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Magnetic Resonance Imaging with Intermolecular Double Quantum Coherences

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Abstract : Recently a new method for magnetic resonance imaging based on the detection of relatively strong signal from intermolecular multiple quantum coherences (iMQCs) is reported. Such a signal would not be observable in the conventional framework of magnetic resonance; it originates in long-range dipolar couplings that are traditionally ignored. In this paper, we present the results of experimental studies to assess the feasibility of intermolecular double quantum coherences (iDQCs) imaging in humans. We show that the iDQC images are readily observable at 4T and that they do indeed provide different contrast than appears in conventional images.
Keyword: MRI, distant dipolar field, intermolecular double quantum coherences

INTRODUCTION

In the traditional treatment of magnetic resonance, the magnetic fields generated by the bulk magnetization of nuclear spins themselves are neglected. At the high magnetic field strengths currently being used for *ex vivo* and even *in vivo* MR, however, the bulk magnetization can lead to such unusual phenomena as trains of large amplitude echoes generated by just two RF and gradient pulses.[1-10] While these effects can be described using classical physics, the use of quantum theory enables the interpretation of the phenomena as the result of dipolar couplings between distant spins which can lead to intermolecular multiple quantum coherences (iMQCs). Recently a new type of MRI based on detection of

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intermolecular zero-quantum coherences (iZQCs) both *in vitro* and *in vivo* has been demonstrated.[11-13] These coherences correspond to simultaneously flipping two water spins in opposite directions on molecules separated by 10 μm – 10 mm. Therefore the contrast in iMQC images is expected to be fundamentally different from contrast in conventional gradient and spin echo sequences.[7-9,11-13]

In two-spin dipolar interactions, besides of iZQCs, there are also intermolecular double quantum coherences (iDQCs) corresponding to simultaneously flipping two water spins in *same* directions on distant molecules. The imaging of iDQCs was first demonstrated in coaxial tubes using a two-quantum CRAZED sequence (90-t_1-gradient-90-{double-area gradient}-t_2),[5] and recently van Zijl et al. obtained iDQ-images of cat brains.[14] In general iDQC imaging might give poorer contrast than iZQC imaging due to dephasing effects of DQCs during the evolution period (twice of conventional single quantum coherences). However, the iDQC-imaging will be more sensitive to motion and flow. The purpose of this research is to show that the phantom and human brain iDQC images are readily observable at 4T and the contrast is different from that in conventional images.

THEORY and METHOD

A prototype spin-echo iDQC imaging sequence, consisting of two 90° pulses and a refocusing 180° pulse, is shown in Figure 1. Two correlation gradient pulses are used to select iDQCs. The second correlation gradient length is twice of the first one. A conventional treatment, therefore, would predict no signal since there are no magnetization doubly modulated in spatial. Instead, this sequence produces signal because intermolecular dipolar couplings convert normally neglected terms (multi-spins) from the equilibrium density matrix into transverse magnetization. Susceptibility variations of iDQCs (during τ_{DQ}) are refocused by a delay of $2\tau_{DQ}$ proceeding the TE period. The signal arises from pairs of nuclear spins, separated by approximately the "correlation distance" $d=\pi/(\gamma G_c T)$ which is half the repeat distance of the helix created by the correlation gradient.[7] Thus iMQC signal is sensitive to dynamics and structural variations on this distance scale, which is dictated by the length and strength of the correlation gradient (typically 100 μm – 1 mm). As discussed in the previous studies,[7,11] the initial 90° pulse creates two-spin intermolecular iDQCs and iZQCs as well as the conventionally observed one-spin, one-quantum coherences. The correlation gradient pair eliminates all but the iDQCs such as $I_i^+ I_j^+$. During the delay, τ_{DQ}, this coherence evolves at the sum of resonance offsets of the spins i and j. The second rf-pulse (β) transfers parts of these DQ coherences into two-spin single quantum terms such as $I_{xi}I_{zj}$. The second gradient (twice of the first one) rephases the helical structure of these coherences. Finally, the magnetization can be rendered observable by a number of small intermolecular dipolar couplings, which remove the I_z term, leaving one-spin single quantum terms for detection. A coherence transfer pathway for the iDQCs in the prototypical pulse sequence we are using to detect images can be written briefly as

$$\begin{aligned} &I_{zi}I_{zj} \xrightarrow{\pi/2} I_i^+ I_j^+ \xrightarrow{GT} I_i^+ I_j^+ \exp(i2\gamma GT) \\ &\xrightarrow{\pi/2} I_{xi}I_{zj} \exp(i2\gamma GT) \xrightarrow{2GT} \xrightarrow{D_{ij} I_{zi} I_{zj}} I_i^- \end{aligned} \quad (1)$$

