Characterization of Single Wall Carbon Nanotubes as anysotropic contrast agents for MRI

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Introduction

The increased use of Magnetic Resonance Imaging (MRI) methods as clinical diagnostic tools has prompted for the development of new, more powerful and selective MRI contrast agents (CAs)[1]. Effectiveness of diagnosis by MRI is joined to the design of new MR sequences as well as the development of new CAs increasing the quality, resolution and specificity of the MR images[2,3]. In the last two decades, our research group actively work in this field contributing to the preparation and evaluation of new paramagnetic CAs for MRI[4,5], and others responsive CAs such as, pH probes aimed to measure the extracellular pH within tumours through Proton Magnetic Resonance Spectroscopic Imaging (^{1}H MRSI)[6,7]. At present, we are interested in the development of a new generation of paramagnetic CAs with anisotropic magnetic properties, being the Single Wall Carbon Nanotubes (SWNTs) the ideal systems[8]. Functionalization of SWNTs constitutes an active area because of their applicability as organic materials or even used as vehicles in drug delivery systems. Furthermore, many synthetic organic transformations of SWNTs have been reported in order to modulate their solubility properties in water or in organic solvents, making them as promising candidates in biotechnology and nanomedicine[9] [8].

Methods

Our aim is the development of a new generation of paramagnetic CAs with anisotropic magnetic properties. We propose the utilization of anisotropic materials in order to distinguish between laminar or turbulent flow in the normal or pathologic biological systems. With this goal, commercial SWNTs were purified by treatment with concentrated HCl. Then, the structures were either treated with $GdCl_3$ to obtain nanotubes Gd containing, or oxidized with HNO_3 to yield the corresponding acids. These can be used to chelate gadolinium in a covalent manner in order to improve the paramagnetic character of the SWNT. Relaxivity measurements of the new structures were made at low field in a 0.5 T Bruker Minispect ®. MRI *in vitro* studies were carry out at high filed in a 7 T Bruker PharmaScan®).

Results

Single Walled Carbon Nanotubes SWNTs synthesized by chemical vapor deposition (CVD) with a purity of 10-40 % have been used in these studies. Dimension of SWNTs: 0.7-1.2 nm diameter, and 2-20 μm length. Characterization was performed by the following thecniques:

TEM. Commercial and treated SWNTs images (100 kV) show different characteristics depending on the SWNTs modification. SWNTsCOOH and SWNTsCOOHGd [III] appear as diffuse images being necessary high resolution TEM analysis.

TG. Thermogravimetric profiles show the presence of carboxylic groups for the SWNTsCOOH and SWNTsCOOH-Gd [III] samples. In both cases, CO_2 loss is observed in a temperature range between 200 to 300 ºC. For the samples SWNTs-Gd [III] and SWNTsCOOH-Gd [III], calcination residues correspond approximately to the Gd contents determined as Gd_2O_3.

TXRF. Total Reflection X-ray fluorescence provided quantitative information of metals expressed as % weight. The paramagnetic metals residues such as Ni, and Co on SWNTsCOOH are responsible for the magnetic properties.

MRI. Magnetic SWNTs induce an anisotropic relaxivity being the intensities of the MRI acquired parallel to Bo bigger than those acquire perpendicular to Bo, as it is depicted in the intensity histograms.

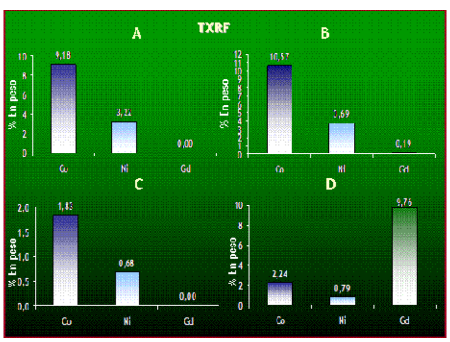

Figure 1: TXRF Profile of A) SWNTs, B) SWNTs-Gd(III), C) SWNTsCOOH D) SWNTsCOOH-Gd(III)

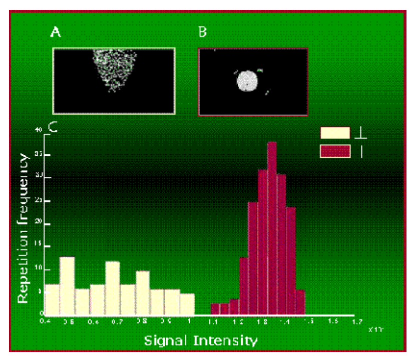

Figure 2: T1 weighted images A) perpendicular to B0, B) parallel to B0, C) Intensity histogram of A and B

Conclusion

We have probed that magnetic tubular materials induce anisotropic magnetic properties in MRI. In this line, single wall nanotubes are promising systems for the preparation of anisotropic paramagnetic contrast agents able to distinguish between laminar (normal) and turbulent (pathologic) flow.

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