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New Radiobiological and Nanodosimetric Insights into Proton Therapy

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While the number of patients treated with Proton Therapy (PT) has largely increased, associated and unexpected late effects have been observed over the last few years, which could be related to the uncertainties in the increased relative biological effectiveness (RBE) of protons stopping in organs at risk. The accepted clinical practice is the use of a constant RBE value equal to 1.1, derived from in vitro and in vivo experiments at the early days of PT. However, we now know that this value disregards experimental evidence that, in fact, RBE is a quantity that depends on many factors, such as dose per fraction, tissue type, Linear Energy Transfer (LET) and biological endpoint.
The main goal of this project is to go beyond the state-of-the-art approach and replace the use of the constant RBE value with a nanodosimetric approach, proving the hypothesis that ionisation detail (ID) at the nanometer scale can predict, better then LET, RBE and microdosimetric quantities, the biological effects associated with proton radiation. ID is a unique nanodosimetric characteristic of ionizing radiation that can be calculated using Monte Carlo Track Structure (MCTS) simulations and measured using a compact gas-based nanodosimeter. To achieve this, we propose to systematically study the frequency of larger ionisation clusters in small target volumes of DNA-size experimentally with low-pressure gas based nanodosimetry and with MCTS simulations (Geant4-DNA/TOPAS-nBio) and correlate them with radiobiological studies.

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