With uniform magnetization, and ignoring both relation and inhomogeneous broadening, the exact signal at the echo time TE obtained from either the quantum or classical treatment is;[11]

$$\begin{aligned} &M^+ = iM_0 2(\tau_d / \Delta_s TE) J_2(-\Delta_s TE/\tau_d); \\ &\Delta_s = \{3(\hat{\mathbf{s}} \cdot \hat{\mathbf{z}}) - 1\}/2, \; \tau_d = (\gamma \mu_0 M_0)^{-1} \end{aligned} \quad (2)$$

where J_2 is the second-order Bessel function; s is the direction of the gradient pulse; τ_d is the dipolar demagnetizing time ($\tau_d \approx 240$ ms for pure water at room temperature in a 4 Tesla magnet). Note that this signal can be quite substantial since the maximum value of the Bessel function J_2 is xxx. In most realistic imaging applications, spin relaxation makes such a long TE impractical, and the iDQC signal is weaker than a conventional image. Therefore, the real utility of the iDQC images comes from different contrast. In the conventional picture ignoring dipolar couplings, the signal vanishes completely because the correlation gradient wipes out the magnetization.

All experiments were done on a 4 T whole-body magnet (GE Signa Echospeed 5.8, GE Medical Systems, Waukesha, WI) at the University of Pennsylvania Medical Center. A standard GE quadrature birdcage head coil was used to obtain both silicone oil phantom and human brain images. The pulse sequence in Fig. 1 was used to generate iDQC images by

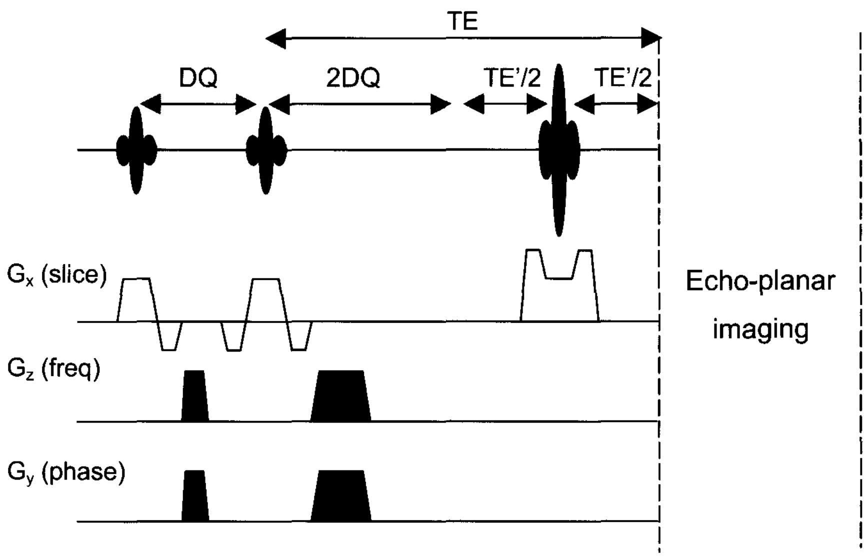

Fig.1. Schematic diagram of intermolecular double quantum coherence (iDQC) imaging pulse sequence with EPI readout

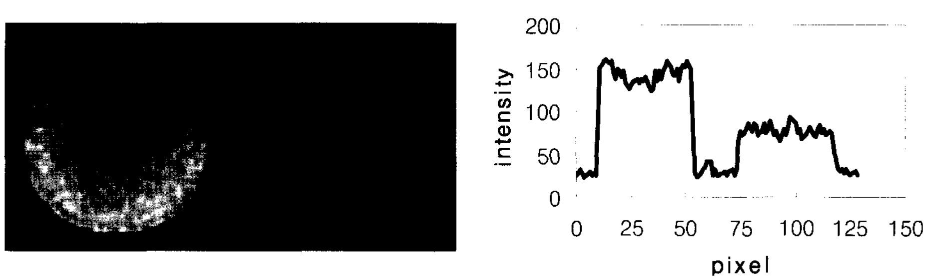

Fig. 2. iDQC images with z (left) and y (right) correlation gradients and the corresponding (absolute) intensity graph.

applying a correlation gradient along the z and/or y axes. Axial images were obtained using the following imaging parameters: matrix size 128 × 64, field-of-view 24 cm, slice thickness 10 mm, number of signal accumulations 16, and TR 5 sec. The longer values of TR were used to eliminate the possibility of interscan stimulated or shift stimulated echoes.[14]

For iDQC imaging, the correlation gradient amplitude was usually set to 2.2 G/cm and the duration was 2~4 msec. This combination of gradient parameters produces a phase variation across the voxel with a periodicity of 600~300 μm (helix pitch = $2\pi/\gamma GT$). The iDQC signal is primarily determined by coupling between spins at half helix pitch (correlation distance). This distance is much smaller than a typical voxel dimension (>1 mm) but much larger than the diffusion distance of water.

