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NMR Relaxation in Systems with Magnetic Nanoparticles: A Temperature Study

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Abstract

Purpose—To measure and model NMR relaxation enhancement due to the presence of Gd substituted Zn-Mn ferrite magnetic nanoparticles at different temperatures.

Materials and Methods—Relaxation rates were measured at 1.5 T using FSE sequences in samples of agarose gel doped with uncoated and polyethylene glycol (PEG) coated $Mn_{0.5}Zn_{0.5}Gd_{0.02}Fe_{1.98}O_4$ nanoparticles over the temperature range 8 to 58°C. Physical characterization of the magnetic nanoparticles synthesized using chemical co-precipitation included scanning (SEM) and transmission (TEM) electron microscopy, inductively coupled plasma (ICP), dynamic light scattering (DLS), and magnetometry.

Results—Relaxivity (in $s^{-1} mM^{-1} Fe$) for the uncoated and coated particles, respectively, increased as follows: from 2.5 to 3.2 and 0.4 to 0.7 for T_1 , while for T_2 it increased from 162.3 to 253.7 and 59.7 to 82.2 over the temperature range 8 to 58°C. T_2 data was fitted to the echo limited motional regime using one fitting parameter that reflects the degree of agglomeration of particles into a cluster. This parameter was found to increase linearly with temperature and was larger for the PEG coated particles than the uncoated ones.

Conclusion—The increase of $1/T_2$ with temperature is modeled successfully using echo limited motional regime where both diffusion of the protons and nanoparticle cluster size increase with temperature. Both transverse and longitudinal relaxation efficiencies are reduced by PEG coating at all temperatures. If prediction of relaxation rates under different particle concentrations and operating temperatures is possible then the use of MNP in temperature monitoring and hyperthermia applications may be achieved.

Keywords

nanoparticles; NMR relaxation; coating; contrast agents; agglomeration; hyperthermia

INTRODUCTION

Recent engineering and biotechnical developments have led to increased attention directed towards multi-functionalized nanoparticles. Two important biomedical applications for magnetic nanoparticles (MNP) are currently receiving attention (i) MRI contrast agents (1,2); and (ii) magnetic particle hyperthermia agents for cancer therapy (3,4). Both of these applications depend, in different ways however, on the magnetic properties of the nanoparticles. In MRI the magnetic field possessed by the MNP disturbs the homogeneous field of the scanner and therefore enhances protons' relaxation. In hyperthermia, self-regulating heat dissipation through the use of materials with a Curie temperature close to the target temperature (i.e. for killing cancerous cells) is controlled by a significant change in the material's magnetization (5). Furthermore, if $T1$ and $T2$ relaxation rates are shown to be temperature-sensitive in the presence of MNP it is anticipated that these agents would then be used as thermometry agents and hence improve the efficacy of many clinical procedures, such as hyperthermia treatment. In order to achieve this goal, however, these sensitivities need to be large and linear.

In this work we measure and model both $T1$ and $T2$ relaxation rates in the presence of different concentrations of nanoparticles over a wide temperature range that covers many biomedical applications including MNP hyperthermia. Both uncoated and polyethylene glycol (PEG) coated nanoparticles are used and the effect of PEG on relaxation is clearly demonstrated.

MATERIALS AND METHODS

Synthesis of the Nanoparticles

Various samples of Gd substituted Mn-Zn Ferrite nanoparticles were synthesized using chemical co-precipitation method and ferritization (6). In this method a 0.1 M solution of the metal salts $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$, $\text{GdCl}_3 \cdot 6\text{H}_2\text{O}$, and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ was added to an 8 M solution of NaOH. The mixture was stirred vigorously at 90°C for 40 mins. Thereafter the synthesized nanoparticles were filtered and washed 3 times with distilled water and 3 times with acetone. In the last wash the precipitate was collected via filtration and dried at room temperature. In this work the Gd concentration was according to the chemical formula $\text{Mn}_{0.5}\text{Zn}_{0.5}\text{Gd}_{0.02}\text{Fe}_{1.98}\text{O}_4$. More detail about the synthesis process can be found in reference (7). As shown before particles with this Gd concentration possess the appropriate Curie temperature ($\sim 43^\circ\text{C}$) for hyperthermia applications (6,8). The element mass proportions obtained from inductively coupled plasma (ICP) measurements were used to work out the concentrations (in mM) of Fe per kg mass (or Liter) of agar gel. The nanoparticles were finally prepared in the form of either powder or colloid for characterization.

