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Supplementary information
for

Multifunctional β-$NaGdF_4:Ln^{3+}$ (Ln=Yb, Er, Dy) nanoparticles with NIR to visible upconversion and high transverse relaxivity: A potential bimodal contrast agent for high-field MRI and optical imaging

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Experimental

Materials

All reagents and solvents used were obtained from Acros Organics (Geel, Belgium), ABCR (Karlsruhe, Germany), Sigma-Aldrich (Bornem, Belgium), Alfa Aesar (Ward Hill, USA), Chemlab (Zedelgem, Belgium) and all the lanthanide oxides were purchased from Heraeus (Hanau, Germany) and were used without further purification.

Instrumentation

IR spectra were measured using a Bruker Vertex 70 FT-IR spectrometer (Bruker, Ettlingen, Germany) equipped with a Platinum ATR accessory and data were processed with OPUS 6.5 software. Lanthanide concentrations were obtained using a TXRF Bruker S2 Picofox with a Bruker AXS sample carrier. An internal standard a Chem-Lab gallium(III) standard solution (1000 µg mL-1, 2-5% HNO_3) was further diluted to 20 ppm and added to an equivolume of the sample. The resulting solution was dropcasted on a hydrophobic Quartz plate and dried in an oven to remove all solvent. Three Quartz plates were made in the same manner and as such used to determine the concentrations. The collected data were processed with excel to retrieve the average value. Powder X-ray diffraction patterns were recorded with a Huber Guinier

Camera G670 equipped with an image plate and utilizing Mo-$K\alpha_1$-radiation. Rietveld refinement in the range 9-80°2θ with the GSAS software package[1, 2] served to determine the lattice constants, using atomic parameters of pure hexagonal $NaGdF_4$ as starting model. Transmission electron microscopy measurements were performed using a 80 kV Zeiss EM-900 using 300 mesh Formvar/carbon coated copper grids. Distribution data were calculated by ImageJ. Oleic acid-coated nanoparticles were dispersed in toluene while the citrate-coated nanoparticles were dispersed in ethanol and subsequently deposited onto the grid. Nanoparticles were dispersed using a 180 W Bandelin Sonorex RK 510H sonicator. Photon correlation spectroscopy was performed at room temperature with a BIC multiangle laser light scattering system with a 90° scattering angle (Brookhaven Instruments Corporation, Holtsville, USA). Analysis was done using Igor Pro 6.20 software. Photophysical data were recorded with an Edinburgh Instruments FS920 steady-state spectrofluorimeter. This instrument was equipped with a 230 mW diode laser (980 nm, Power Technology), a 450 W Xenon arc lamp and a high energy microsecond flashlamp µF900H and an extended re-sensitive photomultiplier (185-1010 nm, Hamamatsu R 2658P). All spectra were analyzed with Edinburgh software and corrected for the instrumental functions. Proton Nuclear Magnetic Relaxation Dispersion (NMRD) profiles were measured with a Stelar Spinmaster FFC, fastfield cycling NMR relaxometer Stelar, Mede PV, Italy. Measurements were performed on samples (0.6 mL) contained in 10 mm (outside diameter) Pyrex tubes. Relaxation rates at 20, 60, 300 and 500 MHz were obtained with a Minispec mq20, a Minispec mq60, a Bruker Avance 300 and Bruker Avance 500 spectrometer, respectively (Bruker, Karlsruhe, Germany). The reported values of r_1 and r_2 are the average of three different measurements.

