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ANALYTIC AND ITERATIVE RECONSTRUCTION ALGORITHMS IN MYOCARDIAL PERFUSION SPECT: A COMPARATIVE STUDY

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by

MOHD SYAHIR BIN MANSOR

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LIST OF ABBREVIATIONS AND SYMBOLS

Name	Definition
2D	Two Dimensional
3D	Three Dimensional
^{99m}Tc	Technetium-99-metastable
^{201}Tl	Thallium-201
AC	Attenuation Correction
ASNC	American Society of Nuclear Cardiology
ART	Algebraic Reconstruction Technique
ANOVA	Analysis of Variance
BTR	Background to Target Ratio
CAD	Coronary Artery Disease
CRC	Contrast Recovery Coefficient
COR	Center Of Rotation
CFOV	Central Field Of View
cm	Centimeter
DRC	Detector Response Correction
ECG	Electrocardigram
FBP	Filtered Back Projection
FWHM	Full Width Half Maximum
FOV	Field Of View
FT	Fourier Transform
GH	General Hospital

g	Gram
HUSM	Hospital Universiti Sains Malaysia
HLA	Horizontal Long Axis
keV	Kilo Electronvolt
LCX	Left Circumflex Artery
LHR	Lung to Heart Ratio
LPO	Left Posterior Oblique
LVEF	Left Ventricular Ejection Fraction
LEHR	Low Energy High Resolution
LEAP	Low Energy All Purpose
mCi	Millicurie
mL	Millilitre
mm	Millimetre
MBq	Megabequerel
ML-EM	Maximum Likelihood Expectation Maximization
MAP	Maximum A Posteriori
MP	Myocardial Perfusion
NaI	Sodium Iodide
NaI(Tl)	Sodium Iodide activated with Thallium
OS-EM	Ordered Subset Expectation Maximization
PMT	Photo Multiplier Tube
Pb	Plumbum
ROC	Receiver Operating Characteristic
ROI	Region Of Interest
RAO	Right Anterior Oblique

SAX	Short Axis Slice
SC	Scatter Correction
SD	Standard Deviation
SNR	Signal to Noise Ratio
SPSS	Statistical Package for the Social Sciences
SPECT	Single Photon Emission Computed Tomography
TLD	Thermo luminescent dosimeter
UFOV	Useful Field Of View
VLA	Vertical Long Axis
υ_c	Cut-off frequency
f_c	Critical frequency
N	Order
γ	Gamma

ALGORITMA PEMBENTUKAN IMEJ ANALITIK DAN PENGULANGAN SEMULA DALAM KAJIAN PERFUSI JANTUNG SPECT: KAJIAN PERBANDINGAN

ABSTRAK

Tujuan kajian ini adalah untuk membandingkan kualiti imej SPECT yang telah dihasilkan menggunakan kaedah analitik atau lebih dikenali sebagai ‘Filtered Back Projection’ (FBP) dan kaedah lelaran berdasarkan ‘Maximum Likelihood Expectation Maximization’ (ML-EM) dalam perfusi miokardium SPECT. Kajian dalam fantom menggunakan pelbagai nisbah aktiviti latar belakang kepada aktiviti sasaran [background to target ratio (BTR)] 0.2, 0.4, 0.6 dan 0.8 bagi mensimulasikan nisbah yang berlainan aktiviti di dalam peparu kepada jantung untuk pesakit-pesakit yang menjalani perfusi miokardium SPECT. Bagi FBP, pemotongan frekuensi di antara 0.4 dan 0.6 kitaran/cm dengan perintah (order) 5 telah digunakan bagi proses penghasilan imej manakala bagi kaedah ML-EM bilangan lelaran yang digunakan adalah 4, 8, 12, 16, 24, 32, 40, 48, 64, 80, 96 dan 128. Kontras pekali pemulihan [contrast recovery coefficient(CRC)] dan nisabah isyarat kepada hingar [signal to noise ratio(SNR)] dinilai untuk kualiti imej bagi menentukan parameter penghasilan imej yang optima. Parameter yang optima bagi FBP adalah 0.4 kitaran/cm manakala bagi ML-EM, 40 lelaran adalah disyorkan bagi penghasilan imej SPECT. Bagi setiap nilai LHR sebanyak dua data pesakit perfusi miokardium telah digunakan untuk penghasilan imej dengan menggunakan parameter yang optima bagi setiap kaedah penghasilan imej. Parameter kualiti imej yang dinilai adalah artifak, hingar dan ketajaman imej. Ujian statistik menggunakan Kruskal Wallis telah digunakan untuk membandingkan kualiti imej di kalangan nilai LHR yang berbeza (0.2, 0.4, 0.6 dan 0.8) bagi setiap kaedah penghasilan imej. Ujian statistik yang ke dua adalah Wilcoxon signed rank untuk membandingkan kualiti imej yang dihasilkan oleh FBP dan ML-EM bagi setiap nilai LHR. Yang terakhir adalah ujian bagi perbandingan antara kedua-dua kaedah tanpa mengambil kira setiap kumpulan LHR menggunakan ujian Wilcoxon signed rank. Berdasarkan analisis statistik, tiada perbezaan yang ketara dalam imej kualiti di antara nilai LHR yang berlainan bagi kedua-dua kaedah penghasilan imej($p>0.05$, ujian Kruskal Wallis). Kualiti imej yang dihasilkan oleh ke dua-dua kaedah penghasilan imej adalah sama bagi setiap nilai LHR ($p>0.05$, ujian Wilcoxon). Tanpa mengambil kira nilai-nilai LHR, tiada perbezaan ketara dalam kualiti imej yang diperhatikan di antara kedua-dua kaedah penghasilan imej ($p>0.05$, ujian Wilcoxon). Berdasarkan keputusan yang dihasilkan, kaedah penghasilan imej (ML-EM) boleh dijadikan satu alternatif bagi penghasilan imej dalam perfusi miokardium SPECT.

