Relaxivity of Cobalt Nanoparticles, a Novel MR Contrast Agent

L. M. Parkes[1], R. Hodgson[1], L. T. Lu[2], I. Robinson[2], D. Fernig[3], and N. T. Thanh[2,3]

[1]MARIARC, University of Liverpool, Liverpool, Merseyside, United Kingdom, [2]Department of Chemistry, University of Liverpool, United Kingdom, [3]Centre for Nanoscale Science, University of Liverpool, United Kingdom

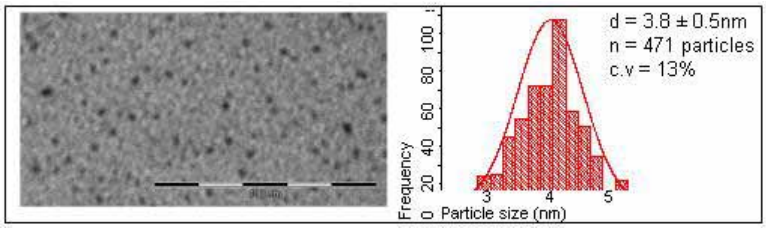
Introduction Magnetic nanoparticles offer a unique opportunity for cell tracking *in vivo*. By incorporating magnetic nanoparticles inside cells, their position within the body can be tracked with MRI. Magnetic nanoparticles composed of iron oxides are currently used as contrast agents in magnetic resonance imaging (1, 2). However iron oxides have a relatively low saturation magnetisation, requiring the use of larger particles. Transition metal nanoparticles, e.g. those made from cobalt, have a much higher saturation magnetisation value, allowing the use of smaller particles (< 5 nm), without compromising sensitivity.
This work describes the relaxation properties of cobalt nanoparticles, a novel MR contrast agent. We report T1, T2 and T2* relaxivity values at a range of temperatures at both 1.5T and 3T. The particles have comparable properties to USPIOs but at a smaller core diameter of 4nm.

Methods

Particle synthesis and properties

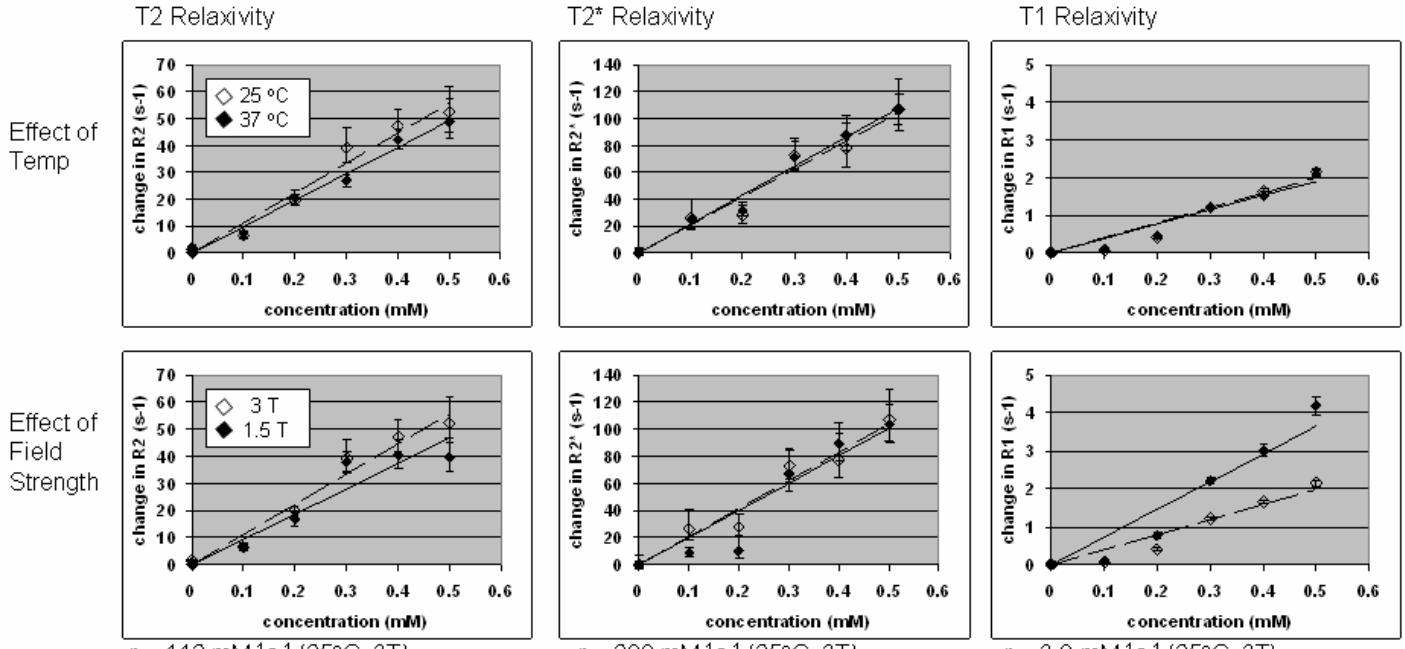
Monodispersed water-soluble cobalt nanoparticles of 3.8 nm diameter were formed by the reduction of cobalt salt in aqueous solution in the presence of alkyl thioether end-functionalized poly(methyacrylic acid) stabilizer with sonication.

