

## Advances in Skeletal Dosimetry through Microimaging: Bone-Specific Assessment of Marrow Cellularity by H-NMR Spectroscopy. Aim 4- Human Adult H-MRS Cellularity Study

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### Introduction

The current gold-standard method for measuring bone marrow (BM) cellularity is histological analysis of a BM biopsy from the iliac crest. Problems with this method are that it is painful and highly invasive—which limits its use for repeated measurements—, it is based on a very small tissue volume, and cellularity measured at the iliac crest is most likely not indicative of cellularity values at other bone sites. Several studies have used proton magnetic resonance imaging (H-MRI) and proton magnetic resonance spectroscopy (H-MRS) to measure marrow cellularity non-invasively in humans. Cellularity is measured as the water fraction (WF)—the ratio of water volume to total volume. Few studies have investigated the accuracy of these methods using water/lipid phantoms and in vivo, comparing MR measurements to iliac crest biopsy measurements. In aim 3 we determine the accuracy and reproducibility of the H-MRS method compared to histology at the same location on thirteen bones of fresh large dog cadavers. This current study corresponds to aim 4, consisting of a pilot study of cellularity measurements via H-MRS on human volunteers.

### Experimental

Forty (40) healthy volunteers will be recruited to cover the following age ranges: 21-25 yrs old, 29-35 yrs old, 40-50 yrs old, and 60-80 yrs old. Each age group will contain ten (10) volunteers, 5 male and 5 female.

Volunteers will be recruited by means of a mail-in flyer. People interested in the study who fit the description provided in the flyer will call the applicant. The initial phone interview will be used to reject volunteers that are pregnant, have pace makers or metal implants, were recently hospitalized, taking medication, or with a strong family history of cancer. Volunteers that pass the initial screen will be interviewed in person to discuss the information in the 'informed consent' form that they will need to sign. Once the 'informed consent' form is signed, volunteers will be screened for hematological diseases by a standard blood test and female subjects of reproductive age will undergo an additional serum-based pregnancy test. All volunteer protocols are presently being reviewed by an IRB committee at the University of Florida.

Each volunteer will be subject to H-MRS measurements at the bone sites listed in Table 1 using the VOI size and the method selected in aim 3. Given the short duration of each spectroscopic measurement (less than a minute), patient motion should not be a problem. Just in case, measurements will be taken in duplicate and compared. Depending on each volunteer's availability and patience being inside the MR unit, measurements may be completed on the same day or on different dates. Joy Kidder an in-house 3T Phillips-trained operator with over 15 years of clinical MR experience will assist to ensure that appropriate coil selection and patient positioning is used for measurements in each bone site.

Cellularity values for each bone site will be averaged for each age group and sex. A standard deviation will also be provided. A table will be produced showing average cellularity for each bone site by age group for each sex.

**Table 1.** Bone sites that contain active marrow in adults as identified in ICRP Publication 70.

Craniofacial bones, mandible (1), scapulae (2), clavicles (2), sternum (1), ribs (12), cervical vertebrae (7), thoracic vertebrae (12), lumbar vertebrae (5), sacrum (1), os coxae (1), proximal femora (2), and proximal humeri (2).

### Results and Discussion/Conclusions

This project has not been started. We will be submitting an RO1 proposal to receive funds from the National Institute of Health (NIH) on March 2008. We are currently waiting for IRB approval.