research article

Segmenting CT images of bronchogenic carcinoma with bone metastases using PET intensity markers approach

Iman Avazpour[1], Ros Ernida Roslan[1], Peyman Bayat[1], M. Iqbal Saripan[1], Abdul Jalil Nordin[2], Raja Syamsul Azmir Raja Abdullah[1]

[1]Department of Computer and Communication, Faculty of Engineering, Universiti Putra Malaysia 43400 Serdang, Selangor, Malaysia, [2]Faculty of Medicine and Health Sciences, University Putra Malaysia, 43400 Serdang, Selangor, Malaysia

Background. *The evolution of medical imaging plays a vital role in the management of patients with cancer. In oncology, the impact of PET/CT imaging has been contributing widely to the patient treatment by its large advantages over anatomical imaging from screening to staging. PET images provide the functional activity inside the body while CT images demonstrate the anatomical information. Hence, the existence of cancer cells can be recognized in PET image but since the structural location and position cannot be defined on PET images, we need to retrieve the information from CT images.*
Methods. *In this study, we highlight the localization of bronchogenic carcinoma by using high activity points on PET image as references to extract regions of interest on CT image. Once PET and CT images have been registered using cross correlation, coordinates of the candidate points from PET are fed into seeded region growing algorithm to define the boundary of lesion on CT. The region growing process continues until a significant change in bilinear pixel values is reached.*
Results. *The method has been tested over eleven images of a patient having bronchogenic carcinoma with bone metastases. The results show that the mean standard error for over segmented pixels is 33% while for the under segmented pixels is 3.4%.*
Conclusions. *Although very simple in implementation, region growing can result in good precision ROIs. The region growing method highly depends on where the growing process starts. Here, by using the data acquired from other modality, we tried to guide the segmentation process to achieve better segmentation results.*

Key words: computed tomography segmentation; dual modality imaging; PET/CT

Received 24 February 2009
Accepted 28 May 2009

Correspondence to: M. Iqbal Saripan, Department of Computer and Communication, Faculty of Engineering, University Putra Malaysia, 43400 Serdang, Selangor, Malaysia. Phone: +603-89464344; Fax: +603-86567127; E-mail: m.i.saripan@gmail.com or iqbal@eng.upm.edu.my

Introduction

Bronchogenic carcinoma normally known as cancer of the lung is the most frequently diagnosed "major" cancer in the world.[1] It is a common disease and a leading cause of death in many countries.[2,3] Lesions occur in breast, lung, prostate and kidney comprised 80% of all metastases to bone. In 1990, estimated 1.04 million new cases of lung cancer were diagnosed; representing 12.8% of total cancer incidence worldwide.[1] The prevention and early diagnosis of lung cancer thus assumes a major public health issue. Bone scan demonstrates the possible evidence of bone metastasis. The study by Kiho Kim *et al.*[4] suggests that bone scanning with 99m- monodiphosphate detected early bone metastases in patients with bronchogenic carcinoma before their lesions became evident clinically or radiographically. A group of researchers from Clinical Radiology of Kyushu University studied the comparison of Positron Emission Tomography (PET) using 18-F-Fludeoxyglucose (18-F-FDG PET) with 99mTc-HMDP scintigraphy for the detection of bone metastases in patients with breast cancer. Their results showed that 18-F-FDG PET tends to be superior to bone scintigraphy in detecting osteolytic lesions, but inferior in the detection of osteoblastic lesions.[5] The evolution of the imaging plays a vital role in managing the patients with lung cancer. The role of imaging ranges from screening lung cancer in high risk individuals to staging bronchogenic carcinoma in advanced stages of the disease.[6]

Tomography is a tool that provides information on what is actually happening inside the body. Positron Emission Tomography (PET) scans and Computerized Axial Tomography (CAT) scans or also known as Computed Tomography (CT) scans are all used to provide information about possible tumours and metastases of cancer. Tomographic imaging methods are important since proper staging of cancer is basic in planning the best treatment.[3,6]

PET images provide information about the functional and metabolic activity of a lesion while CT images demonstrate the anatomical location and the structural information. Integration of Positron Emission Tomography with Computed Tomography (PET/CT) imaging is becoming more popular and useful in the clinical application for an early tumour and cancer detection.[7-9] Superimposing the images of functional activity on structure gives the best of both imaging modalities – the anatomical detail of the CT and the ability to find small clumps of viable cancer cells of the PET. Initial studies by De Wever W *et al*.[2] demonstrate better results for PET/CT in the staging of lung cancer in comparison with PET alone, CT alone or visual correlation of PET and CT.

