NMR Analysis of Age-Related Bone Properties

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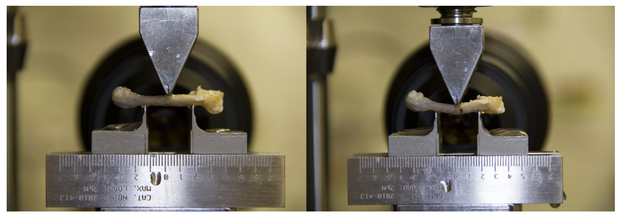
Introduction

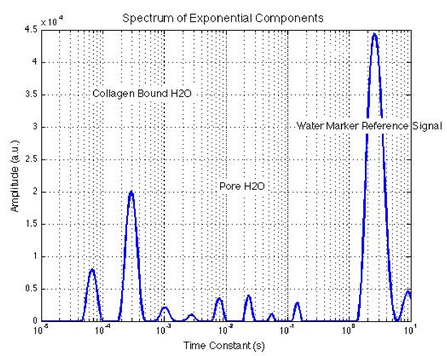
- Fracture risk is affected by several different bone properties including microstructure, mineral density, and bone quality (as defined by collagen integrity)
- ^{1}H NMR can be used to measure amounts of collagen-bound and pore water characteristic of bone quality in humans
- The aim of this study is to use ^{1}H NMR to explain age-related trends in bone properties of the Fischer F344 rat, namely stress intensity factor (K_c), peak stress, and displacement at failure
- It is hypothesized that age-related trends of the rat bone will mimic those of human bone

Methods

- Notched left femurs of rats sacrificed at 6, 12, and 24 months were subjected to three-point bending testing until failure to obtain mechanical properties

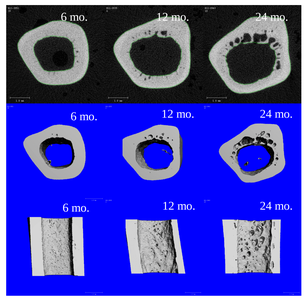


- Segments of bone approximately 4 millimeters in length were cut from the proximal end of the fractured femur nearest to the fracture site (the fracture site was cut off to produce a smooth end)
- NMR was performed on the bone segments using a 4.7T magnet, low proton RF coil, and a CPMG pulse sequence with 100μs echo spacing and TR=15s
- Bound and pore water signals were distinguished by T2 values and calibrated in units of mol 1H/L bone[1]



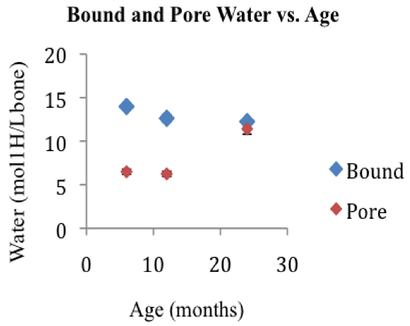
Methods (cont.)

- Micro-computed tomography (μCT) using a Scanco μCT 50 was performed to measure bone volume (needed to normalize the NMR data) and porosity (The scan was acquired using a 70kV energy source with 20μm resolution)



Results

- Bound water concentration of the 6-month old rat femurs was significantly greater than those of the 12 and 24 month old rat femurs
- Pore water of the 24 month old rat femurs was significantly higher than those of the 6 and 12 month old rat femurs



- Bound water concentration significantly correlated with porosity, toughness (Kc), peak stress, and displacement at failure (no r2 value was higher than 0.20)
- Pore water also significantly correlated with porosity, K_c, and displacement at failure (r2 values were greater than 0.30 for porosity (0.81), peak stress (0.31), and displacement at failure (0.35)
- Porosity and K_c were found to significantly increase with age
- Peak stress and displacement at failure were found to significantly decrease with age

Discussion

- The increase in K_c and decrease in displacement at failure suggest that the bone becomes tougher and more brittle with age (stronger on a micro-scale)
- However, the increase in K_c is not consistent with the age-related K_c trend of human bone which was shown to decrease with age
- The increase in porosity causes the bone to become less dense with age (weaker on a macro-scale as supported by the decrease in peak stress)
- The decrease in bound water with age may result from a reduction of water binding sites within the collagen matrix due to increased fiber cross-linking (this would cause the bone to become more brittle, thereby accounting for the decrease in failure at displacement)
- The relatively low bound water signals for rat femurs (10.6-15.5mol 1H/L bone) compared to those previously measured from human femurs (17.4-24.8mol 1H/L bone)[1] is consistent with the known higher collagen to mineral ratio in human bone compared to rat bone[2]

Conclusions & Future Work

A decrease in water binding sites resulting from an increase in cross-linking of collagen fibers with age is a likely explanation for the mechanical trends observed. However, because stress intensity factor K_c, or toughness, of the rat femurs failed to display the same trend as human cortical bone, additional studies are needed to asses the Fisher F344 rat as a model for human bone.

Acknowledgements

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References

1. Horch, et al., 2010, Magnetic Resonance in Medicine, v. 64, p. 680-687.
2. Aerssens, et al., 1998, Endocrinology, v. 139, p. 663-670.