

Novel core-shell nanoparticles with promising properties as negative Contrast Agents for MRI

A. Carvalho¹, T. Silva², V. Ferreira³, J. F. Henriques³, I. Domingues³, M.C. Gonçalves²

¹CENIMAT-I3N/DCM/FCT/UNL, Campus da Caparica, 2829-516 Caparica, Portugal

²Dep. Chemical Eng., IST, UTL, Av. Rovisco Pais, 1049-001 Lisboa, Portugal, and ICEMS, Av. Rovisco Pais, 1049-001 Lisboa, Portugal

³Department of Biology & CESAM, University of Aveiro, Campus Universitário de Santiago, 3810-193 Aveiro, Portugal

- New core-shell NPs with interesting properties as efficient negative CA agent for MRI.
- SPION of roughly 6 nm in diameter, coated with inorganic or hybrid silica.
- Core-shell NPs diameter in the range 20 to 300 nm.

Core_shell	TEM d (nm)
TEOS	38.6
GPTMS	22.0
APTES	250

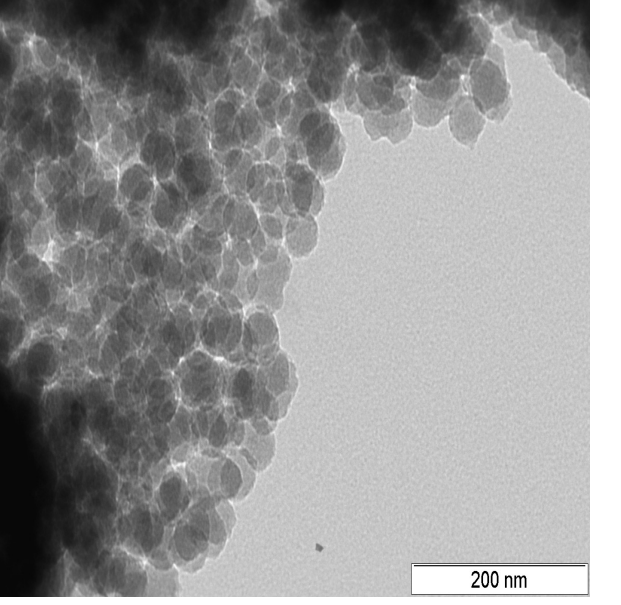


Figure 1: TEM diameters and image of SPION coated with silica.

CA efficiency: relaxivities.

$$1/T_i = 1/T_{(0)i} + r_i [\text{Fe}]$$

	r_1 (mMs) ⁻¹	r_2 (mMs) ⁻¹
TEOS	0.016	13.8
GPTMS	0.026	14.4
APTES	0.006	40.6
Endorem (Guerbert)	2.2	182.0

- i=1 longitudinal, i=2 transverse
- $1/T_i$ relaxation rate longitudinal or transverse
- $1/T_{(0)i}$ relaxation rate in the NPs absence
- r_i relaxivity longitudinal or transverse
- [Fe] iron oxide concentration

