Simultaneous fat, water and T2* mapping for quantitative characterization of bone marrow pathology

Pippa Storey[1], Stephen Honig[2], David R. Stoffel[1], and Sandra L. Moore[1]

[1]*Radiology Department, New York University School of Medicine, New York, NY, United States,* [2]*Division of Rheumatology, New York University School of Medicine, New York, NY, United States*

Introduction: Routine clinical MRI protocols for evaluating bone marrow comprise T1-weighted and fat-suppressed T2-weighted fast spin echo sequences, and are adequate for diagnosing neoplastic lesions larger than 1cm. However, early marrow infiltration, characterized by small or diffuse lesions, is more difficult to assess accurately using these morphological sequences. For example, multiple myeloma, which is the second most common hematological malignancy in the United States, cannot be detected reliably by MRI in its early stages. The standard clinical workup for myeloma involves the use of skeletal survey to screen for lytic lesions. However, trabecular destruction is not apparent on radiographs until approximately 50% of trabeculae are lost. So-called 'micro-MRI', with spatial resolution in the range of 100 – 400 μm, provides exquisite depiction of trabecular bone [1], but has limited applicability because of long acquisition times and SNR issues, which have restricted its use to the distal extremities. A further diagnostic consideration is the need to differentiate trabecular loss due to malignancy from that due to osteoporosis, which is common in older adults. One feature that can potentially distinguish osteoporosis from malignant infiltration is fat content, since trabeculae lost through osteoporosis are usually replaced by fat [2], while those destroyed by malignant processes are replaced by neoplastic cells. The goal of this work was to develop and test a technique to quantify trabecular loss and fat content simultaneously within a clinically feasible scan time. The presence of trabeculae is known to shorten T2* since trabecular bone has different magnetic susceptibility from soft tissue [3]. Furthermore, gradient echo sequences used to measure T2* are also sensitive to fat content due to the effects of chemical shift. Thus we hypothesized that a multiple gradient echo technique could be used to detect alterations in bone density and marrow fat content simultaneously. The approach was tested in patients with osteoporosis or osteopenia, using healthy young men as a control group.

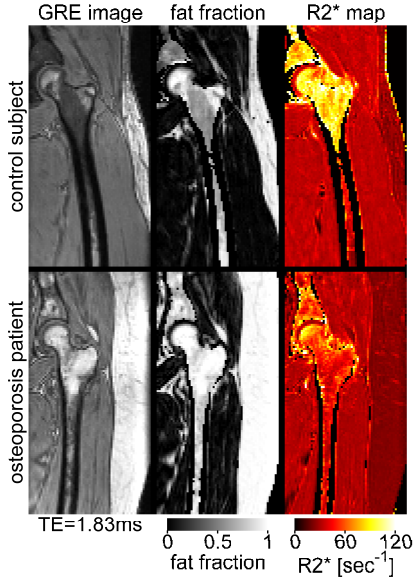

Fig. 1: Single slice from a healthy 24 year old man (top) and a 61 year old woman with osteoporosis (bottom). Images from the first gradient echo (left) are shown together with maps of fat fraction (center) and R2* (right).

