PROTOTWIN-PET: Patient-Specific Deep Learning Models for 3D Dose Verification in Proton Therapy with PET

Pablo Cabrales, Víctor V. Onecha, José Manuel Udías, David Izquierdo-García, Joaquín L. Herraiz

***Abstract*—In this work, we present PROTOTWIN-PET (PROTOn therapy digital TWIN models for dose verification with PET), a patient-specific GPU- and deep learning-based workflow to predict realistic dose deposition deviations in a proton therapy treatment with a PET scanner. Existing PET-based dose verification approaches do not consider realistic clinical deviations, are implemented in 1D or 2D with CPU systems, or lack reliable conversions from detected PET activity to deposited dose. To solve this, the proposed workflow begins with the simulation of realistic treatment plan deviations in patient positioning and physical parameters with GPU Monte Carlo software FRED. Then, the obtained activation images are transformed into the expected activity images with in-house GPU PET simulation and reconstruction software. Finally, a deep learning model is trained to predict the 3D dose deposition from the activity images. We demonstrate this workflow in an oropharynx cancer treatment. Using the SwinUNETR deep learning model, we improve the Gamma Passing Rate (1mm, 3%) from 61.2% to 99.8%. Furthermore, we implement a Deviation Predicting Branch (DPB) on the model that predicts the positioning displacement values within 0.2mm and 0.2º. The entire data generation and model training can be completed in the time interval between the treatment plan CT and the first treatment session, where it can be deployed to detect dose deviations in milliseconds from a PET scan.**

***Index Terms*—Bragg Peak (BP), Convolutional Neural Network (CNN), Deep Learning (DL), Deviation-Predicting Branch (DPB)**

I. Introduction

Proton therapy (PT) conforms the radiation dose to the tumor more precisely than traditional radiotherapy due to the sharp dose fall-off after the Bragg Peak (BP). However, the usefulness of PT is hindered by the risks of deviations in dose deposition with respect to the treatment plan, which may lead to insufficient treatment of the tumor or excessive radiation to healthy tissues. To detect these deviations, imaging of activated positron-emitting isotopes with PET scanners was proposed.

Mapping the detected PET events to the actual deposited dose requires a series of simulations and models. However, current approaches are either not realistic enough (e.g. lacking a reconstruction of deposited dose from detected activity [1] or considering unrealistic dose distributions [2]), not fast enough (e.g. relying on CPU-based systems to generate training datasets [3]), or use old 1D and 2D Deep Learning (DL) architectures to map activity to dose [4].

In this work, we propose using patient-specific DL models to reconstruct 3D dose from PET-detected activity in proton therapy. The models are trained with a set of patient-specific, or digital twin, GPU-based simulations that include realistic deviations with respect to the treatment plan that may occur in the clinical practice. We developed and named this workflow PROTOTWIN-PET, which stands for PROTOn therapy digital TWIN models for dose verification with PET.

This summary was submitted for review to the 2024 IEEE Nuclear Science Symposium, Medical Imaging Conference, and Room-Temperature Semiconductor Detectors Symposium on May 7th, 2024. This work was supported, in part, by the Prototwin Project (TED2021-130592B-I00), funded by the MCIN/AEI/10.13039/501100011033 and the European Union NextGenerationEU/PRTR. Additionally, Pablo Cabrales received support from the Complutense University Predoctoral Fellowship.

Pablo Cabrales (e-mail: pcabrale@ucm.es), José Manuel Udías (e-mail: jmudiasm@ucm.es), and Joaquín L. Herraiz (e-mail: jlopezhe@ucm.es) are with the Group of Nuclear Physics, Complutense University of Madrid, Madrid, Spain.

Víctor V. Onecha (e-mail: vonecha@mgh.harvard.edu) and David Izquierdo-García (e-mail: dizquierdogarcia@mgh.harvard.edu) are with Massachusetts General Hospital & Harvard Medical School, Boston, US.

II. Methods

The proposed workflow consists of three main steps: First, a patient-specific dataset of pairs of 3D volumes of reconstructed PET activity distribution and deposited dose is generated with GPU-accelerated software tools. Second, the dataset is used to train the DL model to convert PET activity into dose. Finally, the model is deployed and ready to use after the treatment session.