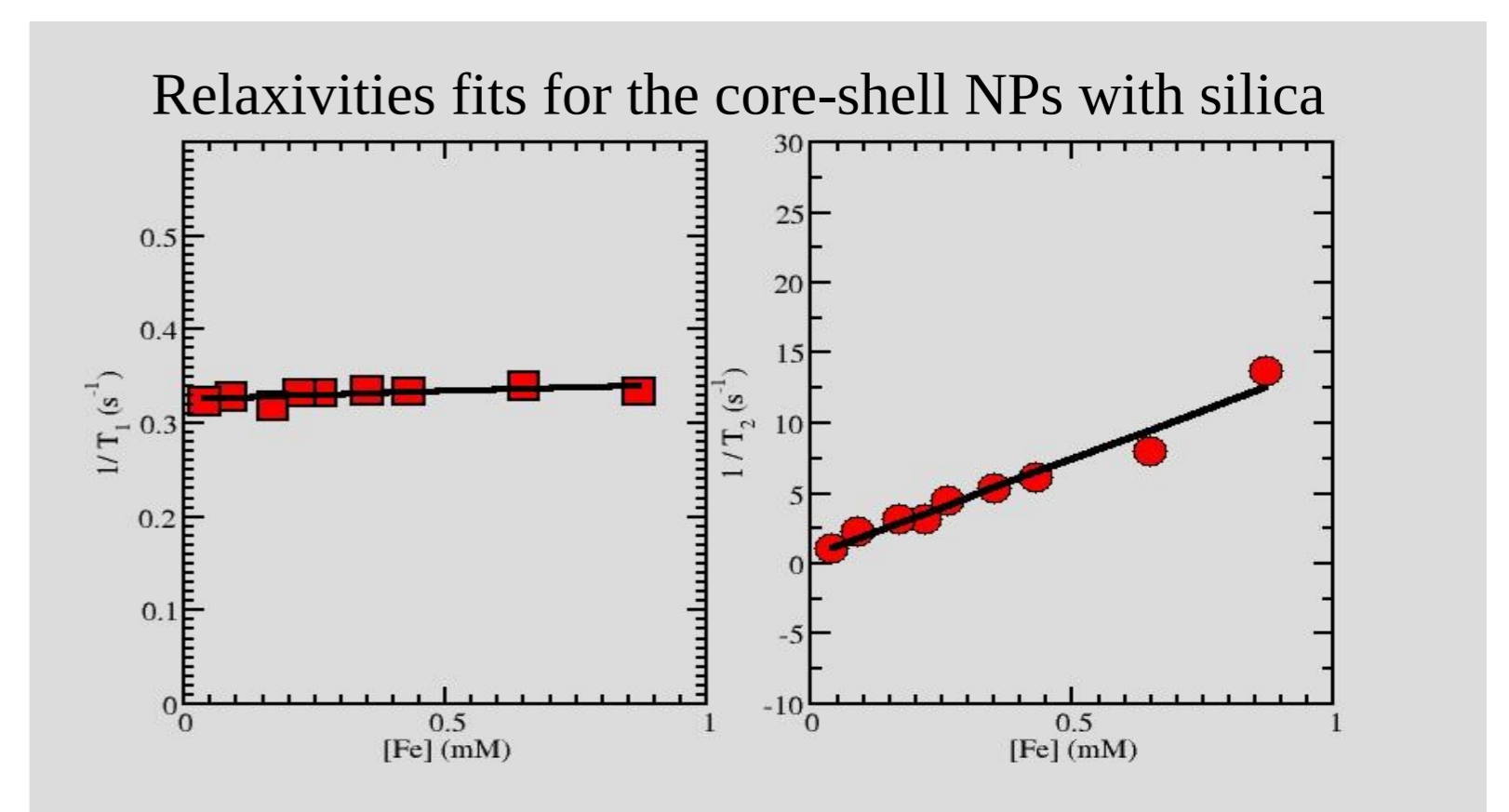


Table 1: Relaxivities measured at 7 T in a Bruker Avance III NMR spectrometer, of the core-shell NPs with silica (TEOS), and functionalized silica with (3-Glycidioxypropyl) methyldiethoxysilane (GPTMS), and (3-Aminopropyl) triethoxysilane (APTES). Endorem relaxivities are presented for comparison.

- The contrast enhancement of the core-shell NPs is presented in a series of MRI micro-images (7 T magnetic field) equipped with an imaging gradient of 160 G/cm of adult zebra-fish (*Danio rerio*).
- NPs were injected to a group of zebra-fish. Animals were euthanized and preserved in Dietrich's fixative.

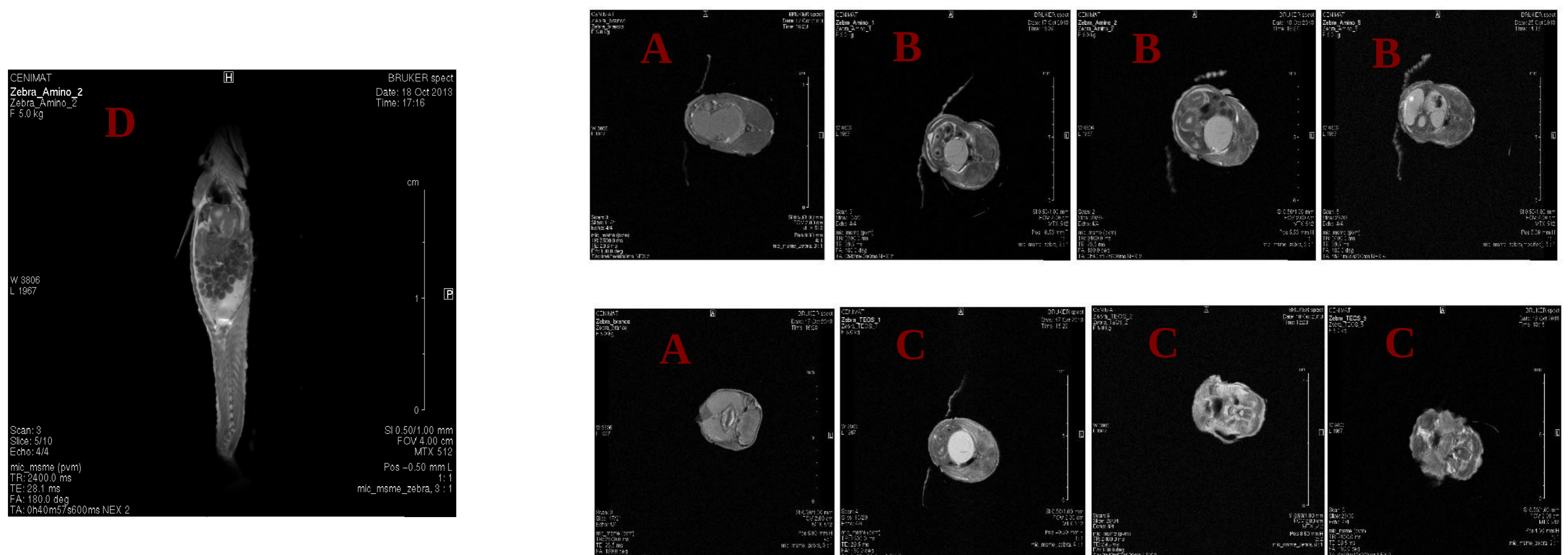


Figure 2: MR micro-images of: axial slices of blank (A), APTES (B) and TEOS (C) core-shell NPs, injected zebra fish, and MR micro-image of a 0.5 mm coronal slice of a zebra-fish injected with APTES core-shell NPs (D).

Conclusion: The novel core-shell NPs have a very small effect on water/tissue longitudinal relaxation time and a moderate effect on the water/tissue transverse relaxation time, inducing a very high r_2/r_1 ratio, the signature of a very efficient negative contrast agent for MRI.

The core-shell NPs strong effect on MRI contrast is clear on the zebra-fish images. The silica functionalization affects the efficiency of the core-shell NPs as a negative CA for MRI.

The amina functionalized core-shell NPs show better performance than the silica core-shell NPs.