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Advanced treatment planning: robust optimization and proton RBE

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Dirk Wagenaar

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university of
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Advanced treatment planning: robust optimization and proton RBE

PhD thesis

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the decision by the College of Deans.

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by

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Abstract

Treatment planning needs to account for setup uncertainty in photon therapy and for setup, range and biological uncertainty in proton therapy. This thesis outlines several undergone studies aimed at mitigating the setup, range and biological uncertainties in radiotherapy planning.

The benefit of composite minimax robust optimization for photon volumetric arc therapy (VMAT) in head and neck cancer patients was demonstrated. Two VMAT plans were generated using both planning target volume (PTV)-based and robust optimization for ten head and neck cancer patients. All 20 treatment plans were evaluated on daily acquired cone beam CT (CBCT) scans to simulate actually delivered dose. The results were a small increase in the near-minimum dose (i.e. the dose to 98% of the volume, D_{98}) of the clinical target volume (CTV) of 1.5 Gy on average and a reduction in normal tissue complication probability (NTCP) for tube feeding dependence and xerostomia of 0.9% and 2.8% respectively.

The effect of different setup and range uncertainty settings was tested in ten proton therapy head and neck cancer patients by evaluating treatment plans with different uncertainty settings on weekly verification CTs. Random and systematic setup and range uncertainties were taken into account in a probabilistic dose accumulation. The results substantiate a safe transition to a 2 mm/3% setup and range uncertainty setting which is expected to result in a 6% reduction in total NTCP for xerostomia, tube feeding dependence and dysphagia combined.

Measurements and independent calculations were done to validate the dose-weighted average linear energy transfer (LET_d) calculation of an experimental version of a commercial treatment planning system (TPS). The results were that 90% of the measurement points were within 6%/2 mm of the calculation of the voxelwise product of dose and LET_d ($D \cdot LET_d$). This type of validation is very important as the LET_d is an important parameter in calculating the additional biological dose in relative biological effectiveness (RBE) models for proton therapy.

The linearity of the relation between RBE and LET_d was investigated by fitting a RBE model with a linear dependency on LET_d to the clinically relevant dosimetric parameters of 60 patients across three body sites with different prescribed fraction doses. The results were that the coefficient of agreement (R^2) was at

least 0.94 for the McNamara and at least 0.87 for the Wedenberg RBE models for α/β values between 1 and 10 Gy. Furthermore, the difference between a linear fit and the McNamara RBE model was in the same order of magnitude as the difference between the McNamara and Wedenberg RBE model.

The possibility of deriving the slope of the RBE-LET_d relation was investigated using a simulation based on 100 head and neck cancer patients. From these patients, different dataset sizes were simulated from which NTCP models were generated using both D and D·LET_d parameters as independent predictors. Due to lack of variation in beam setup, the LET_d was similar for organs-at-risk among the 100 included patients resulting in a high covariance between D and D·LET_d parameters. The required sample size was at least 15.000 patients for all considered toxicities.

Lastly, the thesis concludes with future perspectives and recommendations on the mitigation of the biological uncertainty in proton therapy for current clinical practice using LET_d calculations.