

**THE EFFECT OF CALIBRATION FACTOR
GEOMETRIES ON THE ACCURACY OF ^{99m}Tc
SPECT/CT ACTIVITY QUANTIFICATION**

AZMIN NUR AINA BINTI AZMI

**SCHOOL OF HEALTH SCIENCES
UNIVERSITI SAINS MALAYSIA**

2025

THE EFFECT OF CALIBRATION FACTOR
GEOMETRIES ON THE ACCURACY OF $^{99\text{m}}\text{TC}$ SPECT
ACTIVITY QUANTIFICATION

by

AZMIN NUR AINA BINTI AZMI

Dissertation submitted in partial fulfilment of the
requirements for the degree of Bachelor of Medical
Radiation (Honours)

June 2025

CERTIFICATE

This is to certify that the dissertation entitled “The Effects of Calibration Factor Geometries on The Accuracy of ^{99m}Tc SPECT/CT Activity Quantification” is the bona fide record of research work done by Azmin Nur Aina Binti Azmi during the period from October 2024 to May 2025 under my supervision. I have read this dissertation and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation to be submitted in partial fulfilment for the degree of Bachelor in Medical Radiation (Honours).

Main supervisor



.....
Dr. Marianie Binti Musarudin
Lecturer
School of Health Sciences
Universiti Sains Malaysia
Health Campus
16150 Kubang Kerian
Kelantan, Malaysia

Date: 29 July 2025

Co supervisor



.....
Assoc. Prof. Dr. Mohammad Khairul
Azhar Abdul Razab
Lecturer
School of Health Sciences
Universiti Sains Malaysia
Health Campus
16150 Kubang Kerian
Kelantan, Malaysia

Date: 29 July 2025

DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated and duly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research and promotional purposes.



.....
AZMIN NUR AINA BINTI AZMI

Date: 30 July 2025

ACKNOWLEDGEMENT

In the name of Allah, the most Beneficent and most Merciful. All praises to Allah SWT and peace upon His Messenger. I am grateful to Allah SWT who has given me the grace and strength to finish this final year project with ease and smooth. I have received wonderful help from many people that I would like to record in the immense pleasure and deep gratitude.

My sincere appreciation goes to my main research supervisor, Dr. Marianie Binti Musarudin and co-supervisor, Assoc. Prof. Dr. Mohammad Khairul Azhar Abdul Razab with their guidance, helps, and precious time to guide me throughout my training period. This endeavour would not have been possible without their assistance, dedicated involvement, and constant encouragement. I also could not have undertaken this journey without my defence committee, who generously provided knowledge and expertise.

I am also grateful to my field-supervisor, Mr. Ahmad Thaifur Khaizul who helped me performing a test and analysing a data using a complicated software at Nuclear Medicine Department. I am also thankful to the Nuclear Medicine department's staff for all the considerate guidance. Furthermore, I wholeheartedly dedicate this journey to my beloved family, whose unwavering support and encouragement through every high and low have been my greatest strength.

TABLE OF CONTENTS

LIST OF TABLES	IX
LIST OF FIGURES	X
LIST OF ABBEREVIATIONS	XII
LIST OF SYMBOLS	XIII
ABSTRAK.....	XIV
ABSTRACT.....	XVI
CHAPTER 1	1
INTRODUCTION	1
1.1 Background of Study	1
1.2 Problem Statement.....	3
1.3 Objectives	4
1.3.1 General Objective	4
1.3.2 Specific Objectives	4
1.4 Significant of Study	5
CHAPTER 2	6
LITERATURE REVIEW	6
2.1 SPECT/CT Quantification	6
2.1.1 SPECT/CT Reconstruction	10
2.1.2 CT-Based Attenuation Correction.....	12
2.2 Calibration Factor	13
2.3 Partial Volume Effects (PVE).....	17
2.3.1 Recovery Coefficients.....	19

