Controlled Anchoring of SPIO Nanoparticles on Silica Templates as Sensitive MRI Probes

Jing Tian[1], Na Ma[1], Yuchao Guo[1], Zhiyong Wang[1], Chunchao Xia[2], Fabao Gao[2], Qiyong Gong[2], Bin Song[2], Hua Ai[1,2,*]
[1]National Engineering Research Center for Biomaterials, Sichuan University, Chengdu, China
[2]Department of Radiology, West China Hospital, Sichuan University, Chengdu, China

Introduction: Controlled self-assembly of organic/inorganic hybrid materials have important applications in magnetic resonance imaging (MRI). In this study, hydrophobic superparamagnetic iron oxide (SPIO) nanocrystals coated with alkylated PEI are controlled anchored on the silica nanoparticles. The multilayer ball-on-ball structure obtained from LbL technique is particularly attractive as efficient MRI probes, since their special structures can greatly improve their T_2 relaxivity. At the magnetic field of 1.5 T, SiO_2/Alkyl-PEI-SPIO Nanocomposites has relatively higher T_2 relaxivities up to more than 400 Fe $mM^{-1}s^{-1}$ than T_2 relaxivity of 171 Fe $mM^{-1}s^{-1}$ with single Alkyl-PEI-SPIO. Next, we labeled SKOV-3 with single Alkyl-PEI-SPIO and SiO_2/Alkyl-PEI-SPIO Nanocomposites. Composites have shown much better biocompatibility during cell labeling than the single Alkyl-PEI-SPIO, and composite labeled cells displayed higher image contrast.

Materials: Tergitol NP-9,1-hexanol, NH4OH (35%), tetraethyl orthosilicate (TEOS, 99%) and cyclohexane were purchased from Fluka. 1-iodododecane , Branched PEI2K, 1,2-hexadecanediol, oleic acid, oleylamine, Iron(Ⅲ) acetylacetonate, benzyl ether, Poly(allylamine) hydrochloride (PAH, Mw 15kD), Poly(anetholesulfonic acid, sodium salt) (PAS, Mw 10kD) were purchased from Aldrich Chemical Co.. Fetal bovine serum, RPIM 1640 medium, penicillin/streptomycin were purchased from Hyclone.

Methods: 1) Branched PEI2K was obtained from Aldrich and reacted with 1-iodododecane in ethanol following literature procedures[1]. Silica templates[2], SPIO nanocrystals[3] and Alkyl-PEI-SPIO nanocomposites are prepared following previous publication. 2) Self-Assembly of SiO_2/Alkyl-PEI-SPIO nanocomposites: SiO_2 nanotemplates were first coated by two bilayers of PAH/PSS through LbL self-assembly, then positively charged Alkyl-PEI-SPIO were controlled anchored onto $SiO_2/(PAH/PSS)_2$ through adjusting salt concentration and the presence of free Alkyl-PEI2k. The imaging sensitivity of SiO_2/Alkyl-PEI-SPIO system was examined under a clinical MRI scanner (Siemens) at the field of 1.5 Tesla. 3) Cell Viability and Cell Labeling efficiency: SKOV-3 cells were cultured in 10% fetal bovine serum RPIM 1640 medium with 1% penicillin/streptomycin at 37℃ in 5% CO_2. MTT test was performed to quantify the cell viability. MRI study of these cells was performed at 3 Tesla (Siemens) using a clinical knee coil.

Results: The LbL self-assembly process was verified by DLS and zeta-potential (Fig. 1). DLS analysis shows that the peak of nanocomposite diameter shifted from 68 to 106 nm for subsequent coatings respectively, indicating that polyelectrolytes are successfully incorporated on nanoparticle surface during self-assembly (Fig. 1-a). Zeta-potential results also demonstrate the successful assembly of multilayers of PAH/PAS/ Alkyl-PEI-SPIO on silica templates. (Fig. 1-b)

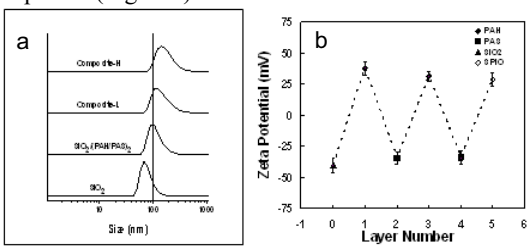

Fig. 1. (a) Number-weighted distributions of hydrodynamic diameters of nanoparticles determined by DLS measurement. (b) Zeta-potential of bare and coated silica nanoparticles versus the number of adsorption steps.

To evaluate the effect of SiO_2/Alkyl-PEI-SPIO in MRI imaging, nanocomposites are tested under a 1.5T MRI scanner. The MRI signal intensity was compared between Alkyl-PEI-SPIO and SiO_2/Alkyl-PEI-SPIO composites. Alkyl-PEI-SPIO has a T_2 relaxivity of 171 Fe $mM^{-1}s^{-1}$. In comparison, our nanocomposites have a relatively higher T_2 relaxivity of 260 Fe $mM^{-1}s^{-1}$ and 412 Fe $mM^{-1}s^{-1}$, showing that higher anchoring density with higher T_2 relaxivity. The MTT results indicate that the SiO_2/Alkyl-PEI-SPIO has the better biocompatibility than Alkyl-PEI-SPIO (Fig. 2).

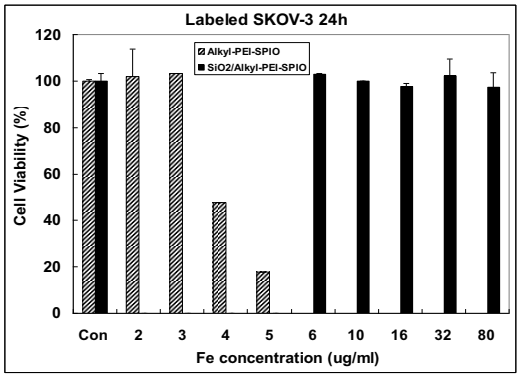

Fig. 2. Cytotoxicity test of the Alkyl-PEI-SPIO and SiO_2/Alkyl-PEI-SPIO formulation with SKOV-3.

Conclusion: Controlled self-assembly of Alkyl-PEI-SPIO on silica templates led to the discovery of MRI probes with high T_2 relaxivity. SiO_2/Alkyl-PEI-SPIO has better biocompatibility comparing to Alkyl-PEI-SPIO nanoparticles. This kind of composites may be used as sensitive MRI probes.

References: 1. Liu G, et al. Biomaterials, in press; 2. Chang, S. et al. J. Am. Chem. Soc.1990; 116, 6739; 3. Sun, S., et al. J. Am. Chem. Soc. 2004, 126, 273.