

Hyperpolarized PASADENA ¹³C tracers for true MR metabolic imaging

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The PASADENA (Parahydrogen And Synthesis Allows Dramatically Enhanced Signal Alignment) increases the MR sensitivity through hyperpolarization subsequent to molecular addition of dihydrogen. Hyperpolarized magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) with signal enhancement over 100,000 fold offer multiple advantages including subsecond experimental time, which is especially attractive for cardiac and metabolic applications. Here, we present our progress toward development of two different classes of hyperpolarized contrast agents potentially useful for performing true metabolic imaging to provide 'virtual biopsy' to delineate the onset of deadly diseases such as cancer and atherosclerotic plaque and provide metabolic information superior to Positron Emission Tomography (PET).

Specifically, we demonstrate the utility of ¹³C hyperpolarized 2,2,3,3-tetrafluoro-propyl propionate targeting atherosclerotic plaque by means of a fluorocarbon moiety essential for lipid affinity [1]. This class of agents potentially enables the subsecond noninvasive MRI study of cardiac plaque formation with increased spatial resolution and high chemical specificity. The hyperpolarized carboxylic acids exemplified by 1-¹³C-succinate [2] potentially allow true metabolic imaging of cancer energetics after hyperpolarized intermediates enter biochemical pathways in vivo.

Furthermore, we demonstrate the utility of ¹³C (and potentially ¹⁵N) for spin storage of hyperpolarization followed by ¹H detection theoretically providing up to $\sim(\gamma_{1H}/\gamma_X)^2$ additional gain in sensitivity in hyperpolarized biomedical MR. While protons are ideal nuclei for detection, but short spin lattice relaxation time T_1 prevents direct ¹H hyperpolarized MR in biomedical applications, which is avoided by storing the hyperpolarized spin order on low- γ nucleus with much longer spin lattice relaxation time. Proton detection has additional practical advantage in biomedicine, since clinical MR scanners are typically equipped with proton detection hardware only.

[1] Chekmenev, E.Y. et al. *J. Phys. Chem. B*, **2008**, *112*, 6285-6287.

[2] Chekmenev, E.Y. et al. *J. Am. Chem. Soc.* **2008**, *130*, 4212-4213.