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Efficient Semi-automatic Annotation System based on Deep Learning

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Abstract : This paper presents the development of specialized software for annotating volume-of-interest on ^{18}F-FDG PET/CT images with the goal of facilitating the studies and diagnosis of head and neck cancer (HNC). To achieve an efficient annotation process, we employed the SE-Norm-Residual Layer-based U-Net model. This model exhibited outstanding proficiency to segment cancerous regions within ^{18}F-FDG PET/CT scans of HNC cases. Manual annotation function was also integrated, allowing researchers and clinicians to validate and refine annotations based on dataset characteristics. Workspace has a display with fusion of both PET and CT images, providing enhance user convenience through simultaneous visualization. The performance of deeplearning model was validated using a Hecktor 2021 dataset, and subsequently developed semi-automatic annotation functionalities. We began by performing image preprocessing including resampling, normalization, and co-registration, followed by an evaluation of the deep learning model performance. This model was integrated into the software, serving as an initial automatic segmentation step. Users can manually refine pre-segmented regions to correct false positives and false negatives. Annotation images are subsequently saved along with their corresponding ^{18}F-FDG PET/CT fusion images, enabling their application across various domains. In this study, we developed a semi-automatic annotation software designed for efficiently generating annotated lesion images, with applications in HNC research and diagnosis. The findings indicated that this software surpasses conventional tools, particularly in the context of HNC-specific annotation with ^{18}F-FDG PET/CT data. Consequently, developed software offers a robust solution for producing annotated datasets, driving advances in the studies and diagnosis of HNC.

Keywords : Image annotation, Deep learning, Head and neck cancer, PET/CT, Embedded software

Ⅰ. Introduction

Positron emission tomography (PET) is a molecular imaging technique used for diagnosing diseases and conducting scientific research, particularly in oncology. It provides information about the metabolic activity of tissues, allowing for the identification of areas with abnormal activity, such as cancerous lesions. The PET scans are particularly useful in oncology to differentiate between benign and malignant tumors, characterize tissues, determine disease stages, and assist in treatment decisions. However, their spatial resolution of functional imaging techniques such as CT might not be high enough to precisely pinpoint the exact anatomical location of these lesions. On the other hand, morphological imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) offer detailed structural information about the body's anatomy. They are excellent for visualizing tissue structures and their relationships, aiding in diagnosing cancer, staging its progression, and determining the extent of tumors and their involvement with nearby tissues. However, these techniques might not be sensitive enough to detect very small lesions or subtle metabolic changes that can be indicative of early stage cancer [1, 2].

To overcome these limitations and offer a more comprehensive diagnostic approach, hybrid imaging technologies have been developed. One notable example is the PET/CT scan, which merges the functional information from PET with the precise anatomical localization provided by CT. By performing both scans simultaneously, the resulting combined images can provide a clearer understanding of both the metabolic activity and the exact location of abnormalities within the body [3]. This collaborative approach improves diagnostic accuracy and proves especially valuable in cases where

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distinguishing between benign and malignant conditions or identifying early metastatic lesions presents challenges.

The radioactive pharmaceutical fluorine-18 fluorodeoxyglucose (^{18}F-FDG) is widely used PET tracer for measuring increased glucose metabolism in malignant tumors [4]. This tracer assists in cancer staging, detecting unknown primary lesions, evaluating treatment response, as well as identifying of residual and recurrent lesions. Moreover, recent studies [5-7] have shown that ^{18}F-FDG PET/CT is excellent for early-stage determination and monitoring of therapeutic response in head and neck cancer (HNC), one of the most commonly occurring cancers worldwide.

