Hyperpolarized ^{15}N MR: PASADE^{15}NA & D^{15}NP

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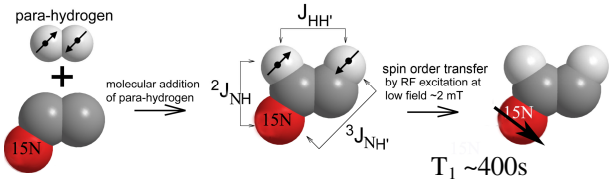
Background & Purpose: Several significant biological and biomedical questions have been addressed by use of ^{15}N MR. However, structural ^{15}N NMR is hampered by the need for complex chemical substitutions and ^{15}N enriched biomedical applications which are time consuming, limited by enzyme flux measurements of mmoles over seconds to minutes. Hyperpolarization of ^{15}N by Parahydrogen And Synthesis Allows Dramatically Enhanced Nuclear Alignment (PASADENA) and Dynamic Nuclear Polarization (DNP) was explored as a means of broadening the biomedical utility of ^{15}N MR imaging and spectroscopy.

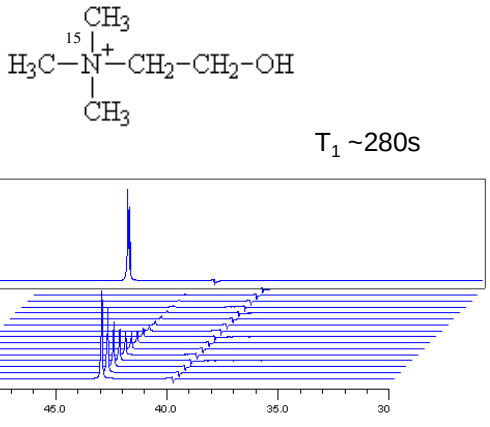
Results: A. An unsaturated precursor of ^{15}N-choline, a known biomarker of many human cancers was synthesized and subsequently hyperpolarized by PASADE^{15}NA to generate hyperpolarized ^{15}N-choline. Compared to hyperpolarized ^{13}C choline, T_1 (longitudinal relaxation time) of ^{15}N choline was carefully extended so that a second biomarker, choline kinase enzyme flux could potentially be determined *in vivo*. Preliminary *in vivo* applications of ^{15}N hyperpolarization towards cancer imaging in rodent models will be demonstrated.

B. D^{15}NP hyperpolarization has also resulted in high levels of hyperpolarization on ^{15}N labeled choline, glutamine, ATP and nucleotides like adenosine and cytosine with relatively long T_1 times. Hyperpolarization of these metabolites has permitted acquisition of single shot ^{15}N MR spectra.

The long T_1 times of ^{15}N molecules compared to that of ^{13}C will provide longer imaging and spectroscopic time window (5X T_1 which translates to over 7 mins in case of hyperpolarized ^{15}N Choline) to observe and monitor metabolic events.



^{15}N NMR Spectrum of PASADE^{15}NA hyperpolarized Choline



^{15}N NMR Spectrum of D^{15}NP hyperpolarized Choline

The different values of T_1s of Choline hyperpolarized by two methods is due to the fact that the methyl groups are deuterated in the PASADENA precursor of ^{15}N Choline.

Conclusions and outlook: Specific advantages of ^{15}N NMR over ^{13}C NMR can now be exploited by hyperpolarization. High resolution fast MR and chemical shift imaging of ^{15}N-labeled metabolites can have significant impact in the understanding of urea cycle, glutamine-glutamate and choline metabolism *in vivo*. Furthermore, hyperpolarized ^{15}N NMR can be utilized for structure elucidation of proteins and oligonucleotides.

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References: Bhattacharya, P. & Ross, B. D. (2008) "Hyperpolarized ^{15}N NMR: D^{15}NP and PASADE^{15}NA" *Handbook of Neurochemistry and Molecular Neurobiology*, Vol 4, 2008, in press