Supporting Information

Manuscript title: A $T_1$, $T_2$ magnetic resonance imaging (MRI)-fluorescent imaging (FI) by using ultrasmall mixed gadolinium-europium oxide nanoparticles

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(1) XRD pattern

An XRD pattern of the as-prepared powder sample is shown in Fig. S1. Among the known three phases (i.e., Ln(OH)$_3$, LnOOH, and Ln$_2$O$_3$, Ln = Gd and Eu),$^1$ the obtained XRD pattern is close to that of Ln$_2$O$_3$. The broad XRD pattern is due to ultrasmall particle diameters of nanoparticles, similarly to that observed in ultrasmall Gd$_2$O$_3$ nanoparticles.$^2$ After TGA analysis up to 900 °C, however, sharp peaks (222), (400), (440), and (622) corresponding to a highly crystallized form of Ln$_2$O$_3$ with a cubic structure were observed (Fig. S1). Note that the peaks from both Gd$_2$O$_3$ and Eu$_2$O$_3$ occur at very similar positions and thus, can not be distinguished from each other in the XRD pattern. The estimated cell constant ($a = 10.84$ Å) is consistent with the weighted average of those of Gd$_2$O$_3$ ($a = 10.81$ Å) and Eu$_2$O$_3$ ($a = 10.86$ Å) given by JCPDS-International Center for Diffraction Data, PCPDFWIN, Version 1.30.$^3$
**Fig. S1** XRD patterns of powder samples of lactobionic acid coated ultrasmall mixed gadolinium-europium oxide nanoparticles: (bottom) as-prepared and (top) after TGA analysis up to 900 °C. The assignments are the Miller indices (hkl).

**(2) 3 tesla \( T_1 \) and \( T_2 \) MR images**

A series of 3 tesla coronal \( T_1 \) MR images of a mouse kidney and artery are shown in Fig. S2. Positive contrast enhancements can be clearly seen after injection of an aqueous sample solution into a mouse tail vein. After 30 minutes, however, signal decayed away due to excretion of nanoparticles through kidneys. A series of 3 tesla axial \( T_2 \) MR images of a mouse liver are also shown in Fig. S3. Negative contrast enhancements can be clearly seen after injection. The negative contrast enhancement in liver was kept longer than the positive contrast enhancement in kidney because clearance of nanoparticles through liver takes a longer time than through kidneys.
Fig. S2 A series of 3 tesla coronal $T_1$ MR images of kidney (indicated as K) and artery (indicated as A) before and after injection of a sample solution into a mouse tail vein.

Fig. S3 A series of 3 tesla axial $T_2$ MR images of liver (indicated as L) before and after injection of a sample solution into a mouse tail vein.

(3) Solubility and stability of nanoparticles in sample solutions

Sample solutions of lactobionic acid coated nanoparticles dispersed in PBS solution, DMEM solution used for incubation of NCTC1469 cell, and RPMI1640 solution used for incubation of DU145 cell were tested for solubility and stability of lactobionic acid coated nanoparticles in them. The lactobionic acid coated nanoparticles were completely dispersed in all solutions, implying that they are soluble in all solutions. In case of stability, we measured the precipitation times of lactobionic acid coated nanoparticles at various Gd&Eu concentrations after they were dispersed in
solutions (Fig. S4). The stability of lactobionic acid coated nanoparticles, depending on the solution type, was decent. Pictures of sample solutions (Gd&Eu concentration = 11 mM) after dispersion and after precipitation of lactobionic acid coated nanoparticles in solutions are provided in Fig. S5. The less stability in PBS solution than those in both DMEM and RPMI1640 solutions is likely related to the salt effect of PBS solution.

![Graph showing precipitation time vs Gd&Eu concentration](image)

**Fig. S4** Stability tests of sample solutions of lactobionic acid coated nanoparticles dispersed in three solutions (PBS, DMEM, and RPMI1640).

![Images of sample solutions](image)

**Fig. S5** Pictures of sample solutions (a) after dispersion and (b) after precipitation of lactobionic acid coated nanoparticles in solutions. Square and arrow indicate the area of precipitation.
References


3 JCPDS - International Centre for Diffraction Data, card no. 43-1008 ($a = 10.86$ Å) and 43-1014 ($a = 10.81$ Å) for Eu$_2$O$_3$ and Gd$_2$O$_3$, respectively.