The treatment of HNC primarily involves a combination of a monoclonal antibody drug known as cetuximab and radiation therapy [8]. However, therapy can give rise to various challenges, including severe damage to healthy tissues, persistence of lesions caused by tumor heterogeneity, metastasis, and the development of secondary malignant tumors. To overcome these limitations, researchers have been actively engaged in radiomics studies that leverage ^{18}F-FDG PET/CT data in the field of HNC research. Radiomics involves the extraction and analysis of large amount of quantitative image features from medical images [9]. This approach enables the generation of personalized treatment plans through the automated medical image segmentation and reproducible analytical methodologies. Beyond efforts to overcome the treatment limitations of HNC, there is also vigorous exploration of Computer-aided diagnosis (CAD) systems driven by advancements in artificial intelligence (AI) technology. CAD serves as a system utilized for the analysis and interpretation of medical images, offering supports to medical professionals in disease diagnosis. Notably, the development of CAD systems necessitates the integration of AI algorithms. Consequently, the performance of CAD systems is intricately tied to the quality of annotation. By ensuring the acquisition of accurate and systematic data through annotation tasks, the effective functioning of CAD systems and the credibility of research outcomes are enhanced.

In the context of HNC research and diagnosis, annotation of lesions on ^{18}F-FDG PET/CT images is essential for CAD system, and constant and accurate annotation of tumors and surrounding tissues is critical. Despite their importance, annotated PET/CT data are rare in public data sets, in contrast to readily available CT or MRI images. Currently, the segmentation and annotation of PET/CT datasets are manually produced by radiologists or nuclear medicine physicians [10]. Manual annotation is time-consuming, inefficient, operator-dependent, and labor-intensive; however, it is considered the definitive gold standard. Specifically, ^{18}F-FDG PET/CT data demands the simultaneous consideration of both metabolic activity and anatomical information, which can lead to issue in terms of reproducibility. In this sense, it is necessary to develop a semi-automatic annotation software for ^{18}F-FDG PET/CT images of HNC patients, enabling efficient work with overlaid PET/CT images.

Our research is grounded in this motivation and aims to develop efficient tools and methods to improve the accuracy and efficiency of ^{18}F-FDG PET/CT of HNC annotation. In doing so, we week to offer the potential to enhance patient care and treatment processes while providing researchers and clinicians with valuable tools.

Over the past few years, research in medical image annotation and deep learning models has rapidly advanced. Yu et al. [11] introduced a deep learning-based approach for the segmentation of HNC in noisy CT images, demonstrating excellent segmentation accuracy. Similarly, Philbrick et al. [12] developed a deep learning-based anatomical tissue annotation software for MRI, CT, and US imaging, successfully segmenting brain, abdominal organs, tumors, and other tissues.

These prior studies have successfully applied deep learning techniques to medical image annotation, thereby improving the accuracy and efficiency of patient diagnosis. However, our research, while building upon these prior works, seeks to go further by innovating in the realm of semi-automatic annotation of PET-CT in the context of HNC.

To date, there has been a notable absence of effective annotation tools for HNC that leverage deep learning. Furthermore, there is a dearth of tools that allow annotation on fused PET and CT images. Currently, most semi-automated annotation tools are primarily trained organ segmentation in anatomical images such as MRI or CT, often relying on complex voxel-based iterative annotation procedures. In this study, our research is uniquely focused on two main objectives: the capability to achieve precise segmentation on fused PET and CT images, and the implementation and incorporation deep learning-based detection and segmentation model for HNC.In this study, we aim to develop the semi-automated annotation software for HNC using a deep learning segmentation model that emerged victorious in the annual deep learning competition known as Hecktor (head and neck tumor segmentation challenge) [13, 14] in 2020. This model was applied to the Hecktor 2021 dataset to assess its effectiveness across diverse datasets.

Notably, Hecktor competition participants have concentrated on enhancing model performance by refining architecture or introducing novel attention modules [13-16]. Hence, we have chosen to adopt the deep learning model that has demonstrated its efficacy through success in the Hecktor competition. Furthermore, this semi-automated software allows medical professionals to review and accurately modify the detected areas.

II. Methods

1. Dataset

^{18}F-FDG PET/CT dataset obtained from Hecktor 2021 containing images of the head and neck regions was used for the medical image segmentation model and annotation software. A total of 224 anonymized image datasets were collected from five different medical centers (CHGJ, CHMR, CHUM, CHUS, and CHUP). Each dataset consists of ^{18}F-FDG PET data in SUV, CT data from low-dose PET/CT, and a binary contour data with the annotated ground truth of the primary gross tumor volume (GTVt). All data were 3D and provided in Nifti format.

