Computerized Medical Imaging and Graphics 70 (2018) 1–7

Contents lists available at ScienceDirect

Computerized Medical Imaging and Graphics

journal homepage: www.elsevier.com/locate/compmedimag

Semi-automatic lymphoma detection and segmentation using fully conditional random fields

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ARTICLE INFO

Article history:
Received 2 March 2018
Received in revised form 4 July 2018
Accepted 4 September 2018

Keywords:
Positron Emission Tomography (PET)
Lymphoma detection and segmentation
Fully connected conditional random fields
Anatomical atlas

ABSTRACT

The detection and delineation of the lymphoma volume are a critical step for its treatment and its outcome prediction. Positron Emission Tomography (PET) is widely used for lymphoma detection. Two common types of approaches can be distinguished for lymphoma detection and segmentation in PET. The first one is ROI dependent which needs a ROI defined by physicians. The second one is based on machine learning methods which need a large learning database. However, such a large standard database is quite rare in medical field. Considering these problems, we propose a new approach that combines PET (metabolic information) with CT (anatomical information). Our approach is semi-automatic, it consists of three steps. First, an anatomical multi-atlas segmentation is applied on CT to locate and remove the organs having physiologic hypermetabolism in PET. Then, CRFs (Conditional Random Fields) detect and segment a set of possible lymphoma volumes in PET. The conditional probabilities used in CRFs are usually estimated by a learning step. In this work, we propose to estimate them in an unsupervised way. The final step is to visualize the detected lymphoma volumes and select the real ones by simply clicking on them. The false detection is low thanks to the first step. Our method is tested on 11 patients. The rate of good detection of lymphoma is 100%. The average of Dice indexes for measuring the lymphoma segmentation performance is 84.4% compared to the manual lymphoma segmentation. Comparing with other methods in terms of Dice index shows the best performance of our method.

1. Introduction

Lymphoma is a group of blood cancers that develops in lymphatic system, notably lymph nodes. Its high morbidity and mortality, notably for aggressive types like diffuse large B cell lymphoma (DLBCL), have drawn an important attention by physicians and related researchers. In particular, it has been shown that the whole volume of the lymphoma is an important prognostic factor (Cottereau et al., 2016) which supports the need to find an algorithm measuring automatically the volume of the disease.

Positron Emission Tomography (PET) is a nuclear medicine functional imaging technique which can observe the metabolic activity of tumors. Despite of the low resolution and poor SNR as described in (Zaidi and El Naqa, 2010), the positron emission tomography using 18F-FDG is one of the most widely used approaches for the lymphoma detection, as most lymphoma subtypes have high (18)F-FDG activity (Weiler-Sagie et al., 2009). To identify a lymphoma from PET it needs to overcome the following difficulties. Firstly, lymphoma's metabolism on PET image in terms of standardized uptake value (SUV) is not fixed. Its metabolism varies from patients, subtypes and activities of lymphoma. Therefore, there are not a standard SUV for them. Secondly, as lymphatic system belongs circulatory system, lymphoma can appear in many parts of body. In addition, the shape of lymphoma varies from one to another and it contains very little texture information. A visual representation of a PET/CT of lymphomas is visible in Fig. 1.

The lack of image characteristic and shape information of lymphoma makes them difficult to be automatically detected. Different approaches have been reported for this task in the literature. They can be separated into two common types. The first type consists of ROI-dependent methods, where the ROI is usually defined by a physician, leading to a human time-consuming processing. The most widely used segmentation approach of this type in clinical application is a thresholding by 41% of the maximum SUV in ROI. But in many situations, the SUV values in a ROI are not homogeneous leading this threshold approach to provide poor results. Thus, different methods (Black et al., 2004; Nestle et al., 2005; Vauclin et al., 2009; Chen et al., 1999) are proposed to improve it. Vauclin's

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https://doi.org/10.1016/j.compmedimag.2018.09.001
0895-6111/

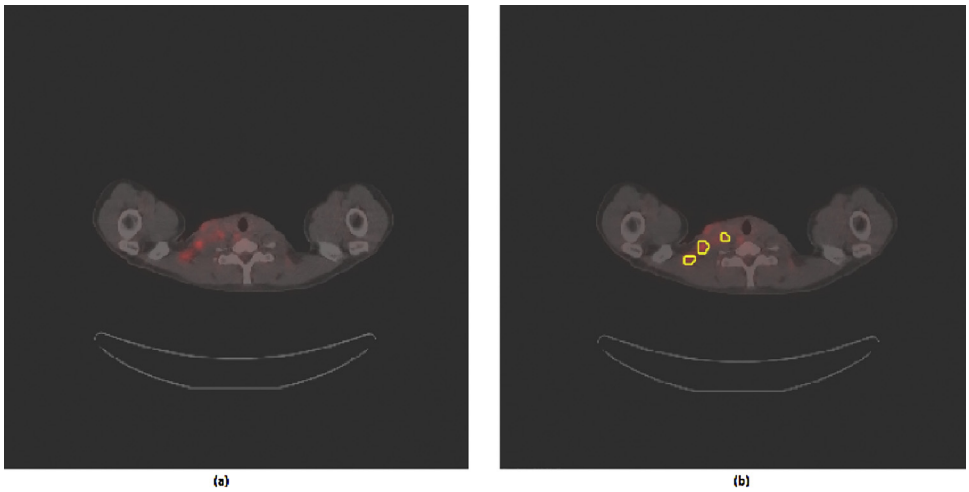

Fig. 1. (a) Combination of PET image (in red) and CT scan. (b) The ground truth of lymphoma sites contoured in yellow in PET and CT (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).

