Translational water diffusion influences magnetization transfer processes in a pH dependent manner

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Introduction.

Magnetization Transfer (MT) between water and the exchangeable hydrogens of biomolecules (BM), constitutes a powerful source of endogenous contrast in the images obtained by Magnetic Resonance methods. Basically, two mechanisms have been proposed for MT processes. Direct exchange of magnetization between the water and the exchangeable protons of BM (OH, NH, etc…) or exchange of magnetization between water molecules with restricted rotational dynamics solvating BM and the freely moving water molecules in bulk solvent. Both mechanisms involve water diffusion but the direct influence of this parameter on MT has not been sufficiently evaluated previously.

Methods.

We investigated the influence of the apparent diffusion coefficient (ADC) of water on MT transfer in solutions of 1M L-Glutathione containing or not 50% Glycerol. Z-spectra (360.13 MHz, 22^0C) representing the ratio of intensities Ms/Mo of the water resonance were obtained at 8.4 Tesla before (Mo) and after (Ms) presaturation (5s) over a range of frequencies at pH 4.0, pH 7 and pH 9.0 using a Bruker AM-360 NMR spectrometer. ADC´s for water were determined using the PFG method.

Results.

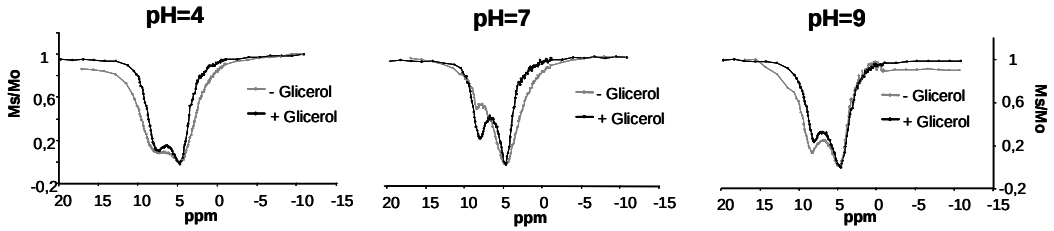

Figure 1. Z spectra (360.13 MHz, 22^0C) of 1M oxidized glutathione solutions in the absence (-) and presence (+) of 50% w/v glycerol.

Z spectra depicted two overlapping MT peaks at 4.7 ppm and 8 ppm, respectively. The peak at 4.7 ppm corresponds to MT transfers between water molecules while the peak at 8.0 ppm reflects MT transfers between the NH groups of oxidized glutathione and water. The presence of glycerol, decreased the apparent diffusion coefficient of water from 1.5 to 0.3 10^{-5} cm^2 s^{-1}. This effect in the translational diffusion of water resulted in appreciable and characteristic effects on the z-spectra at the different pH´s. In particular at pH 7.0, decreased water ADC increased the efficiency of the MT transfer between the NH groups of glutathione and the surrounding water molecules.

Conclusion.

Recently, a variety of Magnetic Resonance Imaging methods have been proposed to measure extracellular pH using MT methods (Ward and Balaban, Mag. Res. Med 2000, 44, 799-802; Zhang et al, 1999, Angew. Chem, 38, 3192-3194). Our results suggest that, in addition to tissue pH, the diffusion coefficient of water may influence considerably the MT processes affecting concomitantly the pH measurement. In order to implement successfully these methods in vivo, appropriate correction factors must be introduced to account for the effects of the different diffusion environments where the pH probe may be distributed in situ.

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