UNIVERSITI PUTRA MALAYSIA

IMPROVEMENT OF THORACIC HYBRID PET/CT REGISTRATION USING HYBRID FEATURE WITH COMBINED INTENSITY MULTIMODAL DEMON WITH PET SINOGRAM FILTERING

SITI SALASIAH BINTI MOKRI

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By

SITI SALASIAH BINTI MOKRI

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

May 2016

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DEDICATIONS

To my beloved parents, my family members and especially to my children,

Aliff Mustaqim, Ariff Muhaymin and Aqiff Muhammad.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

IMPROVEMENT OF THORACIC HYBRID PET/CT REGISTRATION USING HYBRID FEATURE WITH COMBINED INTENSITY MULTIMODAL DEMON WITH PET SINOGRAM FILTERING

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May 2016

Chair: Prof. Dr. M. Iqbal Bin Saripan, Ph.D.

Faculty: Engineering

Accurately registered and fused PET/CT images are required for better tumor interpretation and the following tumor management in oncology and radiotherapy purposes. Although the hybrid PET/CT machine is supposedly solves the problem of misregistration between the PET/CT images, the offered solution is not optimal. The nonlinear misregistration due to physical and physiological motions stays on, declining the performance of the hybrid PET/CT machine. Therefore, the aim of this thesis is to solve the misregistration problem inflicting the PET/CT images acquired from the hybrid PET/CT scanner. Overall, the proposed registration method consists of three major steps. The first step is to perform 3D hybrid mean-median filtering based on the weighted average scheme on the PET sinogram domain. The second step is to segment selected structures of the thorax region which are the lungs, the heart and the tumor in both PET/CT images using a specific segmentation method for each structure excluding the heart in the PET image in which the segmentation is manually done. The main focus at this part is to design segmentation methods for the PET lung and the CT heart as these two subjects are rarely addressed. These segmented structures are used as “features” in the third stage where hybrid feature combined intensity multimodal demon registration is carried out to register both images. This method which is an improved version of multimodal demon registration uses a combination of mutual information (MI), sum of conditional variations (SCV) and multimodality independent neighborhood descriptive (MIND) similarity measures. The PET sinogram filter is tested on the NCAT based PET sinograms generated using ASIM PET simulator of different signal to noise ratio (SNR) and is compared with standard filter as used in analytical filtered-backprojection (FBP) reconstruction method. Aside from FBP, the improvement made by the filter on the iterative maximum likelihood expectation maximization with median root prior (MRP-MLEM) reconstruction method is also investigated. The filter significantly improves the global and local SNR of the PET image by more than 40% and more than 150% when compared to Hanning filtered FBP and MRP-MLEM reconstructed images without filtering. In terms of contrast to noise ratio (CNR), the proposed filter constantly generates improved CNR for all datasets in both analytical and statistical reconstruction methods. In the second stage, the proposed segmentation methods are evaluated on simulated NCAT based PET/CT and 21 clinical patient datasets. Apart from satisfactory subjective evaluation through visual displays, the segmentation of two structures, CT heart and PET lung are validated against expert segmentation on 10 datasets. The achieved mean Dice and Jaccard coefficients for both structures are more than 0.8. Then, the proposed improved intensity multimodal demon registration is tested on simple images and various types of medical images and the registration results are satisfactory. Specific to PET/CT registration problem, the proposed hybrid feature intensity multimodal registration method is tested on the simulated NCAT PET/CT images acquired at different breathing phases as well 21 clinical hybrid PET/CT datasets. Experimental results show that the combination of SCV and MIND based similarity measures produces the best registration result for PET/CT misregistration problem. In particular to clinical datasets experiment, the mean NMI improvement achieved by the proposed hybrid feature combined intensity multimodal demon registration is twice than the established free form deformation (FFD) registration method. The success of the registration of the patient datasets is also validated through improved lung volume overlap between the PET lung and the CT lung post registration according to Jaccard and Dice coefficients calculations. The registration method increases the Jaccard and Dice measures by 7.78% and 4.46% in average respectively after registration.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PENAMBAHBAIKAN REGISTRASI PET/CT PADA TORAKS MENGGUNAKAN HIBRID FITUR DENGAN KOMBINASI KEAMATAN MULTIMODAL DEMON DENGAN PENAPISAN SINOGRAM PET