Synthesis

Oleate-capped Nanoparticles

The oleate capped AC/AS UNCP's were synthesised using a multi-step process starting with the preparation of the lanthanide trifluoroacetate precursors, followed by thermal decomposition reaction. The lanthanide precursors were generated via the addition of 10 mL of a water/TFA (1:1) mixture to the required amount of lanthanide oxides and the suspension was left to reflux until the solution was clear, where after it was dried under atmospheric pressure at 333 K. In the second step 12.5 mL of oleic acid and 12.5 mL of 1-octadecene were added to a 3-neck round bottom flask. The solution was degassed at 423 K for 30 minutes under vacuum (A). To the dried lanthanide precursors 7.5 mL oleic acid, 7.5 mL 1-octadecene and 340.0 mg (2.50×10^{-3} mol) CF_3COONa were added (B). B was successively degassed at 323 K, 348 K and 403 K respectively for 10 minutes under vacuum. Subsequently, A was placed under a gentle flow of argon and heated to 583 K. Using a syringe and pump system B was added at a rate of 1.5 mL min^{-1} to A. After addition the mixture (A+B) was left stirring for 60 minutes at 583 K and meanwhile solution C was formed by adding 340.0 mg CF_3COONa and 5 ml oleic acid/1-octadecene (1:1) to the shell precursor. Solution C was degassed and heated in the same way as solution B and added to the nanoparticle mixture at a rate of 30 ml/h using a syringe pump. After the addition of C, the mixture was left stirring for another 60 minutes at 583 K and then the solution was cooled down to room temperature and the nanoparticles were precipitated with ethanol and recovered via centrifugation. The nanoparticles were dispersed in cyclohexane, precipitated and purified using ethanol. A general production under these conditions delivers 1g nanoparticles and was stored as a wet solid under ethanol at room temperature.

FT-IR (ṽ, cm^{-1}):

NP1: 1461 ($\nu_{s\ C=O}$), 1550 ($\nu_{as\ C=O}$), 2976 ($\nu_{s\ CH}$), 2926 ($\nu_{as\ CH2}$), 2854 ($\nu_{s\ CH2}$), 3003 ($\nu_{s\ CH}$)

NP2: 1461 ($\nu_{s\ C=O}$), 1551 ($\nu_{as\ C=O}$), 2976 ($\nu_{s\ CH}$), 2927 ($\nu_{as\ CH2}$), 2854 ($\nu_{s\ CH2}$), 3004 ($\nu_{s\ CH}$)

NP20: 1461 ($\nu_{s\ C=O}$), 1550 ($\nu_{as\ C=O}$), 2977 ($\nu_{s\ CH}$), 2927 ($\nu_{as\ CH2}$), 2853 ($\nu_{s\ CH2}$), 3004 ($\nu_{s\ CH}$)

NP4: 1460 ($\nu_{s\ C=O}$), 1550 ($\nu_{as\ C=O}$), 2976 ($\nu_{s\ CH}$), 2927 ($\nu_{as\ CH2}$), 2854 ($\nu_{s\ CH2}$), 3004 ($\nu_{s\ CH}$)

Citrate-capped Nanoparticles

200 mg of oleate-capped nanoparticles were dispersed in 20 mL of a 0.2 M citric acid buffer (pH=3) and subsequently shaken for 3h at 800 rpm. The solution was extracted with cyclohexane (3×) and diethylether (3×). The particles were then precipitated with acetone and recovered via centrifugation. After recovery the particles were dispersed in 20 mL of a 0.2M citric acid buffer (pH=6) and subsequently shaken for 12h at 800 rpm. The solution was again extracted with cyclohexane (3×) and diethylether (3×) and 180 mg citrate-capped nanoparticles were obtained via precipitation with acetone and centrifugation and stored at room temperature under ethanol.

FT-IR (ṽ, cm^{-1}):

NP1: 1290 ($\nu_{s\ C=O}$), 1402 ($\nu_{as\ C=O}$), 1571($\nu_{s\ C=O}$), 3550-3000 ($\nu_{s\ O—H}$), 1263 ($\delta_{O—H}$)

NP2: 1289 ($\nu_{s\ C=O}$), 1402 ($\nu_{as\ C=O}$), 1570 ($\nu_{s\ C=O}$), 3550-3000 ($\nu_{s\ O—H}$), 1263 ($\delta_{O—H}$)

NP20: 1290 ($\nu_{s\ C=O}$), 1402 ($\nu_{as\ C=O}$), 1571 ($\nu_{s\ C=O}$), 3550-3000 ($\nu_{s\ O—H}$), 1264 ($\delta_{O—H}$)

