Supporting Information

Size-Tunable, Ultra-Small NaGdF₄ Nanoparticles: Insights into their T₁ MRI Contrast Enhancement

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Ligand exchange of nanoparticles (Additional Information)

The ligand exchange of the oleate-stabilized nanoparticles to get PVP-stabilized nanoparticles was done following our previously published procedure (Ref. 43 in the manuscript). No major modifications were done to this procedure, except for the amount of polyvinylpyrrolidone-10 (PVP-10) used. In a typical exchange procedure, 0.2 ml of 1 wt% oleate-stabilized nanoparticles in toluene (this amount was kept constant for all nanoparticle sizes) was slowly added to 5 ml of 1:1 dichloromethane (DCM)/dimethylformamide (DMF) under continuous stirring to obtain a clear solution. Subsequently, 5 ml solution of PVP-10 in 1:1 DCM/DMF (see Table S1 for PVP-10 used for different NP sizes) was added. The resulting mixture was refluxed at 100 °C for 6 h, and then cooled to room temperature. The polymer-coated NPs were then precipitated by pouring the reaction mixture into excess ethyl ether (250 ml) and the precipitate was collected by centrifugation (1800g), washed with ethyl ether and dried overnight at 70 °C to obtain a thin oily product. This material was dispersed in 30 ml of deionized water and purified by dialysis as explained in the experimental section. After purification, the water from the colloidal dispersion of NPs was removed by rotary evaporation and fresh deionized water was added (3-4 ml) for relaxivity measurements. For higher concentrations two different batches were added and concentrated to 3-4 ml. The final concentrations of these nanoparticle dispersions were determined using ICP-MS.

Table S1. Reagent concentrations used for ligand exchange of different sized nanoparticles*

NP size (nm)	NP concentration (μ M)	PVP-10 concentration (mM)
	(5 ml DCM/DMF)	(5 ml DCM/DMF)
2.5	14	17
4.0	3.5	11
6.5	0.81	6.6
8.0	0.42	5.3

*Note that the PVP-10 used was calculated such that there were ~ 60 PVP-10 molecules per nm^2 of NP surface. The PVP-10 concentration increases with decrease in NP size as surface area increases with decreasing size for the given mass of NPs.

Supplementary Figures

Figure S1. Low resolution TEM images of (A) monodisperse NaYF₄ NPs, and (B) polydisperse NaGdF₄ NPs grown at the same conditions

Figure S2. Low resolution TEM images of as synthesized oleate-coated NaGdF₄ NPs (A) 2.5 nm, (B) 4.0 nm, (C) 6.5 nm, and (D) 8.0 nm, *Scale bar = 100 nm*

Figure S3. Low resolution TEM images of ligand exchanged hydrophilic PVP-coated NaGdF₄ NPs, (A) 2.5 nm, (B) 4.0 nm, (C) 6.5 nm, and (D) 8.0 nm, *Scale bar = 100 nm*

Figure S4. T_2 relaxivity plot of 2.5 nm PVP-coated NaGdF₄ NPs measured at 1.5 T

Figure S5. Powder X-Ray Diffraction spectra of A) NaGdF₄/Yb³⁺/Tm³⁺ core, and B) NaGdF₄/Yb³⁺/Tm³⁺ /NaGdF₄ core/ shell NPs matched with β -NaGdF₄ reference pattern

Relaxivity Calculations*

The concentration of Gd^{3+} ions determined by ICP-MS in the stock solution was used to calculate the molecular mass of $NaGdF_4$ in the specimen using the ratio

$$m(Gd) / m(NaGdF_4) = 0.6137$$

This was used to calculate the r_1/M (**Mass relaxivity**) values.

The $NaGdF_4$ NPs synthesized have Hexagonal closed pack (HCP)- crystal structure and the density of HCP $NaGdF_4$ 5.65 g/cc was used to determine the mass of a NP, considering that the NPs are perfect spheres and their volume determined using

$$V = 4/3 \pi R^3 \text{ (where R is the radius of the NP)}$$

Comparing the mass of the single NP and the total mass determined from ICP-MS the total number of NPs (N) in the stock solution was determined and used to calculate the r_1/NP (**Nanoparticle or per probe relaxivity**) values

The surface area (SA) of the NP was then calculated using

$$SA = 4\pi R^2 \text{ (where R is the radius of the NP)}$$

Using that the total surface area of the NP in the stock solution was calculated

$$\text{Total surface area (TSA)} = N * SA$$

TSA value was used to determine the r_1/SA (**relaxivity per m² of nanoparticle surface**) values.

* Average ionic relaxivity values were used to calculate the r_1/M , r_1/NP , r_1/SA .

Tumbling time of the NPs (τ_R)

$$\tau_R = 4\pi\eta a^3/3k_B T$$

Where, η dynamic viscosity = 10^{-3} pa.s, $k_B T = 4 \times 10^{-21}$ J, a = hydrodynamic radius of the NP, $T = 298$ K.