Ultrasmall catechol-PEG-anchored ferrite nanoparticles for high sensitive magnetic resonance angiography

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Experimental procedures

Reagents and Materials

Erucic acid, sodium hydroxide, sodium carbonate anhydrous, oleyl alcohol, N'N-dicyclohexylcarbodiimide, N-hydroxysuccinimide, dopamine hydrochloride and methyl thiazolyl tetrazolium (MTT) were brought from Shanghai Aladdin Biochemical Technology Co., Ltd (Shanghai, China). Iron (III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$), Mn (II) chloride tetrahydrate ($MnCl_2 \cdot 4H_2O$), oleic acid, dibenzyl ether and bis-carboxymethyl acid polyethylene glycol (HOOC-PEG-COOH, molecular weight (MW)= 600) were obtained from Sigma-Aldrich CO., Ltd (Shanghai, China). Methyl alcohol, n-hexane, cyclohexane, chloroform, N,N-dimethylformamide were provided by Concord Technology Co., Ltd (Tianjin, China). All of reagents and materials were used as received without further purification.

Synthesis of Iron erucic acid and Manganese-Oleate complexes

For the synthesis of iron erucic acid complex, $FeCl_3 \cdot 6H_2O$ (2.7 g, 10 mmol) and (10.2 g, 30 mmol) of erucic acid were dissolved in 50 mL of methanol under magnetic stirring at 40 °C. Subsequently, sodium hydroxide (1.2 g, 30 mmol) dispersed in 100 mL of methanol was dropped into the above solution at a rate of 2 mL min^{-1} and stirred another 1.5 h. After the completion of the reaction, the precipitate comprising the iron erucic acid complex was subjected to three rounds of washing using deionized water and methanol. The as-obtained iron erucic acid complex was dried under vacuum conditions for a duration of three days.

For the synthesis of manganese oleate complex, $MnCl_2 \cdot 4H_2O$ (1.979 g, 10 mmol) and oleic acid (5.65 g, 20 mmol) were dissolved in 50 mL of methanol under magnetic stirring at 40 °C. Subsequently, sodium hydroxide (0.8 g, 20 mmol) dispersed in 100 mL of methanol was dropped into the above solution at a rate of 2 mL min^{-1} and stirred

another 1.5 h. After the completion of the reaction, the precipitate comprising the manganese-oleate complex was subjected to three rounds of washing using deionized water and methanol. The as-obtained manganese-oleate complex was dried under vacuum conditions for a duration of three days.

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Supplementary Figures (Fig. S1-S7)

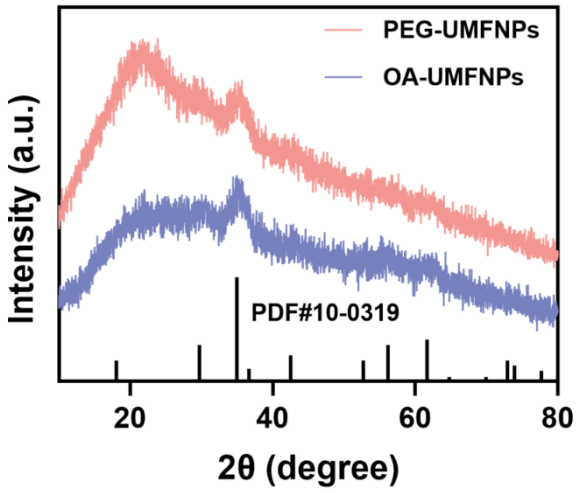

Figure. S1 The XRD spectrum of OA-UMFNPs and PEG-UMFNPs.

