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Uncertainty of RBE model in proton radiotherapy based on α / β ratio and linear energy transfer.

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Living systems exhibit complex response to radiation during and after radiotherapy with protons beams. The response, measured usually by cell survival is mostly affected by the quantity of absorbed radiation. Many other factors, including cell type, dose rate and beam energy have also non-negligible effect on cell-survival.

In proton radiotherapy constant value of the relative biological effect (RBE) is assumed in clinical practice. Many studies based on in-vitro and in-vivo experiments suggest that variable proton RBE would improve the treatment outcome. Several models based on data extracted from in-vitro experiments relate RBE variations with linear energy transfer (LET) and α / β ratio in linear-quadratic (LQ) model. In our study we selected Wedenberg model and extended it by adding prediction of RBE statistical distribution. Such approach propagates uncertainties of in-vitro cell experiments into higher level quantities such as RBE and dose-volume-histograms.

The model is based on experimental data for 10 different cell lines irradiated with monoenergetic proton beams with LET values ranging from 6 keV/um to 30 keV/um. We reconstructed parameters of Wedenberg model by performing least-square fitting to the mean values of the cell survival. Then the model was improved by subsequent fitting including statistical uncertainty of cell survival which produced distributions of correlated α and β parameters of LQ model. We used bootstrapping - resampling technique, to mimic new data generation, by drawing modified samples (in this case: parameters α , β and q). The model outcome was a skew RBE distribution. Mean value of predicted RBE distribution is in agreement of few percent with original Wedenberg model.

We estimated that uncertainties of LQ model parameters α and β at 10% - 15% lead to RBE uncertainty at 9% level. Introduced model predicts RBE distribution which enable better inter-model testing than simple comparison of mean values. Uncertainty of the RBE allows for richer treatment plan comparison.

References:

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