Although fusion techniques have helped visual perception of dual modality images, hundreds of images that are taken for each patient using this modality and analyzing all of them take time and expertise. The image segmentation procedure simplifies the image presentation and canalization. The importance of segmentation in medical images is to extract and characterize anatomical structures with respect to some input features or expert knowledge.[10] The medical image segmentation is a challenging task due to the various characteristics of the images which lead to the complexity of segmentation. In general, the autonomous segmentation is one of the most difficult tasks in digital image processing.[11] To address the problem, we introduced a new algorithm based on the supervised automatic segmentation which, we believe, can improve the diagnosis of bronchogenic carcinoma with bone metastases.

Conventionally, monitoring, treatment arrangement and assessment of response after the radiation therapy (RT) are mainly based on CT and MRI.[12,13] These methods, also called anatomical imaging, have the major advantage of viewing the anatomy with a high resolution and drive to the contribution on the highly sophisticated RT techniques such as the three-dimensional, conformal RT, stereotactic RT and radio surgery, intensity modulated RT (IMRT) and RT with heavy particles.[13,14] All these techniques aim to concentrate the irradiation dose on the lesion area with high precision to spare the normal tissue. Generally, the higher the irradiation dose, the higher is the rate of local tumour control, whereas the lower irradiation dose in normal tissue leads to lower side effect risks.

High activity lesions in PET images always appear with higher intensity due to more absorbent of radio isotope tracer and higher rate of radio activity.[15] Cancer cells have higher activity compare to normal tissue, hence, they absorb more tracer material and the amount of radio activity increases in these cells. PET detectors detect photons propagated by this radio activity and produce an image, showing high activity pixels differently.

Methods

In this study, the patient was fasted overnight prior to the scanning day and injected with *18F-fluorodeoxyglucose (*18F-FDG) radionuclide 45 min before the scan. All imaging studies were performed on a dual-modality PET/CT device (Biograph 6, Siemens Medical Solutions Inc.). PET/CT images were acquired with the patient in the supine arms-up position and acquisition time was 3 min per bed position with seven bed positions covering from vertex to the mid thigh. CT imaging was performed prior to PET imaging with the patient in the same position. A bolus injection of 100 mL iodinated contrast media (Omnipaque 300, Amersham Health) was given intravenously. Acquisition parameters for 6 slices CT were 130 kV, 60 mAs, 0.8 s per CT rotation, 2.5 mm slice thickness, pitch 1.5.

Previously, one bed position of the oncological body investigation would take around 5 min to complete but scanners of the last generation need at least 1 – 3 min. The oncological whole body scan consisting of 6 to 8 bed positions still takes about 10 – 20 min.[13] Due to the limitations of PET imaging device on a relatively low spatial resolution, the restricted anatomic tumour location and limited possibilities to be co registered separately, new PET/CT scanners have been developed on a same platform and the patient will be imaged for both PET and CT at the same time and lying on the same bed with unchanged patient positioning.[16] Thus, little or no patient movement helps registration process not to be too complicated.[17]

Registration and segmentation are important steps in image post processing for radiotherapy. Here, images have been registered using the cross correlation.[18] The cross correlation coefficient matrix of both images has been calculated and the maximum value in that matrix which shows where images are best correlated has been selected. The location of this maximum value indicates where the images are best correlated. Images are then transformed and registered on each other to the position which they are best correlated.[11]

Our segmentation procedure starts by looking through PET image and selecting pixels with maximum value as candidate points that represent high activity and may lead to cancer tumours. Coordinates of these pixels will be used to segment the Region of Interest (ROI). Note that at each step the highest pixel value will be selected, so defining different brightness and contrast will not affect the pixel selection procedure. The overall segmentation procedure is shown in Figure 1.

