

CONSIDERING THE SPATIAL ORGANIZATION OF DNA TO ASSESS PROTON THERAPY RELATIVE BIOLOGICAL EFFECTIVENESS

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Increased use of computer simulations in treatment planning for cancer has highlighted the need for more effective methods in modelling nuclear organisation. Current models aim to predict treatment outcomes by simulating the induction of double strand breaks in the DNA of irradiated cells. In proton therapy, this is achieved via use of Geant-4 software, which tracks electron activity after irradiation with a proton beam. Predictive assays can then be used to assess the value of the relative biological effectiveness (RBE) for protons. Currently, the proton RBE value of 1.1 is taken from results in clinical practice; with proton therapy machinery calibrated using depth dose distribution in water for beams of varying energies. It is thought that a more appropriate value could be computed by analysing to what extent proton beams cause chromosome aberrations, a form of genomic reorganisation that indicates damage to the cell nucleus. For this objective to be realized, the geometric organisation of the nucleus needs to be accurately modelled so that it can be integrated with cellular irradiation simulations. This review describes and evaluates some of the modelling approaches for chromosome territories, and aims to recommend a particular approach that research groups involved in proton therapy can use in their work.

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