

DETERMINATION OF BIODISTRIBUTION OF GOLD NANOPARTICLES USING SPECTRAL PHOTON-COUNTING COMPUTED TOMOGRAPHY K-EDGE IMAGING IN VIVO

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Presenter

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Organisation

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 643694



DISCLOSURES

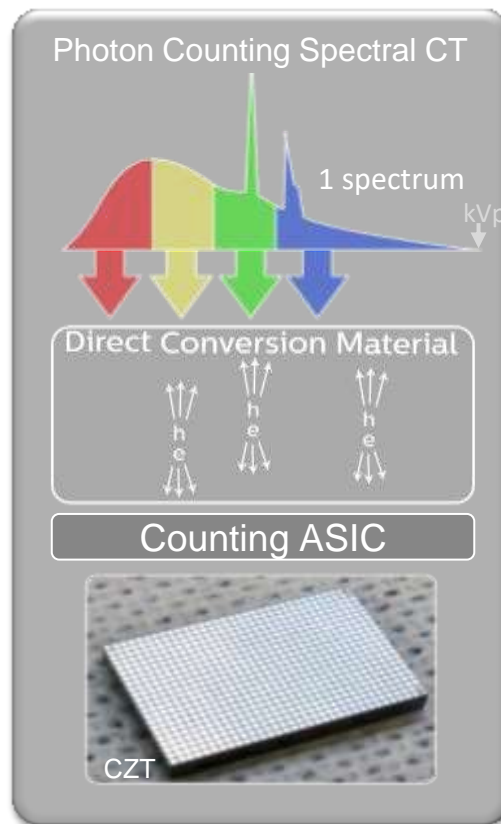
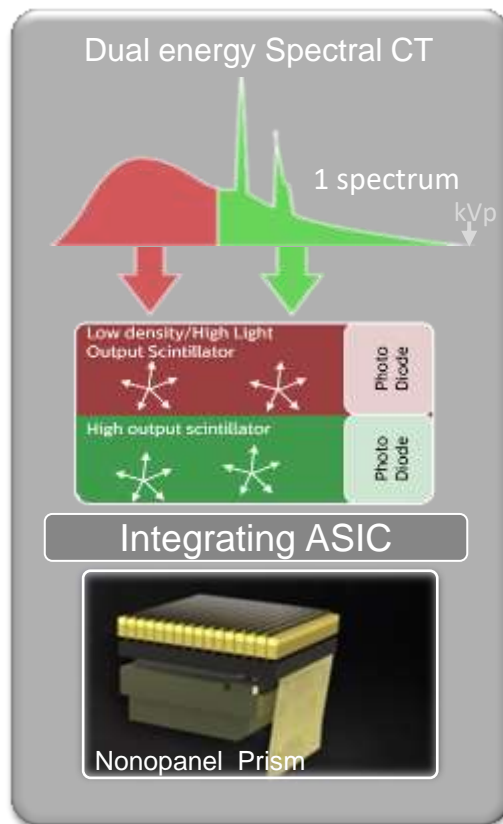
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Nothing to disclose: Monica Sigovan
Nothing to disclose: Caroline Bouillot
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Nothing to disclose: Loic Bousset
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BACKGROUND



OBJECTIVE

To investigate the feasibility of a spectral photon-counting computed tomography system (SPCCT) for specific characterization and quantification of a gold nanoparticle contrast agent's organ biodistribution *in vivo* over time

MATERIAL/METHODS

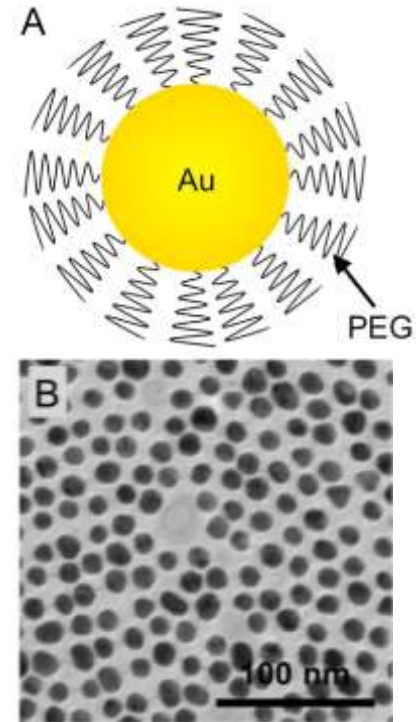
- Spectral photon-counting CT system
 - Photon-counting detectors
 - Modified clinical base
 - Conventional X ray tube
 - Field of view of 160 mm
 - Gantry rotation time of 1 second
 - Parameters used:
 - Tube current of 100 mAs
 - Tube voltage of 120 kVp