ANALYTIC AND ITERATIVE RECONSTRUCTION ALGORITHMS IN MYOCARDIAL PERFUSION SPECT: A COMPARATIVE STUDY

ABSTRACT

The purpose of this study was to compare the quality of images reconstructed using analytic or more commonly known as filtered back-projection (FBP) and iterative method based on maximum-likelihood expectation maximization (ML-EM) in myocardial perfusion (MP) single photon emmision computed tomography (SPECT). Phantom studies using different ratios of background activity to target activity (BTR) of 0.2, 0.4, 0.6 and 0.8 were used to simulate the different ratios of the activity in the lung to the activity in the heart (LHR) for patients undergoing MP SPECT. For FBP, the cut off frequency ranged from 0.4 to 0.6 cycle/ cm with order of 5 were used to reconstruct the image while for ML-EM method the number of iterations examined were 4, 8, 12, 16, 24, 32, 40, 48, 64, 80, 96 and 128. Contrast recovery coefficient (CRC) and signal to noise ratio (SNR) were assessed for image quality to determine the optimum reconstruction parameters. The optimum filter parameters for FBP was 0.4 cycle/ cm with order of 5 and 40 iterations were recommended for ML-EM method. MP SPECT raw data from two patients of each LHR group were used for image reconstruction using the optimized reconstruction parameters for image quality comparison between the two methods. The image quality parameters evaluated were artefact, noise and sharpness. The Kruskal Wallis test was used to compare the image quality among different LHR values (0.2, 0.4, 0.6 and 0.8) for each reconstruction method. Then, the image quality produced by FBP and ML-EM was compared using Wilcoxon signed rank test for each LHR groups. Finally, the image quality produced by FBP and ML-EM was compared using

Wilcoxon signed rank test independent of LHR values. Based on the statistical analyses, there was no significant difference in image quality between different LHR values for both reconstruction methods ($p>0.05$, Kruskal Wallis). The image quality obtained by both image reconstruction methods was about the same for each LHR values ($p>0.05$, Wilcoxon rank signed test). Regardless of LHR values, no significant difference in image quality was observed between the two methods ($p>0.05$, Wilcoxon rank signed test). Based on the data, the iterative reconstruction algorithm (ML-EM) could be an alternative for SPECT slices reconstruction in MP SPECT.

CHAPTER 1

INTRODUCTION

1.1 Myocardial Perfusion SPECT Imaging

The most widely used nuclear cardiology procedure is the myocardial perfusion (MP) study using single photon emission computed tomography (SPECT). This procedure is a non-invasive imaging modality routinely used for diagnosis of coronary artery disease and heart muscle damage following an infarction. MP SPECT images provide 2D slices from 3D section of myocardium for assessment. The MP SPECT requires a suitable radiotracer or radiopharmaceutical for the imaging procedure. The radiotracer is chosen on the basis of some properties, such as distribution in the myocardium in linear proportion to blood flow; efficient myocardial extraction from the blood on the first pass through the heart; stable retention within the myocardium during the scan but also rapid elimination allowing repeat studies under different conditions; be readily available; and have good imaging characteristics which emit gamma rays with energy of 100 to 200 keV (Kathryn, 2009). The most commonly used radiopharmaceutical for MP SPECT are ^{201}Tl thallous chloride, ^{99m}Tc sestamibi or ^{99m}Tc tetrofosmin. The use of the former gold standard ^{201}Tl has decreased in favour of the ^{99m}Tc labelled radiopharmaceuticals. This is because the ^{99m}Tc radiopharmaceuticals produce higher quality images due to the higher energy photons produced and with a shorter half life than ^{201}Tl, which in turn allows larger amounts of radiopharmaceutical to be administered with a lower radiation dose to the patient. Further advantages of ^{99m}Tc sestamibi or tetrofosmin are that imaging can be delayed for a short while after injection and scans can also be repeated without loss of sensitivity. The MP SPECT consists of two types of procedures, the one day and two days imaging protocols. Each procedure consists of rest and stress parts. According to the American Society of Nuclear Cardiology (ASNC) imaging guidelines, it requires two separate injections of ^{99m}Tc -labelled myocardial perfusion imaging agent. One injection during stress and the other one are at rest. Ideally, stress and rest imaging with ^{99m}Tc labelled agents are performed on two different days, the 2-day protocol. One can then administer for each imaging session the maximally allowed activity of radiopharmaceutical (30–40 mCi/day). Thus, images be expected to be of optimal quality, i.e., good count density and not contaminated with "shine-through" from previously administered radioactivity. For one-day imaging protocol, the total activity is divided into two injections: first a low dose and later a high dose injection. In order to get a minimum contamination of radiation on the second image, the first image should be injected of about 1/4 of the total dose, i.e., 10–15 mCi, while the second image should be injected of about 3/4 of the total dose, i.e., 30–35 mCi (Wackers *et al.*, 2008). For the ^{99m}Tc usage in MP, a positive correlation was observed between lung- heart ratios (LHR) values and left ventricular ejection fraction at rest and stress (Giubbini *et al.*, 1995). The LHR measured by ^{99m}Tc-sestamibi imaging, gives clinically useful information. Both resting and post exercise values are correlated with ejection fraction and give prediction for left ventricular dysfunction (Giubbini *et al.*, 1995). They found that for the patients with LHR of higher than 0.47 will have the ejection fraction of <40%. There were several other parameters that involve in MP SPECT procedure such as the application of Electrocardiogram (ECG) Gating, acquisition and reconstruction process. The details of parameters that involve in scanning procedure are discussed in detail in Appendix A.1.

1.2 SPECT Reconstruction Algorithms

The basic principle of nuclear medicine imaging is the following: a γ-emitter–labelled pharmaceutical is administered to a subject and an external device, the gamma camera, detects the radioactivity coming from the body, from 1 or several angles of views. The image obtained at one angle of view is the projection of the 3-dimensional (3D) distribution onto the 2-dimensional (2D) detector plane. So, when the 3D distribution were seen from one angle, no information regarding the depth at which disintegrations occur is available; moreover, activities coming from separate structures may overlap each other on the detector plane, and the contrast may be low. With only one projection image, it is impossible to determine the activity distribution because an infinite number of distributions can yield the same projection. To tackle this problem, the tomography imaging was developed.

In the tomography imaging, it is difficult to find two values knowing only their sum. However, the overlap observed in the projections depends on the relative positions of the detector and of the structures inside the body. So, more information about the relative positions can be obtained by acquiring projections over a large number of angles of view around the subject. The basic idea of SPECT imaging is that to obtain as accurately as possible of the γ-emitter distribution in any slice of the body, using projections of images that acquired by a rotating gamma camera from several angles of view. Although many different algorithms for SPECT slices reconstruction exist, there were two common types of reconstruction methods which are filtered back projection (FBP) and iterative method. Both algorithms are basically having different mathematical approaches to reconstruct the SPECT slices. The FBP involves analytical process of data. On the other hand, iterative method involves an iteration of data. There are several types of iterative reconstruction methods commercially available. The maximum likelihood expectation maximization (ML-EM) for emission tomography was first developed by Shepp and Vardi (1982). Later, Hudson and Larkin (1994) proposed an ordered-subset expectation maximization (OSEM) implementation of the algorithm. Introduction of the latter algorithm decreased the reconstruction time considerably and made it feasible to apply OSEM in daily clinical routine. Despite of the acceleration, the quality of the reconstructed image is identical between both ML-EM and OS-EM. The detail of the FBP and iterative algorithms are discussed in the Appendix B.

