

Relationship between the optimum cut off frequency for Butterworth filter and lung-heart ratio in ^{99m}Tc myocardial SPECT

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Background: We investigated whether the lung-heart ratio parameter (LHR) can be used to identify the optimum cut off frequency for Butterworth filter in ^{99m}Tc myocardial SPECT imaging. **Materials and Methods:** This study involved a cardiac phantom system consisting of cardiac insert in which 1.10 cm cold defect was inserted into its myocardium wall and filled with 4.0 $\mu\text{Ci/ml}$ (0.148 MBq/ml) ^{99m}Tc concentration. The cardiac insert was then put into a cylindrical tank which filled with six different ^{99m}Tc concentrations as background. Thus, six target-background concentrations ratios (T/B) were carried out. The LHR was determined for every SPECT raw image obtained corresponding to each T/B. Then, 130 different combinations of filter parameters from Butterworth filter were utilized to reconstruct each SPECT raw image. The determination of count in myocardium, background, and defect regions of interest (ROI) were performed for every reconstructed image. All the count values were then used to calculate contrast, signal-to-noise ratio (SNR), and defect size. Each criterion was graded (1 to 100) and then summed together to obtain total grade. The optimum cut off frequency for each LHR was determined from the total grade. The relation between optimum cut off frequency for Butterworth filter and LHR was established using linear regression. **Results:** There were good relationship between the optimum Butterworth cut off frequency and LHR ($R^2 = 0.864$, $p < 0.01$). The optimal cut off frequency correspond to the change in LHR can be expressed by the equation: Optimum cut off frequency = $0.715 \times \text{LHR} + 0.227$. **Conclusion:** This study suggests that the optimum cut off frequency for Butterworth filter should be determined by referring to LHR in each patient study. *Iran. J. Radiat. Res., 2010; 8 (1): 17-24*

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INTRODUCTION

In clinical practice, filter is used during filtered back-projection (FBP) reconstruction to reduce image noise, increase contrast

and signal-to-noise ratio (SNR), and enhance the ability to detect any abnormalities. In principle, filter is a mathematical function that is applied to pixels in an image. The goal of filtering is to eliminate as much noise and retain as much signal as possible ⁽¹⁾. This includes smoothing, edge enhancement and resolution recovery ⁽²⁾.

Butterworth filter is one of the most popular low-pass filters used in SPECT imaging especially in nuclear cardiology ⁽³⁾. It is because of its ability to balance between contrast, SNR, and size accuracy which allow better image quality and accurate quantification ⁽⁴⁾. Butterworth filter in spatial frequency domain (f) has two parameters; the cut off frequency (f_c), and the order of the filter (n) as shown in equation 1 ⁽³⁾.

$$B(f) = \frac{1}{1 + \left(\frac{f}{f_c}\right)^{2n}} \quad (1)$$

In myocardial SPECT imaging, the choosing of the appropriate filter parameters is usually a matter of trial and error ^(5, 6). According to Laere *et al.* (2001), it should be chosen depends on the several factors: number of counts which related to study time, organ of study, background of noise level, and choice of interpretation ⁽²⁾. Inappropriate filtering of the raw back-projected tomographic data may significantly degrade image quality and affect the accuracy of

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quantitative results ⁽⁷⁻¹⁰⁾. The emphasis should be on the cut off frequency, which is found more affecting the image quality compared to the order of filter.

Several approaches have been investigated in order to optimize the cut off frequency. Minoshima *et al.* (1993) in optimizing Butterworth filter for brain SPECT revealed that the optimum cut off frequency and total counts were well correlated. They suggested that the cut off frequency of Butterworth filter should be determined by referring to total counts in each study ⁽¹¹⁾. While that, Ohnishi *et al.* (1997) in their study of filtering for myocardial SPECT found that the optimum cut off frequency was dependent on the amount of radiopharmaceutical administered to patient ⁽¹²⁾. However, because of the different distribution volume in each subject, accumulation of tracer injected into a target organ differs from subject to subject even if the same dose is administered ⁽¹¹⁾. This means that, the amount of radiopharmaceutical administered to patient is not an accurate indicator for determination of the optimum cut off frequency.

This study was carried out to find the alternative indicator in determination of the optimum cut off frequency for myocardial SPECT imaging. In this study, the relationship between the lung-to-heart ratio (LHR) parameter and the optimum cut off frequency was investigated by using the following methods.