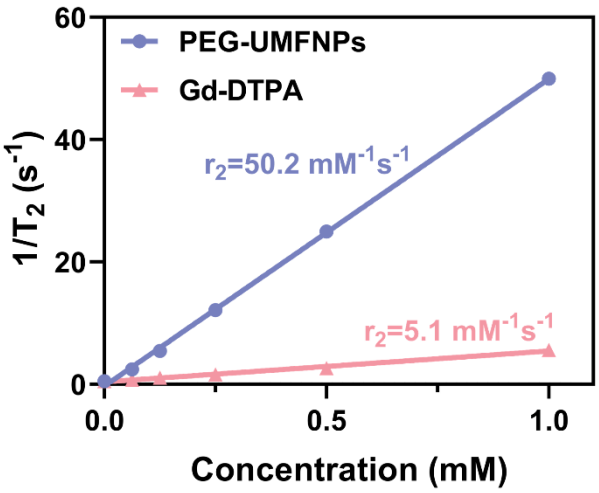

Figure. S2 T_2 relaxivitives of PEG-UMFNPs and Gd-DTPA.

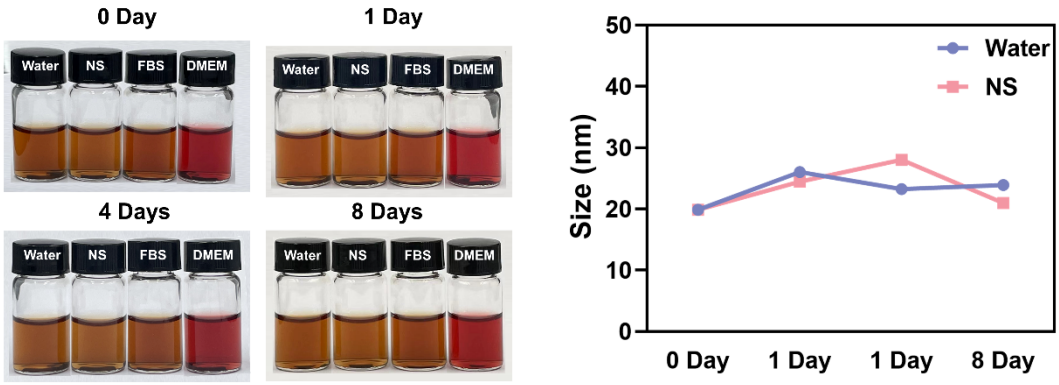

Figure. S3 The photos of PEG-UMFNPs dissolved in various solution including water, normal saline (NS), FBS, DMEM and the hydrodynamic size of PEG-UMFNPs dissolved in water and NS at different time points.

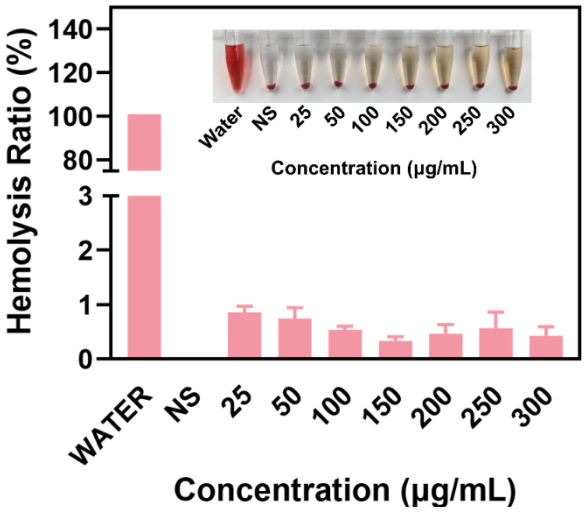

Figure. S4 Blood compatibility evaluation of PEG-UMFNPs at various concentration (n = 3). The data show means ± SD.

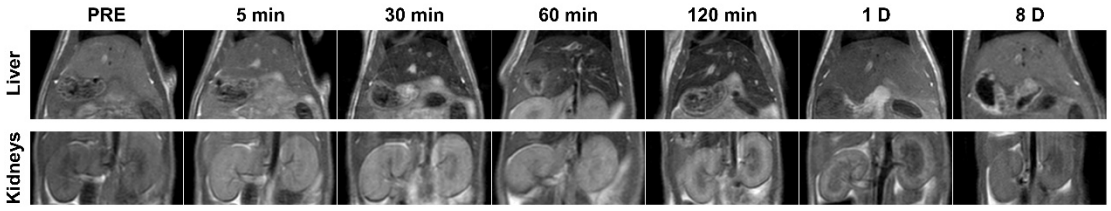

Figure. S5 T_1-weighted MR imaging of the liver and kidneys at various time points after intravenous injection of 0.1 mmol [Fe + Mn] kg^{-1} dose of PEG-UMFNPs in normal rats.

