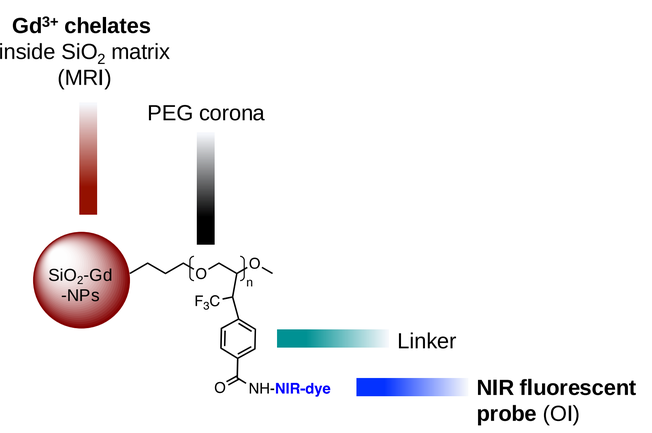
Functionalized Silica Nanoparticles: Design, Characterization, and Multimodal Imaging Applications

Sarah Garifo[1], Dimitri Stanicki[1], Sébastien Boutry[1,2], Lionel Larbanoix[1,2], Robert N. Muller[1,2], Sophie Laurent[1,2]

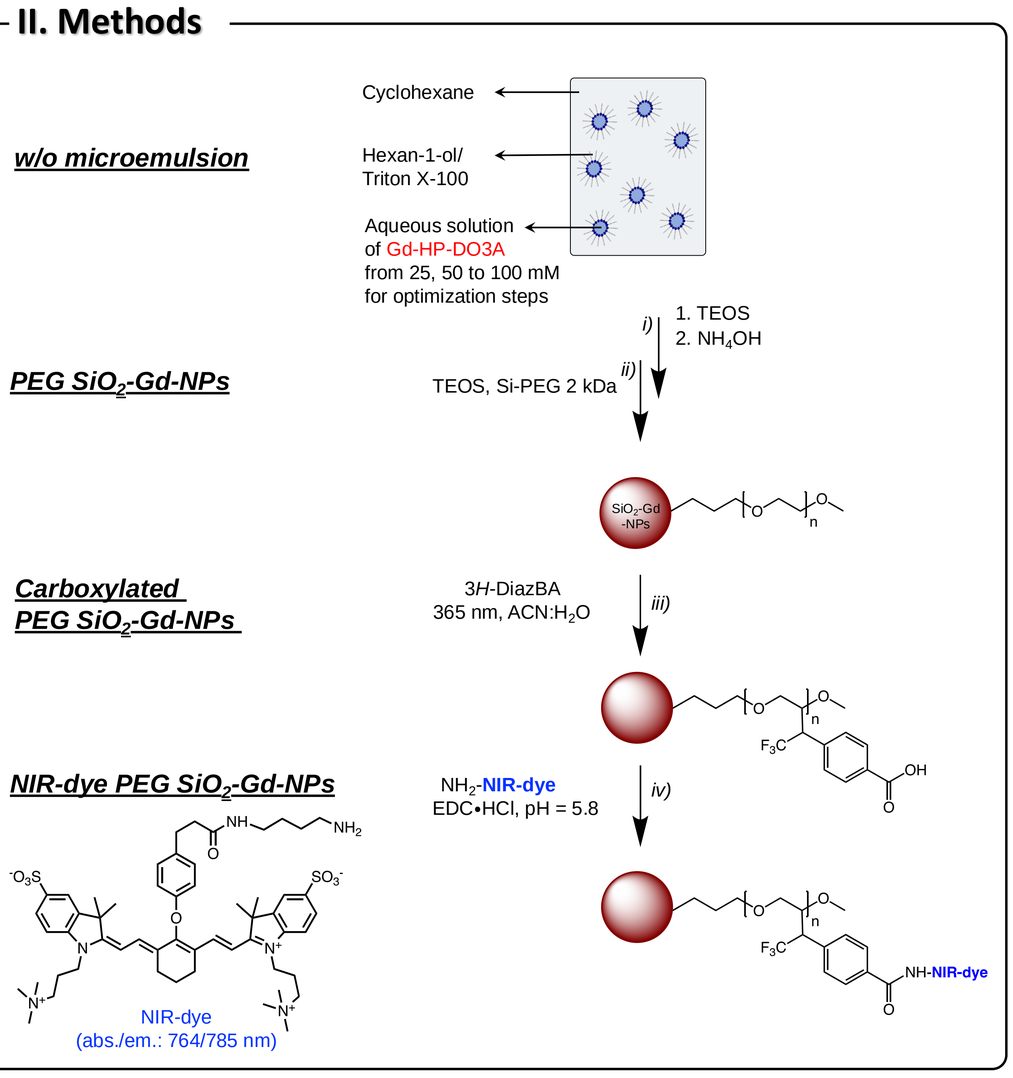
[1] General, Organic and Biomedical Chemistry Unit, NMR and Molecular Imaging Laboratory, University of Mons (UMONS), 7000 Mons, BELGIUM
[2] Center for Microscopy and Molecular Imaging (CMMI), 6041 Gosselies, BELGIUM

