Nuclear spin properties of hyperpolarized solid-state MRI agents.

Maja Cassidy[1], Henry Chan[2], Jingzhe Hu[3], Nicholas Whiting[3], Charles Marcus[1,4], and Pratip Bhatttacharya[2,3]
[1]*Harvard University, Cambridge, MA, United States,* [2]*Huntington Medical Research Institutes, Pasadena, CA, United States,* [3]*The University of Texas MD Anderson Cancer Center, Houston, TX, United States,* [4]*University of Copenhagen, Copenhagen, Denmark*

Introduction – Hyperpolarization of solid-state nanoparticles such as ^{29}Si nuclei in silicon nanoparticles (SiNP) [1,2] and ^{13}C nuclei in diamond [3] are emerging medical imaging modalities for non-invasive targeted diagnostics using MRI. These nanoparticles are attractive due to their negligible in-vivo toxicity [4] and lack of *in-vivo* background signal, while their surface chemistry and variable porosity makes them ideal for targeted drug delivery [5]. The unique nuclear spin properties of these solid state systems leads to multi hour spin relaxation (T_1) times that are unaffected by changes in magnetic field or temperature [6], and depend only on the particle size, isotopic concentration and materials purity [1]. Here we investigate the ^{29}Si nuclear spin properties of bare and functionalized SiNPs suitable for targeted gastrointestinal imaging agents.

Methods – SiNPs (approximately 2 um in diameter) were sourced commercially from Alfa Aesar. A two-step surface functionalization process with aminopropyltriethoxysilane (APTES) and polyethylene glycol (PEG) was carried out to enhance biocompatibility and hydrostability. Hyperpolarization of the ^{29}Si nuclear spins was undertaken at low temperatures using a home-built dynamic nuclear polarization (DNP) polarizer operating at 81 GHz and 3 K located next to a 4.7 T animal imager. *In-vivo* experiments were carried out on normal murine animal models with hyperpolarized SiNPs (~50 mg) diluted in saline (0.5 ml) and delivered into the gastrointestinal tract via a catheter. ^{29}Si spectroscopy was undertaken with a custom built surface coil using a variable flip angle sequence. Signal quantification was obtained via a co-located trimethoxysilane sample (1 ml) positioned above the coil. ^{29}Si imaging was performed using a fast spin-echo sequence with parameters (1 slice, slice thickness = 60 mm, α= 90°, TR = 1.5 ms, TE = 0.74 ms, FOV = 40 x 40 mm, 64 x 64 pixel resolution), with a total imaging time of 300 ms.

Results -

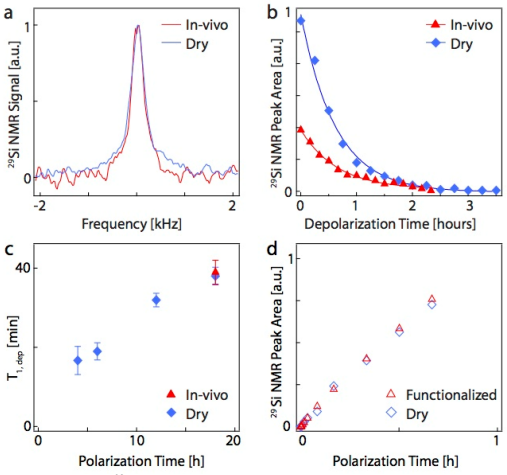

Figure 1 – (a) ^{29}Si NMR spectrum of HP SiNPs recorded in-vivo (red) and dry (blue) 30 min after delivery to the imaging magnet (b) Decay of ^{29}Si nuclear polarization of hyperpolarized SiNPs in-vivo (red) and dry (blue) after 18 h of DNP. Both show depolarization times of approximately 40 min. The difference in signal is attributed to sample loss in the dilution and injection process. (c) Characteristic ^{29}Si depolarization time constants in dry particle phantoms recorded in the imager for polarization times of 4, 6, 12, and 18 hours. (d) Time evolution of the ^{29}Si nuclear polarization under DNP conditions for particles with and without surface functionalization with PEG.

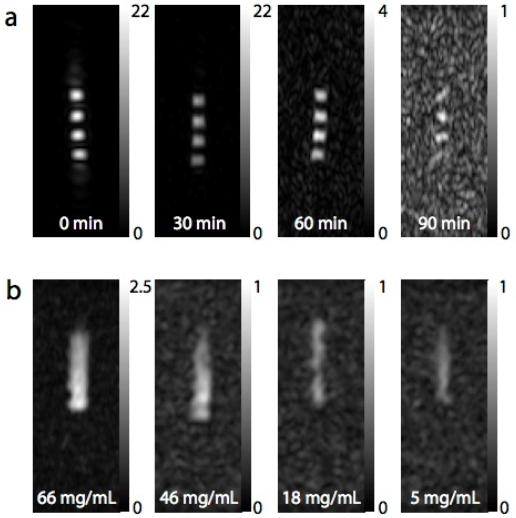

Figure 2 - (a) ^{29}Si MRI of a pixelated phantom containing silicon particles (□ 15 mg in each pixel) with a delay of 0, 30, 60 and 90 min from when the phantom was loaded into the magnet until imaging. (b) ^{29}Si MRI of a cylindrical concentration phantom with particle concentrations of 66 mg/mL, 46 mg/mL, 18 mg/mL and 5 mg/mL. Images have been cropped from 40 mm to 15 mm in the horizontal dimension after processing.

Discussion - DNP in silicon particles is driven by electronic defects that exist at the particle surface and the nuclear hyperpolarization is carried into the center of the particles by nuclear spin polarization. Increasing the polarization time results in an increase in ^{29}Si signal together with longer depolarization times. After long periods of hyperpolarization, the polarized ^{29}Si nuclei in the core of the particle are protected from relaxation sources located at the particle surface such as those due to surface functionalization or the *in-vivo* environment. Single shot ^{29}Si images can be obtained up to 90 min after delivery to the imaging magnet, and down to concentrations of 5mg/mL, corresponding to sub-picomolar SiNP concentrations.

References – [1] Aptekar et al. ACSNano (2009) [2] Cassidy et al (2012) [3] Rej et al (2011) [4] Park et al Nature Materials (2009) [5] Tanaka et al, Cancer Research (2010) [6] Lee et al. PRB (2010).
Acknowledgements – Support was provided by the NIH (1R21 CA118509, 1R01NS048589), the NCI (5R01CA122513), the Tobacco Related Disease Research Program (16KT-0044), NSF BISH (CBET-0933015), the NSF through the Harvard NSEC, and the R.G. Menzies Foundation.