Introduction: Hyperpolarized 13C metabolic MR spectroscopic imaging of pyruvate and its down-stream metabolites alanine and lactate allows real-time in-vivo studies of energy metabolism in healthy and tumor tissue [1]. At the same time, tumor perfusion can be studied using metabolically inactive hyperpolarized agents such as urea [2], whereas hyperpolarized acetate can be used to examine short chain fatty acid metabolism in vivo [3]. Research facilities and clinics perform spectroscopic magnetic resonance imaging (MRSI) experiments at increasingly higher magnetic field strengths B0 (1T, 3T, 7T, 14T) because of availability, higher spectral resolution and better thermal signal to noise ratio (SNR). Recently, it was shown that hyperpolarized experiments at even lower fields can theoretically be more sensitive than high-field MRI [4]. Long longitudinal relaxation times (T1) could favor experiments at low magnetic field strengths even further. In this study, we systematically measured T1 times for the aforementioned 13C hyperpolarization agents at clinically available field strengths (1.05T, 3.0T, 7.0T) and 14.1T under constant conditions (pH, temperature, concentration), facilitating a proper design of time critical hyperpolarization experiments at varying field strengths.

Methods: All labeled compounds ([1-13C]pyruvate, [1-13C]alanine, [13C]urea, [1-13C]acetate, [1-13C]lactate) and TRIS buffer were dissolved 1:1 (c/c) in distilled water, each compound at a concentration less than half of their maximum solubility. All solutions were neutralized and titrated with NaOH or HCl into the physiological pH value around 7.4. All experiments were conducted at room temperature. On all systems, an inversion recovery (IR) sequence was set up with equally spaced inversion times (TI), one excitation per TI and covering a range from 0s to 5xT1. The repetition time (TR) was set to five times the expected T1 or longer. The signal equation was used to estimate the equilibrium magnetization $S_0$, the flip angle $\alpha$ and the longitudinal relaxation time $T_1$ from a three-parameter non-linear least squares fit.

$$S(T) = S_0[1 - (1 - \cos \alpha) \exp(-T/T1)]$$

1T: Experiments at 1.05T were performed with custom made 3.5mL spherical phantoms in a 1H-13C dual tuned mouse coil on an Aspect M2 permanent magnet small animal scanner (Aspect Magnet Technologies, Netanya, Israel), where a standard inversion recovery (IR) sequence was implemented in NITNMR (Tecmag, Houston, USA). Prior to each 13C scan, a 90° pulse proton navigator scan was performed to determine the actual proton resonance frequency and calculate the corresponding 13C frequency to be used in the upcoming 13C scan. Low SNR data were line broadened and peak maxima were corrected according to the Rice distribution [5]. Matlab (MathWorks, Natick, USA) was used both for real-time control of the scanner via a software interface to NITNMR and for post-processing.

7T: Experiments at 7.0T were performed with 3.5mL spherical phantoms on a 13C home-built solenoid coil in a Discovery MR750w (GE Healthcare, Milwaukee, USA), where a standard IR sequence was implemented.

14T: Experiments at 14.1T were conducted in a dual tuned coil with a D2O glass capillary added to a standard 5mm 600uL NMR tube on an Avance600 NMR spectrometer (Bruker BioSpin, Rheinstetten, Germany) using an available TI IR sequence with higher order shimming and frequency locking to D2O.

Results: $T_1$ times were measured for all five compounds at all four fields, each IR sequence taking between 1h and 3h depending on the expected $T_1$. Temperature dependent magnetic field drifts at the 1T Aspect scanner of up to 1 Hz per second were successfully compensated by performing a 90° pulse proton navigator scan during the TR directly before each 13C scan determining the actual 13C resonance frequency without disturbing the 13C relaxation mechanism (see fig. 1). The application of line broadening and the correction of maxima according to the Rice distribution allowed achieving sufficient low measurement uncertainties with just one scan per TI even at relatively low SNR (see fig. 1 and 2). Reproducibility was shown by performing the same IR experiment for the same sample several times (see fig. 2). Within the statistical uncertainty, we found that $T_1$ decreases with increasing $B_0$ for all substances. Concentration dependencies have to be studied.

Conclusion and Discussion: The $T_1$ times for acetate are comparable to the ones measured from Miéville et al. for a 3M solution in D20 using the shuttling technique [7]. The $T_1$ for pyruvate at 1T is comparable to the one measured by Chattergoon et al. using hyperpolarized field cycling. The goal of this study was to investigate $T_1$ times for a larger number of frequently used hyperpolarization agents under comparable experimental conditions at all field strengths currently clinically available. While pH and temperature could be held constant, concentrations were initially chosen to avoid solubility problems for each compound separately. A series of current experiments studies the dependence of $T_1$ on compound concentration and TRIS buffer concentration to also allow for a comparison between different compounds. Planning of hyperpolarized experiments could not only take into account the spectral resolution dependency on $B_0$, but could also consider the type of biological information that can be extracted from the varying duration of the experiment due to the $T_1$ dependency of the 13C hyperpolarized agent on $B_0$.