Philips Spectral Photon Counting CT
pre-clinical prototype UCBL, CERMEP, Lyon,
France

MATERIAL/METHODS

- Gold nanoparticles
 - Characteristics
 - capped with thiol-PEG-2000 (fig A)
 - core size of 12.5 nm determined by transmission electron microscopy (fig B)
 - mean hydrodynamic radius of 18 nm
 - concentration: 65 mg/ml
- Blood pool effect
- Good candidate for K-edge imaging ⁽¹⁾
- Known to be taken up by the mononuclear phagocyte system (MPS) ⁽²⁾

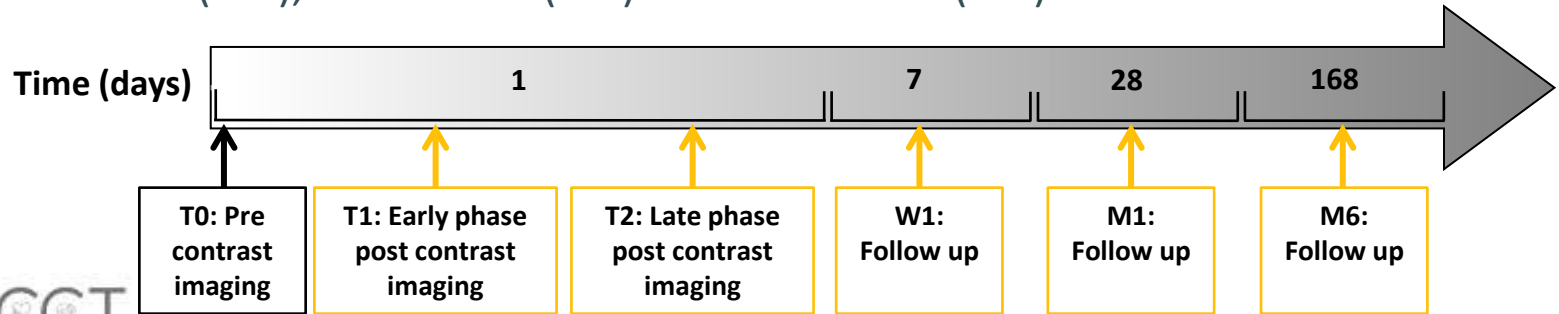
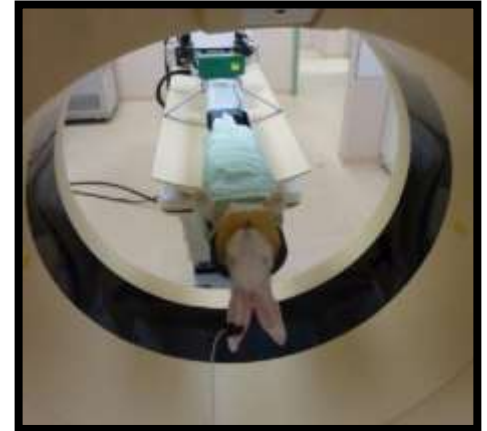


(1) Naha PC et al. *Publ Assoc.* 2015

(2) Cai Q-Y et al. *Invest Radiol.* 2007

MATERIAL/METHODS

- 3 adults NZW rabbits (3.3 ± 0.4 kg)
- Injection of 12 ml of AuNP
- Imaging protocol
 - D1: pre-injection (T0), 30-45 seconds (T1), 7-8 minutes (T2) after injection
 - Repetitive acquisitions over 6 months follow-up at one week (W1), one month (M1) and six months (M6)



