Towards Real-time Metabolic And Molecular Imaging Of Cancer By Three Different Modalities Of Hyperpolarization

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**Purpose:** Hyperpolarized magnetic resonance is a non-toxic, non-radioactive method for assessing tissue metabolism and other physiologic properties. Hyperpolarization allows for over 10,000-fold signal enhancement relative to conventional magnetic resonance imaging (MRI) or spectroscopy (MRS). After hyperpolarization, the signal enhancement can be retained on the metabolites of the hyperpolarized molecules for several minutes prior to relaxing. Several laboratories are working on techniques to extend this relaxation time so that more detailed imaging studies over longer time scales can be considered.

**Methods:** My laboratory has worked on three different modalities of hyperpolarization, both on technique development as well as advancing novel in vivo applications. The research described is focused on the different in vivo applications of Parahydrogen Induced Polarization (PHIP) (and subsequent transfer to 13C), continuous flow Dynamic Nuclear Polarization (DNP) of water (1H), and long lived DNP hyperpolarized signal of Silicon nanoparticles (29Si) as molecular imaging agents.

**Results:**

a) By PHIP, we have hyperpolarized diethyl succinate and used this endogenous compound to image the downstream metabolites of the Krebs cycle in real time in rodents within one minute (1). Efforts are underway to fingerprint the 13C resonances of the TCA cycle metabolome in different cancer models in vivo and to correlate that with the gene expressions (Fig 1).  

b) Employing continuous flow DNP of hyperpolarized water, we were able to obtain perfusion contrast for (1H) MR imaging, thereby providing localized angiography in vivo in rat models (Fig 2) (2). This sensitivity gain of water rivals that of gadolinium-based contrast agents.

c) We have extended the hyperpolarized applications in nanoparticles by demonstrating direct in vivo imaging of hyperpolarized 29Si nuclei in silicon particles using MRI (3). 29Si hyperpolarization was generated by low-temperature DNP using naturally occurring defects at the particle surface, and showed a characteristic decay time of over 40 min, unaffected by particle tumbling in solution, surface functionalization, or the local in vivo environment. Applications in gastrointestinal, intraperitoneal, intravascular and perfusion imaging at sub-picomolar concentrations have been shown (Fig 3). Efforts are underway to develop this technique for non-invasive colonoscopy to detect colon polyps and tumors at an early stage as well as functionalize the nanoparticle surface for targeted receptor imaging in pancreatic and ovarian cancers in vivo.

**Conclusion:** The three different hyperpolarized imaging modalities have opened up the possibilities for visualizing metabolism and other molecular events in real time wherein the local status of cancer can be interrogated on the time scale of seconds to tens of minutes with unprecedented chemical specificity and MR sensitivity, where both early detection as well as the efficacy of cancer therapy can be imaged.


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