Electronic Supplementary Material (ESI) for Nanoscale.

Electronic Supplementary Information

Europium-engineered iron oxide nanocubes with high T_1 and T_2 contrast abilities for MRI in living subjects

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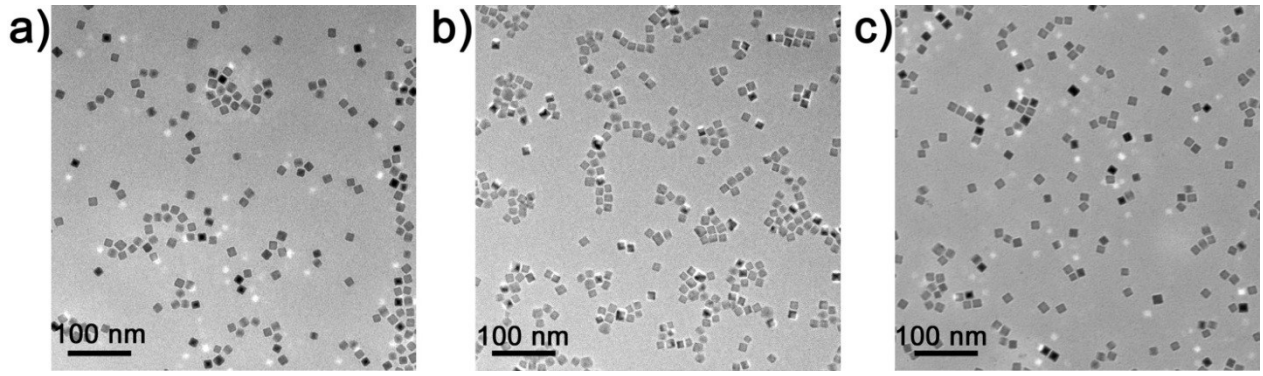

Figure S1. Representative TEM images of monodisperse EuIO nanocubes with different Eu molar ratios. (a) 6.4%, (b) 10.3% and (c) 15.1%, respectively. The metal concentrations were measured by ICP-AES.

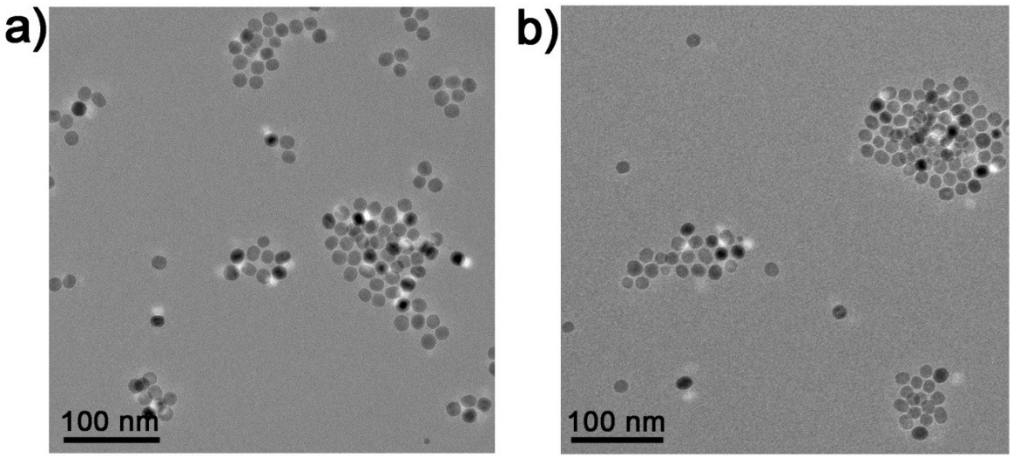

Figure S2. TEM images of (a) Fe_3O_4 and (b) Eu_2O_3 nanoparticles with similar diameter of about 14 nm.