MATERIAL/METHODS

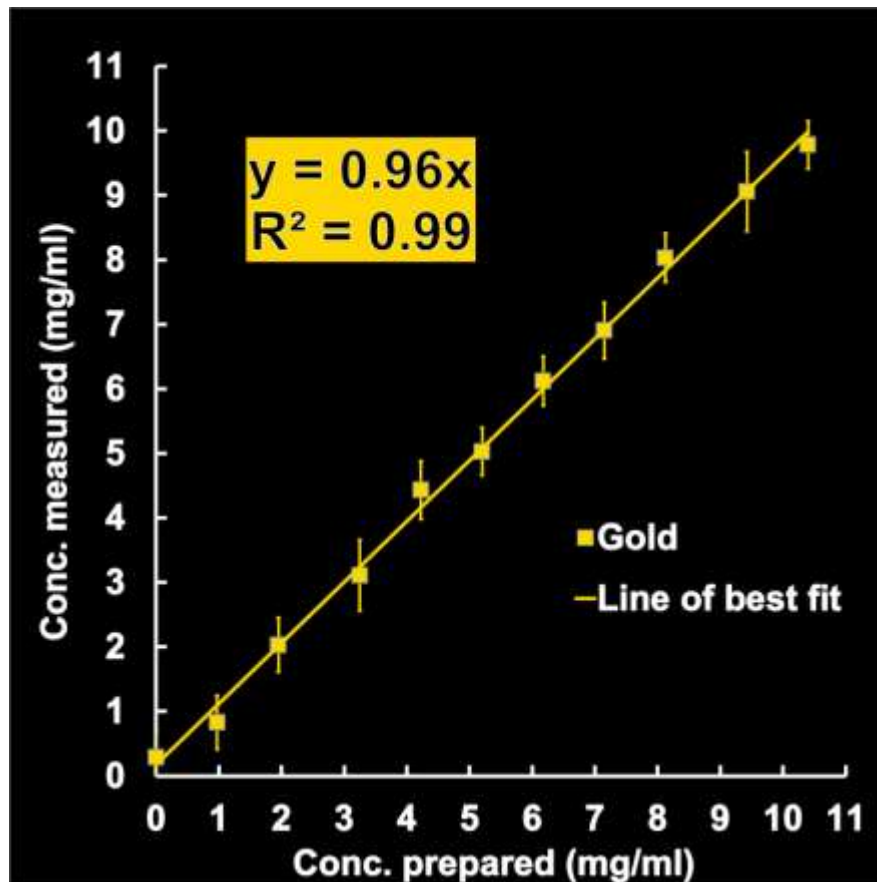
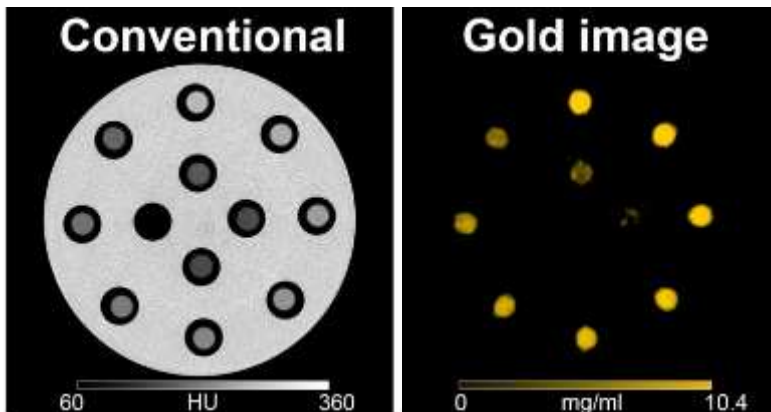
- Image reconstruction
 - Conventional images: HU units
 - Specific Gold images: mg/ml units
- Analysis
 - Regions of interest
 - Heart, kidney, brain
 - Organs of the mononuclear phagocyte system (MPS)
 - spleen, liver, bone marrow, lymph node

