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Microdosimetric and Biokinetic Modelling of Alpha-Immuno-Conjugate Transport in Endothelial Cells

Background and Objective:
The characterization of the Alpha-Immuno-Conjugate (AIC) targeted delivery process under vascular environment is very challenging due to the small scale of AIC particles, decay chain of the labeled radionuclide and the complex in vivo vascular system. To understand such a complex system, computational biokinetic model and microdosimetric model have been developed at Canadian Nuclear Laboratories (CNL) to help understand the AIC targeted delivery process and efficacy. The overall aim is to assist in the optimization and personalization of the treatment of patients.
Methods:1) Biokinetic model based on computational fluid dynamics (CFD) method is developed to study the blood flow through a two-dimensional Endothelial Cell (EC) embedded in a solid tumour or a normal cell. This model includes the collision model to handle the interactions of multiple particles in an administered conjugate. Immersed boundary method was used to handle the multiple moving particles in the capillary after the intravenous injection of AIC. A mesoscale modeling is applied in order to gain an understanding of AIC transport in capillary so that the time-dependent location of the AICs can be predicted. The resulting locations of radiation sources can be used as an input by the dosimetric model to predict the absorbed dose. 2) Microdosimetic modeling based on alpha Monte Carlo simulation toolkit was developed in FORTRAN programming language to calculate the amounts of the energy deposited in a simplified nucleus model from internal moving emitters and evaluate the single-event spectra for alpha particle emitters. The model can handle various alpha kinetic energies based on emitters with long decay chains. 3)The coupled biokinetic and Monte Carlo models would be integrated into a generic coupling framework such as SALOME as reusable modules in order to capture the rapid changes involving the phenomenological interdependencies in biological effects to evaluate the efficacy and toxicity of the AIC. The resulting large amount of data calculated by the coupled high fidelity CFD simulation and microdosimetric analysis can be processed in real time by a visualization tool.

Results and Discussions: A coupled model based on a simplified and the Geant4 Monte Carlo micro-dosimetry technique and Computational Fluid Dynamics analysis for multiple particle movement was established. The transient AIC delivery process and the absorbed dose to the EC cells in the capillary are investigated to determine the transient toxicity of the AIC. The model to implement the decay scheme for radionuclide such as 225Ac is under development. The Multiphysics model presented in this abstract demonstrates the feasibility of combined biokinetic and microdosimetric modeling to evaluate the efficacy of the TAT.

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