Segmentation algorithms are mostly categorized in two approaches. One is the region based which relies on homogeneity of features and the other which is based on boundary finding and discontinuity measures.[19] Among these methods Region Growing has become very useful and practical due to simplicity of implementation.[20] Seeded Region Growing (SRG) has been chosen as segmentation algorithm of choice to segment CT image and candidate points found on PET have been used as seeds to a guide segmentation procedure.

Seeded Region Growing algorithm operates by using the coordinates given to it as starting points and expanding the Region of Interest (ROI) by checking their bilinear neighboring pixels. Each pixel value which is in a significant difference interval with the candidate point will be added to the ROI. This interval is set manually by the user so the sensitivity of region growing process can be defined depending on which part of body is going to be diagnosed. The growing process will continue until there is no other bilinear neighboring pixel that falls in the defined interval. Once all the relatively similar pixels have been added to the region, the growing process will stop.

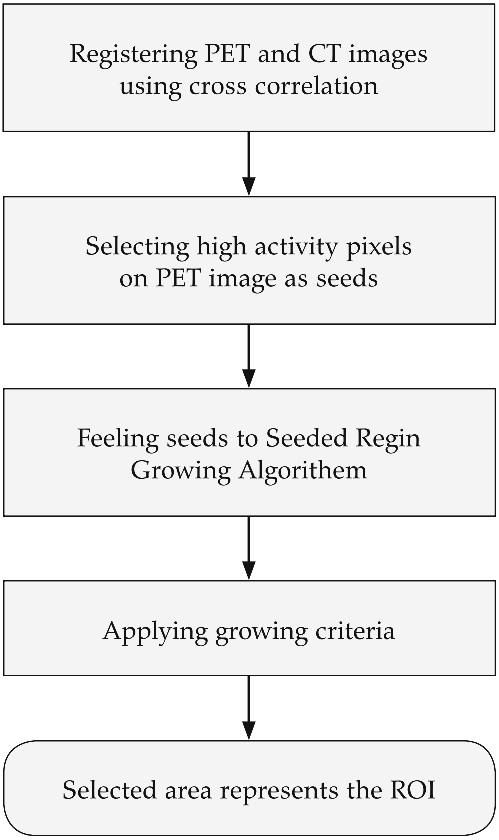

Figure 1. The overall segmentation procedure.

Results

In this experiment, 11 images from dual modality PET/CT imaging device (Biograph 6, Siemens Medical Solutions Inc.) have been used. Figure 2 shows a series of CT (first row), PET (second row) and PET/CT fused images (third row) of a patient having Bronchogenic Carcinoma with Bone Metastases. Areas of highest activity have been marked with arrows and can be easily seen in PET and PET/CT fused images.

In order to evaluate the segmentation process, areas of interest have been selected manually and surveyed by a professional radiologist as benchmarked images. Images shown on Figure 3 (second row) show the manually segmented region which we address as desired ROIs. The method has been applied on all images and the significant interval has been set for each image to make the segmented area as close to ideal segmentation as possible. Figure 3 (first row) shows the result of segmentation on image series shown in Figure 2. As can be seen in Figure 3, the first and last images show relatively same segmentation results with the desired ROI. The segmentation result on second image shows spots of under segmentation. In general, the method has been able to search and find the correct ROI, and visually, there is not much differ-