CHAPTER 3	22
MATERIALS AND METHODS	22
3.1 Materials	22
3.1.1 Discovery NM/CT 670 Pro SPECT/CT.....	22
3.1.2 NEMA 2007 / IEC 2008 Phantom	23
3.1.3 Technetium-99m (^{99m} Tc).....	24
3.1.4 Syringe and Plastic Tube.....	24
3.1.5 Petri Dish	25
3.1.6 Fillable Sphere	25
3.1.7 Well Type Ionisation Chamber Dose Calibrator	26
3.1.8 Xeleris Workstation.....	26
3.1.9 Q Metrix Software	27
3.2 Methodology	28
3.2.1 Determination of Calibration Factor.....	29
3.2.2 Phantom Preparation.....	32
3.2.3 Image Acquisition	35
3.2.3 Evaluation of Calibration Factor (CF)	36
3.2.4 Evaluation of Recovery Coefficient (RC).....	37
3.2.5 Evaluation of Quantification Accuracy.....	39
CHAPTER 4	41
RESULT AND DISCUSSION	41
4.1 Phantom Preparation.....	41
4.2 Image Reconstruction	42
4.3 Calibration Factors.....	43
4.4 Recovery Coefficient	45

4.5 SPECT/CT Quantification	47
CHAPTER 5	52
CONCLUSION.....	52
5.1 Conclusion	52
5.2 Limitation of Study	53
5.3 Recommended in Future Research	54
REFERENCES	55
APPENDICES	60
APPENDICES A - THE IMAGE RECONSTRUCTION AND SEGMENTATION ..	60
APPENDICES B – RAW DATA OF CF, RC, QUANTIFIATION ERROR	
EVALUATION	63

LIST OF TABLES

Table 2.1	Controllable and uncontrollable factors that influence the quantitative accuracy of activity concentration measurements obtained from SPECT-CT images	8-9
Table 3.1	The detail of three geometry phantom	30
Table 3.2	Summarize of activity needed during phantom preparation for three geometries	31
Table 3.3	Summarize of activity needed for TBR 5:1 and 10:1	33
Table 4.1	The pre-injection and post injection of ^{99m}Tc for geometry 1, 2, and 3	41
Table 4.2	The pre-injection and post-injection for TBR 5:1 and 10:1	42
Table 4.3	The value obtained from image reconstruction for geometry 1, 2, and 3	43
Table 4.4	The value obtained from image reconstruction of TBR 5:1 and 10:1	43
Table 4.5	The RCs calculated for different sphere diameter	46

LIST OF FIGURES

Figure 2.1	NEMA IEC image quality phantom filled with 99mTc at 10:1 contrast in three different sphere configurations reconstructed with 3 iterations and 6 subsets (upper set of images) and 20 iterations and 6 subsets (lower set of images) (Dickson et al., 2022).	10
Figure 2.2	Analyses of calibration factor for each SPECT/CT in the SET-I and SET-II study (Mehrotra et al., 2023).	15
Figure 2.3	The calibration factor and sensitivity of the SPECT based on increasing matrix size (Mohd Akmal Masud et al., 2023).	16
Figure 2.4	Demonstration of the impact of the partial volume effect for two different spatial. resolution values (7 and 18 mm FWHM) in the IEC Body Phantom. A and C are the image from PET while B and D are the images from SPECT imaging (Marquis, Willowson and Bailey, 2023).	18
Figure 2.5	A schematic overview of the generation of the dataset utilized in this study of the position dependence of RCs in ¹⁷⁷ Lu-SPECT/CT reconstructions – phantom simulations and measurements (Leube et al., 2024).	21
Figure 3.1	Discovery NM/CT670 Pro SPECT/CT	22
Figure 3.2	NEMA 2007 IEC/2008 Phantom	23
Figure 3.3	A 25-cc syringe and plastic tube	24
Figure 3.4	Petri dish used for geometry 1	25
Figure 3.5	A 5 cm fillable sphere	25
Figure 3.6	Well type ionisation chamber dose calibrator	26

Figure 3.7	Xeleris Workstation	26
Figure 3.8	The workflow chart of the study	29
Figure 3.9	The phantom configuration for CF. a) The whole phantom filled with ^{99m}Tc with no cylindrical phantom and sphere. b) The geometry 3 with a sphere attached to the cylindrical phantom in NEMA phantom.	32
Figure 3.10	The phantom preparation for TBR 5:1 and 10:1. a) ^{99m}Tc were diluted in 50 ml water. b) The diluted ^{99m}Tc were injected into each spheres using the syringes and plastic tube. c) ^{99m}Tc were injected to the background before the scanning.	34
Figure 3.11	Measurement of distance between collimator and petri dish	35
Figure 3.12	The positioning of all phantom during imaging	36
Figure 3.13	The coronal, sagittal, and transaxial image of the phantom	36
Figure 3.14	The segmentation and OSEM reconstruction. a) The image of geometry 2. b) The image of geometry 3.	37
Figure 3.15	The segmented and contoured of all spheres in TBR 5:1	38
Figure 3.16	The segmented and contoured of all spheres in TBR 10:1	39
Figure 4.1	The graph of RCs of each geometry	45
Figure 4.2	The quantification error for geometry 1 with and without PVC	48
Figure 4.3	The quantification error for geometry 2 with and without PVC	48
Figure 4.4	The quantification error for geometry 3 with and without geometry	49

