Detection and assignment of phosphocreatine signal *in vivo* in ^{1}H NMR spectra at 9.4 Tesla

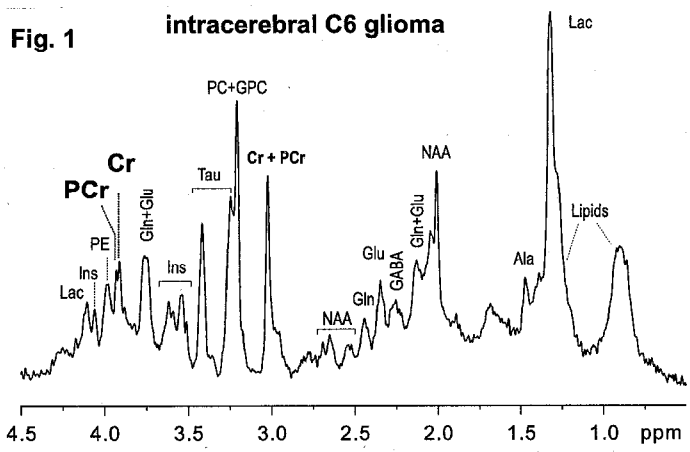
Josef Pfeuffer, Ivan Tkac, Kamil Ugurbil, Michael Garwood, and Rolf Gruetter
Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN 55455, USA

Introduction: Recent improvements in spectral resolution at 9.4 Tesla have shown that the creatine methylene peak is split into two distinct signals in brain (1), potentially permitting quantification of phosphocreatine (PCr) in the ^{1}H NMR spectrum without further editing. However, recent studies also suggested splitting of this peak in muscle tissue, with an orientation-dependence (2). The aim of this study was to demonstrate that PCr can be measured by ^{1}H NMR *in vivo* at 9.4 Tesla by observing changes of metabolite levels during hypoxia/ischemia.

Methods: Male Sprague-Dawley rats were measured at 400 MHz (9.4 T) with a quadrature ^{1}H surface coil. The spectra were acquired from 63 µL volumes by a 2-ms echo time STEAM sequence with VAPOR water suppression and outer volume saturation (3). Breathing gas was switched to N_2O with 2% isoflurane to induce hypoxia prior to euthanasia. First- and second-order shimming was done with a fully adiabatic version of FASTMAP (1) and the singlet linewidth was 0.02-0.025 ppm. For quantification with LCModel (4), water was used as an internal standard assuming 0.83 ml/g. The concentrations of metabolites and macromolecule resonances were repeatedly determined from 2-min spectra (32 scans).

Results: Splitting of the Cr methylene peak into two distinct chemical shifts was consistent with phantom results (not shown) and observed consistently in rat hippocampus, striatum, C6 glioma and cortex at 9.4 Tesla, whenever excellent shimming was present and/or resolution enhancement was added to the processing. Fig.1 shows a spectrum of an intracerebral C6 glioma in rat (TE = 2 ms, nt=640, 63µL). In addition to the highly resolved spectrum, the Cr and PCr resonances at 3.911 and 3.931 ppm indicate splitting as in previous studies (1). To further validate the assignment, ^{1}H NMR spectra were measured during euthanasia induced by hypoxia/KCl injection respectively. Fig.2 shows the spectra before and after cardiac arrest. Clearly, the fine structure of the peak after global ischemia was reduced and the linewidth narrowed consistent with complete PCr depletion and conversion to Cr.

Fig. 1



Using LCModel analysis, the signals of more than 15 metabolites were measured simultaneously (5). Fig.3 shows the time course of PCr depletion during progressive hypoxia/anoxia and the concomitant increase in Cr. Noteworthy is the remarkable numerical stability of total creatine signal. The rapid depletion of PCr coincided with complete elimination of brain glucose and lactate increase.

Conclusions: High sensitivity and excellent shimming permits detection of PCr and Cr changes in rat brain and experimental tumors at very high magnetic fields. These measurements permit the non-invasive monitoring of phosphorylation potential via PCr/(PCr+Cr). While detection of PCr signal in C6 glioma points to the feasibility of such measurements in other tissues, it remains to be determined whether such advances are possible also in skeletal muscle.

References: **1**.Gruetter R et al, *JMR* 135,260,1998. **2**. Ntziachristos V et al MRM 38, 33, 1997. **3**. Tkac I et al. *MRM,* 1999, in press. **4**. Provencher SW, *MRM* 30,672,1993. **5**. Pfeuffer J et al. *MAGMA* 6 S1, 15, 1998.

Supported by NIH R01 CA64338, P41 RR08079, W.M.Keck and Whitaker Fdn.

Fig. 2

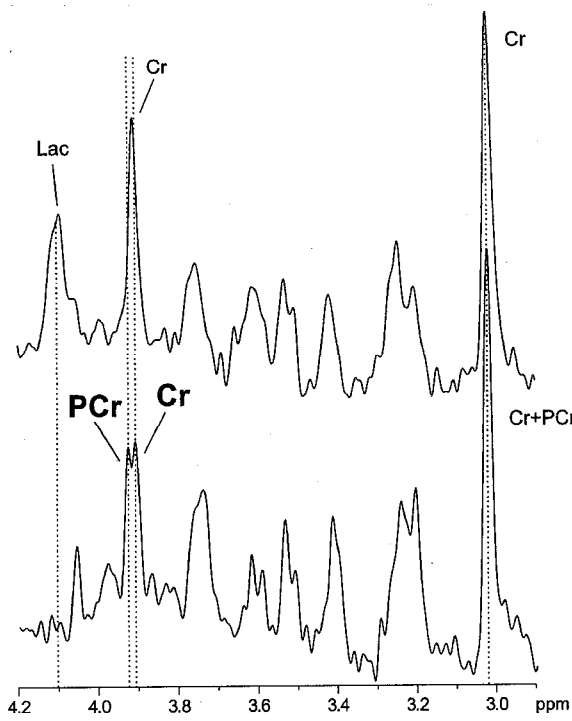


Fig. 3