$T_{1\rho}$ fMRI at 9.4 T: different contrasts in the parenchyma and at the cortical surface

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Introduction Most current functional magnetic resonance imaging (fMRI) techniques measure changes in water T_2* caused by blood oxygenation-level dependent (BOLD) contrast. A well-known drawback of these blood susceptibility based methods is that the fMRI signal dominates at large draining veins and surroundings areas and thus is not localized to sites of neuronal activity. Recently, Hulvershorn et al. found that $T_{1\rho}$ increases during activation of human visual cortex at 3 T [1]. $T_{1\rho}$ is the spin-lattice relaxation time (T_1) in the rotating frame during application of an on-resonance spin-locking (SL) pulse. The functional elevation of $T_{1\rho}$ was mostly attributed to an increase in cerebral blood volume since the $T_{1\rho}$ of blood water was found to be much higher than that of tissue at 3 T. In order to study whether similar $T_{1\rho}$ contrast can be detected at higher magnetic fields and its spatial characteristics, we measured the functional response of $T_{1\rho}$ at 9.4 T using high spatial resolution.

Materials and methods All MR experiments were carried out on a 9.4T/31-cm magnet (Magnex) interfaced to a Unity INOVA console (Varian). Four adolescent cats were anesthetized and kept under normal physiological conditions. A 1.8-cm diameter surface coil was used to achieve high spatial resolution and high sensitivity. Shown in Fig. 1A is a double spin-echo EPI sequence with a non-selective SL preparation pulse, where after a 2-ms adiabatic half passage pulse the RF amplitude is decreased to the desired SL field (B_1) and then held constant for the spin-locking time (TSL) [2]. Following SL, transverse spins were imaged with double spin-echo EPI acquisition. Since surface coil excitation induces inhomogeneous B_1 field, the spin-locking field in the sample ($B_{1,SL}$) is consequently spatially inhomogeneous. This $B_{1,SL}$ heterogeneity is shown in Fig. 1B, where $B_{1,SL}$ at a region of interest (ROI) close to the coil (red square) is 0.25 G, ~37% higher than that (0.18 G) of another ROI (blue square) further from the coil. Despite the $B_{1,SL}$ heterogeneity, the $R_{1\rho}$ map shows only a small amount of spatial inhomogeneity, with about 2% difference between the $R_{1\rho}$ (=1/$T_{1\rho}$) values of the two ROIs (Fig. 1C). For fMRI, a transverse slice was chosen with imaging parameters: 2 × 2 cm^2 FOV, 2 mm slice thickness, 64 × 64 matrix size, TE = 28 ms, and a repetition time (TR) of 2 s. The SL amplitude was $B_{1,SL}$ = ~0.06 G at the near-coil ROI. An fMRI run of single-shot SE-EPI images with TSL of 0 or 50 ms duration was acquired in an interleaved manner. The runs with and without the SL preparation gave the $T_{1\rho}$-weighted fMRI and SE-BOLD responses, respectively. The visual stimulus was a high contrast black and white square-wave drifting grating. The block-design stimulation paradigm was 20 s control, 20 s stimulation, and 30 s control. Functional $R_{1\rho}$ responses were calculated from the SE-BOLD and $T_{1\rho}$-weighted fMRI data, by pixel-wise fitting to a mono-exponential decay on TSL for each time point. The percentage change maps were calculated for SE-BOLD, $T_{1\rho}$-weighted fMRI and $R_{1\rho}$ responses, where activated pixels pass a cross correlation coefficient (CCC) threshold of 0.4 and a minimal cluster size of 3 pixels.

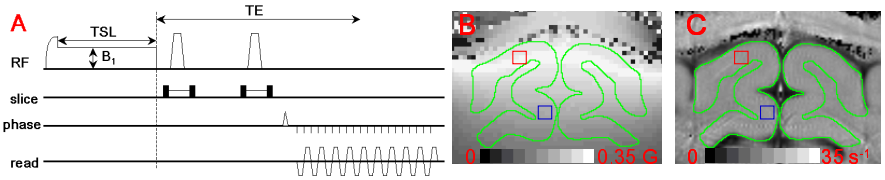

Fig. 1. (**A**). Diagram of the pulse sequence consists of a spin-locking preparation pulse followed by a double spin-echo EPI acquisition. For our surface coil, the $B_{1,SL}$ map shows significant spatial inhomogeneity (**B**). However, the map of $R_{1\rho}$ (=1/ $T_{1\rho}$) shows little spatial variation (**C**). Gray matter areas are outlined in green.

