Abstract

The aim of this dissertation was to determine the relationship between the nanometre-scale structure of radiation tracks and the radiobiological response of normal and tumour cells irradiated with protons, α particles, and carbon ions. I investigated whether parameters describing ionization cluster size distributions could serve as radiation-quality descriptors complementary to conventional quantities such as linear energy transfer (LET) and relative biological effectiveness (RBE). In the experimental part, I characterized a ^{241}Am source and constructed a system for irradiating cells with α particles. The source model developed in Geant4 was validated using a silicon detector and EBT3–Unlaminated radiochromic films. Using the developed setup, I irradiated PC3 and DU145 prostate cancer cells and assessed their response with a clonogenic assay. Ionization cluster size distributions were determined from Geant4-DNA simulations by counting ionizations within cylindrical volumes corresponding to a DNA segment of approximately 10 base pairs. From the resulting distributions, I calculated the mean cluster size M_1, the cumulative probabilities F_k, and the weighted cumulative probability fraction, hereafter denoted as the R_2 parameter. The results showed that particles with similar LET values may produce different ionization cluster size distributions, indicating that LET does not uniquely describe the local spatial distribution of ionizations at the DNA scale. The R_2 parameter was a more stable descriptor than the individual threshold parameters F_k. I related the nanodosimetric parameters to the effective cell-inactivation cross section $\sigma_{5\%}$, determined, among other quantities, from the α and β parameters of the linear-quadratic model. For normal cell lines, I obtained the relationship $\sigma_{5\%} = KR_2 + B$, from which I estimated the value of the parameter K, comparable to the cross-sectional area of the cell nucleus. Differences in the radiosensitivity of tumour cell lines were described using the parameter p, representing the probability of lethal damage accumulation in the R_2 model. This parameter was inversely related to the area under the survival curve for reference radiation, commonly used as a measure of radiosensitivity. The results indicate that nanodosimetric parameters provide information unavailable from a description based solely on LET and dose. Combining the R_2 parameter, which describes the physical structure of the radiation track, with the parameter p, being associated with the individual radiosensitivity of cells, may provide a basis for a more universal description of the biological response to charged-particle radiation.

Keywords:

nanodosimetry, radiation track structure, ionisation clusters, ICSD, R_2 model, probability of sublethal damage, Geant4-DNA, cell survival, linear energy transfer, relative biological effectiveness, linear-quadratic model