The particles were then divided into two groups for the purpose of coating with PEG (Molecular Weight: 8,000, Polyscience Inc, USA). One of them was sonicated in deionized water for five minutes before adding dissolved PEG and mixing lightly to keep the particles dispersed within the PEG layer. The particles were dispersed in viscous solution of agarose gel followed by sonication to ensure homogeneous distribution. Solutions were then left to dry and solidify in glass tubes (20×3 cm). The agarose gel is a high resolution electrophoresis grade (Invitrogen, concentration 1.5%) with a strength 500 g/cm^2 and melting point 70°C (as powder). The concentrations of MNPs used in this study were in the range 0.0 (control: pure gel) to 0.17 mM Fe per kg gel.

Characterization of Nanoparticles

Inductively coupled plasma spectroscopy (Varian Vista-MPX CCD Simultaneous ICP) was used to yield the chemical composition of the synthesized nanoparticles. Magnetization curves were obtained at different temperatures using superconducting quantum interference device (Quantum Design MPMS SQUID VSM dc Magnetometer). SEM and TEM analysis (EDX, Jeol Model JSM-5600) was performed to extract the average diameter of the nanoparticles as well as their size distribution. Dynamic light scattering (DLS) was used to measure the particle size at different temperatures (Zetasizer, Malvern Instruments, UK). Uncoated particles were diluted in deionized water (concentrations 10 µg/ml) and sonicated vigorously to ensure that the solution is homogeneous before obtaining DLS measurements.

T1 and T2 Measurement

Measurement of $T1$ and $T2$ was performed at different temperatures at a magnetic field strength 1.5 T using a GE SIGNA MR Scanner (Twin Gradient Echo Speed, General Electric, Milwaukee, WI, USA). The temperature of the samples was raised gradually in a controlled manner using an electrical water bath outside the magnet. Sufficient time (~10 minutes) was given to allow temperature inside the gel to equilibrate with that of the water bath. This was confirmed using invasive temperature measurements at interior locations on similar tubes (not used for MRI). Inside the magnet the tubes were immersed in a water bath and were well insulated.

For the $T1$ measurement an inversion recovery fast spin-echo (IR-FSE) sequence was used with TE = 15 ms and TR = 6s. Eight values for the inversion time (TI) were used: 50, 100, 250, 700, 1200, 2000, 3000, and 4000 ms. The fast spin-echo (FSE) imaging sequence had the following parameters: FOV 20 cm, matrix 256×256 , NEX = 1, slice thickness = 5 mm, Echo Train = 16, BW = 15.63 kHz, flip = 90°. For the measurement of $T2$ seven values of TE were used to generate $T2$ -weighted images with a TR = 4 s: TE = 12, 23, 35, 47, 58, 105, and 152 ms. Image analysis was carried out using Analyze software (Version 4.0, Biomedical Imaging Resource, Mayo Clinic, Rochester, MN, USA). Signal intensities were sampled from ROIs covering 112 pixels (the tube covered 391 pixels in total). Mean values were then fitted to a single exponential curve using non-linear programming (Levenberg-Marquardt) minimizing the sum of squares of the differences between the fitted curve and the data. An additional ROI was also sampled outside the phantom and the standard deviation of its pixels' intensities was subtracted from all signal mean values prior to fitting the data in order to correct for errors associated with background noise (9). This analysis generated longitudinal and transverse relaxation time values at different concentrations and temperatures.

Relaxation Theory

The enhancement of proton's relaxation due to the presence of magnetic nanoparticles is governed by many factors such as the particle's size and magnetic moment, particle concentration and spatial distribution. The ability of the protons to experience spatially varying magnetic fields produced by the nanoparticles depends on, among other factors, the temperature of the sample which controls viscosity and diffusion. Relaxation theory is well developed (10–18) and was reviewed by Laurent (19). For short diffusional times (τ_D) compared to the variation in the precessional frequency, i.e. $\omega_\gamma \tau_D \ll 1$ relaxation is within the motionally averaged regime (MAR); however, when $\omega_\gamma \tau_D \gg 1$ relaxation is in the static dephasing regime (SDR) where the diffusion coefficient is irrelevant and $T2$ decay originates from the inhomogeneity of a nearby particle. ω_γ , the r.m.s. Larmor frequency (14) experienced by the proton at the surface of the particle or cluster of particles of radius r is given by (S.I. units)

$$\omega_r = \sqrt{4/5} \mu_0 M \gamma / 3 = \sqrt{4/5} \frac{\mu_0}{4\pi} \gamma \mu / r^3 \quad [1]$$

γ is the proton gyromagnetic ratio, μ_0 is the permeability of free space, M is the particle magnetization (A/m), and μ is the magnetic moment of the particle (A.m²). Note that ω_r is independent of the particle size and only material dependent. $\tau_D = r^2/D$ is the diffusion correlation time (time taken by the proton with diffusion coefficient D to diffuse around a particle of radius r).

