Journal of Magnetic Resonance **136,** 22–26 (1999)
Article ID jmre.1998.1594, available online at http://www.idealibrary.com on IDEAL®

Self-Diffusion Imaging by Spin Echo in Earth's Magnetic Field

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Received March 6, 1998; revised July 30, 1998

The NMR of the Earth's magnetic field is used for diffusion-weighted imaging of phantoms. Due to a weak Larmor field, care needs to be taken regarding the use of the usual high field assumption in calculating the effect of the applied inhomogeneous magnetic field. The usual definition of the magnetic field gradient must be replaced by a generalized formula valid when the strength of a nonuniform magnetic field and a Larmor field are comparable (J. Stepišnik, *Z. Phys. Chem.* 190, 51–62 (1995)). It turns out that the expression for spin echo attenuation is identical to the well-known Torrey formula only when the applied nonuniform field has a proper symmetry. This kind of problem may occur in a strong Larmor field as well as when the slow diffusion rate of particles needs an extremely strong gradient to be applied. The measurements of the geomagnetic field NMR demonstrate the usefulness of the method for diffusion and flow-weighted imaging. © 1999 Academic Press

Key Words: **magnetic resonance imaging; self-diffusion; geomagnetic; earth's magnetic field; magnetization prepolarization; gradient approximation; strong nonuniform magnetic field; convection; weak magnetic field.**

INTRODUCTION

In magnetic resonance a nonuniform magnetic field, $\mathbf{B}_g(\mathbf{r}, t)$, is used to encode the molecule position in the phase of spin precession. It enables the detection of the translation displacement of molecules via the change of spin precessional motion. The method is almost as old as NMR itself (*2–5*). It is a noninvasive and nondestructive method and, therefore, attractive to use for studying the molecular random migration in various systems. At the magnetic resonance imaging (*6*) a nonuniform magnetic field is used for spin positional phase encoding to get the image of spin distribution in sample. In the past decade NMR imaging technique has been combined with motion encoding for mapping velocity and diffusion (*7, 8*) to become a practice tool in science.

In this paper the nuclear magnetic resonance in the Earth's magnetic field is used to test the methods of diffusion-weighted measurements (*1, 9, 10*) in extremely weak magnetic fields. It is the first experiment in such a weak field where the methods for position and motion encoding are combined in order to get information about the spatial distribution of molecular motion.

Particle migration across the inhomogeneous magnetic field causes a dephasing of the spin induction, which leads to the attenuation of the spin signal. The attenuation depends on the strength of the nonuniform magnetic field, its duration, and the rate of particle migration. The technique uses the spin-echo RF sequence in combination with pulses of the magnetic field gradient. The spin relaxation limits the time of spin-echo sequence, and sometimes a slow migration of molecules requires application of a strong inhomogeneous magnetic field, so strong that the approximation of the magnetic field "gradient" (MFG) fails. The gradient approximation is significant when a nonuniform magnetic field is weaker than the main uniform magnetic field B_{zo}. Namely, the inhomogeneous magnetic field at a point shifted from the initial position by $d\mathbf{r}$ can be written as

$$\mathbf{B}(\mathbf{r} + d\mathbf{r}, t) = \mathbf{B}_o + \mathbf{B}_g(\mathbf{r} + d\mathbf{r}, t) \quad [1]$$

$$= \mathbf{B}_o + G(t)d\mathbf{r} \quad [2]$$

with G being a tensor. According to Maxwell's equations there is always more than one field component different from zero. In the case of $|\mathbf{B}_g(\mathbf{r}, t)| \ll B_{zo}$ the magnetic field components perpendicular to the static magnetic field can be neglected, and the remaining row of the tensor is called the magnetic field gradient. This approximation has no significance whenever the applied nonuniform magnetic field is on the order of, or larger than, the main magnetic field (*1*).

Herein, we are dealing with NMR in the Earth's field to measure the self-diffusion and obtain diffusion-weighted NMR images. In such a weak Larmor magnetic field, only very weak nonuniform magnetic fields can fulfill the gradient requirements, but the spins may not accumulate measurable signal dephasing in the interval between the gradient pulses. Therefore, a stronger nonuniform magnetic field must be applied that may no longer satisfy the condition of the gradient approximation. Its strength could be greater than that of the main magnetic field, and the perpendicular components of the nonuniform magnetic field must be taken into account. Therefore, the usual formula for the diffusion spin echo attenuation must be replaced with a more general expression that considers such a strong nonuniform magnetic field (*9*).