MATERIALS AND METHODS

Preparation of cardiac phantom system

Myocardial wall chamber (250 ml) in the cardiac insert was filled with 1000 μCi (37 MBq) of $^{99\text{m}}\text{Tc}$ which was equal to 4.0 $\mu\text{Ci/ml}$ (0.148 MBq/ml) of $^{99\text{m}}\text{Tc}$ concentration. The 1.1 cm thick plastic rod was inserted into the myocardium wall to be used as cold defect (figure 1). The cardiac insert was then placed into the cylindrical tank (10 litres) with six different concentrations of $^{99\text{m}}\text{Tc}$ as background: (i) 0.75 $\mu\text{Ci/ml}$

(0.028 MBq/ml), (ii) 1.0 $\mu\text{Ci/ml}$ (0.037 MBq/ml), (iii) 1.2 $\mu\text{Ci/ml}$ (0.044 MBq/ml), (iv) 1.5 $\mu\text{Ci/ml}$ (0.056 MBq/ml), (v) 2.0 $\mu\text{Ci/ml}$ (0.074 MBq/ml), and (vi) 3.0 $\mu\text{Ci/ml}$ (0.111 MBq/ml). Thus, six target-background concentrations ratios (T/B) were carried out: T/B = 5.3, 4.0, 3.3, 2.7, 2.0, and 1.3.

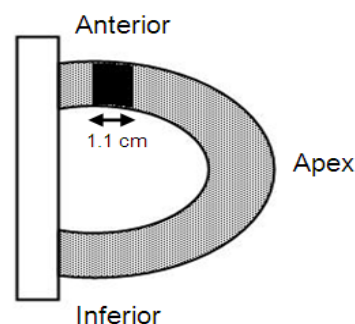


Figure 1. The plastic rod (cold defect) was located at the anterior position of cardiac insert (viewed from vertical axis).

Data acquisition

Data acquisition was obtained with dual head, large field of view gamma camera (ADAC Forte Imaging System), equipped with low energy high resolution (LEHR) collimators. 64 projections (25 sec per projections) was used in 64 x 64 matrix using step and shoot acquisition over 180° arc from 45° right anterior oblique (RAO) to 45° left posterior oblique (LPO) position, with radius of 29.7 cm. The distance between detectors and phantom was approximately 2 cm. A single energy window at 140 keV was used.

Lung-heart ratio determination

The lung-heart ratio (LHR) was determined for each SPECT raw image corresponding to each T/B using Lung-Heart Ratio program. Two regions of interest (ROI) were defined over the cardiac zone and a representative background region of an anterior or left anterior oblique (LAO) 45° projection image. Then, the program automatically determined the counts ratio.

Data processing

All SPECT slices reconstructions were performed using Auto SPECT program

employing filtered back-projection (FBP) method. Butterworth filter with following combination of filter parameters were utilized: cut off frequency from 0.20 to 0.80 Nq with 0.05 step and order of filter from $n = 3$ to $n = 12$ with 1 step. Thus, a total of 130 different combinations of filter parameters were used to carry out SPECT slice reconstruction on each SPECT raw image corresponding to each T/B.

Contrast, signal-to-noise ratio, and defect size determination

For each combination of filter parameters used in filtering, one of the slices in vertical long axis view which has the clearest defect appearance was chosen for analysis. ROI was drawn to determine the maximum count in myocardium ($R_{max} (myo)$), the minimum count in heart hole ($R_{min} (hole)$), and the minimum count in the defect ($R_{min} (def)$). All the count values were then used to calculate contrast and SNR. To determine

the defect size, count profile along the line passing through the defect and myocardium was obtained. The number of pixel between the lower peak and the steep of the other peak having same count (N_{pixel}) was used to determine defect size (figure 2). All of these measurements were performed using Count Profile program. The contrast (C), SNR (S), and defect size (D) were calculated using formulae below:

$$MaxContrast, C = \frac{R_{max} (myo) - R_{min} (def)}{R_{max} (myo)} \quad (2)$$

Note: C is the maximum contrast for defect detection.

$$SNR, S = \frac{R_{max} (myo) - R_{min} (def)}{R_{min} (hole)} \quad (3)$$

Note: S is the SNR for defect diagnosis.

$$Defect\ Size, D = N_{pixel} \times 6.47\ mm \quad (4)$$

Note: D is the determination of defect size where size of a pixel = 6.47 mm.