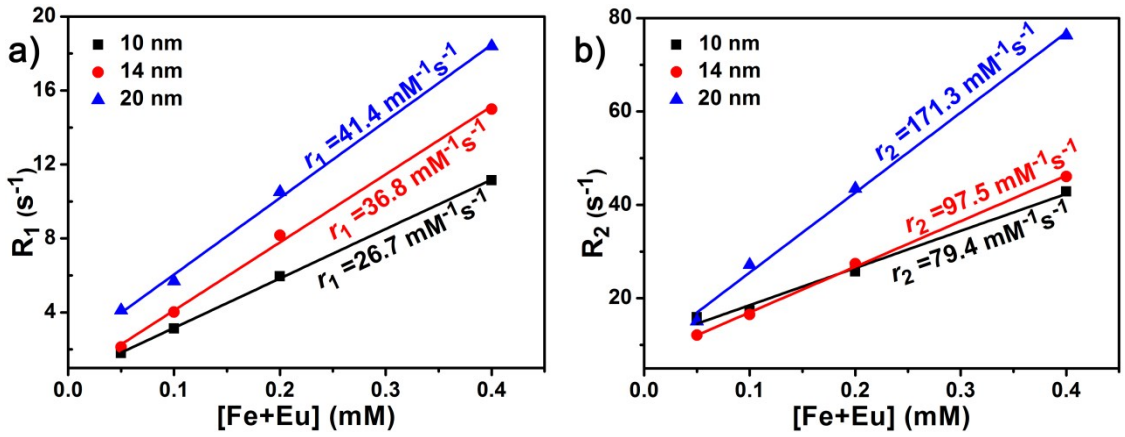

Figure S3. Relaxivitity measurements of EuIO nanocubes with different sizes. (a) R_1 and (b) R_2 of 10, 14 and 20 nm EuIO nanocubes on a 0.5 T scanner. The relaxivity values r_1 and r_2 were obtained from the slopes of linear fits of experimental data.

Table S1. Comparisons of the r_1 and r_2 values of EuIO nanocubes with different sizes at 0.5 T.

Sizes (nm)	r_1 (mM^{-1}s^{-1})	r_2 (mM^{-1}s^{-1})	r_2/r_1
EuIO-10	26.74±0.33	79.44±2.29	2.97
EuIO-14	36.79±1.16	97.52±2.16	2.65
EuIO-20	41.43±1.34	171.32±4.12	4.14

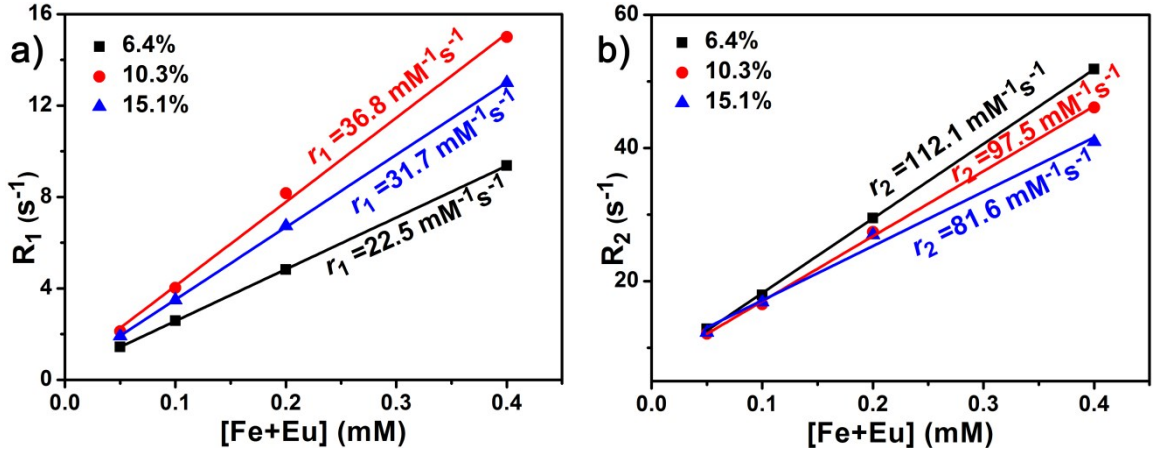

Figure S4. Relaxivitity measurements of EuIO nanocubes with different Eu molar ratios. (a) R_1 and (b) R_2 of EuIO nanocubes with Eu molar ratios of 6.4%, 10.3% and 15.1% on a 0.5 T scanner.

Table S2. Summary of the r_1 and r_2 relaxivity of 14 nm sized EuIO nanocubes with different Eu molar ratios on a 0.5 T MR scanner.