MATERIAL/METHODS

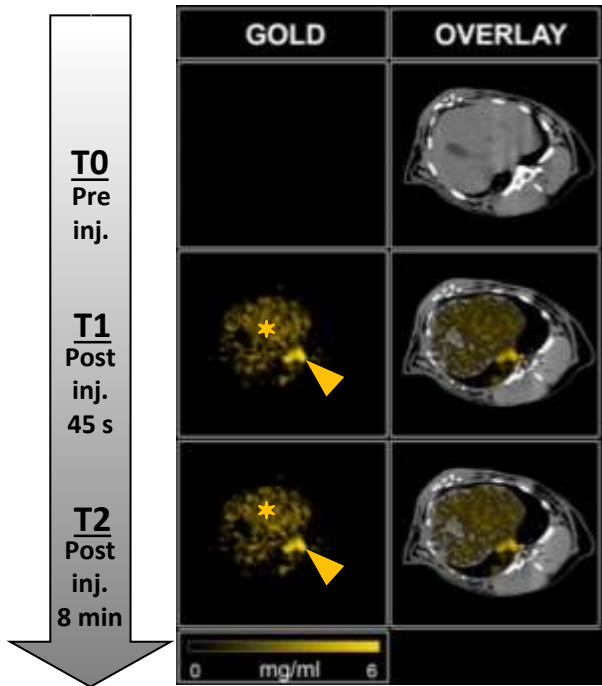
- Ex vivo analysis of the biodistribution of the gold nanoparticles by transmission electron microscopy (TEM)
- Correlation with inductively coupled plasma-optical emission spectrometry (ICP-OES)

