Subject (M1-M2): "Radiotherapy sparing effect on the circulating lymphocytes: development of a time-dependent framework to score the dose"

Host structure

The Institut Curie is a major player in cancer research and treatment. It consists of a hospital and a research center with more than 3,000 employees and a strong international presence. The Orsay Proton therapy Center (CPO) founded in 1991 is part of the radiation oncology department at Institut Curie hospital group, which is one of the European-wide recognition as a Comprehensive Cancer Center of excellence. This internship will be carried out as part of a research project whose goal is to investigate **new dose calculation tools for FLASH ultra-high dose rate radiotherapy**, and is an exciting opportunity to join the radiation therapy research activities in Orsay, within the hospital and the research center.

Subject description

Within the medical physics research team based at the Institut Curie Orsay (91), we are looking for a student, with a strong interest in translational research on cancer radiation therapy. As part of the activities of our team, the student would be expected to **develop a time-dependent framework to score the dose to the circulating lymphocytes during the course of radiotherapy**.

Indeed, radiation therapy is currently one of the main techniques used for cancer treatment. More than 50% of patients treated for cancer - about 180,000 per year in France - benefit from it. Over the last thirty years, numerous technical advances have made it possible to considerably improve the conformation of irradiation to the specific characteristics of each tumour and to reduce their side effects. Nevertheless, **the tolerance of healthy tissues** remains the main limitation of this type of treatment, particularly in the case of particularly radiosensitive patients, such as children, for whom controlling the side effects of radiotherapy remains a major therapeutic challenge. Recently, pioneering work conducted at Institut Curie has shown that ultra-high dose rate irradiation (known as **FLASH**) has a major effect in sparing healthy tissue - while preserving anti-tumor efficacy (Favaudon et al 2014). Photons or charged particles (protons or electrons) radiotherapy with intensity modulation and pencil beam scanning techniques are now the reference techniques for the majority of treatments (Figure 1) and can also be used to implement FLASH therapy.

Radiation-induced lymphopenia (RIL) describes the depletion of circulating lymphocytes by external radiation fields. RIL has been reported to correlate strongly with overall survival and tumor recurrence in various cancers. Indeed, lymphocytes circulating in the blood (being highly radiosensitive already at 2Gy) could constitute one of the targets of radiation and could be quantified by assessing the proportion of blood irradiated during irradiation (much smaller in volume but at higher doses if the dose rate is increased). One hypothesis to explain the biological effects of FLASH therefore relates to the different modulation of immune effects depending on the type of irradiation and the dose rate, a variable quantity in space and time.

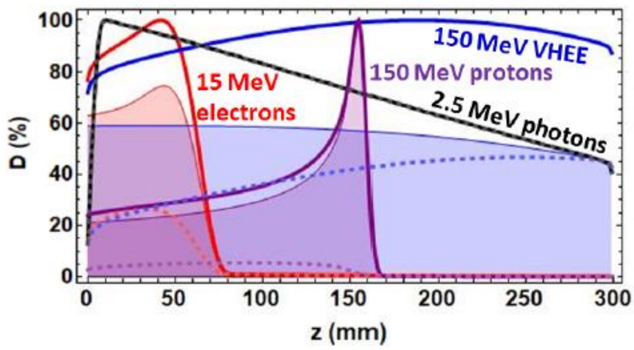

Figure 1: Depth dose distribution in water for several radiation types (photons, electrons, protons, Lagzda 2019).

Dose calculations in radiotherapy are mainly based on fast but accurate dose calculation algorithms, such as superposition/convolutions or Monte Carlo simulations, which do not currently take into account the temporal aspects of the dose delivery. However, this physical parameter has started to be taken into account and more precise characterisation of irradiation is now available in research tools.

Several 4D blood flow models to compute the dose to circulating blood during brain irradiation also already exist (Shin et al 2021, Hammi et al 2023), usually neglecting whole-body blood dynamics and re-circulation. The aim of this work will be to implement such a hematological dose framework to compute blood dose volume-distribution for radiotherapy to any treatment site based on various organs with appropriate accounting of probabilistic blood flow and dose. This 4D computational framework will be tested for time-dependent radiation field delivery of modern intensity modulated radiation therapy (IMRT) techniques, and then for FLASH pencil beam scanning proton therapy, by simulating the blood flow during a realistic radiotherapy delivery and thereby determining the dose delivered to the lymphocytes. Correlations on series of patients already treated (breast cancer with IMRT) or prospective simulations (FLASH PT) will then be carried out.

Profile required

The candidate must be enrolled in a master degree (or equivalent) in physics • Radiation matter interactions / radiation therapy • Preferred experience in programming skills (Python or MATLAB) – Monte Carlo simulations (eg Geant4). You will also be expected to work as part of a multidisciplinary team.

Informations sur le contrat

Type of contract: Internship
Contract duration/Starting date: *4 months*
Working hours: Full time – *39h/week*
Remuneration: according to our current standards.
Benefits*:* Collective restaurant, 70% reimbursement of the transport ticket, company mutual insurance
Location: Institut Curie, Centre de protonthérapie d'Orsay, France
Reference: LC

Contact

Please apply by e-mail (CV + application letter) to ludovic.demarzi@curie.fr and pierre.loap@curie.fr

Institut Curie is an inclusive, equal opportunity employer and is dedicated to the highest standards of research integrity. All our opportunities are open to people with disabilities.

References

Favaudon V, Caplier L, Monceau V, et al. Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. Sci Transl Med. 2014;6(245):245ra93. doi:10.1126/scitranslmed.3008973

Shin J, Xing S, McCullum L, Hammi A, Pursley J, Correa CA, Withrow J, Domal S, Bolch W, Paganetti H, Grassberger C. HEDOS-a computational tool to assess radiation dose to circulating blood cells during external beam radiotherapy based on whole-body blood flow simulations. Phys Med Biol. 2021;66(16):10.1088/1361-6560/ac16ea.

Hammi. (2023). 4D dosimetric-blood flow model: impact of prolonged fraction delivery times of IMRT on the dose to the circulating lymphocytes. Physics in medicine and biology, 68(14), 10.1088/1361-6560/acdcdc