Eu molar ratios (%)	r_1 (mM^{-1}s^{-1})	r_2 (mM^{-1}s^{-1})	r_2/r_1
EuIO-6.4	22.51±0.46	112.07±0.97	4.98
EuIO-10.3	36.79±1.16	97.52±2.16	2.65
EuIO-15.1	31.68±0.25	81.63±3.15	2.57

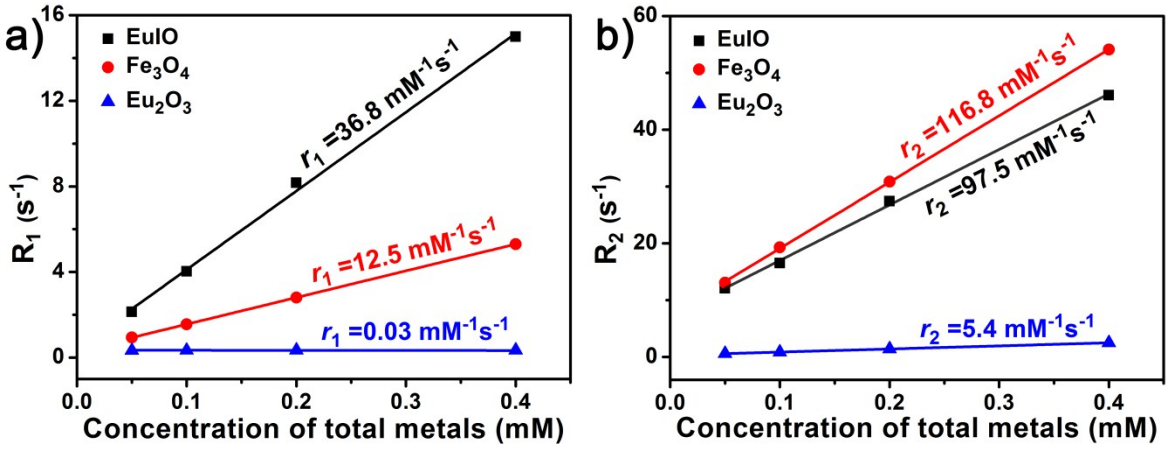

Figure S5. Relaxivity (a) r_1 and (b) r_2 values of EuIO nanocubes, Fe_3O_4 nanoparticles and Eu_2O_3 nanoparticles with similar size at 0.5 T.

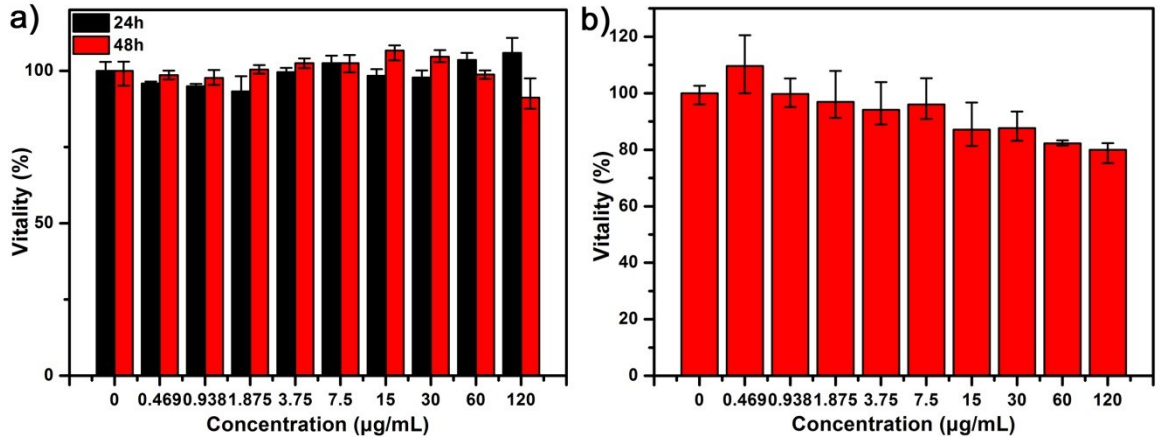

Figure S6. Biocompatibility of EuIO nanocubes. (a) MTT assay of SMMC-7721 cells incubated with EuIO nanocubes for 24 h and 48 h (n = 5/group), (b) MTT assay of MRC-5 normal cells incubated with EuIO nanocubes for 24 h (n = 5/group). Concentration correspond to total metal ions [Fe+Eu] measured by ICP-AES.

