## On the feasibility of PD-weighted MRI-based FE modeling of the proximal femur under sideways fall

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INTRODUCTION: Hip fractures account for nearly 20% of all fragility fractures [1], and while osteoporosis is the disease most associated with hip fracture, recent data indicate that rates of hip fracture are equal or higher for those with osteoarthritis (OA) vs. without OA [2,3]. Computed-tomography (CT) is the current standard for patient-specific, image-based finite element (FE) modeling for predictions of bone strength [4,5]; however, CT scans are not always part of routine screening, particularly in OA. Magnetic Resonance Imaging (MRI)-based FE modeling has emerged as a promising, radiation-free alternative for patient-specific assessment of fracture risk [6,7]. Although prior studies on MRI-based FE modeling have used T2-weighted MRI and reported good agreement with mechanical testing [7,8], other MRI sequences, such as Proton Density (PD)-weighted spin echo sequences, are also used for assessing bone [9-11] and evaluating OA progression [12-14]. PD-weighted MRI-based FE modeling could open another avenue for opportunistic assessment of bone strength and fracture risk but has not yet been evaluated. Therefore, the goal of this work was to compare PD-weighted MRI-based FE modeling to paired CT-based FE models, for assessment of femoral strength and failure location under sideways fall.

METHODS: MRI and CT scans were performed on human cadaveric femora (n=10, 4F/6M, age range = 25-84 years) immersed in water. Proximal femur geometry was semi-automatically segmented and converted to a second-order tetrahedral volume mesh (mean element size = 2.5 mm) (MITK-GEM, SimTK). Similar to published methods for MRI-based material mapping [6,8], bone volume fraction (BV/TV) was approximated by an inverted linear scaling that assigned the upper and lower 2.5% of MRI gray values in the segmented volume to be pure marrow (0% BV/TV) and pure bone (100% BV/TV), respectively. Element-wise elastic modulus for the MRI models was assigned as linearly proportional to the mean BV/TV value [7], and Poisson's ratio was set to 0.3. The CT scans used a calibration phantom to obtain CT density and then converted to apparent density [15]. Element-wise material property assignments for the CT models followed an established density-modulus power relation [16]; again, Poisson's ratio was set to 0.3. Boundary conditions representative of sideways fall (10-deg adduction, 15-deg internal rotation) were applied to the femur [17] with the distal end fully fixed, a roller constraint on the greater trochanter, and a distributed vertical load of 2000 N applied to the femoral head (Abaqus, Dassault Systemes Simulia). Whole bone stiffness, 90th percentile minimum and maximum principal strains, and femoral strength were computed, the latter via an asymmetric maximum principal strain criterion (0.73% tension, 1.04% compression) to predict failure load and location [18]. Paired t-tests and percent difference were used to compare whole bone stiffness, 90th percentile minimum and maximum principal strains, and failure load between MRI- and CT-based FE approaches.

RESULTS: The MRI-based models were of comparable volume, but slightly smaller (-8.1%, p<0.001), than their CT-based counterparts, while the median elastic modulus assignment was on average 266.9% higher (p<0.001) in the MRI- vs CT-based models (Fig.1). As compared to CT-based FE, MRI-based FE over-predicted whole bone stiffness (138.1%, p=0.003, Fig.2A) and under-predicted minimum (-40.6%, p<0.001) and maximum principal strains (-56.2%, p<0.001). No difference was found in failure load (72.2%, p=0.111), but MRI- and CT-based measures showed poor correspondence with each other, Fig.2B). CT models predicted compressive failure on the supero-lateral aspect of the proximal femur, predominantly in the mid-neck and trochanteric fossa regions. All but two of the MRI models predicted compressive failure in the same location, though in several the location of predicted failure was towards the head-neck junction (Fig.3).

DISCUSSION: This is the first study to investigate FE analysis of PD-weighted MRI scans to assess bone stiffness, strength, and failure initiation of the proximal femur, here for a sideways fall scenario. In general, MRI-based FE-predicted measures did not match paired CT-based FE-predicted measures. However, MRI-based FE-predictions of failure location did agree with CT-based FE-predicted failure for 8 out of 10 femora. These mixed results may be an indication that MRI segmentation is sufficient for ascertaining patient-specific shape of the proximal femur, and that shape is the dominant determinant of failure location, but that other features that contribute to stiffness and strength, such as material properties [19], are not represented well in the MRI models. Different material mapping methods resulted in an overestimation of modulus from MRI (p<0.001), which we attribute to underlying differences in MRI and CT imaging modalities. Future investigation into relationships between MRI values and measures of density and elastic modulus would prove a critical contribution towards the utility of an MRI-based FE framework as a tool for opportunistic assessment of fracture risk in patient populations for which MRI, rather than CT, is available.

SIGNIFICANCE/CLINICAL RELEVANCE: While MRI-based FE modeling may offer a radiation-free alternative to CT-based FE modeling, the ability of MRI-based FE models to predict the mechanical response of the proximal femur hinges on the relationship between MRI signal and tissue material properties. Our results indicate that a prior relationship developed for T2-weighted MRI does not extrapolate to PD-weighted MRI.

REFERENCES: [1]Johnell et al. 2006; [2]Chudyk et al. 2012; [3]Chan et al. 2014; [4]Adams et al. 2018; [5]Fleps et al. 2022; [6]Chang et al. 2015; [7]Rajapakse et al. 2020; [8]Rajapakse et al. 2018; [9]Majumdar et al. 2002; [10]Wehrli et al. 2007; [11]Jerban et al. 2020; [12]Roemer et al. 2011; [13]Lee et al. 2015; [14]Schwaiger et al. 2016; [15]Schileo et al. 2008; [16]Morgan et al. 2003; [17]Dragomir-Daescu et al. 2011; [18]Schileo et al. 2014; [19]Helgason et al. 2016

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## IMAGES AND TABLES:

