Supplementary Material (ESI) for Chemical Communications

ELECTRONIC SUPPLEMENTARY INFORMATION

Preparation of Gd_n^{3+}@US-tubes

For the solution-phase filling, 100 mg of US-tubes and 100 mg of anhydrous $GdCl_3$ were were stirred together in 100 ml deionized (DI) HPLC grade water and sonicated in a 30 W batch sonicator for 60 minutes. The solution was left undisturbed overnight whereupon the Gd^{3+}-loaded US-tubes (Gd_n^{3+}@US-tubes) flocculated from the solution. The supernatant solution was then decanted off. The sample was next washed with 25 ml portion of fresh DI and batch sonicated to remove any unabsorbed $GdCl_3$. Once again, the $Gd^{3+}{}_n$@US-tubes flocculated from solution and the supernatant solution was removed by decantation. This procedure was repeated 3 times. Multiple samples were prepared to demonstrate reproducibility. The sample was air dried and an ICP analysis performed showed the Gd content to be 2.84 % (m/m).

Confirmation of absence of free (non-encapsulated) Gd^{3+} ion

This ligand $TTHA^{6-}$ forms a highly stable complex with Gd^{3+} which contains no inner-sphere water molecule (1). Thus, $[GdTTHA]^{3-}$ with no inner-sphere water molecule has a much lower relaxivity than (Gd^{3+}-OH_2) centers and hence any decrease in relaxivity observed upon addition of $TTHA^{6-}$ would signal the presence of free Gd^{3+} ion. For both the solutions, the relaxation rates with and without $TTHA^{6-}$ were identical, implying the absence of accessible (exo US-tubes) aquated Gd^{3+} ions.

ICP sample preparation

In preparation for the ICP measurements, the solutions were treated with cc. 90% HNO_3, then carefully heated until a solid residue was obtained. They were then further treated with a 30% H_2O_2 solution and again carefully heated to completely remove any

remaining carbonaceous material. This solid residue was dissolved in 2 % HNO_3 and analyzed by ICP.

ICP Analysis

Apart from the presence of Gd, the ICP analysis also showed 0.1 to 0.5 ppm of Ni (catalyst) present as impurity, but Y (catalyst) was not detected within the limits of the instrument (1 ppb). The large T_1 values of the unloaded US-tubes demonstrate that the presence of the Ni in the sample has no influence on the relaxation rates. This has been further corroborated by the SQUID magnetization data on an unloaded US-tube sample (Supplementary, Fig. S3), which characterized the sample as having no observable magnetization. Indeed, Ni^{2+}-doped materials have been previously used to make phantom materials that have similar relaxation times to tissue (2).

Instrumentation details

ICP

ICP analysis were performed on a Varian Vista Pro Simultaneous Axial Inductively Coupled Atomic Emission Spectrometer (ICP-OES) with a CCD detector. The selected experimental conditions were as specified elsewhere (4). Gd lines at 335.05 nm, 342.35 nm and 376.84 nm were initially chosen. Seven scans were performed for each sample (relative standard deviation (RSD) = 0.2%). The Gd line at 376.84 showed a higher intensity and was chosen for the final Gd concentration. Sc (λ = 361.38 nm) was used as the internal drift standard.

TEM

TEM imaging was carried out on a JEOL 2000 FX electron microscope operating at 130 kV. Samples were mounted on a copper grid coated with amorphous carbon-holey film.

TEM analysis included conventional, high-resolution TEM imaging, selected area electron diffraction (SAED), and energy-dispersive X-ray spectroscopy (EDS).

Cryo-TEM

Sample solutions were plunge-frozen over Quantifoil grids using Vitrobot^{TM} (FEI company). Images of the vitrified specimens at 93K were recorded on a JEOL 2010F microscope operated at 200kV using a 4K x 4K gatan CCD camera. The nominal magnification was 60000x with a dose of 30 $e^{-}/Å^{2}$. Focal pairs were collected as a part of the experiment and a focal pair merging technique was used to produce composite images with reduced contrast transfer function artifacts and improved contrast (3).

XRD

X-ray powder diffraction (XRD) were performed using a Rigaku DMAX-IIIB diffractometer with a Cu target. The scanning is from 10° to 70° at 0.04°/step. The profile was analyzed using a search /match program with ICDD cards.

