Can Hyperpolarized ^{89}Y be used as a Molecular Imaging Agent?

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Introduction

Hyperpolarization of nuclear species for magnetic resonance (MR) studies has already opened new avenues for *in vivo* metabolic imaging. The chemical information available in an MR spectrum differentiates it from positron emission tomography which only measures total tracer activity. Carbon-13 is the most commonly used nucleus for hyperpolarization experiments to date. The most significant drawback for experiments with hyperpolarized ^{13}C is the short T_1's of protonated carbons; even quaternary carbons typically have T_1's of 1 minute or less in solution. Longer nuclear T_1's would allow longer times for delivery to a site of interest *in vivo* and would allow more time for detection of a metabolic event. Yttrium-89 is a spin-1/2 nucleus with exceptionally long T_1 values and has the advantage of being a 100% naturally abundant isotope. Furthermore, the ionic radius and hydration number of Y^{3+} is similar to that of Gd^{3+} so the coordination chemistry of these two ions are similar. In this study, we have initiated investigations to measure the potential of using hyperpolarized ^{89}Y for molecular imaging of responsive complexes in a biological medium.

Methods

Samples of either YCl_3 or Y^{3+} complexed with high affinity ligands were dissolved in 50:50 water:glycerol along with 16.6 mM trityl radical. Dynamic Nuclear Polarization (DNP) was carried out at 3.35T using an Oxford Hypersense DNP system. The samples were frozen at 1.4K and irradiated with a microwave frequency of 94.118 GHz at 100 mW for 2.5 hours. The samples were ejected from the Hypersense using 4 mL of boiling H_2O. An aliquot (~1.2 mL) was transferred to an 8 mm NMR tube and positioned entirely within the coil volume of a probe tuned to 29.37 MHz in a Varian INOVA 14.1 Tesla NMR. Data were collected using a train of 10 degree pulses separated by 11 seconds.

Results

Figure 1 illustrates the magnetization decay curve as a function of time for a sample of 15 mM hyperpolarized YCl_3. The data was modeled using the equations of Patyal, *et. al.*, yielding a T_1 of nearly 10 minutes. (1) Localization of the sample within the active volume of the MR probe was necessary to remove the effects of diffusion which artificially lengthen the apparent T_1. The measured enhancement for this sample was estimated at 246 times that of the thermal signal using 3M YCl_3 as a thermal standard. Similar experiments using $Y(DOTP)^{5-}$ and $Y(DOTA)^{-}$ were even more promising, showing enhancements of 1042 and 1527 times the thermal equilibrium signal, respectively.

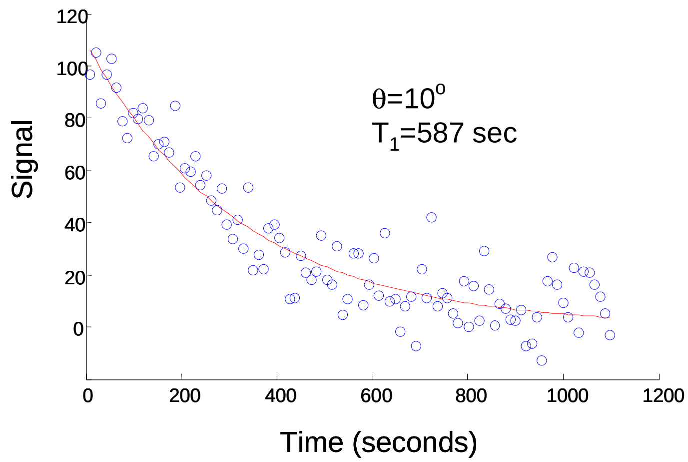

Figure 1. Decay of MR signal of hyperpolarized YCl_3 as a function of time. Using a 90 degree pulse for detection results in a greater signal amplitude but destroys all the hyperpolarized signal rendering T_1 estimates impossible.

Conclusions

Historically, NMR detection of ^{89}Y has been limited by the low sensitivity of this nucleus. We show here that ^{89}Y can be hyperpolarized to modest levels using a commercial DNP system and stable electron free radicals optimized for ^{13}C. The long T_1 of ^{89}Y and its similar coordination chemistry to Gd^{3+} makes this an attractive nucleas for molecular imaging. It is noteworthy that the beta emitter, ^{90}Y, is currently used in radioimmuno-therapy for treatment of non-Hodgkins lymphomas. Once optimized, hyperpolarized ^{89}Y surrogates of the drug could potentially serve to monitor delivery of the pharmaceutical *in vivo* by MRI.

REFERENCES

1. Patyal BR, Gao J, Williams RF, Roby J, Saam B, Rockwell BA, Thomas RJ, Stolarski DJ, Fox PT. Longitudinal Relaxation and Diffusion Measurements Using Magnetic Resonance Signals from Laser-Hyperpolarized ^{129}Xe Nuclei. Journal of Magnetic Resonance 1997;126:58-65.