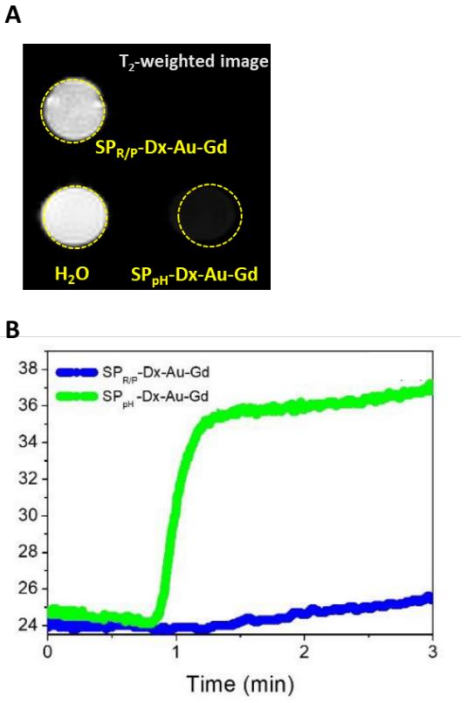
Title "Improving theranostic properties of SPIONs: surface coating influence "

Vital C. Ferreira-Filho[1], Beatriz Morais[1], Bruno J. C. Vieira[1], João Carlos Waerenborgh[1], Maria João Carmezim[2,3], Csilla Noémi Tóth[4], Sandra Mêmе[4], Sara Lacerda[4], Daniel Jaque[5], Dirk H. Ortgies[5] Célia T. Sousa[6], Maria Paula C. Campello[1] and Laura C. J. Pereira[1]

[1] *CTN, DECN, Instituto Superior Técnico, Universidade de Lisboa, EN10, km 139,7, 2695-066 Bobadela, Portugal;*
[2] *CQE, DEQ, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisbon, Portugal;*
[3] *ESTSetúbal, CDP2T, Instituto Politécnico de Setúbal, 2910-761 Setúbal, Portugal;*
[4] *CBM, CNRS, UPR 4301, Université d'Orléans, Rue Charles Sadron, 45071 Orléans, CEDEX 2, France;*
[5] *DFM, Universidad Autonoma de Madrid, Avda. Francisco Tomás y Valiente 7, 28049 Madrid, Spain;*
[6] *DFA, Universidad Autonoma de Madrid, Avda. Francisco Tomás y Valiente 7, 28049 Madrid, Spain;*

Superparamagnetic iron oxide nanoparticles (SPIONs) play a crucial role in cancer therapy and imaging, mostly due to their non-invasiveness and high-throughput imaging studies. A multifunctional single entity containing both imaging and therapeutic properties, named theranostic, allows the possibility to acquire in real-time information about delivery and, eventually, the effects of therapeutic agents when administered to patients [1,2]. However, there is a need for comprehensive studies to optimise the synthesis methods, coatings, and characterization techniques to enhance their applicability in biomedicine [3]. In this study, the development of multifunctional SPION nanoplatforms for both cancer imaging and therapy was investigated.



SPIONs were synthesised via two different methods, reduction–precipitation ($SP_{R/P}$) and co-precipitation at controlled pH (SP_{pH}), to explore and assess the influence of the synthetic method and the coatings (dextran and gold) on its magnetic and hyperthermia properties. These SPIONs were further functionalized with gadolinium for magnetic resonance imaging (MRI), which also can be further functionalized with Lu-177 via DOTA to act in target radionuclide therapy. Parameters such as size, stability, morphology, and magnetic behaviour were subjected to a detailed analysis. Relaxitivity (at 7T) and hyperthermia experiments were conducted to assess their effectiveness in imaging and therapy, respectively. All samples exhibited superparamagnetic behaviour at room temperature and good saturation magnetization (Ms) values, crucial for the desired applications. The presence of Gd enables a longitudinal relaxivity contribution, with SPIONs displaying similar or higher r_1 relaxivities than Gd-based MRI contrast agents in clinical use.

Synthesis SP_{pH} led to better theranostic particles, with superior magnetic and hyperthermia properties, as shown via higher T_2-contrast (A) and better hyperthermia profile (B).

These encouraging SP_{pH} SPION properties will be later tested *in vitro* and *in vivo* (PC3 and RWPE cells/murine models). Furthermore, SPIONs optimisation with targeting moieties, via their gold layer, will endow them with targeting ability, which should improve in vivo applications.

Funding

This work was partially supported by FCT, Fundação para a Ciência e a Tecnologia, I.P, through contracts UID/Multi/04349/2019 and LTHMFL-NECL LISBOA-01-0145-FEDER-022096 and PhD doctoral grant to V.C.F.F. (PRT/BD/154845/2023).

REFERENCES

[1] J. Kim, J. E. Lee, S. H. Lee, J. H. Yu, J. H. Lee, T. G. Park, T. Hyeon, Adv. Mater **20** (2008) 478.
[2] R. D. Piazza, W. L. Viali, C. C. Dos Santos, E. S. Nunes, R. F. Marques, Mater. Res. Express **7** (2020) 015078.
[3] T. Ahmed, H. Bae, I. Rhee, Y. Chang, S. U. Jin, S. Hong, J. Nanosci. Nanotechnol **12** (2012) 5132.