

## TOWARDS MULTIFUNCTIONAL CORE-SHELL NANOPARTICLES FOR BIOLOGICAL APPLICATIONS

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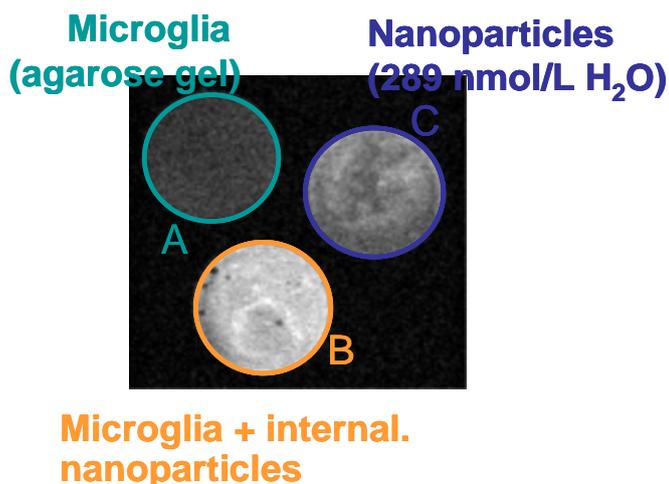
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There is therefore a real need to design multifunctional contrast agents, which can produce multiple targeting and visualization of organs or cells (detectable changes in the MR signal intensity<sup>1</sup> of the target tissue or organ by changing its MR relaxation properties and detectable optical signals for example<sup>2, 3</sup>). These contrast agents require (i) a large number of paramagnetic centers selectively bound to the target tissue and (ii) a sufficiently high molecular weight of the MRI agents in order to extend their vascular retention and thus slow their tissue clearance. For this reason, the development of biocompatible nanoparticles with an external shell of high-spin paramagnetic lanthanide contrast agents like gadolinium chelate (seven unpaired electrons), europium fluorescent probes and a superparamagnetic core, appears to be an interesting solution for targeted imaging.

Indeed, the lanthanides species are both active in the detection of the target using different techniques. Gd<sup>3+</sup> nucleus generates a hypersignal with a T1 weighted sequence, even at high magnetic field and, consequently, a much easier interpretation of the MRI images. However, these low molecular weight gadolinium chelates accumulate in the extracellular space where the “blood brain barrier” breakdown has occurred. They undergo rapid diffusion through the interstitial and as well as renal elimination and therefore have the limitation of providing a time-dependent image of tumor margins. We show in this communication that the chemical grafting of such contrast agent on *metal oxide nanoparticles* can be an alternative route to change their biodistribution, with the desired half-lives, inducing their internalization by macrophages, and having a hypersignal with T1 weighted sequence (Figure 1).



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Silica nanoparticles, for example, would be an excellent carrier for the lanthanides chelates. Silica is porous enough so that water can freely move in and out of the frame. The size of the particles will slow the rotational movement of the chelates and improve the relaxation of water. Additionally, the nontoxic silica can be easily derivatized and targeted contrast agents can be synthesized. Nanosized silica, with a size between 10 and 20 nm, are small enough to pass through the body, and above all are able to enter cells. New sets of Ln<sup>3+</sup> modified nanoparticles were synthesized and investigated for their MRI contrast agents' properties and for their ability to be internalized and allow the spatial detection of cell populations able of phagocytosis such as microglial cells. We will also present preliminary results on the introduction of a superparamagnetic oxide in the silica and study the interactions in between the shell and the core with respect to the silica shell thickness.

### References:

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