LIST OF ABBEREVIATIONS

AC	Activity concentration
CF	Calibration factor
cps	Count per second
DICOM	Digital Imaging and Communications in Medicine
FOV	Field of view
LEHR	Low Energy High Resolution
ML-EM	Maximum Likelihood Expectation Maximisation
NEMA	National Electrical Manufacturers Association
PACS	Picture Archiving and Communication System
PET	Positron Emission Tomography
PVC	Partial volume correction
PVE	Partial volume effect
RC	Recovery coefficient
SPECT	Single Photon Emission Computed Tomography
SUV	Standard Uptake Value
TBR	Tumor-to-background ratio
VOI	Volume of interest
3-D OSEM	3-Dimension Ordered Subset Optimisation Maximisation
^{131}I	Iodine-131
^{177}Lu	Lutetium-177
$^{99\text{m}}\text{Tc}$	Technetium-99m

LIST OF SYMBOLS

$^{\circ}$	Degree
cc	Cubic-centimeter
λ	Decay constant
ml	Millilitre
MBq	Megabacquerel
mCi	Millicurie

ABSTRAK

Pengimejan SPECT kuantitatif semakin penting dalam diagnosis dan pemantauan penyakit. Penentuan kuantiti mutlak taburan radioisotop penjejak yang tepat adalah penting untuk terapi radionuklid peribadi berasaskan dosimetri. Salah satu komponen utama dalam ketepatan kuantifikasi SPECT/CT ialah faktor penentukuran (CF). Kajian ini bertujuan untuk menilai kesan CF dan pekali pemulihan (RC) yang diperoleh daripada geometri penentukuran yang berbeza terhadap ketepatan kuantifikasi SPECT/CT. Tiga jenis geometri fantom telah dikaji: cawan petri dipenuhi dengan ^{99m}Tc (Geometri 1), seluruh badan NEMA fantom dipenuhi dengan ^{99m}Tc (Geometri 2), dan sfera yang diisi dengan ^{99m}Tc yang dilekatkan pada silinder dalam fantom NEMA (Geometri 3). CF dikira bagi setiap geometri, manakala RC diperoleh bagi enam sfera dengan pelbagai diameter (1.0 hingga 3.7 cm). Ralat kuantifikasi dianalisis sebelum dan selepas penggunaan pembetulan isipadu separa (PVC).

Geometri 1 menghasilkan CF tertinggi, terutamanya disebabkan oleh kepekatan aktiviti yang berbeza digunakan. Ini menyebabkan RC yang lebih rendah dan ralat kuantifikasi yang lebih besar, yang sebahagian besarnya disebabkan oleh kesan isipadu separa (PVE) yang ketara. Oleh itu, hasil daripada Geometri 1 tidak boleh dibandingkan secara langsung dengan geometri lain kerana perbezaan dalam kepekatan aktiviti. Geometri 2 menunjukkan nilai RC yang paling tepat dan konsisten, mencecah setinggi 1.03, menandakan syarat ideal untuk kuantifikasi. Geometri 3 menunjukkan prestasi sederhana, walaupun terdapat kesan tumpahan masuk diperhatikan pada saiz sfera yang lebih kecil. PVC meningkatkan ketepatan kuantifikasi dengan ketara bagi sfera kecil dalam semua geometri. Walau bagaimanapun, ralat lebihan anggaran berlaku bagi sfera bersaiz besar, terutamanya dalam Geometri 1 dan 3. Kesimpulannya, pemilihan geometri penentukuran memberi kesan yang ketara terhadap ketepatan kuantitatif dalam

pengimejan SPECT/CT. Kajian ini menekankan pemilihan strategi penentuan yang sesuai serta pembetulan khas geometri bagi meningkatkan ketepatan klinikal dalam terapi radionuklid.

