Automatic Detection of Abnormality in the Lung Images taken by Positron Emission Tomography with 18Fluorodeoxyglucose

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論文内容の要旨

Chapter1. Introduction

Lung cancer is the most common cause of death by malignancy in men and women. Approximately 3 million cases arise each year worldwide. Lung images taken by Positron Emission Tomography (PET) using ^{18}Fluorodexyglucose (FDG) have shown many progressions in detecting the abnormality. Therefore, in this study, these images were used. However, the PET images suffer from noises. Small lung nodule could be overlooked due to noise. Visual inspection for detecting tumor can lead to an error due to fatigue of the medical doctor. Therefore, a system of automatic detection is an urgent need.

Objective of this thesis was to develop a methodology and a system of automatic detection of abnormality in FDG-PET image of lung. Abnormality in the lung is usually detected as high intensity region. The suspicious area could be cancerous cell, tumor, or inflammation. The system receives the 3 dimensional emission and transmission image as inputs and the output is a 3 dimensional image which contains only the abnormal part of the image.

Chapter 2. Automatic Segmentation of Lung Tissue in the Emission Image

Materials used in this thesis were ^{18}FDG-PET images from Cyclotron and Radioisotope Center (CYRIC), Tohoku University. The data contains 21 healthy subjects' images, and 22 lung cancer patients' images. Both patients and healthy subjects images were taken using Shimadzu PET SET-2400W. The images were reconstructed using Ordered Subset Expectation

Maximization (OSEM). Voxel values of the emission images were converted into Standardized Uptake Value (SUV).

To increase the efficiency, the input images were down-sized. The downsized images were built by representing 27 voxels into 1 voxel. Value of the resulting voxel was the median of the 27 voxels.

In a transmission image, the border of the lung can be seen clearer than in emission image. Therefore segmentation of the lung was done first in the transmission image. The transmission image was clustered into 2 clusters. From the highest cluster, the lung voxels were searched from the center of body cavity up to the upper part of the body.

The region growing algorithm should be restricted by the border of the patient's body. This border was obtained by clustering the image until the air surrounding the patient was found. Negative of the air is the patient's body. Border of the patient was obtained by applying the first derivative to this image.

Missing part of the lung caused by abnormality was closed using median filter continued with dilation and erosion. The lung coordinates of the transmission image was applied to emission image for segmenting the lung in the emission image.

Results and analysis of lung segmentation: For image of the subject without abnormality, the algorithm succeeded in segmenting the lung completely. For image of the lung cancer patient with abnormality in the middle of the lung, the algorithm also works very well. For the lung with abnormality located on the border, it depends on the voxel value. If the voxel value is not very high then it would be segmented together with the lung tissue, otherwise, it is excluded. This abnormal part was excluded during clustering process where high intensity abnormal tissue was grouped in to the higher cluster together with other tissue. In chapter 3, this problem is solved.

Chapter 3 Automatic Detection of Abnormality in Lung

It is broadly known that lower part of the lung has higher intensity than the upper part. From observation done in this study, it is clear that the more the tissue located near mediastinum, the higher the intensity is. From these facts, it is clear that the judgment for a voxel whether or not it is abnormal, depends on its location.

Other fact that should be taken into consideration in judging the abnormality in the lung is mean of SUV (Standardized Uptake Value). Capability of absorbing FDG tracer is different from one patient to another.

By having comprehended the facts mentioned above, the idea proposed in this thesis was creating a multiple regression model for judgment of abnormality of voxels in the lungs. A point located in the center of chest cavity (c), was determined. Distance of the voxel under examination from point c, coordinates of the voxel relative to c, and mean of SUV become explanatory variables. Multiple linear regression model of FDG activation in healthy subject's left lung is:

Estimated value = 1.783873 mean of SUV - 0.006440 distance - 0.061818 x - 0.028532 y - 0.025683 z,

while that of healthy subject's right lung is:

Estimated voxel value = 1.192548 mean of SUV + 0.026833 distance + 0.053990 x - 0.029837 y - 0.013159 z.

Judgment of the abnormality depends on the actual voxel value whether or not it is higher than 1 standard deviation or 2 standard deviation of the estimated value. The estimated value was calculated using model of the healthy subject's lungs images and that of the patient's lung images itself.

Results and analysis of automatic detection in lung images: The algorithm has been tested for detecting abnormality in 22 patients' images. Judgment for voxel abnormality using model of healthy lung images was more sensitive than using that of patient images itself. Abnormality determination using estimated value+1 standard deviation is more sensitive than that using estimated value+2 standard deviations. Because the result of lung segmentation suffers from under segmentation if the abnormality is located on the border, the segmentation of abnormality was also not completed. Chapter 4 discusses the solution of this problem.

Chapter 4. Detection of Abnormality of Lung Tissue near Mediastinum

Abnormal tissue that was not detected was located near mediastinum. This is due to the clustering process where they are clustered together with other tissue whose intensity is high. Therefore, abnormality detection should be continued for the mediastinum.

Heart, which is located in the mediastinum, should be excluded in the detection process. Heart in FDG-PET image of the patient with high metabolism has high intensity in its ventricle. Therefore, it would be detected together with the abnormal tissue. Also, high intensity of the ventricle affects the sensitivity of the detection.

Variations in the voxel intensity among different patients make the heart segmentation a challenging task. The idea proposed in this study was to register the chest of a healthy subject's image whose intensity is high in its ventricle with the patient's chest image. Chest was used here with consideration of better efficiency than if whole body is used in the registration process.

