X-ray Fluorescent Nanoparticles for *in vivo* Bioimaging

G. M. Saladino*, C. Vogt, Y. Li, K. Shaker, B. Brodin, M. Svenda, H. M. Hertz and M. S. Toprak

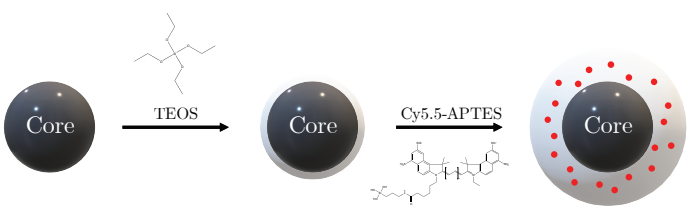
Department of Applied Physics, KTH Royal Institute of Technology
SE 10691 Stockholm, Sweden

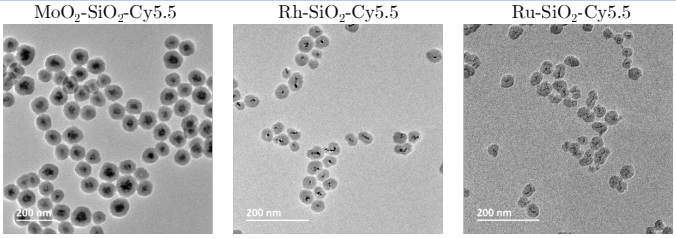
*saladino@kth.se

Introduction

X-ray Fluorescence Tomography (XFCT) was recently demonstrated to be a new bioimaging technique, for preclinical research and tumor detection [1], employing MoO_2, Rh and Ru Nanoparticles (NPs) as X-ray Fluorescence (XRF) contrast agents, among the others [2,3]. Multiple functionalities and high biocompatibility constitute indispensable tools for expanding the knowledge. Dual mode core-shell NPs were synthesized to empower both optical and XRF properties, as microscopic and macroscopic imaging contrast agents [4].

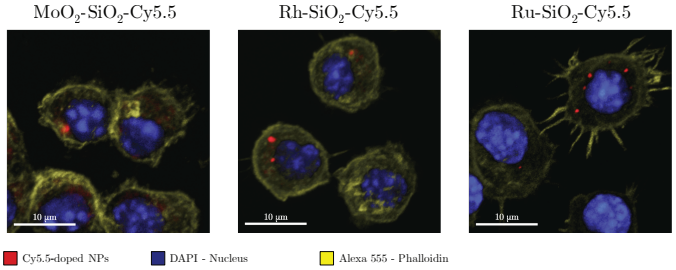
Dye-Doped Silica Coating on X-ray Fluorescent Contrast Agents



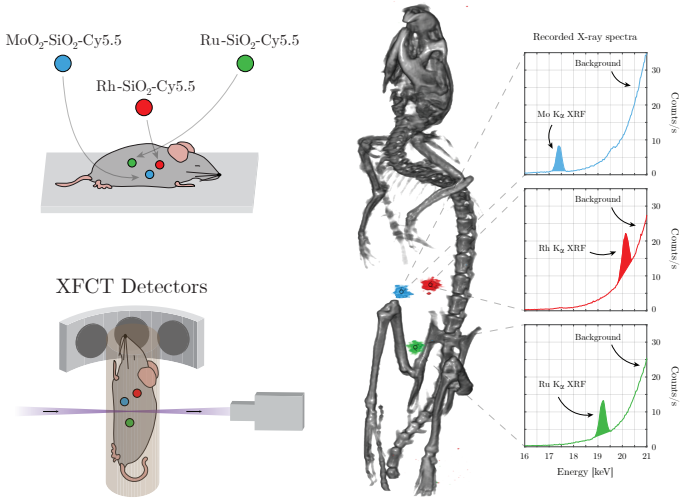


Three XRF core NPs, based on MoO_2, Rh and Ru, were coated with silica using TEOS (Tetraethyl orthosilicate). A commercial dye (Cy5.5) conjugated with APTES, was used to dope the silica shell, providing the NPs with optical fluorescence property. The core-shell NPs present uniform morphology and strong negative surface charge.

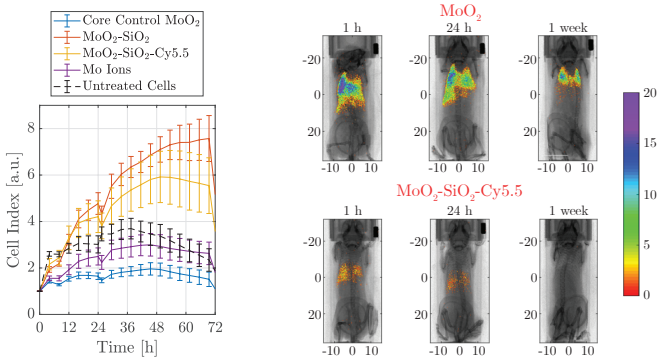
Dual Mode Nanoparticles for Microscopic and Macroscopic Imaging



The optical fluorescence property was tested *in vitro* with RAW 264.7 macrophages, allowing to localize the NPs in the intracellular environment. *In situ* XFCT on a dead mouse demonstrated the multiplexing property of the method, localizing NPs with the three different cores with a single scan. Thus, these core-shell NPs constitute potential contrast agents for *in vivo* studies.



Cytotoxicity and Biodistribution



The core-shell NPs exhibited reduced cytotoxicity with Real-Time Cell Analysis (RTCA) Assay on RAW 264.7 macrophages, while keeping the same core concentration. Preliminary *in vivo* studies on mice highlighted the different biodistribution of the core-shell (MoO_2-SiO_2-Cy5.5) NPs, where the silica coating prevented unwanted uptake in the lungs. Furthermore, a more rapid clearence was observed on core-shell NPs, with no signal detected after 1 week. These results pave the way to passive and active targeting and detection of tumors with XFCT.

References

[1] K. Shaker *et al.*, IEEE Trans. Med. Imaging. 39, 3910-3919 (2020)
[2] Y. Li *et al.*, Contrast Media Mol. Imaging 2018, 1 (2018)
[3] Y. Li *et al.*, Nanomaterials 10 (11), 2129 (2020)
[4] G. M. Saladino *et al.*, ACS Nano 15 (3), 5077-5085 (2021)