Ecole Doctorale des Sciences Fondamentales

Title of the thesis: Monte Carlo simulations of microdosimetry and radiolytic species production for very high dose rate preclinical proton and alpha beams using GATE and Geant4-DNA.

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Summary:

Among the recent developments in the field of preclinical radiotherapy, the remarkable sparing of normal tissue obtained after irradiation at very high dose rate (VHDR), the so-called FLASH effect, is really promising. The Physics laboratory of Clermont is collaborating with ARRONAX, Subatech and Institut de Cancérologie de l'Ouest (ICO) in order to set up Monte Carlo simulations of microdosimetry experiments performed under VHDR (till 10 kGy/s) proton (67 MeV) and later on alpha preclinical beam lines with Spread Out Bragg Peaks (SOBP).

The role of oxygen in FLASH irradiation is of high concern. Like specified in the theoretical review of FLASH therapy; Spitz et al. (Spitz 2019) explain that VHDR irradiations consume all available oxygen in tissue and liberate significantly more electrons to ionize the medium and organic hydroperoxides (ROOH) instead of conventional dose rates. This is impacting then the free radical chemistry during the irradiation and in the end, the cell damage. The Geant4-DNA Monte Carlo track structure code, the first open source and open access simulation platform dedicated to nanodosimetry and radiation biology is now proposing the simulation of chemical yields resulting from water radiolysis or Fricke dosimetry with possible scavengers under VHDR beams.

The PhD thesis will be segmented in three main topics:

- First, the candidate will have to reproduce VHDR proton and alpha beam lines using the GATE Monte Carlo platform in order to simulate water radiolysis and Fricke dosimetry at different depth along the SOBP through Geant4-DNA. Results will be validated with experimental measurements of radiolytic species (H_2O_2 and $OH^{\cdot}$) under normoxic or hypoxic conditions performed by collaborators from Subatech.
- The candidate will use the quantification of chemistry products responsible for indirect tissue and cell damage to calculate the biological dose delivered to cells and xenograft tumours on small animals. To that purpose, the PhD student will adapt a specific tool, the BioDoseActor, developed within the open-source GATE Monte Carlo platform to predict cell survivals under preclinical and clinical ion beams at the voxel scale. This tool needs to be validated and adapted for VHDR beams.
- Finally, the candidate will validate simulated cell survival fractions with experimental data from ICO and Subatech collaborators for different cell lines.

The candidate will join a dynamic group whose research is at the interface between physics and life sciences, this group includes physicists, computer engineers, biologists and chemists.

This thesis requires skills in medical physics and computer science. Knowledge of different Monte Carlo algorithms and / or software will be highly appreciated, especially the knowledge of the C ++ and Python programming languages.