Automated measurements of metabolic tumor volume and metabolic parameters in lung PET/CT imaging

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Abstract. Patients with lung tumors or inflammatory lung disease could greatly benefit in terms of treatment and follow-up by PET/CT quantitative imaging, namely measurements of metabolic tumor volume (MTV), standardized uptake values (SUVs) and total lesion glycolysis (TLG). The purpose of this study was the development of an unsupervised or partially supervised algorithm using standard image processing tools for measuring MTV, SUV, and TLG from lung PET/CT scans. Automated metabolic lesion volume and metabolic parameter measurements were achieved through a 5 step algorithm: (i) The segmentation of the lung areas on the CT slices, (ii) the registration of the CT segmented lung regions on the PET images to define the anatomical boundaries of the lungs on the functional data, (iii) the segmentation of the regions of interest (ROIs) on the PET images based on adaptive thresholding and clinical criteria, (iv) the estimation of the number of pixels and pixel intensities in the PET slices of the segmented ROIs, (v) the estimation of MTV, SUVs, and TLG from the previous step and DICOM header data. Whole body PET/CT scans of patients with sarcoidosis were used for training and testing the algorithm. Lung area segmentation on the CT slices was better achieved with semi-supervised techniques that reduced false positive detections significantly. Lung segmentation results agreed with the lung volumes published in the literature while the agreement between experts and algorithm in the segmentation of the lesions was around 88%. Segmentation results depended on the image resolution selected for processing. The clinical parameters, SUV (either mean or max or peak) and TLG estimated by the segmented ROIs and DICOM header data provided a way to correlate imaging data to clinical and demographic data. In conclusion, automated MTV, SUV, and TLG measurements offer powerful analysis tools in PET/CT imaging of the lungs. Custom-made algorithms are often a better approach than the manufacturer’s general analysis software at much lower cost. Relatively simple processing techniques could lead to customized, unsupervised or partially supervised methods that can successfully perform the desirable analysis and adapt to the specific disease requirements.

1. Introduction

Positron emission tomography/computed tomography (PET/CT) is a hybrid imaging technique that combines, in a single gantry, a PET scanner and a CT scanner. Sequential images are acquired from these scanners in the same session and could be fused into a single image. PET/CT combines functional information provided by PET with anatomic information provided by CT [1]. Two- and three-dimensional image reconstruction may be rendered as a function of a common software and control system. The tracer commonly used in oncological PET imaging is fluorine-18 flurodeoxyglucose (FDG) and is a glucose analog that is taken up by glucose-using cells and undergoes phosphorylation by hexokinase, an enzyme whose mitochondrial form is at much higher levels in rapidly-growing malignant tumors [2]. FDG is absorbed by the cells causing intense radiolabeling of areas with high glucose uptake.
such as the brain, most cancers, and inflammations. This process is used for diagnosing, staging, and monitoring of disease [1]. Various metrics are used clinically to determine the FDG uptake of lesions and differentiate benign from malignant or inflamed areas. The standardized uptake value (SUV) is commonly calculated and reported today as a prognostic marker. There are several ways to estimate SUV, two commonly used parameters are the SUV\textsubscript{max} and SUV\textsubscript{mean} that are based on the maximum and mean pixel values respectively within an ROI. Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) are additional markers that prove to have significant prognostic values [3]. Lung tumors or inflammatory lung disease are not usually diagnosed by PET/CT scans. Patients undergo a series of primary diagnostic procedures which define the type and extend of the disease. There is increasing interest, however, to broaden the application of PET/CT and make it more standardized and quantitative. Computer methodologies offer robust tools for the automation and standardization of the measurements and could significantly enhance the role of PET/CT in diagnosis and treatment. The purpose of this study was to develop and evaluate a generic computer algorithm for PET/CT images of the lungs for the detection and quantitation of disease.

2. Materials and Methods

Medical image processing algorithms vary according to the nature of each imaging. Thresholding is the simplest method of image segmentation. From a grayscale image, thresholding can be used to create binary images. The simplest thresholding methods replace each pixel in an image with a black pixel if the image intensity $I$ is less than some fixed constant $T$ (if $I < T$) or a white pixel if the image intensity is greater than that constant (if $I > T$). [4]. Adaptive thresholding, is the process where the value $T$ is changing for each image according to the $I$ of the specified image. The developed algorithm included 5 steps as follows:

I. Segmentation of the lung areas on the CT slices was achieved by adaptive thresholding and labelling. Adaptive thresholding was based on the mean value of a customized frame that included lungs, trachea and a small part of thorax. The threshold was adapted for each image and each patient. Labeling separated the lung regions (left-right). This first step of the algorithm was semi-automated. The user could manually customize the segmentation process by changing the threshold value $T$ for the desired result that included only the true lung area.

II. Registration of the segmented lung regions from CT on the PET image was performed in the second step to determine the boundaries of the lungs on the functional data and, hence, facilitate the detection of the lung lesions on the PET data.

