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## Biological dose calculations with variable RBE for proton therapy using Monte Carlo code FRED

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The Monte Carlo (MC) codes are extensively used to support proton therapy clinical practice due to high accuracy of dose calculations in heterogeneous media. The MC platforms offer different methods to model radiobiological effectiveness (RBE) and to calculate biological dose (constant RBE, biophysical and phenomenological models). Such functionality allows to quantify the influence of the variable RBE on biological dose distribution in human body.

Currently available clinical treatment planning systems (TPS) for proton beam therapy (PBT) allow for biological dose calculation only with constant  $RBE=1.1$ . The recent studies show that the use of  $RBE=1.1$  can lead to inaccurate calculations of biological dose deposited in patient body (Giovannini et al. Radiation Oncology (2016) 11:68, Chen et al. Phys. Med. Biol. (2018) 63 195001), mostly because of diverse tissue radiosensitivity and proton beam quality.

The GPU-accelerated MC code FRED (Fast paRticle thErapy Dose evaluator) offers dose calculation with various RBE models (McNamara, Carabe, Wedenberg) accounting for variation of linear energy transfer (LET) of proton beam and RBE model parametrization. FRED was experimentally validated in the Krakow PBT centre showing maximum dose difference up to 2% with respect to measurements. Based on treatment plans of head and neck patients treated in Krakow, we compare biological dose distributions calculated with FRED MC using different RBE models in order to systematically quantify physical and biological dose uncertainties accounting for variable RBE. The dose delivered to the planning target volume (PTV) and organs at risk (OARs) were evaluated.

The quantification of dose uncertainties in PBT using FRED code and RBE models will be discussed. The information about the influence of variable RBE on dose deposited in patients can eventually improve the quality of PBT treatment.

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