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PTCOG 2025 award: Mapping intratumoral heterogeneity through PET-derived washout and deep learning after proton therapy

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The distribution of produced isotopes during proton therapy can be imaged with Positron Emission Tomography (PET) to verify dose delivery. However, biological washout, driven by tissue-dependent processes such as perfusion and cellular metabolism, reduces PET signal-to-noise ratio (SNR) and limits quantitative analysis. In this work, we propose an uncertainty-aware deep learning framework to improve the estimation of washout parameters in post-proton therapy PET, not only enabling accurate correction for washout effects, but also mapping intratumoral heterogeneity as a surrogate marker of tumor status and treatment response. We trained the models on Monte Carlo-simulated data from eight head-and-neck cancer patients, and tested them on four additional head-and-neck and one liver patient. Each patient was represented by 75 digital twins with distinct tumoral washout dynamics and imaged 15 minutes after treatment, when slow washout components dominate. We also introduced "washed-out" maps, quantifying the contribution of medium and fast washout components to the loss in activity between the end of treatment and the start of PET imaging. Trained models significantly improved resolution and accuracy, reducing average absolute errors by 60% and 28% for washout rate and washed-out maps, respectively. For intratumoral regions as small as 5 mL, errors predominantly fell below thresholds for differentiating vascular status, and the models generalized across anatomical areas and acquisition delays. This study shows the potential of deep learning in post-proton therapy PET to non-invasively map washout kinetics and reveal intratumoral heterogeneity, supporting dose verification, tumor characterization, and treatment personalization. The framework is currently being validated using phantom experiments at Clínica Universidad de Navarra, Spain, and clinical data at Massachusetts General Hospital, USA. The implementation code is available at https://github.com/pcabrales/ppw.

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