The coordinates of the central pharyngeal regions and the bounding box information containing lesion coordinates were employed to train the segmentation model. To address potential minor movements in the pharyngeal area during PET scan following CT scan, a rigid-body transformation model for PET/CT co-registration was applied. The co-registration was performed using SPM12 (statistical parametric mapping 12), an open-source tool in MATLAB R2021a (Mathworks, Inc., USA).

2. Deep learning model

The deep learning model for image segmentation utilized here is based on the SE-Norm-Residual Layer [17]-based U-NET architecture, which demonstrated outstanding performance in segmenting ^{18}F-FDG PET/CT images of the HNC in the Hecktor 2020 challenge (see Fig. 1). The Hecktor 2021 data used in this study includes 23 more samples compared to the data used by Iansen et al. [17] in Hecktor 2020.

The U-Net architecture leverages SE-Norm-Residual convolutional operations as building blocks, and the numbers represents the number of channels in the blocks. To enhance the predictive performance while preserving the inherent Skip-connection structure of a conventional U-Net, Iantsen et al. replaced typical Convolutional Layers with SE-Norm-Residual Layers, effectively

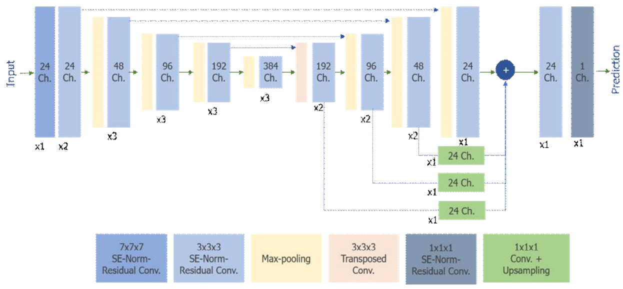

Fig. 1. SE-Norm-Residual-based U-Net Structure

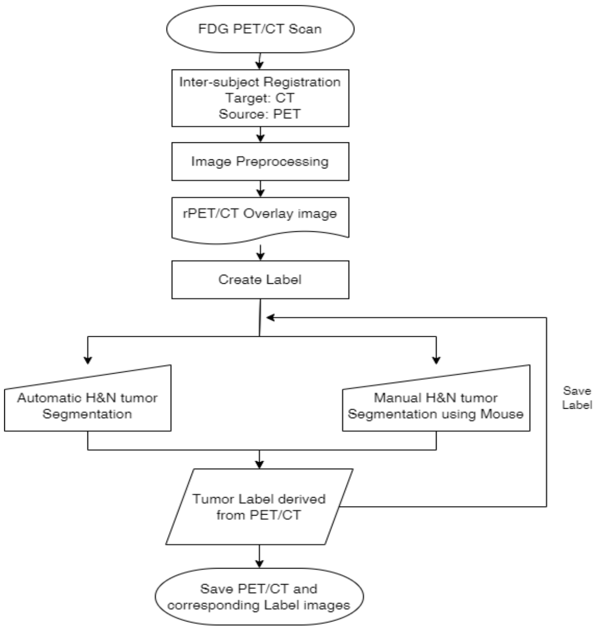

Fig. 2. System flow chart of proposed annotation software

controlling model parameter growth [17]. The SE-Norm-Residual Layer comprises a fusion of Instance Normalization and sequential Channel Attention applied to input features, combined with Residual Blocks.

Furthermore, each feature map generated by the decoder underwent additional Convolutional Layer, facilitating accurate image segmentation. The aggregation of these upsampled feature maps at different resolutions is referred to as Hypercolumn [18].

3. Annotation software design

In order to develop the annotation software for HNC in ^{18}F-FDG PET/CT images, Python (Python Software Foundation) and Qt framework (The Qt Company, Ltd., Finland) were utilized. We designed this software as standalone application, enabling the loading of medical images stored on the computer for annotation purposes. The workflow of the semi-automatic annotation software is depicted in Fig. 2, and the sequence of operations is detailed.

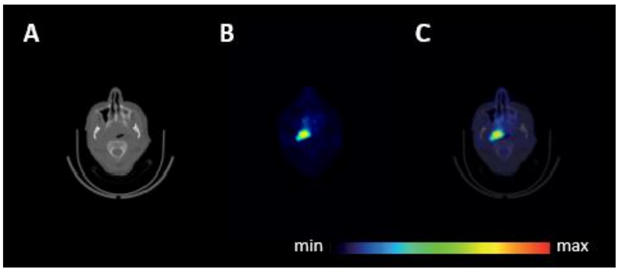

Fig. 3. The representative images of a head and neck cancer patient. (A) The CT images encoded in grayscale. (B) The PET images encoded using JET colormap, representing the positron emission activity. (C) Fusion image of PET and CT images.

The preprocessed PET/CT fusion image is displayed in the software viewer section. CT data representing anatomical information are encoded in grayscale, while PET data representing functional information are encoded using Jet colormap (see Fig. 3).

Labeling is an essential part of medical image annotation for dataset expansion, update, and maintenance. It enables the collaboration and data sharing among multiple operators and reuse or modification of identical annotations. Therefore, we integrated labeling generation and storage function into our software.

Two core functionalities were incorporated: the deep learning segmentation model, as discussed in the **Deep learning model** section, and a manual annotation tool resembling traditional methods. The deep learning segmentation model enables automatic segmentation of potentially concerning regions related to HNC within ^{18}F-FDG PET/CT images, which then can be verified using a viewer. The manual tool encompasses brush style, size, and color selection option, as well as an eraser function. These functions facilitate the participation of users, including researchers and clinicians, thereby contributing the establishment of the definitive criterion. In addition, an opacity adjustment function of the labels was implemented. This provide a visual confirmation of whether the annotations are accurately aligned from a functional/anatomical perspective.

Ⅲ. Results

1. Image preprocessing

The ^{18}F-FDG PET/CT image preprocessing was conducted to improve data quality and segmentation model performance. First, a resolution of 1×1×1 mm^3 was obtained through 3D linear interpolation to adjust the resolution of the acquired data. The resampled data were then modified to form a 144×144×144 mm^3 cubic volume

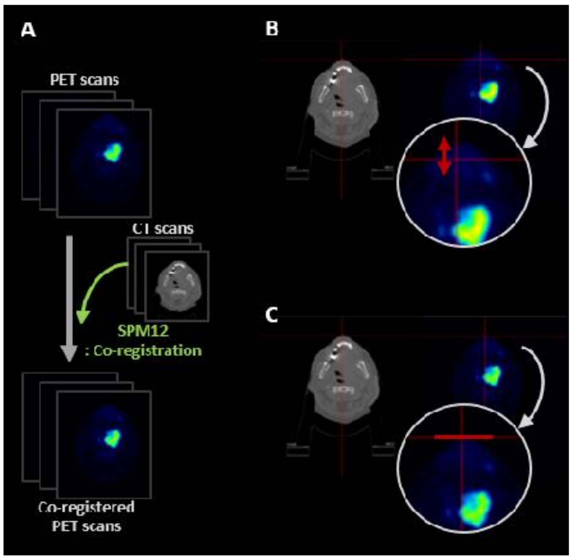

Fig. 4. Within-subject co-registration results. (A) Overall co-registration processing. (B) Pre-registration PET and CT images with misalignment (red arrow). (C) Post-registration images.

(Image cropping). For CT images, Hounsfield units (HU) values beyond the interval of [-1024, 1024] were set to 0 using thresholding. Subsequently, the images were normalized within the range of [-1, 1] (CT image normalization). In cases of PET images, each dataset underwent z-normalization (PET image normalization). Finally, a rigid-body transformation model was employed to co-register PET/CT images from the same subjects onto a uniform coordinate space (Within-subject co-registration) (see Fig. 4).

