Magnetically Decorated Multi-Walled Carbon Nanotubes as Dual MRI and SPECT Contrast Agents

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ABSTRACT SUMMARY
The present study developed radio-labeled iron oxide decorated multi-walled CNTs (MWNT) as dual magnetic resonance (MR) and single photon emission computed tomography (SPECT) imaging agents. The delicately synthesized hybrid displayed distinct stability and was shown to be capable of dual MR and SPECT imaging in vivo.

INTRODUCTION
MWNTs are cylinder-structured nanomaterials composed of layers of rolled-up graphene sheets. Their impressive inherent electrical/thermal conductivity and mechanical properties have led to tremendous applications in industry since firstly described in the 1990s. Moreover, benefiting from their capability of further chemical modifications, MWNTs have been considered as revolutionary biomaterials, serving as carriers for drug/gene delivery or as probes for biomedical imaging.

MR and nuclear imaging are currently the mainstream clinical diagnostic approaches. The former offers excellent spatial and temporal resolution, and good soft tissue contrast (1) and the latter including SPECT and positron emission tomography (PET) involves the use of radioisotopes and has the advantages over other modalities of high sensitivity and the possibility to perform functional imaging (2). Multimodal imaging is expected to be important in future diagnosis which integrates the advantages of each imaging tool and compensates their limitations.

Studies have been conducted to employ CNTs for MRI by incorporating superparamagnetic iron oxide nanoparticles (SPION) into CNTs. In this work, we further proposed CNTs as dual MRI and SPECT contrast agents by decorating SPION onto MWNTs and using bisphosphonates (BPs) to link SPION with radionuclides due to the strong binding affinity of BPs to the surface of SPION. Physicochemical and magnetic properties of the MWNT-SPION hybrids were characterized. The efficiency of radio-labeling SPION/MWNT hybrids was examined, followed by biodistribution studies and SPECT and MR imaging in vivo.

EXPERIMENTAL METHODS
MWNT-SPION hybrids were synthesized by in situ generation and were extensively characterized by thermogravimetric analysis (TGA), magnetic measurements, high resolution transmission electron microscopy (HRTEM), fast Fourier transform simulations (FFT), X-ray diffraction (XRD) and X-ray photoelectron spectroscopy (XPS). For radio-labeling, MWNT-SPIONs were mixed with technetium-99m bisphosphonate conjugates (99mTc-BP) at 37°C for 30min. Radio-labeling efficiency was determined by measuring the radioactivity in the supernatants and the pellets after centrifugation. For in vivo studies, SPECT/CT imaging was carried out on C57/Bl6 mice i.v. injected with 99mTc-labeled MWNT-SPION immediately after injection and up to 24 h. Detailed organ biodistribution profiles of 99mTc-labeled MWNT-SPION were assessed by gamma counting of major organs sampled at up to 24 h post injection. Post-mortem histological and TEM examinations were also carried out on selected organs. Phantom and in vivo MR imaging were performed at a 7 Tesla MR scanner. T2*-weighted MR images of agar phantom samples with different concentrations and mice injected with different doses of MWNT-SPIONs were acquired. The decay of
the signals was analyzed by Image J and plotted against iron concentrations to obtain the relaxation profiles.

RESULTS AND DISCUSSION

The loading of SPIONs on MWNTs after synthesis was determined by TGA as shown in Fig. 1a. Hybrids containing 11.5-48.0wt% of SPION were obtained. Hysteresis loops depict the saturation magnetization of the hybrids is dependent on the SPION concentration (Fig 1b) and Fig. 1c-d show the TEM images of the hybrids. Designated peaks shown in XRD analysis (Fig. 1f) denote the presence of iron oxide particles which was further confirmed by XPS as γ-Fe₂O₃.

Fig. 1: Characterization of MWNT-SPION hybrids. (a-b) TGA and hysteresis loops of hybrids containing different amounts of SPIONs (S-MWNT 1-4) at 10 K; (c-d) TEM images; (f) XRD pattern of SPIONs decorating MWNTs.

Successful and stable radio-labeling was achieved with around 80% labeling efficiency and more than 90% stability in either 50% PBS or human serum. SPECT/CT imaging of mice injected with ⁹⁹mTc-labeled hybrids displays lung, liver and spleen accumulation after injection (Fig. 2a). In MRI studies, the hybrid show reduction of T₂* signals in both phantom and liver (Fig. 2b) equivalent in efficacy to clinically approved MRI contrast agents. No abnormality was found by histological examination with good in vivo stability confirmed by TEM analysis on liver and spleen samples.

CONCLUSION

This is the first study documenting the use of CNTs/iron oxide hybrids for dual MR and nuclear imaging. SPION-MWNT was radio-labeled with ⁹⁹mTc through a functionalized bisphosphonate, permitting quantitative in vivo biodistribution studies as well as dual SPECT-MR imaging.

REFERENCES

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