The major advantage of iterative reconstruction techniques is that they permit the emission and detection process to be accurately modelled (Hutton *et al.*, 1997). In contrast, the filtered back projection algorithm makes no allowance for the physics of emission including attenuation and scatter of the emitted photons. The iterative model can be quite comprehensive, to include the variation of resolution with source-detector position, the incorporation of measured variable attenuation, as is essential for accurate myocardial reconstruction, the modelling of scatter in three dimensions, or even inclusion of knowledge of patient motion or tracer kinetics.

The final reconstructed noise using iterative algorithm tends to be much more acceptable than that present using FBP. In FBP the noise is constant across the reconstructed field when no attenuation is present. In iterative, the noise level is correlated with the signal: i.e. the noise amplitude is lower in regions of low counts. Probably more striking is the absence of streaking artefacts, which are common in noisy FBP studies, particularly when there is a focus of high activity. Although the noise structure and distribution have appeal, it must be noted that, as iteration number increases, noise increases. Due to the dependency of noise on the iteration numbers, the smoothness of the images needs to be maintained when applying higher iterations number. To maintain smoothness of the reconstructed slices in ML-EM method, regularisation is introduced which usually involves control of the difference between neighbouring pixels throughout the reconstruction process. An alternative approach for noise reduction, from which similar results can be obtained, is to use post-reconstruction filtering (e.g. using a Gaussian filter).

The other advantage of the ML-EM reconstruction is that it has much better properties for reconstruction of noisy data with much less evident streaking. However several artefacts have been reported by Snyder *et al*., (1987), particularly edge artefacts exist when there is a sharp transition from areas with activity to background levels outside the area of interest. These effects are not unlike the ring artefacts commonly observed when using restoration filtering in FBP method. Also there can be hotspots near body boundaries, especially when there are low in counts. ML-EM has the property that when there are zero counts on a projection this enforces zero counts along the corresponding ray in the reconstruction. This is a sort of truncation effect, which results in a build up of counts near body boundaries. However, in general, artefacts tend to be less evident using ML-EM compared to FBP.

1.3 Literature Review

The most common method for image reconstruction in SPECT imaging is the FBP. It has been widely used in all SPECT procedure. The reconstructed SPECT slices using FBP have a tendency to incorporate with higher noise level, negative pixel values and lower contrast. In clinical Myocardial Perfusion SPECT, certain region of the cardiac image will be reduced in the uptake. This is due to filtering the projection with a ramp filter will generate the negative pixel value near the liver, and thus resulting in reduced counts in the inferior and posterior myocardial walls as study done by Germano *et al.*, (1997). This phenomenon can be lead to the misdiagnosis of the patients with coronary artery disease (CAD). As the several previous studies done, the usage of iterative reconstruction method could give a better quality image compared to the FBP method (Pan *et al.*, 1997 and Blocklet *et al.*, 1999).

The application of ML-EM/ OS-EM to the clinical data shows an improvement, qualitatively and quantitatively compare to FBP reconstruction (Bai *et al.*, 2001 and Zakavi *et al.*, 2006). These reconstruction methods, ML-EM/ OS-EM actually are able to incorporate various correction techniques, including scatter, attenuation and spatial resolution corrections. Iterative technique demonstrates less severe artefacts than does FBP and can tolerate at least four missing projections in clinical Myocardial Perfusion SPECT (Hatton *et al.*, 2004). Iterative algorithm also can reduce the star artefact in bone study and clinical myocardial study (Blocklet *et al.*, 1999 and Bai *et al.*, 2001). Recent advance in computer technology and the use of ordered subset expectation maximization OS-EM reconstruction have provided acceptable calculation time in EM reconstruction (Hutton *et al.*, 1997).

It has been reported that the ML-EM reconstruction of an object is dependent on the activity surrounding (background) the object (Stamos *et al.*, 1988). The investigation of this dependence can be clinically important when small lesions are embedded in background activity. Using the ML-EM/ OS-EM reconstruction with or without the attenuation correction (AC) and detector response correction (DRC), the introduction of background activity may degrade dramatically the contrast of the point source (Pan *et al.*, 1997). In the reconstruction of cardiac images, the activity in the liver has been shown to affect the activity reconstructed in the myocardium region when the ML-EM reconstruction with attenuation correction is performed (Nuyts *et al.*, 1995, King *et al.*, 1996).

Several reports have addressed the usefulness of iterative reconstruction method on the clinical myocardial imaging as studies done by Bai *et al.*, (2001) and Zakavi *et al.*, (2006). The finding has shown that iterative method contributed to the reduction of the count-loss artefacts in inferior and posterior walls and easy recognition of hypoperfusion in the left circumflex artery (LCX) area of the heart (Bai *et al.* 2001). The iterative method shows the higher tolerance to the missing data and less tolerance to motion artefacts in SPECT slices compare to FBP method (Hatton *et al*., 2004 and Zakavi *et al.* 2006). Gutman *et al*., (2003) have studied the optimal number of iterations and the use of post filtering in phantom and patients. Both the iterations number and post filtering were found depended on the medical application and the gamma camera used. In order to test the detection of the lesion visibility, the usage of higher number of iteration should be followed by the use of mild post filtering. In that study, the author has used 40 iterations with post filtering to get the same image quality with 32 iteration number without post filtering. The usage of the post filtering is to suppress the noise level to the acceptable value. To reduce the effect of motion on the image, Zakavi *et al.*, (2006) use post filtering to reduce the noise to the optimum level in the Myocardial Perfusion SPECT studies.

According to Seret (2004), the inexperienced user should always use 16 iterations for ML-EM while at least eight subsets with two iterations in OS-EM reconstruction for SPECT myocardial perfusion images. With the low number of iteration, this will generate reconstructed image with low noise level, but at the expense of biased contrast. In other words, a smaller number of iteration results in smooth image, but with low contrast, especially in poorly perfused region in myocardium (Hutton *et al.*, 1997 and Seret 2004).