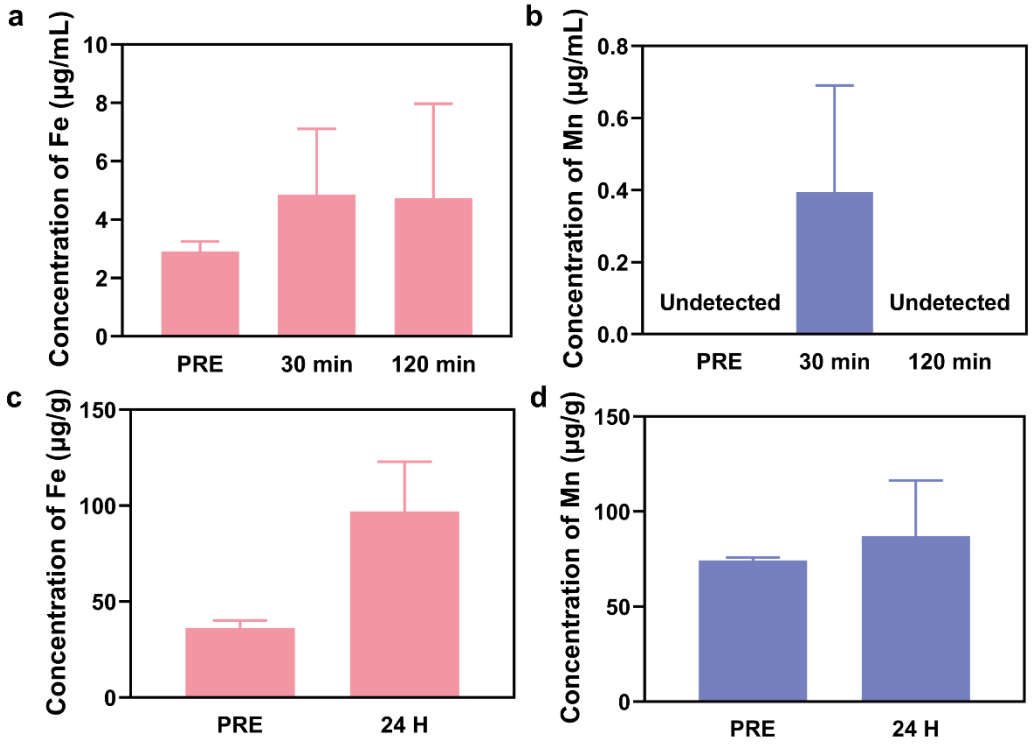

Figure. S6 The concentrations of the Fe and Mn elements in urine (a and b) and feces (c and d) collected from normal rats administrated with 0.1 mmol [Fe + Mn] kg^{-1} dose of PEG-UMFNPs.

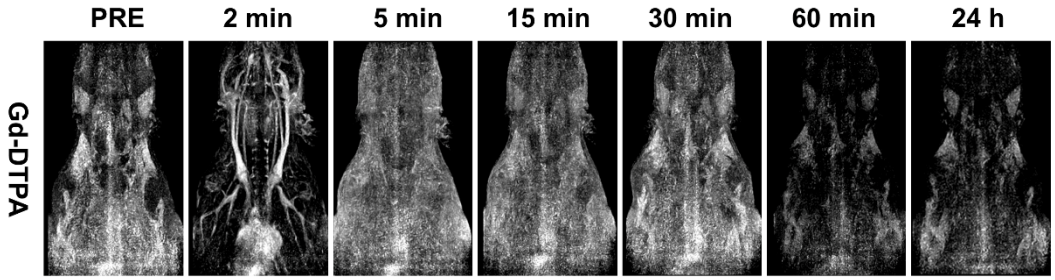

Figure. S7 Contrast enhanced MRA (CE-MRA) images of head and neck vessels in SD rats treated with at a dosage of 0.1 mmol Gd kg-1 on a clinical 3.0 T scanner.

