Monte Carlo Simulation of the Effect of Fat Spatial Distribution in Trabecular Bone Marrow on the DDIF MR Signal

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Target Audience – Musculoskeletal radiologists, Metabolic bone disease specialists, Diffusion MR specialists, MR physicists

Purpose – To assess the application of DDIF (Decay due to Diffusion in the Internal Field) MR in characterizing bone marrow fat distributions. The DDIF MR technique measures properties of porous materials. We have shown in a clinical study that DDIF MR readily detects changes in trabecular bone of the spine[1]. The DDIF effect is based on the change in the magnetic susceptibility across the boundary between the pore spaces and the solid bone[2-4]. Diffusive motion of the water molecules through the induced locally varying field leads to signal dephasing. The DDIF technique involves the acquisition of a stimulated echo for a range of diffusion (mixing) times T_M and records the MR signal decay as a function of T_M. DDIF MR data can be acquired either spectroscopically or as an image.

Bone marrow is a complex tissue containing water and fat and it plays an important role in DDIF MR: since fat has a magnetic susceptibility that differs from both solid bone and water, the field gradients in the pore spaces depend not only on the microstructure of the solid bone but also on the water-fat ratio and spatial distribution of the marrow fat within the pores. The spatial distribution and amount of fat cells in human bone marrow varies significantly among healthy people, depends on body weight, gender, race and age, and is affected by diseases such as osteoporosis, anorexia, multiple myeloma and bone metastasis. In this work we aimed to assess in more detail whether the DDIF MR technique can characterize bone marrow fat spatial distribution. This could have enormous value in detecting and evaluating bone marrow alterations and certain diseases. As a first step towards this goal, we simulated the effect of the spatial distribution of bone marrow fat cells on the DDIF MR signal for three typical clinical cases.

Methods –The influence of marrow fat cells on the DDIF MR signal was studied by Monte Carlo simulations. Three different marrow cases were studied: **I)** Healthy: low fat content, homogeneous fat cell distribution; **II)** Osteopenia: non-fat cells (water signal) in the centers of pores, paratrabecular layer of fat cells; **III)** Multiple myeloma with paratrabecular infiltration: fat in the centers of pores, paratrabecular layer of non-fat cells (water signal). Examples of bone biopsies for each marrow case are shown in Fig. 1a [5]. In these biopsies, the solid bone is dark red and the fat cells are the white circular dots.

One solid bone model, a 3D μCT data set of a sample of veal femur of size 10.24 mm^3 at 20 μm^3 spatial resolution, was used for all marrow cases to isolate the effects of changes related to the marrow composition. In the pore spaces of the binary solid bone model, fat cell 'seeds' were randomly distributed in 1 out of 350 (**I,II**) and 1 out of 50 (**III**) pore space locations. Using a region growing technique, these seeds were turned into fat cells by adding a 2 pixel thick layer around every seed. For models **II** and **III**, additionally, a 7 voxel thick paratrabecular layer of fat (**II**) or water (**III**) was added by region growing. The solid bone and fat areas were masked out to define a restricted volume in which water molecules may freely diffuse via random walk in the simulations. Solid bone, water, and fat were assigned the following susceptibilities: $\chi_{solid\ bone}$ = –11.3 ppm[6], χ_{water} = –9.04 ppm[7], χ_{fat} = –7.79 ppm[6] and the 3D susceptibility model was smoothed. Subsequently, the 3D field distribution was computed in the Fourier domain[8]. Monte Carlo software was written in MATLAB (Mathworks, Natick, MA, USA). The center 100^3 voxels of the restricted region model as well as the magnetic field map were linearly interpolated to a 2x2x2 mm^3 volume with 1000^3 voxels. Random walks of a total duration of 1 second at a temporal resolution of 0.2 ms were simulated for 10,000 protons. Protons were allowed to diffuse in the water-only spaces of the whole volume. Random walks were confined to the pore space by recalculation of the random walk from the time point at which the restricted region was encountered. The water self diffusion coefficient was set to 0.5 x 10^{-3} mm^2/sec[9] and the main magnetic field strength was set to B_0 = 3T. Subsequently, the DDIF MR signal decay was calculated for a range of mixing times (TM = 10 ms to TM = 900 ms at 5 ms intervals) and an echo time of TE = 20 ms using:

$$S_{B_i}(T_M) = \frac{1}{N}\sum_{n=1}^{N}\exp\left(i\cdot\gamma\int_0^{T_E} B_i(x_n(t))dt + \gamma\int_{T_E+T_M}^{2T_E+T_M} B_i(x_n(t))dt \right)$$

where S_{Bi} denotes the MR signal, which dephases in the internal field, N is the total number of protons and $x_n(t)$ is the random walk over time of a single proton n.

