Structural Characterization of Trabecular Bone Using Bulk NMR Measurements of Intermolecular Multiple-Quantum Coherences

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Synopsis. Magnetic resonance imaging based on intermolecular multiple-quantum coherences (iMQC) is an emerging new technique with potentially useful applications to materials science and in vivo studies. It has been proposed that its sensitivity to long-range dipolar interactions be used to characterize the mean pore size distribution of porous materials such as bone. Previous published structural studies using multiple spin echoes (MSE) may be limited by problems with coherence pathway selection.

Introduction. Bulk measurements of multiple spin echoes as function of dipolar correlation distance have been proposed [1] to characterize the pore size of bone samples. A method which could differentiate structural features of normal from osteoporotic bone would have significant clinical implications. The approach chosen in Ref. 1, does not discriminate between the various coherence transfer pathways which are all expected to contribute to the bulk signal. This results in a convoluted curve which contains contributions from the random bone structure as well as sample boundary effects. Thus, without phase cycling, a two-quantum CRAZED sequence, as well as a second echo MSE sequence is expected to contain contributions from zero- (ZQC), single- (SQC) and higher order quantum coherences due to the highly structured geometry. Specifically, non-phase cycled measurements may contain significant contributions by single-quantum coherence arising from partial helix cycles at the sample tube boundaries or at the inclusions within the sample itself. In this work, we show that an appropriate phase cycling scheme provides significantly improved coherence selectivity and thus simplifying the interpretation of the resulting measurements.

Methods. Bulk NMR measurements were done on a 4T GE scanner using a home-built probe with a 3.4 cm-diameter solenoidal rf coil. Two demarrowed human distal tibia bone specimens were cut in cylinders of 2.5cm diameter and 1cm thickness, and placed in saline-filled cylindrical plastic containers. Spacers were added to minimize the amount of free water. The high-resolution image of Fig. 1 shows trabecular structure and water-filled marrow pores. Samples were centrifuged to remove air bubbles prior to each experiment. iMQC measurements were done with a 2-quantum MODCRAZED [2] sequence (θ=120°, τ=30ms, TE=200ms, TR=5s, Thk=12mm, correlation gradients along B_0, specimen axis perpendicular to B_0) with BIR-4 non selective excitation pulses and slice-selective hyperbolic secant refocusing pulses to provide volume selection over the bone region only. Adiabatic pulses are required for uniform excitation. The signal amplitude was measured as the average magnitude of 5 adjacent points sampled (RBW=12 kHz) on top of the echo, with 16 accumulations to provide an estimate of the noise (smaller than the symbols on all plots).

Results and Discussion. Non phase cycled measurements versus correlation distance (Fig. 2) have large oscillations or dips at several values of the helix pitch. Similar oscillations are seen with CRAZED or MSE sequences. For a structured sample, this sequence is expected to be contaminated by SQC and higher order pathways. When a four-steps phase cycle (first rf pulse: 90x,90-x,90y,90-y with a corresponding receiver phase x,x,-x,-x) is used, the SQC contribution is eliminated and the dips disappear (Fig. 3). Fig. 4 is a similar non-phase-cycled run on a tube (same diameter) filled only with water. The modulations arise from boundary effects. A peak-to-peak distance in a SQC pathway modulation is expected to have a period of 1 helix pitch, an effect which is readily seen in Fig. 4. Hence, some of the dips of Fig. 2 can be attributed to the shape of the cylindrical container. The remaining dips are attributed to the highly structured geometry of the sample, which may exhibit peaks at characteristic lengths, depending on the extent of constructive interference from those structures. The DQC pathways (Fig. 3) likely reflect average information about pore size, rather than fine structural details.

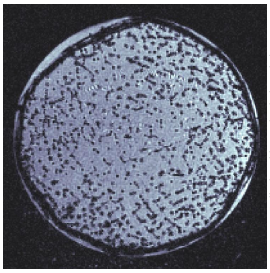

Fig 1. Bone specimen

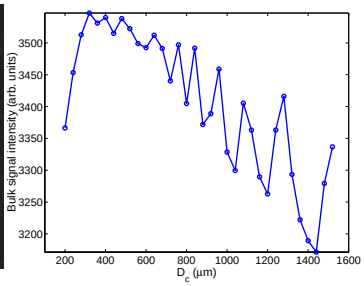

Fig 2. No phase cycling

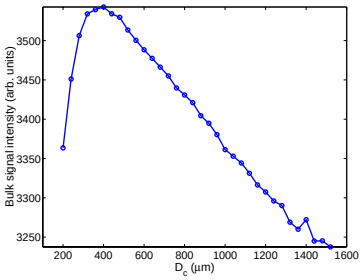

Fig 3. 4 steps cycle (divided by 4)

High resolution 3D SPGR images (156×156×200μm^3 voxel size) were thresholded into a binary map and used to compute the 3D isotropic lineal path function L(z) for this medium [2]. The results indicate a lack of short-range order, often characteristic of random media.

Conclusion. Imaging or bulk measurements may help to characterize bone, but the complex geometry causes several quantum coherence pathways to simultaneously contribute to the observed signal, even for a simple 2-quantum sequence. Simple phase cycled data with a smaller number of pathways (Fig.5) may contain physiologically important features: the initial rise out of the diffusion-limited regime, the position of the maximum and the slope of the decay. Since the functional dependence of iDQC signal is different than conventional signal, combining results from different coherence pathways can extract additional information, but there currently exist no simple models to retrieve such structural characteristics.

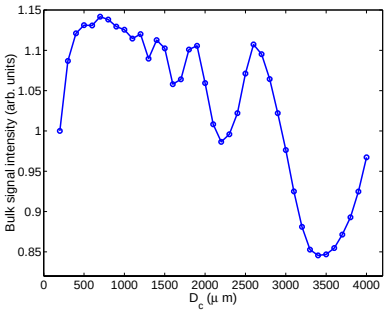

Fig 4. Pure water (no phase cycle)

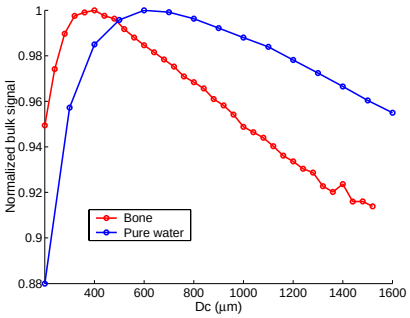

Fig 5. Water vs. bone (4 steps)

References. [1] S. Capuani et al., MRM 46:683 (2001) [2] S. Garrett-Roe, JMR 146, 1-13 (2000) [3] S. Torquato, Random Heterogeneous Materials, Springer (2002)