SELF-ASSEMBLED MULTIFUNCTIONAL Fe/MgO NANOSPHERES FOR MRI AND HYPERTHERMIA

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We report on the fabrication of nearly spherical crystalline Fe particles covered by a uniform 3 nm thick MgO epitaxial shell (Figure), presenting advanced magnetic properties, and their potential forthcoming exploitation as contrast agents for magnetic resonance diagnosis and heating mediators for cancer therapy through hyperthermia.

Herein, We explored the potential use of the ferromagnetic properties of the Fe/MgO particles for cancer therapy by carrying out heating experiments. We found that under field amplitude H = 250 Oe and frequency *f* = 765 kHz nanoparticles solutions exhibited significant temperature increases over time (Figure). A very high specific absorption rate (SAR) in the order of 450 W g^{-1} (per Fe gram) was found. Typically, ferrofluid samples investigated in literature show SAR values in the order of 100 W g^{-1}. This demonstrated Fe/MgO NPs as high performance therapy vectors capable of induce heat at lower doses than existing materials.

We also present results on particles biodistribution. In preliminary *in vivo* animal experiments, we intravenously injected 10 µl g^{-1} of saline solution at 1 mM Fe^0 molar concentration into mice (total iron dose about 0.6 mg kg^{-1}). No apparent acute toxicity or side-effects health problems were observed over a monitoring period of 3 weeks, though of fear of raising the likelihood of blood vessel blockage due to particles-cluster formation by magnetic interaction. Animals were imaged using MRI (Figure). The distribution of particles in the mouse 24 h post injection is similar to that reported previously for iron oxides particles with similar physical characteristics.[1] This particles display a tendency to undergo phagocytic system clearance in the liver, spleen and kidneys. Significantly, the values measured for MRI are consistent with the magnetic data analysis of excised organs. The primary accumulation in liver, kidneys and spleen showed a gradual decrease within the 3 weeks monitoring period, for which urinary, and eventually hepatobiliary excretion into the intestinal tract, are considered as possible clearance pathways. A remarkable result was that the hysteresis cycle taken from tissue several days after injection resembled that of the NPs powder, demonstrating the particle *in vivo* solidity. Even in case the magnetic nanoparticles start to break down, any Fe and Mg amount will be diluted and regulated within the body. Given that a clinical dose would likely include a few milligrams of Fe per kilogram body mass, the prospect of iron overload is highly unlikely.[2] Although our studies may be considered as a first proof-of-principle approach, further work is still needed to investigate the biocompability of the nanocrystals in various *in vivo* applications.

Referentes
(1) H. Pardoe et al. *Mag. Res. Imag.* **2003,** *21*, 483
(2) P. Gould, *Nanotoday,* **2006,** *1*, 34

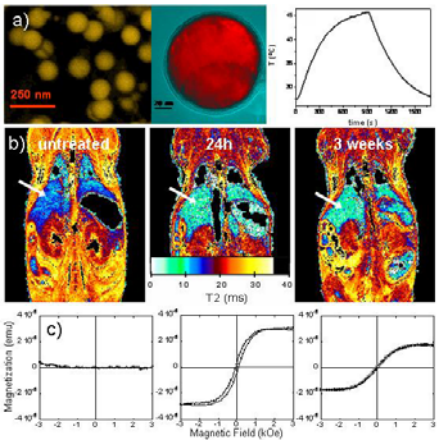

Figure
a) Tem image of Fe/MgO particles, Heating performance of particles aqueous suspensions under 250 Oe and 765 kHz (right)
b) T_2 MR images of mouse body before (left) and after injection of nanoparticles. MRI show a decrease in T_2 values in the liver after contrast administration (arrow).
c) Comparison of magnetic signal from targeted liver at the same time points as imagined by MRI.