Magnetic Susceptibility Measurement Using a Double-DANTE Tagging (DDT) Sequence

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Preliminary results are presented for the nuclear magnetic resonance (NMR) measurement of field gradients generated by differences in magnetic susceptibility. The DDT technique maps the resonant frequency throughout the sample in a single image. Regions of paramagnetic and diamagnetic susceptibility are differentiated with a single magnitude-calculated image. © 1991 Academic Press, Inc.

INTRODUCTION

There is growing appreciation for the effects of magnetic susceptibility in biological nuclear magnetic resonance (NMR) spectroscopy and imaging. Techniques to measure susceptibility effects may provide additional clinical information, such as determining regions of calcification (1) or hemorrhage (2, 3). The measurement of susceptibility-induced line broadening has been suggested as a means for mapping brain iron (4). It has been demonstrated that the susceptibility effects of contrast agents such as Gd-DTPA in combination with echo-planar imaging techniques can provide a method for evaluating tissue perfusion (5–7). Observable bulk magnetic susceptibility effects are not uncommon in the clinical population. In a study using phase mapping of the magnetic field, Collins and colleagues found that in 50% of the 150 studies performed for a variety of brain disorders, local field perturbations were in excess of 0.2 ppm (8). The prevalence of susceptibility effects and the potential for providing useful clinical information necessitate a quantitative, rapid method for their measurement.

Previous methods for measuring susceptibility effects were based on the detection of phase (9–11) or frequency (12–17) shifts induced by differences in the static magnetic ($B_0$) field. Several factors limit the clinical utility of these sequences. First, most methods require a minimum of two images to obtain a map of the $B_0$ field. To differentiate susceptibility effects from the inherent $B_0$ inhomogeneity of the magnet, the sequences must then be repeated on homogeneous phantoms. In practice as many as three images per study are recommended to evaluate susceptibility differences (18). These studies require excessively long imaging times, and are often impractical in the clinical setting. Second, when magnitude-calculated images are employed, the images describe only the difference and not the absolute field strength. With these images it is not possible to determine whether the observed field changes are due to paramagnetic or diamagnetic species. As a result, regions of calcification cannot be unequivocally differentiated from
regions with iron-containing metabolites with a single image (1). Third, phase methods are sensitive to the phase shifts induced by motion in the presence of a field gradient. This limits the accuracy of the susceptibility measurement. Fourth, since signal intensity is a function of many properties, the interpretation of phase contrast images may be complicated in heterogeneous samples where these properties vary spatially. These difficulties have limited the measurement of tissue magnetic susceptibility in the clinical setting despite the potential for obtaining useful diagnostic information.

In this communication we describe the use of the Double-DANTE Tagging (DDT) sequence for mapping the field changes generated by differences in bulk magnetic susceptibility in a single NMR image. This technique previously described for the evaluation of sample motion (19) utilizes a DANTE pulse train in the presence of a frequency-encoding field gradient to irradiate a grid pattern of thin planes in the sample. The spacing between the planes or "tags" is inversely proportional to the magnitude of the frequency-encoding gradient, and the DANTE interpulse delay. Following tag placement the sample is imaged, and the tagged regions appear as dark lines. By using very small tagging gradients, the placement of these lines is sensitive to the local magnetic field. For homogeneous fields the lines are straight. Regional variations in the $B_0$ field shift the line according to the magnitude of the local field. The displacement of the lines can be used to determine absolute field shifts within the image.

**METHODS**

Initial studies were performed on a Bruker AM 400 WB spectrometer equipped with microimaging capability and operating at 400 MHz for protons. Studies utilized a phantom consisting of a 20-mm NMR tube filled with a 5 m $M$ EDTA solution. After maximizing the homogeneity of the $B_0$ magnetic field, two microspheres containing 10 m $M$ FeCl$_3$ and 500 m $M$ CaCl$_2$, respectively, were inserted into the tube. A single-slice spin-echo imaging sequence with a $256 \times 256$ matrix was used to image the tagged sample orthogonal to the $B_0$ field. The images had a slice thickness of 500 $\mu$m and an in-plane resolution of $100 \times 100$ $\mu$m. All images were $T_1$ weighted with an echo time (TE) of 25 ms, a repetition time (TR) of 1090 ms, and are displayed with increasing frequency to the left and bottom of the image.

A 16-pulse DANTE train with an interpulse delay of 6.25 ms was used in the presence of a 0.0928 G/cm tagging gradient to generate a grid pattern of tags within the sample. The phase of the DANTE pulse train was modulated (0–180–0–0°) to produce evenly spaced tags at a 40-Hz interval. With the gradient strength chosen, a 0.1-ppm change in the local $B_0$ field results in a 1-mm shift in the grid line. The total time to generate the tagged regions was approximately 125 ms per axis. This generates a line 200 $\mu$m thick covering approximately 2 pixels in the image. The sensitivity of the technique is limited by the change in $B_0$ field needed to shift the tag a distance of 1 pixel. For these studies this would be a field change of 0.01 ppm, with a spatial resolution of 100 $\mu$m. Greater sensitivity and resolution would be possible by decreasing the pixel size and tagging gradient strength.