The figure shows a TEM image (left) and histogram (right) of 3.8nm polymer stabilized Co nanoparticles dispersed in water, bar 100 nm.



MR methods The nanoparticles were dispersed in tubes of 2% agarose gel at a range of concentrations. The tubes were placed in a water bath at 40°C and the temperature was monitored. T1, T2 and T2* mapping was performed on Siemens 1.5T and 3T systems.
T2 quantification: A multi-echo spin echo sequence was used with the following parameters: TE: 6 echo times from 15 to 90ms, TR=2.5s, resolution 0.9x0.9x3mm.
T1 quantification: An inversion recovery turbo spin echo sequence was used with inversion times: 100,570,750,1500,3000ms, TR=5.9s, TE=12ms, res 0.9x0.9x3mm.
T2* quantification: A 3D gradient echo sequence was used with echo times: TE= 10,20,30,40ms, TR=70ms, 1.5mm isotropic resolution.
Matlab was used to fit the signal intensity of the images on a voxel by voxel basis to the appropriate mono-exponential model using least squares minimization to produce maps of T1, T2 and T2*. A region of interest was identified in the centre of each tube (containing 50 voxels for the T1 and T2 images and 16 voxels for T2* images). The mean and standard deviation of the relaxation rates were recorded for each ROI to produce plots of relaxation rate versus concentration. A linear fit gave the relaxivity value r in units of $mM^{-1}s^{-1}$. Note that mM refers to millimoles of cobalt atoms per litre.

Results and Discussion



r = 112 $mM^{-1}s^{-1}$ (25°C, 3T)
r = 98 $mM^{-1}s^{-1}$ (37°C, 3T)
r = 93 $mM^{-1}s^{-1}$ (25°C, 1.5T)

r = 208 $mM^{-1}s^{-1}$ (25°C, 3T)
r = 215 $mM^{-1}s^{-1}$ (37°C, 3T)
r = 201 $mM^{-1}s^{-1}$ (25°C, 1.5T)

r = 3.8 $mM^{-1}s^{-1}$ (25°C, 3T)
r = 4.0 $mM^{-1}s^{-1}$ (37°C, 3T)
r = 7.5 $mM^{-1}s^{-1}$ (25°C, 1.5T)

The figure shows that there was no detectable effect of temperature on any of the relaxivities. Field strength however had a significant effect with 1.5 T giving approximately double the T1 relaxivity compared to 3 T but reducing the T2 relaxivity. This T1-specific field strength dependence is in accordance with the theory of Roch and Muller (3). The opposite effect of field strength on T1 and T2 relaxivities is supported by empirical evidence from a study of USPIOs (4). The values for T2 and T1 relaxivity of 100 and 8 $mM^{-1}s^{-1}$ respectively at 1.5T are similar to those reported for USPIOs of larger size (4) and the T1 relaxivity is greater than that of Gd-DTPA (3.3 $mM^{-1}s^{-1}$ at 1.5T, ref 5). Hence, these cobalt nanoparticles offer potential as a positive contrast agent.

References 1. Pankhurst, Q.A., et al., Journal of Physics D-Applied Physics, 2003. 2. Kim, D.K., et al., Scripta Materialia, 2001. 3. Roch and Muller, J Chem Phys 1999, 4. Simon et al, European Radiology 2006. 5. Roher et al, Invest. Radiol. 2005.