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Dose prescription in spatially fractionated radiation therapy (SFRT)

A wealth of preclinical evidence is demonstrating superior tumour control and less side effects for SFRT. Particularly, the normal tissue tolerance towards extremely high peak doses is the promoting argument for SFRT. However, recent research is showing that peak dose is not the determining factor for toxicity or tumour control. The many parameters required to define the radiation field are a challenge in SFRT. Multiport irradiations have even more degrees of freedom. For dose prescription in clinical translation, an equally effective conventional dose equivalent is highly desirable!
Classical radiation biology is based on cellular survival and the linear quadratic model (LQM). The LQM has been clinically employed for the prediction of equal effective temporal fractionation schedules, based on only a single parameter, α/β. Relative biological effectiveness is another well-established concept based on cellular survival in clinical proton therapy treatment planning. Can such classical models be extended to SFRT? We introduce the equivalent uniform dose (EUD) as a method of dose prescription in SFRT and couple it with RBE and EQD2. We used the concept for retrospective treatment planning in realistic clinical cases.
Preclinical studies demonstrate that neither peak, nor valley, nor mean dose are reliably describing outcomes in SFRT. In vitro data demonstrate that EUD is a much better predictor of cell survival, particularly for non-tumour cells. But there are also considerable deviations between conventional and SFRT treatments when compared at equal EUD.
The strength of EUD is its mechanistic approach in predicting SFRT outcomes. It is based on individual, independent survival of cells. Of course, this assumption may not hold true in SFRT, and not surprisingly EUD does not accurately predict biological endpoints in vivo. However, usage of EUD allows the quantification of systemic influences on SFRT outcomes (bystander signalling, immune response, vascular effects etc.). Furthermore, working with EUD reveals that the extraordinary tissue tolerance observed in the early days of SFRT at synchrotrons may be explained with established models of radiobiology.

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