Titre Thèse	**Computer Simulation and Experiments of Radio-Induced Cell Senescence**	
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Résumé du sujet :

Medical use of radiations for treating cancers and other diseases rests on a vast amount of empirical knowledge, accumulated over the past century. However, rather little attention is yet paid to the biological specificity of the individual cell response to ionizing radiation. Computer modelling of DNA damage and repair aims to give quantifiable depictions of the DNA damage response following therapeutic irradiation. Notably, a severe complication of radiation therapy is identified in the development of secondary sarcomas around the irradiated field, a very rare, difficult to predict, but often lethal pathology. According to a number of experimental indications, accumulated by our groups and others, it is supposed that normal cells around the treated primary cancer might be affected by scattered ionizing radiation, which diffuse in uncontrolled way from the irradiated main volume, and that the peculiar type of damage accumulated in this way could induce these cells into senescence; upon exiting from this state at much later times, defects latently accumulated in some such cells could evolve the secondary sarcoma.

We propose to develop a complete computer model of the cell treatment, starting from the detailed description of the irradiation source by Monte Carlo dosimetry and micro-dosimetry; include a multicellular, evolutive description of the irradiated tissue; radiation damage and repair will be treated in full details at the scale of each single cell, including competitive pathways for different types of DNA and cell damage; dedicated high-resolution biology experiments will define ranges of values for fitting the model parameters, and provide benchmarks to test and improve the computer simulations.

The candidate PhD student will work at the mathematical and computer developments, and take part in the biology experiments, in our **two laboratories of IEMN (UMR8520)** and **CanTher (UMR8161) in Lille**. Part of the model development will take place in the **Cancer Sciences Division at the University of Manchester, UK**. The resulting computational/experimental protocol would represent an important step forward into the domain of high-precision, personalized healthcare, by defining a general approach by which the detailed biological effects of different types of cell damage could be predicted by mathematical modelling.

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