In Vivo Hip Fracture Strength Assessment from Microstructural MR Images Acquired in a Six-minute Scan

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INTRODUCTION: Osteoporosis is a disease of weak bone and increased fracture risk. Each year, nine million fragility fractures worldwide are caused by osteoporosis. Of these, hip fractures are the most devastating and costly. 20 to 24% of patients experiencing hip fracture expire within the first year, and hip fractures account for 72% ($12 billion) of the total direct annual costs in fracture care. Dual energy X-ray absorptiometry (DXA) is the clinical standard for the assessment of osteoporosis. However, it has a sensitivity of <50%, making it a poor predictor of osteoporotic fracture risk. Previous works both within and outside the authors' laboratory have demonstrated the feasibility of magnetic resonance imaging (MRI) techniques to interrogate the three-dimensional trabecular microstructure of the proximal femur *in vivo* – these studies have demonstrated that information on the trabecular microstructure can complement measures of bone mineral density acquired by DXA[1-3].

Notably, a recent study from the authors' laboratory used parallel imaging and compressed sensing to reduce the duration of these high-resolution scans to six minutes without substantial degradation in trabecular bone image quality[4]. Hence, *in vivo* assessment of whole proximal femur trabecular microstructure may potentially be feasible for research studies and clinical translation. Briefly, agreement was found between local anatomical measures of hip trabecular bone quality derived from fully-sampled (18-minute) and 3-fold accelerated (six-minute) MRI scans. The objective of the present work is to extend the image analysis of Vu et al.[4] and simulate a global, "sideways-fall" hip fracture injury. Towards this end, a finite element model was used to acquire and compare whole-bone stiffness measurements derived from 18-minute and six-minute scans.

METHODS: A subset of the proximal femur MRI data acquired for a previous study[4] was used (8 healthy volunteers, 5 male and 3 female, average age: 35 y.o., median age: 29 y.o.). MRI was performed on a Siemens Prisma 3-Tesla scanner using an 18-channel body matrix coil array wrapped around the left hip. A 3D balanced steady-state free precession was used to image at the largest fat peak corresponding to methylene protons. Fully-sampled (18-minute) and 3-fold accelerated (six-minute) versions of the sequence were developed, and model-based iterative methods were used to reconstruct the images. Wavelet regularization (compressed sensing) was used for the accelerated acquisitions. Like in previous studies[5], the periosteal border of the whole proximal femur was manually segmented for all MR images in ImageJ, and the grayscale values of the images were linearly scaled from 0% (voxel containing pure marrow) to 100% (pure bone). This conversion of the images to bone volume fraction maps accounts for partial volume effects. These bone volume fraction maps were used to create a finite-element mesh, which represents each voxel in the segmented maps with an equally sized linear hexahedral finite element. The tissue modulus of elasticity for each element was set proportional to the grayscale intensity of the corresponding voxel in the bone volume fraction map, with 100% intensity (pure bone) assigned a value of 15 GPa for bone tissue and 0% intensity (pure marrow) assigned a value of 0 GPa. The Poisson ratio was set at 0.3 for each model.

RESULTS: **Figure 1** illustrates the loading conditions designed to mimic forces sustained by the femur during a sideways fall. **Figure 2** contains a correlation plot to assess agreement between stiffness measurements acquired from the whole-femur finite element model applied to 18-minute and six-minute scans. Overall, the median percent error across subjects in proximal femur stiffness between 18- and six-minute scans was found to be 5.2%, and the intraclass correlation coefficient (ICC) assessing agreement was 0.90. The mean bias was 0.003 ± 0.011 (mean ± S.D.).

DISCUSSION: This work proposes a rapid and high-resolution MR image-based technique for *in vivo* assessment of the whole hip trabecular bone compartment. This finite element-based technique was tested in a healthy cohort of 8 volunteers, and high agreement in whole-femur stiffness measurements was found between the finite element models derived from fully-sampled (18-minute) and 3-fold accelerated (6-minute) scans of the proximal femur trabecular microstructure. While this study was performed on a cohort of nominally healthy volunteers, future work will focus on recruiting participants with and without osteoporosis and/or osteopenia to assess differences in hip trabecular bone quality for the whole compartment.

SIGNIFICANCE: A six-minute MRI-based method for *in vivo* assessment of stiffness of the whole hip trabecular bone compartment by a finite element model was proposed and evaluated in a healthy cohort of 8 individuals.

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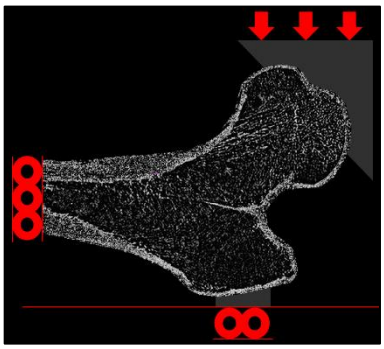
IMAGES

Figure 1: Diagram of sideways fall orientation illustrating the direction of applied force and side restrictions for a 56-y.o. female volunteer.



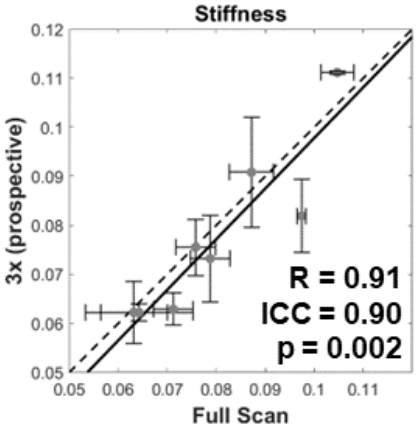


Figure 2: Correlation plot to assess agreement between stiffness measurements from the 18-minute scan and the six-minute scan. Pearson and intraclass correlation coefficients are listed. Error bars are given by the standard error for each pair of measurements.