Insight into intravoxel incoherent motion: appearance of signal from interstitial fluid

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Target Audience: MR Physicist, Radiologist

Purpose: Blood flow in capillaries has been believed to be intravoxel incoherent motion (IVIM) whose MR signal appears in diffusion weighted imaging (DWI) at low *b* values as well as MR signal from free water. We questioned this belief and investigated T2 changes along with *b* values. Then we focused on the existence of interstitial fluid (ISF) and the oxygen concentration dependency of its T2 was quantified.

Methods: Six healthy volunteers underwent brain DWI with 3-T MRI. A single-slice which includes enough gray matter was imaged using a single-shot SE-EPI with FLAIR: TI, 2650 ms; *b* value, 0, 10, 20, 50, 100, 200, 400, 600, 800, 1000 s/mm^2; FOV, 220 × 220 mm^2; matrix size, 64 × 64; slice thickness, 5 mm. To calculate T2, this imaging was performed at two different TEs (54, 100 ms). This series of experiment was repeated 10 times. Gray matter was segmented on each image and T2 value of gray matter was obtained at each *b* value. Then, to investigate how the transverse relaxation rate (R2) of ISF mimetic solution changes along with the oxygen concentration, a test tube filled with saline was scanned with 1.5-T MRI using a single-slice SE sequence: TR, 2000 ms; TE, 10, 100, 200, 300 ms; FOV, 240 × 240 mm^2; matrix size, 256 × 256; slice thickness, 10 mm. The T2 of saline solution was adjusted to that of ISF[1] by doping $CuSO_4$. The oxygen concentration of the solution was varied by bubbling (nitrogen and oxygen) and exposure to the atmospheric pressure; three partial pressures of oxygen (PO_2: 0, 152, 760 mmHg) was employed. The temperature of the imaged tube was kept at 36℃ with a water bath controlled by a constant-temperature circulator.

Results and Discussion: The T2 value of gray matter increased with decreasing *b* values (Fig. 1). This increase was well explained by the existence of ISF; the volume fraction is 15 - 20% and T2 value is 340 - 460 ms[1]. Whereas blood in capillaries which has been believed as IVIM component does not explain the observed increase of T2 because of small volume fraction (2 - 3%) and low T2 (averagely less than 100 ms). Since T2 of grey matter stays constant at *b* values larger than 1000[2], Fig. 1 indicates that signal from ISF is gradually suppressed with increasing *b* values up to 1000. This result reflects the various situation of ISF: from the Starling's flow near capillaries to the slow pseudo diffusion in the restricted intracellular space. On the other hand, the pseudo diffusion property of the blood flow in capillaries is calculated to be suppressed at *b* values larger than 50 by the theory of anisotropic directional distribution model[3] of vessel segments with the average kink angle of 135°. This estimation tells that blood flow in capillaries is rather intravoxel coherent motion (IVCM). Because the previous model of the blood flow in capillaries employs the random directional distribution model which does not represent the actual structure of capillaries[4], this model underestimates the pseudo diffusion coefficient and the belief that blood flow in capillaries is IVIM should be reconsidered. The R2 of the saline mimetic solution increased with an increase in oxygen concentration reflecting the paramagnetic effect of oxygen molecule. The oxygen concentration dependency of R2 was 1.6×10^{-4} [1/(s·mmHg)] and this value well explains quantitatively the previously reported phenomenon that fMRI signals obtained by using DWI at *b* = 250 showed conspicuous time course which has dimple[5]. This dimple may reflect the increase in oxygen concentration in ISF causing a decrease in signal from ISF. The standard deviation of T2 tends to decrease along with an increase in *b* values (Fig. 1). This deviation is supposed to be caused by the fluctuation of the magnetic field distortion along the capillaries[6] which depends on the blood oxygenation. This magnetic field distribution affects the ISF near capillaries but does not spread to the neuronal cell area, interpreted from Fig. 1 showing small standard deviation at *b* = 1000. This structural consideration also explains the previously reported results that showed a rapid decrease in fMRI signal of DWI with *b* = 1800 and a slow decrease in that with *b* = 250 after the end of the stimulation[5]; DWI with *b* = 1800 may mainly reflect the signal from neuronal cell area where activated signal changes rapidly, and DWI with *b* = 250 includes signal from ISF near capillaries where the magnetic field distortion due to blood oxygenation changes slowly.

Conclusion: The signal from ISF may appear in DWI and the interpritation of IVIM component should be reconsidered.

References:

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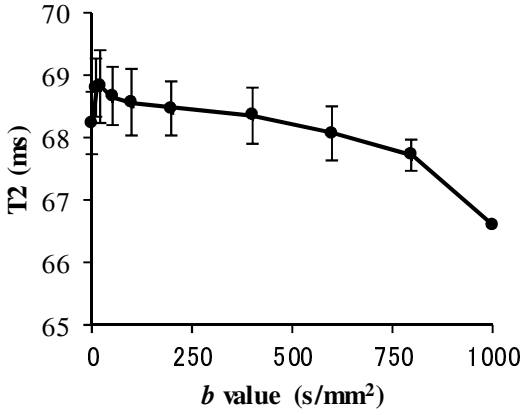

Figure 1 T2 versus *b* value in gray matter.