Localized ^{31}P saturation transfer in rat brain

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Introduction: Phosphorus saturation transfer experiment is useful for studying chemical exchange processes such as creatine kinase and ATP-ase reactions *in vivo* in human or animal brain, heart or skeletal muscle (1). This technique, however, is sensitive to several experimental imperfections. Direct partial saturation of the observed phosphocreatine (PCr) during selective saturation of the neighboring γ-ATP signal has to be considered in the measurement setup and in data processing of the creatine kinase reaction study (2). The use of transmit/receive surface coils makes complete saturation of the γ-ATP peak difficult and sophisticated saturation schemes such as BISTRO (3) are necessary (4). Since the 3D localized spectroscopy mode reduces drastically SNR and can lead to large chemical shift displacement errors, the ^{31}P signal is usually localized by the active volume of a surface coil alone. In such a case, however, the measurement accuracy of saturation transfer in brain can be affected by a mismatch between saturated and excited volumes of tissue. In experiments on rodent brain, the masticatory muscle tissue containing a high concentration of PCr can also be excited by a nonselective excitation pulse transmitted by a surface coil, thus forming a contamination of the observed PCr signal, usually as a broad (poorly shimmed) signal component. This contamination can lead to systematic errors of the calculated rate constants and fluxes. Thus, we aimed to compare creatine kinase saturation transfer experiments in rat brain with and without outer volume presaturation of surrounding tissues, using one-dimensional (1D) ISIS localization in the horizontal direction in both cases.

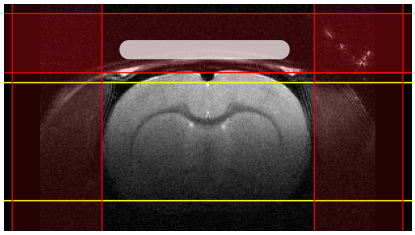

Fig. 1. Position of the ^{31}P RF coil, the 1D ISIS excitation region (yellow lines) and the respective outer volume saturation regions (red demarcated and shaded areas).

Experimental: The experiments were performed on five adult Sprague-Dawley rats. ^{31}P spectra were obtained on a 9.4 T spectrometer (Varian/Magnex Scientific) using a home-built coil consisting of a 20 mm diameter proton quadrature coil and a linearly polarized 10 mm diameter phosphorus coil, both used as transceivers. The γ-ATP signal was saturated by a BISTRO pulse train consisting of a series of 40 ms hyperbolic secant pulses with variable amplitudes and having a total length t_{ir} from 0.324 s to 10 s. Interleaved with BISTRO, 2.5 ms hyperbolic secant outer volume saturation (OVS) pulses were applied as shown on Fig. 1. Afterwards, a 2.5 ms adiabatic pulse inverted the magnetization in the relevant region of brain in alternate scans, followed by a 1 ms broadband nonselective adiabatic half passage pulse and a signal acquisition with alternated phase. Field homogeneity in the brain was adjusted by FASTMAP (5) using water signal. Sixty to eighty scans were collected for each of 8 different saturation times and for a control scan with irradiation offset in the mirror position relative to the PCr peak. The PCr peak intensities were obtained by fitting to a Lorentzian function using AMARES (6) from the jMrui software (http://www.mrui.uab.es/mrui). The forward creatine kinase rate constant k_{for} and the apparent T_1 relaxation time of PCr during the γ-ATP saturation (T_{1sat}) were obtained from a nonlinear regression of relative PCr signal intensities $M(t_{ir})/M(0)$ as a function of t_{ir} according to the equation:

$$M(t_{ir})/M(0) = (1 - k_{for}\, T_{1sat}) + k_{for}\, T_{1sat} \exp(-t_{ir}/T_{1sat}) \,. \qquad [1]$$

Results: Fig. 2 depicts experimental and AMARES-estimated peaks of PCr at different values of t_{ir} from experiments with and without outer volume saturation. The peaks measured by the combination of 1D ISIS + OVS had a Lorentzian shape and the fit of signal intensities to the equation [1] provided the k_{for} value = 0.43±0.05 s^{-1}. The peaks measured by 1D ISIS without the OVS showed an extra broad component, which distorted the Lorentzian shape of the PCr peak. Peak intensities obtained from this series gave the k_{for} value of 0.34±0.04 s^{-1}.

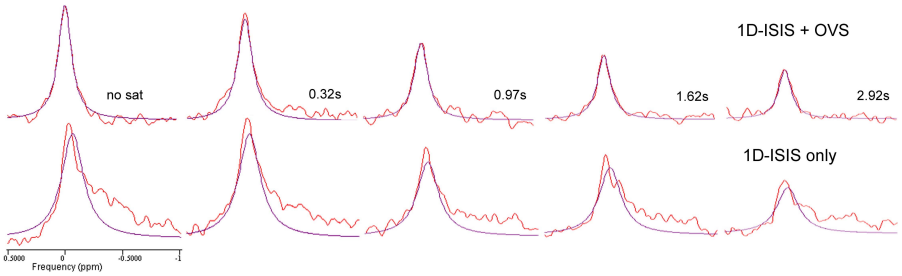

Fig. 2. Experimental (red) and fitted (violet) peak of PCr measured by a saturation transfer experiment using a 1D ISIS localization combined with outer volume saturation (upper row) and the 1D ISIS only (lower row). Numbers denote irradiation times t_{ir} of the γ-ATP peak.

Conclusions: Localization by 1D ISIS should not affect the accuracy of a saturation transfer experiment since the duration of the localization sequence (< 5 ms) is much shorter than t_{ir}, T_{1sat} and $1/k_{for}$. The results suggest that the contribution to the brain PCr signal from cranial muscles is not negligible in a saturation transfer experiment, even when a small surface ^{31}P coil is used. Neglecting this contamination can lead to an underestimation of the calculated rate constant of the creatine kinase reaction.

Acknowledgments
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