Following (19) the expressions for $1/T_2$ for the above mentioned two motional regimes are given by

$$1/T_2^{MAR} = \frac{16}{45} f \omega_r^2 \tau_D \quad [2]$$

$$1/T_2^{SDR} = \frac{2\pi}{\sqrt{27}} f \omega_r \quad [3]$$

Here, f is the particulate volume fraction. For large particles, or agglomeration of particles, where the refocusing RF pulses are not effective and the diffusion time τ_D is larger than a characteristic time τ_L given by

$$\tau_L = (1.49/\omega_r) x^{1/3} (1.52 + f x)^{5/3} \quad [4]$$

$x = \omega_r \tau_{CP}$, the theoretical model for T_2 , known as the echo limited regime (ELR), applies and is given by the following equation (19)

$$1/T_2^{ELR} = 1.8 f x^{1/3} (1.52 + f x)^{5/3} / \tau_D \quad [5]$$

τ_{CP} is half the echo time (TE). According to the experimental values used in our study equation 5 can be simplified to be written as

$$1/T_2 \approx A M^{1/3} D / r^2 \quad [6]$$

A is a constant in equation 6.

RESULTS

A group of T_2 weighted images is shown in figure 1 with the sample tubes arranged in two groups for the coated (left) and uncoated particles (right). TEM images of the uncoated and coated particles are shown in figures 2 and 3, respectively. The uncoated particles, which were suspended in water before submitting to TEM, show a degree of clustering that is not apparent in the PEG coated particles.

All R_1 and R_2 results in this work refer to the incremental (paramagnetic) relaxation rates after subtracting the pure gel diamagnetic relaxation rates. The variation of relaxation rates $R_1=1/T_1$ and $R_2=1/T_2$ with nanoparticle concentration at the two temperatures 18 and 58°C are shown in figures 4 and 5, respectively. They clearly show the effect of PEG coating in reducing both relaxation rates with similar effect for all other temperatures not shown in the

figures for clarity. Linearity of $R1$ and $R2$ versus concentration of nanoparticles is also demonstrated. We concentrate on analyzing transverse relaxation data since these particles have the potential to act as negative contrast agents since $R2 \gg R1$, and attempt to fit the $R2$ data to the theoretical model. The enhancement of the $R2$ temperature coefficient (i.e. the rate of change of transverse relaxation rate $R2$ per degree temperature change) with nanoparticle concentration is shown in figure 6 for both coated and uncoated particles with similar, but much smaller, pattern for the $R1$ coefficient (not shown). In figure 7 we display the transverse relaxivity ($r2$) variation with temperature for both uncoated and coated particles. Similar pattern is observed for the longitudinal relaxivity ($r1$) parameter (not shown). In both figures 6 and 7 the increase in the plotted parameters is larger for the uncoated particles than for the coated ones. Relaxivity (in $s^{-1}mM^{-1}Fe$) for the uncoated and coated particles, respectively, increased as follows: from 2.5 to 3.2 and 0.4 to 0.7 for $R1$; while for $R2$ it increased from 162.3 to 253.7 and 59.7 to 82.2 over the temperature range 8 to 58°C (figure 7). The relaxation rate temperature coefficient increased monotonically with concentration. The coefficient values (in $s^{-1}^{\circ}C^{-1}$) at the largest concentration for the uncoated and coated particles, respectively, were as follows: 2.96×10^{-3} and 8.48×10^{-4} for $R1$; while for $R2$ they were 0.31 and 0.09 (figure 6). It should be noted that the coefficient value of zero (at $C = 0.0$) reflects the incremental paramagnetic contribution of the particles only; the gel itself exhibits monotonically decreasing $R1$ (from 0.55 to 0.34 s^{-1}) and non-monotonically decreasing $R2$ variation (from 9.91 to 6.10 s^{-1}) over the temperature range (8–58°C). As stated before all relaxation values reported here are relative to the pure gel relaxation values at all temperatures. This is important because the gel relaxation values change with temperature. Therefore, if a different type of matrix is used (or even a PEG of different concentration or an in vivo data is acquired) then baseline relaxation values (with no nanoparticles) have to be measured at all temperatures for the data to be meaningful.

