Magnetic susceptibility anysotropy of oriented Single Walled Carbon Nanotubes suspensions as measured by SQUID induces water relaxation anysotropy as detected by MRI

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Introduction.
The relaxation of water molecules induced by classical contrast agents occurs in an isotropic manner, becoming not possible to determine the molecular orientation of the contrast agent molecule from water relaxivity measurements. In this work we report on a novel family of contrast agents endowed naturally with anisotropic relaxivity (1,2) and thus able to reveal the molecular orientation of the contrast agent probe from non invasive, water relaxivity measurements. Single Walled Carbon Nanotubes (SWCNTs) preparations are shown to be useful systems for this purpose since they align along the magnetic field and may depict different magnetic properties in the longitudinal and axial directions. In this communication we report, for the first time to our knowledge, measurements of the directional magnetic susceptibility of SWCNTs suspensions using a SQUID magnetometer and of the resulting anisotropic water relaxivity using an MRI scanner.

Materials and Methods.
We used commercial SWCNTs (Sigma-Aldrich, Barcelona, ES) dissolved in Fetal Bovine Serum (2mg/ml, GIBCO, Alcobendas, ES) and ultrasonicated (15 min, Branson Ultrasound, Hospitalet de Llobregat, ES). For the SQUID experiment, samples were cooled down to a final temperature of 5K, starting from the liquid state (room temperature), under a magnetic field of 5T used to maintain oriented the carbon nanotubes during the cooling process. First magnetization curves and hysteretic loops were measured at 5 K in two directions, parallel and perpendicular to the direction of the cooling field. For the Magnetic Resonance Imaging measurements, we mixed the suspension with melted agarose (333 K), and cooled down (to 275K) inside a 7T magnet (Bruker Biospin, Rheinstetten DE) to obtain an oriented SWCNT gel. The SWCNTs oriented sample was placed in an Eppendorff tube accommodated to a home made PVC goniometer (Fig. 1A), allowing the rotation of the tube inside the magnet. We measured T2 values varying the orientation of the sample with respect to B0, using spin-echo sequences as implemented in a Bruker Biospin 7T scanner.

Results. A different behaviour of the hysteretic loop and magnetic susceptibility is observed in the parallel and perpendicular directions (Fig. 1B). Notably, in the perpendicular direction a higher magnetic field is necessary for the sample to reach the saturation value and the corresponding initial susceptibility is higher (see inset), suggesting a significant degree of alignment of the nanotubes. Fig.1C demonstrates the variation of T2 varying the orientation of the nanotubes with respect to the direction of B_0. A significant decrease is observed when the nanotube suspension is oriented perpendicular to B_0.

Discussion. An important point is to explain the effects of the magnetic susceptibility of the SWCNTs, as measured by SQUID, on the water relaxivity, as determined by MRI. We suggest that the local magnetic field is higher in the nanotube tips, inducing a relative increase in the T_2 relaxation times of the water molecules located there (Fig. 1D).

Conclusions. We show that oriented suspensions of commercial SWCNTs depict anisotropic relaxivity in T_2, a property that may allow the unravelling of the molecular orientation of the probe from relaxivity measurements in vivo. In addition, we report a convenient method for obtaining magnetically oriented SWCNTs suspensions, able to maintain the orientation within a solid agarose matrix. By changing the orientation of the agarose matrix inside the magnet we were able to prove the directional dependence of relaxivity in the SWCNTs suspension

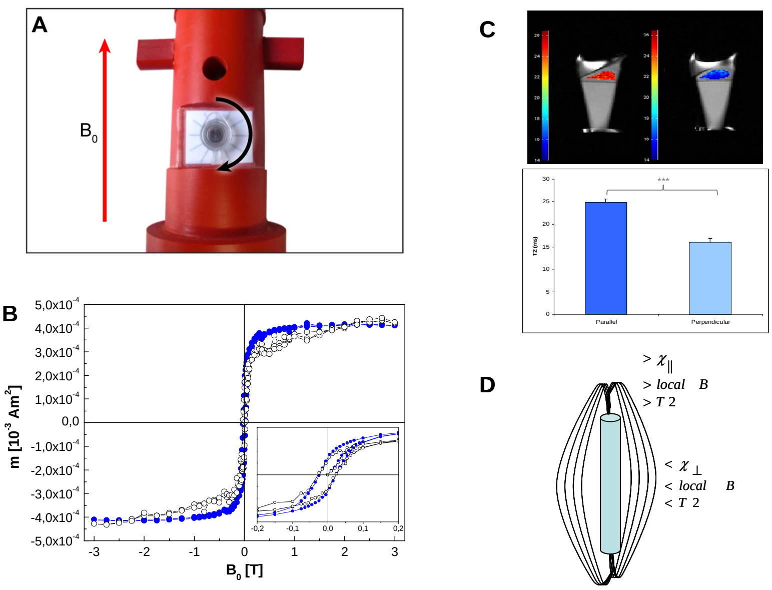

Figure 1. A: Home made PVC goniometer. B: Magnetization curves of carbon nanotubes measured by SQUID with the field applied parallel (blue) and perpendicular (white) to the cooling field.C:T_2 maps obtained from oriented SWCNTs in agarose. Note the different values of T_2 (mean ± sd) in the parallel and perpendicular orientations ($p<0.01$). D: Scheme showing the higher magnetic flux density at the tips of the nanotube than at the sides. The higher magnetic field at the tips results in longer relaxation times when the nanotube is aligned with the external magnetic field

Bibliography.
(1) V. Negri, A. Cerpa, P. López-Larrubia, L. Nieto-Charques, S. Cerdán, P. Ballesteros. Nanotubular Paramagnetic Probes as Contrast Agents for Magnetic Resonance Imaging Based on the Diffusion Tensor. Angewandte Chemie 2010, 49: 1813-1815.
(2) J.Tumpane, N. Karousis, N. Tagmatarchis, B. Nordén. Alignment of Carbon Nanotubes in Weak Magnetic Fields. Angewandte Chemie 2008, 47: 5148-5152.