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Probabilistic Treatment Planning for Carbon Ion Therapy

Intensity-modulated scanned particle therapy in combination with the characteristic depth dose deposition of carbon ions entail a higher sensitivity to physical changes of the patient geometry compared to photons. As a result, carbon ions stop at different spatial locations than predicted during treatment planning thereby potentially compromising the quality of the radiation treatment plan. The resulting uncertainty level in dose requires a patient specific uncertainty analysis and uncertainty mitigation. On the basis of a concept called APM initially proposed by (Bangert et al., 2013) to quantify uncertainties of the proton dose deposition modeling setup and range errors alongside fractionation effects in closed-form, this manuscript presents the extension of APM to carbon ion treatment planning.

Unlike protons, carbon ion treatment planning needs to account for the increased nonlinear cell killing of carbon ions in a mixed radiation field which increases the treatment planning complexity. With respect to uncertainties, not only the location of dose deposition is uncertain for carbon ions but also their effectiveness which consequently introduces biological uncertainties to treatment planning.

Different to scenario based approaches, this work presents exact and approximated nonlinear closed-form calculations of the expectation value and covariance of the RBE weighted dose accounting for setup-, range- and biological-uncertainties in fractionated carbon ion therapy. The developed analytical pipeline allows propagating linearly correlated Gaussian input uncertainties through the carbon ion pencil beam dose calculation algorithm to obtain uncertainties in dose.

With I and J being the number of voxels and pencil beams, respectively, low-rank tensor approximations were derived for the expectation value and standard deviation reducing the computational complexity from $O(I\,x\,J^2)$ to $O(I\,x\,J)$and from $O(I\,x\,J^4)$ to $O(I\,x\,J^2)$ with minimal loss in accuracy. The consideration of biological errors introduces a new uncertainty structure in the analytical pipeline without increasing the computational complexity. The calculation of expected dose and variance influence information via APM allows performing a subsequent probabilistic optimization.

A proof of concept and several aspects such as accuracy, fractionation and the impact of different probability densities to model input uncertainties were studied in detail on a one-dimensional phantom case. Further, basic three-dimensional dose calculation and optimization functionalities were implemented in the open-source treatment planning system matRad. A subsequent validation against a clinical reference system revealed excellent agreement for elementary pencil beams and patient cases as indicated by g-pass rates above 99.67%. Theoretical APM derivations were implemented on top and were then applied to clinical carbon ion patient cases. The expectation value and standard deviation of the RBE weighted dose were compared to estimated analogs stemming from 5000 random samples. The γ-pass rate exceeded 94.95% in all patient cases thereby proving the validity of the proposed analytical pipeline. A subsequent probabilistic optimization avoided underdosage of the target volume, reduced the integral dose and resulted in carbon ion treatment plans with a minimized standard

deviation of RBE weighted dose. Thus APM facilitates a flexible, effective and accurate probabilistic description of the radiation treatment plan and generalizes to probabilistic optimization.