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MEDICIS-PROMED: MEDICIS-Produced Radioisotope Beams for Medicine an Innovative Training Network

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MEDICIS-PROMED aims to develop a network of academic, medical and industrial partners providing an extensive doctoral program to 15 young scientists in the field of new personalized treatments using radioisotope beams, notably for treatment of ovarian cancer.
This field is expected to expand rapidly and provide new types of treatments combining imaging and personalized treatment with the same radiopharmaceutical and different types of isotopes, emitting positron or gamma light for imaging on one side, and Auger electron, beta and alpha radiation for treatment on the other side, known as theranostics pairs [1]. In addition, positron emitting isotopes such as ^{11}Carbon can personalize hadron therapy treatments by imaging the dose distribution of the implanted ions [2,3].
In this scheme, CERN, the European Organization for Nuclear Research is the coordinating partner, and collaborates with local hospitals which are able to exploit short-lived isotopes produced in the newly constructed CERN-MEDICIS facility. It also fits within an extended network of high-technology companies and leading academic research institutes, which will design new components for the development or tests of innovative radiopharmaceuticals and imaging agents for personalized treatment. It brings world-class researchers together in the field of lasers and isotope mass separation, accelerators, material science, oncology, entrepreneurial radiopharmaceutical production, and imaging, to propose new solutions to the second deadliest cancer for women.
The program will develop along three R&D work packages integrating multidisciplinary intersectorial training teams:
• Development of new radioisotopes and techniques using isotope mass separation for medicine and based on CERN-MEDICIS.
• Development and test of ^{11}Carbon PET-aided hadron therapy.
• Synthesis & tests of radiopharmaceuticals to diagnose and treat ovarian cancer.
Because of the unique capability of CERN-MEDICIS to produce medical batches of innovative isotopes, such as ^{149}Terbium [4] and thanks and to the new generation of young scientists that will be trained in the relevant fields the MEDICIS-PROMED innovative training network will significantly advance the use of radioisotopes for personalized medicine in Europe and go beyond the present common practices.

Keywords: Radiopharmaceuticals, Nuclear Medicine, Pre-Clinical and Clinical Strategies

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Investigating the impact of a variable RBE on proton dose fractionation across an actively scanned spread-out Bragg peak.

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Purpose: Experimental data for the impact of fractionated proton beam exposures is limited. Using acute exposures, the current clinical adoption of a generic, constant cell killing RBE has been shown to underestimate the effect of the sharp increase in Linear Energy Transfer (LET) in the distal regions of the spread-out Bragg peak (SOBP). Here we aim to investigate the clinical implications of a variable Relative Biological Effectiveness (RBE) on proton dose fractionation.
Methods and Materials: Human fibroblasts (AG01522) were irradiated with 219.65 MeV protons at four depth positions along a clinical SOBP. These were delivered as fractionated regimes with an inter-fraction period of 24 hours at the Prague Proton Therapy Centre. Cell killing RBE variations were measured using standard clonogenic assays and were further validated using Monte Carlo simulations and parameterized using a Linear-Quadratic formalism.
Results: Consistent with previous studies of a single fraction response for both survival and DNA damage (DSB foci) (1,2), significant variations in the cell killing RBE for fractionated exposures along the proton dose profile were observed. The RBE increased sharply towards the distal position, corresponding to a reduction in the cell sparing effectiveness of fractionated proton exposures at lower energies and higher LET. The effect is more pronounced at smaller doses per fraction. Experimental survival fractions were adequately predicted using a Linear Quadratic formalism assuming full repair between fractions. The data were also used to validate a parameterized variable RBE model based on linear alpha parameter response with LET that showed considerable deviations from clinically predicted isoeffective fractionation regimes.
Conclusions: The biologically effective dose calculated using the clinically adopted generic RBE of 1.1 significantly underestimates the biological effective dose from variable RBE for single and fractionated regimes with low doses per fraction. Coupled with an increase in effective range in fractionated exposures, the study indicates the needs for the optimization of proton therapy particularly in the move towards hypofractionation.

Keywords:
RBE protons fractionation