Supporting Information

Synthesis of Au-Fe_3O_4 heterostructured nanoparticles for in vivo computed tomography and magnetic resonance dual model imaging

Jing Zhu, Yinjie Lu, Yonggang Li, Jiang Jiang, Liang Chen, Zhuang Liu, Liang Guo, Yue Pan,* Hongwei Gu*

Experimental Section

Materials

Oleylamine (99%), oleic acid (99%), 1-octadecene (99%) and $Fe(CO)_5$ were purchased from Sigma-Aldrich. $HAuCl_4 \cdot 4H_2O$ was purchased from Sinopharm group CO. Ltd.

Synthesis of 11-nm Au nanoparticles

20ml of oleylamine (OAm) was stirred under a gentle flow of argon at 80 ^oC for 20 min. Then a solution (1ml hexane and 1ml OAm) of 96mg $HAuCl_4 \cdot 4H_2O$ was added to the reaction at 80 ^oC under vigorous magnetic stirring. The solution was then heated at 80 ^oC for 5 hours and then cooled down to room temperature. Ethanol was added to the solution, and gold nanoparticles were separated by centrifugation. Then the nanoparticles were washed by ethanol several times, and redispersed in hexane.

Synthesis of heterostructured Au-Fe_3O_4 nanoparticles

1ml oleic acid(OA) and 1ml OAm were added to Au nanoparticles (1-octadecene as solvent), then heated to 120^oC by bubbling argon through the solution for 20 min. 0.30 ml $Fe(CO)_5$ (2mmol) was then injected into the hot solution. The mixture was heated to reflux (~320 °C) for 1 hour, and then cooled to room temperature and exposed to air for extra several hours to form a heterostructured Au-Fe_3O_4 nanoparticles. After purification with ethanol, the nanoparticles were redispersed in hexane.

Modification of Au-Fe_3O_4 nanoparticles

Au-Fe_3O_4 nanoparticles, 300mg tetramethylammonium hydroxide (TMAOH), 15ml acetic acid were added to 25ml water, then the solution was ultrasounded for a while. The extra surfactants were removed by dialysis using a dialysis bag (MWCO 10000) for 24 hours in water.

In vitro cytotoxicity assay by methylthiazoletetrazolium(MTT)

The effect of Au-Fe_3O_4 nanoparticles on the cell viability was carried out by the MTT assay. The Hela cells seeded in 96-well plates (1×10^4 cells per well) for 24 h. Afterwards a series of concentrations of Au-Fe_3O_4 nanoparticles were added into the cell culture. After 24h incubation, 20 ml of MTT solution was mixed in each well for another 4 h. After that, dimethyl sulfoxide (DMSO) was added into the well. Finally, the cell viability was measured by a microplate reader (Model 680 Bio-RAD).

In vitro CT and MR imaging

The CT imaging was obtained using a GE LightSpeed VCT clinical imaging system (GE Medical Systems) with a tube voltage of 120 kV, an electrical current of 333 mA, a slice thickness of 238 mm.

The MR imaging of Au-Fe_3O_4 nanoparticles in all samples were scanned using a 1.5 T clinical MRI scanner (GE Medical systems, Signa HDX) at room temperature. The T_2 values at different iron concentrations were measured by a manually drawn region-of-interest (ROI) after obtaining the T_2-weighted MR imaging.

In vivo CT and MR imaging

CT and MR images in New Zealand rabbits were obtained on GE LightSpeed VCT clinical imaging system (GE Medical Systems) and 1.5 T system (Philips medical system, Eclipse) respectively. After the rabbits were anesthetized, imaging of the heart was acquired before and 5 s, 25 s, 45 s after injection with Au-Fe_3O_4 nanoparticles and commercial iodine agent (Iohexol) respectively.

Ex vivo study of Au element in the liver

The livers of the New Zealand rabbits were collected and weighed after injection the nanoparticles at 10min. The livers were then completely dissolved in a digestion solution (aqua regia: perchloric acid= 3:1) by heating at 300°C for 4 h until clear liquid was obtained. Au^{3+} contents were then determined using ICP-AES. The Au level in liver were about 38 ±8 μg/ g (liver).