Table 1. Standard error of the segmentation process

	Over Segmented Pixels	Under Segmented Pixels
Mean Standard Error	33%	3.4%

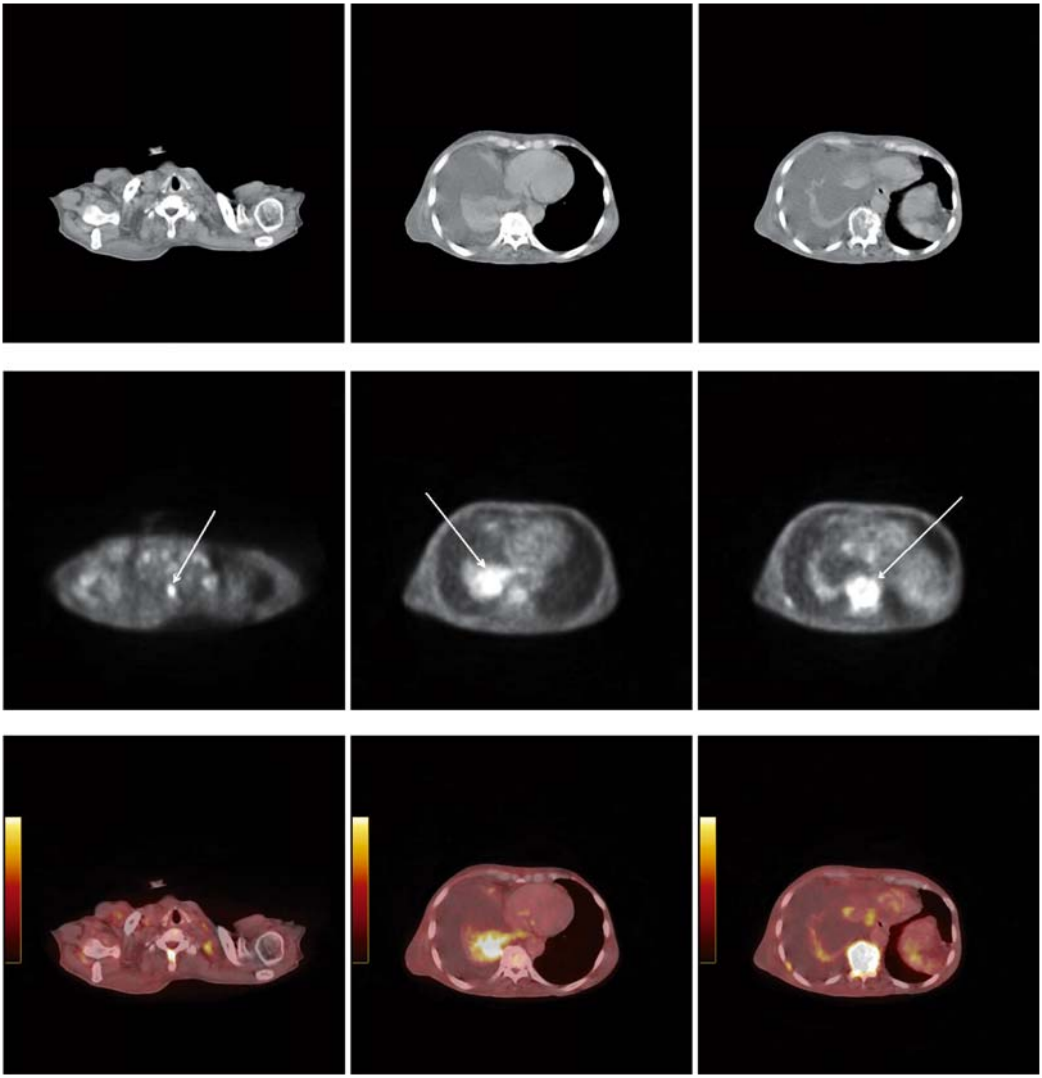

Figure 2. First row CT images, second row PET and the third row PET/CT fused image of a patient having Bronchogenic Carcinoma with Bone Metastases. The arrows indicate the highest activity areas.

ence between the proposed method and the benchmark data.

To look into the details, a standard error percentage has been calculated based on the number of pixels over and under segmented compare to desired segmentation for each image and their average has been calculated. Table 1 shows the percentage of over and under segmentation cause by SRG process.

