Fracture Risk Discriminators based on Statistical Shape and Density Modeling of the Proximal Femur

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INTRODUCTION
The structural integrity of an individual bone in any mechanical loading environment is dependent on the bone mineral density (BMD) distribution and the macroscopic morphology of the bone, as well as hierarchical interaction between complex and interrelated characteristics at the levels of the cortical and trabecular bone microstructure and the organic and inorganic matrix. However, at present, clinical fracture risk assessment is limited to simple univariate imaging data (i.e. DXA, CT or MRI), severely limiting our ability to increase the accuracy (i.e. specificity) with which individuals at highest risk are identified.

A statistical shape and density model (SSDM) describes multivariate geometry and BMD distribution variation contained implicitly within 3D imaging data for a set of bones. Without making a priori assumptions regarding the importance of discrete measures, a variable reduction method (i.e. principal component analysis) reduces high fidelity descriptions of 3D geometry and BMD distribution into a small set of variables (i.e. principal components (PCs)) that describe independent and uncorrelated combinations of geometry and BMD distribution traits [1]. By definition, each femur in the SSDM is described more efficiently and compactly in terms of the average femur and a weighted linear combination of PCs, as compared to the original descriptions.

In this preliminary study, we retrospectively investigated the performance of two fracture risk discriminators based on femur SSDMs to identify individuals at risk for future hip fracture and compared the performance of the multivariate methods to that of BMD alone. The goal of this research program is to generate the fundamental knowledge required to develop and implement a risk assessment tool that is easily accessible in the clinic.

METHODS
The Osteoporotic Fractures in Men (MrOS) Study is a multi-center observational study investigating the determinants of fracture in a group of older men (n=5,995, age ≥ 65) [2]. Both QCT data and hip areal BMD data (aBMD, DXA QDR 4500W; Hologic) were available at baseline for 3,561 individuals. After enrollment, the men were observed for an average of 5.6 years and any reported hip fractures were validated by physician review of radiology reports or X-rays. Baseline QCT and aBMD data scans for 40 individuals, including 20 randomly selected from the group who did not (NF) (n=3,519), were used to retrospectively develop fracture risk discriminators by regressing measures were used to investigate the performance of aBMD alone, fracture risk discriminators based on inclusion of increasing numbers of PC weighting factors (i.e. Method 1), and the multivariate fracture risk discriminator based on comparing individual fracture cases to the NF control SSDM (i.e. Method 2).

RESULTS
Method 1: Weighting factors for 3 PCs were found to be significantly different between the F and NF groups: PC4, PC15, and PC18 (p < 0.05 for all PCs). These 3 new combined trait variables describe the independent, complex, and subtle differences in 3D shape and bone density between individuals with and without fracture.

Method 2: T2 statistics determined using weighting factors for all PCs. These T2 statistics greater than the UCL indicated significant differences between baseline traits of individuals in the F group compared to the NF group.

DISCUSSION
Statistical shape and density modeling methods compactly and efficiently described the total geometry and bone density distribution variability within this small set of proximal femur models defined from the MrOS cohort. More importantly, SSDM provides a means of identifying the independent complex combinations of interrelated bone geometry and BMD distribution traits that appear to act as indicators of the likelihood of future fracture risk. The description of sample variation using a SSDM allows investigation of the important structural differences that may allow improved prediction of those at risk of subsequent hip fracture.

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REFERENCES

Figure 1: ROC curves Indicate Relative Risk Discriminator Performance

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