**Multitracer Lesion Segmentation in FDG-18 and PSMA Whole-Body PET/CT scans using augumented labelling approach: AutoPET III challenge**

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**Abstract:**

Automatic segmentation of lesions in multi radiotracer setting using deep learning models is instrumental for determining treatment response, optimizing dosimetry, and advancing theranostic applications in oncology. However, the presence and diversity of organs with elevated radiotracer uptake between different radiotracers, such as the liver, spleen, brain, and bladder, often leads to challenges, as these regions are often misidentified as lesions by deep learning models. To address this issue, we propose a novel approach of segmenting both organs and lesions, aiming to enhance the performance of automatic lesion segmentation methods. In this study, we assessed the effectiveness of our proposed method using the AutoPET II challenge multi radiotracer dataset (PSMA and FDG-18), which comprises 1278 subjects with 1611 studies. We evaluated the impact of inclusion of additional labels and data in the segmentation performance of the model. In addition to the expert-annotated lesion labels, we introduced nineteen additional labels for organs, including the adrenal, thyroid, small bowel, intestine, duodenum, esophagus, gall bladder, pancreas, prostate, skull, liver, kidneys, urinary bladder, spleen, lung, brain, heart, and stomach. These labels were integrated into the dataset, and a residual XL 3D UNET model was trained within the nnUNet framework. Our results demonstrate that our method achieved the top ranking in the held-out test dataset, underscoring the potential of this approach to significantly improve lesion segmentation accuracy in FDG-18 and PSMA Whole-Body PET/CT scans, ultimately benefiting cancer patients and advancing clinical practice.

**Introduction:**

Whole-body Positron Emission Tomography/Computed Tomography (PET/CT) is a vital tool for imaging tumors, aiding in early detection of metastatic lesions, quantifying metabolically active tumors, and contributing significantly to cancer diagnosis, staging, treatment planning, and recurrence monitoring. Recent studies suggest its potential for personalized therapy response assessment. Among PET radiotracers, 18-Fluorodeoxyglucose (18F-FDG) is the mostly used due to its ability to target increased glucose metabolism in malignant tumors, demonstrating high sensitivity for metastasis detection in solid tumors. 1–5. Another promising PET tracer is Prostate-Specific Membrane Antigen (PSMA), which targets PSMA receptors highly expressed in prostate cancer cells, allowing for enhanced detection of prostate cancer metastasis. PSMA PET imaging has shown superior sensitivity and specificity in identifying both primary and metastatic prostate cancer lesions compared to conventional imaging techniques.

Simultaneously, the evolution of deep learning algorithms has brought about a revolution in the field of medical imaging, fostering more precise and efficient segmentation of cancerous lesions within acquired images6–9. These algorithms possess the remarkable ability to autonomously delineate tumor boundaries, even in scenarios where conventional methodologies fail due to the intricacy, variability, or subtlety of the lesions. The integration of deep learning algorithms into the molecular theranostics framework holds immense promise, streamlining the interpretation of diagnostic data and optimizing subsequent therapeutic strategies. This includes precise radiotracer dose estimation, treatment planning by monitoring treatment response, and the staging of cancer.

Radiotracer uptake exhibits interpatient variability, and the inherent design of radiotracers may lead to heightened accumulation in normal organs with high metabolic activity, such as the brain, or cleansing organs like the liver, kidneys, and urinary bladder. Automatic lesion segmentation algorithms often struggle to differentiate between normal uptakes in these organs and actual lesions, presenting a significant challenge. Consequently, we hypothesize that segmenting high-uptake organs alongside lesions can provide the model with valuable discernment between the two. Our preliminary study10, training a multiclass model to segment lesions in 40 prostate cancer subjects with WB Ga-68 PSMA-11 PET/CT scans and testing on A close-up of a ct scan

Description automatically generated10 held-out subjects, revealed that the proposed multilabel model significantly outperformed the single-label model, which focused solely on lesion segmentation. We achieved first ranking in AutoPETII using the same approach11.

Figure 1: **Training data**: Representation of the Whole-Body CT (left), PET (middle), and labels (right) employed to train the final model.

In this research paper, we extend our investigation by including a larger cohort from the AutoPET challenge. We leveraged a Residual XL 3D UNet model within the nnUNET framework and employed a rigorous 5-fold cross-validation approach for evaluation.We trained a final model using a 5-fold cross-validation technique to segment lesions and other high-uptake organs, incorporating all 1611 studies from the AutoPET training dataset. An ensemble of the final model across all five folds was created and submitted to the AutoPET challenge for benchmarking against other methods. This comprehensive methodology and evaluation process allowed us to assess the performance of our approach within the context of the AutoPET challenge and make comparisons with other submitted techniques. Significantly, our proposed method achieved the top-ranking position in the AutoPET III challenge, highlighting its potential as a clinical utility in the field of molecular theranostics.

**Methods:**

**Data and Preprocessing**

The models were trained using whole-body FDG-PET/CT data from 900 patients, including 1014 studies and PSMA PET/CT data from 378 patients including 597 studies provided by the AutoPET challenge III 202412,13. A held-out dataset consisting of 200 patients, was used as a test dataset to assess the robustness and generalizability of the algorithm. In the preprocessing step, the CT data was resampled to the PET resolution and normalized. Two experts annotated the training and test data. A radiologist with 10 years of experience in Hybrid Imaging and experience in machine learning research at the University Hospital Tübingen annotated all data. A radiologist with 5 years of experience in Hybrid Imaging and experience in machine learning research at the University Hospital of the LMU in Munich annotated all data. We randomly split the training data into 5-fold and trained the 3D Residual XL UNet model within nnUNet framework to segment multiple organs and lesions. The final model is the ensemble of the five folds and is uploaded into the challenge portal for testing in docker format.

**Model Training Methodology**

**Model Architecture**:

The nnUNET pipeline has consistently demonstrated top-tier performance in various medical imaging segmentation competitions.14. The 3D Residual XL UNet model variant was utilized, incorporating skip connections for training. The input image dimensions are set to 192x256x256 with a single channel, utilizing CT scans as input data. During training, models are trained over five folds using a loss function combining the Dice Sorensen Coefficient (DSC) and weighted cross-entropy loss to mitigate overfitting. Augmentation techniques such as random rotations, random scaling, random elastic deformations, gamma correction, mirroring, and elastic deformations are employed to enhance model robustness. Each of the five models is trained for 1000 epochs with a batch size of eight, utilizing the SGD optimizer with a learning rate of 0.01. Performance assessment includes metrics such as Dice Similarity Coefficient (DSC) and normalized surface dice (NSD) to evaluate various aspects of the segmentation methods.

**Results:**

**AutoPET II Challenge**

Our method achieved top ranking in AutoPET III challenge by achieving xx dice, yy FPV and zz FNV.

**Discussion and Conclusion:**

In conclusion, our research demonstrates that the inclusion of high radiotracer uptake regions and other anatomical structures as multiple labels significantly enhances lesion segmentation performance, even when working with smaller datasets.

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