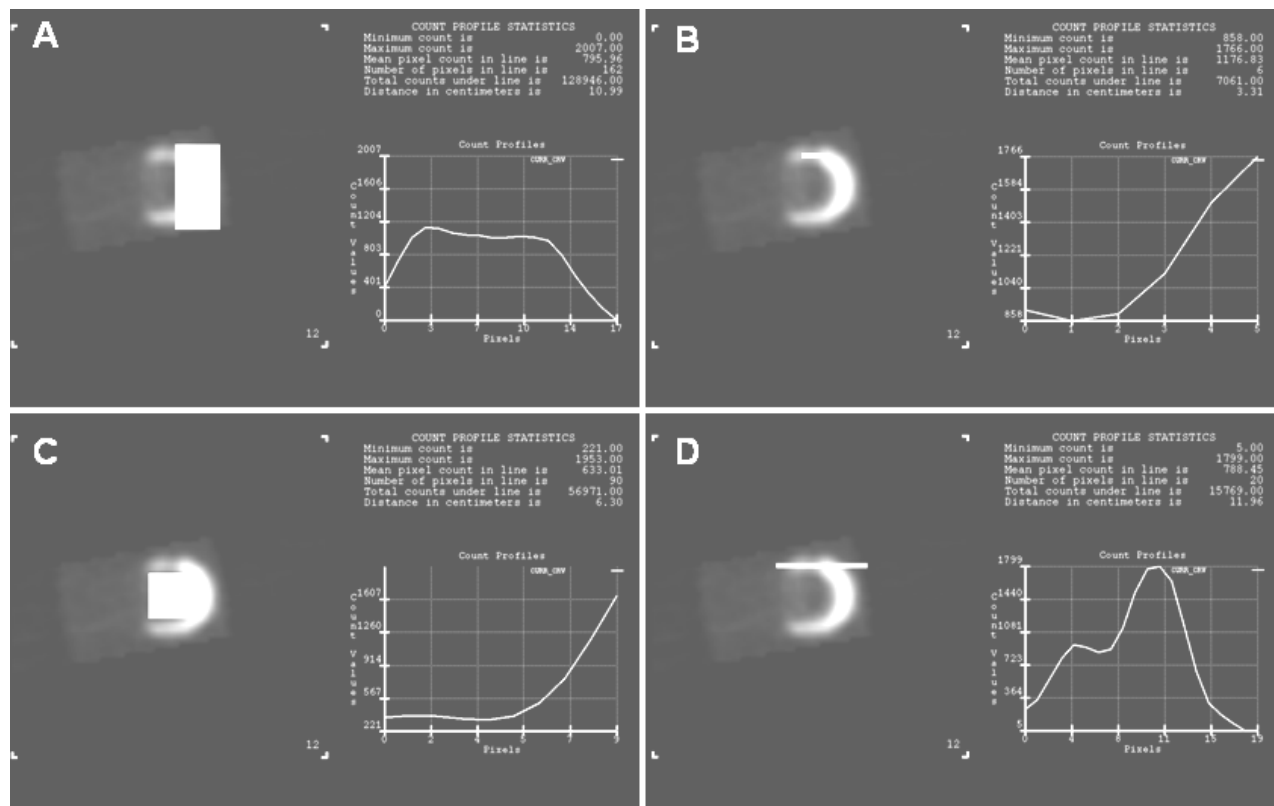


Figure 2. The measurements of maximum count in normal myocardium ($R_{max} (myo)$) (A), minimum count in defect ($R_{min} (def)$) (B), minimum count in background or heart hole region ($R_{min} (hole)$) (C), and number of pixel between the smaller peak and the steep of the other peak having same count (N_{pixel}) (D) using Count Profile program.

The optimum filter parameters determination

The parameter chosen to represent the optimum filter parameters for Butterworth filter is the total grade which is the trade-off of contrast, SNR, and defect size accuracy. To determine the total grade, first the contrast, SNR, and defect size values for each filter parameter combinations (cut off frequency and order of filter) were graded from 1 to 100. 1 is for the worst contrast and SNR, and 100 is for the best case. For defect size, 1 is for the least accurate and 100 is for the value very close to true size. Then the total grade for each combination of filter parameters was determined based on the average of contrast, SNR, and defect size grades. The combination of filter parameters which produced the highest value of total grade represents the optimum filter parameters for each T/B.