The SEM determined radii of the uncoated and coated particles were, respectively, $r_{SEM}^u = 16.8$ nm and $r_{SEM}^c = 31.5$ nm (at 27°C), while the magnetization data yielded the volume magnetization $M = 66k$ A/m. Using values for the particles' density (5.2 g/cm³), M_s , and μ an estimate for the particle radius is calculated in a similar way as used by Giessen (20) to be equal to $r_{MAG}^u = 8.7$ nm (almost half the value obtained from SEM) - where the superscripts "u" and "c" refer to uncoated and coated particles, respectively. Using these values we notice that the condition for motional averaging $\omega_\gamma \tau_D \gg 1$ is not fully met for our particles. Indeed, using the measured magnetization values in equation 1 and the definition of τ_D we obtain a value $\omega_\gamma \tau_D = 6.6$ at 26°C. To take account of large particle size caused by possible agglomeration of particles we use equation 5 to fit the $R2$ data for the uncoated particles as shown in figure 8. The model fits the data well over the whole ranges of temperature and particle concentration. For each temperature we have used a fitting parameter "packing factor α^u " that accounts for the agglomeration of particles and the volume of the non-magnetic part of the formed cluster (21,7) with $\alpha^u = (r_{REL}^u / r_{MAG}^u)^3$ and r_{REL}^u is the modified radius value of the uncoated particles where "REL" refers to relaxation. As shown in figure 9 the ratio r_{REL}^u / r_{MAG}^u (or the cubic root of α^u) increases with temperature almost linearly from 4.4 at 8°C to 6.7 at 58°C. In equation 5 we used values of D for water molecules diffusing in agarose gel of concentration 1.5% at various temperatures obtained from (22). The values are slightly smaller than the self-diffusion coefficient for water as expected due to networking introduced by the agarose gel.

To model the $R2$ data for the coated particles we not only have to account for the larger particle size introduced by the presence of the PEG layer, but also, the reduced effective magnetization since the coating layer is non-magnetic. The ratio of $R2$ for the uncoated particles to that of the coated ones is shown in figure 10 as a function of temperature for all particle concentrations, along with the mean value (2.31) of all data points.

DISCUSSION

For nanoparticles to be used as hyperthermia agents as well as MRI contrast media for the purpose of temperature measurement we need to quantify MRI relaxation enhancement at a wide range of temperatures. There are many physical parameters that will interact in a complex way in defining relaxivity and heat dissipation for the above two mentioned applications, particularly, the magnetic moment and the size of the particle and their dependence on temperature. This can be further manipulated by the presence of the surfactant layer which is important to insure biocompatibility, targeting, and also to prevent agglomeration.

In this study we have confirmed previous results (23, 7) that PEG coating reduces relaxation efficiency, however, we have extended this result to be applicable for a wider temperature range 8–58°C. The R_2 data was successfully modeled using the echo limited motional regime by the use of a temperature dependent packing factor which expresses the ratio of the cluster to the individual particle radius. The linear increase in this ratio with temperature is attributed in our view to mainly the agglomeration of the particles. This agglomeration occurs due to the particles' dipolar coupling induced by easily thermally agitated loose spins at the nanoparticles surface. It can also be enhanced by the uniform MRI fields as was used e.g. by Hong et al (24) to determine viscosity by MRI. Although the non-magnetic part of the cluster, trapped between the individual particles, can play a role in increasing the inter-particle distances (as used by Noginova (21)), we think that this is insignificant in magnitude compared to agglomeration. In fact, polymers may contract with temperature; however, PEG would have a very small contraction rate within this temperature range. It is believed that shrinkage in the PEG physical network with temperature occurs due to the breaking of physical bonds which are known to be much weaker than chemical ones. Clustering, as reflected by the packing factor, takes place due to dipolar interactions (25) in nanoparticles of ferrimagnetic materials with dimensions bigger than 10 nm and magnetic moments larger than 10^4 Bohr magnetons. The dipolar interaction energy E_d between moments μ separated by a distance d is on the order of (25)