I. Introduction

Among the numerous imaging techniques, magnetic resonance imaging (MRI) has imposed as a powerful diagnosis tool owing to its high spatial resolution, unlimited tissue penetration and non-ionizing nature. In addition, its combination with optical imaging (OI) offers a better sensitivity especially in the field of molecular imaging. The goal of this project is to develop a multimodal nanoplatform. To improve relaxation process, an encapsulation inside nanostructures has been considered. Thanks to their inherent properties (*i.e.,* biocompatibility, chemical stability, low toxicity) silica nanoparticles (SiO_2-NPs) have been chosen as a matrix. They offer the possibility of molecule incorporation in their core during the water and oil (w/o) synthesis[1,2]. To ensure colloidal stability, the surface of the particles was modified by means of treatment using PEG-silane, and further functionalized photochemically using a diazirine linker bearing carboxylic functions[3]. Optical properties were obtained by the covalent grafting of a near-infrared emitting probe[4] (NIR-dye) on the resulting platform. Preliminary imaging experiments complete this study and confirm the potential of the presented system for preclinical imaging experiments.



II. Methods



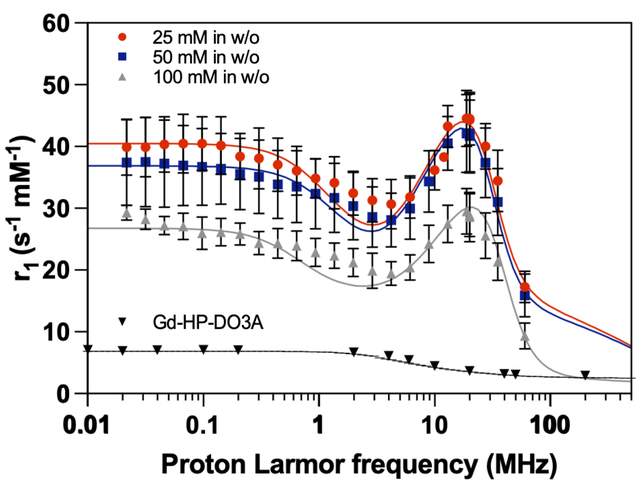
III. Results

Targeted system: properties

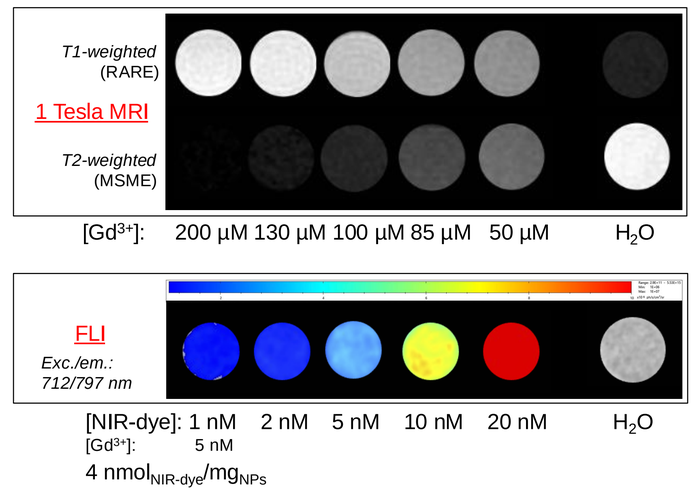
[Gd-HP-DO3A] in w/o	D_H^{DLS} (nm)	D^{TEM} (nm)	r_1^{para} B_0: 0.47 T, 37°C (s^{-1} mM^{-1})	D^{NMRD} (cm^2 s^{-1})
25 mM	33.4 ± 1.2	15.9 ± 2.8	44.9 ± 2.4	2.5 e^{-6}
50 mM	39.1 ± 4.6	18.1 ± 3.1	42.2 ± 3.9	2.8 e^{-6}
100 mM	66.9 ± 4.7	25.6 ± 5.7	28.9 ± 3.4	1.9 e^{-5}
Gd-HP-DO3A	_	_	3.6	3.3 e^{-3}

Relaxometric studies over various [Gd-HP-DO3A] in w/o reached optimal conditions using 25 mM (20 nmol of Gd^{3+} per mg of particles) which have proven the efficiency of the prepared paramagnetic nano-assembly by the decrease of T_1 and T_2 ^1H spins. The NMRD profiles exhibit a bump at higher field which confirms the encapsulation of the complexes inside the matrix. NIR-dye functionalized SiO_2-Gd-NPs sized 15.6 ± 1.9 nm (PDI=1.05) were then studied with phantoms and *in vivo* healthy hairless SKH1 mice via MRI/OI.

NMRD profiles (37°C)