NP4: 1290 ($\nu_{s\ C=O}$), 1402 ($\nu_{as\ C=O}$), 1571 ($\nu_{s\ C=O}$), 3550-3000 ($\nu_{s\ O—H}$), 1263 ($\delta_{O—H}$)

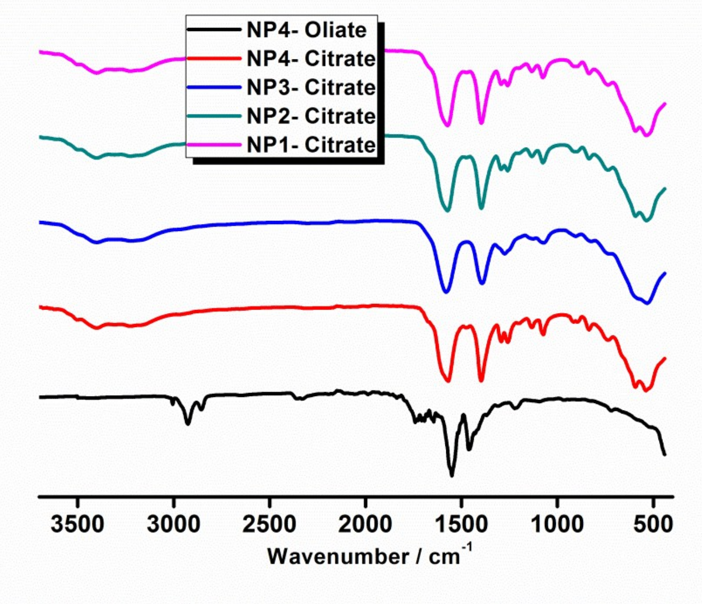

Fig. S1 FT-IR spectra of citrate capped **NP1-NP4** and oleate capped **NP4**.

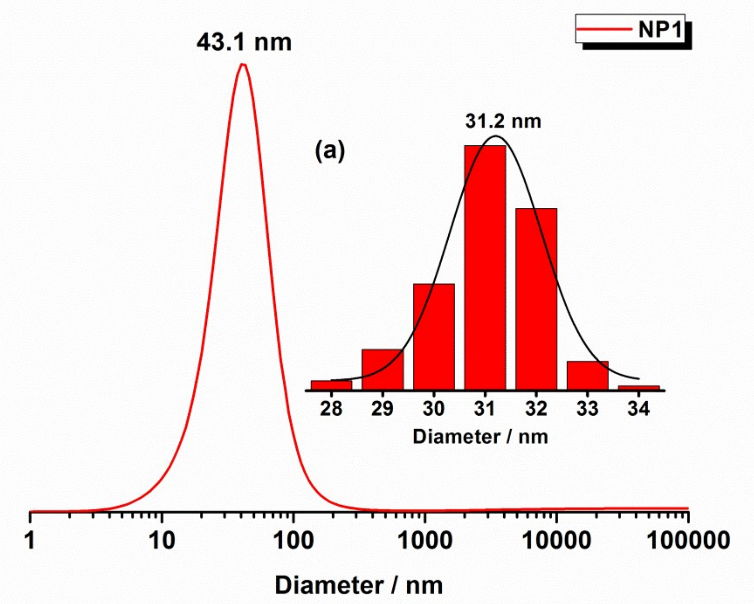

Fig. S2 DLS measurement of the nanoparticles **NP1** and (a) its size distribution obtained from TEM analysis, considering 150 particles.