$$E_d \approx \frac{\mu_0 \mu^2}{4\pi d^3} \quad [7]$$

Depending on the concentration of the nanoparticles in the sample (i.e. inter-particle spacing), magnetic dipole interactions can result in ordering (26, 27) of the magnetic moments of the nanoparticles below a critical temperature T_0 given by

$$E_d \approx T_0 k_B \quad [8]$$

For our sample, the values of the ratio $E_d/T_0 k_B$ varies from 14 and 40, suggesting that agglomeration is not excessive but is still possible in the sample used in this work if PEG coating is not used (27). Uncoated particles were suspended in agarose gel in this initial study to prevent any further agglomeration beyond that produced during the solidification stage of the molten gel or during heating. If strong dipolar coupling exists then synthesized particles must be kept small in size and must not be left suspended in liquids for long time prior to coating and use. Thermally induced agglomeration of particles would continue up to certain temperature T_0 at which thermal energy agitation would overcome dipolar interaction produced by possible thermally increased surface spin. This may explain the plateau in R_2 data above 40°C (figure 8) which is further confirmed using the DLS measurements shown in figure 11. The measured diameter of the agglomerate peaks around 50°C which is very close the particle's Curie temperature (43°C). The loss of the particle's magnetic moment

around this temperature leads to the weakening of dipolar interactions and thereafter the loss of agglomeration.

The reduced $R1$ and $R2$ for the PEG coated particles was due to the increased hydrodynamic particle size caused by the coating layer which has many effects on relaxation. Firstly, it shields the water protons from the magnetic moment of the magnetic core of the particle (i.e. increased minimum distance of approach); secondly, depending on the density of the PEG it may decrease the diffusion coefficient of water molecules around the particle ($D^c = D_{H_2O/PEG}$) compared to that of water molecules in the agarose gel ($D^u = D_{H_2O/Agarose}$); thirdly, it places a limit on the density of particles within a cluster because it prevents excessive agglomeration of the particles; finally, the coated particle magnetization can be interpreted as a reduced effective magnetization as compared to that of the uncoated value due to the increased volume of the non-magnetic coating layer. A recent study (28) confirmed that minor changes in particles' aggregation (e.g. polymer type and particle loading) plays the dominant role in controlling proton relaxivity over other factors such as exclusion of protons or diffusivities. A counter effect (23) that may lead to increasing $R1$ is the fact that protons may have an increased residence time (under the influence of the particle's magnetic field) due to the reduced diffusion coefficient of the PEG layer. Therefore, we estimate the ratio of uncoated particle magnetization (M^u) to that of the coated particle magnetization (M^c) as given by

$$M^c = M^u \left(V_{REL}^u / V_{REL}^c \right) = M^u \left(r_{REL}^u / r_{REL}^c \right)^3 = M^u \left(\frac{\alpha^u}{\alpha^c} \right) \quad [9]$$

V_{REL}^u and V_{REL}^c are the volumes of the uncoated and coated particles using the modified radii, respectively, and $\alpha^c = (r_{REL}^c / r_{MAG})^3$ can be obtained in a similar way to α^u . This estimate assumes that each particle along with its coating is identical to others within the crystal, and the crystal will have a uniform magnetization. A simpler analysis would assume that magnetization remains the same in both uncoated and coated particles ($M^c = M^u$), however, with agglomeration density and mobility in gel and PEG absorbed in the modified radius r_{REL}^c and the diffusion coefficient D^c . The theoretical ratio of $R2$ for the uncoated particles to that of the coated ones may then be given by (using equation 6)

$$\frac{R2^u}{R2^c} \approx \left(\frac{M^u}{M^c} \right)^{\frac{1}{3}} \frac{\tau_D^c}{\tau_D^u} = \frac{D^u}{D^c} \left(\frac{\alpha^c}{\alpha^u} \right)^{\frac{2}{3}} \quad [10]$$

Substituting $D^u = 2.188 \times 10^{-9} \text{ m}^2\text{s}^{-1}$ (22), $\alpha^c / \alpha^u = 1.71$ from figure 9, and the above value of $R2^u / R2^c = 2.31$ (figure 10), we obtain an estimate for the factor $D^c = 1.35 \times 10^{-9} \text{ m}^2\text{s}^{-1}$. This is a reasonable estimate since we know it must lie between the minimum permissible value $D^c = 0.150 \times 10^{-9} \text{ m}^2\text{s}^{-1}$ (29) which corresponds to protons diffusing in pure PEG enveloping the nanoparticles, and the maximum value $D^c = D^u$ corresponding to pure gel (i.e. no coating). The ratio (α^c / α^u) being larger than unity means that PEG coating increases inter-particle distance within the cluster or equivalently reduces agglomeration.