The ratio of activity in the lung to activity in heart or lung to heart ratio (LHR) has been shown to be an effective indicator of the severity of coronary artery disease in cardiac SPECT using ^{201}Tl (Soares *et al.*, 1995). Increased pulmonary ^{201}Tl uptake has a strong correlation with high pulmonary capillary wedge pressure, elevated left atrial pressure, prolonged pulmonary blood transit time, and left ventricular dysfunction (Bingham *et al.* 1980). Therefore, it is accepted that increased pulmonary ^{201}Tl activity detected by scintigraphy is a marker of either transient (Boucher *et al.*, 1980) or persistent left ventricular dysfunction. Patients at risk for future cardiac events can be identified by the presence of increased ^{201}Tl uptake in conjunction with an abnormal perfusion pattern (Kaul *et al.*, 1988). In general, the lung/heart ratio for ^{201}Tl has been shown to have an upper limit of 0.54 for normal patients (Aksut *et al.*, 1995). The data for ^{99m}Tc sestamibi suggested that the upper limit of 0.44 (Bacher-Stier *et al.*, 2000). Morise *et al.*, (1995) noted that the LHR could be used as an indicator whether the patients are having cardiac problems.

1.4 Problem Statement

SPECT imaging of the heart is a widely used procedure for diagnosing coronary artery disease. For many years, the clinical SPECT image reconstruction method was the Filtered Back Projection (FBP) method. Over the years, the iterative method gained popularity compared to FBP method due to several advantages qualitatively and quantitatively. The one major disadvantage of iterative method (ML-EM/ OS-EM) is that it consumes more calculation time as compared to FBP. But, with the advancement in computer technology and the use of OS-EM, reconstruction has provided acceptable calculation time in expectation maximization (EM) based reconstruction method.

The main problem with the FBP method is that the SPECT images reconstructed tend to have the streak artefacts due to the analytical approach of the FBP method. The other major problem that arises when using the FBP method is that the lower signal to noise ratio (SNR) in SPECT slices. The iterative method could reduce the streak artefacts (Blocklet *et al.*, 1999 and Bai *et al.*, 2001) and increase the SNR value in SPECT slices (Defrise *et al*., 2003).

Previously, the numbers of iteration used depended on trial and error method to get the “best” reconstructed SPECT slices. There was one study done in phantom and patients to find the optimum number of iteration in hot spot and lung cancer patient using dual head camera by Gutman *et al*., (2003). But for the Myocardial Perfusion SPECT study, it is still unclear how many iterations are required to produce the optimum quality. The determination of the optimum number of iteration is very crucial because it will provide the best image diagnostic value for Myocardial Perfusion SPECT. If we use too large number of iterations, the image structure will be diminished due to the existence of higher statistical noise level. Conversely, if we use too small number of iteration, this will introduce low image contrast. Thus the optimum number of iterations for specific gamma camera needs to be evaluated.

By determining the optimum number of iterations for iterative method and optimum cut off frequency for FBP method based on phantom studies, the comparison of image quality in patients were carried out to assess whether the iterative method will give any advantage or can be used as an alternative to the FBP method for image reconstruction in Myocardial Perfusion SPECT.

1.5 Aims and Objectives

The aim of this project is to compare the image quality of images reconstructed using FBP and iterative method in ^{99m}Tc Myocardial Perfusion SPECT studies. The objectives are;

1. To determine the optimum filter parameters to be used in FBP for different background to target ratio (BTR) simulating the clinical conditions based on phantom studies.
2. To determine the optimum number of iterations needed in iterative (ML-EM method) to produce the best image quality based on phantom studies.
3. To compare the image quality of the reconstructed images using the optimized FBP and ML-EM method in clinical MP SPECT studies.

CHAPTER 2

MATERIALS AND METHODS

2.1 Research Design

This project consists of two parts; the cardiac phantom system SPECT studies and Myocardial Perfusion SPECT studies on patients as shown in Figure 2.1 and 2.2 respectively. The SPECT phantom studies were done using four different values of background to target ratio (BTR) which are 0.2, 0.4, 0.6 and 0.8. The BTR values for phantom studies were based on the chosen same lung to heart ratio (LHR) values of the patients undergoing Myocardial Perfusion SPECT in the Nuclear Medicine Department Penang General Hospital (GH). The SPECT images were reconstructed using two different reconstruction algorithms which were Filtered Back Projection (FBP) and Iterative [Maximum Likelihood Expectation Maximization (ML-EM)] methods. The first part of the project was to determine the optimum parameters for Butterworth filter to be used in FBP, and to determine the optimum number of iterations for ML-EM algorithm will produce good quality images. The second part of this project was to compare the image quality obtained using the two reconstruction methods in patient studies based on the results in phantom studies. The SPECT studies using phantom were performed at Nuclear Medicine, Radiotherapy and Oncology unit in Hospital Universiti Sains Malaysia (HUSM).

In Penang GH 100 male patients who underwent stress and rest Myocardial Perfusion SPECT were evaluated to determine the LHR values. Male patients were chosen as the number of female patients was very small. Four different LHR values (0.2, 0.4, 0.6 and 0.8) reflecting the various heart conditions were chosen. The LHR has been shown to be an effective indicator of the severity of coronary artery disease in cardiac SPECT. In the patients who had the cardiac problems, the higher magnitudes of LHR value were observed. This was due to the uptake in the lung was higher compared myocardium. Each of LHR was selected within the range of ±10% from 0.2, 0.4, 0.6 and 0.8. As an example, patients which have a range of LHR between 0.18 and 0.22 will be classed into LHR 0.2 group. The LHR of 0.2 represents the normal lung uptake while LHR of 0.4 is near the upper limit of normal heart condition. The LHR of 0.6 and 0.8 reflect the moderate and severe degree of left ventricular dysfunction respectively where the uptakes of radioactivity in the lung are high.

