Pharmacokinetics of Radiolabelled Graphene Oxide Sheets after Intravenous Administration

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Abstract

Graphene-based materials designed for biomedical applications have been recently of great interest. One of the key limitations for such applications is the determination of the possible interactions with the biological milieu [1,2]. In this work, thin GO sheets were chemically functionalized with DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid), a radiometal chelating agent, by an epoxide opening reaction. The resulting sheets became smaller in lateral dimension, with an increase in thickness. We investigated the tissue distribution of the functionalized GO sheets labelled with radioactive indium (^{111}In) after intravenous administration in mice. Whole body single photon emission computed tomography (SPECT/CT) imaging, gamma counting studies, Raman microscopy and histological examinations were used. Our results indicated no acute tissue damage, with extensive urinary excretion and spleen accumulation. Intact GO sheets were detected in the urine of injected mice by Raman spectroscopy, high resolution transmission electron microscopy (HR-TEM) and electron diffraction. These results offer a previously unavailable pharmacological understanding on how chemically functionalized GO sheets of certain lateral dimension and thickness characteristics transport in the blood stream and interact with physiological barriers that determine their body excretion and tissue accumulation.

References

[1] Kostarelos, K., Novoselov, K. Science, 344 (2014) 261-263.
[2] Kostarelos, K., Novoselov, K. Nature Nanotechnology, 9(10) (2014) 744-745.

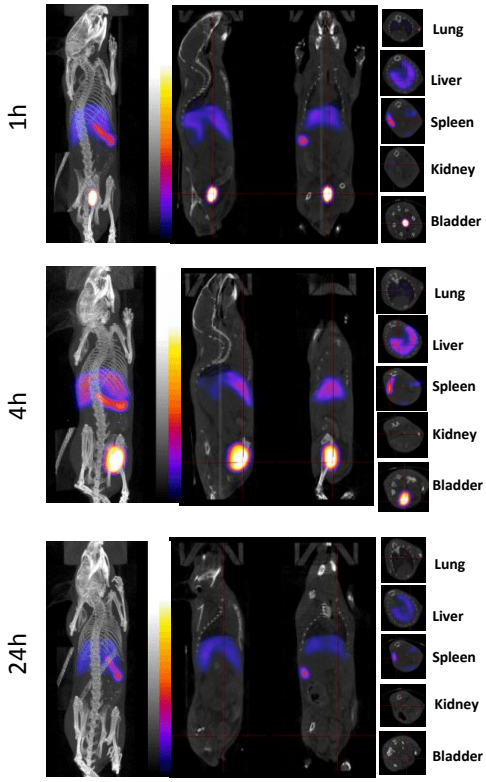

Figure 1: Whole body SPECT/CT imaging of a C57BL/6 mouse injected with 50 µg of GO-DOTA[^{111}In], showing from left to right whole body, sagittal, coronal and transverse views at different time points from injection.