Oleh

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Registrasi dan jajaran imej PET/CT yang tepat adalah perlu bagi mencapai proses interpretasi dan pengurusan tumor yang baik di dalam aplikasi onkologi dan radioterapi. Walau pun mesin hibrid PET/CT dikatakan dapat menyelesaikan masalah misregistrasi PET/CT, penyelesaian yang ditawarkan oleh mesin ini adalah tidak optimum. Masalah misregistrasi tak linear yang disebabkan oleh gerakan pesakit dan fisiologi masih wujud lalu mengurangkan prestasi mesin tersebut. Oleh itu, tesis ini bertujuan untuk menyelesaikan masalah misregistrasi yang terdapat di antara imej PET/CT dari mesin hibrid PET/CT disebabkan oleh gerakan fizikal dan fisiologi. Algoritma registrasi yang dicadangkan mengandungi tiga langkah utama. Langkah pertama adalah menjalankan proses penapisan menggunakan penapis purata-median 3D berasaskan purata pemberat terhadap data sinogram PET. Langkah kedua ialah melakukan segmentasi struktur-struktur yang terpilih di bahagian toraks (paru-paru, jantung dan tumor) pada kedua-dua imej. Oleh itu, tesis ini mencadangkan algoritma segmentasi khusus bagi setiap struktur kecuali jantung yang terdapat pada imej PET di mana proses segmentasi dijalankan secara manual. Fokus utama diberikan kepada segmentasi paru-paru PET dan jantung CT kerana kedua-dua subjek kurang diberi perhatian di dalam literasi penyelidikan. Segmentasi struktur-struktur yang diperoleh dijadikan sebagai ciri yang akan digunakan di dalam kaedah registrasi hibrid ciri-keamatan pelbagai modaliti demon pada langkah seterusnya. Kaedah ini merupakan versi tambah-baik registrasi pelbagai modaliti demon yang menggunakan gabungan metriks kesamaan *mutual information* (MI), *sum of conditional variations* (SCV) dan *multimodality independent neighborhood descriptor* (MIND). Penapis sinogram PET diuji ke atas sinogram PET NCAT tersimulasi dengan SNR yang berbeza yang dijana menggunakan simulator ASIM PET dan dibandingkan dengan kaedah rekonstruksi imej FBP. Selain FBP, sebarang penambahbaikan ke atas kaedah rekonstruksi imej menggunakan kaedah rekonstruksi *maximum likelihood expectation maximization with median root prior* (MRP-MLEM) turut dikaji. Penapis yang digunakan menambahbaik

SNR global dan lokal imej PET masing-masing sebanyak 40% dan 150% apabila dibandingkan dengan FBP berasaskan Hanning dan MRP-MLEM tanpa penapisan sinogram. Penapis yang dicadangkan juga menambahbaik CNR pada imej untuk setiap data yang digunakan pada kedua-dua kaedah rekonstruksi analitikal dan statistik. Pada tahap yang kedua, kaedah segmentasi yang dicadangkan diuji pada imej PET/CT simulasi NCAT dan 21 data pesakit. Selain daripada penilaian subjektif yang memuaskan melalui visual, segmentasi kedua-dua struktur, paru-paru PET dan jantung CT dibandingkan dengan segmentasi oleh pakar ke atas 10 data. Bacaan purata Dice dan Jaccard untuk kedua-dua struktur adalah melebihi 0.8. Kaedah registrasi tambah baik berasaskan keamatan pelbagai modaliti demon yang dicadangkan diuji ke atas imej mudah dan pelbagai jenis imej perubatan dan keputusan registrasi adalah memuaskan. Untuk masalah misregistrasi PET/CT, kaedah registrasi hibrid ciri-keamatan pelbagai modaliti demon dilaksanakan ke atas imej PET/CT simulasi NCAT yang diambil pada fasa pernafasan yang berbeza dan juga terhadap 21 imej pesakit. Keputusan eksperimen menunjukkan gabungan metriks kesamaan SCV dan MIND menghasilkan keputusan registrasi yang terbaik. Khususnya, keputusan eksperimen ke atas data pesakit menunjukkan bahawa kaedah registrasi yang dicadangkan menghasilkan penambahbaikan peratusan NMI sebanyak dua kali ganda berbanding nilai yang diperoleh dengan menggunakan kaedah registrasi “free form deformation” (FFD). Kejayan proses registrasi juga disahkan melalui ukuran tindihan isipadu paru-paru CT dan PET sebelum dan selepas registrasi berdasarkan pengiraan Jaccard dan Dice. Kaedah registrasi yang dicadang menambahbaik ukuran Jaccard dan Dice masing-masing sebanyak 7.78% dan 4.46% secara purata selepas proses registrasi.