MIGRATING SPINS IN AN INHOMOGENEOUS MAGNETIC FIELD

The signal of a pixel at position R_j is given by

$$S(\mathbf{R}_j, t) \propto \rho(\mathbf{R}_j) e^{-t/T_2(\mathbf{R}_j)} \left\langle \sum_i e^{i \int_0^t \gamma B(\mathbf{r}_i, t') dt'} \right\rangle, \qquad [3]$$

where i runs over spins of pixel subensemble. For now we want to describe the signal of one pixel so we can drop the subscript j. A random migration of spin-bearing particles in the nonuniform magnetic field brings about a dephasing of the signal. It results in attenuation of the spin echo (*8*) as

$$S(t) \propto \sum_i e^{-\beta_i(t)}. \qquad [4]$$

In the case of an isotropic molecular random walk, the attenuation in Eq. [4] is

$$\beta_i(t) = D \int_0^t \left| \mathbf{F}(\mathbf{r}_i, t') \right|^2 dt' \qquad [5]$$

with D being the self-diffusion coefficient and

$$\mathbf{F}(\mathbf{r}_i, t) = \int_0^t \nabla \omega_{\text{eff}}^{\pi}(\mathbf{r}_i, t) dt. \qquad [6]$$

Here

$$\omega_{\text{eff}}^{\pi}(\mathbf{r}_i, t) = (-1)^{\pi(t)} \times \sqrt{(\omega_o + \gamma B_{gz}(\mathbf{r}_i, t))^2 + \gamma^2 B_{gy}(\mathbf{r}_i, t)^2 + \gamma^2 B_{gx}(\mathbf{r}_i, t)^2}, \qquad [7]$$

where $(-1)^{\pi(t)}$ denotes a unit function changing the sign after each π pulse. Reference (*9*) shows the details of this calculation.

In the gradient field approximation, the perpendicular components of a nonuniform magnetic field are neglected, and migration along the gradient of a component parallel to the main field is responsible for the signal attenuation. In our case all the components of the magnetic field play a part. Instead of the gradient of the z component of the magnetic field, the gradient of the total magnetic field magnitude must be considered. Thus, the spin dephasing $\mathbf{F}(\mathbf{r}_i, t)$ is the gradient of Larmor frequency $\omega_{\text{eff}}(\mathbf{r}_i, t)$. By taking into account the relation $\nabla \times \mathbf{B} = 0$, spin dephasing is proportional to

$$\nabla \omega = \gamma \frac{(\mathbf{B}\nabla)\mathbf{B}}{|\mathbf{B}|}. \qquad [8]$$

Thus the gradient of the effective Larmor frequency in Eq. [8] is proportional to the change of the magnetic field along the direction of the field line. We call it "the line gradient of the magnetic field" (LGMF) (*1, 9*). Now the spin dephasing does not result from the molecular motion along the gradient of the z component of the magnetic field but along LGMF. At first sight the form of Eq. [5] may resemble Torrey's formula, but there is significant difference in the definition of gradient. Both equations are identical only when a nonuniform magnetic field with particular symmetry is applied (*1, 9*).

A quadrupolar gradient coil (*11*) with its axis perpendicular to the main field B_o creates a nonuniform magnetic field that together with the main field gives the total field, which in the linear approximation is equal to $\mathbf{B} = (-Gz, 0, -Gx + B_o)$. Here G is the first derivative of a nonuniform magnetic field at the point where the co-ordinates x, y, and z are zero. In our case with a gradient coil of 35 cm diameter and 10 cm sample space, the linear approximation is justified and the gradient nonlinearity (*1*) can be neglected. Thus, the gradient of the magnetic field magnitude is

$$\nabla|\mathbf{B}| = G \frac{(-Gx + B_o, 0, -Gz)}{|\mathbf{B}|}. \qquad [9]$$

Since its magnitude is

$$|\nabla|\mathbf{B}||^2 = G^2, \qquad [10]$$

the expression for the normalized echo attenuation, which follows from Eq. [5], is

$$\ln S(t) = \gamma^2 D \int_0^t \left| \int_0^u G(t') dt' \right|^2 du. \qquad [11]$$