As shown on Table 1, SRG suffers from over segmenting to homogenous neighboring areas. The small percentage of under segmentation is due to relatively bright or dark spots inside the segmented ROI which could not be prevented. An example of under segmentation can be seen in segmentation results on Figure 3 second image, which shows small dark spots in the segmented area. The individual segmentation

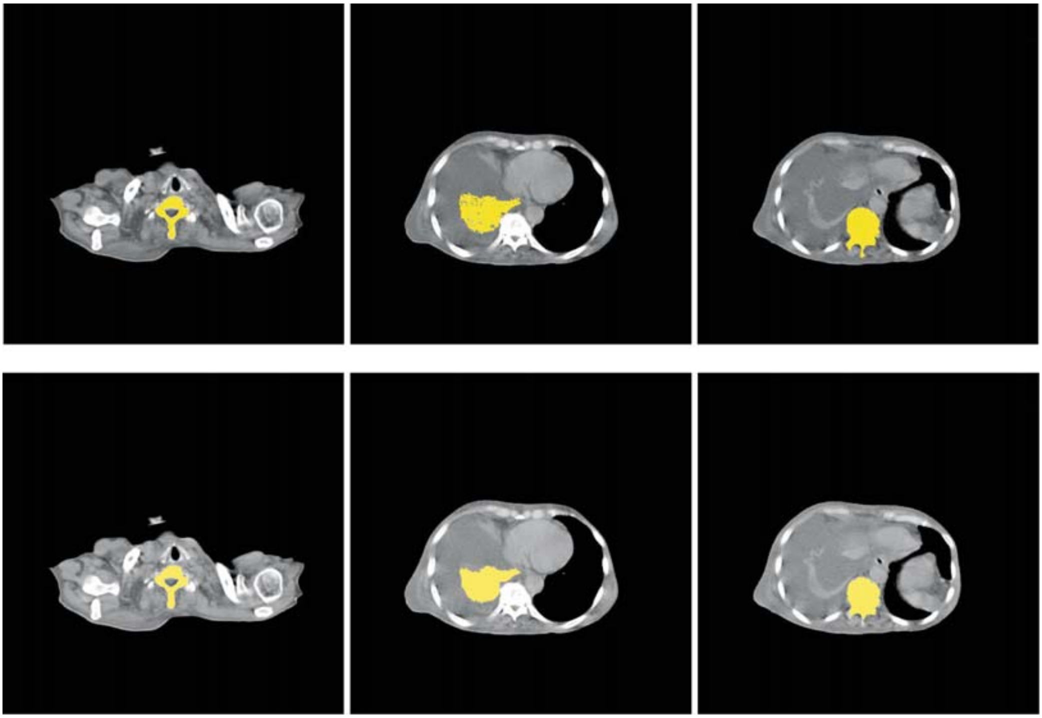

Figure 3. First row segmentation results and second row the desired ROI.

errors on each image have been shown as a chart on Figure 4.

Discussion

The image segmentation is a blind task and there have been lots of researches to guide segmentation in a way that results in the better precision ROI selection. Here, by acquiring dual modality imaging we have used PET image to guide segmentation on CT image.

Region growing algorithm highly depends on where the growing process starts and how to control it in order to avoid over growing to homogenous neighboring area.[21] The method described here uses predefined data to start segmentation, so from the starting point the area to be segmented is a part of the desired ROI but the whole segmentation process may be improved by

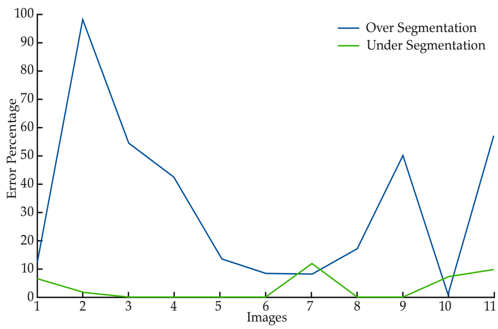

Figure 4. Over and under segmentation percentage of the SRG process.

using other aspects of region growing than manually selection of growing criteria.

This method is considered as a supervised automatic segmentation since at each step the growing interval needs to be defined by the user. Although the method has proven that it is possible to guide seeded region growing segmentation using hot spots from other modality, there still exist a limitation on the selection of high activity points since it is not necessarily the highest active point that represents malignancy.

