Metabolic reactions studied with ^{13}C-DNP-MR *in vitro* and *in vivo*

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Introduction: The strong enhancement of the nuclear polarization, which has been obtained using DNP-MR [1], has profound impact on MR spectroscopy. Sensitivity improvement by many orders of magnitude widens the scope of MR to analytical areas not accessible by current state of the art MR techniques. By virtue of the method, MR analysis is completed in a time frame of the nuclear T_1 (seconds for ^{13}C). The method allows MR studies to be performed at physiological realistic concentrations in complex biological systems such as whole cells and living animals. Enzyme kinetics as well as metabolic profiles may be studied providing new insight to biochemical pathways.

Results and discussion: The DNP-NMR method has been developed for the measurement of kinetics in cellular systems [2,3]. When fumarate is ^{13}C-labelled at the C_1 and the C_4 position the hydration of fumarate by fumarase leads to $^{13}C_{1,4}$ malate, where the broken symmetry produces two signals (C1-malate 182.1 ppm, C4-malate 180.9 ppm). Both signals can be observed in immortalized cells after injection of hyperpolarized $^{13}C_{1,4}$-fumarate, figure 1. From one DNP experiment global kinetic parameters for the metabolic system may be obtained.

With use of commercially available equipment liquid state sample polarisations of up to 40% has been obtained for several compounds in tenth of mM concentrations at physiologically acceptable conditions. The metabolism of these substrates has been studied *in vivo* in animals with the purpose of developing disease diagnostic tools. One example has been studied in detail, the metabolism of acetate. Significant differences in the ratio between the two observed products from acetate, acetyl CoA and acetyl carnitine, are observed by single aquisition spectra localized over the heart or liver regions. This metabolic ratio is significantly different in the two studied organs, Figure 2.

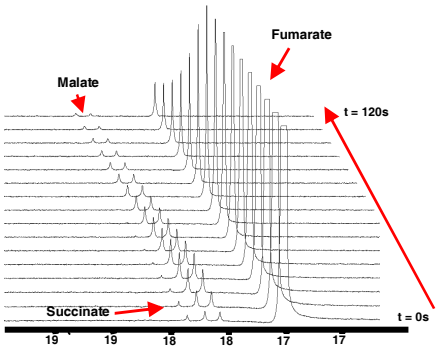

Figure 1. Metabolism of $^{13}C_{1,4}$-fumarate in immortalized cancer cells. ^{13}C NMR spectra of hyperpolarized $^{13}C_{1,4}$-fumarate (176.8 ppm) and the build up of $^{13}C_1$ (182.1 ppm) and $^{13}C_4$ malate (180.9 ppm) is seen as a function of time.

References: 1 Ardenkjaer-Larsen et al PNAS, 2003 ;100(18):10158. 2 Karlsson et all, Proc. Intl. Soc. Mag. Res. Med, 2007. 3. Andersson et al Proc. Intl. Soc. Mag. Res. Med, 2007

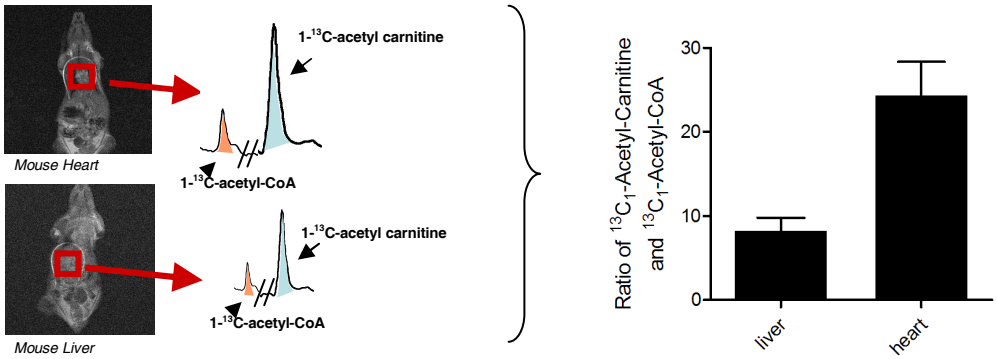

Figure 2. Distribution of the ratio of 1-13C-acetyl-Carnitine and 1-13C-acetyl-CoA in mouse heart and liver (n=6) following an i.v injection of hyperpolarized 1-13C-acetate. All experiments have been performed with a surface coil placed over the organ of interest.