Gold Nanoparticles with Stably Embedded Cu-64 and Their Use in Nanoparticle Research - DTU Orbit (18/12/2018)

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$^{64}$Cu is a popular radionuclide for PET imaging and when $^{64}$Cu$^{2+}$ is mixed with gold nanoparticles (AuNPs) it adheres to the gold surface. Taking advantage of this, we developed methods to trap the $^{64}$Cu within the AuNPs by embedding under additional layers of gold. This resulted in radiolabelling efficiencies around 53 ± 6%. EDTA challenge for two days revealed the embedded $^{64}$Cu to possess excellent stability with 94-98% of the radioactivity remaining associated with the AuNPs. Testing for two days against serum likewise showed no loss of $^{64}$Cu from the $^{64}$Cu-AuNPs. Accordingly, the technology was shown to yield a very stable radiolabel that can accurately trace AuNPs in vivo. Such chelator-free radiolabelling removes traditional concerns over the use of chelators for $^{64}$Cu, notably instabilities of chelators, such as DOTA, and their ability to alter the surface and thus the biodistribution of the compounds onto which they are attached. Radiolabeled $^{64}$Cu-AuNPs were prepared in biomedically relevant sizes of 20-30 nm and decorated with three different coatings, in order to investigate their in vivo performance by PET imaging in a murine xenograft model. We found the longest plasma half-life (T½ about 9 hours) to result from a polyethylene glycol (PEG) coating, while faster elimination from the bloodstream was observed for both a Tween-20 stabilized coating and a zwitterionic coating based on sulfonic acids and quarternary amines. Accordingly, our data concluded the PEG coating to be most beneficial for long circulation in vivo. In the in vivo model, the $^{64}$Cu was observed to closely follow the AuNPs for each coating, again attributing to the excellent stability of the radiolabel. Further, $^{64}$Cu-AuNPs were prepared in three different sizes ranging from 30 to 70 nm and injected intravenously (I.V.) or intratumorally (I.T.) in murine xenograft models, either coated with PEG or stabilized by citrate (only 30 nm). In the I.T. experiments, citrate-stabilized $^{64}$Cu-AuNPs were retained best in the tumors with about 100 %ID/g after 24 hours. For the PEG-coated $^{64}$Cu-AuNPs, a tendency for increased retention as larger particles were injected was observed (30 nm: ~ 30 %ID/g, 70 nm: ~ 60%ID/g). In the I.V. experiments, the opposite tendency was observed, with smaller particles showing higher tumor accumulation and citrate stabilized $^{64}$Cu-AuNPs being rapidly taken up in liver and spleen. Our group continues work with embedding of radionuclides in solid nanoparticles and further results will be presented as available.

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