## From Plasmid DNA to FLASH Radiotherapy: Experimental and Computational Insights

Radiotherapy, along with chemotherapy and surgery, is one of the basic methods of treating oncological patients. The goal of radiotherapy is to deliver a maximum dose of ionizing radiation to the tumor volume to kill its cells while simultaneously minimizing the dose delivered to the healthy tissues surrounding the tumor. Researchers are continuously looking for better ways to limit side effects, especially by understanding how different types of radiation affect the body. Recently, intense research has been conducted on a new method known as "FLASH radiotherapy", which involves delivering extremely high doses of radiation in a fraction of a second. This method has shown promise in reducing damage to healthy tissues while still effectively killing cancer cells. The FLASH phenomenon mechanisms are not fully understood yet, hindering its safe and effective clinical use.

The aim of this project is to investigate how FLASH radiotherapy protects healthy tissues, with a particular focus on the effect of radiation on DNA. When radiation reaches cells, highly reactive molecules are formed, which can damage DNA. Certain proteins present in cells prevent some of this damage by neutralizing the reactive molecules. The level of oxygen in the cell also affects the amount and severity of damage. The research conducted in this project will provide new insights into the protective effect on healthy tissues with FLASH radiotherapy over traditional methods.

To achieve this, the project will combine advanced experimental assays and state-of-the-art computer simulations. In the experimental part, scientists will irradiate, under unprecedented controlled oxygenation levels, DNA using high-intensity FLASH radiation with advanced proton and electron irradiation devices. Sophisticated analysis methods, such as atomic force microscopy (AFM) and other techniques based on DNA separation in agarose gel, will be used to examine the DNA structure and assess the quantity and types of damage. Simultaneously, computer modeling will be developed to simulate the effects of ultra-high-dose-rate radiation, which will help understand the complex physical and chemical processes occurring at the molecular level. By combining experimental and computational approaches, the team aims to develop an improved model of the FLASH effect that could contribute to more effective and safer cancer treatment methods in the future.

The expected outcome of this project is a better understanding of the FLASH effect in radiotherapy, which will lead to the development of more effective cancer treatments in the future, minimizing therapy side effects, improving the quality of life for cancer patients, and making radiotherapy safer and more efficient.