In vivo detection of hyperpolarized 15N Choline in the rat

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Introduction:

^{15}N MRS labeled experiments are especially useful for measuring the rates of synthesis and turnover of amino acids such as glutamate and glutamine, implicated in glutamate neurotransmission (1). However, the very low natural abundance of ^{15}N (0.365%) makes the study of nitrogen metabolism difficult. A recent study has reported relatively long T_1 for some nitrogen compounds (i.e. Choline) (2), suggesting that ^{15}N may be a suitable candidate to be used with hyperpolarization by means of DNP (3). This is of special interest for observing phospholipid metabolism in cancer due to changes in choline metabolism (2).The aim of the present study was to demonstrate the feasibility of detecting hyperpolarized ^{15}N labeled Choline *in vivo* in the rat.

Methods:

All the ^{15}N MRS data were acquired on a 9.4T system (Varian/Magnex Scientific) using a home-built quadrature ^{1}H coil with a single 5-loop 10 mm ^{15}N coil placed on the head of the animal. For the *in vivo* experiments, male Sprague-Dawley rats (~350g) were anesthetized using 1.5% isoflurane and a femoral vein was catheterized for injection. Blood pressure, respiration rate and temperature were maintained within normal range.

^{15}N choline chloride (Sigma Aldrich) solution, prepared at a concentration of 6M in a deuterated water-glycerol solvent doped with 50mM of TEMPO as free radical, was polarized at 3.35 T and 1.2 K using a polarizer described in (4). After dissolution into 5 ml of D_2O, the ^{15}N Cho chloride sample was automatically transferred to a phase separator placed in the bore of the 9.4T system within 6s. An external pump then injected 2.5 ml of the sample over 8s into the rat femoral vein. The concentration of the ^{15}N Cho infusate was ~ 90mM. The injection was repeated two times on the same animal. The *in vitro* and *in vivo* acquisitions were performed using a 3ms 10° BIR4 pulse with 3s interpulse delay. The FIDs were analyzed with AMARES (5).

Results and Discussions:

The polarization in the cryostat reached 4% (corresponding to ~10000 times amplification compared to room temperature polarization at 9.4T). The maximum polarization was obtained after ~2hours, within 1600 s time constant.

In vivo ^{15}N Cho was discernible above the noise level for about the first ~90 s (Figure 1, 2) and the linewidth was 9 Hz. The fit for the *in vivo* ^{15}N Cho T_1 estimation was performed on the last part of the time course shown in Figure 1, from 27 to 105 s .Taking into account the RF flip angle correction, the T_1 was estimated to be approximately 150 s *in vitro* and around 1min *in vivo*. The *in vitro* results on phantom were in agreement with the one *in vitro* study using ^{15}N hyperpolarized Cho (2). The long T_1 combined with the potential to observe hyperpolarized ^{15}N Cho *in vivo* makes this compound useful for early detection of tumors and also for a potential utilization in the assessment of blood flow. The relatively long T_1 of the nitrogen atom may render other nitrogen compounds suitable for DNP studies such as this one. To our knowledge the in vivo detection of hyperpolarized ^{15}N has not been demonstrated to date. We conclude that it is feasible to detect hyperpolarized ^{15}N in live animals.

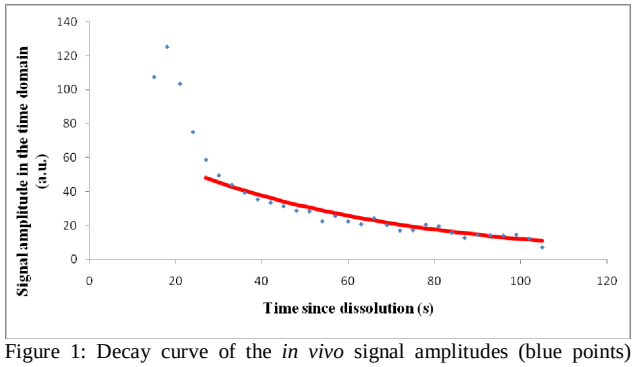

Figure 1: Decay curve of the *in vivo* signal amplitudes (blue points) plotted for the first 31 FIDs (15s-105s). A fit for the last part (27-105 s) of the plotted decay curve is shown in red.

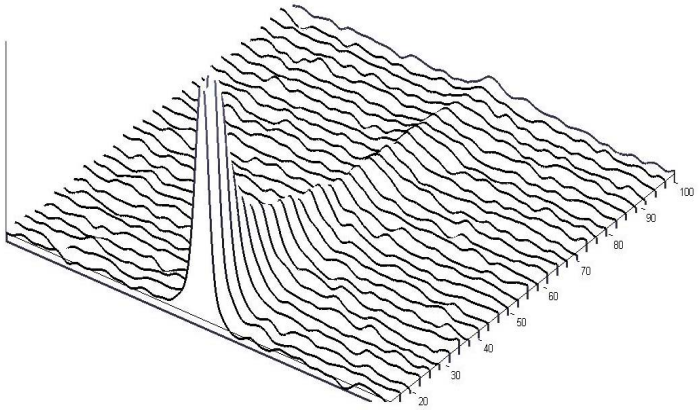

Figure 2: Plot of the first 31 *in vivo* ^{15}N Cho spectra over time (90s).

References:

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