Ultrasmall Doped Iron Oxide Nanoparticles as Dual T_1–T_2 Contrast Agents for MRI

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Ultrasmall superparamagnetic iron oxide nanoparticles, with a mean hydrodynamic diameter below 50 nm, possess characteristics such as biocompatibility, long plasma half-life, and interesting magnetic properties, which make them suitable for a wide range of biomedical applications in both therapy and diagnosis. Magnetic resonance imaging (MRI) is one of the most used techniques in the medical field for the diagnosis of diverse diseases due to its high spatial resolution, rapid acquisition times, and the absence of exposure to ionizing radiation. However, contrast agents (CAs) are frequently needed to distinguish between adjacent tissues, for example to better visualize tumor morphology or coronary angiography. Commonly, CAs are helpful for the enhancement of either T_1 or T_2, e.g. gadolinium chelates work as T_1 and iron oxide nanoparticles as T_2 CAs. However, bimodal T_1–T_2 CAs would help to distinguish interferences, such as hemorrhagic regions, bond calcification, metal deposits, and susceptibility artifacts, leading to a more accurate and early diagnosis. Additionally, bimodal behavior of a single CA platform within the same technique would simplify the acquisition due to identical penetration depths and time scale in both imaging modes.

We report on the synthesis of ultrasmall water-dispersed superparamagnetic iron oxide nanoparticles with manganese as main doping ion for T_1–T_2 enhancement in MRI. The nanoparticles were produced by a hydrothermal method in gram-scale quantities. A purification protocol was developed to ensure narrow size distribution and high colloidal stability, avoiding the use of organic solvents and phase-transfer procedures. This procedure was also found to dramatically modify the performance of the nanoparticles in terms of MRI properties and colloidal stability in biological medium.

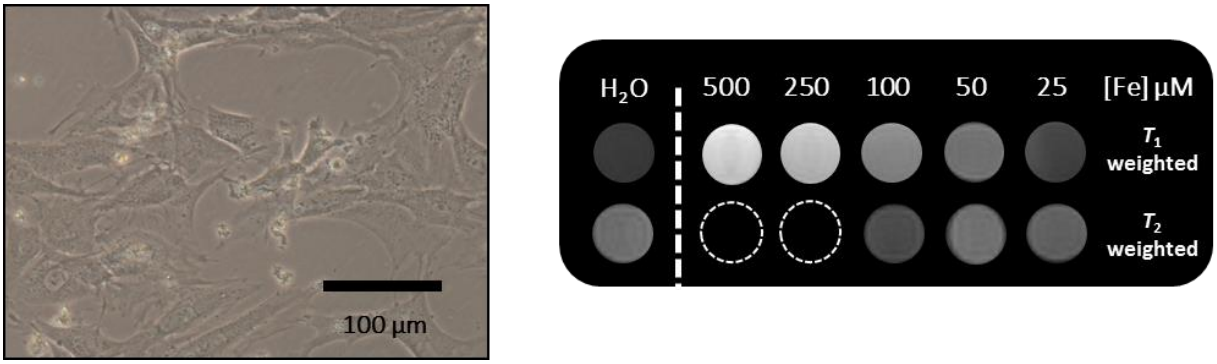

Figure: Nanoparticles incubated with rat mesenchymal stem cells after 16 h (left). Phantom images at 3 T with varying Fe concentration (right).