Nanotubular Superparamagnetic Probes as Contrast Agents for Diffusion Tensor Magnetic Resonance Imaging

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Introduction

Enhanced MRI contrast has been classically induced by reducing the T_1 or T_2 relaxation rates of tissue water either through the administration of the paramagnetic complexes of DTPA or DOTA derivatives or superparamagnetic particles(1-3). More recently, the non invasive imaging of the Apparent Translational Diffusion Coefficient (ADC) of water molecules and its anisotropic orientation has been shown to provide comprehensive information on tissue microstructure and its pathologiess.[4,5] However, no appropriate exogenous molecules have been designed to improve ADC contrast. An important potential exists, therefore, to increase the information content of ADC weighted Images through the use of contrast agents modifying selectively the ADC properties of tissue water. In this communication, we provide the proof of concept for this novel approach demonstrating that exogenous paramagnetic nanotubular structures induce anisotropic water diffusion detectable by MRI methods.

Materials and Methods

Commercial Single Walled Carbon Nanotubes (SWNTs:2-10 nm diameter, 1-5 □m length) produced by Chemical Vapor Depoasition (CVD) and containing paramagnetic metals (% weight); Ni (17) and Y (4); were oxidized with nitric acid for 48 h and resuspended in an aqueous solution of 2% sodium dodecylbenzene sulphonate (2 mg/mL). Transmission Electron Microscopy (300 kilovols) revealed a average length of 100-200 nm (Figure 2). Axial diffusion weighted images across a 2,5 ml plastic syringe containing the suspension, were acquired with a Bruker Pharmascan spectrometer (horizontal magnet 7.0 Tesla/16 cm diameter) using the diffusion weighted spin- echo imaging sequence (matrix size = 256 x 256, TR = 500 ms, TE = 10,6 ms; section width = 1mm, Number of averages = 3, Field of view = 3,8 x 3,8 cm, Diffusion time D= 20 ms and diffusion gradient duration d=4 ms) equipped with an Echo Planar Imaging (EPI) readout. Ortoghonal ADC maps of three consecutive slices were acquired, with the diffusion encoding gradient oriented in the H-F (B_o), L-R or A-P directions with six b values (100, 200, 300, 500, 800, 1200 mm^{-2}.s), respectively. ADC values were calculated pixel by pixel by fitting the expression $I_g = I_o\, e^{-b.ADC}$ (MATLAB 7.4.0 R2007a). T1 and T2 of the water resonance in the SWNT´s suspensions were determined using inversion-recovery and Carr-Pucell.Meiboom.Gill sequences at 1.5T in a Bruker Minispec platform.

Results

The presence of the embedded paramagnetic metals Ni and Y, enabled the nanotube suspensions with superparamagnetic properties reducing the T_1 and T_2 values of the water resonance to 2s and 0.3s, respectively. Superparamagnetic SWNT,s align with the magnetic field Bo inducing an anisotropic diffusion of the water molecules in the suspension (Figure 1). Under these conditions, the Stokes-Einstein formalism(6) predicts smaller obstructions in the Bo direction than in the perpendicular plane. To investigate this, we obtained maps of the water ADC with the diffusion encoding gradient oriented in the head-feet (H-F), left-right (L-R) or anteroposterior (A-P) directions (Figure 3, left panels). The average ADC values measured in the H-F direction (parallel to B_o) were significantly higher than those determined in the perpendicular plane (L-R and H-F directions).This can be realized by the evident increased abundance of red pixels in the H-F map as compared to the A-P or L-R maps. The bar graphs (Figure 2, right panels) show more quantitatively the statistically significant differences among the three orthogonal directions (H-F; blue bars, L-R; green bars, A-P: red bars) in the three slices. Grey bars on the right illustrate the average ADC values (and SD) in the three directions. The ADC anisotropy observed (ADC_{H-F}>ADC_{L-R} or ADC_{A-P}) in these sSWNT´s upensions opens the possibility to use these preparations to alter selectively the ADC of water molecules in tissues in an MRI detectable manner.

Conclusion

We demonstrate that SWNT´s supensions originate anisotropic ADC movements of the surrounding water molecules, opening the possibility to use these nanostructures as novel contrast agents in diffusion weighted and diffusion tensor imaging by magnetic resonance methods.

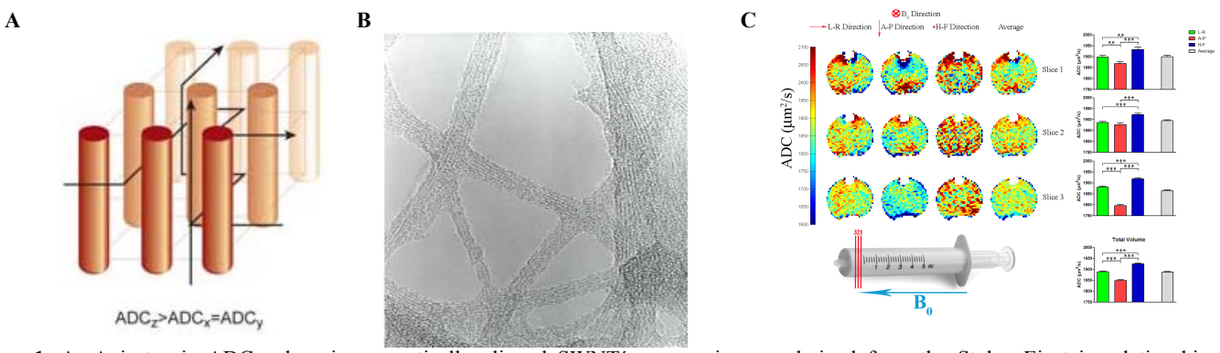

Figure 1. A: Anisotropic ADC values in magnetically aligned SWNT´s suspensions as derived from the Stokes-Einstein relationship. B: Transmission Electron microscopy (300 kV) of a non oriented SWNT´s suspension, C. Left panels: ADC maps from three consecutive axial slices (1-3) across a syringe containing a SWNT suspension (2mg/mL) obtained with the diffusion encoding gradient oriented in the L-R, A-P or H-F directions. The orientation of the syringe with the H-F exis parallel to the B_0 field is shown in the bottom. Right panels: Barg graphs (mean± sd) of the ADC values measured in the L-R (green), A-P (red), H-F (blue) or average of the three directions (grey).

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