To demonstrate the workflow, a realistic, three-field oropharynx cancer treatment plan with approximately 30000 pencil beams was obtained with MatRad [5]. The 3D volumes have a resolution of 1.95 mm $\times$ 1.95 mm $\times$ 1.5 mm, a size of 128x96x128 voxels, and were generated with GPU Monte Carlo simulation software FRED [6] and a single RTX 4080Ti GPU. PET acquisitions between 10 and 40 minutes after the treatment were simulated with MCGPU-PET [7] and the simulated PET data was reconstructed with in-house GPU-based software to generate realistic PET images.

A dataset of 189 clinically plausible plan deviations was generated assuming potential set-up errors in couch or patient positioning ($|\Delta x_{max}| = |\Delta y_{max}| = 5mm$, $|\Delta\theta_{max}| = 5°$) [8], as well as uncertainties of up to 10% in mean excitation energies and densities obtained from the patient's CT [9]. The plan deviations constitute the patient's digital twins. The DL model used to estimate 3D doses from the PET activity was the SwinUNETR [10], where we also introduced a *Deviation-Predicting Branch* to predict the values of Δx, Δy, and $\Delta\theta$. The model was trained for 200 epochs using the MSE loss.

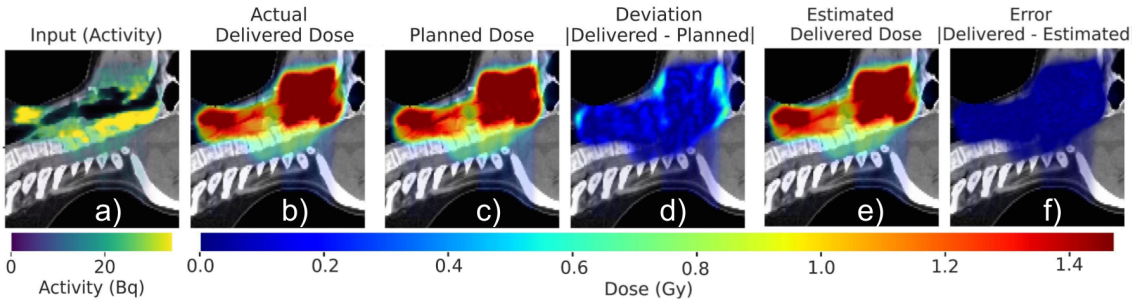

Fig. 1. For a sample case, the deviated delivered dose (b) is compared to the planned dose (c) in (d) and to the estimated dose predicted by the model (e) in (f). The color map is truncated at 1.5 Gy to showcase these differences.

III. Results

In Table I, the MSE, as well as the Gamma Index and Gamma Passing Rate (1mm, 3%) [11] are shown. The baseline is the average difference between the deviated and planned doses. The model was trained in under 3 hours and the inference time was 16ms per image.

TABLE I
Comparison of Model Performances. Lower MSE Loss and Gamma Index and higher passing rate are better.

Model	**MSE Loss** ($\times 10^{-4}$ **Gy**^{2})	**Gamma Index**	**Gamma Pass. Rate (%)**
Baseline (No Correction)	59.2	1.01	61.2
SwinUNETR	**1.4**	**0.18**	**99.8**

For a sample deviated plan, the difference between the planned dose and the deviated, actual delivered dose and the difference between the delivered dose and the delivered dose estimated by our model from the PET activity are shown in Fig. 1.

Furthermore, the differences between expected and predicted positioning set-up errors are $\Delta x = 0.15 \pm 0.09mm$, $\Delta y = 0.06 \pm 0.05mm$, and $\Delta\theta = 0.13 \pm 0.08°$.

IV. Discussion

The clear improvements shown in Table I regarding the baseline underscore the model's capacity to accurately reconstruct the dose from the PET activity even for slight positioning errors.

Moreover, Fig. 1 highlights the importance of detecting subtle deviations, as they can yield dose deposition differences greater than 0.7 Gy. This can be seen in the hard palate region in the fourth image from the left (d). As shown in the rightmost image (f), our model is able to detect these deviations.

