Radiation Roulette and Cell Survival

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Background:
Mathematical and computational models, which describe the complex biophysical processes associated with radiation induced cell death, have been used since the early 1960s. In 1973, Chadwick first presented a mathematical formula which accurately fit experimental data of cell survival as a function of absorbed dose. It was the first model that attempted to consolidate theories of *macroscopic* dose deposition and *micro/nanoscopic* damages caused by ionising radiation. In macroscopic radiobiological models (such as Chadwick's) small scale behaviour is consolidated into a set of analytical equations representing the large scale behaviour of the system. While these models are fast in terms of computation time, they are not robust enough in order to predict outcomes for a wide range of input parameters. As physical, chemical and biological interactions of radiation within an organic medium are stochastic processes, a stochastic type model is required for their accurate description. As a result, with improvements to the speed and general availability of computer hardware, a transition is occurring from simple analytical models to more physically realistic stochastic (i.e. Monte Carlo) models. The Monte Carlo Damage Simulation (MCDS) software developed by Semenenko in 2004 was a significant step towards developing such a model, based on several adjustable physical and biological parameters: the number of strand breaks and the number of base damages per gray of radiation per cell, as well as the DNA segment length which defines the minimum separation between isolated ionisation events to be considered as two separate lesions.

Current work:
At our institution, we have developed an integrated radiobiological model by combining several "in-house" generated models with existing Monte Carlo particle tracking toolkits (GEANT4). The result is a simulation that can: grow a tumour/cell structure composed of individual cells (with realistic chemical composition and geometry), irradiate the cells, record the microdosimetric track structure in each cell, cluster spatially correlated ionisation events into DNA double strand breaks and then predict the likelihood that any given cell will survive. The novelty of this model is its ability to predict both the microscopic and macroscopic outcome of radiobiology experiments while varying input parameters such as: cell line, radiation type, tumour geometry, dose etc. This model was applied to the novel treatment modality of radiation sensitisation of cells by gold nano-particles. The photon energy, gold concentration dependence, contribution from Auger electrons and the effect of delivery method were investigated. In another simulation, low energy (0.76 MeV) protons were used to irradiate a mono-layer of V79 CHO cells and to predict the cell survival fraction, replicating a published experiment in the attempt to validate the model in its entirety by comparing modelled cell survival with experimental data.

It is hoped that this model will be used to improve our understanding of the mechanisms of biological damage of photons, electrons, protons and other perticles in both the clinical and space environments.