ABSTRACT

Quantitative SPECT imaging has become increasingly important in disease diagnosis and monitoring. Achieving accurate absolute quantification of radiotracer distribution is essential for dosimetry-based personalized radionuclide therapy. A key determinant of SPECT/CT quantification accuracy is the calibration factor (CF). This study aimed to evaluate the impact of CFs and recovery coefficients (RCs) derived from different calibration geometries on SPECT/CT quantification accuracy. Three phantom geometries were assessed: a petri dish filled with ^{99m}Tc (Geometry 1), a whole body NEMA phantom filled with ^{99m}Tc (Geometry 2), and a sphere filled with ^{99m}Tc attached to the cylindrical in NEMA phantom (Geometry 3). CFs were calculated for each geometry, and RCs were obtained for six spheres with varied diameters (1.0 to 3.7 cm). Quantification errors were analysed both before and after the application of partial volume correction (PVC).

Geometry 1 yielded the highest CF, primarily due to the use of a different activity concentration. This resulted in lower RCs and greater quantification errors, largely attributable to pronounced PVE. Consequently, the results from Geometry 1 are not directly comparable to those of the other geometries due to the disparity in activity concentration. Geometry 2 demonstrated the most accurate and consistent RCs reaching values as high as 1.03 indicating optimal conditions for quantification. Geometry 3 yielded moderate performance, although spill-in effects were observed at smaller sphere sizes. PVC substantially improved quantification for small spheres across all geometries. However, overestimation errors emerged in larger volumes, especially in Geometries 1 and 3. In conclusion, the choice of calibration geometry has a significant influence on the quantitative accuracy of SPECT/CT imaging. These findings highlight the importance of

selecting appropriate calibration strategies and applying geometry-specific corrections to improve clinical accuracy in radionuclide therapy.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Single photon emission computed tomography (SPECT/CT) is one of the modalities in nuclear medicine that used for diagnostic purpose. It used a radioactive substance to create 3-dimensional image. It used gamma ray to visualize the perfusion and functionality of the structures inside of the body. Even though positron emission tomography (PET) is the standard technique for absolute quantification in emission tomography. Recently, SPECT/CT has been used mostly for qualitative and semiquantitative clinical investigations; by consequence the signal at the pixel level (in units of counts) is proportional to the number of measured events (Gnesin et al., 2016). Both SPECT/CT and PET have its own benefits as in terms of quantitative value and absolute radioactivity quantification. Hence, the internal dosimetry is the most important fields of SPECT/CT application. Accurate absolute quantification of radiotracer distribution is crucial for the purpose of dosimetry customised radionuclide therapy. It may also enhance treatment follow-up, toxicity effect prevention, and therapy response prediction. Quantitative study of SPECT/CT has been increasingly used in diagnosis and disease monitoring. There has been continuous improvement of SPECT/CT as a molecular imaging modality to produce qualitative as well as accurate quantitative images and yet further to normalised uptake using the standard uptake value (SUV) (Kaur, 2025).

The primary aim for quantitative SPECT/CT is to produce a tomographic image with voxel values representing activity concentration (Dickson et al., 2022). Accurate dosimetry is strongly depended on SPECT/CT quantification. Furthermore, the SPECT/CT quantification accuracy also depend on few factors, including the necessary

use of a collimator, the varying detector trajectory, and the need for more complicated scatter correction and attenuation correction (Peters et al., 2019). Hence, to ensure the improvement of accuracy of the quantified activity, attempts are made to correct those factors. One of the statistical iterative techniques that is based on one of the reconstruction algorithms is used in emission tomography. Based on RIMD Pamphlet No.23 (Dewaraja et al., 2012), the requirement of SPECT/CT quantification for dosimetry are described. The quantification accuracy for Technetium 99m (^{99m}Tc) is $\pm 10\%$ of the known concentration of the radiotracer in vivo (Bailey & Willowson, 2013). It is important to obtain calibration images using the same values utilised for patient studies since the calibration factor depends on radionuclide image, geometry, and imaging system parameters.