In conclusion these new contrast agents exhibit linear variation of relaxation enhancement with temperature. If prediction of relaxation rates under different particle concentrations and operating temperatures is possible then the use of MNP in temperature monitoring and hyperthermia applications may be achieved. Current work is concentrating on controlling the PEG thickness layer, the quantification of water diffusion coefficient in mixtures of

coating materials of different thicknesses, and testing other types of coating materials under different temperatures.

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Figure 1.

The phantom used in this study comprising two groups of tubes for the uncoated (right) and coated (left) nanoparticles suspended in agarose gel. Each of the two groups contained eleven tubes with different samples. Right column (from bottom tube upwards) contained: distilled water doped with 0.1 mmol/L Gd-DTPA, distilled water, and pure agarose gel. Middle column (from top tube downwards) contained gel deoped with nanoparticles with Fe concentrations (mmol/L): 0.014, 0.029, 0.058, and 0.115; while the left column contained the following Fe concentrations (from bottom tube upwards): 0.173, 0.288, and 0.403.

Figure 2.
The uncoated nanoparticles shown in this image were suspended in water before submitting to TEM, i.e. prior to sonication and dispersion into agarose gel. Some agglomeration exists.

Figure 3. TEM image for iron oxide PEG coated particles prior to sonication and dispersion into agarose gel. It is clear that less agglomeration exists now than in figure 2 and that the particles are farther separated from each other.

Figure 4.

Linearity of $T1$ relaxation enhancement by nanoparticles for both uncoated and coated nanoparticles is evident for the two temperatures 18 and 58°C. Also evident is the effect of PEG coating in reducing $1/T1$, and of temperature in increasing $1/T1$. Other temperatures exhibit similar relaxation curves (not shown). Linear regression analysis performed on the data sets yields the following r-squared values 0.99 and 0.99 for the uncoated particles (18 and 58°C respectively), and 0.88 and 0.98 for the coated particles.

Figure 5.

Linearity of T_2 relaxation enhancement by nanoparticles for both uncoated and coated nanoparticles is evident for the two temperatures 18 and 58°C. Also evident is the effect of PEG coating in reducing $1/T_2$, and of temperature in increasing $1/T_2$. Other temperatures exhibit similar relaxation curves (not shown). Linear regression analysis performed on the data sets yields the following r-squared values 0.98 and 0.99 for the uncoated particles (18 and 58°C respectively), and 0.86 and 0.90 for the coated particles. One data point is missing for the coated particles due to poor SNR.

Figure 6.

The transverse relaxation rate temperature coefficient ($1/T_2$ per degree) is plotted versus variation nanoparticle concentration. Sensitivity of $1/T_2$ to temperature is linear for all concentrations (reflected by the same r-squared value 0.98 for both types of particles) and is larger for the uncoated nanoparticles than the coated ones. One data point is missing for the coated particles due to poor SNR.

Figure 7.

Transverse relaxivity ($1/T_2$ per mM of Fe) is plotted against temperature for both the uncoated and coated particles. The r-squared value for the uncoated particles 0.98 is larger than that for the coated particles 0.91.

Figure 8. R_2 echo limited regime fitting of the data with temperature for all nanoparticle concentrations (Filled symbols: experimental data; Open symbols: ELR model). The concentrations (in mM/L Fe) are as follows: ▼0.014, ■0.029, ▲0.58, ●0.115, and ◆0.173.

Figure 9.

The ratio of the modified particle radius to the value obtained from magnetic measurements (i.e. the cubic root of the packing factor). The values for the coated particles are larger than those for the uncoated ones by a constant value (1.71) at all temperatures.

Figure 10.

Ratio of $R2$ for the uncoated and coated values at different temperatures ($R2^u/R2^c$) is shown for the various nanoparticle concentrations. Also shown is the mean value (dotted line). One data point is missing for the coated particle due to poor SNR. The concentrations (in mM/L Fe) are as follows: ▼0.014, ■0.029, △0.58, ●0.115, and ◇0.173.

Figure 11.

Cluster diameter measured using dynamic light scattering clearly shows the maximum size reached around 50°C – a temperature close to the Curie temperature of the particles. The sample was suspended in water and concentration was 10 $\mu\text{g/mL}$.