RESULTS

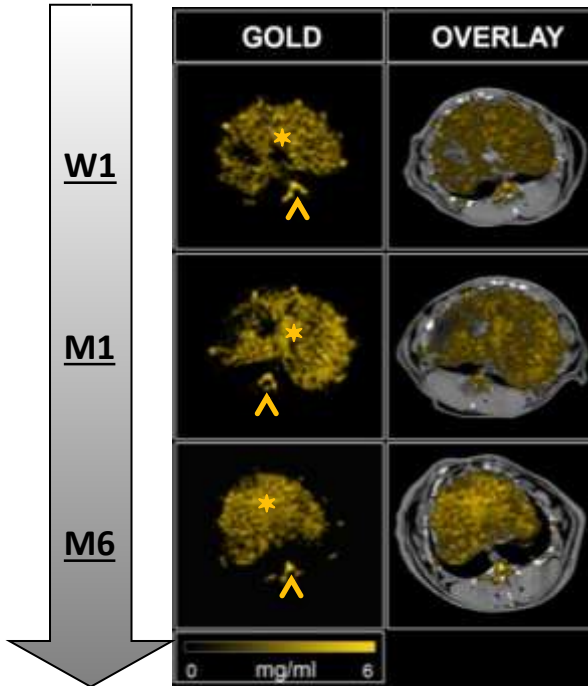
- In vitro imaging



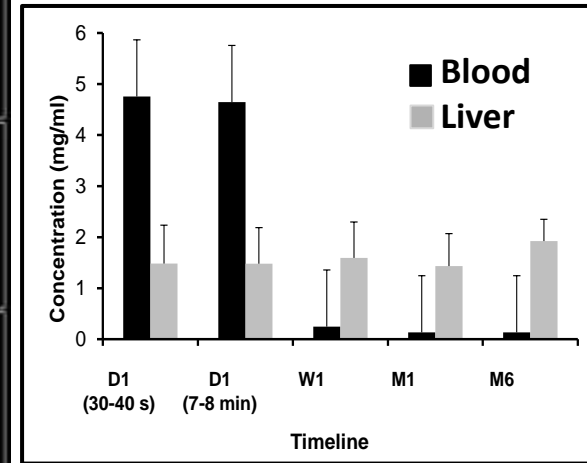
RESULTS



Day of injection: Perfusion imaging
=> **Blood pool effect**

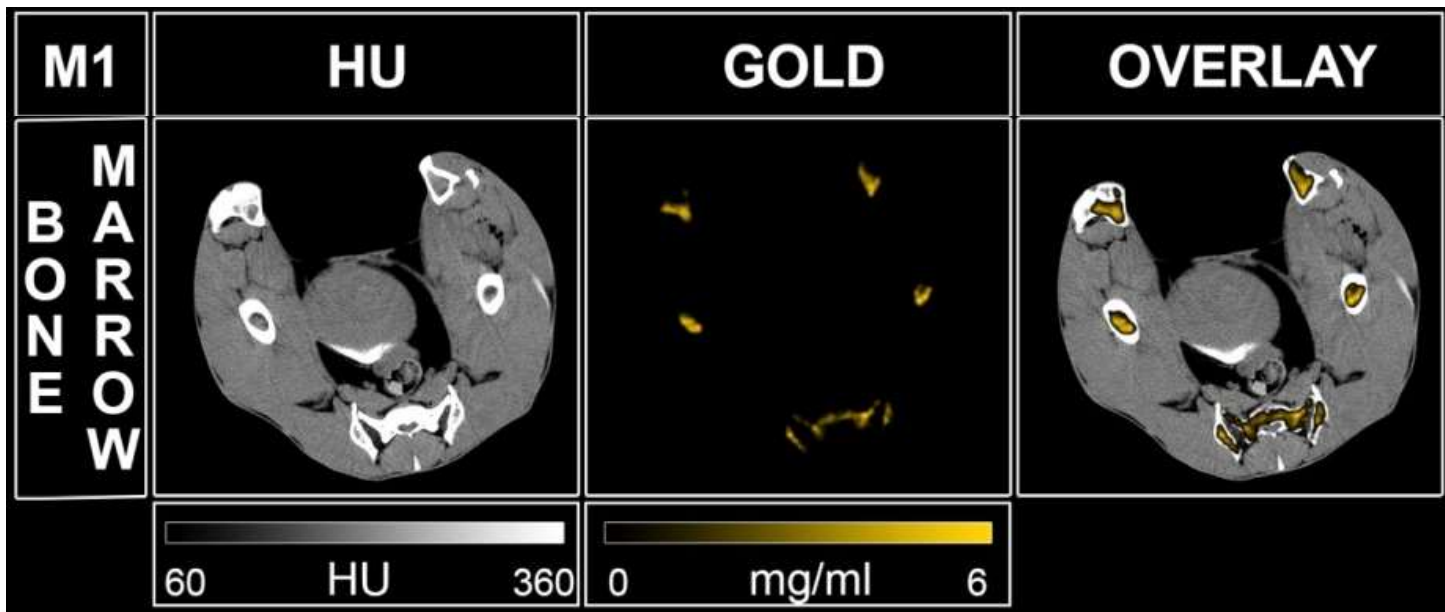


Follow up: Uptake imaging
=> **Mononuclear phagocyte system**



RESULTS

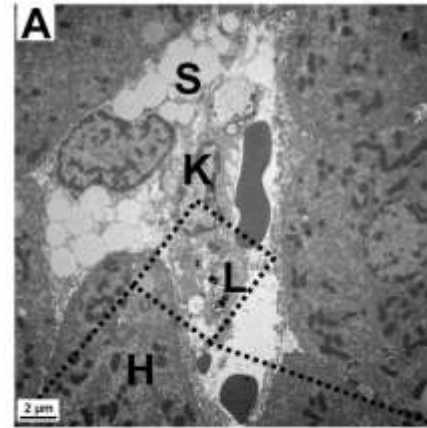
- Signal in the bone marrow at 1 month



RESULTS

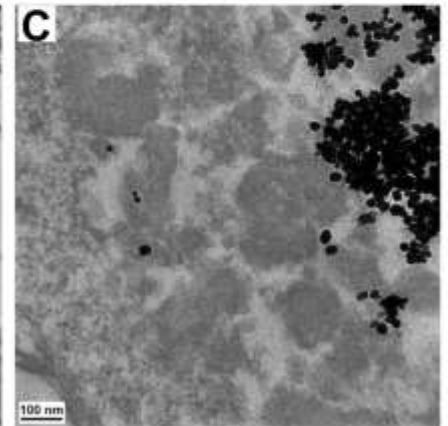
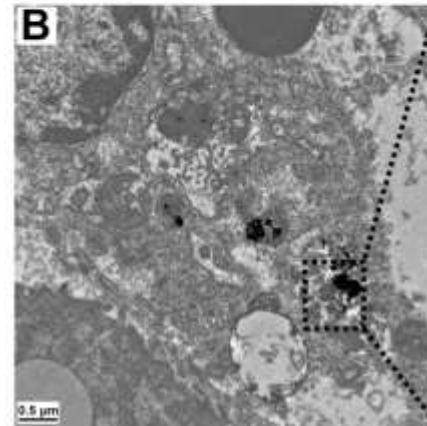
- Uptake in the organs of the MPS
 - Bone marrow
 - Liver
 - Spleen
 - Lymph node
- Aggregation in the macrophages⁽¹⁾