CARDIAC PHANTOM SYSTEM SPECT STUDIES

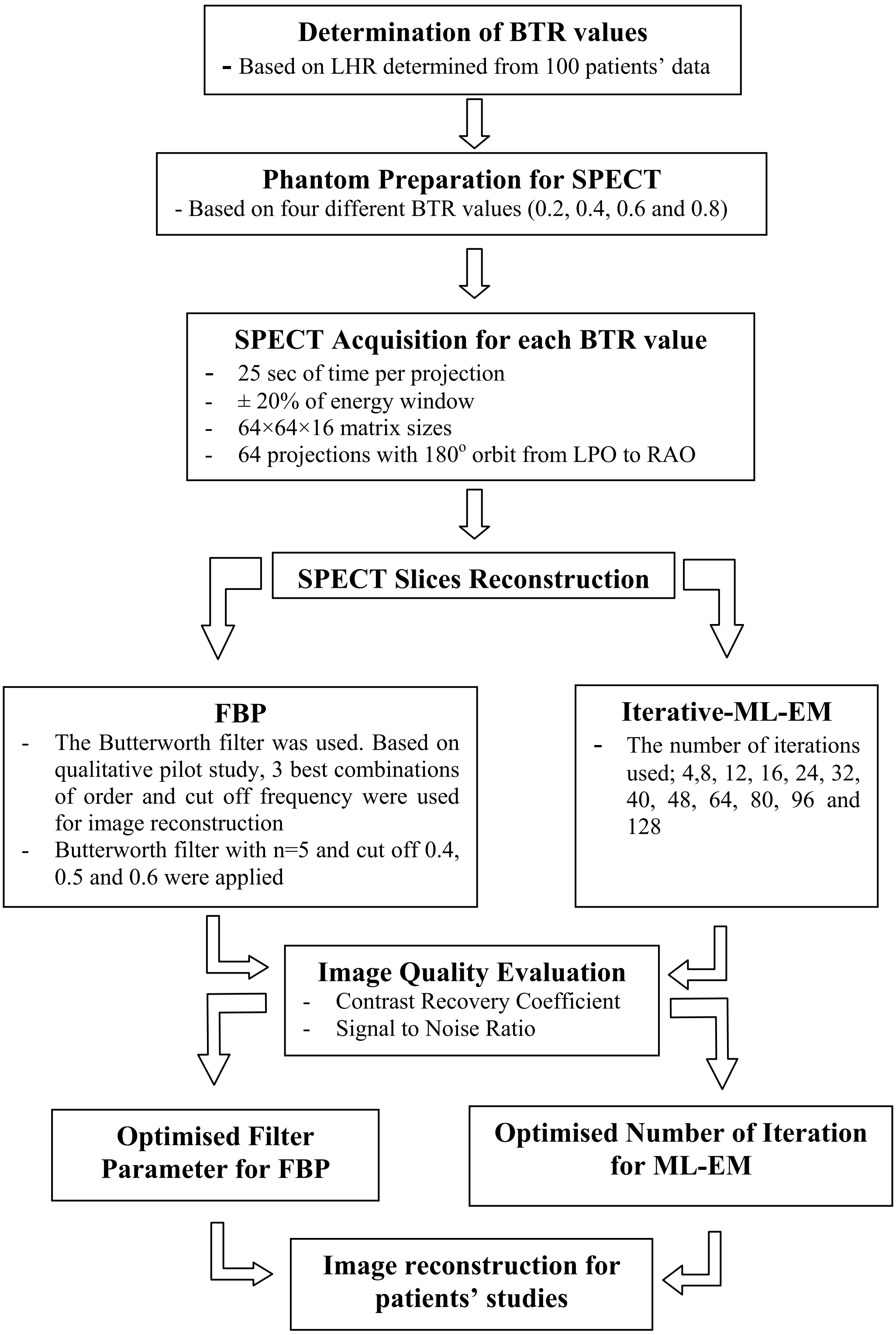

Figure 2.1 The flow chart of phantom SPECT studies

MYOCARDIAL PERFUSION SPECT STUDIES

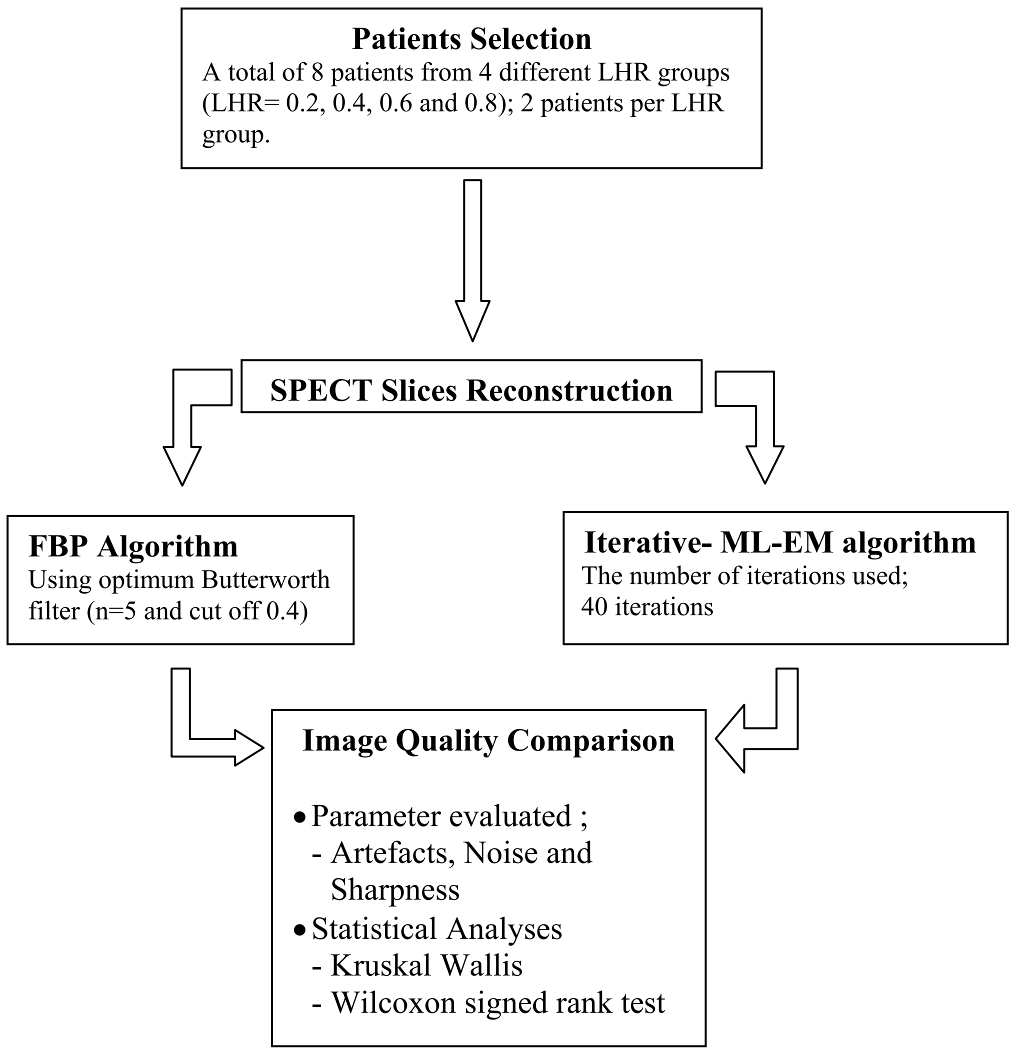

Figure 2.2 The flow chart of image quality comparison in MP SPECT studies in patients

A total of four SPECT phantom studies (4 different BTR values) were carried out and the images were reconstructed using FBP and ML-EM reconstruction algorithms. Butterworth filter was utilized for FBP reconstruction using 3 different cut off frequencies (0.4, 0.5 and 0.6) with order, n=5. The image reconstruction performed using ML-EM algorithm with different number of iterations (4, 8, 12, 16, 24, 32, 40, 48, 64, 80, 96 and 128) though the recommended number of iterations as suggested by the vendors were 12 and 16. The quality of reconstructed images was evaluated in term of contrast recovery coefficient (CRC) and signal to noise ratio (SNR). The optimum filter parameters for FBP and the optimum number of iterations for iterative method obtained were used in image reconstruction for patients' studies.