Furthermore, the main component of the accuracy of SPECT/CT quantification is the calibration factor (CF). Errors in this CF will lead to systematic bias in quantitative values derived from the images (Dickson et al., 2022). The CF can be divided into two components: (1) the sensitivity of the collimator and detector for the specific collimator, system and radionuclide used for the imaging and (2) protocol specific factors including residual errors resulting from the image processing and compensation methods and scaling factors sometimes used when images are stored (Quantification | IAEA, 2021). From the study of Gnesin et al., (2016), the construction parameters influence recovery coefficient (RC) and thus standardized uptake value (SUV), and optimization is recommended according to clinical requirements which resulted in SPECT/CT quantification can improve monitoring clinical processes and their evolution with therapy. J. Wevrett et al., (2017) has demonstrated that it is feasible to use a combination of simplistic phantom geometries to standardise the calibration of gamma cameras for quantitative imaging (J. Wevrett et al., 2017). Moreover, RCs for partial volume

correction (PVC) can easily be determined in phantom studies where true activity and object size can be measured (Ramonaheng, van Staden and du Raan, 2021). Hence, this study focused on assessing how each CF and their corresponding RCs affecting the accuracy of ^{99m}Tc SPECT/CT image quantification using different phantom geometries.

1.2 Problem Statement

In many SPECT/CT system, the reconstructed SPECTS images are routinely provided in units of counts. Therefore, system sensitivity or CF must be applied to obtain SPECT/CT reconstructed images in units of radioactive concentration. This value is critical for accurate dosimetry and treatment planning in nuclear medicine. Various CFs geometries have been proposed to convert SPECT data into units of activity concentration (Keamogetswe Ramonaheng et al., 2021). However, a standardized CF geometry has yet to be established. According to Nadège Anizan et al., (2014), the study focused on evaluating the factors affecting the repeatability of a CF measured using a planar image of an in-air calibration source. The authors highlighted the importance of accurate and precise preparation and measurement of the calibration source activity. Another study by M. D'Arienzo et al., (2016), assessed the gamma camera CF using four different reference geometries. The CFs were obtained from a point source in air, a 16 mL Jaszczak sphere in air, a 16 mL Jaszczak sphere surrounded by non-radioactive water and a 20 cm diameter cylinder filled with water uniformly mixed with radioactive $^{177}\text{LuCl}_3$. From the study, all CF are corrected for the major effects which are scatter and attenuation that contribute to image degradation and hinder the absolute quantification. However, it is generally accepted that the CF with a source geometry that incorporates photon attenuation and scatter properties in the acquisition (Keamogetswe Ramonaheng et al., 2021).

The lack of a consensus on a standard and optimal CF geometry creates inconsistencies across clinical sites, impacting the comparability and reproducibility of

quantitative SPECT/CT measurements. Superior quantification has been reported for some CF geometries over the other due to several factors, including the high sensitivity to the selected volume of interest (VOI) size for the CF obtained with a point source in air, underestimation of triple energy window (TEW) scatter approximation and attenuation correction for the CF obtained using sphere in non-radioactive background, activity calibration and characterisation of the system. In addition to that, the quantification accuracy also strongly dependent on the accuracy of the reconstructed image. Low spatial resolution image and image noise are the effect of the inaccuracies of SPECT/CT quantification. This variability of CF can lead to inconsistencies in dosimetry calculations, affecting treatment planning and potentially impacting patient outcomes, as it may lead to under- or over-estimation of the actual activity concentration. Inaccuracies in absolute quantification are likely to lead to decreased effectiveness or a higher frequency of unfavourable side effects.

The optimisation process of quantitative SPECT/CT must evaluate the influence of the controllable variables on the accuracy and reproducibility of image derived measurements (Dickson et al., 2022). It also has the potential to improve the monitoring medical process and the evaluation with the therapy. The study aims to reinforces the need to standardised the CF in purpose of SPECT quantification accuracy.

1.3 Objectives

1.3.1 General Objective

To investigate the impact of phantom geometries on calibration factors and ^{99m}Tc SPECT quantification accuracy.

1.3.2 Specific Objectives

- i. To determine the CFs using three different phantom geometries.

- ii. To assess the accuracy of activity quantification based on each CF geometries by calculating the recovery coefficients.
- iii. To compare the quantified activity value with and without the application of partial volume correction (PVC).