2. Deep learning model training

Data augmentations such as RandomCrop, RandomRotation, and HotrizontalFlip were used to train the deep learning model. The batch size was set to 8 and a total of 300 epochs were performed. In addition, Adam optimizer along with Cosine annealing scheduler was utilized during the training. The maximum learning rate was set to 1e-3, the minimum to 1e-5, and the cycle to 25. We used a combination of Cross-Entropy and Focal loss. Both loss functions were used in equal proportions and the evaluation metric was Dice score. The performance of the deep learning model was evaluated via CUDA version 11.3 with two RTX 6000 GPUs. All experiments were conducted using the same random seed to ensure reproducibility of the results.

5-Fold Cross Validation was performed to achieve robust predictive performance unbiased towards a specific dataset. Each fold consisted of an 8:2

Table 1. Deep learning model prediction performance on automatic segmentation of head and neck cancer

Fold	Recall	Precision	Dice score
1	0.798	0.810	0.774
2	0.798	0.745	0.735
3	0.749	0.765	0.745
4	0.810	0.768	0.749
5	0.762	0.755	0.726
Average	0.783	0.769	0.750

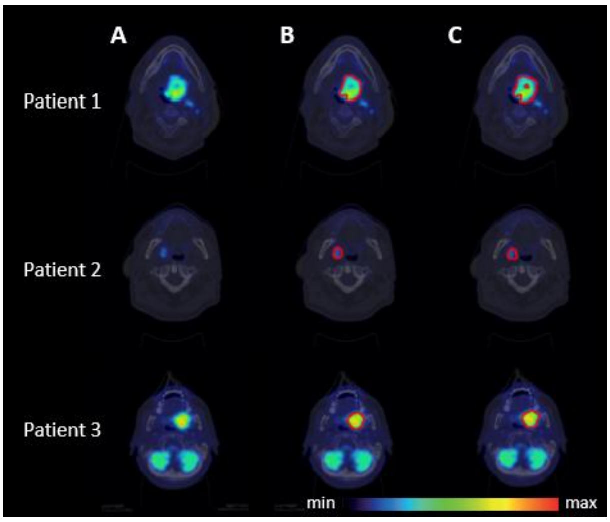

Fig. 5. Representative image of segmentation results using the deep learning model.
(A) Network input. (B) Network output. (C) Ground truth.

training-to-validation dataset ratio. The Dice score for each fold is presented in Table 1. Ultimately, an ensemble of five models was employed within the semi-automatic annotation software to predict suspicious lesion in ^{18}F-FDG PET/CT images. The representative image of the segmentation results using the deep learning model and the ground truth is presented in Fig. 5.

Additionally, for the 1-Fold, we compared the performance of the model trained in this study with the SE-Norm-Residual Layer-based U-NET architecture used by Iansen group [17]. The validation set was maintaine, and both models were compared using the Hecktor 2020 data with/without the additional 23 samples. The performance of both models is presented in Table 2.

3. Annotation software development

In this study, the semi-automatic annotation software for ^{18}F-FDG PET/CT images of HNC patients was developed (see Fig. 6). The software enables operators to upload preprocessed PET and CT images along with an

Table 2. Performance comparison between our U-Net and the U-Net from Iansen group.

Model	Recall	Precision	Dice score
U-Net [17]	0.776	0.808	0.766
U-Net (Ours)	**0.798**	**0.810**	**0.774**

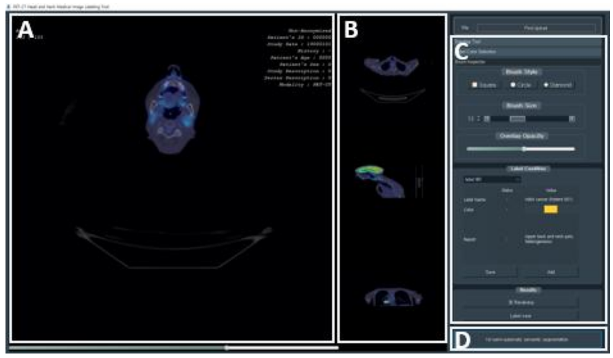

Fig. 6. A semi-automatic annotation software for ^{18}F-FDG PET/CT in Head and Neck cancer.
(A) The main viewer for annotation. (B) Sub viewer for annotation. (C) Manual annotation tools. (D) Deep learning-based automatic lesion segmentation function.

