31P spectroscopic imaging of human brain at 7T

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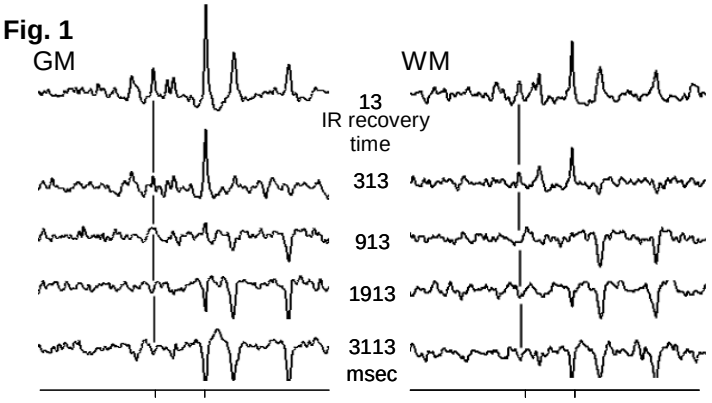
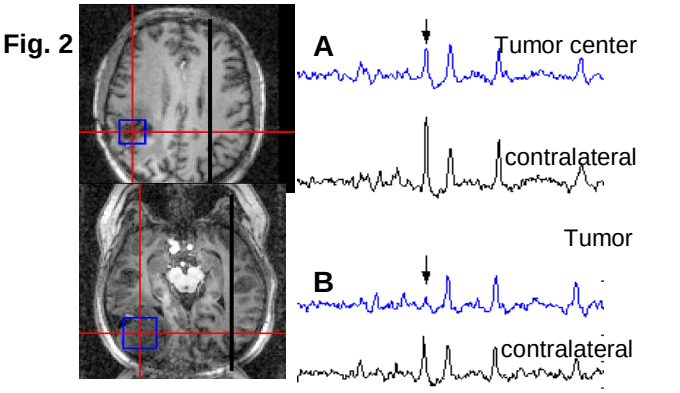
Introduction: Due to reduced spectral overlap and reduced sensitivity to B0 inhomogeneity in comparison to 1H MRSI, 31P MRSI can be advantageous for whole brain SI studies. 31P MRS is also sensitive to chemical exchange and the creatine kinase (CK) reaction, this aspect not being widely utilized in studies of the human brain. The primary limitation of 31P MRSI (SNR) can be offset by acquiring data at 7T. At 7T the 31P frequency is 120mHz, equivalent to the 1H frequency at 3T; as a result 31P TEM volume coils can provide whole brain coverage. To optimize the acquisition we measured the T1 values of PCr, ATP and inorganic phosphate at 7T using a multi-tip inversion recovery sequence and a three site exchange model. We have implemented this to demonstrate that in brain tumors there is dramatic reductions in PCr, while ATP levels are largely maintained and argue that the reduced content is not due to chemical exchange differences, but rather true decrements in PCr content.

Methods: 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 1^{st} - 3^{rd} order shims was performed over the entire head (1), achieving a whole brain B0 standard deviation of 25Hz within 3min. For the T1 measurements, a multiply sampled IR acquisition was used (TR=6, tip angle 32). The T1 analysis was performed with/without chemical exchange using the Bloch McConnell equations (2). For gray matter voxels, reported rate constants $k_{PCr\rightarrow ATP} = 0.30\ sec^{-1}$, $k_{ATP\rightarrow Pi} = 0.05\ sec^{-1}$ (3) were used. For white matter, a lower $k_{ATP\rightarrow Pi} = 0.017\ sec^{-1}$ was used, reflecting the differences between white and gray matter cerebral metabolic rates (ref). Because white (WM) and gray matter (GM) ATP concentrations are minimally different, data were referenced to an ATP concentration of 2.5mM. The time dependent three site exchange model was implemented using a least squares fit of the time course data evaluating T1 and concentrations. N=7 healthy volunteers were studied. For patient studies, parameters for optimal SNR were used, with a pulse acquire spectroscopic imaging sequence (32deg, TR 0.5s) and sparse gaussian weighted spherical sampling (1219 encodes, ~7cc resolution, 42 min acquisition).

Results: Fig. 1 shows the IR time course for GM and WM summed spectra (6, 4 voxels). While the time courses of PCr and Pi recovery are similar between gray and white matter, ATP appears to have a faster WM recovery. The $T1_{intr}$ and $T1_{obs}$ for PCr from GM, WM are not significantly different ((4.04±0.59s, 4.13±0.24s respectively for $T1_{intr}$; 2.79±0.22sec and 2.61±0.09 sec for $T1_{obs}$). However, the $T1_{intr}$ for ATP from GM, WM are different (0.73±0.06s vs. 0.47±0.03s, $p<0.05$, two tailed t test). Fig. 2 shows 31P data from two tumor patients. Spectra from a previously treated glioblastoma patient (Fig. 2A) show substantially depressed PCr but relatively normal ATP. The low PCr may result from several effects including changes in concentration, T1 and exchange rates. In considering the 3-site exchange model, decreased CK rates would increase the $T1_{obs}$ value of PCr towards $T1_{intr}$, which, under saturating conditions will reduce PCr. Assuming normal concentrations and relaxation values, show that a total loss of exchange would reduce PCr/ATP by 25% at most. From Fig. 2A it is clear that the decrement in PCr (~65%) compared to the homologous location in the contralateral hemisphere can not be solely due to exchange. Thus the loss of PCr is probably due to decreased tumor cell PCr. This perspective is supported by data from another tumor patient with a low grade astrocytoma (Fig 2B) who shows virtually no PCr in the tumor.





Discussion: The PCr T1 values are in agreement with previously reported values and consistent with dipolar interactions dominating PCr relaxation at in vivo conditions. The shorter T1 of WM ATP is consistent with in vitro studies suggesting that chemical shift anisotropy of the triphosphate chain dominates with a squared dependence on field strength (4). The short values for ATP T1 imply that the measured ATP levels may be influenced more by intrinsic T1 saturation rather than by chemical exchange, likely explaining the reports of higher ATP concentrations in WM compared to GM (5). In tumors, several simultaneous processes can result in substantial abnormalities e.g., changes in 31P T1 values, differences in ATP and PCr concentration and exchange. Independent of chemical exchange, glial tumors appear to have dramatic reductions in PCr content. 31P SI studies may be especially useful for the therapeutic management of glial tumors: i.e. necrotic areas are likely to display both reductions in PCr and ATP, while recurrent tumors will have intact ATP and reduced PCr.

Refs: (1) Hetherington 2006; (2) Spencer and Fishbein 2000; (3) Du 2007; (4) Mathur-Devre 1990; (5) Hetherington 2001