MRI Measurements of Bound and Pore Water for the Radius Correlate with Whole Bone Strength

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Disclosures: M. Manhard: None. S. Uppuganti: None. J.S. Nyman: None. M.D. Does: None.

Introduction: The current gold standard for diagnosing fracture risk include X-ray based methods, such as Dual X-ray Absorptiometry (DXA) to measure areal bone mineral density (aBMD), and quantitative computed tomography (qCT) to measure volumetric BMD (vBMD). However, these imaging methods only give measures related to hard tissue. As such, the contribution of the soft tissue characteristics, such as collagen or water bound to the organic matrix, to fracture resistance is not assessed. This may explain why there is a disproportionate increase in fracture risk relative to the age-related decrease in bone density. Bone hydration (1), intracortical porosity (2), and collagen integrity are also important determinants of fracture resistance (3), and Magnetic Resonance Imaging (MRI) has been shown to produce quantitative measures of both water bound to the collagen matrix (bound water) and water residing in the pores (pore water) in cortical bone. These MRI measurements can be produced using a ultra short echo time (UTE) sequence with T2 selective preparation pulses to discriminate between compartments of water in bone (4). In previous studies, Nuclear Magnetic Resonance (NMR) measurements of bound and pore water in small samples of cortical bone were found to correlate with the mechanical properties of these samples, such as peak bending strength and flexural modulus (5). In this study, whole bones were imaged with 3D MRI using clinically practical parameters. These bones were also imaged with DXA and μCT as a comparison to current gold standard measurements. These imaging measures were compared to the biomechanical properties of the whole bone as determined using a 3-point bend test. The objective of this study was to find correlations between imaging methods and whole bone fracture tests to demonstrate the potential of MRI for determining fracture risk.

Methods: The Vanderbilt Donor Program supplied cadaveric arms from elbow to fingertip. DXA measurements were acquired on the whole arm using a GE Lunar iDXA system to obtain aBMD measurements at the upper distal and distal third sites of the radius. The arms then underwent MRI scans using a 3T Philips Ingenia system with an 8-channel knee coil for the receive signal. Pore water maps were obtained using the Double Adiabatic Full Passage (DAFP) sequence, which plays two consecutive broad-bandwidth adiabatic full passage pulses to drive the short T2 magnetization (bound water) to saturation while rotating the long T2 magnetization (pore water) through 360°, leaving it unaffected. The Adiabatic Inversion Recovery (AIR) sequence was used to acquire bound water maps by using one adiabatic inversion pulse followed by an appropriate delay to null pore water magnetization while the bound water magnetization experiences a saturation recovery process. A reference marker with known concentration was used to convert signal into absolute units of mol H1/L. After MRI measurements, the radii were dissected out of the arms, and the distal third region was scanned using a Scanco μCT50 system at isotropic voxel size of 40 μm (80keV & 200 μA). These were evaluated to find several parameters, including Tissue Mineral Density (TMD). After imaging, 3-point bend tests (6) of hydrated radii at the distal third site were performed using an MTS Bionix 858 to get force vs. displacement curves. From these curves, biomechanical properties such as peak force and yield force were calculated. These measures were then correlated to the imaging results to assess the relative contribution of bound and pore water, as well as BMD measurements, to the strength of the radius at the fracture site.

Results: Figure 1 shows a slice from a conventional UTE image of a representative cadaveric arm, with the corresponding bound and pore water maps of the cortical bone in the radius at the distal third location. These were calculated from the AIR and DAFP sequences to get measures of concentration. The mean bound and pore water signal from these maps were correlated with the peak force and yield force.
Preliminary results from four radii are shown in Figure 2 of yield force and peak force correlations with bound and pore water, along with correlations with aBMD from DXA and TMD from μCT at the distal third site.

Discussion: These MRI imaging methods show promising results for bound and pore water mapping as a predictor for fracture risk. Measuring both bound and pore water has the potential to increase the information obtained to more fully evaluate fracture risk. There are strong linear relationships between mechanical properties of bone and bound and pore water, as well as μCT and DXA. This study will be continued on the radius, as well as on the femur, femoral neck, and vertebrae to obtain a more comprehensive evaluation of bound and pore water and the relation to whole bone mechanical properties.

Significance: These results validate the potential of MRI for yielding diagnostically useful information for clinical bone imaging to determine fracture risk across the cortical bone volume. Non-ionizing MRI methods that can measure soft tissue characteristics of bone offer a fundamentally new diagnostic measure, which may be valuable in both researching the mechanisms of increased fracture risk and in developing new drugs to mitigate these fracture risks.

Acknowledgments: The authors acknowledge support from NIH grant EB14308.

References:
