## <sup>68</sup>Ga-DPD-Fe<sub>3</sub>O<sub>4</sub> as a dual-modality contrast agent: biodistribution study on mice and biocompatibility with peripheral human blood cells

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Radiolabeled Fe<sub>3</sub>O<sub>4</sub> nanoparticles are promising candidates as dual-modality contrast agents (DMCA) for diagnostic applications. Accordingly, the biocompatibility of a DMCA is of significant clinical importance for subsequent *in vivo* applications. Thus, we focused on the realization of biocompatibility and biodistribution tests both *in vitro* and *in vivo*, of a DMCA, namely Fe<sub>3</sub>O<sub>4</sub> nanoparticles radiolabeled with <sup>68</sup>Ga. The *in vitro* biocompatibility of the DMCA was performed after incubation with donated human blood cells, namely red blood cells (RBCs), white blood cell (WBCs) and platelets (PLTs) coming from five healthy individuals. The advanced atomic force microscopy (AFM) technique was employed for the investigation of the morphological characteristics of all blood cells at the nanoscopic level. The kinetics of the *in vivo* biodistribution of the DMCA was evaluated in normal mice. The obtained *in vitro* and *in vivo* data prove that the specific DMCA is biocompatible, thus promising for future *in vivo* applications [1, 2].

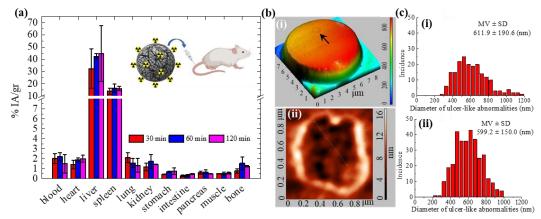


Figure 1: (a) The accumulation of [<sup>68</sup>Ga]Ga-DPD-Fe<sub>3</sub>O<sub>4</sub> DMCA in the organs of normal mice, expressed as percentage injected activity per gram of tissue (% IA/g) at 30, 60 and 120 min post injection. At each time point, the results are expressed as the mean value ± standard deviation (MV±SD) of three mice. (b)(i) Three-dimensional AFM image of a DMCA-incubated RBC at C<sub>DMCA</sub>=0.1 mg/ml (incubation at room temperature for 120 min). The arrow indicates an ulcer-like abnormality on the RBC membrane. (b)(ii) Two-dimensional topography of the ulcer-like abnormality observed on the RBC membrane in (b)(i). (c)(i)-(ii) Quantitative data of the diameter of ulcer-like abnormalities observed in RBCs coming from (i) DMCA-free after 120min incubation and (ii) DMCA-incubated samples at C<sub>DMCA</sub>=1 mg/ml. The MV ± SD expresses the mean value and standard deviation of all data obtained from five healthy donors.

## References

- [1] Karageorgou M. A. et al., Mater. Sci. Eng. C. 115, 111121 (2020).
- [2] Karageorgou M. A. and Stamopoulos D., Sci. Rep. 11, 9753 (2021).

M. A. Karageorgou acknowledges the NKUA for financial support through the "S. Tsakirakis" Scholarship.

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