Convolutional neural networks predict the linear energy transfer for proton-beam radiotherapy of patients with brain tumours

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Abstract

Proton therapy is a promising option for cancer treatment, even though its radiobiological properties are not yet fully considered in clinical practice. In this context, the relative biological effectiveness (RBE) of protons is the most important quantity, which is strongly related to their linear energy transfer (LET). LET distributions can be provided by commercial treatment-planning systems based on Monte Carlo simulations. However, such systems require a considerable amount of computational resources, are not yet available in every proton-therapy centre and may not be applicable to assess retrospective patient data. Here, we provide proof-of-concept for inferring LET distributions using convolutional neural networks (CNN) based on proton therapy radiation dose distributions and treatment-planning computed tomography (CT). We further evaluate established models for estimating treatment-related side effects after proton therapy of brain tumours and observe good agreement between CNN and MC based outputs.

Keywords: proton therapy, linear energy transfer, relative biological effectiveness, convolutional neural networks.

Introduction Over the last years, proton therapy has been clinically established besides conventional photon-based radiotherapy for the treatment of several tumour entities. To further improve proton treatment, radiobiological properties of protons have to be better understood. In this context, the relative biological effectiveness (RBE) of protons is an important quantity, defined as the ratio of photon dose to proton dose required to achieve the same biological effect. In clinical practice, a constant RBE of 1.1 is currently applied. However, there is increasing evidence showing that the RBE varies as a function of physical dose, biological parameters, such as tissue type, and the linear energy transfer (LET) of protons. Ignoring this effect during treatment-planning may cause an increase in treatment-related side effects (Lühr, A. et al., 2018). Nowadays, the gold standard of LET computations available in commercial treatment-planning systems is based on Monte Carlo (MC) simulations which require large amounts of computational resources. However, these algorithms are not readily available in every proton therapy centre and may not be applicable for the analysis of retrospective data. Therefore, we investigate the potential of three-dimensional convolutional neural networks (CNN) for calculating the LET based on the available dose distribution and treatment-planning computed tomography (CT) images. The results are compared with MC simulations, translated into RBE values, and applied to estimate treatment-related side effects after proton therapy of patients with brain tumours.

Methods We analysed data from 29 patients with primary brain tumours who received double-scattering proton therapy at the University Proton Therapy Dresden. Using the dose distribution and the treatment-planning CT as input channels, we trained a 3D version of UNet with mean absolute error loss to predict the voxel-wise dose-averaged LET available from a MC simulation (Eulitz, J. et al., 2019) in a fivefold cross-validation approach. To assess the quality of our predictions, we compared the predicted LET distribution to the MC ground truth for several organs at risk. Furthermore, we considered the clinically more relevant prediction of normal-tissue complication probabilities (NTCP). NTCP models rely on RBE-weighted dosimetric features in specific organs at risk. Here, these features were evaluated considering a variable proton RBE, calculated by $\mathrm{RBE} = 1 + 0.1 \cdot \mathrm{LET}\ [\mathrm{keV}/\mu\mathrm{m}]$ (Bahn, E. et al., 2020). We compare the results of established NTCP models for fatigue grade ≥ 1 24 months after therapy and memory impairment grade ≥ 2 12 months after therapy, which are based on high dose values in the brainstem and the volume receiving intermediate dose values in the healthy brain, respectively (Dutz, A. et al., 2021).

Results Considering the predicted mean LET for the validation data of the cross-validation folds in the clinical target volume (CTV), brain and brainstem, the median absolute relative deviation between both approaches was 0.03, 0.06 and 0.15, respectively. For these three regions, the Wilcoxon paired signed-rank test showed non-significant differences between both modelling approaches (Figure 1, left). Our CNN produced LET distributions qualitatively similar to the MC ground truth (Figure 1, center). For predicting the probability of fatigue and memory impairment, the median absolute relative deviation between both approaches was 0.01 and 0.007, respectively (Figure 1, right).

Discussion We demonstrated that 3D CNNs can be used to predict LET distributions for proton therapy and have the potential to support investigations of variable RBE effects. While CNN predictions of LET might deviate from the results of MC simulations in certain body regions, these differences did not translate into clinically relevant changes for the

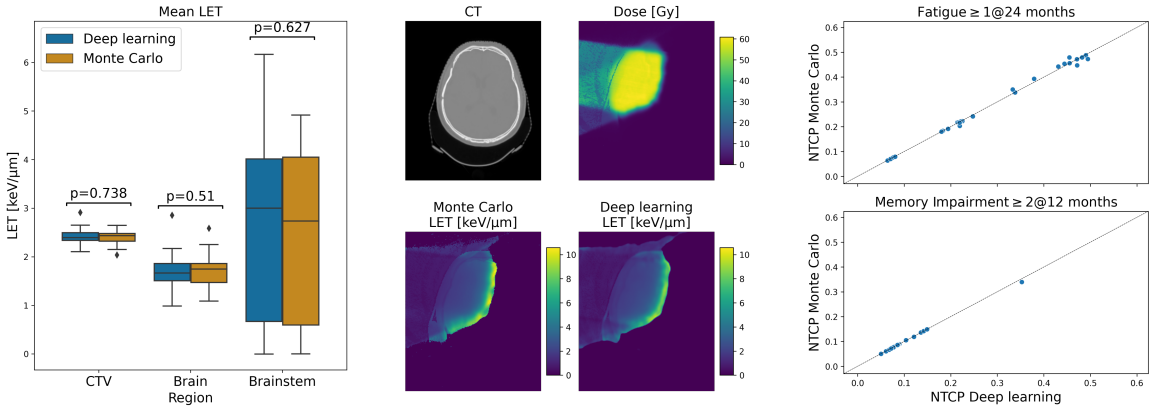

Figure 1: Left: Comparison of LET distributions for organs at risk. Center: Visual comparison between ground truth and prediction. Right: Calibration of NTCP models.

prediction of treatment-related side effects of fatigue and memory impairment. Moreover, CNN predictions can be obtained faster than the often time-consuming MC simulations and require only the easily available dose distribution and treatment-planning CT, while MC simulations require additional information such as the beam model of the proton therapy device. Since this information is not always available in the clinical setting in particular for retrospective studies, our approach offers two main benefits: it provides a rapid way to evaluate LET distributions of retrospective patient data and may be applied by clinics using treatment-planning systems without the possibility to calculate the LET. Further development and validation of our findings on larger and more heterogeneous datasets is required and planned.

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