**RESULTS**

An estimate of the paramagnetic and diamagnetic $B_0$ field shifts due to the microsphere solutions can be made from the mass susceptibility of CaCl$_2$, FeCl$_3$, and water
Fig. 1. A 400-MHz $^1$H microimage demonstrating the effects of local magnetic susceptibility field gradients on the DDT image. A 1-mm displacement in the position of the line corresponds to a 0.1-ppm change in the $B_0$ field. The images are displayed with increasing field strength to the left and bottom of the image. (a) DDT image obtained from 20-mm NMR tube of 5 mM EDTA demonstrating the $B_0$ homogeneity of the system. (b) DDT image obtained following the addition of two 18-pl microspheres containing 10 mM FeCl$_3$ (top) and 500 mM CaCl$_2$ (bottom). The local gradients due to differences in magnetic susceptibility shift the tag position in the region of the microspheres.

which are $-54.7 \times 10^{-6}$, $1.52 \times 10^{-2}$, and $-12.97 \times 10^{-6}$ (cgs units) respectively (20). According to the rule of mass susceptibility ($X_m$) the susceptibility of a solution is a weighted average of the individual species as

$$X_m = \frac{m_1X_1 + m_2X_2}{m_1 + m_2},$$

where $m_1$ is the mass of solute 1 whose susceptibility is $X_1$ and $m_2$ is the mass of the solvent whose mass susceptibility is $X_2$. The final $B_0$ of the solution can be determined as

$$B_0 = u_0u_rH,$$

where $u_0$ is the permeability of free space, $u_r$ is the relative permeability which is equal to $1 + X_m$, and $H$ is the applied magnetic field. Neglecting geometric considerations, a shift of $+0.39$ ppm is predicted within the 10 mM FeCl$_3$ solution, and a shift of $-0.04$ ppm is expected within the 500 mM CaCl$_2$ microsphere.

As demonstrated in Fig. 1 the DDT sequence is sensitive to the distortion in field generated by the microspheres. Figure 1a illustrates the background $B_0$ homogeneity within the EDTA solution. As shown in Fig. 1b the addition of the microspheres results in local field perturbations. Near the region of the iron-containing solution, the lines are shifted to the left and bottom of the image as a result of perturbation in the local $B_0$ field of greater than 0.09 ppm. The field shift within the microsphere could not be determined due to the short $T_2$ of the solution. The lines near and within the calcium-containing microsphere are shifted due to a local decrease in field. Within
the CaCl$_2$ solution the field is quite uniform as indicated by the straight lines with a measured field shift of approximately $-0.05$ ppm. The blurring of tags at the glass–water interface indicates regions having a large field gradient.

DISCUSSION

The DDT sequence has several advantages over previous techniques for mapping the magnetic field. The spatial variation in resonant frequency can be rapidly determined with a single image. This significantly reduces the time needed to obtain field maps. Typical imaging times were less than 5 min. Since the field calculations require only the ability to discriminate the tagged grid, the signal to noise can be reduced without a loss in accuracy. Rapid spin-echo images with acquisition times under 2 min should be possible. As with all techniques used to evaluate susceptibility effects the images must be compared to images obtained with phantoms in order to differentiate the $B_0$ inhomogeneity of the system from the susceptibility effects of the sample.

A useful feature of this method is the ability to measure absolute field strength with a single image. This is a distinct advantage when measuring susceptibility effects in heterogeneous samples. As demonstrated in these preliminary results, the diamagnetic effects of calcium are easily differentiated from the paramagnetic effects of iron and agree well with theoretical estimates. The ability to discriminate between these two species provides important diagnostic information that can assist in the interpretation of images obtained with other MRI techniques (1, 21).

The effects of diffusion are different from those observed with phase mapping techniques. Microscopic random motions produce a mixing of tagged and untagged spins. Unlike phase techniques, random motions do not displace the line and therefore do not result in an error in the field calculation. Since for typical tagging times the line thickness is significantly greater than the diffusion distance of water, diffusion does not decrease line resolution. This allows susceptibility effects to be evaluated independent of diffusion. Gross sample motion, such as that of a beating heart will cause a translational displacement of the lines which could be mistaken for a change in field. However, most forms of motion are obvious and have a characteristic pattern. For cases in which motion cannot be ruled out, increasing the tagging gradient strength will allow motional processes to be observed in the absence of susceptibility effects. Motional artifacts can be minimized by gating acquisition to the periodicity of the movement.

With the DDT sequence, the sensitivity to $B_0$ inhomogeneity can be adjusted independently of spatial resolution allowing the sequence to be optimized for specific applications. The sensitivity is inversely proportional to the magnitude of the tagging gradient. Once an appropriate gradient strength has been chosen, the line spacing may be adjusted by varying the length of the DANTE interpulse delay. Due to the narrow excitation profile of the DANTE sequence, thin lines may be produced even in the presence of very small tagging gradients. As a result the DDT sequence can be made extremely sensitive to $B_0$ variations while still maintaining excellent spatial resolution.

In conclusion, we have presented preliminary results illustrating the use of a unique sequence for the measurement of susceptibility field shifts. This sequence has several advantages over previously described techniques. Theoretical calculations agree well
with the observed field changes suggesting that this method may allow semiquantitative analysis of mass susceptibility. Although initial studies have been performed on a high field instrument, the technique may be easily adapted for low field clinical imagers.

REFERENCES