Heart of the healthy subject was segmented by first, calculating gradient magnitude of all voxels inside it. Then the voxels that were not locally maximum were suppressed. The process was continued by adding the voxels that were known as part of the heart. Closing algorithm was done by applying dilation and erosion.

Model of FDG uptake in the mediastinum was then obtained using the same process performed for creating the model of FDG uptake in the lungs. The model is written as follows:

Estimated voxel value = (1.662263 mean of SUV) – (0.013505 distance) – (0.048033 x) – (0.008235 y) - (0.021689 z)

Results and analysis: The abnormality located near mediastinum was successfully detected here. The problem discussed in the previous chapter has been solved. Even the nodules with high intensity located in the border were detected. Beside the positive determination, there were also negative determinations, where the nodules were not detected. The problem existed because those nodules were located in the high intensity neighborhood, for instance, because of other higher intensity nodules located nearby.

Chapter 5. Discussion on Related Works

There exist some related works in the literature. Most of them use a threshold for SUV > 2.0 for judging the abnormality of voxels. One of them is the work of Haiying Guan, et.al, of SIEMENS, "Automatic Hot Spot Detection and Segmentation in Whole Body FDG-PET Images", 2006 IEEE International Conference on Image Processing - ICIP 2006).

Other work has been performed using Gaussian Mixture Model as opposed to fix thresholding, however their method needs the user to input a certain parameter. It means that the process is not fully automatic (Michalis Aristophanousa, et.al "A Gaussian mixture model for definition of lung tumor volumes in positron emission tomography", Medical Physics (34)11, Nov 2007).

It is clear that the methods proposed in this thesis are better than the existing methods. There is no thereshold used in this study. In some cases, adenocarcinoma, a kind of lung cancer disease, have mean of SUV below 2.0. Using the methods proposed in this thesis, the nodules whose value is below 2.0 can be detected. The system developed in this study is fully automatic. No parameter is needed to be input.

Chapter 6. Conclusion

An algorithm that is better than the existing algorithms has been proposed in this study to detect abnormality in lung cancer patient image which is taken using FDG-PET. The algorithm is better since it does not use any threshold for detecting the abnormality and because the system, developed as the application of the algorithm, is fully automatic. Novel linear models were proposed in this study for modeling activation of FDG in the right lung, left lung, and mediastinum. Using these linear models, the abnormality, whose value is below 2.0, can be successfully detected. The algorithm can be used to build atlas of the healthy lungs. To our knowledge, no such algorithm was available yet.

The system has been tested to detect 22 lung cancer patient images. In those images, there are 27 nodules. 24 of those nodules were detected. Small nodule (1 cm) can also be detected. The system was only failed in detecting 3 nodules. Those undetected nodule were located in high intensity neighborhood, so that they are considered as normal by the system. Those nodules are located, for instance, in the high intensity mediastinum, or in the lung that has other higher intensity nodule. Part of the method proposed in this study is segmentation of the heart of healthy subject. Segmentation of heart in FDG-PET image can be hardly found in the literature.

In some cases, there exists false detection where noise was also detected. But using the images from current technology (high resolution PET image), the noise can be certainly reduced. In some cases, mis-alignment of the heart was found. Big nodule can affect the shape and intensity of the lung that leads to mis-alignment of the heart. The fact is that the research in alignment of organs containing abnormality is currently performed worldwide. A deep research in this area could lead to a new research topic that is out of the scope of this study.

The key achievements of this thesis, as described above, make it clear that the methods proposed in this thesis are better than the existing systems.

論文審査結果の要旨

本論文は、^{18}FDG-PET の肺画像において病巣等の異常部位を自動的に検出する手法を提案するものである。この手法は、固定のしきい値を用いた従来法と異なり、大きな肺腫瘍のみならず微小な腫瘍をも自動的に検出することを目的としている。

本論文は全6章で構成されている。

第1章は、背景と目的である。

第2章では、本論文で提案する肺形状の抽出のためのセグメンテーションアルゴリズムについて述べている。加えて、肺の ^{18}FDG-PET 画像のサイズ縮小により、全プロセスを高速化する手法について説明している。

第3章では、第2章で説明した手法によりセグメンテーション化された肺画像から、異常部位を自動的検出するアルゴリズムを提案している。さらに、肺の異常部位を検出するのに有効な、新たな数学的モデルに関して言及している。すなわち、肺の PET 画像から、しきい値を設けることなく異常の検出を可能にしたものである。

第4章では、肺の縦隔に対するセグメンテーションと異常部位の検出のアルゴリズムについて論じている。ここで、縦隔周辺に位置する異常部位のセグメンテーションに関する不完全性の問題が解決されている。また、これまでほとんど研究されていない心臓のセグメンテーションのためのアルゴリズムが提案されている。さらに、縦隔での ^{18}FDG 集積に対する新しい数学的なモデルが示されている。

本手法を実装した完全自動システムを 22 件の肺がんの臨床画像（27 個の腫瘍が存在）に適用し、心臓の極近くに位置した癌（3 個）以外の 24 個の検出に成功している。

第5章では、本研究に関しての考察と検討が為されている。既存のシステムとの比較の結果、本研究で実装された方法とシステムが優れていることが示されている。本研究において提案された方法が、重篤な腫瘍部位の中心を発見するだけでなく、1cm 程度の小さな腫瘍も検出できることが確認されている。

第6章では、本論文の結論が述べられている。

以上、要するに本論文は、^{18}FDG-PET 画像に関するセグメンテーション法の高度化により、癌などの異常部位を自動的に検出することを可能にしたことを示したものであり、医工学の発展に寄与するところが少なくない。

よって、本論文は博士（医工学）の学位論文として合格と認める。