The axial symmetry of the field created by a quadrupolar coils gives a spin echo diffusion attenuation of identical form to that of Torrey's well-known equation (*4*). However it is true only in the case of isotropic diffusion since all nonzero components of strong nonuniform magnetic field have the same first derivative. Whenever the diffusion rate is directionally dependent, the spin attenuation becomes nonuniform within the sample, and both equations are no longer identical (*1, 12*). Thus, the measurement or imaging of the diffusion in a weak magnetic field must fulfill certain requirements regarding the symmetry of the applied nonuniform magnetic field.

Equation [3] describes the signal of one pixel. The complete signal is a sum of the signals of all the pixels, and each pixel's attenuation corresponds to the self-diffusion properties of the region containing the pixel. Using the spin-warp imaging technique (*6*), we can extract the signal of each pixel from the complete signal.

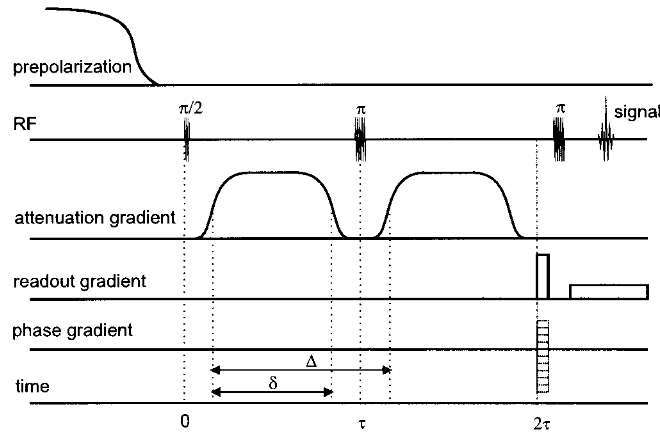

FIG. 1. The pulse sequence used for the 2D spin-warp imaging of the self-diffusion distribution in a geomagnetic field: It starts with a prepolarizing magnetic field, perpendicular to the main field, used to compensate for a weak magnetization of the geomagnetic field. After excitation with a $\pi/2$ RF pulse, two LGMF pulses directed perpendicular to the main field and parallel to the cylinder axis produce the diffusion attenuated of spin echo. At the moment of anticipated echo, the spin-warp imaging gradients are applied in the plane perpendicular to the axis of the cylindrical phantom.

EXPERIMENTAL RESULTS

Measurements have been carried out on a phantom consisting of three plastic, 5-cm diameter, 10-cm length cylinders each filled with a different liquid: water, ethanol, or propanol. The cylinders were stacked horizontally with their axes oriented perpendicular to the Earth's magnetic field and along the axis of the polarizing coil. The images were taken on a homemade setup for MRI in the Earth's magnetic field. The signal was amplified by polarizing the sample in a field of about 50 mT applied perpendicularly to the Earth's magnetic field. In order to get polarized spins in the direction of the Earth's magnetic field the polarizing field was switched off slowly relative to the Larmor precession in the Earth's field (about 2 kHz). After spin excitation with a $\pi/2$ RF pulse, two LGMF pulses with a π RF pulse in-between are applied to the sequence. The duration of each pulse is δ, and the two pulses are separated by Δ. The π RF pulse is applied at time τ. The sequence creates spin echo at time 2τ.

The nonuniform magnetic field of a quadrupolar gradient coil with its axis perpendicular to the Earth's magnetic field provides the spin-echo attenuation as

$$\beta(2\tau) = \gamma^2 G^2 \delta^2 D\left(\Delta - \frac{\delta}{3}\right). \qquad [12]$$

In our experiment G, Δ, and τ were fixed while δ was varied from 0 to 250 ms. The strength of the gradient field was $G = 1.8 \times 10^{-3}$ T/m. This means $B_g \approx 0.7 \times 10^{-4}$ T at the edges of the sample, which is larger than the Earth's magnetic field being 0.5×10^{-4} T. To obtain an image of the phantom the spin-warp pulse sequence is applied at the time of the spin echo. It is composed of a weak phase gradient parallel to the Earth's magnetic field (changed in steps) and a weak frequency (readout) gradient perpendicular to the main field. The sequence of fields and pulses and their directions are shown in Fig. 1. This sequence of pulses gives us a 2D distribution of plane projection of spin density attenuated by the diffusion process. We could get a 3D distribution if we use a slice selection gradient during the excitation with a $\pi/2$ RF pulse.