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Last but not least, to my beloved parents, my siblings, my family, my children and my dear friends who support me throughout my phd journey. Thank you for the support, patience, trust and belief in my undertakings.

I certify that a Thesis Examination Committee has met on 12 May 2016 to conduct the final examination of Siti Salasiah Mokri on her thesis entitled "Improvement of Thoracic Hybrid PET/CT Registration Using Hybrid Feature with Combined Intensity Multimodal Demon with PET Sinogram Filtering" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

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LIST OF ABBREVIATIONS

ADF	Anisotropic diffusion filter
AMPCM	Adaptive modified probabilistic curvature motion
BM3D	Block matching 3 dimensional
CMB	Combined intensity demon
CNR	Contrast to noise ratio
CT	Computed Tomography
DCT	Discrete cosine transform
DIBH	Deep Inspiration Breath Hold
DICOM	Digital imaging in communication and medicine
DRLSE	Distance regularised level set
EPD	Edge preserved denoising
FBP	Filtered Backprojection
FDG	Flurodeoxyglucose
FFA	Free fatty acid
FFD	Free form deformation
GUI	Graphical user interface
FOV	Field of view
HU	Hounsfield unit
ICA	Independent component analysis
LOR	Line of response
MAP	Maximum a posteriori
MI	Mutual information
MIND	Multimodality independent neighbourhood descriptor
MLEM	Maximum Likelihood Expectation Maximisation

MRP	Median Root Prior
MRI	Magnetic Resonance Imaging
NCAT	NURBS cardiac and torso phantom
NCC	Normalised cross correlation
NLM	Non local means
NMI	Normalised mutual information
NMSE	Normalised mean square error
NSCLC	Non-small cell lung cancer
NURBS	Non uniform rational b-spline
OSEM	Ordered subset expectation maximisation
PC	Phase correlation
PD	Proton density
PET	Positron Emission Tomography
PPDN-UPM	Pusat Pengimejan Diagnostik Nuklear – Universiti Putra Malaysia
RFP	Ratio false positive
RFN	Ratio false negative
ROI	Region of interest
RIU	Ratio image uniformity
SCV	Sum of conditional variance
SFCM	Spatial fuzzy C means
SNR	Signal to noise ratio
SPECT	Single Photon Emission Computed Tomography
SSD	Sum square distance
SUV	Standardised uptake value

TBD	Texture based denoising
TNM	Tumour-lymph node-metastasis
TPS	Thin plate spline
TV	Total variation
VOI	Volume of interest

CHAPTER 1

INTRODUCTION

1.1 Background

There are two types of medical imaging devices that are commonly used in oncology cancer diagnosis and radiation therapy. The first type is anatomical based devices such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) (Alessio et al., 2004). The second type is functional based devices such as Single Photon Computed Tomography (SPECT) and Positron Emission Tomography (PET) (Alessio et al., 2004). PET image depicts the distribution of the radiotracer that is injected into the patient prior to the scanning session. With this knowledge, the radiologist and physician are able to interpret physiological processes such as metabolism and blood flow as well as to assess the acuteness of any cancerous cells. At the early stage, the PET scanner is mainly used for oncologic cancer diagnosis. However, the localisation of possible metastatic cancer based on the PET image alone could be less than accurate due to the noisy, blurry, low resolution characteristics of the image itself. Thus, the idea of integrating PET and CT images for cancer diagnosis comes into sight (Pan & Mawlawi, 2008). The CT image provides the necessary anatomical descriptions such as the size and the shape of the lesion while the PET image tells about the degree of malignancy. The integration of PET/CT images improves the accuracy of the localisation in general.