RESULTS and DISCUSSION

All iDQC images were obtained using a two-step phase cycling for the first RF pulse designed to suppress conventional signals (e.g. single-quantum contaminations). In general, multiple-quantum dipolar field effects are proportional to $3\cos^2\theta-1$ where θ is the angle between the correlation gradient direction and the dipolar field. Warren et al. have shown that magic-angle gradients suppress these effects and the directional dependence was also demonstrated for multiple quantum coherences.[8,15] The iDQC signal using a correlation gradient perpendicular to the field (x or y direction) is -1/2 of the iZQC when the gradient is along the main field (z direction). Fig. 2 illustrates the gradient direction effects (absolute intensities of images with z and y direction gradients; TE=150 ms), which can verify that the signal is not contaminated by conventional signal or stimulated echoes. For the iZQC images (without the second correlation gradient), a correlation gradient chopping method has been also employed to removed the conventional single quantum signal generated by the second RF pulse.(ref)

As shown in Eq. (2), the iDQC signal grows during the echo delay, whereas new transverse magnetization would decay with $T_{2,\mathrm{DQ}}$ relaxation during this time. In Fig. 3 iDQC images of a silicone oil phantom and the intensity graph are shown as a function of echo time which show an increase in signal intensity up to an echo time of ~150 ms followed by

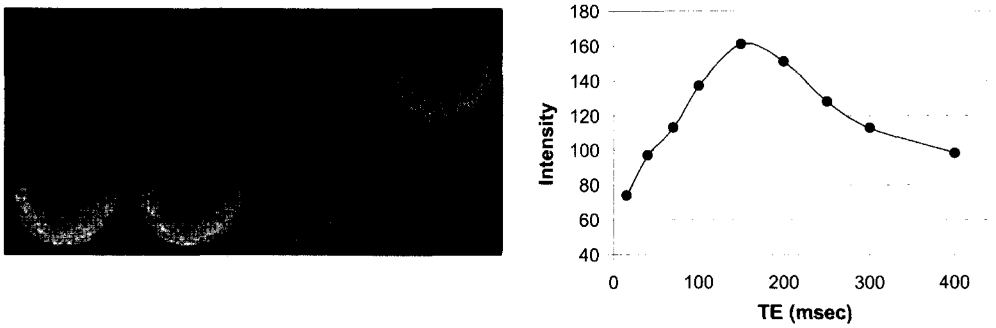

Fig. 3. iDQC images and the intensity graph of Si phantom, taken for a fixed τ_{DQ} (10ms) and different TE's (15, 40, 70, 100, 150, 200, 300 and 400 ms from top left).

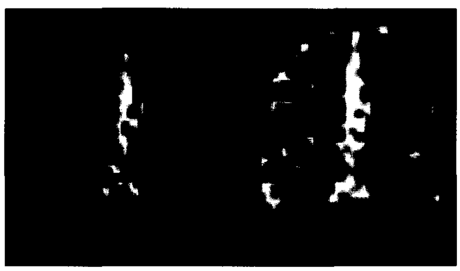

Fig. 4. iDQC images of human brain with different TE's, 20 ms (left) and 50 ms (right) : matrix size 64x64, slice thickness of 10 mm, τ_{DQ} = 10 ms, NEX = 16, TR = 5s.

decreasing signal. This is similar to the previous experimental works on iZQC images.[8,11] This experimental result also verifies that these images are not contaminated by other conventional signals. The initial signal growth with increasing TE is inconsistent with either conventional single quantum contamination and interscan stimulated echoes which should be simply decayed with TE. Fig. 4 shows iDQC human brain images (TE = 20ms, 50 ms), which also show an increase in signal intensity for the longer TE. For short values of τ_{DQ}, the iDQC has a magnetization squared weighting since the signals mostly come from two-spin correlations.[8,11] In general, as discussed elsewhere,[7,8,14] iDQC images may give relatively poorer contrast than iZQC images due to dephasing effects of DQCs during the evolution period (twice of conventional single quantum coherences). However, the iDQC-imaging will be more sensitive to motion and flow.

In this paper, the feasibility of the iDQC imaging has been investigated by changing the experimental parameters – echo time (TE), direction of the correlation gradient, and double quantum evolution time (τ_{DQ}). All the experimental results agree well the theoretical expectation and those of the previous iZQC imaging. Despite the intrinsically low intensity, the iDQC images can highlight different features than conventional images.

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