NMR Relaxation of Mn0.5Zn0.5GdxFe(2-x)O4 Hyperthermia Nanoparticles: Effects of Coating

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Introduction: Recent technical advances have made available magnetic nanoparticles (MNPs) of different compositions, coating, sizes, and size distributions leading to different chemical and physical properties and a range of applications (e.g. molecular imaging). We studied the 1/T1 and 1/T2 behaviour with MNP concentration and also explored the effect of the coating for a new class of MNPs composed of elements Zn, Mn, Gd and iron oxides. These particles have already been used as hyperthermia agents and are being considered as MRI contrast agents.

Material & Methods:

Nanoparticles Synthesis: Various samples of Gd substituted Mn-Zn Ferrite nanoparticles were synthesized using a chemical co-precipitation method and ferritization. In this method a 0.1 M solution of the metal salts $MnCl_2$, $FeCl_3$, $FeSO_4$, $ZnSO_4$ and $GdCl_3$ was added to an 8 M solution of NaOH. The mixture was stirred vigorously at 90ºC for 40 minutes followed by filtration, washing, and drying. Samples made were of the form $Mn_{0.5}Zn_{0.5}Gd_xFe_{(2-x)}O_4$ with x = 0.02. MNPs were dispersed in viscous solution (agarose gel) followed by ultrasonication to ensure homogeneous distribution. A range of concentrations C (in mM of MNPs) was prepared from C = 0.0 to 0.3 mM for both naked and PEG-coated MNPs.

MR Relaxometry: Measurement of T1 and T2 was performed (at 1.5 T) using a GE SIGNA MR Scanner (Twin Gradient Echo Speed, General Electric, Milwaukee, WI, USA). A fast spin-echo (FSE) imaging sequence was used with the following parameters: FOV 20 cm, 256 x 256, NEX = 1, slice = 5 mm, Echo Train Length = 16, BW = 15.63 kHz, flip = 90^o. For the T1 measurement an inversion recovery FSE sequence was used with TE = 15 ms and TR = 6s, and eight values for the inversion time: 50 - 4000 ms. T2-weighted images were generated using seven values of TE: 12 - 152 ms. Mean signal values were then fitted to a single exponential curve.

Results: The magnetic moment (μ) was measured to be 13.07 EMU/g at 27^oC. ICP measurements gave the following concentrations (μg/mL): Gd 60, Mn 810, Fe 1874, and Zn 511. Figure 1 below shows SEM images of uncoated MNPs. The average diameter for the uncoated and coated MNPs were 36 and 63 nm, respectively, as determined automatically by image processing software. The coating affects not only the particle size and size distribution, but also agglomeration properties of the particles. 1/T1 and 1/T2 are plotted as a function of concentration in Figure 2. The 1/T2 relaxation mechanism is the classical outer-sphere relaxation enhancement by diffusion through field gradients created by MNPs [1,2]. The increase of R1 and R2 with MNPs concentration is larger for the uncoated particles than for the coated ones. This can be explained by the larger distance separating the gel protons from the nanoparticles in the coated case. Any disagreement between theoretical ($1/T2=16\,\nu\,\Delta\omega\tau_D/45$; ν is the volume fraction occupied by the MNPs, $\Delta\omega$ is the angular frequency at the equatorial line of the MNP, τ_D is the time taken by protons to diffuse a distance similar to MNP radius) and experimental results can be due to the agglomeration of the particles, which effectively increases the particle size, and the distribution of sizes. For the PEG-coated particles we have also calculated the theoretical 1/T2 using a reduced radius since water molecules diffuse through the PEG layer. The dotted line shows a better agreement between theoretical and experimental results when the effective radius is reduced to 80% of the true radius.

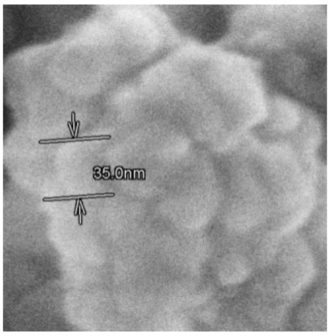

Fig. 1: SEM images of naked MNPs.

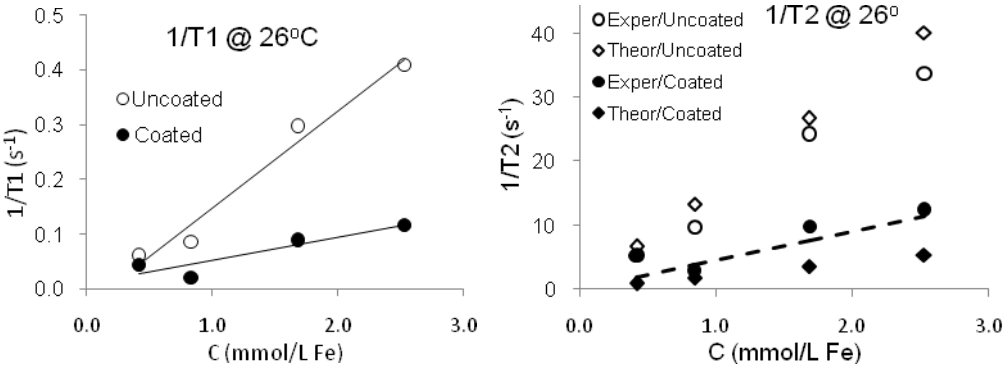

Fig. 2: Experimental & theoretical 1/T1 and 1/T2 are plotted vs. concentration of MNPs.

Conclusions: Results obtained here indicate that coating plays an important role in reducing relaxation efficacy. The coating layer prevents the water from diffusing near the MNP so that the sampled magnetic field gradients will be smaller. The thickness of the layer need only be small because the field decreases with the third power of distance (dipole). We are investigating the use of these MNPs particles, in addition to their role as contrast agents, in temperature monitoring and hyperthermia applications.

References: (1) Brooks RA, Moiny F, Gillis P. On *T*2-shortening by weakly magnetized particles: the chemical exchange model. Magn Reson Med 2001;45: 1014–1020. (2) Alain Roch, Yves Gossuin, Robert N. Muller, Pierre Gillis. Superparamagnetic colloid suspensions: Water magnetic relaxation and clustering. Journal of Magnetism and Magnetic Materials 293 (2005) 532–539.

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