Trimodal probes for NIR luminescent, high-field MRI and CT bioimaging based on lanthanide vanadate nanoparticles

Manuel Ocaña,[1] Elisabet Gómez-González,[1] Daniel González-Mancebo,[1] Nuria O. Núñez,[1] Carlos Caro,[2] Maria L. Garcia-Martin,[2] Ana I. Becerro[1]

[1]Instituto de Ciencia de Materiales de Sevilla (CSIC-US), c/Américo Vespucio, 49, 41092 Sevilla, Spain
[2]Instituto de Investigación Biomédica de Málaga y Plataforma en Nanomedicina (IBIMA-Plataforma BIONAND) and CIBER-BBN, Málaga 29590, Spain

mjurado@icmse.csic.es

Multimodal bioimaging involves the combined use of several imaging techniques to improve medical diagnosis by overcoming the limitations of the single-mode techniques regarding tissue penetration depth, spatial resolution, and cost, among others [1]. Lanthanide (Ln)-based nanoparticles (NPs) have been highlighted as very promising candidates as bimodal luminescent and magnetic resonance imaging (LI-MRI) contrast agents (CAs) owing to the luminescent properties and paramagnetic character of lanthanide cations [2]. Regarding the luminescent component, the selection of the Ln^{3+} cation is essential as a high penetration depth of luminescence is required for *in vivo* imaging. This can be achieved by working in the biological windows, which lie in the near-infrared (NIR) region of the spectrum, in which the excitation and emission of Nd^{3+} cations take place [2]. Concerning MRI, increasing the signal-to-noise ratio is currently pursued to improve diagnosis accuracy, which can be achieved by the application of higher magnetic fields (up to 9.4 T) [3]. Under such conditions, new CAs are required, those based on Dy^{3+} cations being the most promising candidates because the high magnetic moment of such cations ensures a high magnetization and, therefore, a high magnetic relaxivity at high field [4].
In this work, we describe the synthesis and characterization of a bimodal bioimaging probe for near-infrared luminescent imaging (NIR-LI) and high-field magnetic resonance imaging (HFMRI), based on uniform core-shell-shell nanoparticles (Fig. 1) [5]. Such architecture consists of a $DyVO_4$ core as the HFMRI component, coated by a Nd^{3+}-doped $LaVO_4$ outer shell which confers the luminescent property. An intermediate undoped $LaVO_4$ shell was introduced to increase the separation distance between the Dy and Nd ions which should minimize energy transfer process that might quench the luminescence of the Nd^{3+} cations. Such nanoparticles presented a magnetic relaxivity (r2) value at high field (9.4 T) among the highest ever reported for this kind of probe, and an intense luminescence in the NIR region when excited with NIR radiation. In addition, they were chemically stable, could be dispersed in a physiological medium owing to their one-pot surface functionalization with polyacrylic acid, and were non-toxic for human fibroblast cells. The potentiality of such a probe as multimodal contrast agent for near-infrared luminescent imaging and high-field magnetic resonance imaging is demonstrated through *in vivo* assays with an animal model.

References

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Figures

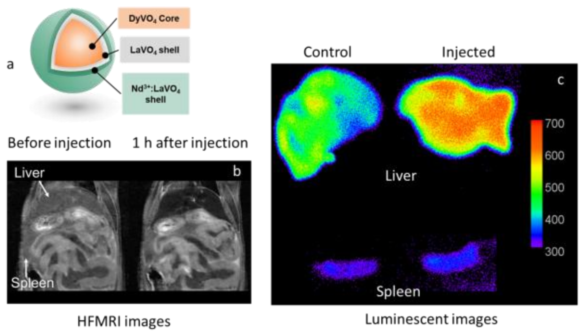

Figure 1. a) Schematic representation of the core-shell-shell nanoparticles. b) *In vivo* T2-weighted HFMRI images of a BALB/c mouse before and after nanoparticles injection (10 mg Dy/Kg animal). c) *Ex vivo* NIR luminescent images of different organs.