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Journal of Magnetic Resonance 176 (2005) 27–36
JMR Journal of Magnetic Resonance
www.elsevier.com/locate/jmr

Structural anisotropy and internal magnetic fields in trabecular bone: Coupling solution and solid dipolar interactions

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Received 19 February 2005; revised 27 April 2005
Available online 13 June 2005

Abstract

We investigate the use of intermolecular multiple-quantum coherence to probe structural anisotropy in trabecular bone. Despite the low volume fraction of bone, the bone–water interface produces internal magnetic field gradients which modulate the dipolar field, depending on sample orientation, choice of dipolar correlation length, correlation gradient direction, and evolution time. For this system, the probing of internal magnetic field gradients in the liquid phase permits indirect measurements of the solid phase dipolar field. Our results suggest that measurements of volume-averaged signal intensity as a function of gradient strength and three orthogonal directions could be used to non-invasively measure the orientation of structures inside a sample or their degree of anisotropy. The system is modeled as having two phases, solid and liquid (bone and water), which differ in their magnetization density and magnetic susceptibility. A simple calculation using a priori knowledge of the material geometry and distribution of internal magnetic fields verifies the experimental measurements as a function of gradient strength, direction, and sample orientation.

PACS: 76.60.Jx

Keywords: Distant dipolar field; Intermolecular multiple-quantum coherence; Porous materials; Trabecular bone; Material anisotropy; Microstructure

1. Introduction

The potential of intermolecular multiple-quantum coherence in non-invasively probing material microstructure in liquid state NMR has been acknowledged [1–3]. Pulse sequences exist that generate signals which are proportional to the strength of the distant dipolar field (DDF) [1]. These signals can be spatially resolved, as in the case of magnetic resonance imaging, or can be averaged over larger regions—or voxels—to provide high signal-to-noise bulk measurements. In both cases, the localized or unlocalized signals encode information about the material microstructure and its underlying geometry.

Biphasic materials modeled with a solid phase that does not contribute to the measured signal, and a NMR-sensitive liquid phase that encodes the geometry of the solid phase, are of interest to the biomedical and materials sciences. It was recently shown [4] that the volume-averaged DDF can be decoded to reconstruct simple material geometries. Thus, bulk measurements of the DDF would constitute imaging experiments in their own right, with the added advantages that sensitivity is not lost by having to use smaller imaging voxels and structural information below the voxel size can be obtained. It was also shown [5,3,6] that spatially resolved measurements in imaging experiments can remotely detect changes in magnetization density

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doi:10.1016/j.jmr.2005.05.012

occurring at distances beyond the size of the imaging voxel. These changes can, moreover, be quantitatively predicted by theory [5]. Beyond porous materials, the method has found applications in functional imaging [7], tumor detection [8,9], and amplification of weak NMR signals [10,11].

Most studies to date have focused on magnetization density differences in a structured material and their effects on modulating the DDF, while the effects of internal magnetic field gradients remain poorly characterized. Internal field gradients can be useful in tumor detection [8,9], functional imaging [7], and also for structural studies in the case where a large enough susceptibility difference exists between the phases of a material but the volume fraction of the solid phase is too low to modulate the DDF significantly. The present article studies the DDF dependence of trabecular bone on pulse sequence parameters and sample orientation. The bone volume fraction is typically 14% or less, while the water and bone phases differ significantly in their magnetic susceptibilities (by 2.28 ppm): pure water has a magnetic susceptibility of -9.03 ppm in SI (système international) units while the solid phase of trabecular bone is at -11.31 ppm. See Hopkins and Wehrli [12].

Trabecular bone consists essentially of an array of interconnected struts and plates arranged in such a fashion as to optimally withstand the stresses to which it is subjected. The structural elements are aligned with the major stress lines, forming a structurally anisotropic network [13]. The internal magnetic field gradients that are generated by the interface of the two phases offer the possibility of further characterizing the geometry. To assess the feasibility of modeling trabecular bone, we are interested in knowing the dependence of the DDF on sample orientation and internal magnetic field gradients. Such modeling, if it could lead to a reliable method for probing architectural parameters, would be of clinical interest since bone loss, as it occurs in postmenopausal osteoporosis or extended exposure to microgravity, is associated with architectural changes that include anisotropy. For example, it is known that trabecular bone becomes more anisotropic through preferential loss of transverse trabeculae (i.e., those perpendicular to the loading direction), therefore making the bone more prone to failure by buckling.

Other examples of anisotropic biological materials include neural fiber and capillary networks. In many cases where MRI and other imaging modalities cannot spatially resolve the structures, alternative methods which non-destructively probe the structural integrity of complex heterogeneous materials are needed.

In this article, we investigate the dependence of NMR measurements of the magnetic DDF on gradient strength and direction, evolution time, and sample orientation. This functional dependence in specimens of trabecular bone shows a strong sensitivity to trabecular orientation with respect to the gradient direction, thus offering new possibilities for using this technique in monitoring microstructural anisotropy and integrity of porous materials. We find that a linear model for the time expansion of the magnetization evolution is adequate for calculating DDF-dependent signals and corroborates experimental measurements in our system of trabecular bone in which the marrow was replaced by water as the NMR-active medium.

1.1. Calculating the CRAZED signal

The three-dimensional biphasic medium is described in terms of the indicator function $\chi(\mathbf{r})$ of the fluid phase $\Omega \in \mathbb{R}^3$ [4], which equals 1 when $\mathbf{r} \in \Omega$ and 0 otherwise (i.e., $\chi(\mathbf{r})$ is the simple "step" function that takes the value 1 when the vector $\mathbf{r}$ points to the liquid region and equals 0 when $\mathbf{r}$ points elsewhere). Since the solid phase generally differs in magnetic susceptibility, we must specify the susceptibility shift, which in turn determines the distribution of resonance frequency offsets $\omega(\mathbf{r})$. $\omega(\mathbf{r})$ therefore provides an indirect measurement of the coupling between the liquid phase magnetization and the dipole field of the solid phase. $\omega(\mathbf{r})$ can be directly measured by high-resolution MRI [14], or may be calculated either by summing the dipoles of the solid phase, or equivalently, by adding the individual fields from induced surface charge elements [15].

For a double-quantum CRAZED sequence, consisting of preparation and detection periods [1,9], and with conditions of weak DDF encountered in most clinical experiments, the expected CRAZED signal is most conveniently calculated in the linear approximation, where the signal intensity is directly proportional to the DDF. See Ramanathan and Bowtell [3] for the conditions of validity of this regime.

Insight pertaining to the behavior of DDF measurements can be gathered by solving the forward problem which consists of calculating the expected CRAZED signal for a given geometry and distribution of local magnetic fields and comparing to the experimental measurements. Also of interest are solutions to the inverse problem for reconstructing the material geometry from DDF measurements [4]. The inverse problem is not treated in this study, but could be addressed by extending the reconstruction method [4] with the addition of a DDF calculation which models the solid phase and its altering of the resonance frequency distribution over the liquid phase.

The primary role of the forward problem is to validate the experimental measurements by confirming the various trends observed. These trends, as will be seen later, reveal that the method is highly sensitive to internal magnetic field gradients over specific length scales and this dependence suggests a potentially useful tool for probing the architecture of trabecular bone or other