Since the diffusion constants of the liquids in the cylinders are different, we expected different contrasts of their images. In order to get a real image of diffusion rate we must take into account different relaxation times T_2 of the liquids. It was done

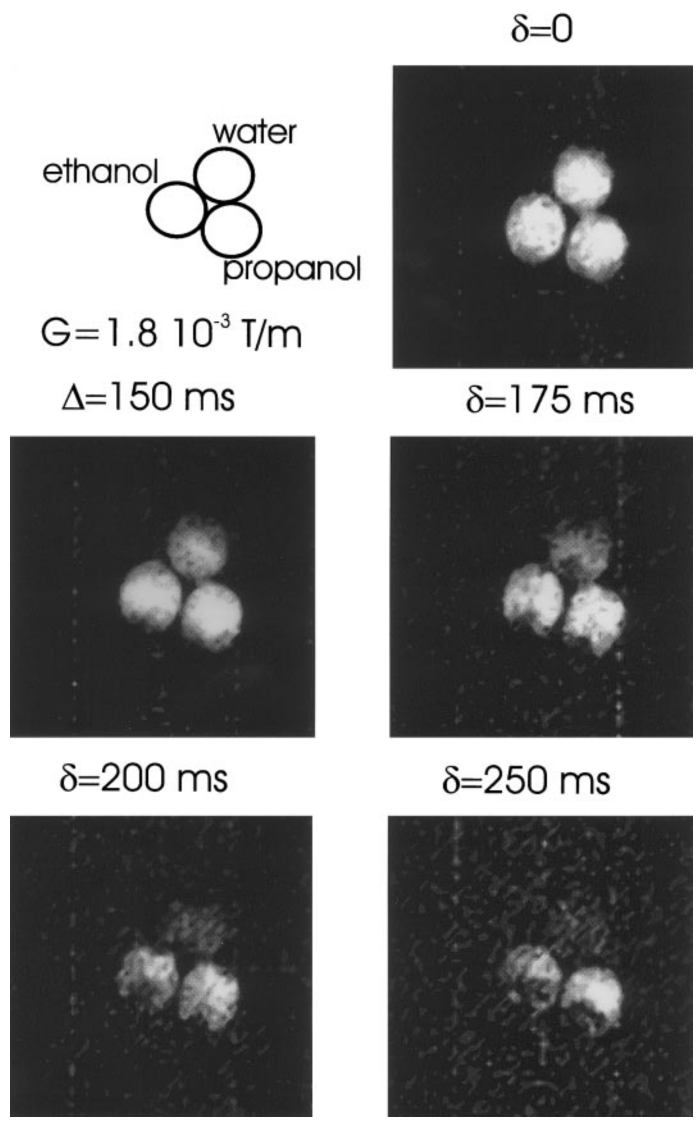

FIG. 2. The sequence of images shows how self-diffusion attenuation increases with the duration δ of LGMF pulse. The brightness of the water sample diminishes faster than that of the ethanol and propanol samples. The patches at the bottom and top of the circles in the images are due to a convection flow.

