Subject 1 : **Evaluation of the effectiveness of FLASH irradiation in the presence of AGuix® nanoparticles**

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To improve the effectiveness of conventional radiotherapy, the use of a new irradiation technique has been proposed: high dose rate (>100 Gy/s) radiotherapy (UHDR) called RT FLASH. This consists of delivering the prescribed radiation dose over a very short time interval (a few milliseconds). By increasing the differential effect between the tumor and the healthy tissues, it makes it possible on the one hand to limit toxicities on the organs at risk while guaranteeing anti-tumor efficacy comparable to that of conventional treatments [1]. With equivalent toxicity, RT-FLASH also makes it possible to increase the dose delivered to the tumor to increase local control and therefore proves to be promising for the treatment of radioresistant tumours. In order to further increase the therapeutic window, we propose to couple this new irradiation modality with the use of metallic nanoparticles of Gadolinium (AGuIX®), capable of preferentially enriching tumors and locally amplifying the effect of radiation [2]. These two innovative treatment strategies have already demonstrated their effectiveness in preclinical studies and are currently being transferred to the clinic in several trials [3-4]. However, although the respective potential of each approach has been demonstrated, there is currently no work aimed at studying the synergy of these two techniques, in particular on the maintenance of the radioamplifier effect of nanoparticles under irradiation conditions. UHDR. The proposed internship will aim to investigate this possibility of combination by first evaluating its effectiveness at the cellular level. This will be done using a 3D cell model, in this case spheroids composed of B16-F10 cells (mouse melanoma). Several irradiations will be carried out in RT (Gustave Roussy) and RT FLASH (CHUV Lausanne, Switzerland), with and without nanoparticles. The efficacy of the proposed treatment will be assessed through clonogenic assays to obtain cell survival curves. If it exists, the radioamplifier effect obtained with RT FLASH (> 100 Gy/s, irradiation duration < 100 ms) will then be compared to that obtained with conventional RT (0.03 Gy/s, irradiation duration > 500 sec). Finally, the cell death processes at the origin of the FLASH effect, in the presence or not of NPs, can be characterized by flow cytometry. This internship subject, which aims to establish a proof of concept of the combination, will serve as a basis for subsequent studies aimed at studying the influence of the degree of tumor oxygenation in the effectiveness of the combination and the impact of the temporal parameters of the beam of RT FLASH on the synergy studied.

Internship duration : 6 months
Your profile: M2 in Medical Physics, M2 SERP or any other M2 interfacing Physics/Chemistry/Biology/Medicine
Gratification : 591.51 €/month

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