Two patients for each LHR value were selected for image quality comparison giving a total of eight SPECT raw data to be reconstructed using the two methods. The image quality was evaluated based on artefact, noise and sharpness of the image reconstructed. For each LHR value about 10 slices were reconstructed. A total of 160 images were reconstructed and presented in random order to two experienced nuclear medicine physicians blinded to the reconstruction methods and LHR values. The two doctors evaluated the image quality using a four point scale to grade the sharpness, the presence of artefacts and noise. Statistical analyses were then used to compare the image quality produced by the two reconstruction methods.

2.2 Cardiac Phantom SPECT Study

2.2.1 Material

2.2.1 (a) Cardiac Phantom System

The cardiac phantom system used in this study consists of cardiac insert placed inside a cylindrical water tank (Nuclear Associates, Hicksville, NY) as shown in Figure 2.3. The insert consisted of a hollow inner cylinder (7 cm in diameter) placed within a larger hollow outer cylinder (9 cm in diameter). The volume of space (1 cm wide) between the two hollow cylinders was about 275 mL. The insert was used as a 3-dimensional model of the left ventricle. The volume of the cylindrical water tank was about 9225 ml simulating the thorax/lungs in human. The cardiac insert chamber has the same activity with the cylindrical water tank due to the communication between the cardiac insert chamber and cylindrical tank.

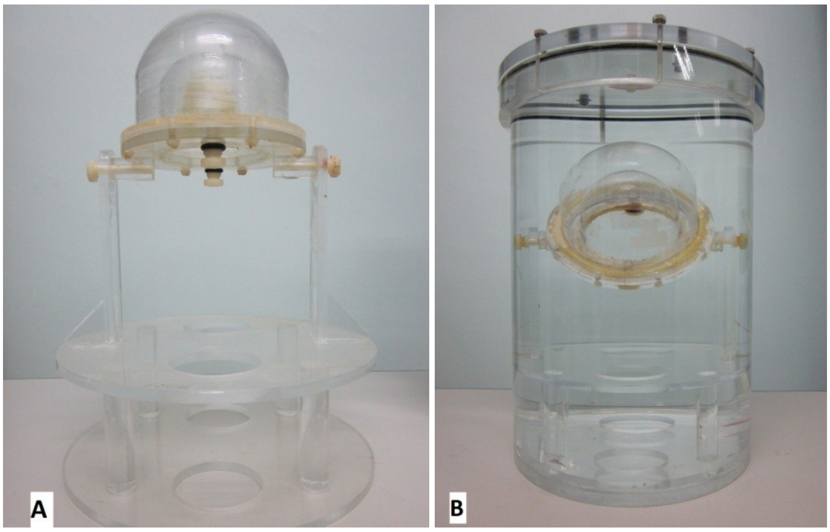

Figure 2.3 Image of the cardiac phantom

Note:
A. The cardiac insert attached to a stand **B**. Cardiac phantom system: Cardiac insert in the cylindrical water tank.

2.2.1 (b) Gamma Camera Imaging System

The gamma camera used was Phillips ADAC Forte (Philips Medical System, Milpitas, CA) with dual heads. The workstation used was Pegasys Ultra workstation with SUN Microsystems platform. Each camera head consist of a rectangular with 508mm × 381mm field of view (FOV). The camera equipped with 9.5mm thickness of NaI (Tl) scintillation crystal and 55 photo multiplying tubes (PMT), low energy high resolution (LEHR) collimator as in Figure 2.4A.

Figure 2.4 Gamma Camera Imaging System in HUSM

Note:
A. ADAC Forte gamma camera systems with dual detector head **B.** The Pegasys Ultra workstation with SUN Microsystems platform. **C.** Acquisition computer.

2.2.1 (c) Dose Calibrator

The measurement of radionuclide activity was performed using Atomlab 100 (Atomic Product Corp, Shirley, NY) with well type detector. This dose calibrator was covered with 0.25 inches of lead (Pb). This equipment was covered using lead glass as in Figure 2.5.

Figure 2.5 Dose calibrator

2.2.1 (d) Radionuclide

For this study, the ^{99m}Tc was used and it was drawn from the Elumatic III ^{99m}Tc generator (IBA Molecular, Yvette, Cedex, France). The elution was done early in the morning.

2.2.1 (e) Radiation monitoring and protection equipments

There were several items that were considered for radiation monitoring and protection purposes. The personal monitoring equipment used was thermo luminescent dosimeters (TLDs) chip ring wore at both hand. This equipment was important to record the radiation exposure received when preparing the ^{99m}Tc. The lead gown was also used in order to perform the preparation of ^{99m}Tc in phantom. The other equipments that have been used were lead syringe shield. The radiation protection and protection equipments were shown in Figure 2.6.

