Localised Phosphorus Spectroscopy of the Brains of 7-Day Mouse Pups

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Introduction: Phosphorus (^{31}P) magnetic resonance spectroscopy (MRS) can be used to study the effects of hypoxia-ischemia (HI) in neonatal brain. In particular the ratio [phosphocreatine (PCr)]/[inorganic phosphate (Pi)], has great prognostic utility[1]. In experimental models, ^{31}P MRS is an important tool for the investigation of cerebral HI injury and the assessment of putative therapeutic agents. We have employed a modified Rice –Vannucci model[2], comprising ligation of the left carotid artery followed by a period of hypoxia, in 7 day old mouse pups. This produces a HI insult to the left hemisphere. We describe here methods for the acquisition of ^{31}P spectra from day 7 mouse pups, localised to a single hemisphere, using a single shot technique based on SIRENE[3].

Methods: The SIRENE technique localises signal to a voxel of interest by saturating signal from the surrounding tissue and we have implemented this method on a 7 Tesla Bruker Biospec spectrometer. The brain was centred in a single-turn surface coil. Adiabatic full-passage hyperbolic secant (sech) inversion pulses (bandwidth: 16,300 Hz) invert the signal outside the volume of interest. After an inversion time, TI, 3 sets of 6 sech saturation pulses (bandwidth: 15400Hz) are applied to saturate the remaining signal from outside the voxel. The transmitter pulse amplitudes for the saturation pulses were calibrated interactively in set-up mode with the spectrometer tuned to ^{1}H frequency. Calibration measurements were used to derive the required ^{31}P transmitter pulse amplitudes. In set-up mode the inversion pulses are not switched on; the user views a profile of the sample perpendicular to the plane of the surface coil and adjusts the pulses amplitudes so as to minimise the signal from saturation bands which are parallel to the coil (saturation bands 1 and 2; see figure 1). Pulse gains for saturation bands perpendicular to the coil (bands 3-6) are calculated automatically. For the first saturation set, the pulse gains for saturation bands 3-6 are set so that maximum saturation occurs at a quarter of the distance between saturation bands 1 and 2. The position of maximum saturation is incremented with saturation set number so that it occurs at half and three quarters of the distance between saturation bands 1 and 2 respectively for set 2 and 3 (see figure 1). This is done to ensure uniform saturation perpendicular to the surface coil in spite of B_1 non-uniformity. Following saturation of the outer volume a non-selective excitation pulse is applied. In the application described here the voxel was positioned such that one hemisphere of the brain was saturated leaving signal localised to the other hemisphere.

A one-pulse spectroscopy sequence with an adiabatic inversion preparation was used to calibrate the optimum TI for nulling the ^{31}P metabolites in the saturation band. A TI of 1200ms yielded good attenuation of signal across the whole spectrum from a 7-day mouse pup. The other acquisition parameters are: TR = 5s, 384 averages; giving a scan time of ~ 32 mins.

Results: Figure 2 shows an axial scout image of the 7-day mouse pup brain together with an image acquired using SIRENE showing the saturation of the right hemisphere; the field of view is the same for both images. The width of the saturation band is ~ 3 times larger in ^{31}P mode due to the ^{31}P and proton gyromagnetic ratios; thus in ^{31}P mode the signal seen on the extreme right of figure 2b is saturated also. Figure 3 shows spectra from an un-operated 7-day mouse pup: (a) localised to the left hemisphere, (b) localised to the right hemisphere and (c) with the saturation band positioned so as to saturate the whole brain.

Discussion: 7-day mouse pups have brains less than 1cm across. This small size presents a great challenge to localised ^{31}P spectroscopy; care must be taken to preserve enough signal for spectrum acquisition in a period of time consistent with physiological stability. Conventional PRESS and STEAM localisation sequences utilise three selective pulses to localise the signal to the volume of interest. When used with a surface coil, voxels that have dimensions of a similar order to those of the coil (typically the case with ^{31}P spectroscopy) can have poor signal profiles due to the B_1 inhomogeneity. SIRENE uses a single excitation pulse and so results in much improved voxel profiles and thus more efficient signal acquisition. We have used SIRENE to successfully acquire spectra localised to a single hemisphere in a 7-day mouse pup. To our knowledge this is the first report of localised ^{31}P spectroscopy in 7-day mouse pups. It is proposed to use this ^{31}P spectroscopy technique along with the modified Rice-Vannucci model to study the evolution of perinatal HI injury and the effects of putative therapeutic agents.

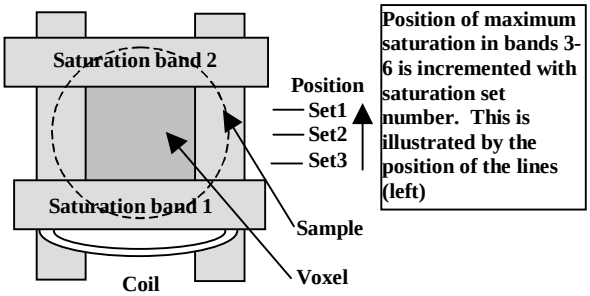

Figure 1: Position of the saturation bands

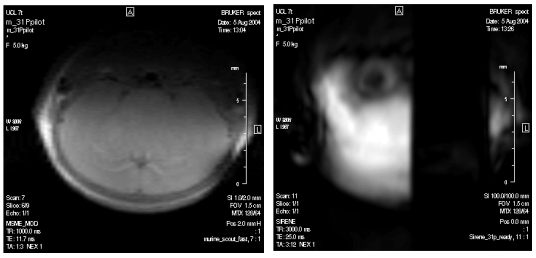

Figure 2: (a) scout image of the 7-day mouse pup brain, (b) SIRENE image showing saturation of the right hemisphere.

References:

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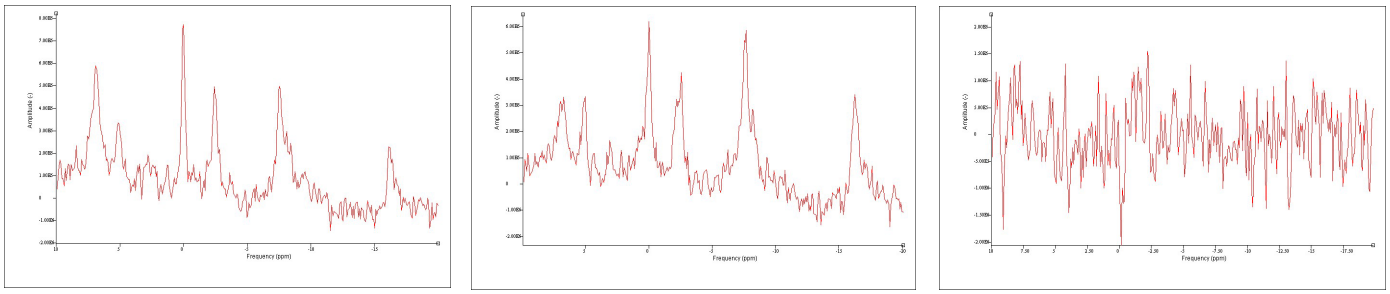

(a) **(b)** **(c)**

Figure 3: Spectra from a 7-day mouse pup displayed with 30 Hz line broadening: (a) left hemisphere, (b) right hemisphere; (c) whole brain saturation