addition of LSR to BMD and TBS increases AUC to a small extent (from AUC 0.72 for BMD+TBS to 0.74 for BMD+TBS+LSR).