Results – (Samples of) the simulated 3D susceptibility distribution are shown for all three marrow models in Fig. 1b. The corresponding field maps are shown in Fig. 1c. The DDIF MRI signal curves are shown in Fig. 1d. The signal curves for the marrow models **II** and **III** are different from the healthy marrow model **I**. Paratrabecular fat cells decrease the DDIF MR signal decay rate (**model II**), where paratrabecular water with high fat content in the centers of the pores results in an enhanced DDIF decay rate (**model III**).

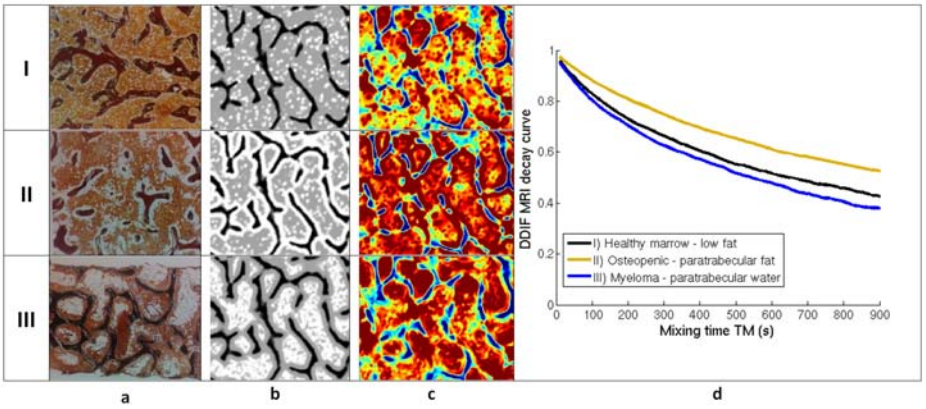

Figure 1. For 3 bone marrow models (**I** top row, **II** middle row, **III** bottom row) the following data is shown **a)** a bone biopsy[5] **b)** (part of) the simulated magnetic susceptibility distribution **c)** the magnetic field map computed based on the susceptibility distribution and **d)** the DDIF MR signal decay curves.

Discussion & Conclusion – Our results suggest that DDIF MR is sensitive to the spatial distribution of fat cells in the bone marrow and may be used as a tool to probe specific disease related bone marrow fat cell patterns. In the simulations we have studied three distinct marrow fat cell distributions. By using a trabecular bone structural model derived from real biological bone, and then varying only the spatial distribution of the marrow components, the effect of the marrow fat spatial distribution could be isolated. In this setting, we have observed an impact of the fat cell spatial distribution on the DDIF MR signal. This is a remarkable level of sensitivity to subtle tissue effects, and suggests that DDIF MR could serve as a powerful tool for performing histological assessments of marrow noninvasively, which is currently not possible by any other technique. In vivo, there is a full spectrum of possible fat cell distributions which varies amongst people, diseases, bone locations and also within a single bone on a smaller dimensional scale. Investigating the capability of DDIF MR in the differentiation of solid bone changes form marrow composition will be our next step.

References [1] Sprinkhuizen S.M. et al. Influence of Bone Marrow Composition on Measurements of Trabecular Microstructure using Decay due to Diffusion in the Internal Field (DDIF) MRI: Simulations and Clinical Studies Magn Reson Med. 2013 (in press) [2] Hurlimann, M. JMR 1998 . 131(2): p. 232-40. [3] Song et al. Concepts in Magnetic Resonance Part A, 2003. 18A(2): p. 97-110 [4] Song, Y.Q. et al. Nature, 2000. 406(6792): p. 178-81. [5] Bartl, R. and B. Frisch, Biopsy of Bone in Internal Medicine, Vol. 21. 1993: Kluwer Academic Publishers [6] Hopkins, J.A. et al. Magn Reson Med, 1997. 37(4): p. 494-500. [7] Schenck, J.F. Med Phys, 1996. 23(6): p. 815-50. [8] Sprinkhuizen, S.M. et al. Magn Reson Med, 2010. 64(5): p. 1360-72. [9] Yeung, D.K. et al J Magn Reson Imaging, 2004. 19(2): p. 222-8. **Support** Schlumberger-Doll Research, Martinos Center for Biomedical Imaging, NIH grant P41EB015896.