Targeted MRI In Vivo by Hyperpolarized Silicon Nanoparticles

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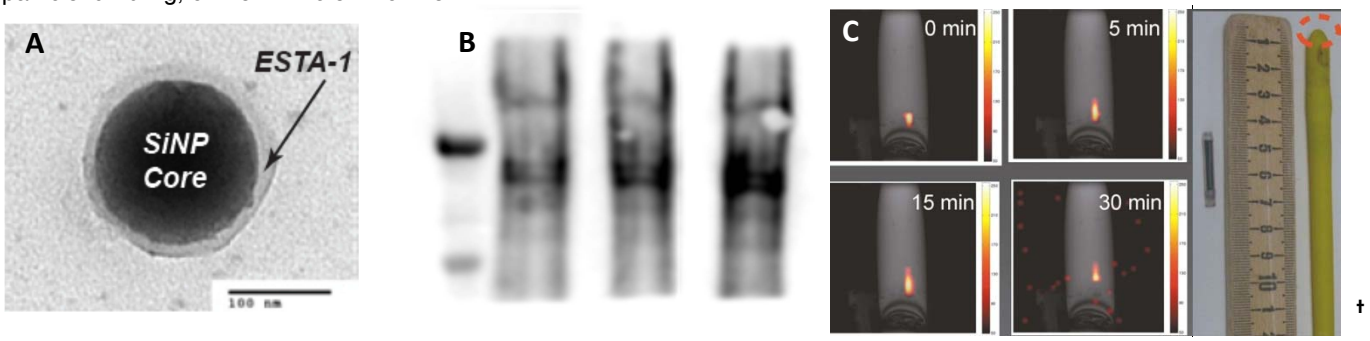
Purpose: Nanomedicine is an emerging field that offers great promise in the development of non-invasive strategies for the diagnosis and treatment of disease. The complexity of the *in-vivo* response to these nanomaterials means that it is crucial to develop platform technologies that suit a wide range of potential applications. Silicon and its oxide derivatives are one such material that has emerged for targeting and drug delivery that may suit a range of applications[1,2]. Silicon nanoparticles are easily surface functionalize, are biocompatible and biodegradable. Additionally, silicon oxide is frequently used as a biocompatible coating of other materials, and is a common food additive. Hyperpolarized silicon nanoparticles has opened up the possibility of performing targeted MRI *in vivo* in real time with over 10,000 fold sensitivity enhancement via Dynamic Nuclear Polarization (DNP).

Methods: We have developed a new technique for background-free imaging silicon nanoparticles *in-vivo* using hyperpolarized ^{29}Si magnetic resonance imaging (MRI)[3]. The ^{29}Si nuclear hyperpolarization is generated via low temperature dynamic nuclear polarization (DNP) before the sample is transferred to the MRI system for imaging, in a technique similar to that pioneered by Ardenkjær-Larsen[4]. Unlike many other DNP techniques, additional radicals are not required for hyperpolarization, as unbonded electrons naturally occur at the particle surface and are ideal for DNP. Silicon particles have extremely long spin-relaxation times, ranging from minutes to several hours[5,6], depending on the particle size and materials properties, and their relaxation times are unaffected by surface functionalization, particle tumbling, or the *in vivo* environment[3].



Results: We are now pursuing a number of applications for targeted imaging of disease using hyperpolarized silicon nanoparticles. We have developed protocols for functionalizing silicon particles with short-chain antibodies to target mucine produced by tumors in the gastrointestinal tract as well as target overexpressed proteins in pancreatic and ovarian cancers by functionalizing aptamers to silicon nanoparticles (Fig A: A representative SEM image of 70nm SiNP functionalized with aptamers). We have demonstrated that these antibodies can readily survive the hyperpolarization process and retain their binding properties (Fig B: MUC1 antibody pre- and post-liquid Helium treatment. The antibody retained its ability to bind the MUC1 epitope found in a pancreatic cancer cell line). We have also developed a catheter tip made of silicon particles that can be hyperpolarized and tracked via ^{29}Si MRI for over half an hour (Fig C).

Discussion: Magnetic resonance offers not only the possibility of structural imaging, but also functional imaging of flow, particle binding, or the local environment through surface functionalization. The lack of *in-vivo* ^{29}Si background signal has the potential for quantification of the ^{29}Si magnetic resonance label, opening up the possibility to track the particle biodistribution systematically over long time periods, analogous to the use of nuclear tracers.

Conclusion: The broad positive impact of hyperpolarized imaging employing SiNPs when translated to clinic are that *(a)* it is non-invasive, non-toxic and non-radioactive, *(b)* the technique can be utilized by the widely available MR imaging tool, and *(c)* it can provide rapid feedback for decision-making related to patient selection, disease staging, and treatment monitoring.

References: [1]Tasciotti et al. Nature Nano (2008) [2]Park et al. Nature Mat. (2009) [3]Cassidy et al. Nature Nano. (2013) [4]Ardenkjær-Larsen et al. PNAS (2003) [5]Atkins et al ACS Nano [6]Aptekar et al ACS Nano (2009).