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MIRTO: A microdosimetric study and RBE measurement with 62 MeV clinical proton beam

CATANA (Centro di AdroTerapia ed Applicazioni Nucleari Avanzate) was the first Italian protontherapy facility dedicated to the treatment of ocular neoplastic pathologies. Since 2002, it is in operation at the LNS Laboratories of the Italian Institute for Nuclear Physics (INFN-LNS), to date 400 patients have been successfully treated. Nowadays, a slightly increased biological effectiveness (with respect to reference low-LET radiation) is considered in clinical proton treatment planning by assuming a fixed RBE of 1.1 for the whole radiation field. However, data emerging from various studies suggest and highlight how variations in RBE, which are currently neglected, might actually result in deposition of significant doses in healthy organs. Accurate knowledge of the RBE increase in eye protontherapy is of extreme importance as the distal part of the Spread-Out Bragg Peak (SOBP) often involves critical anatomical regions like optic nerve and the macula for which an excess of biological dose could lead to patient's vision loss. To our knowledge, while comprehensive literature exists on the clinical results of protontherapy treatment of uveal melanoma, no in-vitro data on the cellular radioresponse of uveal cancer cells along a clinical proton SOBP are available, with the exception of one study by Courdi et al (1994), who found an RBE of 1.27 at the distal end of a 65 MeV proton SOBP. In this study, however, melanoma derived from a metastatic axillary lymph node was used. Instead, we used a uveal melanoma cell line (MP38), deficient in BAP1 (BRCA1 associated protein-1), a known hallmark of aggressive disease. In addition, to evaluate damage incurred by a typical organ at risk, normal epithelial cells from the retina was used.

A collaboration, between INFN-LNS, CMRP UoW, INFN-NA, IBFM-CNR, INFN-LNL, INFN-MI and INFN-TIFPA was established to perform an experimental measurement of major microdosimetric parameter the dose average lineal energy yd to derive RBE value along a typical SOBP for eye protontherapy. Microdosimetry measurements along the SOBP were carried out using silicon-based detector microdosimeter, a MicroPlus probe, mini-TEPC and a TEPC followed by application of MKM for RBE10 calculation.

In parallel, radiobiological measurements was performed irradiating the MP38 cells at the same positions along the SOBP. ARPE-19 cells from retinal pigmented epithelium will be also investigated in the distal end region. Radiation-induced cell death was evaluated by clonogenic assay and RBE values was calculated from constructed dose-response curves using the LQ model.

Monte Carlo (MC) simulations of the whole experimental set-up, including the physical characteristics of the proton beam, was implemented using the Geant4 toolkit. The spectra generated by these simulations was used as the physical input for the radiobiological simulations based on the MKM model, from which an estimation of the RBE along the SOBP was evaluated and compared with the experimental data.

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