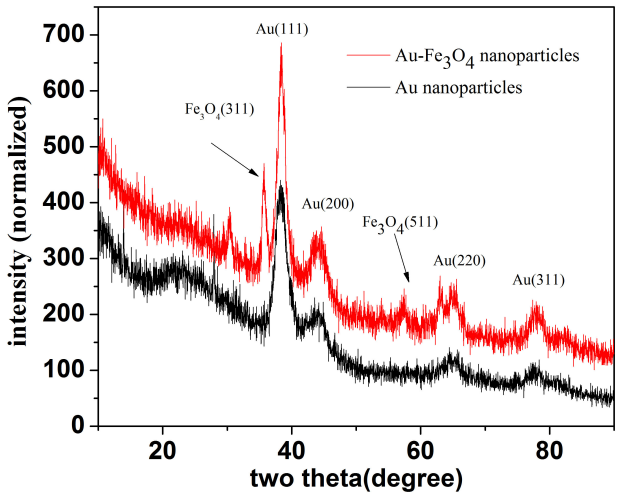

Figure S1. X-ray diffraction (XRD) patterns of Au nanoparticles (black) and Au-Fe_3O_4 heterostructured nanoparticles (red). The samples were deposited from their hexane dispersion on Si (100) substrates and dried under ambient conditions.

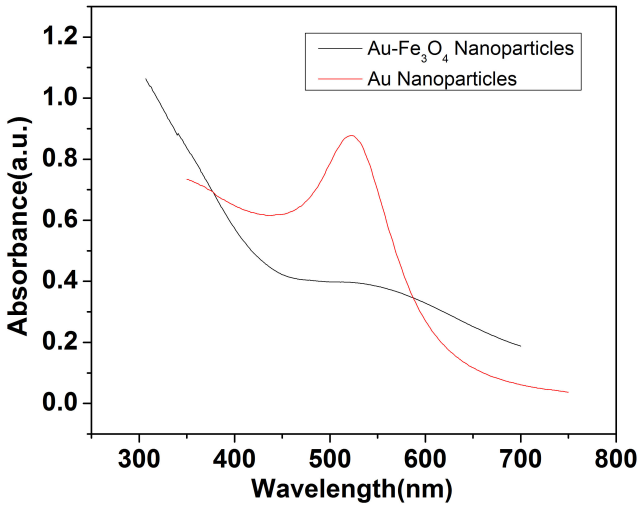

Figure S2. UV-Vis absorption spectra of Au and Au-Fe_3O_4 heterostructured nanoparticles in water.

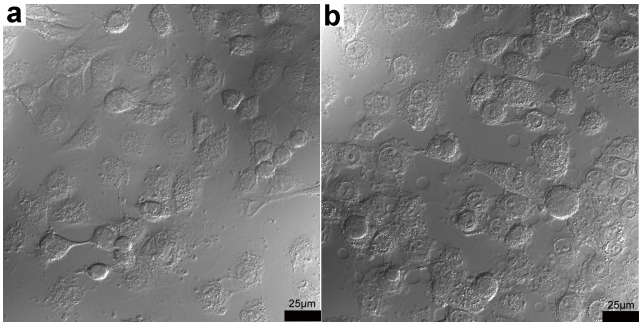

Figure S3. The cell morphology before (a) and after (b) treated with Au-Fe_3O_4 heterostructured nanoparticles imaged with phase contrast microscopy.

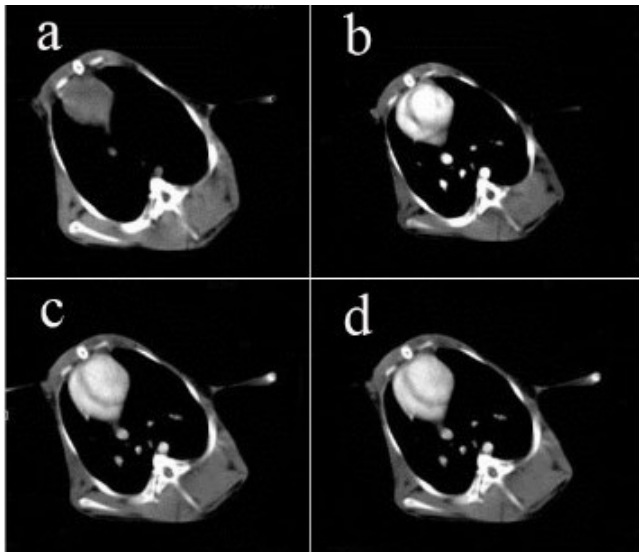

Figure S4. CT images of a rabbit heart. (A) Before injection (B) 5 s (C) 25 s (D) 45 s after intravenous injection of 4ml (300mg/ml) commercial iodine agent (Iohexol).

Time	before	5 s	25 s	45 s
Au- Fe_3O_4	50	56	239	80
Iodine agent	50	298	262	181

Table S1. HU values of rabbit heart before and after the injection of Au-Fe_3O_4 heterostructured nanoparticles and iodine agent respectively.