Methods: Fourteen adults participated in the study, all of whom provided informed consent under an IRB-approved protocol. The subjects included 6 women (mean age 61, range 55 – 68 years) who had undergone a clinically-indicated dual-energy x-ray absorptiometry (DXA) scan within the previous 2 months ('patient group'), and 8 healthy young men (mean age 24, range 22 – 28 years), who were assumed to have normal bone density by virtue of their age and gender ('control group'). None of the patients were taking bisphosphonates for osteoporosis. The DXA scans were performed on GE Lunar systems (n=4) or Hologic machines (n=2). MRI was conducted at 1.5T (Avanto, Siemens) using body phased array coils in combination with spine coil elements in the patient table for signal reception. 3D volume imaging was performed in an oblique coronal slab encompassing both proximal femora using a multiple gradient echo sequence with a scan time of 4min 58sec. Parameters included: 16 echoes with monopolar readout gradients, minimum TE = 1.83ms and echo spacing = 1.83ms; receiver BW = 1000Hz/pix; FOV = 400mm x 400mm; base resolution = 192, phase resolution = 100% and phase oversampling = 17%; 24 partitions with slice thickness = 4.2mm, slice resolution = 100% and slice oversampling = 16.7%; TR = 47ms; and FA = 18°. This FA was chosen as a compromise between maximizing SNR and minimizing T1 weighting. Images were reconstructed offline, and maps of fat, water and R2* (= 1/T2*) were generated by performing a pixel-by-pixel fit of the complex-valued image data as a function of echo time. The model used for the fitting procedure assumed a single relaxation rate R2* for water and lipid components within the same voxel, and took into account the multiple spectral peaks of fat by using the signal from subcutaneous fat as a reference, normalized by the area of the principal lipid peak. The fat fraction was calculated from (fat signal)/(fat + water signals). Note that this ignores the effect of slight T1 weighting in the signal, which will introduce a small positive bias into all the estimates of fat fraction. Mean R2* values and fat fractions for each subject were evaluated by averaging the R2* and fat fraction maps over the entire volume of both hips from the proximal border of the femoral neck to a level 1 cm distal to the lesser trochanter. The femoral head was excluded for purposes of comparison with DXA, which is a projection technique and cannot be used to evaluate the femoral head since it is enclosed within the acetabulum.

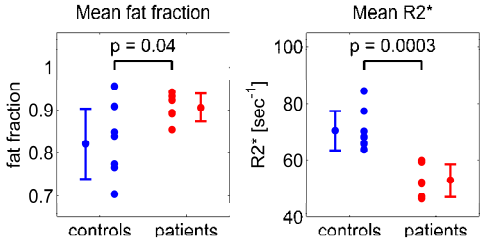

Fig. 2: Fat fraction (left) and R2* (right) averaged over both hips for control subjects (blue) and patients with osteopenia or osteoporosis (red).

Results: Of the patients, three had osteoporosis (*T*-score < -2.5) in one or both hips as determined by DXA, while the remaining three were classified as having osteopenia (*T*-score between -2.5 and -1.0). The *T*-score signifies the number of standard deviations by which the patient's bone mineral density (BMD) differs from the mean value for young adults of the same gender and ethnicity. Figure 1 shows example MRI results from a control subject (top) and a patient with osteoporosis (bottom). Note that, in the hip, the fat fraction is higher in the patient than the control subject, while R2* is lower. Figure 2 compares the mean fat fraction and R2* values between patients and control subjects. The fat fraction is significantly higher in patients than control subjects (p = 0.04), although there is considerable overlap in the values. R2* shows no overlap between patients and control subjects, and the difference is highly significant (p = 0.0003). Figure 3 compares the MRI and DXA results over the patient cohort. Fat fraction is negatively correlated with BMD (r = -0.89 and p = 0.02) while R2* shows a positive correlation with BMD (r = 0.88 and p = 0.02).

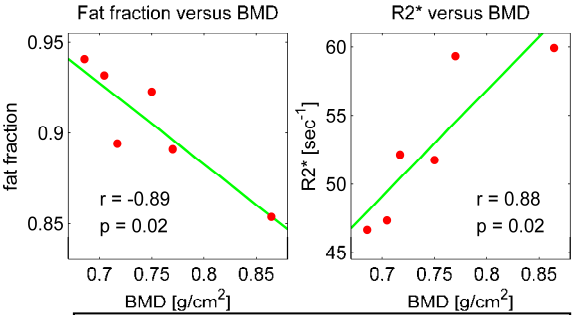

Fig. 3: Fat fraction (left) and R2* (right) as a function of bone mineral density (BMD) evaluated by DXA in all patients. Data represent means over both hips.

Discussion: Our results suggest that the multiple gradient echo approach is sensitive to changes in bone mineral density and fat content associated with osteopenia and osteoporosis. Further work will be needed to validate the technique in a larger group of patients, and to apply it to different pathologies such as early multiple myeloma and osseous carcinomatosis, in which trabecular loss is expected to be associated with reduced fat content. Differentiation of malignant infiltration from dense reconverted hematopoietic marrow may require exploration of complementary techniques such as quantitative diffusion imaging.

References: [1] Wehrli FW *et al.*, NMR Biomed. 2006;19:731-764, [2] Shen W *et al.*, Osteoporos Int. 2007;18:641-7, [3] Majumdar S *et al.*, MRM 1991;22:111-27