Linear regression analysis

Linear regression analysis was used to evaluate the relationship between the optimum cut off frequency for Butterworth filter and lung-heart ratio (LHR).

RESULTS

The calculated lung-heart ratio

Figure 3 shows the calculated lung-heart ratio (LHR) for each target/background concentration ratio (T/B). When the T/B decreased from 5.3 to 1.3, the LHR values were found increased from 0.24 to 0.90. LHR values were 0.24, 0.43, 0.60, 0.72, 0.80, and 0.90 for T/B 20.0, 4.0, 3.3, 2.7, 2.0, and 1.3 respectively.

and 1.3 respectively.

The optimum filter parameters

Table 1 demonstrates the total grades for different target-background concentration ratio (T/B) using Butterworth filter. The optimum filter parameters are 0.40 Nyquist (Nq) and order 12 (for T/B = 5.3), 0.45 Nq and order 8 (for T/B = 4.0), 0.75 Nq and order 12 (for T/B = 3.3), 0.80 Nq and order 8 (for T/B = 2.7), 0.80 Nq and order 11 (for T/B = 2.0), and 0.80 Nq and order 11 (for T/B = 1.3).

Relationship between the optimum cut off frequency and LHR

Figure 4 shows a linear regression model, which demonstrates the variation of optimum cut off frequency determined from Butterworth filter correspond to the change in lung-heart ratio (LHR). The LHR represents their respective target-background concentration ratio (T/B) set up in phantom study. The regression analysis shows that the optimum cut off frequencies determined from Butterworth filter are well correlated with LHR. The plotted line is expressed by the equation $Y = AX + B$, which Y is optimum cut off frequency, A is coefficient (0.715), X is LHR, and B is constant (0.227). The analysis of variance (ANOVA) shows that the model is significant ($p < 0.01$) which indicates the acceptability of the model from a statistical perspective. The R Square of this model is high ($R^2 = 0.864$) which indicates that about 86.4% of the variation in optimum cut off frequency is explained by the LHR.

Table 1. Summary of the optimum filter parameters for Butterworth filter and each T/B.

T/B	LHR	Optimum Filter Parameters	
		Cut off Frequency (Nyquist)	Order of Filter (n)
5.3	0.24	0.40	12
4.0	0.43	0.45	8
3.3	0.60	0.75	12
2.7	0.72	0.80	8
2.0	0.80	0.80	11
1.3	0.90	0.80	11

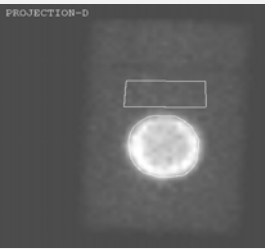





Target/Background Concentration Ratio (T/B)	Lung-Heart Ratio (LHR)
T/B = 5.3	<div>PROJECTION-D</div> <div></div> <div>LUNG-HEART RATIO</div> <div>Normalized Counts</div> <div>Heart : 11513.584270</div> <div>Lung : 2737.409836</div> <div>Ratio : 0.237755</div>
T/B = 4.0	<div>PROJECTION-D</div> <div></div> <div>LUNG-HEART RATIO</div> <div>Normalized Counts</div> <div>Heart : 26258.840000</div> <div>Lung : 11268.579832</div> <div>Ratio : 0.429135</div>
T/B = 3.3	<div>PROJECTION-D</div> <div></div> <div>LUNG-HEART RATIO</div> <div>Normalized Counts</div> <div>Heart : 18691.195652</div> <div>Lung : 11246.857143</div> <div>Ratio : 0.601720</div>
T/B = 2.7	<div>PROJECTION-D</div> <div></div> <div>LUNG-HEART RATIO</div> <div>Normalized Counts</div> <div>Heart : 25807.961538</div> <div>Lung : 18508.438095</div> <div>Ratio : 0.717160</div>
T/B = 2.0	<div>PROJECTION-D</div> <div></div> <div>LUNG-HEART RATIO</div> <div>Normalized Counts</div> <div>Heart : 28119.116505</div> <div>Lung : 22550.890110</div> <div>Ratio : 0.801977</div>
T/B = 1.3	<div>PROJECTION-D</div> <div></div> <div>LUNG-HEART RATIO</div> <div>Normalized Counts</div> <div>Heart : 20162.216667</div> <div>Lung : 18174.946429</div> <div>Ratio : 0.901436</div>

Figure 3. The calculated lung-heart ratios (LHR) for each situation of target/background concentration ratios (T/B).

