Towards Powerful T1 and T2 MRI Contrast Agents: Noncovalent Functionalization of Carbon Nanotubes with Amphiphilic Gd3+ Chelates

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INTRODUCTION

Carbon nanotubes are ultra-small cylinders of few micrometers in length and several nanometers in diameter, exclusively made of carbon atoms. Recently, we have reported the noncovalent functionalization of carbon nanotubes via chemical adsorption of various anionic surfactants [1]. We report herein the first example of noncovalent functionalization of the outer surface of carbon nanotubes by amphiphilic Gd^{3+} chelates and their effect on water proton relaxation *in vitro* and *in vivo* [2].

MATERIAL AND METHODS

Aqueous solutions of the complex at different Gd^{3+} concentrations (from 1 mM to 1 µM) were prepared and adsorbed on multiwalled carbon nanotubes. The resulting suspensions are stable for several days.

Longitudinal r_1 and transversal r_2 water proton relaxivities have been measured at 20, 300 and 500 MHz (20 MHz Bruker relaxometer and 300 and 500MHz Bruker Avance spectrometers).

In vivo images were recorded on anesthetized mice at 300 MHz (Varian NMR spectrometer; Inova, Palo Alto, US, and Bruker Biospec 70/18 spectrometer, Wissembourg, France) using SE and GE sequences.

RESULTS AND DISCUSSION

The r_1 values show a strong dependence on the GdL concentration, particularly at low field. The proton relaxivities are particularly high at 20 MHz with 0.1 and 0.05 mM GdL concentrations: 34.5 and 50.3 $mM^{-1}s^{-1}$ respectively, in comparison to 4.7 $mM^{-1}s^{-1}$ for GdDTPA (Magnevist), under the same conditions.

Transverse relaxation times, T_2, have also been measured on these samples at three different proton Larmor frequencies: 20, 300 and 500 MHz The T_2 values at all frequencies and any GdL concentrations are remarkably lower than that of pure water and they are practically independent of both the frequency and the GdL concentration (8.5-13.8 ms for MWNT/GdL).Consequently, the T_2 effect is exclusively related to the presence of the suspension of carbon nanotubes, and independent of Gd^{3+}. Carbon nanotubes can be viewed as giant conjugated molecular wires with a conjugation length corresponding to the length of the tube which create strong inhomogeneities and potential magnetic susceptibility effects related to the electronic states of the nanotubes [3].

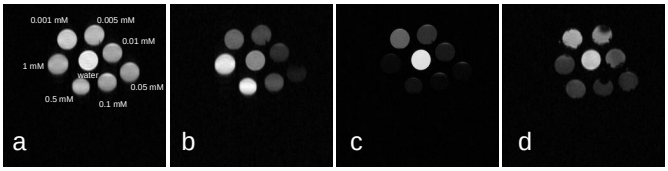

Fig 1 MRI images of the MWNT/GdL complex with different weightings and concentrations measured at 300 MHz. a) rho-weighted SE TR/TE = 15s/10ms, b) T_1-weighted SE TR/IR/TE = 15s/1s/10ms with hyper signal for the Gd concentrated complex, c) T_2-weighted SE TR/TE = 15s/33ms with hyposignal for the concentrated Gd complex, d) T_2*-weighted with relative signal intensity as c) GE TR/TE = 15s/9ms FOV = 5cm, final 256x256 matrix resolution

An i*n vivo* feasibility MRI study has been performed at 300 MHz in mice. A negative contrast could be well observed after injection of a suspension of functionalized nanotubes into the muscle of the leg of the mice (Fig 2)

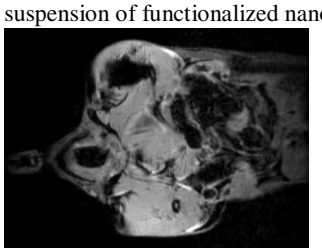

Fig 2 T_2*-weighted GE image of the mouse legs after MWNT/L injection (left leg, white muscle arrow) and reference solution injection (right leg).

CONCLUSION

In summary, we report the first example of carbon nanotubes noncovalently functionalized by amphiphilic GdL chelates as potential MRI contrast agents. The functionalized nanotubes proved to be simultaneously powerful positive and negative CA. Their use as potential contrast agent for *in vivo* applications is under investigations.

REFERENCES

[1] Richard, C. et al. *Science* 2003, *300*, 775-778 [2] Richard et al. *Nano Lett*. 2007 accepted [3] Minot, E, et al. *Nature*, **2004**, *428*, 536-539