

The effect of polymer coating on the hepatic uptake and clearance of iron oxide nanoparticles studied by Magnetic Resonance Imaging

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Engineered nanoparticles have attracted widespread interest in biology and medicine. Studies have shown that in biological fluids such as intra or extra cellular media, the nanoparticles are coated with proteins and agglomerate, resulting in noticeable changes of their properties [1]. Fewer reports have addressed the issue of their *in vivo* behavior, and in particular in the blood circulation system. Here, we report on the pharmacokinetics of iron oxide nanoparticles coated with phosphonic acid poly(ethylene glycol) (PEG) copolymers. The uptake and clearance of iron-based probes were investigated in Magnetic Resonance Imaging (MRI) [2] by monitoring the signal intensity of the liver, spleen and arteries of mice as a function of the time. The time scale explored ranges from one minute to seven days after injection. Results show that phosphonic acid PEG-copolymers with multiple anchors build a 5 nm thick PEG layer around the particles [3] and are able to prolong their lifetime in the blood circulation by a factor 50 as compared to benchmarks. We demonstrate also that coating is the primary parameter that affects the liver uptake kinetics and elimination from the blood pool. In contrast, the clearance is independent on the core size, coating or particle stability. By comparing different polymer coats, we show that colloidal stability is a necessary but not a sufficient condition for prolonged circulation *in vivo*.

References

- [1] Safi, M.; Courtois, J.; Seigneuret, M.; Conjeaud, H.; Berret, J.-F., The effects of aggregation and protein corona on the cellular internalization of iron oxide nanoparticles. *Biomaterials* **2011**, *32*, 9353-9363.
- [2] Vuong, Q. L.; Berret, J. F.; Fresnais, J.; Gossuin, Y.; Sandre, O., A Universal Scaling Law to Predict the Efficiency of Magnetic Nanoparticles as MRI T2-Contrast Agents. *Adv. Healthc. Mater.* **2012**, *1*, 502-512.
- [3] Torrisi, V.; Graillot, A.; Vitorazi, L.; Crouzet, Q.; Marletta, G.; Loubat, C.; Berret, J.-F., Preventing Corona Effects: Multiphosphonic Acid Poly(ethylene glycol) Copolymers for Stable Stealth Iron Oxide Nanoparticles. *Biomacromolecules* **2014**, *15*, 3171-3179.