XPS

A Physical Electronics Model 5700 XPS instrument was used with photo-emissions produced via a monochromatic Al K_{α} x-ray source (1486.6 eV) operated at 350 W. Photo-emissions were acquired at a take off of 45^{o} as defined relative to the surface plane. These were passed through a hemispherical analyzer operated in the fixed retard ratio mode at a pass energy of 11.75 eV. Curve fitting and quantification were accomplished following the application of a Shirley background subtraction routine.

Proton Relaxivity Measurements

Single point relaxation measurements were performed at 60 MHz on a Bruker Minispec (mq60) NMR spectrometer. The $1/T_1$ NMRD profiles measurements were performed on a

Stelar Spinmaster FFC fast field cycling relaxometer covering a continuum of magnetic fields from 2.35×10^{-4} to 0.47 T (corresponding to a proton Larmor frequency range 0.01-20 MHz) equipped with a VTC90 temperature control unit. The temperature was fixed by a gas flow. At higher fields, the ^{1}H relaxivity measurements were performed on Bruker Minispecs mq30 (30 MHz), mq40 (40 MHz) and mq60 (60 MHz) and on ARX 400 (9.4 T, 400 MHz). In each case, the temperature was measured by a substitution technique.

Magnetization

Measurements for field cool and zero field cool DC magnetization measurements were obtained using a Quantum Design model MPMS magnetic property measurement system (SQUID magnetometer).

DLS

Measurements were conducted on a Wyatt Technologies, Dawn EOS instrument equipped with a 30 mW GaAs laser at λ = 690 nm, with a scattering angle fixed at 90° and a temperature of 25 °C. Data analysis and size distribution computations were performed using the DYNALS regularization algorithm and a multi-τ digital recorder (Wyatt QELS).

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Supplementary Figures

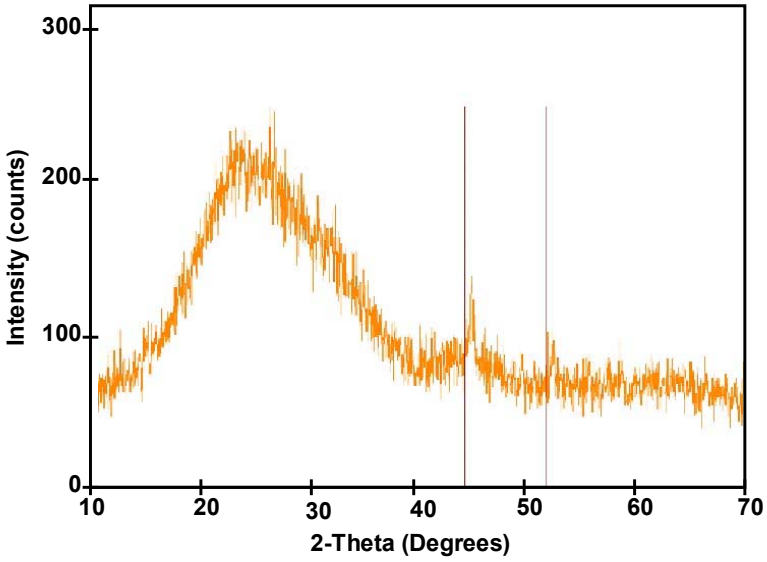

Figure S1: XRD powder pattern of Gd^{3+}_n@US-tubes showing only carbon peaks.

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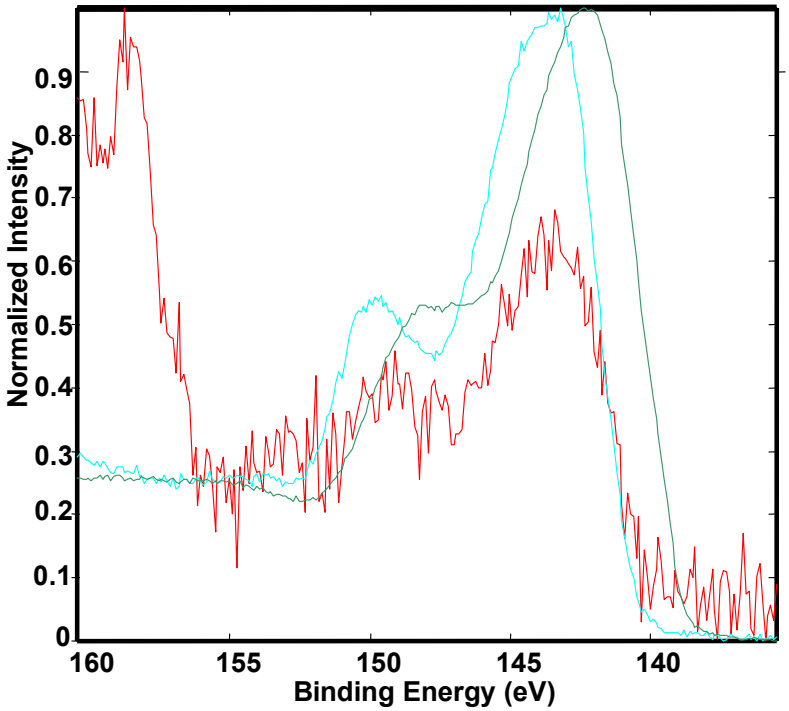