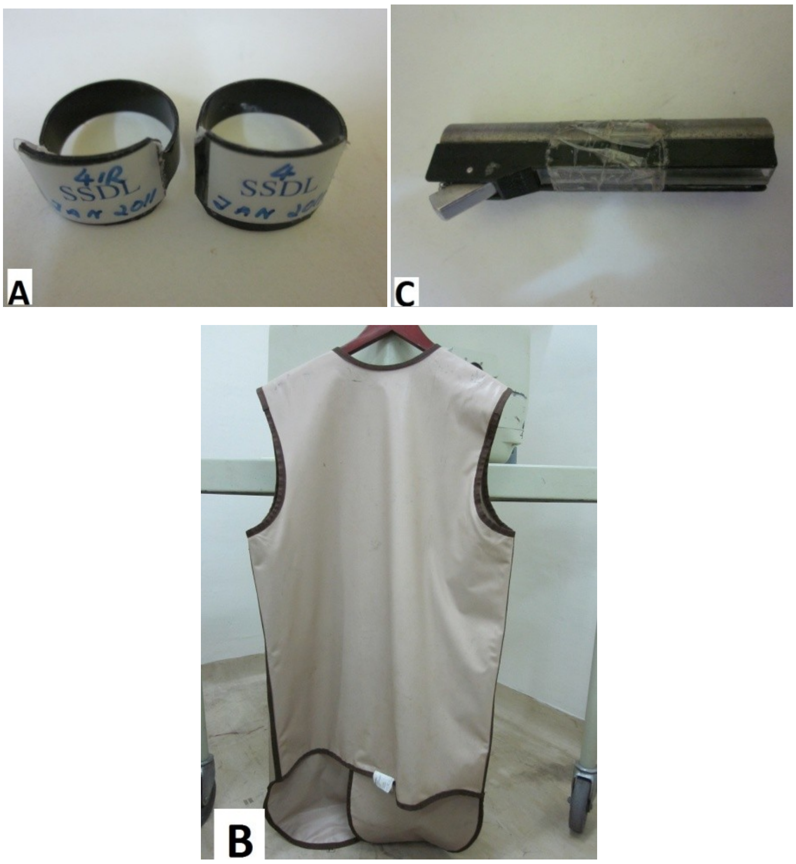

Figure 2.6 The radiation protection and monitoring equipment

Note:
A. The TLD chip rings **B.** The lead gown **C.** The lead syringe shield

2.2.2 Methods

Quality control of SPECT was performed according to the manufacturer's protocol. A good quality assurance program is essential to minimize the adverse effects of various factors on the quality of SPECT images: 20% symmetric energy window, centred at 140 keV of ^{99m}Tc photo peak, uniformity, centre of rotation (COR) and sensitivity were done prior to the studies. The result of the quality control test is shown in Appendix C.

2.2.2 (a) Cardiac Phantom SPECT Study

The BTR values to be used for phantom studies were based on the ratio of activity in the lung to the activity in the heart (LHR) from cardiac patients undergoing Myocardial Perfusion SPECT in Nuclear Medicine Department, Penang General Hospital. The usage of MP SPECT data from Nuclear Medicine Department, Penang General Hospital in this study was due to the unavailability of MP SPECT procedure in Hospital Universiti Sains Malaysia (HUSM). The data from 100 male patients underwent myocardial perfusion scans were used in determining the LHR values. From the analysis, four LHR groups were identified based on the patients' clinical condition: 0.2, 0.4, 0.6 and 0.8. Each of LHR was selected within the range of ±10% from 0.2, 0.4, 0.6 and 0.8. As an example, the patients which have a range of LHR between 0.18 and 0.22 will be classed into LHR 0.2. The LHR of 0.2 represents the normal lung uptake while LHR of 0.4 is very close to the upper limit of normal value which is 0.44 for ^{99m}Tc. The LHR of 0.6 and 0.8 reflecting the moderate and severe degree of left ventricular dysfunction. These LHR values were then used for BTR values in the phantom studies.

The method of calculating the lung to heart ratio (LHR) was based on the technique described by Giubbini *et al* (1995) to correlate the activity in the lung and myocardial dysfunction. The process of calculating the LHR was started by recalling the SPECT raw data. The anterior side or Left Anterior Oblique (LAO) 45^{o} position of the projection data sets from the raw image was selected. To reduce the counts bias, 3 frames/ projection were chosen from raw data. A 3×3 pixels region of interest (ROI) was drawn on the hottest region of the myocardium and on the hottest part of the lung. The two ROIs drawn must be separated by at least 5 pixels distance. The process was carried out for all 100 SPECT patients both in rest and stress groups. As all 100 patients undergone one day MP SPECT imaging procedure, the effect of shine trough on the patients' images has been avoided. The average counts per pixel in each ROI were then determined to calculate mean LHR based on the average value from the 3 frames.

The activity of ^{99m}Tc used inside cardiac insert was ≈0.68 mCi corresponding to the concentration of 2.5×10^{-3} mCi/ ml. The concentration used was based on the average myocardial tracer uptake of 2.5% of a regular injected dose 30 mCi) for an average heart weighing 300 g (≈300 mL), in standard clinical cardiac SPECT imaging (Liu *et* al 2002). Then a fixed concentration of ^{99m}Tc were prepared inside cardiac insert and four varying concentrations in cylindrical tank to obtain BTR values of 0.2, 0.4, 0.6 and 0.8 as shown in Table 2.1.

Table 2.1 Administered activities inside the cardiac insert and cylindrical tank to obtain various BTR values

BTR	Phantom Activity	
	Cardiac Insert Concentration (mCi/ml)	Cylindrical Tank Concentration (mCi/ml)
0.2	2.5×10^{-3}	5×10^{-4}
0.4	2.5×10^{-3}	1×10^{-3}
0.6	2.5×10^{-3}	1.5×10^{-3}
0.8	2.5×10^{-3}	2×10^{-3}

The phantom with different BTR was then placed on the camera bed. It was placed about 5 cm on the left from the central x axis. It needs to be angled about 30^{o} off x axis to the left and about 45^{o} to the anterior plane of cylindrical phantom as in figure 2.7. The low energy high resolution (LEHR) collimator was used with 20% of energy window width. The standard matrix size used was 64 × 64 × 16 with 25 sec per stop. The measured pixel size was about 9.98mm. A total of 64 projections were obtained with step and shoot mode with 180^{o} acquisition orbit, started from left posterior oblique (LPO) and ended at right anterior oblique (ROA) as in Figure 2.7 and 2.8. The total counts for the SPECT raw data was about 9.4 million.

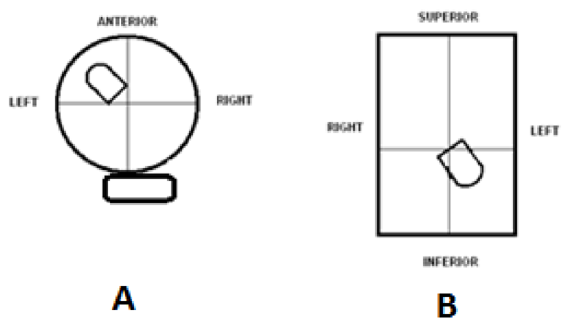

Figure 2.7 Diagram of phantom

Note:
A. Superior view of the phantom. **B.** The anterior view of phantom.

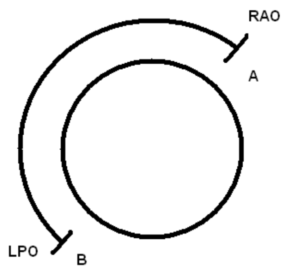

Figure 2.8 The orbit used for the acquisition

Note:
The camera head will travel from B to A.

