Introduction of Hyperpolarized C-13 MR: What is it?

How do you do it?

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Highlights

- Producing non-equilibrium Boltzmann polarizations is a method for enhancing MR sensitivity
- Enhancement of polarization is possible through multiple methods
- The most general is the Dynamic Nuclear Polarization (DNP) mechanism
- Dissolution DNP produces hyperpolarized, metabolic contrast agents
- The selectivity of the MR experiment allows multiple reactions to be detected simultaneously

Target Audience: Researchers with an interest in technical and applied aspects of hyperpolarized imaging, and those interested in imaging metabolism and physiology.

Objectives

1. To provide an overview of methods for producing hyperpolarized samples
2. Develop an intuitive approach to understanding the DNP experiments
3. Describe technical challenges and opportunities for future development

Background

Metabolic imaging using magnetic resonance has tremendous potential due to the selectivity inherent in the MR experiments because of the chemical shift. However, the relatively low sensitivity of the MR experiment has typically prevented its application as a molecular imaging modality. This is especially true in the case of carbon-13 based spectroscopy and imaging methods. With the advent of the fast dissolution DNP method(1), carbon-13 based metabolic imaging is now possible on 1 second time scales in humans(2). The physical processes that allow the production of highly polarized samples have been described for many years, but due to the application of DNP to multiple research fields, understanding which regime current pre-polarizers operate in can be difficult.

Methods

When used for the production of hyperpolarized contrast agents, the essential goal is producing the highest physical polarization in the solid state and rapidly melting and delivering the agent to the subject. DNP requires the presence of a free radical electron to be located proximal to the nuclei that are the targets for enhancement. The DNP process exploits the dipolar interactions between the electron Zeeman system (EZS), the electron dipolar system (EDS), and the nuclear Zeeman system (NZS) to produce non-Boltzmann population distributions for the nuclei. Microwave irradiation at the electron Zeeman frequency ± electron dipolar linewidth/2 reduces the temperature of the EDS, which is strongly coupled to the NZS. Current commercially available systems operate at either 3.35 T or 5.0 T, field strengths sufficient to produce near

unity electron polarization, which boosts the final nuclear enhancement. Reduction of the sample temperature will also produce large gains in sample polarization. Dissolution of the sample is accomplished by injection of an aliquot of superheated water using a high pressure, helium gas driven dissolution wand.

Results

DNP typically produces ^{13}C nuclear polarizations of ~20 % at 3.35 T and 1.4 K. Lower temperatures achieved through more powerful pumping systems produce nonlinear gains in sample polarization versus the achieved sample temperature. At these field strengths, a minimal amount of microwave power (< 20 mW) will typically produce maximum polarizations. Higher powers simply heat the sample and reduce the available polarization.

Discussion

Hyperpolarized carbon-13 imaging is not readily achievable without the gains in sensitivity available through the DNP method. The strength of the method is the kinetic information that is readily obtained by observing the generation of products from a bolus of hyperpolarized imaging agent. Downsides of the method include the need to inject high concentrations of the imaging agent and the relatively short time period over which the products must be imaged. The high cost of the method also cannot be ignored when planning its possible applications.

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2. Nelson SJ, Kurhanewicz J, Vigneron DB, Larson PE, Harzstark AL, Ferrone M, van Criekinge M, Chang JW, Bok R, Park I, Reed G, Carvajal L, Small EJ, Munster P, Weinberg VK, Ardenkjaer-Larsen JH, Chen AP, Hurd RE, Odegardstuen LI, Robb FJ, Tropp J, Murray JA. Metabolic Imaging of Patients with Prostate Cancer Using Hyperpolarized [1-13C]Pyruvate. Science translational medicine 2013;5(198):198ra108.