Biodistribution of Near-Infrared Fluorescent Nanoparticles: an in vivo study

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Introduction:
Research in new fluorescent nanoparticles is today an important field for preclinical studies in the optical imaging technique area. Great expectation concerns new fluorescent markers engeneered for particular applications (conjugated with antibody or pharmaceutical compounds) or alone to study nano-compound intrinsic behaviour in living organisms. In particular, nanosized fluorescent particles (silica nanopaticles[1] and quantum dots[2-3]) are promising tools for the development of luminescent probes and markers provided by great brightness and high photostability respect to traditional organic fluorophores. Here we present an in vivo study of biodistribution in a small laboratory animal model of silica-core / PEG-shell fluorescent nanoparticles (20-30nm) doped with a CY7 NIR emitting dye ((2-((E)-2-((E)-2-chloro-3-((Z)-2-(3-ethyl-1,1-dimethyl-1H-benzo[e]indol-2(3H)-ylidene) ethylidene)cyclohex-1-enyl)vinyl)-3-ethyl-1,1-dimethyl-1H-benzo[e]indolium iodide). Silica particles, due to the recognized low toxicity of their chemical composition, could be interesting for future clinical applications.

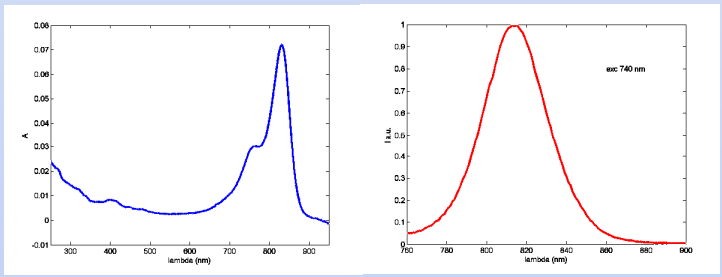

Fig.1: Absorbance (on the left) and emission (on the right) of the near-infrared nanoparticles

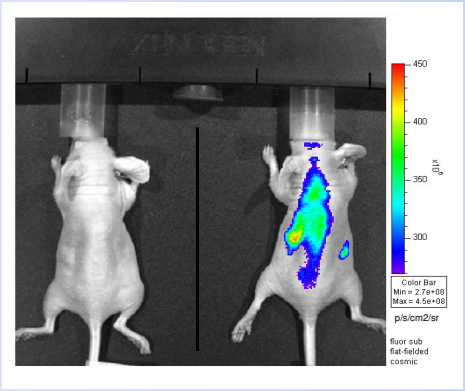

Fig.2: Optical imaging acquisition of control (on the left) and treated (right) nu-nu mice 2h after nanoparticles injection. Exposure time 1 s, binning 8, f/2, excitation filter ICG [710-760 nm], emission filter [810-875 nm].

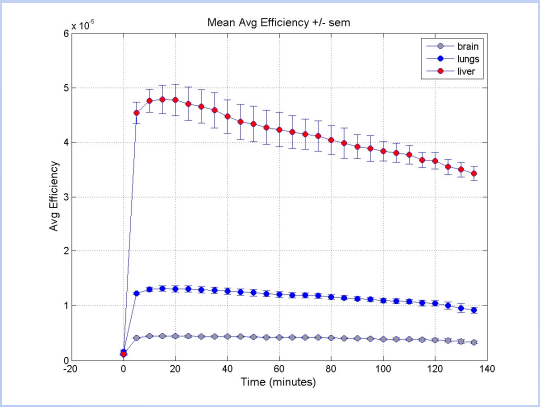

Fig.4: Everage efficency of fluorecensce mesured on three ROIs corresponding to brain, lung and liver versus time. Every value represents the mean from the treated group.

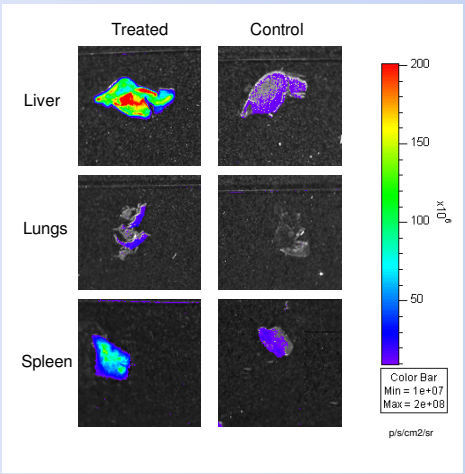

Fig.3: Optical imaging acquisition from extracted liver. On the left we show a treated section and on the right a control. Exposure time 30 s, binning 1, f/1, excitation filter ICG [710-760 nm], emission filter [810-875 nm].

Methods:
Silica fluorescent nanoparticles biodistribution was studied. We have observed with Optical Imager the kinetics of biodistribution and tissue accumulation during three hours immediately after fluorescent tracer administration (10 µl/g body weight, i.v.), in gas anaesthetized mice. Optical images were acquired with IVIS200 Series (Xenogen Corporation, Alameda USA). Data were extracted using Living Image 2.6 software.
Silica nanoparticles, with an emission peak around 810 nm, were excited with ICG excitation filter (710-760 nm) and the fluorescent emission acquired with ICG emission filter (810-875 nm).

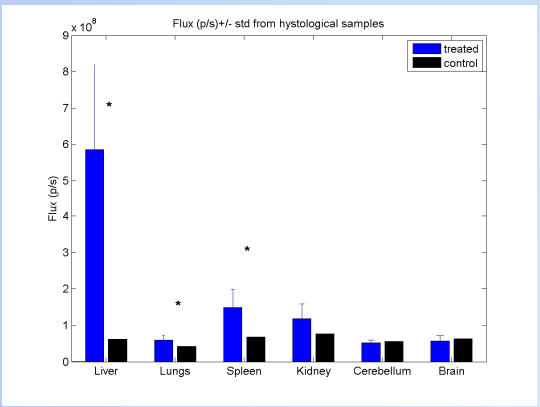

Fig.5: Histogram representing the emitted flux from surgically extracted organs and acquired with optical imaging. The asterix over the columns indicated the significantive differences among ttreated and control samples ($p<0.05$)

Conclusions:
This preliminaruy data give us a good characterization of fluorescent characteristics of the silica-core / PEG-shell nanoparticles. They have showed a very good fluorescent efficiency comparable with commercial semiconductors nanocrystals (quantum dots, QDs) actually used in preclinical research. They can be successfully used for *in vivo* applications allowing to follow the biodistribution and tissues accumulation for hours in a small animal model. The very low intrinsic toxicity of the chemical composition encourages the employ of such fluorescent markers for many *in vivo* applications in preclinical research and to investigate the possibility to engineering them with biomelcules for targeting bio-analytical applications.

References:
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