III. Segmentation of the regions of interest (ROIs) on the PET images was performed based on adaptive thresholding and clinical criteria regarding the uptake of FDG. Several cutoff values from the maximum region intensity were tested on the training set of images (see below). A threshold of 40%, commonly used in clinical practice, was finally selected for the segmentation of sarcoidosis regions.

IV. Estimation of the number of pixels and pixel intensities of the segmented PET ROIs was performed for each slice, each lung, and each patient. Data were saved as a text file.

V. Estimation of four markers, MTV, SUV\textsubscript{max}, SUV\textsubscript{mean} and TLG, was performed from the previous measurements and DICOM header data as defined in the literature [3].

It should be noted that CT images were 512x512 pixels while PET images were 168x168 pixels in size and both had 16 bits/pixel. The difference in spatial resolution of the two image sets required the evaluation of different approaches in the fusion of the lung templates from the CT data with the PET data. In the end, it was given as an option to the user to either resize the PET images to 512x512 to match the CT data or reduce the CT segmentations to 168x168 to match the original PET data; the former approach was preferred by the experts for the sarcoidosis application described below. Both changes were performed with bilinear interpolation to minimize artifacts. The resizing required an additional step to smooth and fill in artificial “gaps” in the resized images in order to avoid underestimates or overestimates of the disease in the following steps.
The above algorithm was trained and tested on PET/CT scans of 57 patients with lung sarcoidosis [5]; 10 patients were used for training and 47 for testing. Each patient underwent a whole body PET/CT scan with a Biograph 6 (Siemens Healthcare, DE) system using the same imaging protocol. The slices that covered the entire pulmonary regions were selected for processing. That yielded an average of 80 CT and 80 PET slices per patient. Results were reviewed by two experts in nuclear medicine and PET/CT. Ground truth data were determined by the same experts for all patients.

3. Results
Representative results are shown in Figs. 1-3. Figure 1 shows a CT slice and a corresponding PET slice of a patient with lung sarcoidosis. Figure 2 shows the segmentation of the lungs from the CT slice that yields a template to superimpose on the corresponding PET slice. Figure 3 shows the segmentation of the areas that correspond to sarcoidosis with increased FDG uptake in the PET scan.

The segmentation results were evaluated qualitatively and quantitatively by two experts in PET/CT. The agreement between experts and the algorithm for the detection of sarcoidosis was around 88%. Segmented metabolic sarcoidosis volume ranged from 14 cm³ to 1136 cm³. Lung volumes estimated from the CT segmentation agreed with lung volumes published in the literature. Average segmented lung volume was 2787 cm³ with a standard deviation of 715 cm³. $SUV_{\text{max}}$ and $SUV_{\text{mean}}$ parameters of the segmented sarcoidosis lesions ranged from 2.5 to 9.8 and 0.7 to 4.3 respectively. The TLG marker ranged from 4.2 to 2384.

The prognostic value of MTV, $SUV_{\text{max}}$, $SUV_{\text{mean}}$, and TLG metrics that were estimated following image segmentation and pixel measurements is currently under investigation in a longitudinal study by experts in sarcoidosis and will be determined by correlating these measurements with laboratory test results and clinical outcome.

4. Conclusions
Hybrid tomographic imaging like PET/CT is expected to grow with expanded applications in cardiology, infectious and inflammatory disease management, orthopedics, and others. New and more efficient protocols are likely to be developed in addition to technological advances of the scanners. Automated processing and analysis of the images will become a clinical necessity and an integral part of their interpretation considering the amount of data to be reviewed by the experts and their complexity.

The proposed algorithm offered a relatively simple approach to the segmentation of lung lesions in PET/CT data. Several unanswered questions remain including that of the optimum matching between CT and PET images and its impact on the segmentation results as well as the selection of optimum
threshold according to the clinical application. Despite these open issues, the method led to the quantitation of important clinical markers in a fast, reliable, and standardized way. Correlation of imaging to demographic and clinical data was facilitated. Such analysis could standardize the interpretation of hybrid examinations and improve patient management in a variety of applications.

Fig. 2. Segmentation of lungs areas from the CT image of Fig. 1.

Fig. 3. Segmentation of PET ROIs that correspond to sarcoidosis (light gray) within the defined lung regions. The number of pixels and the intensities of the pixels within each ROI was calculated and stored as a text file to be used for further quantitative measurements.

5. References

[1] Kapoor V, McCook BM, and Torok FS 2004 An Introduction to PET-CT Imaging Radiographics 24 523
[2] Zhu A and Shim H 2011 Current molecular imaging positron emitting radiotracers in oncology Nucl. Med. Mol. Imaging 45 1
[3] Satoh Y, Nambu A, Ichikawa T, and Onishi H 2014 Whole-body total lesion glycolysis measured on fluorodeoxyglucose positron emission tomography/computed tomography as a prognostic variable in metastatic breast cancer BMC Cancer 14 525
[4] Sharma N and Aggarwal LM 2010 Automated medical image segmentation techniques J. Med. Phys. 35 3
[5] Prabhakar HB, Rabinowitz CB, Gibbons FK, et al 2008 Imaging Features of Sarcoidosis on MDCT, FDG PET, and PET/CT AJR 190 S1