Results and discussions Fig. 2A and 2B show the percentage signal change maps from a representative study. The baseline $R_{1\rho}$ values of tissue and cerebrospinal fluid (CSF) water are measured to be ~20 s^{-1} and ~4 s^{-1} at 9.4 T, respectively. Parenchymal signal intensity is significantly attenuated in the $T_{1\rho}$-weighted image, whereas CSF signal is only slightly reduced as compared to the SE image (Fig. 2B vs. 2A). Functional signal increase within the gray matter is detected in both SE-BOLD (2A) and $T_{1\rho}$-weighted maps (2B), but the percentage change within the parenchyma is higher (more yellow pixels) with SL preparation. As a result, the calculated relative $R_{1\rho}$ change map shows decrease of $R_{1\rho}$ in the parenchyma, consistent with the observation of $T_{1\rho}$ increase in human visual cortex. The averaged relative $R_{1\rho}$ decrease at the middle of the cortex was ~0.8% (n = 4), also similar to that reported in humans (0.7%). In contrast, $R_{1\rho}$ increases at the boundary of parenchyma and CSF. This spatially opposite contrast of $R_{1\rho}$ was consistently observed for all studies (n = 4).

Because $R_{1\rho}$ values of arterial and venous blood water are unknown at 9.4 T, it is premature to determine the exact signal sources of the observed $R_{1\rho}$ contrast. For voxels at the cortical surface, a $R_{1\rho}$ increase is likely caused by a functional change of the CSF partial volume, which may be induced by a dilation of surface vessels, or a shift (expansion) of tissue volume because of the CBV increase at the parenchyma. Because CSF has a much smaller $R_{1\rho}$ value than tissue, a functional decrease in CSF partial volume will lead to a $R_{1\rho}$ increase in these surface voxels. A small functional decrease of CSF partial volume was reported recently with simultaneous nulling of blood and CSF signal, though the sensitivity was low after double nulling [3]. If the change of CSF partial volume could be confirmed, it may be important for the understanding of hemodynamic responses, and for modeling of BOLD signal. Because $T_{1\rho}$ is close to T_2 at low $B_{1,SL}$ field and the T_2 of venous blood is much shorter than that of tissue at 9.4 T [4], an increase of venous CBV may also contribute to $R_{1\rho}$ increase if venous $R_{1\rho}$ is larger than that of tissue.

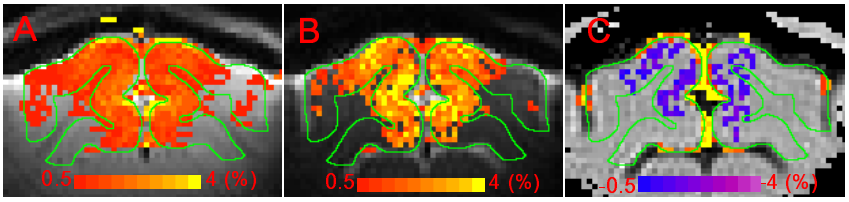

Fig. 2. Percentage signal change maps obtained by SE-BOLD (**A**) and $T_{1\rho}$-weighted fMRI with TSL = 50 ms (**B**). $\Delta R_{1\rho}/R_{1\rho}$ map (**C**) overlaid on a baseline $R_{1\rho}$ image was calculated from SE-BOLD and $T_{1\rho}$-weighted maps. $R_{1\rho}$ decreases at the parenchyma whereas increases at the boundary of parenchyma and CSF. Gray matter areas are outlined.

Because tissue $R_{1\rho}$ is insensitive to the susceptibility changes in blood [5], functional decrease of $R_{1\rho}$ at the parenchyma was mostly ascribed to CBV dilation at 3 T because the blood $T_{1\rho}$ value is significantly (30-50%) longer than that of tissue water [1]. Given similar T_2 (and T_1) values of arterial blood and tissue water at 9.4T, the difference in $R_{1\rho}$ may be much smaller. A preliminary computer simulation based on a three-compartment model (tissue, arterial and venous blood) indicated that CBV increase and blood oxygenation level change could not fully explain the observed $R_{1\rho}$ decrease (results not shown), suggesting other mechanisms may contribute.

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References: [1]. Hulvershorn J et al., *MRM* 54:1155-1162 (2005). [2] Grohn HI et al., *MRM* 51:4-8 (2004). [3]. Donahue MJ et al., *MRM* 56:1261-1273 (2006). [4]. Lee SP et al., *MRM* 42 :919-928 (1999). [5]. Kettunen MI et al., *MRM* 48:470-477 (2002).