Supporting Information

Zinc Ferrite Nanoparticles as MRI Contrast Agents

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Syntheses of superparamagnetic Zn-SPIO nanoparticles. Monodispersed Zn_xFe_{1-x}O·Fe_2O_3 nanoparticles were prepared from iron acetylacetonate (Fe(acac)_3), zerovalent diethyl zinc (Et_2Zn), 1,2-hexadecanediol (5 mmol), oleic acid (3mmol), and hexadecylamine (3mmol). The value of x was calculated based on the molar ratio of Zn and Fe, keeping the total sum of (Zn + Fe) molar fractions equal to 3. The actual reaction batch was carried out on a 1 mmol total metal scale. As an example for x = 0.34: first, a mixture of Fe(acac)_3 (0.83 mmol), along with 1,2-hexadecanediol (5 mmol), oleic acid (3mmol), and hexadecylamine (3mmol) and octyl ether (5mL) was heated at 150 °C for 30 min under argon in a three-neck flask. Et_2Zn (0.17 mmol), was then injected into the reaction and temperature was raised to 275 °C and held at that temperature for additional 30 minutes. Typically, two to three times excess of Et_2Zn was added to the reaction to get the desired stoichiometric amount of Zn incorporation. After the mixture was cooled to room temperature, ethanol (40 mL) was added to the mixture to precipitate the Zn-SPIO.
The Zn-SPIO was isolated by centrifugation (6000 rpm, 10 min) and then redispersed in hexane.

**Characterization of SPIO nanoparticles.** TEM images were obtained using an FEI Tecnai G2 Spirit BioTWIN at 120 kV. All samples were prepared by allowing a small drop of nanoparticle suspension in hexane to dry on carbon-coated copper grids. TEM images of $\text{Zn}_x\text{Fe}_{1-x}\text{O} \cdot \text{Fe}_2\text{O}_3$ ($x = 0, 0.14, 0.26, 0.34, 0.76$) are shown in Figure S1. Size analyses of the nanoparticles were carried out using Image J software (NIH). XRD patterns were collected on a Philips PW 1710 diffractometer with Cu Kα radiation (wavelength $\lambda = 1.54056 \text{ Å}$) (Figure S2). The XRD patterns were assigned to the (220), (311), (400), (422), (333), (440), (620), (533), and (444) reflections for an inverse spinel structure of magnetite ($\text{Fe}_3\text{O}_4$; JCPDS no. 79-0418). All samples were deposited on glass substrates from their hexane dispersions.

**Figure S1.** TEM images of Zn-SPIO, $x = (a) 0$, (b) 0.14, (c) 0.26, (d) 0.34, and (e) 0.76 (scale bar = 100 nm).
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**Figure S2.** XRD patterns of Zn-SPIO, x = (A) 0, (B) 0.14, (C) 0.26, (D) 0.34, and (E) 0.76.

**Encapsulation of SPIO nanoparticles in PEG-DSPE.** A solution mixture of iron oxide nanoparticles and DSPE-5kPEG was prepared by mixing a stock solution of iron oxide nanoparticles in hexane (0.5 mg SPIO) with a stock solution of DSPE-PEG in THF (10 mg DSPE-PEG) in a 15-mL conical flask. The mixture was later dried with a flow of argon, while vortexing, generating a thin blended film of DSPE-PEG and SPIO. The film was rehydrated with pH 7.4 HEPES buffer (5 mL) at 70°C. The mixture was vortexed for 5 min and incubated at 70°C for 3 h with intermittent vortexing. The resulting mixture was then filtered through a nylon filter membrane (size cutoff 0.2 μm).

**Encapsulation of SPIO nanoparticles in PEG-PLA micelles.** A stock solution of PEG5k-PLA5k in THF (0.5 mg polymer) and a stock solution of SPIO in hexane (0.5 mg SPIO) were mixed in a 5-mL vial. The mixture was dried with a gentle flow of argon, and the film was dissolved in THF (1 mL). This solution was added dropwise to DI water (5 mL) while being vigorously sonicated. The organic solvent was allowed to evaporate slowly at ambient conditions overnight. The final volume was adjusted to 5 mL with DI water, and the micelles solution was filtered through a nylon filter membrane (size cutoff 0.2 μm).
TEM analyses of SPIO-encapsulated micelles. TEM images were obtained using the same FEI Tecnai G2 Spirit BioTWIN shown in Figure S3. Formvar coated-copper grids were glow discharged using a Vacuum Coating Unit. For each micelle sample, a glow discharged grid was allowed to float on a small drop of the micelle solution for 2 min, and the excess solution was removed by blotting the grid against a filter paper. For the negative staining (dark field) image, the grid was then treated with 2% phosphotungstic acid (PTA) solution for 30 s and dried in the same manner as described. All TEM images of SPIO-micelles were obtained at an accelerating voltage of 120 kV.

Figure S3. Representative bright-field TEM images of Zn-SPIO (a) single DSPE-PEG and (b) clustered PEG-PLA micelles (insets show the dark-field TEM images as counterstained by 2% PTA solution).

Magnetization measurements. Samples for magnetization measurements were prepared by drying hexane suspensions of SPIO nanoparticles. All measurements were conducted at room temperature using an alternating gradient magnetometer (Princeton Measurements) (Figure S4).
**Figure S4.** Magnetization curves for Zn$_x$Fe$_{1-x}$O·Fe$_2$O$_3$ nanoparticles at room temperature.

**Atomic Absorption Spectrometry.** The metal concentrations in micelles were determined using a Varian SpectrAA 50 spectrometer. All micelle samples were freeze-dried and the solid samples were digested in an aqua regia solution at 80 °C for 3 hours. The samples were diluted to the appropriate concentration and ionized using an air/acetylene flame.

**MRI Measurement.** Samples for T$_2$-weighted imaging were prepared by diluting the stock solution to the appropriate concentrations. Then 100 μL of diluted sample were pipetted into a 4 x 7 wells. MR imaging was performed on a 4.7 T Varian INOVA scanner (spin-echo sequence, TR = 6 s, TR varied from 30 to 90 msec) at room temperature.
**Figure S5.** Sensitivity plot for Feridex® and Zn-SPIO (x = 0.34) (TE = 90 ms).