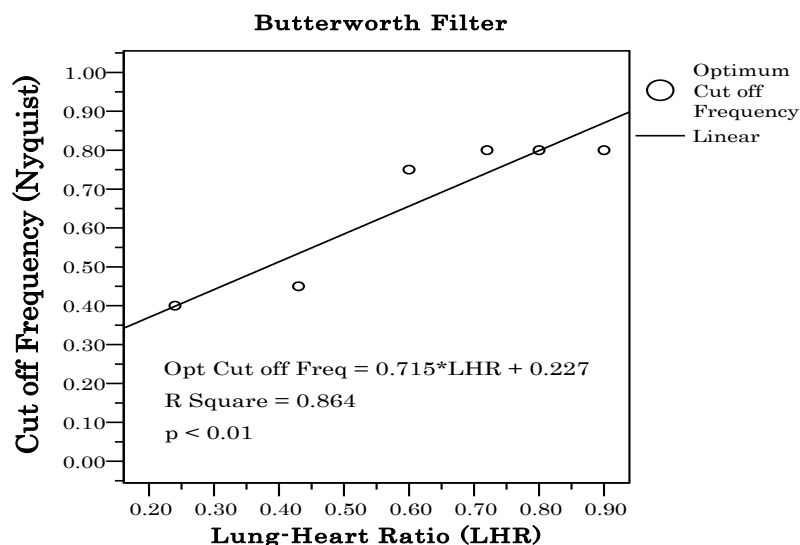


Figure 4. A linear regression model which demonstrates the variation of optimum cut off frequency determined from Butterworth filter corresponds to the change in lung-heart ratio (LHR).

DISCUSSION

^{99m}Tc concentration in myocardial wall

In the determination of the exact amount of ^{99m}Tc concentration that should be used in myocardial wall chamber for the cardiac phantom study, several conditions were taken into consideration. First, the amount of ^{99m}Tc concentration used should be related to the human myocardial uptake. However, it is difficult to determine the absolute concentration absorbed by the myocardium in patient studies due to the nonuniform uptake, varying background, and the numerous acquisition and image processing parameters that affect the final counts ⁽¹³⁾. According to Higley *et al.* (1993), at 2 hours post-injection, about 0.6% to 1.8% (at rest) and 0.6% to 1.7% (at stress) of the injected activity was taken up by the heart, which the majority of subjects studied had heart uptake exceeding 1.1%, both for rest and stress ⁽¹⁴⁾. However, this percent of uptake was based on the fraction of total counts in the heart comparing to the counts in the whole body. It did not predict the exact amount of concentration in myocardium. Previous studies have shown that different ^{99m}Tc concentrations were used in cardiac phantom SPECT which varied from 2.5 μ Ci/ml (0.093 MBq/ml) to 7.5 μ Ci/ml (0.278 MBq/ml)⁽¹⁵⁻²⁰⁾. In this study, the

amount of 4.0 μ Ci/ml (or 0.148 MBq/ml) ^{99m}Tc concentration (1000 μ Ci in 250 ml) was used for myocardial wall chamber ⁽¹⁷⁾.

Second, the amount of ^{99m}Tc concentration in myocardial wall chamber was fixed for all studies due to the bio-distribution of ^{99m}Tc-tetrofosmin in human hearts especially their retention at 2 hour post-injection. A study showed that heart uptake is rapid with good retention ⁽¹⁴⁾. From 5 minutes to 2 hours after injection, some clearance was seen from the heart, but relatively stable over time, which the heart uptake of ^{99m}Tc-tetrofosmin slightly decreased from 1.3% to 1.0% (at stress) and 1.2% to 1.0% (at rest).