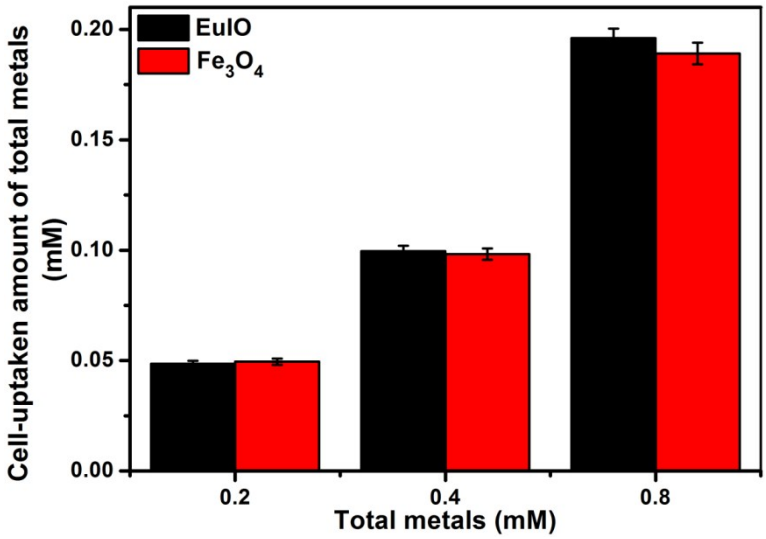

Figure S7. Quantitative analysis of cell uptake by ICP-MS (after subtraction of the inherent Fe inside cells) incubated with EuIO nanocubes (black) and Fe_3O_4 (red) nanoparticles with respect to total metals.

Table S3. MR signal-to-noise ratio (SNR) changes of cells incubated with EuIO nanocubes and Fe_3O_4 nanoparticles with different concentrations in T_1 images (n = 3/group). We calculated the SNR by the equation: $SNR_{cell} = SI_{cell}/SD_{noise}$, where SI represents signal intensity and SD represents standard deviation. The SNR changes were calculated by the equation: $SNR = |SNR_{post} - SNR_{pre}|/SNR_{pre}$.

Total metals (mM)	SNR_{pre} (0 mM) (%)	SNR_{post} (%)	ΔSNR_{post} (%)
EuIO-0.2	100	110.4±5.4	10.4±5.4
Fe_3O_4-0.2	100	103.6±4.3	3.6±4.3
EuIO-0.4	100	127.0±2.3	27.0±2.3
Fe_3O_4-0.4	100	105.9±3.5	5.9±3.5
EuIO-0.8	100	161.4±5.3	61.4±5.3
Fe_3O_4-0.8	100	113.5±4.5	13.5±4.5

Table S4. SNR changes of cells incubated with EuIO nanocubes and Fe_3O_4 nanoparticles with different concentrations of T_2 images (n = 3/group).

Total metals (mM)	SNR_{pre} (0 mM) (%)	SNR_{post} (%)	ΔSNR_{post} (%)
EuIO-0.2	100	84.6±5.3	15.4±5.3
Fe_3O_4-0.2	100	82.5±2.6	17.5±2.6
EuIO-0.4	100	68.4±3.6	31.6±3.6
Fe_3O_4-0.4	100	64.4±2.4	35.6±2.4
EuIO-0.8	100	38.0±1.4	62.0±1.4
Fe_3O_4-0.8	100	31.9±2.8	68.1±2.8

Table S5. SNR changes of region of interests (ROIs) in T_1 imaging before and after intravenous injection of EuIO nanocubes at 3 T (n = 3/group). We calculated the SNR by the equation: $SNR_{heart} = SI_{heart}/SD_{noise}$.

Time (min)	SNR_{pre} (%)	SNR_{post} (%)	ΔSNR_{post} (%)
0	100	100	0
1	100	162.2±2.9	62.2±2.9
3	100	127.1±2.2	27.1±2.2
5	100	119.5±1.9	19.5±1.9

Table S6. SNR changes of ROIs in T_2 imaging before and after intravenous injection of EuIO nanocubes at 3 T (n = 3/group). We calculated the SNR by the equation: $SNR_{liver} = SI_{liver}/SD_{noise}$.

Time (min)	SNR_{pre} (%)	SNR_{post} (%)	ΔSNR_{post} (%)
0	100	100	0
30	100	45.2±2.6	54.8±2.6
90	100	22.7±1.6	77.3±1.6
150	100	31.1±1.3	68.9±1.3