References

1. Shetty C, Lakhkar B, Gangadhar V, Ramachandran N. Changing pattern of bronchogenic carcinoma: a statistical variation or a reality? *Indian J Radiol Imaging* 2005; **15:** 233-8.
2. De Wever W, Stroobants S, Coolen J, Verschakelen JA. Integrated PET/CT in the staging of nonsmall cell lung cancer: technical aspects and clinical integration. *Eur Respir J* 2009; **33:** 201-12.
3. Kovac V, Smrdel U. Meta-analyses of clinical trials in patients with non-small cell lung cancer. Minireview. *Neoplasma* 2004; **51:** 334-40
4. Kim K, Kim KR, Sohn HY, Lee UY, Kim SK, Lee WY. The role of whole body bone scan in bronchogenic carcinoma. *Yonsei Med J* 1984; **25:** 11-7.
5. Abe K, Sasaki M, Kuwabara Y, Koga H, Baba S, Hayashi K, et al. Comparison of 18FDG-PET with 99mTc-HMDP scintigraphy for the detection of bone metastases in patients with breast cancer. *Ann Nucl Med* 2005; **19:** 573-9.
6. Debevec L, Jerič T, Kovač V, Bitenc M, Sok M. Is there any progress in routine management of lung cancer patients? A comparative analysis of an institution in 1996 and 2006. *Radiol Oncol* 2009; **43:** 47-53.
7. Guo H, Zhu H, Xi Y, Zhang B, Li L, Huang Y, et al. Diagnostic and prognostic value of 18F-FDG PET/CT for patients with suspected recurrence from squamous cell carcinoma of the esophagus. *J Nucl Med* 2007; **48:** 1251-8.
8. Miller JC, Fischman AJ, Aquino SL, Blake MA, Thrall JH, Lee SI. FDG-PET CT for tumor imaging. *J Am Coll Radiol* 2007; **4:** 256-9.
9. Goo JM, Im J, Do K, Yeo JS, Seo JB, Kim HY, et al. Pulmonary tuberculoma evaluated by means of FDG PET: findings in 10 cases. *Radiology* 2000; **216:** 117-21.
10. Ting-lei Huang, Xue Bai. An improved algorithm for medical image segmentation. Genetic and evolutionary computing, 2008. WGEC '08. Second International Conference; 2008. p. 289-92.
11. Gonzalez RC, Woods RE, Eddins SL. *Digital image processing using MATLAB*. New York: Prentice-Hall, Inc. Upper Saddle River; 2003.
12. Rajer M, Kovač V. Malignant spinal cord compression. *Radiol Oncol* 2008; **42:** 23-31.
13. Nestle U, Weber W, Hentschel M, Grosu AL. Biological imaging in radiation therapy: role of positron emission tomography. *Phys Med Biol* 2009; **54:** R1-25.
14. Evans PM. Anatomical imaging for radiotherapy. *Phys Med Biol* 2008; **53:** R151-91.
15. Rohren EM, Turkington TG, Coleman RE. Clinical applications of PET in oncology. *Radiology* 2004; **231:** 305-32.
16. Beyer T, Townsend DW, Brun T, Kinahan PE, Charron M, Roddy R, et al. A Combined PET/CT scanner for clinical oncology. *J Nucl Med* 2000; **41:** 1369-79.
17. Townsend DW, Beyer T. A combined PET/CT scanner: the path to true image fusion. *Br J Radiol* 2002; **75:** S24-30.
18. Lewis J. Fast normalized cross-correlation. *Vision Interface* 1995; **10:** 120-3.
19. Hojjatoleslami SA, Kittler J. Region growing: a new approach. *IEEE Trans Image Process* 1998; **7:** 1079-84.
20. Adams R, Bischof L. Seeded region growing. Pattern analysis and machine intelligence. *IEEE Trans Image Process* 1994; **3:** 641-7.
21. Wan S, Higgins WE. Symmetric region growing. *IEEE Trans Image Process* 2003; **12:** 1007-15.