^{99m}Tc concentration in cylindrical tank

Six different ^{99m}Tc concentrations were chosen for background radiation in this study. In this project the cylindrical tank is analogous to the human lung, so the determination of ^{99m}Tc concentrations for the background should consider lung uptake, bio-distribution, and heart-lung ratio. Previous works by Higley *et al.* (1993) and Taillefer (2001) indicated that the lung uptake is initially moderate (from 0.7% to 3.0% of the injected dose) and rapidly clear to almost undetectable level within 4 hours. After injection, heart-lung ratios were 3.1 ± 1.8 at 5 minutes, 4.5 ± 1.5 at 30 minutes,

and improved rapidly to 7.3 ± 4.4 at 60 minutes^(14, 21). Therefore, the ratios of $T/B = 4.0$ ($LHR = 0.4$) and $T/B = 3.3$ ($LHR = 0.6$) were chosen as the normal situations during image acquisition which is performed 15 minutes after intravenous injection and the image produced takes approximately 15-25 minutes. While the ratios of $T/B > 4.0$ and $T/B < 3.3$ were considered as extreme situations. The $T/B = 5.3$ ($LHR = 0.2$) represents a situation where the image acquisition was performed very late after the injection of ^{99m}Tc to patient, or the situation when the background clearance was extremely rapid. $T/B = 2.7$ ($LHR = 0.7$), $T/B = 2.0$ ($LHR = 0.8$), and $T/B = 1.3$ ($LHR = 0.9$) represent situation where the SPECT procedure was performed right after the injection of ^{99m}Tc to patient, or when the background uptake was extremely high.

Normal lung-heart ratio

Lung-heart ratio (LHR) is a quantitative parameter which describes the myocardial uptake relative to the lung uptake. According to Germano (2006), the preliminary data for ^{99m}Tc suggests an upper limit of normal for LHR is 0.44⁽²²⁾. It means that, two of six T/B s in phantom studies can be classified as normal situations, those are $T/B = 5.3$ and $T/B = 4.0$ which their calculated LHR are 0.24 and 0.43 respectively.

Relationship between the optimum cut off frequency and LHR

The purpose of this investigation is to reveal whether the LHR could be used as indicator in the determination of the optimum filter parameter, particularly the cut off frequency. From the data, the optimum cut off frequency determined for Butterworth filter was well correlated with LHR. This means that LHR could be used to identify optimum cut off frequency for filtering to obtain good image quality and accurate quantification.

Minoshima *et al.* (1993) has derived the relationship between the optimum cut off frequency and total counts in brain SPECT

study using Butterworth filter⁽¹¹⁾. While Ohnishi *et al.* (1997) suggested that the cut off frequency of Butterworth filter should be changed depending upon the amount of radiopharmaceutical administered, in which higher cut off frequency was needed for higher activity injected⁽¹²⁾. However, according to Minoshima *et al.* (1993), even if the same dose is administered, the accumulation of tracer injected into a target organ differs from subject to subject because of a different distribution volume which will cause different total acquisition counts in each study⁽¹¹⁾. The total counts will also change according to acquisition time in different protocol. Therefore the amount of radiopharmaceutical injected cannot be an exact indicator in determining the optimum cut off frequency. The use of total counts in determining the optimum filter is good as suggested by Minoshima *et al.* (1993) for brain SPECT study since it determine the noise level in acquired image⁽¹¹⁾. However, for myocardial SPECT study, LHR is better indicator since it represents the relative counts in heart and lung regions which closer to real situation.

CONCLUSION

In clinical practice, the application of filter parameters particularly the cut off frequency cannot be generalized in all situations. An indicator should be identified to make its application more objective. This study revealed that the LHR and optimum cut off frequency for Butterworth filter is related linearly by *Optimum cut off frequency* = $0.715 * LHR + 0.227$ ($R^2 = 0.864$, $p < 0.01$). It is suggested that the optimum cut off frequency for Butterworth filter should be determined by referring to LHR in each patient study.

