Hyperpolarized silicon nanoparticles – Towards 29Si in-vivo imaging

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Introduction – Molecular imaging is a rapidly expanding field of research allowing for the studying of metabolic and cellular processes in real time utilizing a range of technologies such as PET, ultrasound and magnetic resonance spectroscopy. A number of new multimodal techniques are being investigated that combine molecular imaging with the targeted delivery of therapeutics. Surface functionalized silicon nanoparticles (SiNP) have been demonstrated as non-toxic and effective slow-release vehicles for chemotherapy agents [1, 2] that can be imaged by fluorescence in cells and small animal models. Fluorescence imaging has limitations for tissue depths greater than a few cm and so magnetic resonance imaging (MRI) remains an extremely attractive alternative for noninvasive imaging with high spatial resolution. We have recently proposed directly imaging the ^{29}Si nuclei in such particles that have been hyperpolarized to increases the ^{29}Si nuclear polarization by many orders of magnitude so that the particles can be directly imaged in-vivo. SiNP have room temperature T1 relaxation times ranging from tens of minutes to several hours [3], can be hyperpolarized at low temperatures by dynamic nuclear polarization (DNP) [4,5]. Once polarized, the particle core is largely protected from sources of relaxation, and so the T1 times are seen to remain long even in solution and varying magnetic fields. [6]

Methods – Hyperpolarization of the SiNP samples (~100mg) was performed at cryogenic temperatures in a custom built cryostat in a 2.9 T superconducting NMR magnet (f_{NMR} = 24.4 MHz, f_{ESR} = 81 GHz) located adjacent to a 4.7T Bruker Avance animal imager. Microwave irradiation of the sample was provided by a waveguide-coupled 2W microwave source (Quinstar) held at room temperature, allowing for the generation of ^{29}Si nuclear polarizations of ~5% using the thermal mixing effect [5]. A custom built probe allowed for rapid unloading (< 5 s) of the hyperpolarized sample. Following hyperpolarization, the silicon samples were removed from the magnet and diluted in ethanol for measurement. Spectroscopy and co-registered imaging was performed in Paravision with a custom-built dual tuned ^{1}H/^{29}Si coil. The decay of the hyperpolarized ^{29}Si signal was measured with a variable small flip angle sequence. Preliminary animal toxicity studies were undertaken on 6 mice (average body weight 25 g) injected intraperitoneally with suspensions of silicon nanoparticles functionalized with polyethylene glycol (PEG) in saline at concentrations ranging from 60 to 8000 mg SiNP/kg mouse.

Results - ^{29}Si nuclear polarizations of ~5% can be routinely generated in silicon particles (Fig 1). In-vitro T1 decays in the 4.7T imager ranging from 24 to 33 minutes were measured following 3 hours (blue) and 6 hours (red) of hyperpolarization (Fig. 2). No ill effects to the animals were observed for the IP injections for concentrations less than 2000mg/kg over a period of one week (Table 1).

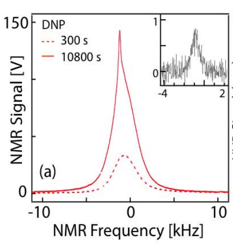

Figure 1: Low temperature DNP of silicon nanoparticles. The room temperature Boltzmann polarization is shown in the inset.

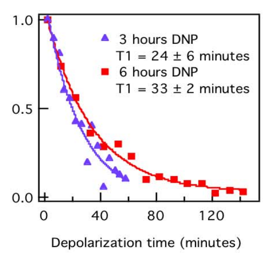

Figure 2: Decay of hyperpolarized SiNP recorded in the animal imager

SiNP dose (mg/kg)	0	60	500	1000	2000	8000
48 Hour Survival	Yes	Yes	Yes	Yes	Yes	Yes
1 week survival	Yes	Yes	Yes	Yes	Yes	No

Table 1: Preliminary animal toxicity results following an intraperitoneal injection of suspensions of silicon nanoparticles in saline.

Discussion – SiNP have a wide range of applications for targeted molecular imaging and therapeutics, in particular for gastrointestinal imaging. The measured in-vitro decay times of greater than 30 minutes offer potential for imaging over clinically relevant time scales. Current efforts are focused on improving our imaging system to record high quality ^{29}Si images in-vivo.

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References - [1] Tasciotti et al. Nature Nanotechnology (2008) [2] Park et al. Nature Materials (2009) [3] Aptekar et al. ACS Nano (2009)[4] Dementyev et al. Phys. Rev. Lett (2008) [5] Cassidy et al. in preparation [6] Lee et al. Phys. Rev B. (2011)