

Radiation therapy (RT) is an effective method of treating cancer and is used in approximately 40- 50% of cancer patients, however, like any other therapy carries a risk of side effects. The optimistic treatment relies on the reduction of damage to healthy tissues. For this purpose, a new therapeutic technology was developed consisting in the treatment of neoplasm using the so-called FLASH radiotherapy. FLASH radiotherapy involves the use of an ultra-high dose rate (20-100 Gy /s) compared to the currently used radiotherapy, which uses conventional (much smaller) dose rates (0.5-5 Gy / min). Studies on an animal model have shown that the use of FLASH radiotherapy reduces the side effects of radiotherapy (increases the tolerance of healthy tissues), while maintaining the effectiveness of the treatment. The aim of the project is to broaden the knowledge of the physical and biological processes that take place in the tumour and healthy tissues (organs) during ultra-high dose electron radiation therapy. The project will verify four hypotheses: (1) the response of detectors placed in the electron beam for conventional and ultra-high dose rate therapy is different and requires the development of calibration factors, (2) oxygenation modifies the response of cancer and healthy cells in vitro after conventional radiotherapy and ultra high dose rate, (3) the Monte Carlo method allows to simulate the processes taking place in biological material at different levels of oxygenation after conventional and ultra high dose radiation therapy, and (4) complications (side effects) in the critical organs located in the chest are smaller after radiotherapy ultra high dose rate than conventional dose rate. In preclinical studies, oxygen deficiency and transient hypoxia have been shown to be responsible for the increased tolerance to FLASH radiation, thus providing a protective effect in healthy tissues but not in tumour cells. The first clinical application of FLASH-RT was described by Bourhis et al., who treated a patient with T-type leukaemia. It is also believed that the use of FLASH-RT can also improve the accuracy of tumour irradiation due to the short delivery time, which eliminates the need to compensate for tissue and tumour movement during radiation delivery. For the wider use of FLASH-RT, much more data, both preclinical and clinical, is needed to elucidate the nature of the interaction of this type of radiation both at the molecular level and at the tissue and organ level, and a better understanding of its clinical effects. Moreover, it is necessary to develop more accurate and more sensitive measurement methods for FLASH radiation. The project will implement four work packages (WPs). A modified AQUIRE-FLASH accelerator, developed in cooperation with the National Centre for Nuclear Research, will be used. In WP1, we will construct appropriate phantoms and measure radiation doses for various detectors. The sensitivity, saturation and linearity of detector responses for megavolt electron radiation at conventional and ultra-high dose rates will be studied. In WP2, radiation-induced biological damage in cells of established normal and neoplastic cell lines under various oxygen concentration conditions will be studied. Human and mouse lung cancer cells and normal heart (HL-1), lung (MRC-5), skin (BJ-5ta) and endothelial cells (HUVEC) will be used. In WP3, after analysing the design of devices involved in the emission, scattering and absorption of radiation from the source to the tissues, a Monte Carlo model will be built to simulate the processes in cells in vitro at different oxygenation levels. In WP4, the complications of organs located in the chest after FLASHRT in the mice model will be examined along with the examination of tumour response. It will also be studied whether the immune response after FLASH-RT is significant for the FLASH effect.