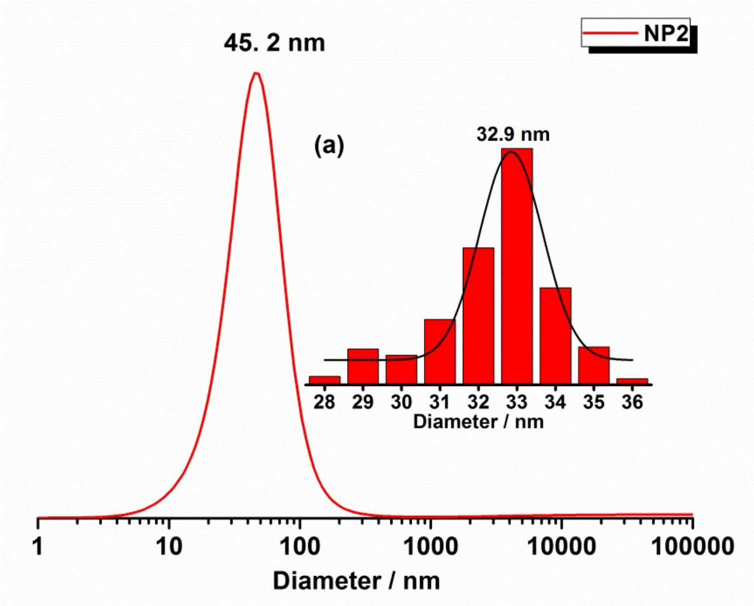

Fig. S3 DLS measurement of the citrate capped **NP2** and (a) its size distribution obtained from TEM analysis, considering 150 particles.

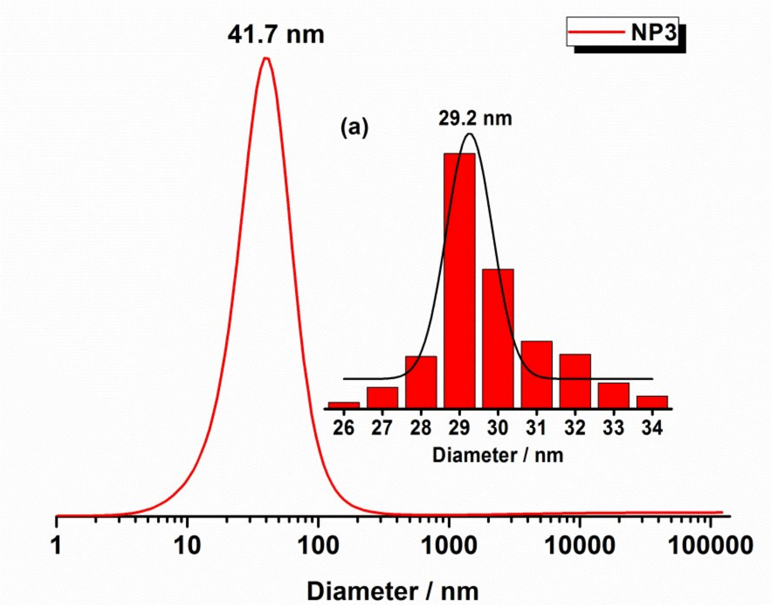

Fig. S4 DLS measurement of the citrate capped **NP20** and (a) its size distribution obtained from TEM analysis, considering 150 particles.

Table S1 Particle size, hydrodynamic diameter and molar composition of **NP1-NP4**

AC/AS-UCNP	**Size (nm)**		**mol%**	**Core**			**Shell**			**Total**			
				Gd^{3+}	Yb^{3+}	Er^{3+}	Gd^{3+}	Yb^{3+}	Dy^{3+}	Gd^{3+}	Yb^{3+}	Er^{3+}	Dy^{3+}
NP1	TEM	31.2	Calcd.	78	20	2	80	20	0	79	20	1	0
	DLS	43.1	TXRF	—	—	—	—	—	—	79.2668	19.8095	0.9237	—
NP2	TEM	32.9	Calcd.	78	20	2	79	20	1	78.5	20	1	0.5
	DLS	45.2	TXRF	—	—	—	—	—	—	78.0460	20.3110	1.0587	0.5843
NP3	TEM	29.2	Calcd.	78	20	2	70	20	10	74	20	1	5
	DLS	41.7	TXRF	—	—	—	—	—	—	74.4590	19.4568	1.0264	5.0578
NP4	TEM	30.9	Calcd.	78	20	2	0	20	80	39	20	1	40
	DLS	43.3	TXRF	—	—	—	—	—	—	40.9138	20.0460	0.9832	38.0570

References

1. A.C. Larson and R.B. Von Dreele, "General Structure Analysis System (GSAS)", Los Alamos National Laboratory Report LAUR 2000, 86-748.
2. B. Toby, *J. Appl. Cryst.* , 2001, **34**, 210-213.