2.2.2 (b) SPECT Slices Reconstruction

2.2.2 (b) (i) Filtered Back Projection (FBP)

The reconstruction of SPECT slices using FBP reconstruction was in the AutoSPECT programme. In this case, the FBP reconstruction algorithm used the combination of ramp and Butterworth filter. There were a wide range of cut off frequencies and order (n) available. The cut off frequency ranged from 0.1 to 2.0 while the order (n), ranged from 0 to 10. Before this project was carried out the qualitative pilot study on image quality was done using different cut off frequencies and order to reconstruct the images. Based on this study, Butterworth filter of n=5 and cut off frequencies (0.4, 0.5 and 0.6) produced good quality images. The Butterworth filter was chosen for image reconstruction in phantom studies with BTR values of 0.2, 0.4, 0.6 and 0.8 as shown in Table 2.2. The number of slices produced depended on the selection of border of cardiac insert from the raw data. About 14 image slices were reconstructed for image quality analyses. There was no attenuation correction applied since the cardiac insert was very close to the cylindrical tank wall during SPECT studies. The reconstructed images were then oriented into three different axis; Short Axis (SAX), Horizontal Long Axis (HLA) and Vertical Long Axis (VLA). The reconstruction and the orientation process are shown in Figure 2.9A. The total counts before reconstruction is about 9 million and the total counts after reconstructions is about 3.7 million. The time required for reconstruction of the SPECT slices was about less than 1 sec.

Table 2.2 Butterworth filters of order 5 (n=5) for FBP reconstruction

B/T Ratio	**Cut off Frequency (cycle/cm)**		
	0.4	0.5	0.6
0.2	×	×	×
0.4	×	×	×
0.6	×	×	×
0.8	×	×	×

2.2.2 (b) (ii) Iterative- ML-EM Reconstruction

The reconstruction of SPECT slices from raw data using the iterative reconstruction ML-EM method was also available in AutoSPECT programme. Various number of iteration (1 to 128) available for SPECT slices reconstruction. The numbers of iterations applied were 4, 8, 12, 16, 24, 32, 40, 48, 64, 80, 96 and 128 for each BTR value. About 14 image slices were reconstructed. The reconstructed images were then aligned into three different axis; Short Axis (SAX), Horizontal Long Axis (HLA) and Vertical Long Axis (VLA) as shown in Figure 2.9.B. In this case, the total counts before and after reconstructions were the same. The time required for reconstruction of the SPECT slices was depended on the iteration number used. The time required for 4 and 16 iterations was about 3.7 sec and 6.0 sec respectively. Meanwhile, the time required for 40 and 128 iterations was about 12.8 sec and 38 sec respectively.

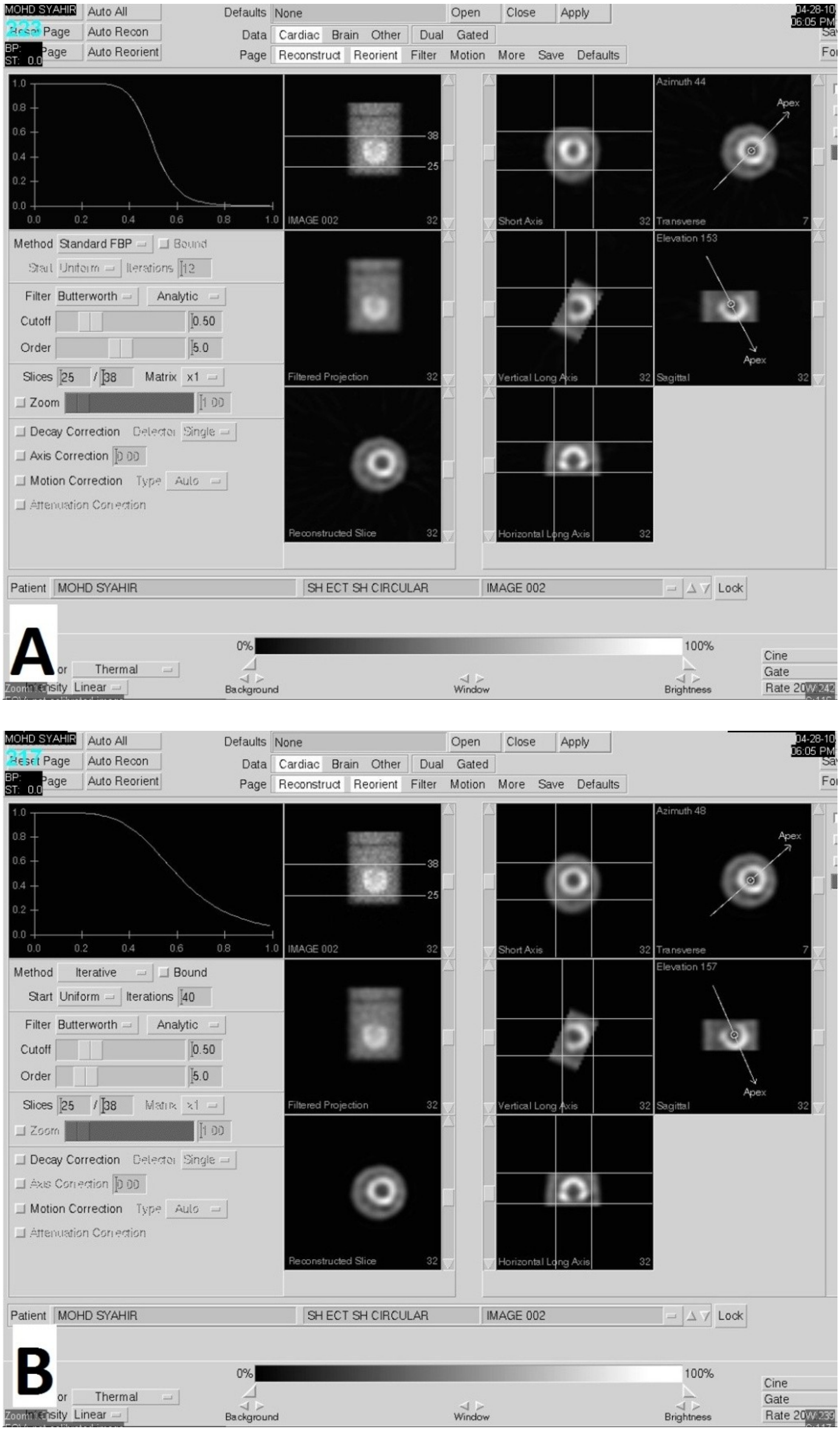

Figure 2.9 Image reconstructed using AutoSPECT in phantom studies.

Note: Left side is reconstruction parameter setting, and reorientation process on the right. **A.** Using the FBP reconstruction method **B.** Reconstructed images using Iterative (ML-EM) reconstruction process.