The physical integration of PET and CT images coming from separate machine is not as straightforward. Due to patient and biological motions such as respiration, heart and bowel movement during screening period, misalignment between the two images may occur (Goerres et al., 2002). Thus, an accurate spatial registration technique to correct the misregistration is needed. In general, there are three approaches to register the PET/CT images; visual, hardware based and computer based registration methods (Townsend et al., 2004). Traditionally, visual registration is done with the physician comparing both images side by side. It is an exhaustive process and inconsistent registration interpretation might occur among different physicians. Hardware based hybrid PET/CT machine emerges based on the idea of physically integrating the PET and CT machines into a single device. There is a centralised operating system with a single scanning bed. As a result, the use of hybrid PET/CT machine compared to standalone PET and CT machines, increases the localisation of metastatic cancer, improves the sensitivity to malignancy and effectively minimises the involved cost. In addition, the CT transmission data is used for noise attenuation correction of the PET emission data. Pelosi et al., (2004) reported a higher percentage of having false interpretation of lesion localisation in independent PET and CT images (15.3%) as compared to hybrid PET/CT (3.4%).

Although hybrid PET/CT scanner literally restrains the patient motion, the problem of misregistration at the thorax region due to the respiratory/heart/bowel movements remains (Mawlawi & Townsend, 2008). During whole body hybrid PET/CT acquisition, CT scanning is performed in less than a minute with the patient engages in breath-hold, compared to PET scan that can lasts up to 20 minutes with the patient engages in tidal breathing. The unmatched respiratory phase between the PET and CT acquisitions produces unaligned PET/CT images at the thorax and the abdomen. As CT transmission data is used for PET attenuation correction, the misregistration leads to the attenuation correction artefacts that eventually cause inaccurate tumour localisation and size estimation (Nehmeh & Erdi, 2008; Osman et al., 2003). Goerres et al., (2002) found that a maximum displacement of 8.29 cm in the diaphragm between the PET and CT images acquired at maximum inspiration. To solve physiologically induced misregisteration between the PET/CT images acquired from combined PET/CT scanner, software based registration technique is used (Camara et al., 2007). Thus, this thesis aims to develop a non-gated postprocessing software based registration technique to solve the PET/CT misalignment problem. In brief, the developed technique is based on hybrid feature intensity multimodal demon registration framework which consists of three major steps: filtering the PET sinogram, segmenting the main structures in the PET/CT images and registering the images using the segmented features and improved intensity based demon registration.

1.2 Problem Statement

Postprocessing image registration software is important for both separate and combined PET/CT systems for better image interpretation and analysis. In thoracic oncology PET/CT diagnosis and radiotherapy, both the functional PET and anatomical CT images are integrated so that accurate oncological diagnosis, radiotherapy planning and monitoring processes can be achieved. Integrating these two images therefore requires good registration strategy as these images are taken at different time and place. Misregistered PET/CT images will cause inaccurate interpretation (underestimation/overestimation) gross tumour volume and tumour malignancy due to variation in standardized uptake value (SUV) in PET as well as inaccurate tumour localisation as the anatomical (CT) and physiological (PET) information do not correlated very well. Exact tumour localisation is important in radiotherapy so that an optimal target volume to be irradiated can be identified while reducing the impact of radiation on healthy tissues. In terms of radiotherapy monitoring, an exact quantification of standardised uptake value is required for the physician to reliably decide the next course of treatment.

Since its beginning until today, the hybrid PET/CT persistently fails to accurately register both the PET/CT images. The PET/CT misregistration problem in hybrid PET/CT scanner is in fact an inherent issue (Pan & Mawlawi, 2008; Sureshbabu & Mawlawi, 2005; Mawlawi & Towsend, 2009; Nye & Faber, 2011; Shekhar et al., 2005 and Alessio et al., 2004) due to nonlinear respiratory, cardiac and bowel motions apart from the patient motion. These motions result in heavily affected misregistration at the thorax and the abdomen compared to the other regions of the body. The most significant artefact is the so called “banana artefact” in the PET image (Sureshbabu & Mawlawi, 2005). The artefact shows underestimated low activity region at the lung base (the diaphragm). Induced misregistration at the thoracic region is mainly due to respiratory motion and the different scan times between the PET and CT scan. The CT scan takes less than one respiratory cycle while the PET scan takes up to 8 minutes per bed position. In obvious, there will always be respiratory phase mismatch in terms of the misaligned lung volumes of the two images. The CT image is considered taken at a certain respiratory phase while the PET image is an image averaged over multiple respiratory cycles and cardiac positions. There are several studies that have been conducted to investigate the frequency of having misregistration at these areas. For example, Pan et al., (2005) reported a percentage of 50% out of 100 patient studies experienced significant diaphragm misalignment between the hybrid PET/CT images with some of the cases showed greater than 2 cm mismatch error. In addition Gould et al., (2007) presented a percentage of 40% false positive results in their cardiac PET/CT diagnostic purpose owing to misregistration artefacts.