V. Conclusions

The results show the capacity of the developed workflow, PROTOTWIN-PET, to recover dose distributions from measured PET activities. The use of GPU-accelerated simulation and reconstruction tools allows training the model within a few hours so that the workflow can be developed and ready for deployment in the time interval of approximately one day between the treatment plan and the first treatment session. Once trained, the dose deposition can be verified in milliseconds to reduce the risks of tumor undertreatment and healthy tissue overdosage with submillimetric accuracy.

Acknowledgment

We extend our gratitude to FRED contributor Keegan McNamara (PSI's Centre for Proton Therapy) for his guidance in the utilization of FRED and to Amit Bennan and Remo Cristoforetti (DKFZ German Cancer Research Center) for their assistance with MatRad's treatment planning.

References

[1] D. Borys, J. Baran, K. Brzeziński, J. Gajewski, N. Chug, A. Coussat, E. Czerwiński, M. Dadgar, K. Dulski, K. V. Eliyan *et al.*, "Protheramon—a gate simulation framework for proton therapy range monitoring using pet imaging," *Physics in Medicine & Biology*, vol. 67, no. 22, p. 224002, 2022.

[2] X. Zhang, Z. Hu, G. Zhang, Y. Zhuang, Y. Wang, and H. Peng, "Dose calculation in proton therapy using a discovery cross-domain generative adversarial network (discogan)," *Medical physics*, vol. 48, no. 5, pp. 2646–2660, 2021.

[3] V. Onecha, P. Galve, P. Ibáñez, C. Freijo, F. Arias-Valcayo, D. Sanchez-Parcerisa, S. España, L. Fraile, and J. Udías, "Dictionary-based software for proton dose reconstruction and submilimetric range verification," *Physics in Medicine & Biology*, vol. 67, no. 4, p. 045002, 2022.

[4] C. Liu, Z. Li, W. Hu, L. Xing, and H. Peng, "Range and dose verification in proton therapy using proton-induced positron emitters and recurrent neural networks (rnns)," *Physics in Medicine & Biology*, vol. 64, no. 17, p. 175009, 2019.

[5] H.-P. Wieser, E. Cisternas, N. Wahl, S. Ulrich, A. Stadler, H. Mescher, L.-R. Müller, T. Klinge, H. Gabrys, L. Burigo *et al.*, "Development of the open-source dose calculation and optimization toolkit matrad," *Medical physics*, vol. 44, no. 6, pp. 2556–2568, 2017.

[6] K. McNamara, A. Schiavi, D. Borys, K. Brzezinski, J. Gajewski, R. Kopeć, A. Rucinski, T. Skóra, S. Makkar, J. Hrbacek *et al.*, "Gpu accelerated monte carlo scoring of positron emitting isotopes produced during proton therapy for pet verification," *Physics in Medicine & Biology*, vol. 67, no. 24, p. 244001, 2022.

[7] J. L. Herraiz, A. Lopez-Montes, and A. Badal, "Mcgpu-pet: An open-source real-time monte carlo pet simulator," *Computer Physics Communications*, vol. 296, p. 109008, 2024.

[8] M. Moglioni, A. C. Kraan, G. Baroni, G. Battistoni, N. Belcari, A. Berti, P. Carra, P. Cerello, M. Ciocca, A. De Gregorio *et al.*, "In-vivo range verification analysis with in-beam pet data for patients treated with proton therapy at cnao," *Frontiers in Oncology*, vol. 12, p. 929949, 2022.

[9] P. Andreo, "On the clinical spatial resolution achievable with protons and heavier charged particle radiotherapy beams," *Physics in Medicine & Biology*, vol. 54, no. 11, p. N205, 2009.

[10] A. Hatamizadeh, V. Nath, Y. Tang, D. Yang, H. Roth, and D. Xu, "Swin unetr: Swin transformers for semantic segmentation of brain tumors in mri images," 2022.

[11] D. A. Low, W. B. Harms, S. Mutic, and J. A. Purdy, "A technique for the quantitative evaluation of dose distributions," *Medical physics*, vol. 25, no. 5, pp. 656–661, 1998.