In-vivo 29Si magnetic resonance imaging of hyperpolarized silicon particles

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Introduction – Silicon-based nanoparticles have gained popularity in a wide range of biomedical applications due to their biocompatibility and biodegradability in-vivo, as well as a flexible surface chemistry that allows drug loading, functionalization and targeting.[1-5] To date, in-vivo imaging and tracking of silicon particles has been realized via optical activation[2] or by the incorporation of imaging agents such as fluorescent markers,[1] paramagnetic compounds for conventional magnetic resonance imaging (MRI)[4], or radionuclides for positron emission tomography (PET).[5] Here we report direct *in-vivo* imaging of hyperpolarized ^{29}Si silicon microparticles by ^{29}Si MRI. Applications to gastrointestinal, intravascular, and tumor perfusion imaging at sub-picomolar concentrations are presented.

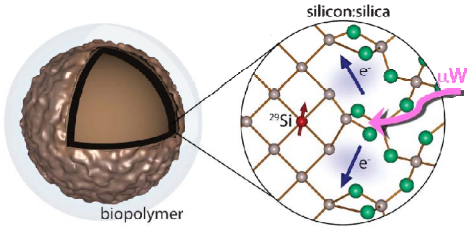

Figure 1 – DNP mechanism in silicon particles

Methods - We used commercially obtained high purity silicon particles with a mean diameter of 2 um and were surface functionalized with polyethylene glycol (PEG). Low temperature DNP was performed in a home-built polarizer operating at 3 T. Defect electrons naturally occurring at the particle surface are used for DNP of the 29Si nuclei and so no free radicals are required (Fig. 1). MRI experiments were performed at 4.7 T in a horizontal bore animal scanner (Bruker) outfitted with a high-resolution gradient set. A dual coil setup was used for co-registered coronal ^{1}H:^{29}Si imaging. Anatomical ^{1}H imaging was performed with a standard MSME spin echo sequence (8 slices, slice thickness = 3 mm, 256 x 256 pixel resolution, FOV = 6 cm). A custom spin echo pulse sequence was written for ^{29}Si imaging (1 slice, slice thickness = 60 mm, α= 20°-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 – For hyperpolarized silicon particles injected via a catheter into the gastrointestinal (GI) tract of a mouse (Fig. 2a), the ^{29}Si image shows the particles accumulating in the stomach and the duodenum immediately following the injection. After 30 min, the ^{29}Si image shows the particles have moved further into the small intestine of the animal, further elucidating internal structure. Delivery into the intraperitoneal cavity reveals detailed external structure of the GI tract imaged over 20 min (Fig. 2b). For particles administered intravenously via a tail vein catheter, the vena cava is visible immediately after injection and continues to be visible several minutes later (Fig 2c). Perfusion imaging of a prostate tumor of a TRAMP mouse is also demonstrated (Fig. 2d). The particles used in this study are too large to enter the cellular structure of the tumor, however they accurately map the blood vessel microstructure inside the tumor, as well as the direction of blood flow within the tumor.

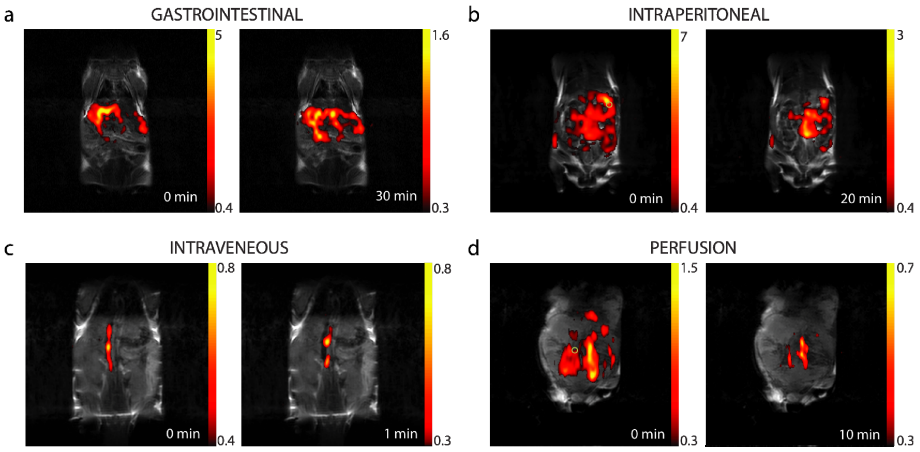

Figure 2 - *In-vivo* coregistered ^{1}H: ^{29}Si MRI of hyperpolarized silicon particles administered (a) intragastrially, (b) intraperitoneally, and (c) intravenously via a tail vein catheter. (d) Perfusion imaging using hyperpolarized silicon particles injected into the tumor of a prostate cancer animal.

Discussion - We have demonstrated in-vivo imaging of hyperpolarized silicon particles by MRI more than 30 minutes after delivery to the animal and investigated a range of potential applications. Magnetic resonance offers not only the possibility of structural imaging, but also 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, analogous to the use of nuclear tracers. These results demonstrate a new background-free imaging modality applicable to a range of inexpensive, readily available, and biocompatible Si particles.

References - [1]Tasciotti et al. Nature Nano (2008) [2]Park et al. Nature Mat. (2009) [3]Singh et al JACS (2011) [4]Gu et al, Small (2010). [5]Tu et al, ACS Med. Chem. Lett. (2011).

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