Long-T_1 Silicon Nanoparticles for Hyperpolarized Magnetic Resonance Imaging

M. C. Cassidy[1], J. W. Aptekar[1], A. C. Johnson[1], R. A. Barton[1], M. Lee[1], C. Vo[1], A. L. Hill[2], R. W. Mair[2], M. S. Rosen[1,2], R. L. Walsworth[1,2], and C. M. Marcus[1]

[1]Department of Physics, Harvard University, Cambridge, MA, United States, [2]Harvard-Smithsonian Center for Astrophysics, Cambridge, MA, United States

Introduction - The use of nanoparticles for biomedical applications has benefited from rapid progress both in the nanoscale synthesis of materials with specific optical [1] and magnetic properties [2], and in the biofunctionalization of surfaces, allowing targeting in-vivo tracking, and therapeutic action [3]. For magnetic resonance imaging (MRI), superparamagnetic nanoparticles [2] have extended susceptibility-based contrast agents toward targeted imaging though achieving high spatial resolution with high contrast remains challenging. An alternative approach is direct MRI of hyperpolarized materials with little or no background signal. Hyperpolarized noble gases for lung imaging [4] and hyperpolarized ^{13}C enhanced biomolecules [5] have demonstrated impressive image contrast, but have been limited by short *in-vivo* enhancement times (~ 10 s for noble gases [4], ~ 30 s for ^{13}C-labeled molecules [5]). Silicon can exhibit multi-hour nuclear relaxation T_1 times at room temperature [6] and can be hyperpolarized via dynamic nuclear polarization [7]. In this study, Si nanoparticles are investigated as a potential hyperpolarized, targetable MRI imaging agent.

Methods - Nuclear T_1 times of the Si nanoparticles were measured at room temperature at a magnetic field of 2.9 T (f_{NMR} = 24.4 MHz) using a spin-echo Fourier transform method with a signal recovery sequence. Following a train of sixteen hard 90° pulses to null any initial polarization, the sample was left at field to polarize for a time τ_{pol}, followed by a CPMG sequence $(\pi/2)_X$–$(\tau$–π_Y–τ–echo$]^n$ with τ = 1ms and n = 200. It is known that in Si and other nuclear-dipole-coupled materials, the CPMG sequence yields echoes that persist for much longer than T_2 (as measured using other sequences) [7]. However, the Fourier amplitude of the echo train still yields a useful measure of initial polarization [8]. Values for T_1 were extracted from fits to an exponential saturation of the Fourier amplitude of the n=200 echoes as a function of polarization time τ_{pol}.

Results - Figure 1a shows T_1 as a function of (volume-weighted) average particle diameter for the various samples. The high-resistivity ball-milled samples follow a roughly linear dependence on size, $T_1 \propto d$, for d ~ 10 um, saturating at T_1 ~ 5 h for larger particles. The trend of increasing T_1 in larger particles is qualitatively consistent a shell-core diffusion model [7] which, however, predicts $T_1 \propto d^2$. The low-resistivity ball-milled particles have T_1 ~ 200 s, independent of size. Submicron commercial particles formed by wet synthesis (Meliorum) and plasma synthesis (MTI) have T_1 times as long as 700 s. The larger commercial particles formed by electrical explosion (NanoAmor) have shorter T_1 than the comparably sized high-resistivity ball-milled particles. Whereas T_1 changes by two orders of magnitude over the range of measured particle sizes, T_2* changes only by factor of ~ 6 over the same range (Fig 1 b).

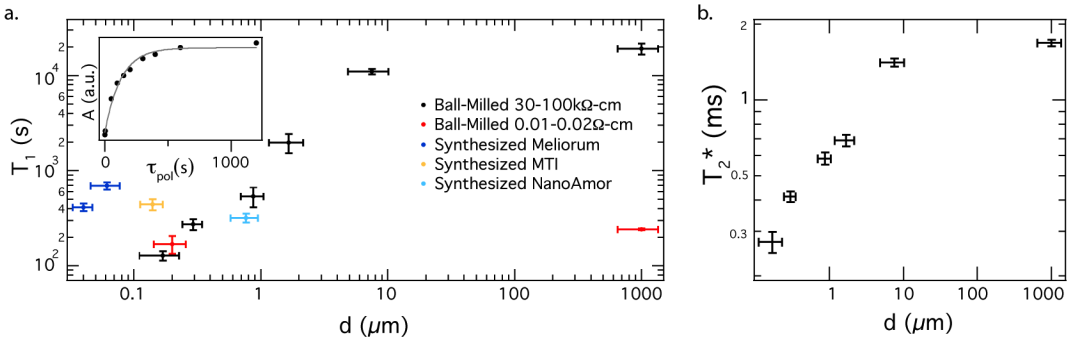

Figure 1 – NMR properties of silicon particles. a. Nuclear relaxation T1 times as a function of particle diameter, d for various Si particles. Vertical error bars are from exponential fits; horizontal error bars Inset. Fourier transformed NMR peak amplitude as a function of polarization time for ball milled particles with d=0.17um. b. T2* as a function of mean particle diameter for ball-milled high-resistivity samples at 4.7T.

Discussion – We have investigated T_1 times in this system as a function of nanoparticle size, dopant concentration and synthesis method. Nuclear T_1 times are found to be remarkably long, allowing for hyperpolarized particles to be transported and administered on practical time scales without significant polarization loss. The modest values of T_2* set the limit to image resolution for MRI applications. However, it is expected that the rapid tumbling of particles in a liquid suspension will narrow the line considerably, restoring resolution. We also note that Si nanoparticles can be combine with other material components to provide MRI tracking of the delivery of drugs or as a therapeutic agent that allows simultaneous MRI tracking.

Acknowledgements - This work was supported by the NIH under grant # 1 R21 EB007486-01A1 and the Harvard Nanoscale Science and Engineering Center and NSF Center.

References –

[1] Akerman, M.E. *et al. Proc. Nat. Acad. Sci. U.S.A* 99, 12617-12621 (2002).
[2] Weissleder, R. *et al. Nat. Biotechnol.* 23, 1418-1423 (2005).
[3] Simberg, D. *et al. Proc. Nat. Acad. Sci. U.S.A* 104, 932-936 (2007).
[4] Leawoods, J.C. *et al. Concepts Magn. Reson.* 13, 277293 (2001).
[5] Golman, K. *et al. Br. J. Radiol.* 76, 118-127 (2003).
[6] Schulman, R.G *et al. Phys. Rev.* 103, 1127-1129 (1956).
[7] Dementyev, A.E. *et al. Phys. Rev. Lett.* 100, 127601 (2008).
[8] Li, D. *et al. Phys. Rev. B.* 77, 214306 (2008).