Automated lattice radiation therapy planning personalised to tumor size, shape and biology

Sarcomas are known to be large, radioresistant tumors. Radiotherapy treatment is generally administered using an intensity-modulated radiotherapy technique, at 2Gy per fraction in 25-30 fractions (1). However, in many cases, dose escalation up to 60Gy or more is impossible due to the tolerance of surrounding organs at risk (OARs). In parallel, stereotactic radiotherapy (SBRT), which consists in delivering higher doses per fraction (typically 6-25Gy), in few fractions (1-5), has shown its efficiency in treating radioresistant tumors, and could be indicated. However, SBRT on the whole volume is prohibited, otherwise it could have a major impact on the OARs.

Spatially fractionated radiotherapy (SFRT) is an innovative irradiation technique using heterogeneous dose distribution, alternately delivering high doses (peaks) and low doses (valleys) within the tumor (2). This technique therefore makes it possible to treat bulky tumors that are inaccessible to SBRT with ablative doses, while limiting potential toxicity to the surrounding healthy tissues. Lattice radiotherapy (LRT) represents the 3-dimensional approach of SFRT. First clinical results of LRT obtained on various tumor types are encouraging (3).

The radiobiological mechanisms of LRT are currently unclear. The main hypotheses for its efficacy are the bystander effect, modulation of tumor vasculature and the immune system. High doses promote the release of tumor antigens, which are recognized by antigen-presenting cells and thus trigger an immune response. However, these high doses also exert an immunosuppressive effect through various mechanisms. Low doses, on the other hand, have an immunostimulatory effect on the tumor microenvironment. Thus, the peak/valley dose distribution characteristic of LRT is thought to enhance the anti-tumor immune response.

In our Cancer Center, few patients have already been treated using the well-described irradiation geometry of Duriseti et al (2). However, this geometry is sometimes limited for certain intermediate-volume tumors. In this context, we propose to:

- Evaluate dosimetrically different geometries (different diameters/spacing) = diameters of spheres (between 10 and 15 mm), evenly spaced 3-6cm from center to center while trying to respect a more or less identical peak/valley dose ratio to control toxicity.
- Perform a dosimetric evaluation under linac: does the precision of the dose distribution become less accurate as the diameter of the sphere decreases?
- Develop a routine which will automatically optimize the spatial distribution and the number of spheres in the GTV, taking into account the geometry of the tumor and the proximity of the OARs.

In a second phase, information on the spatial biology of the tumor will be also considered to further improve the distribution of the spheres within the tumor. To do so, we first plan to use multiparametric-MRI (mp-MRI) sequences. Mp-MRI images will allow identifying tumor sub-regions such as necrosis, viable and proliferating tissue, and hypoxia regions. In parallel we will also explore suitable hypoxic markers to implement in PET/CT to further explore different treatment strategies combining either LRT/MRI or LRT/PET.

The PhD will be conducted in the CREATIS lab, team “tomoradio”, located in the radiation therapy department of the Léon Bérard cancer center, Lyon, France.

References:

(1) Le Péchoux C, Llacer C, Sargos P, Moureau-Zabotto L, Ducassou A, Sunyach MP, Biston MC, Thariat J. Conformal radiotherapy in management of soft tissue sarcoma in adults.Cancer Radiother. 2022 Feb-Apr;26(1-2):377-387.

(2) Duriseti S, Kavanaugh J, Goddu S, Price A, Knutson N, Reynoso F, et al. Spatially fractionated stereotactic body radiation therapy (Lattice) for large tumors. Adv Radiat Oncol. 2021;6(3):100639

(3) Iori F, Cappelli A, D'Angelo E, Cozzi S, Ghersi SF, De Felice F, Ciammella P, Bruni A, Iotti C. Lattice Radiation Therapy in clinical practice: A systematic review. Clin Transl Radiat Oncol. 2022 Dec 20;39:100569.

Applicant profile: Medical physicist, data analysis

Location: Léon Bérard center, radiation therapy department, CREATIS lab, Lyon, France

Length: 3 years starting in February 2024

Contact: Please send your CV and application letter by email to:

- Marie-Claude Biston, Responsable unité de Physique, HDR, Centre Léon Bérard, marie-claude.biston@lyon.unicancer.fr

- David Sarrut, DR CNRS, david.sarrut@creatis.insa-lyon.fr

Applications will be gathered until end of December 2024. Interviews will be conducted by videoconference or in Lyon depending on availability.