Development of ^{13}C and ^{15}N Contrast Agents Employing PASADENA

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Background: Recent advances[1-4] in hyper-polarization techniques has opened up possibilities for sub-second imaging in chemistry, biology and biomedicine. Dynamic Nuclear Polarization[4] (DNP) has proved effective in *in vivo* angiography and imaging, because of its ready application to biological molecules. However, DNP is currently impractical because of preparation times of around 12 hours. Parahydrogen and synthesis allows dramatic enhancement of nuclear alignment (PASADENA) or parahydrogen induced polarization has hitherto been considered unsuitable on the basis of toxicity and its limited range of available ^{13}C and ^{15}N contrast agents.

Aim: Design of ^{13}C hyperpolarizable contrast agents using PASADENA developed by Bowers and Weitekamp[1,2] and employ them for targeted ultra-fast high resolution imaging and spectroscopy.

Method: A family of contrast agents was employed to achieve polarization utilizing PASADENA. Para-hydrogen was produced by passing normal hydrogen gas through a catalyst at a temperature of 14K. The resulting gas consisting of more than 95% parahydrogen was used in a facile hydrogenation reaction to produce the imaging reagents. Using pulse excitation in a low magnetic field, the spin order of the protons originating from para-hydrogen was transferred into polarization of a scalar coupled ^{13}C nucleus[5] which was subsequently employed for sub-second ^{13}C imaging of brain, heart and lungs in animals[5-7].

Results: ^{1}H NMR confirms the formation of para-hydrogenated product. Comparative single shot ^{13}C NMR spectra of the reactant and product shows over 40% polarization transfer to the enriched carbons (representative case) which amounts to more than 1000 fold gain in SNR (Figure1). The molecules were subsequently utilized for targeted ultrafast imaging of heart and brain (Figure 2).

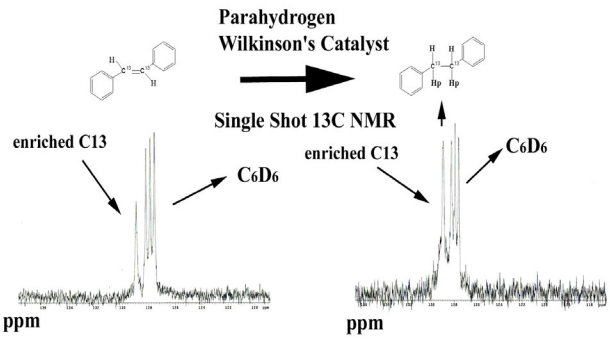

Figure1

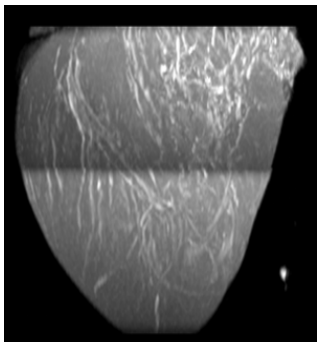

Figure 2

Conclusion: (a) ^{13}C molecular imaging with PASADENA is hereby demonstrated. PASADENA opens up exciting areas of ultra fast high resolution real time MRI, MRS and metabolic mapping. Furthermore, this method is not only applicable to ^{13}C but also to other NMR-active nuclei (e.g. ^{15}N). (b) Extension of PASADENA to real time *in vivo* MRS can be envisaged with the identification of polarized ^{13}C reagents which undergo tissue-specific biotransformation[8]. c) Problems to be addressed before human use include unknown LD_{50} and separation of reagents from catalysts employed by PASADENA.

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