Effect of Lanthanide Ions on Dynamic Nuclear Polarization Enhancement and Liquid State T_1 Relaxation

J. Gordon[1], I. Rowland[1,2], E. Peterson[3], and S. Fain[1,2]

[1]Department of Medical Physics, University of Wisconsin-Madison, Madison, WI, United States, [2]Department of Radiology, University of Wisconsin-Madison, Madison, WI, United States, [3]Department of Biomedical Engineering, University of Wisconsin-Madison, Madison, WI, United States

INTRODUCTION: Dynamic nuclear polarization (DNP) is a process that increases the population difference between the two spin states from parts per million to 20% [1]. Upon dissolution, the spins equilibrate to their Boltzmann distribution with a characteristic spin-lattice relaxation time T_1. Previous work has focused on using commercially available gadolinium contrast agents to enhance the solid-state polarization of $1\text{-}^{13}C$ pyruvate, leading to polarization levels >20% [2,3]. Unfortunately, Gd(III) is also a very effective T_1 relaxation agent in the liquid state, therefore decreasing the available time for liquid state experiments. This work explores the effects of different lanthanide metals on the solid-state amplitude and buildup time of $1\text{-}^{13}C$ pyruvate, as well as the liquid state nuclear relaxation time at 4.7T.

MATERIALS AND METHODS: Lanthanide hydrates ($LnCl_3 \cdot xH_2O$, x = 6 or 7; Sigma-Aldrich, St Louis, MO, USA) were dissolved in water to create stock 1M solutions. The trityl radical OX63 (GE Healthcare) was added to $1\text{-}^{13}C$ Pyruvic acid (Sigma-Aldrich, St Louis, MO, USA) to yield a concentration of 30mM. Solutions were mixed to a concentration of 15mM OX63, 7.1M $1\text{-}^{13}C$ Pyruvic acid and 0.5mM lanthanide. 30μL aliquots were placed into a 3.35T polarizer (HyperSense®, Tubney Woods, Abingdon, Oxfordshire, UK) and irradiated at their frequency of maximum enhancement for one hour. The compounds were rapidly dissolved with 106mM NaOH, 80mM Tris and either 0.43 mM EDTA or 0.22 mM EDTA and 0.275mM DTPA to yield solutions with pH = 7.7 ± 0.2 and a $1\text{-}^{13}C$ Pyruvic concentration of 53mM. T_1 was measured via spectroscopy on a Varian 4.7T scanner with varying TR to separate the effects of RF and T_1 decay.

RESULTS AND DISCUSSION: The effect of different Lanthanides on the solid-state polarization can be seen in Figure 1. At 0.5mM concentrations, only Gd and Ho appreciably increase the solid-state polarization of $1\text{-}^{13}C$ Pyruvate. None of the lanthanides appreciably alter the buildup time at this concentration. Based on these results, experiments with higher concentrations of Gd and Ho were explored, with the results showing markedly different trends. Gd slightly increases the buildup time while exhibiting an asymptotic solid-state enhancement as concentration increases. On the other hand, Ho increases the solid-state polarization at low concentrations, while at high concentrations both the solid-state polarization and buildup times decrease. Finally, T_1 relaxation times at 4.7T are shown in Table 1 for dissolutions with EDTA or EDTA & DTPA. Spin-lattice relaxation times for pyruvate in the presence of paramagnetic lanthanides are increased when dissolved with DTPA, as compared to dissolutions with EDTA alone. As DTPA chelation to lanthanides is well characterized [4], this is likely due to an increase in the distance between the paramagnetic center and the carbon nucleus.

CONCLUSION: While Gd can be used to enhance solid-state polarization [2,3], it is a potent relaxation agent in the liquid state. We show that Ho also increases the solid-state polarization, but interestingly at high concentrations it also significantly decreases the buildup time. Dissolution with DTPA & EDTA in the presence of paramagnetic lanthanides further increases the T_1 of pyruvate in the liquid state, as compared to dissolution with EDTA alone. The data presented here shows that Ho may be used to increase the solid-state polarization or decrease the buildup time while leaving the liquid state T_1 unaffected. Additionally, DTPA rapidly and efficiently chelates free Gd (or any lanthanide) in the dissolution process, allowing for maximum polarization enhancement while minimizing the relaxation effects and toxicity in the liquid state.

REFERENCES: [1] Ardenkjaer-Larsen et al., PNAS 2003; 100: 10158-10163. [2] Ardenkjaer-Larsen et al., Appl. Magn. Reson. 2008; 34: 509-522. [3] Waldner et al., ISMRM 2009; p3263. [4] Caravan et al., Chem. Rev. 1999; 99: 2293-2352.
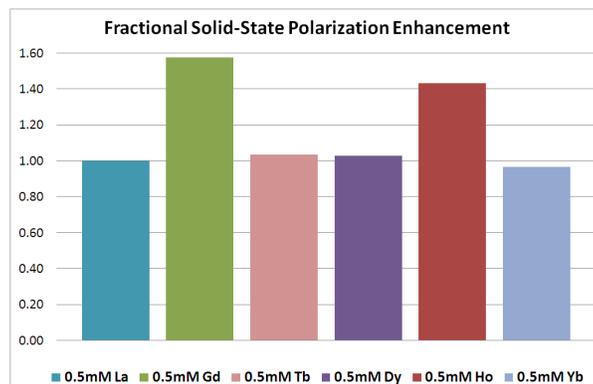
Figure 1. Solid-state enhancement as a function of lanthanide. Solutions were polarized for 1 hour. At 0.5mM concentrations, only Gd and Ho significantly increased the solid-state polarization.
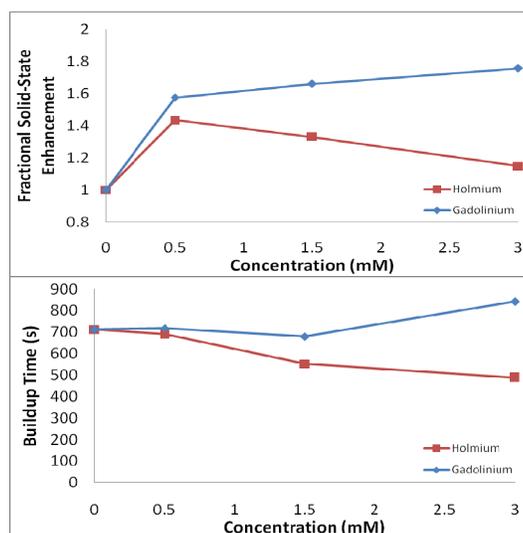

Figure 2. Dependence of the solid-state amplitude (top) and buildup time (bottom) on Gd and Ho concentrations.

Liquid State Lanthanide Concentration	Dissolution Method	
	EDTA	**DTPA & EDTA**
0.0037 mM La	78.3 s	-
0.0037 mM Dy	68	77.0 s
0.0037 mM Ho	75.5 s	76.2 s
0.0112 mM Ho	73.2 s	73.0 s
0.0223 mM Ho	71.2 s	72.3 s
0.0037 mM Gd	23.8 s	57.5 s
0.0112 mM Gd	16.8 s	35.8 s
0.0223 mM Gd	-	29.4 s
0.0037 mM Tb	68.7 s	71.5 s
0.0037 mM Yb	77.0 s	79.0 s

Table 1. T_1 times for 53mM $1\text{-}^{13}C$ Pyruvic acid at 4.7T in the presence of various lanthanides. Dissolution with DTPA and EDTA increases the T_1 markedly in the presence of Gd, as compared to dissolution with EDTA alone. This effect is less pronounced with other lanthanides due to their increased electronic relaxation rates.