method (Vauclin et al., 2009) uses a no linear model to find the threshold by an iterative way. A comparison of the methods based on thresholding is reported in (Tylski et al., 2010a; Tylski et al., 2010b). Cellule automata (CA) (Desbordes et al., 2015) is based on region growing approach with seeds distributed in a ROI. Second type of lymphoma detection and segmentation approach does not need a ROI a priori, it uses machine learning by learning and analyzing a huge database. Different features of lymphoma are learnt and trained from PET image. The main methods of this second type of approach are SVM (Yan et al., 2015), Random Forest, Component-Trees (Eloïse et al., 2017), and recently deep learning (Sharif et al., 2010; Bi et al., 2017). As the lymphoma can appear in many locations in the body and the number of lymphoma can be important, definition of all ROI increases largely physicians' work. In addition, the results of segmentation are highly depended on the defined ROI. The second type of approach is promising. However, it needs a standard and global admitted database which is hard to get and focus principally on lymphoma detection.

CRFs (Conditional Random Fields) algorithm is applied widely in natural language processing and sequential data labelling or parsing. Recent researches show also its significant application in object recognition and multi-class image segmentation (Shotton et al., 2007; Krähenbühl and Koltun, 2011). Considering its efficiency, CRF is developed in our work. As reported in our preliminary study (Yu et al., 2018), we propose to use a new way to detect and segment the lymphoma in 3D. Our method combines an anatomical atlas obtained in CT and a fully connected conditional random field based segmentation to detect and segment lymphoma regions in PET. Firstly, the anatomical multi-atlas segmentation of the CT removes the organs which have a physiological hypermetabolism in PET and are usually not affected by the disease, such as brain, heart, kidneys and bladder. We use the method proposed in (Zhoubing et al., 2015) for this step. As PET/CT are acquired in one acquisition, their registration is not needed. After removing these organs, the CRFs algorithm is applied on PET image volume for lymphoma detection and segmentation. The CRFs model is composed of a unary energy which is based on the probability of lymphoma and a Gaussian kernel pairwise energy which includes the contrast and the spatial distance information. Finally, all the detected regions are visualized in 3D, allowing the user to select the lymphoma to be studied by simply clicking on it. The proposed tool allows to largely reduce the time and improve the precision to measure the lymphoma volume.

In this paper, we focus on the development of CRFs based detection and segmentation. The paper is organized as follows: Section 2 presents our CRFs model and related inference; Section 3 explains our evaluation metrics, the parameters' estimation and our obtained results compared to other segmentation algorithms; Conclusion and perspectives are given in the last section.

2. Materials and method

2.1. Database

PET images were acquired by a PET/CT scanner (Biograph Sensation 16; Siemens®, Knoxville, TN), which includes a 16-slice CT component and a PET system with lutetium oxyorthosilicate crystals. For PET imaging, the emission data were acquired from the base of the skull to the proximal thigh with acquisitions of 3 to 3.5 min per bed position, depending on the patient's body mass index (BMI), each covering 16.2 cm, at an axial sampling thickness of 2 mm per slice. The CT scan parameters were set to 100–120 kVp and 100–150 mA s (based on the patient's BMI) using dose reduction software (CareDose; Siemens Medical Solutions, Knoxville, TN). Both the PET scans and the CT scans were obtained during normal tidal breathing. The PET images were reconstructed with attenuation correction using the CT-derived data and an attenuation-weighted ordered-subsets expectation maximization (AW-OSEM) algorithm. The spatial resolution was 5.3 mm × 5.3 mm × 2 mm.

Our dataset consists of 11 patients. Each patient has approximately 4 tumor sites of lymphoma (type: DLBCL).

2.2. Multi-atlas

The first step of our method is to remove the organs which have a physiological hypermetabolism in PET and can be considered as lymphoma. We use a multi-atlas based segmentation to delineate these organs. The method developed in (Zu et al., 2015) is applied in our work. The Fig. 2 shows the processes of this first step. A new CT is registered to the multi-atlas in order to find the locations of the organs to be removed. This step allows to reduce the number of false lymphoma detection, and results of the registration does not directly influence the segmentation of the lymphoma in the next step.

The second step is to detect and segment the lymphoma volume only on the regions without these organs. We propose to use an automatic approach based on CRFs model.