Nye & Faber (2011) listed several proposed approaches to compensate misregistration artefacts. One example is to instruct the proper breathing protocol named as deep inspiration breath hold (DIBH) to the patient for both CT and PET exams (Nehmeh et al., 2007). However, DIBH requires a breathing coach and the additional respiratory monitoring hardware to be integrated into the hybrid PET/CT machine. The other approach is to specify specific CT protocols slow CT scan, low-pitch CT and cine CT) so that the CT scan can be conducted under free breathing. Another approach is based on respiratory gating (Nehmeh et al. 2008). In this technique, several PET images of different respiratory bins are generated using the gating mechanism. The respiratory motion is estimated from the gated PET emission data and then the motion fields are used to register the static CT image with the PET image of similar respiratory bin. However, this method results in reconstructed PET bin image with reduced signal to noise ratio (SNR) and it requires additional hardware to be embedded in the PET/CT machine, thus increases cost (Nehmeh et al. 2008).

Thus, the thesis aims to improve the image registration between the PET/CT images of hybrid scanner through software based registration algorithm. Although the existing hybrid machines are equipped with commercial registration and fusion software tools, most of the registration software (Steffen et al., 2013; Gong, O’keefe & Scott, 2005) normally solves rigid deformation that is irrelevant for thoracic region. Besides, (Weigert et al., 2008) also concluded that the tested rigid and non-rigid commercial registration software on the whole body combined PET/CT datasets in their experiment failed to meet sufficient registration quality as required. Thus far, there are a number of registration methods have been proposed for thoracic PET/CT images and few works are actually tested their algorithms on combined PET/CT datasets (Jin et al., 2013; Camara et al., 2007; Moreno et al., 2006; Shekhar et al., 2005).

None of these methods considers the pre-processing the PET sinogram through filtering in order to obtain a better quality PET image. It is a well-known fact that the reconstructed PET image is blurry and noisy. These inherent characteristics of the PET image are due to random and scatter effects and the design of the electrical parts that constitute the whole PET machine. Evidently the quantification and interpretation of tumour based on noisy and blurry PET image will be less than accurate. Therefore, the reconstructed PET image should be smoothed and enhanced to attain better tumour interpretation. In terms of solving the PET/CT misregistration problem, the use of a better quality, smoothed and enhanced PET image in the registration process will likely generate better registration accuracy than using blurry, noisy PET image. Based on this notion, this thesis proposes a 3D hybrid mean-median PET sinogram filter as a pre-processing step in the proposed registration framework. Besides improving the registration accuracy, the proposed method is considered as a mean to improve the conventional PET reconstruction method that is filtered back projection (FBP) and advanced reconstruction methods such as iterative maximum likelihood estimation maximisation (MLEM) in PET reconstruction subject (Alessio & Kinahan, 2006). Another aspect that is overlooked in the previous literature is a dedicated registration step for the heart structure. Some of the previous works mainly focused on the lung structure in their integrated intensity-feature based registration by assuming that the heart will be accurately aligned following the deformation fields of the lung registration. However, this assumption is not always valid (Faber et al., 2010). Thus, an independent heart registration is required during the feature based registration implementation. Apart from the heart, the other identified structures are the tumour and the lungs. One might argue on the necessity to have a specific heart registration for thoracic oncologic PET/CT study as it is mainly used for lung cancer diagnosis and management. However, there are reported findings on cardiac masses detection in whole body oncology PET/CT study (Mallia et al., 2009; Zhang, Li & Jiang, 2008).

