31P Exchange Sensitive Imaging in Human Brain at 7T

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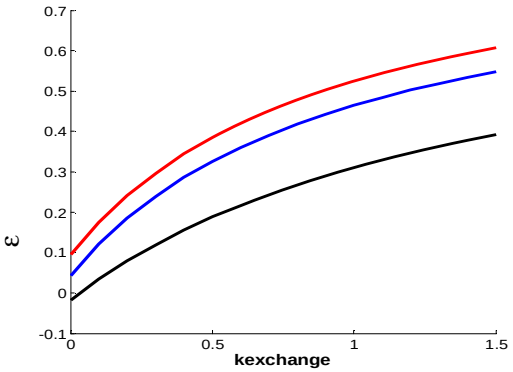
Introduction: 31P MRSI is commonly used as a functional measure of bioenergetic state in human brain. As discussed by several groups, the measurements of PCr and ATP are sensitive to numerous effects, including relaxation, concentration and chemical exchange. However while the sensitivity to creatine kinase has been well used in muscle and heart spectroscopy with saturation transfer experiments (1,2), it has been less developed for brain. This relative lack of development may be due to the known macroscopic heterogeneity of brain tissue thus requiring good spatial resolution. Nonetheless, given that creatine kinase rates have demonstrated sensitivity to physiologic condition (3,4), the development of a 31P acquisition that is specifically sensitive to exchange may be differentially more informative than measures of ratios or concentrations. We implemented exchange sensitive weighting to the 31P acquisition based on 3site exchange simulations to ascertain sensitivity to varying levels of exchange. We demonstrate this approach in controls and epilepsy patients.

Methods: Simulation: Our goal is to implement a saturation transfer experiment that enhances sensitivity to detection of abnormal chemical exchange. This is done by applying saturating rf to γ-ATP as a spectroscopic image (SwST), and compare it to the non-saturated study (SwoST) to calculate the fractional change in signal ε = (SwoST – SwST)/SwoST. Simulation of this experiment uses the variable k_{exch} as a factor between 0 and 1 that proportionately reduces all exchange rates. Under conditions of normal k_{exch}, γ-ATP saturation will reduce the detected PCr signal; with low k_{exch}, γ-ATP saturation will be comparatively less effective to reduce the PCr signal. Thus the fractional change ε declines with depressed k_{exch}. The simulation performed with three tip angles shows a nonlinear sensitivity to k_{exch}, falling rapidly at values less than 0.5. Furthermore, the simulation shows that the ε map is relatively insensitive to minor changes in tip angle, this arising because of the intrinsic normalization of ε.

Fig 1. Plot of ε at three tip angles: 14° (red), 32° (blue) and 60° (black). The model used in this simulation: TR=0.5sec, PCr 3.5mM, ATP 2.5mM, Pi 1mM, k_1 = 0.30, k_2 = 0.05, $T1_{int}$PCr 4sec, $T1_{int}$ATP 0.8sec, $T1_{int}$Pi 4sec, 25Hz irradiating B1 on γ-ATP.



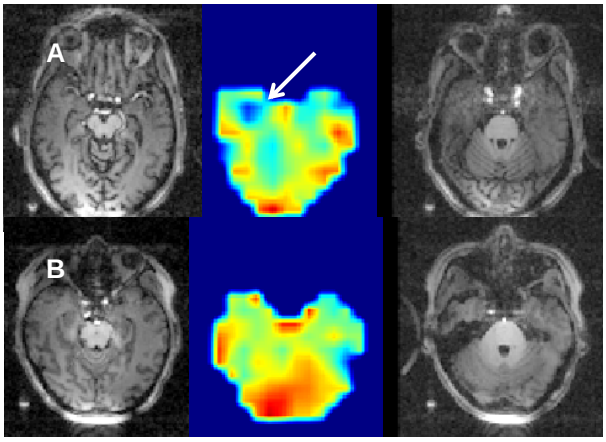


Fig 2. Scouts and ε maps from a control subject (A) and a patient with medial temporal lobe epilepsy (B), both taken through the medial temporal lobe region. The structural images span the spectroscopic imaging slice.

Acquisition: A 68cm head only Varian-Magnex 7T MR system was used with a double tuned 31P-1H TEM head coil (120.7/398MHz). Non-iterative shimming with 1st, 2nd and 3rd order shims was performed over the entire head (5), achieving a typical whole brain water linewidth of 25Hz within 3min. For human studies a pulse acquire spectroscopic imaging sequence (28deg, TR 0.5s) and sparse gaussian weighted spherical sampling (nt=3, 1219 encodes, isotropic FOV 230mm) was used with acquisition time of 30min. Thus for the saturated and symmetrically saturated studies, total acquisition time was 60min. The saturation pulse was applied to γ-ATP for 290msec, with less than 1.5W SAR. The psf of the acquisition provides a FWHM volume of 8.3cc.

Results: Fig. 2 shows the performance of the "Phosphorus Exchange Sensitive Imaging" (PExSI) in a healthy volunteer (Fig. 2A) and in a patient with medial temporal lobe epilepsy (Fig. 2B). Shown are two structural slices that span the slice thickness of the spectroscopic imaging slice. The patient has a region of depressed ε over the right medial temporal lobe (arrow).

Conclusions: Saturation transfer weighting as implemented in a spectroscopic imaging sequence can provide sensitivity to abnormalities in the creatine kinase rate constant in human brain. Additional simulations at a lower PCr concentration of 2.8mM show similar behavior and values for ε, showing it to be relatively robust. As shown in muscle and more recently in brain, the creatine kinase forward rate constant has been shown to be sensitive to physiologic state. Thus if abnormalities in dynamic processes precede changes in concentrations, sensitizing to chemical exchange rather than ratios or concentrations may be advantageous for the detection of pathology. Finally, because of its relatively low sensitivity to Bo inhomogeneity and lesser spectral overlap, 31P spectroscopy can provide whole brain spectroscopic coverage, a significant advantage for cryptogenic focal pathologies.

References: (1) Spencer and Fishbein 2000 (2) Bottomley 2002 (3) Chen W 1997 (4) Sauter and Rudin 1993 (5) Hetherington 2006