Figure S2: Gd $4d_{5/2}$ x-ray photoelectron spectra of Gd^{3+}_n@US-tubes (red trace), commercial $GdCl_3$ (blue trace) and Gd_2O_3 (green trace).

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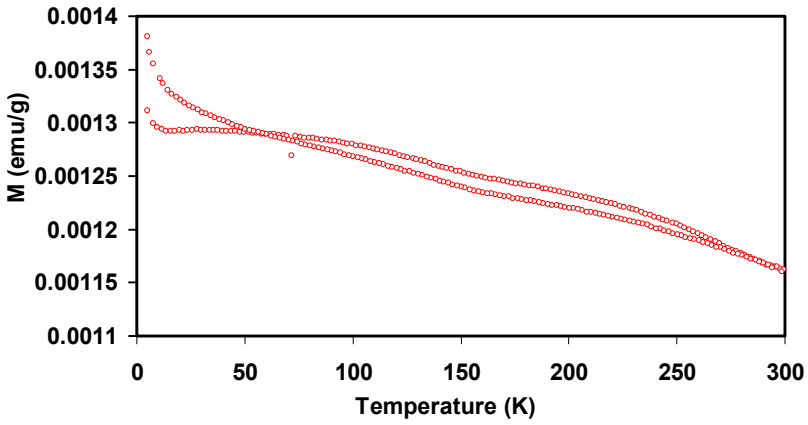

Figure S3: Magnetization (ZFC + FC) vs temperature plot for the US-tubes (control) sample, measured at applied field of 1000 Oe showing no observable magnetization.

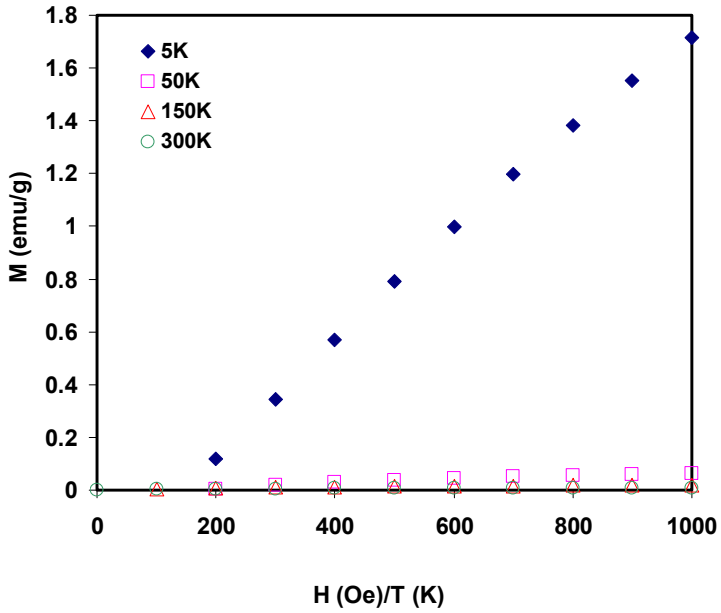

Figure S4: Superposition of the magnetic curves at different temperatures.

SUPPLEMENTARY INFORMATION REFERENCES

1) C. A Chang, H. G. Brittain, J. Telser, and M. F. Tweedle, *Inorg. Chem.* 1990, 29, 4468.

2) P. S. Tofts, B. Shuter, J. M. Pope, *Magnetic Resonance Imaging* 1993, 11, 125-133

3) S. J. Ludtke, And W. Chiu, *Journal of Structural Biology* 2003, 14, 73-78.

4) http://www.varianinc.com/ ICP-OES Application Notes, No. 29.