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REFERENCES

1. Groch MW and Erwin WD (2000) SPECT in the year 2000: basic principles. *J Nucl Med Technol*, **28**: 233-244.
2. Laere KV, Koole M, Lemahieu L, Dierckx R (2001) Image filtering in single-photon emission computed tomography: principles and applications. *Comput Med Imaging Graph*, **25**: 127-133.
3. Germano G (2001) Technical aspect of myocardial SPECT imaging. *J Nucl Med*, **42**: 1499-1507.
4. Yusoff MNS and Zakaria A (2009) Determination of the optimum filter for qualitative and quantitative ^{99m}Tc myocardial SPECT imaging. *Iran J Radiat Res*, **6**: 173-182.
5. Germano G, Nichols KJ, Cullom SJ, Faber TL, Cooke CD (2001) Gated perfusion SPECT: technical considerations. In: *Cardiac SPECT imaging*, (DePuey EG, Garcia EV, Berman DS, eds.), Lippincott Williams & Wilkins, USA.
6. Mann A (2004) Quality control for myocardial perfusion imaging. In: *Nuclear cardiology, practical applications*, (Heller GV and Hendel RC, eds.), The MacGraw Hill Companies Inc, USA.
7. Vera P, Manrique A, Pontvianne V, Hitzel A, Koning R, Cribier A (1999) Thallium-gated SPECT in patients with major myocardial infarction: effect of filtering and zooming in comparison with equilibrium radionuclide imaging and left ventriculography. *J Nucl Med*, **40**: 513-521.
8. Wright GA, McDade M, Martin W, Hutton I (2002) Quantitative gated SPECT: the effect of reconstruction filter on calculated left ventricular ejection fractions and volumes. *Phys Med Biol*, **47**: N99-N105.
9. Manrique A, Hitzel A, Gardin I, Dacher JN, Vera P (2003) Impact of Wiener filter in determining the left ventricular volume and ejection fraction using Thallium-201 gated SPECT. *Nucl Med Commun*, **24**: 907-914.
10. Vakhtangandze T, Hall DO, Zananiri FV, Rees MR (2005) The effect of Butterworth and Metz reconstruction filters on volume and ejection fraction calculations with Tc-99m gated myocardial SPECT. *Brit J Radiol*, **78**: 733-736.
11. Minoshima S, Maruno H, Yui N, Togawa T, Kinoshita F, Kubota M, Berger KL, Uchida Y, Uno K, Arimizu N (1993) Optimization of Butterworth filter for brain SPECT imaging. *Ann Nuc Med*, **7**: 71-79.
12. Ohnishi H, Ota T, Takada M, Kida T, Noma K, Matsuo S, Masuda K, Yamamoto I, Morita R (1997) Two optimal prefilter cutoff frequencies needed for SPECT images of myocardial perfusion in a one-day protocol. *J Nucl Med Technol*, **25**: 256-260.
13. Macey DJ and Giap HB (1995) Quantitative SPECT. In: *Clinical SPECT Imaging*, (Kramer EL and Sanger JJ, eds.), Raven Press Ltd, USA.
14. Higley B, Smith FW, Smith T, Gemmell HG, Gupta PD, Gvozdanovic DV, Graham D, Hinge D, Davidson J, Lahiri A (1993) Technetium-99m-1,2-bis[2-ethoxyethyl] phosphino] ethane: human biodistribution, dosimetry and safety of a new myocardial perfusion imaging agent. *J Nucl Med*, **34**: 30-38.
15. Elkamhawy AA and Chandna H (2001) Minimum detectable defect thickness in SPECT myocardial perfusion test: phantom study with ^{99m}Tc and ^{201}Tl . *J Nucl Med Technol*, **29**: 183-188.
16. Germano G, Kiat H, Kavanagh PB, Moriel M, Mazzanti M, Su H-T, Train KfV, Berman D S (1995) Automatic quantification of ejection fraction from gated perfusion SPECT. *J Nucl Med*, **36**: 2138-2147.
17. Takavar A, Shamsipour G, Sohrabi M, Eftekhari M (2004) Determination of optimum filter in myocardial SPECT: A Phantom Study. *Iran J Radiat Res*, **1**: 205-210.
18. Verberne HJ, Dibbets-Schneider P, Spijkerboer A, Stokkel M, Eck-Smit BLFV, Sokole EB (2006) Multicenter intercomparison assessment of consistency of ventricular function from a gated cardiac SPECT phantom. *J Nucl Cardiol*, **13**: 801-810.
19. Ye J, Liang Z, Harrington DP (1994) Quantitative reconstruction for myocardial perfusion SPECT: an efficient approach by depth-dependent deconvolution and matrix rotation. *Phys Med Biol*, **39**: 1263-79.
20. Liang Z, Ye J, Cheng J, Li J, Harrington D (1998) Quantitative cardiac SPECT in three dimensions: validation by experimental phantom studies. *Phys Med Biol*, **43**: 905-920.
21. Taillefer R (2004) Radionuclide myocardial perfusion imaging protocols. In: *Nuclear Cardiology, Practical Applications*, (Heller GV and Hendel RC, eds.), The MacGraw Hill Companies Inc, USA.
22. Germano G (2006) Quantitative analysis in myocardial SPECT imaging. In: *Quantitative Analysis in Nuclear Medicine Imaging*, (Zaidi H, eds.), Springer Science & Business Media, USA.