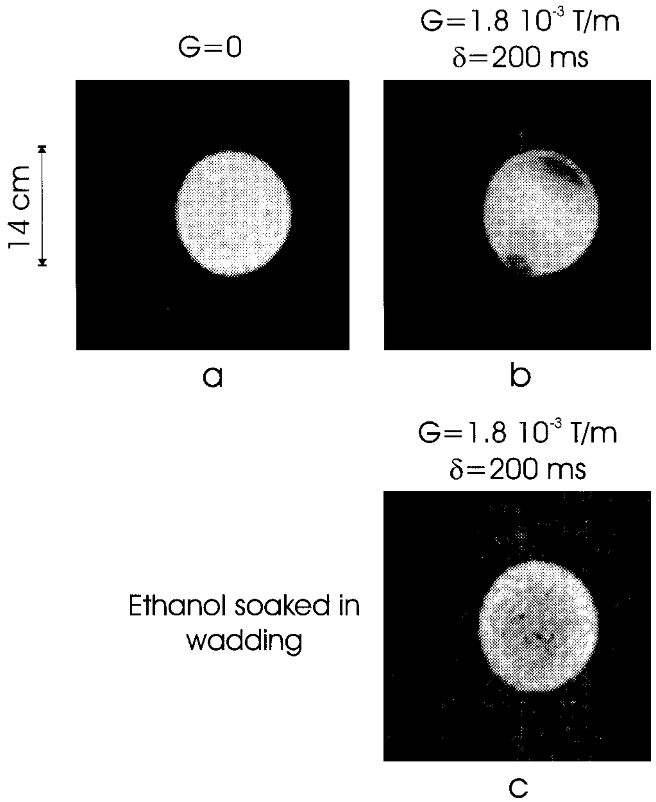

FIG. 3. An image of ethanol taken without (a) and with LGMF pulses (b) clearly shows an additional attenuation due to convection flow that is absent when the ethanol is soaked in wadding (c).

by normalizing the pixel intensity to one obtained without the strong gradient pulses, $\delta = 0$. Indeed we can see in Fig. 2 how the different diffusion rates of the liquids enhance the contrast difference between the samples. In the first image we cannot differ between the liquids whereas in the last image the signal of water is some 8 times weaker than the signal of propanol. The diffusion constants of water, ethanol, and propanol are, respectively,

$$D_{\mathrm{Wa}} = 1.96 \times 10^{-5}\ \mathrm{cm^2/s},$$
$$D_{\mathrm{Et}} = 0.93 \times 10^{-5}\ \mathrm{cm^2/s}, \quad \text{and}$$
$$D_{\mathrm{Pr}} = 0.51 \times 10^{-5}\ \mathrm{cm^2/s}$$

at the temperature of 20°C.

We noticed another interesting effect appearing as patches at the top and the bottom of the cells in Fig. 2. This effect has been amplified when we applied the sequence to a sample in a bigger cell shown in Fig. 3b. The image of a cylindrical phantom filled with ethanol clearly shows shadows on the image edges located at the top and the bottom of the cylindrical crosssection of the bottle. Since the Earth's magnetic field is tilted 30° from the vertical axis, the phantom image is turned the same angle from the vertical line of the figures. One could speculate that these shadows appear as a result of nonlinearity of the nonuniform magnetic field created by the quadrupolar coil, which Eq. [5] may predict. However, one can observe similar shadows in the images of the smaller phantoms, Fig. 2. There the shadows appear in the center of the image, where the nonuniform magnetic field is certainly perfectly quadrupolar. However, we cannot rule out the possibility of a convection flow within the bottle. Although stationary velocity does not attenuate the spin echo (it only changes its phase), the use of a signal averaging technique may produce a diminishing of intensity. Namely, the summation of many slightly phase-shifted echoes results in signal attenuation. When we suppressed the motion of the liquids by filling the bottle with wadding, the image shadows disappeared, Fig. 3c. It proves that the shadows are due to a natural convection flow in the phantom. It may result from temperature differences between the segments of liquid in the bottle. The observed attenuation can be caused by a phase factor varying by an order of a radian on the time scale of a duty cycle which is on the order of seconds (3 s). With the gradient field being constant, the estimated variation of flow velocity is on an order of 1/10 mm/s. The temperature gradient which could invoke such motion is on the order of 1×10^{-3} K/m.

Despite the magnetic resonance in a very low magnetic field (0.05 mT), the images are remarkably good. This is due to the extremely good homogeneity of the Earth's magnetic field, which allows a very efficient refocusing of the spin phase and thus the accumulation of sampling points in a wide interval of spin relaxation.

CONCLUSION

It is shown that the measurement and imaging of diffusion by NMR is not severely limited with respect to the strength of the applied inhomogeneous magnetic field. Taking into account the LGMF approach the measurements of molecular migration by NMR in an extremely low magnetic field are feasible. One should however be cautious of the convection effects. The LGMF approach is useful also in other cases where a low magnetic field or a short spin relaxation limits the application of standard methods (short spin relaxation implies a strong gradient field). We suggest its application to self-diffusion measurements in solids. It may be used also with the EPR spin echo for migration measurement. Thus in both cases the main restriction of a short spin relaxation time remains.

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