Due to this reason, a separate heart registration is proposed in this thesis so that a thorough, extensive investigation of any malignancy at the heart region can be conducted from the well registered PET/CT images. Although (Moreno et al., 2006) has raised the idea of specific heart registration, it has not been practically implemented in their work. They also suggested that the heart should remain rigid during the whole registration process. However, this thesis adopts the approach of independently deforming the heart through non-rigid deformation based on the findings of Bond et al., (2008). They have found that the heart region was better aligned using translation and deformable transformation compared to translation or rigid transformation alone. In order to independently register the heart, the heart regions in both PET/CT images need to be identified or segmented. Therefore, the second step in the proposed registration framework in this thesis performs main structures segmentation in both PET/CT. These structures are the lungs, the heart and the tumour. Automatic segmentation of the whole heart is not an option. It should be done manually due to the inconsistency of the heart uptake of varying patients' datasets (Fukuchi et al., 2007).

Third, based on the latest work by Jin et al., (2013) on PET/CT registration problem, the thesis attempts to improve their modified multimodal intensity demon registration through feature integration as well as merging different similarity measures in their technique so that the algorithm is designed to be more robust towards various medical images as well as simple images. The current work by Jin et al., (2013) showed an improvement of their work in registering PET/CT images compared to the previously proposed method (Mattes et al., 2003). Originating from this work, the multimodal intensity demon registration can be made superior by merging different similarity measures to define the demon energy. The superiority can be justified by testing the algorithms on different kinds of medical and simple images. In specific to thoracic PET/CT registration problem, the newly improved multimodal intensity demon can be combined with feature based demon registration serially in order to obtain optimal registration accuracy.

1.3 Aim and Objectives

The aim of the research is to develop a postprocessing image registration technique for PET/CT images acquired from hybrid PET/CT scanner focusing at the thoracic region. The aim is achieved by specifying the following objectives:

i. To develop a filter for the PET sinogram data in order to obtain a better quality PET image.

ii. To develop segmentation framework for structures (the lung, the tumour and the heart) in thoracic PET and CT images.

iii. To improve the original monomodal demon registration method that works for multimodal registration problem in order to obtain improved registration accuracy between PET/CT images.

1.4 Scope and Limitation of the Study

The thesis studies on improving the registration between PET/CT images acquired from combined hybrid PET/CT scanner. To achieve this, three major steps are identified. The first step is to filter the PET sinogram raw data. Second, is to segment three main structures, which are the lungs, the heart and possible tumours in both images. The third step is to perform hybrid feature-intensity registration based on modified demon registration that can works for multimodal registration cases. A 3D hybrid mean-median filter is proposed to filter the PET sinogram. To evaluate the efficacy of the sinogram filter, four PET sinograms with different SNR are simulated using ASIM PET simulator software (Elston et al., 2012). The simulated phantom used which is inputted into the software is based on NURBS cardiac and torso phantom (NCAT) developed by Segars (2001).

The proposed sinogram filter is tested on the four datasets and is compared with standard mean and median filters as well as four established edge preserving filters, namely Non-local means filter (Buades, Coll, & Morel, 2005), Anistotropic Diffusion filter (Perona & Malik, 1990) and Adaptive Modified Probability Curvature Motion filter, the latest proposed PET sinogram filter by Alrefaya & Sahli, (2013). The comparison is made based on the quality of the reconstructed PET image using FBP method. Another evaluation is to investigate the percentage of improvements made by the filter on the reconstructed image using FBP and iterative based statistical reconstruction method namely Maximum Likelihood Maximisation Estimation – Median Root Prior (MLEM-MRP), (Alenius, Ruotsalainen & Astla, 1998). The image quality is assessed according to visual displays, signal to noise ratio (SNR), local signal to noise ratio, contrast to noise ratio (CNR) and edge preserving quality through the display of the line profile. The limitation of the filter analysis is the lack of the real PET sinogram acquired from hybrid PET/CT machine. This is because the real sinogram could not be retrieved from the hybrid PET/CT machine Biograph 6, Siemens Medical Solutions Incorporated. This hybrid machine which is attached to the UPM Nuclear Diagnostic Imaging Centre (PPDN-UPM), Universiti Putra Malaysia, Malaysia supplies the PET/CT datasets used in the segmentation and registration experiments of this thesis.

The second step deals with segmenting important structures which are the lungs, the heart and the possible tumours, in the PET/CT images. The proposed method for lungs segmentation in CT image is based on thresholding and region growing. The lung segmentation in CT image is considered trivial due to distinct intensity of the lung regions across CT datasets. In opposite, the lung segmentation in PET image is considered difficult. The proposed method uses a combination of edge refinement and spatial fuzzy C mean clustering (Chuang et al., 2006). In terms of heart segmentation in non-contrast enhanced CT image, the thesis proposes an automated determination of the heart volume of interest based on the obtained CT lung volume. Then the fine heart structure is obtained through slice by slice Distance Regularised Level Set (DRLSE) method (Li et al., 2010).

