Nanoparticle-assisted radiosensitization of human glioblastoma cells using high-energy photon and proton beams: Surface engineering for the enhancement of cancer radiotherapy

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Metal nanoparticles are a promising new class of sensitizer agents in cancer treatment using radiotherapy. When colocalized with biological tissue, NPs may augment cell kill induced by high-energy radiation due to specific physical, chemical and biological effects elicited by the particles, which are closely related to their surface properties. In spite of the positive results reported in a large number of pre-clinical studies, the underlying mechanisms behind NP-assisted radiosensitization are not yet fully understood. In this contribution, recent results from our group on the sensitization effects produced by metal nanoparticles of different formulations in human glioblastoma cells irradiated by high energy photons and proton beams will be presented. We explored three classes of NPs: superparamagnetic iron oxide coated with dextran (SPION@DX); gold coated either with dextran (GNP@DX) or PEG (GNP@PEG), and Bi nanoparticles. Two cell lines (U87 and M059J) were exposed to the NPs at various concentrations and subsequently irradiated with either x-rays from a 6 MV linear accelerator, 662 keV ɣ-rays from a 137Cs source, or 150 MeV H+ beams. Several markers were used to monitor the sensitization effect (NP uptake in the cells, cell viability, post- irradiation cell survival via clonogenic assay, production of reactive species, and DNA damage and repair). Enhancement sensitization ratios at 10% survival (SER10%) varying from 3.5 down to 1.0 (i.e. no effect) where observed, depending on the NP´s characteristics and type of cell. We will discuss the effect of the surface coating and nature of the metal core of the NPs and the type of beam on the sensitization effects, and present mechanistic insights derived from such studies.