**Titel: FLASH-Irradiation and Dosimetry in Proton-Beams**

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**Zusammenfassung des Projekts**

In recent years, several radio-biological animal studies have investigated dose-rates of more than 40 Gy/s - the so-called FLASH range - and found in single fraction irradiations significant increase of normal tissue tolerances compared to conventional dose-rates (2-20 Gy/min) with apparently unchanged tumor sensitivity. FLASH-irradiation thus may offer the opportunity to significantly reduce side effects of radiation therapy and still achieve the same outcome or to increase the tumor dose. In summer 2019 the first treatment of a first patient suffering from cutaneous lymphoma using high dose rate electron irradiation was reported, showing a tremendously reduced skin reaction as compared to classical treatments. However, the biological-chemical processes of the apparent radio-protective effect of the high dose rate has so far not been understood. One of the main causes for this is currently still seen in an inconsistent data situation in the area of the temporal and local energy-depositions in the cell and dose-measurements. The origin of these inconsistencies can mainly be found in different accelerator techniques offering either pulsed or continuous dose delivery with X-rays, electrons or protons. An essential base for solving this problem is the accuracte measurement of the spatio-temporal dose distribution during irradiation. Dosimetry in the FLASH range is a significant challenge, since the existing clinical dosimetry measuring systems cannot be simply transferred to the FLASH range due to the high dose rates and the need for spatio-temporal measurement. In this work the methods and tools to perform irradiations at FLASH and conventional dose rates with well-controlled spatio-temporal properties at a beam line of the KVI-CART cyclotron will be developed and implemented. At this beam line, for the first time biological and animal experiments will be possible in different doses-per-pulse in proton beams with full control on the spatio-temporal characteristics of the dose delivery. The beam line will thereby support the systematic search for the onset and origin of the radioprotectivity of this new technique. As an accurate and reliable dosimetry will be essential for FLASH, the dosimetrical characterization and stable monitoring of the beam will be developed by means of several independent detection principles. Detector and electronics failures by radiation interactions will become a major problem in these high-dose rate beams. These failures may play a critical role during radiobiological experiments as repetition or termination of cell- or animal experiments due to faulty equipment must be avoided both scientifically and ethically. Therefore a work package is devoted to the set up and evaluation of a test-environment for these problems. The project will be carried out in an European Consortium with academic and industrial partners from Germany, The Netherlands, France and Switzerland