1.4 Significant of Study

The implication of this study is to validate the absolute quantification of SPECT/CT using ^{99m}Tc . This validation is particularly meaningful for nuclear medicine applications such as internal dosimetry, where precise measurement of radiotracer distribution is essential for personalized treatment planning in therapies like radionuclide therapy. The method used three geometries to obtain the CFs are to creates the consistencies across clinical sites, impacting the comparability and reproducibility of quantitative SPECT/CT measurements. Due to there is no standardised CF established. Assessing different CFs geometry might improve the accuracy of absolute SPECT/CT quantification. Ultimately, this study supports the broader integration of quantitative SPECT/CT in nuclear medicine, positioning it as a valuable alternative and paving the way for more precise diagnostics and treatment monitoring in patient care.

CHAPTER 2

LITERATURE REVIEW

2.1 SPECT/CT Quantification

Producing a tomographic image with voxel values that represent activity concentration is the main goal of quantitative SPECT/CT. The use of absolute quantification in SPECT/CT has been rapidly increasing in the quantitative imaging. The past two decades have seen the continuous improvement of SPECT/CT as a molecular imaging modality to a point where it can produce accurate quantitative images (Schepper et al., 2021). Thus, quantitative SPECT/CT may enhance clinical outcomes with direct applications in other fields like evaluating the course of a disease, determining coronary flow reserve, and imaging the density and occupancy of receptors in the brain using neurotransmitters. The members of The European Association of Nuclear Medicine (EANM) had published a practices guideline for quantitative SPECT/CT on 2022. The guidelines act as an instruction that will helps practitioner and scientist perform high-quality quantitative SPECT/CT and will provide a framework for the continuing development of quantitative SPECT/CT as an established modality (Dickson et al., 2022). The information in the guidelines include the procedural requirements that must be fulfilled in order to achieve and execute quantitative measurements for SPECT/CT imaging. They also list clinical applications where the use of SPECT/CT imaging has already proven successful.

Based on Peters et al., (2019) study investigate about the comparison of absolute quantification for state-of-the-art SPECT/CT systems from different vendors at different imaging centres for ^{99m}Tc . This study used different reconstructed algorithm that are available for quantification comparison. The variability of RC between systems increased

in larger phantom volumes. Furthermore, smaller sphere diameters showed lower quantitative accuracy (lower RC values) indicating that reliable quantification of small volumes (< 10 ml) in larger (patient) volumes is more challenging (Peters et al., 2019). Variation between centres is mainly caused by the use of different reconstruction algorithms or setting. Furthermore, the patient-specific factors such as high patient volume (BMI) may impact quantification accuracy particularly for small lesions. The study suggests that normal to moderately elevated BMIs do not significantly affect results. However, there is study that investigate SPECT/CT quantification for different BMI using larger phantom. This study examines the quantitative accuracy of several SPECT/CT systems, thus became a significant step towards standardising absolute SPECT/CT quantification.

SPECT/CT absolute quantification depends on a lot of factors either controllable and non-controllable. Dickson et al., (2022) suggest some technical factors that influence the absolute quantification. It will influence the accuracy in terms of positive bias which is an overestimation of activity concentration or negative bias which is an underestimation of activity concentration. Based on table 2.1, some technical factors will influence these negative and positive bias such as acquisition time, SPECT/CT orbit radius, and post-reconstruction smoothing filter are the controllable factors that result in positive bias due to image noise. Furthermore, collimator, matrix size, and number of updates (product of iterations and subsets) for iterative reconstruction will influence the accuracy in terms controllable factors in negative bias (Dickson et al., 2022). Mostly happened due to degrading of spatial resolution. Dead-time, lesion or organ size and shape, organ-to-background contrast, organ location, and patient movement are the non-controllable factors that did influence the SPECT/CT quantification accuracy. The optimisation process of quantitative SPECT/CT must evaluate the influence of the controllable

variables on the accuracy and reproducibility of image-derived measurements (Dickson et al., 2022). Additionally, the parameters should be selected in a way that minimises the impact of the uncontrollable factors.