Finally the possible tumours in the PET and CT images are segmented semi automatically using thresholding, region growing and DRLSE methods. The limitation of the proposed structures segmentation methods at this stage is the disability of the methods to handle any PET/CT patient datasets with serious pathology conditions such as patients infected with pleural effusion (fluid build-up) in their lungs due to chronic malignancy, liver failure and others (Yao, Han & Summers, 2009). Apart from this, the proposed methods also could not be applied on PET/CT datasets in which the patients bearing high density very large lung tumours that attached to the chest wall and the mediastinum. In this case, the attached tumours tend to be excluded from the lung boundary due to their intensity similarity with the chest wall. These two examples of severities impede the reliable estimation of the lung boundary in both the CT images and the following PET images as well as the estimation of the initial CT heart volume of interest (VOI).

Therefore, the tested segmentation algorithms are performed on 21 patient datasets out of 27 datasets archived from the previously mentioned hybrid PET/CT machine in which 6 patient datasets show serious lung pathologies. The segmentation results are analysed using visual displays as well as comparison with manual delineation by the expert. The latter analysis is done by measuring several overlapping metrics between the automated segmented structures with that of the manual segmented structures. These metrics are Jaccard coefficient, Dice coefficient, False positive ratio and False negative ratio. Only 10 out of 21 datasets are used to be compared with manual ground truths.

The third step is to register the 21 clinical PET/CT datasets and to analyse any registration improvement before and after the registration process. The proposed filter is based on demon registration that is improved by integrating feature based demon registration as well as upgrading the demon capability to work for multimodal registration. Apart from visual displays, registration analysis is also done based on global similarity metric normalised mutual information (NMI) achievement pre- and post-registration in percentage and comparing the proposed filter with established, commercialised registration technique which is free form deformation method (Rueckert et al., 1999). The use of NMI mutual information is considered a reliable and competent measure to compare the improvement of the proposed registration method on the combined PET/CT datasets post-registration (Modat et al., 2010; Pekar, Gladilin & Rohr, 2006) as the registration accuracy correlates well with the improved NMI measure (Rivest et al., 2010). The registration improvement is also inspected in terms of the lung volume overlap improvement between the PET lung and the CT lung after registration.

1.5 Thesis Contribution

The main contribution of this thesis is the registration improvement between the PET/CT images acquired from hybrid PET/CT machine. To achieve this goal, this thesis proposes an improved registration method that comprises of three major steps, where each of them represents three different image processing areas; filtering, segmentation and registration. In the first step, *first*, this thesis contributes in the development of a new filter on the PET sinogram data in order to obtain a better, enhanced PET image. The filter uses a combination of 3D mean and median filters of specified masks. The mean and median values are estimated according to a weighted average scheme that considers the “similarity” among the voxels which constitute each mask. Furthermore, the filter improves the quality of the PET image when both analytical filtered backprojection (FBP) and statistical iterative reconstruction method, to be specific median root prior – maximum likelihood expectation maximisation (MRP-MLEM) are used.

The second contribution of this thesis is the proposed segmentation framework for structures in the thoracic region in PET/CT images in particular for the heart in non-contrast CT and the lungs in the PET image. Published methods to perform segmentation of these two structures are uncommon. In this thesis, an automated heart segmentation for non-contrast CT is proposed in which the initial heart volume of interest (VOI) is identified automatically compared to manual determination of the VOI in the previously reported work. On the other hand, the PET lungs are segmented using fuzzy based clustering on the priorly estimated lung core. Implementing fuzzy clustering on the lung core allows a fixed number of clusters to be used in the clustering scheme rather than having to heuritiscally determine the parameter as applied in the previous works.

The third contribution is the improvement on the original demon registration for multimodal image registration problem. The previously proposed intensity based multimodal demon using mutual information (MI) is improved by combining two other similarity measures, which are sum of conditional variance (SCV) and multimodality independent neighbourhood descriptor (MIND) in its formulation. This increases the robustness of the method and improves the registration accuracy. The modified multimodal demon has been experimented on various types of simple as well as medical images.

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