Excel file containing bounding box coordinates using the *File Upload* button. Once the Nifti files are loaded, the software displays transverse plane images of the PET/CT fusion in the main annotation viewer and provides transverse, sagittal, and coronal views in the sub-viewers, respectively (see Fig. 6A and 6B).

The implemented deep learning segmentation model was integrated into the software to provide automatic lesion segmentation capability. This integration offers a tool for generating guidelines on how to delineate voxel-of-interests (VOI) (see Fig. 7). This function operates by selecting the *1st semi-automatic semantic segmentation* button to start inference, and when inference is completed, the prediction results are presented to the main viewer (see Fig. 6D).

Depending on the results, the users can manually refine the areas of false positives or false negatives if corrections are needed according to their expertise. A brush tool for manual annotation was integrated into the software, selecting the brush tool creates the labels and allows users to configure and use options for brush type, color, size, and opacity. For greater user convenience, these settings are adjustable while annotating. The users can easily annotate the HNC regions by splitting the VOIs using the left mouse button and de-annotating it using the right mouse button (see Fig. 6C).

Upon completion of the semi-automatic lesion

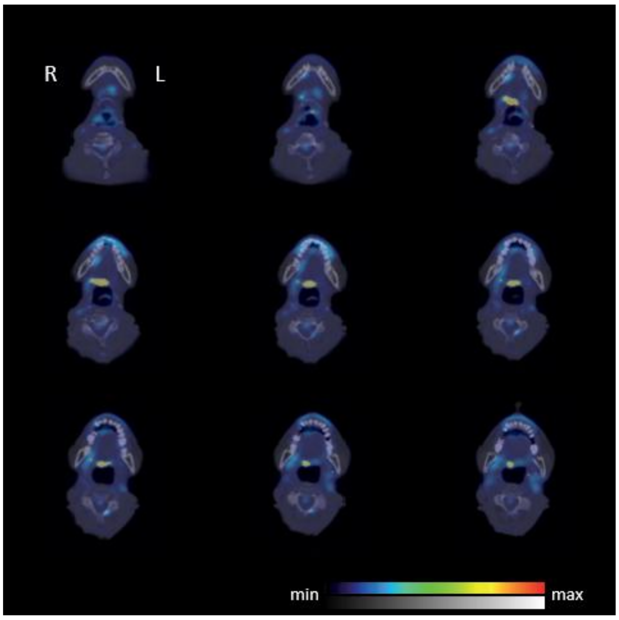

Fig. 7. Thumbnail of main viewer delineating the segmented HNC (in yellow) using a deep learning model.

segmentation, the annotation results can be visualized as 3D rendering by selecting the *3D Rendering* button. Lastly, the *Label Save* button is employed to save both the ^{18}F-FDG PET/CT fusion image and the corresponding annotated binary image for easy application to various fields such as radiomics, CAD, and AI research (see Fig. 6C).

In conclusion, we have implemented a semi-automated approach for annotating the semantic segmentation of suspected regions in HNC within ^{18}F-FDG PET/CT images. Through this system, the PET/CT images and their corresponding annotated data stored within the workstation can be designated for use as input and label data for the previously mentioned studies. Furthermore, it allows for reducing the annotation time for researchers and clinicians and improving the performance of their studies. To the best of our knowledge, proposed system is the first to incorporate automatic detection capabilities among annotation software targeting HNC.

Ⅳ. Discussion

In this study, we have developed a deep learning-based semi-automatic annotation software for ^{18}F-FDG PET/CT images of HNC patients with aim of improving medical imaging diagnosis and research. In addition, it can contribute to overcoming the limitations of existing annotation software by introducing a more efficient and user-friendly solution. To achieve this goal, we initially conducted image preprocessing and training including tasks such as resampling, normalization, and co-registration. Subsequently, the deep learning-based model for HNC segmentation was implemented (Recall=0.783, Precision=0.769, and Dice score=0.75). Furthermore, while maintaining the same model structure, we confirmed that our model outperforms the base model [17] in segmenting HNC (Recall=0.798, Precision=0.810, and Dice score=0.774 for 1-Fold).

