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Intratumoral injections of low-energy photon-emitting gold nanoparticles: a microdosimetry assessment

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Injections of gold nanoparticles (Au-NPs) at the vicinity of low-dose radioactive implants (containing 103Pd or 125I) could enhance the efficiency of prostate cancer brachytherapy. The interaction of low-energy photons with gold produces a large number of photoelectric events that are expected to lead to higher energy deposition. Understanding the impact of intracellular Au-NPs concentration and diffusion on the deposition of dose at the subcellular level is essential to achieve a good control of this emerging treatment. Here we report on the first microdosimetric study based on the microscopic mapping of radioactive Au-NPs injected in prostate cancer tumors.103Pd-doped Au-NPs were synthesized (50 nm diam.) and stabilised with biocompatible polyethylene glycol. The Au-NPs were injected intratumorally in a murine prostate cancer (PC3) xenograft model. CT imaging, transmission electron microscopy (TEM) and optical microscopy were used to follow-up the diffusion and the cell internalization of the Au-NPs. TEM histology maps were used to generate a microdosimetric Monte Carlo dose deposition study. The macroscopic distribution volume of Au-NPs after injection (2mm3), was estimated to 4.1 ± 1.6 mm3 (2h), 3.0 ± 0.9 mm3 (4 days), and 3.1 ± 1.2 mm3 (8 days). TEM and optical microscopy images confirmed the rapid uptake of the Au-NPs by the cells. After 2h, accumulations of Au-NPs were visible in vesicles. The activity in tumors was also measured, which confirmed the retention (80 %) of Au-NPs after 8 days. The microdosimetry assessment showed that energy deposition gradient is very steep and mostly confined inside the vesicles, which indicates that Au-NPs need to get closer of the nucleus to deliver the dose. In conclusion, radioactive nanoparticles were efficiently synthesized and showed good retention in tumors. Energy deposition from radioactive nanoparticles was calculated for the first time according to in vivo conditions and showed that the dose decreases dramatically at the edge of the vesicles.

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