Study on the magnetic relaxation of superparamagnetic nanotubes as magnetic resonance imaging contrast agent

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ABSTRACT SUMMARY

This work describes the synthesis and characterization of magnetic nanotubes (MNTs) as magnetic resonance imaging (MRI) contrast agent. The synthesis of MNTs with well-controlled dimensions and highly enhanced proton magnetic resonance relaxation rates has been demonstrated, making MNTs an ideal candidate for image-guided drug delivery. Both in vitro and in vivo MRI studies were carried out.

INTRODUCTION

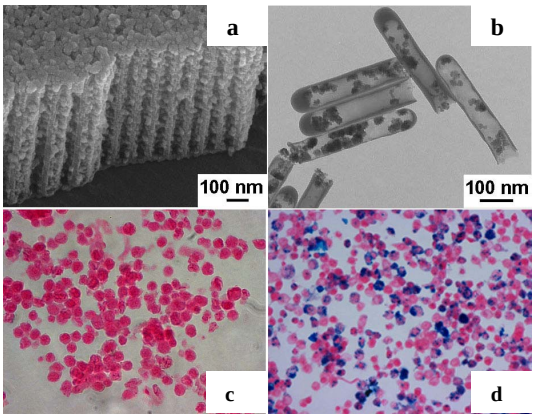
There is an increasing interest in MRI to monitor the temporal and spatial migration *in vivo* behavior of the transplanted cells labeled with superparamagnetic iron oxide nanoparticles[1]. Silica nanotubes, with well-defined, robust, and monodisperse structures, have attracted intensive attention recently as drug delivery vectors[2]. Lee and coworkers[3] have recently demonstrated their potential in applications such as chemical separations, immunobinding, and controlled drug release. In this paper, we describe a method for the synthesis of magnetic nanotubes (MNTs) with highly improved magnetic properties based on a polyol method. The relaxivities of the synthesized MNTs were characterized. Preliminary studies on cell labeling were carried out.

EXPERIMENTAL METHODS

The MNTs were prepared by template synthesis method with aluminum anodic oxide films as templates[4]. The dimensions of the pores in the films can be controlled on nanometer scale. The template was first coated with silica layers via surface sol-gel, and then loaded with superparamagnetic nanocrystalline iron oxide nanoparticles (MIONs) generated by the reflux of iron precursor in propane diol. The inner and outer surfaces of the nanotubes are modified before and after the selective dissolution of the template, respectively. T_1 and T_2 relaxation rates were determined on a clinical 3T MR scanner (Acheiva, Philips Medical System, Best, The Netherlands) using a dedicated 7 cm rat solenoid receive only RF-coil (Philips Research Laboratories, Hamburg, Germany). Rat glioma C-6 cells were used for the *in vitro* studies. MNTs complexed with protamine sulfate (Pro, a transfection agent) were prepared in serum-free media with the concentration of MNTs upto 10 µg/ml. The cells were incubated in the MNT-Pro solution for 2 h before the addition of complete media with a total incubation time of 24 h at 37 °C, 5% CO_2, 95% air. Cytotoxicity of the MNT-Pro complexes was determined with MTS (3-(4,5-dimethylthiazol-2-yl) -5-(3-carboxymethoxyphenyl) -2- (4-sulfophenyl)-2H-tetrazolium) assay. The labeling efficiency was determined with Prussian blue method [5].

RESULTS

The MNTs retained the superparamagnetic characteristics of the MIONs formed in bulk solutions with a saturation magnetization of 95 emu/gFe. The MNTs enhanced water proton relaxivities significantly with r_1 of 1.6 ± 0.3 $mM^{-1}s^{-1}$ and r_2 of 264 ± 56 $mM^{-1}s^{-1}$ with MNT dispersions in phantom. Preliminary studies on *in vitro* cell labeling showed promising results with labeling efficiency about 70%. No significant cellular toxicity was observed *in vitro* and there was no difference in proliferation between labeled and unlabeled cells.



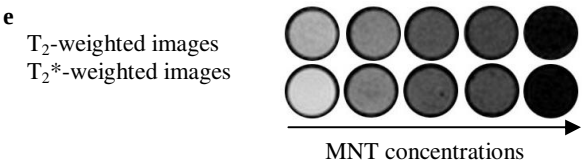


Figure 1. (a) Scanning electron microscopy images of MNTs (len. 2µm, dia. 70 nm) embedded in the pores of alumina template; (b) transmission electron microscopy images of MNTs (len. 500 nm, dia. 60 nm), Prussian blue-stained (c) unlabled cells and (d) MNT-Pro labeled cells, and (e) T_2- and T_2*-weighted images for phantoms dispersed with MNTs (len. 500 nm, dia. 60 nm) with concentration of 0, 3.3, 6.5, 13 and 26 pM, respectively.

CONCLUSIONS

Preliminary *in vitro* cell labeling studies proved that the labeling is effective, and MNTs are not toxic under the labeling condition. We have demonstrated MNTs to be effective T_2 contrast agents and can be used to magnetically label cells.

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