(1) Naha PC et al. *Toxicol. In Vitro.* 2015



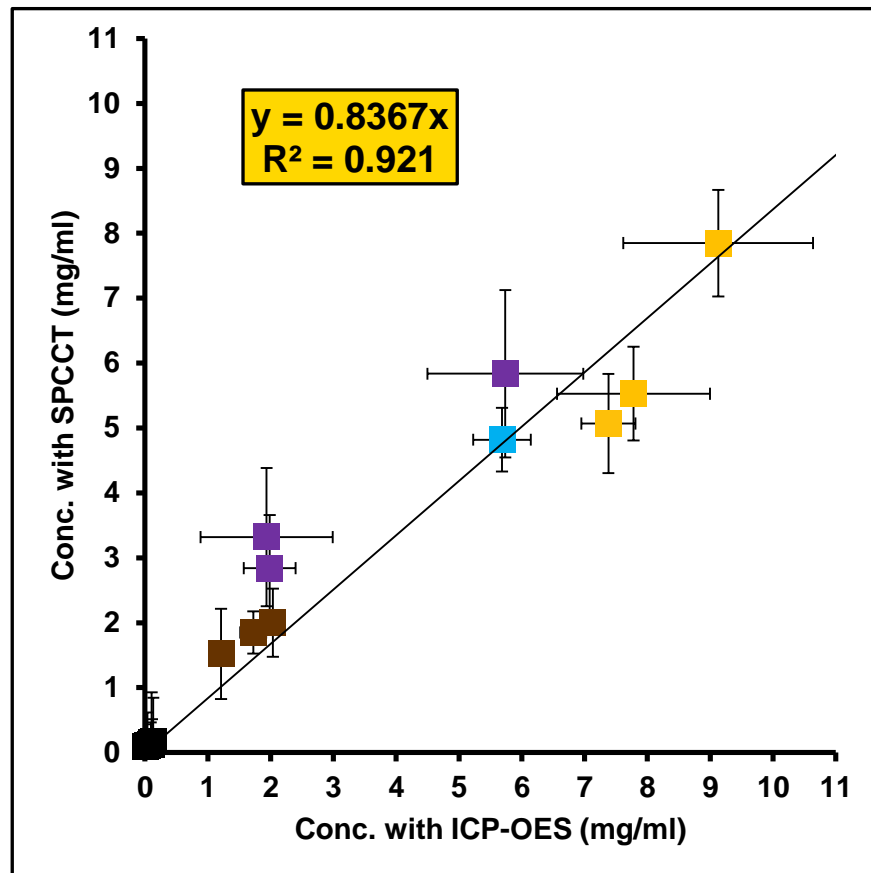
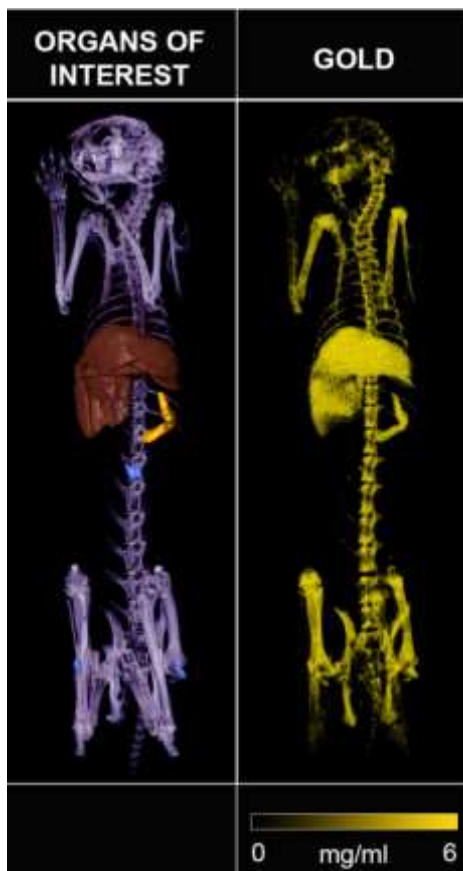
LIVER AT M6

K: Kupffer cell
S: Sinusoid
L: Lysosome
H: Hepatocyte



RESULTS

- Spleen
- Lymph node
- Bone marrow
- Liver
- Kidney, heart, brain, blood



CONCLUSION

- SPCCT is capable of assessing biodistribution of gold nanoparticles and quantitative in-vivo imaging of pharmacokinetics in organs over time.
- Gold nanoparticles appear to be suitable contrast agents for the vascular system initially and for the MPS over time, opening to at least two major applications in the field of cardiovascular disease, and hemato-oncology.
- BUT poor biological elimination leading to potential questions over long-term safety.

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