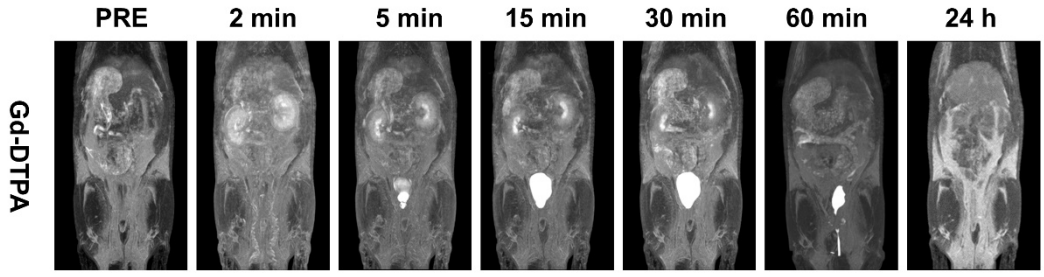

Figure. S8 CE-MRA images of abdominal vessels in SD rats treated with at a dosage of 0.1 mmol Gd kg-1 on a clinical 3.0 T scanner.

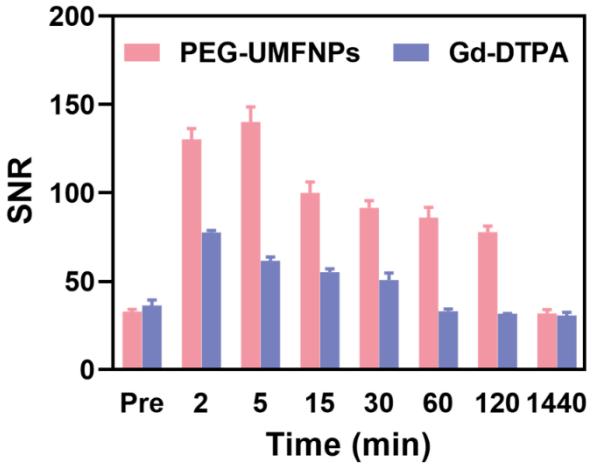

Figure. S9 The changes of the SNR of inferior vena cava (IVC) with time. Error bars represent the standard deviation (n = 3). The data show means ± SD.

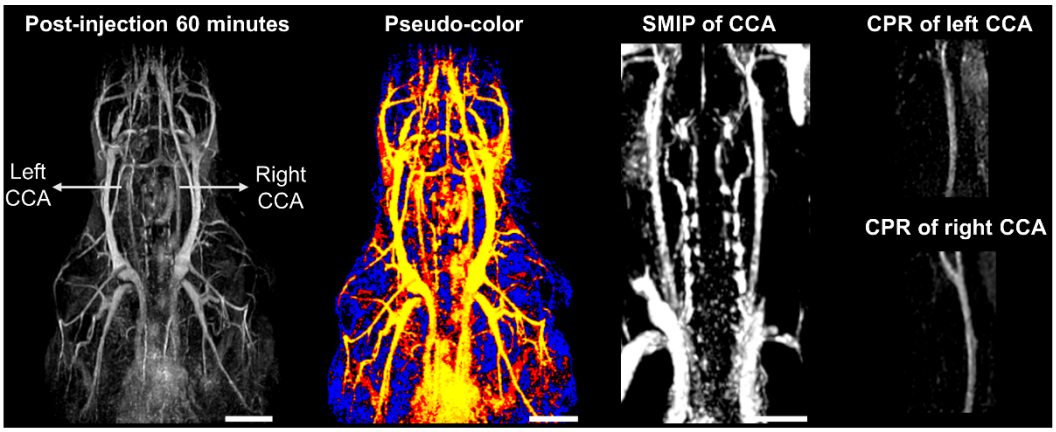

Figure. S10 Maximum Intensity Projection (MIP) images and post-processing images of the common carotid artery (CCA) at 60 min after injection of PEG-UMFNPs. Scale bar = 10 mm.