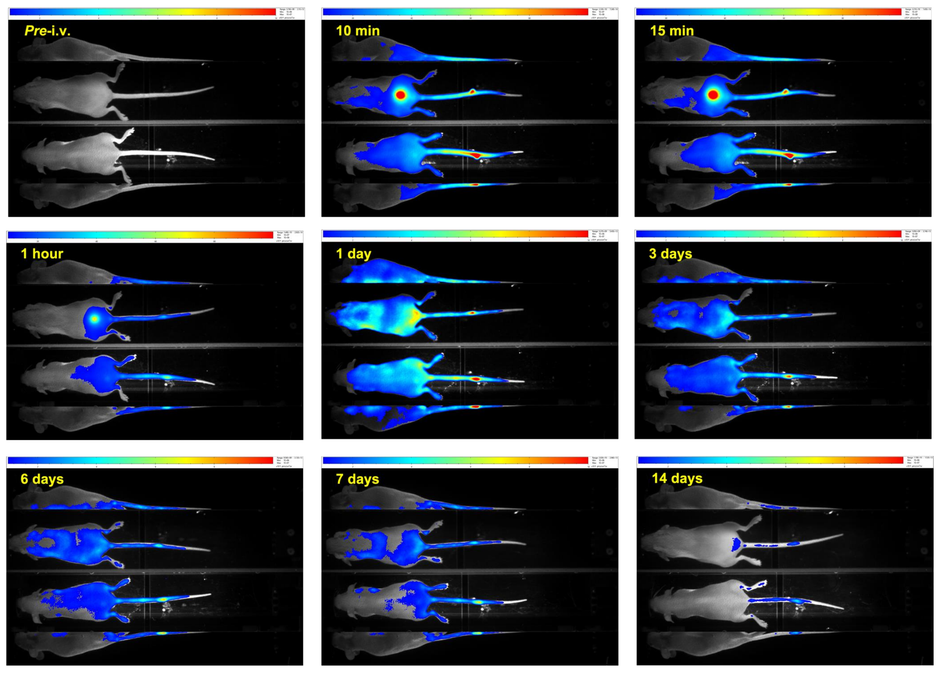


Phantoms MRI and optical imaging by FLI experiments

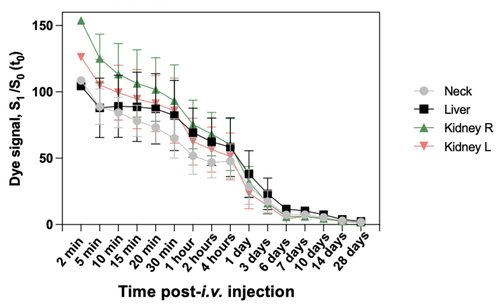


Small animal imaging experiments: biodistribution and elimination studies

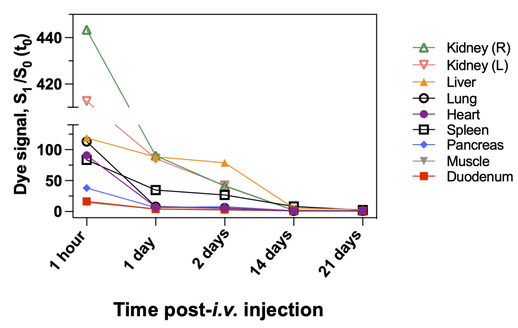
***In vivo* FLI experiments**



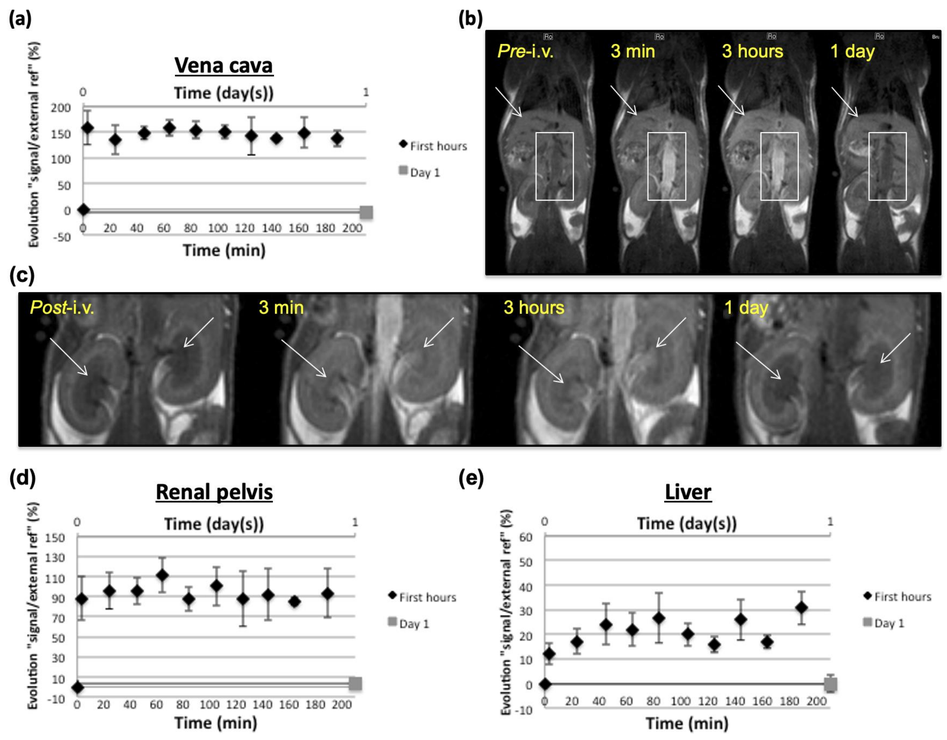
***In vivo* FLI data**



***Ex vivo* FLI data**



***In vivo* MRI experiments**



IV. Conclusions and perspectives

This work aimed to develop an efficient SiO_2-NPs-based platform as a potential contrast agent for both MRI and OI techniques. Relaxometric measurements have proven some promising results as active MRI probe after Gd^{3+} chelates encapsulation during w/o microemulsion. In addition, we proposed to design an innovative strategy to further post-functionalize the NPs through a photochemistry process followed by the grafting of NIR-dyes. By doing this, a stable fluorescent paramagnetic nanoplatform was successfully prepared, characterized and visualized in *in vivo* imaging for 4 weeks.

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References:
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