The currently available software for annotating 3D medical images for segmentation purpose is notably limited. Moreover, semi-automatic medical image segmentation tools that incorporated unsupervised learning technique, like ITK-SNAP [19], are deficient in their ability to detect VOIs, making them inadequate for annotation tasks. In contrast, our software stands out for its distinctive disease-specific segmentation functionalities. Consequently, developed software represents an innovative and impactful tool, particularly well-suited for executing lesion annotation tasks on head and neck ^{18}F-FDG PET/CT images.

Nevertheless, it is important to acknowledge several methodological limitations within the scope of this study. We chose to use the basic segmentation model, namely U-Net, as our primary emphasis was directed towards harnessing the capabilities of annotation software in conjunction with deep learning models. To achieve even greater precision in image segmentation, the adoption of more sophisticated models such as PSPNet [20], FPNet [21], TransUNet [22], and similar alternatives, which have exhibited superior performance, could be imperative. As a result, subsequent investigations involving the implementation of more refined and high-performance models become evident avenue for exploration.

Due to the limitations of hardware specifications used in this study, the original 3D images were downsampled to the dimensions of 144×144×144 mm^3 before training the deep learning model. Nonetheless, downsampling potentially carries the risk of the loss of information and the reduction image segmentation performance. Therefore, maintaining the initial size and proportions of the medical images is expected to improve the efficacy of the deep learning model.

Furthermore, the relatively compact size of lesions in head and neck ^{18}F-FDG PET/CT dataset prompted the enlargement of the primary viewer, thus providing user convenience during annotation tasks. However, the process of image resizing via interpolation might introduce distortion and information loss. To solve this challenge, the further investigation could consider the development of deep learning-based image resizing models [23], such as Convolutional Neural Networks (CNN), as a potential solution.

In spite of these identified limitations, our study effectively and successfully demonstrates the potential of a semi-automatic annotation software for HNC research and diagnosis. The software boasts an intuitive user interface that streamlines the working environment, thereby bolstering usability and reproducibility. The automated lesion detection and segmentation capabilities not only reduce the independence on operator expertise, but also hold promise in reducing instance of false positive and false negatives. Therefore, the findings of this study stand to enhance the robustness of medical image analysis.

In addition to the findings presented in this study, there are several promising avenues for future research in this field. The current study primarily focused on HNC. It would be valuable to broaden the scope to encompass a more comprehensive analysis of other diseases or imaging modalities. Furthermore, the proposed software offers PET/CT fusion image viewers alongside orthogonal multi-planar reconstruction (transverse, sagittal, and coronal) viewers, similar to commonly employed Picture Archiving and Communication System (PACS) by medical practitioners. This design enhances user familiarity and convenience. These potential directions for further research not only expand upon the current study but also contribute on the ongoing development of knowledge in this domain.

This study demonstrated the potential of semi-automatic annotation software for the HNC diagnosis and research using ^{18}F-FDG PET/CT data. It is expected to have an impact on various research fields in terms of theoretical and practical implications.

Ⅴ. Conclusion

In here, we present a procedure for generating semi-automatic annotations for ^{18}F-FDG PET/CT scans of HNC patients. The underlying objective of this approach is to amplify the potency and accessibility of annotations essential for both research and diagnosis. Our results successfully demonstrate the potential of newly devised semi-automatic annotation software, which surpasses prevailing tools in the field.

Furthermore, as we look to the future, it is essential to consider areas for further research. it is imperative to consider areas for further research future research should focus on enhancing the performance of the segmentation deep learning model. Further research in deep learning modeling could extend the accuracy of HNC delineation, thereby reducing the time-consuming annotation tasks for users. Furthermore, expanding the scope to include other target diseases or modalities may prove to be a significant area for future study. The development of semi-automatic annotation software with scalability will be invaluable for research in fields such as radiomics and CAD. Therefore, we intend to conduct future research in a more realistic setting, taking into account deep learning modeling and scalability.

In conclusion, considering our results and future potential, we suggest that our software offers a streamlined and effective solution for conducting annotated datasets in ^{18}F-FDG PET/CT image investigations and diagnostics, thus notably augmenting their practical utility.

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