Abstract:

The increased relative biological effectiveness (RBE) at the end of the proton range might increase the risk of radiation-induced toxicities. This, however, is not accounted for in clinical practice when using the constant RBE of 1.1. This thesis aims to quantify the impact of variable RBE models with uncertainties in the plan evaluation and to include RBE model uncertainties in the robustness evaluation. Moreover, two indirect RBE optimization methods were proposed: (1) Re-optimising the physical dose based on variable RBE predictions from the dose-average linear energy transfer (LET_d) distribution (LET_d-based re-optimisation). (2) Reducing the D_{RBE} in OARs while maintaining the physical target dose by penalising protons stopping in OARs (proton track-end optimisation).

For clinical target volumes (CTVs) with $\alpha/\beta \approx 5$–15 Gy, the RBE-weighted dose (D_{RBE}) using variable RBE models was predicted to be similar to RBE=1.1 (average RBE around 1.05–1.15 for brain/H&N), whereas it was predicted to be higher for CTVs with $\alpha/\beta \approx 1$–5 Gy (average RBE around 1.1–1.3 for breast/prostate). For most organs at risk (OARs), the predicted D_{RBE} was often substantially higher, resulting in higher normal tissue complication probabilities (NTCPs). Inclusion of RBE uncertainties generally broadened the error bands around the nominal dose-volume histograms (DVHs) compared to only including physical uncertainties (e.g. range and patient setup). The largest contribution to the increase originated from the uncertainty in the α/β parameter. The LET_d-based re-optimisation allowed for satisfying target coverage for several variable RBE models and treatment sites. For prostate and breast cases, robust plans fulfilling clinical target and OAR goals were generated. Proton track-end optimisation allowed for substantial reductions in D_{RBE}, LET_d, and NTCP for several OARs compared to only dose-based optimisation, without compromising target coverage or the integral dose. For brain lesions, the near-maximum LET_d could be reduced with approximately 50%, or more, resulting in fulfilment of clinical OAR goals assuming variable RBE models where dose optimised plans failed.

In conclusion, robustness evaluation including RBE uncertainties allows for comprehensive analyses, where potential adverse effects could be evaluated and mitigated on quantitative individual bases. LET_d-based re-optimisation could be used as a pragmatic solution for prostate and breast cases to fulfil clinical goals assuming variable RBE models, whereas proton track-end optimisation might be a generalised indirect RBE optimisation tool that could produce biologically advantageous plans compared to dose-optimised plans, without compromising physical criteria in current treatment protocols.

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