Table 2.1: Controllable and uncontrollable factors that influence the quantitative accuracy of activity concentration measurements obtained from SPECT-CT images

Factors	Controllable?	Impact of quantitative accuracy
Administered activity	Sometimes	• For SUV_{max} and other regions based upon threshold of SPECT voxel values, positive bias can occur due to changes in noise level • Note that geometric regions, manually delineated on whole organs or lesions where all encompassed SPECT voxel values are averaged, are less susceptible to variations in image noise levels • It should be noted that for diagnostic applications, the administered activity is defined locally while, for therapeutic applications, it is likely to be either a fixed activity or defined by the planned therapy absorbed dose for the patient
Acquisition time	Yes	• Positive bias from image noise—see comments above regarding administered activity
Collimator	Yes	• Negative bias due to degrading spatial resolution

Matrix size	Yes	- Negative bias due to changes in spatial sampling - Positive bias due to changes in noise
SPECT orbit radius	Yes	Negative bias due to degrading spatial resolution for larger radii
Number of updates (product of iterations and subsets) for iterative reconstruction	Yes	- Negative bias due to under-converged image - Positive bias due to image noise
Post-reconstruction smoothing filter	Yes	- Negative bias due to additional image blurring - Positive bias due to control of image noise
Dead-time	No	Negative bias due to dead-time effects at very high count-rate levels
Lesion/ organ size and shape	No	Negative bias due to degrading spatial resolution for small volumes
Organ-to-background contrast	No	Variable due to changes in spill-over from surrounding activity
Organ location	No	Negative bias due to increasing distance from the detector
Patient movement	No	Negative bias due to increasing image blurring

2.1.1 SPECT/CT Reconstruction

Reconstruction is an important note to produce accurate SPECT/CT quantification. Based on International Atomic Energy Association (IAEA) Human Health Reports No. 9, absolute and better relative quantification can be obtained with iterative reconstruction using compensation for the image degrading 28 effects (International Atomic Energy Agency, 2014). Emission image reconstruction using the maximum likelihood expectation maximization (ML-EM) algorithm usually does not make assumptions about how the image should look beforehand (Kangasmaa, Constable and Sohlberg, 2021). Ordered Subset Optimisation-Maximisation (OS-EM) is a common type of reconstruction algorithm that is widely used nowadays. Mostly modern SPECT/CT system had this reconstruction algorithm available. Using a distinct subset of the projections for each update, the OS-EM algorithm modifies the estimate several times per iteration. The example from figure 2.1 illustrates that, with a sufficient number of updates, the variability in activity concentration recovery can be effectively aligned across different sphere configurations.

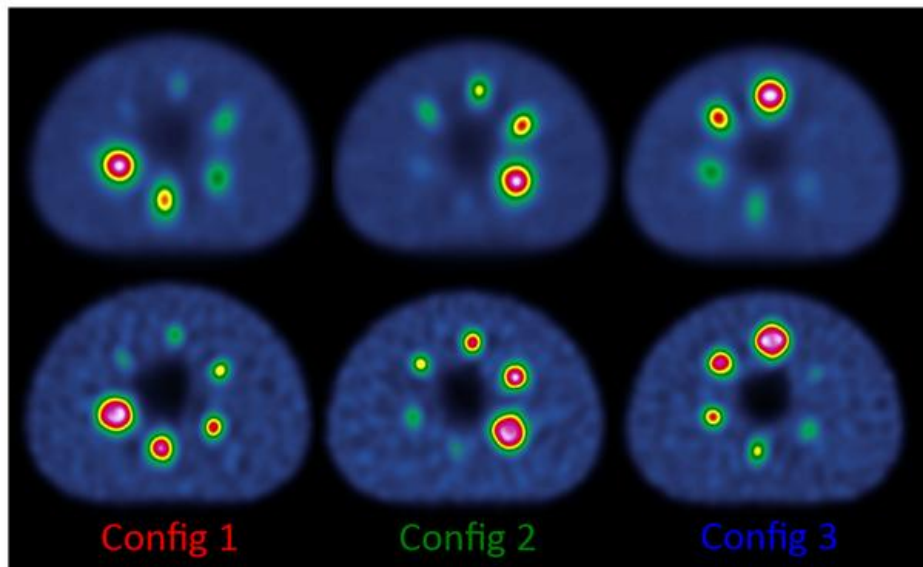


Figure 2.1: NEMA IEC image quality phantom filled with ^{99m}Tc at 10:1 contrast in three different sphere configurations reconstructed with 3 iterations and 6 subsets (upper set of images) and 20 iterations and 6 subsets (lower set of images) (Dickson et al., 2022).

A study by Kangasmaa, Constable and Sohlberg, (2021) investigate about the use of two different type of reconstruction algorithm in the quantitative bone SPECT/CT. Bayesian reconstruction methods and OS-EM algorithm was chose as a comparison. We compared Bayesian reconstruction methods utilizing anatomical prior information from CT (AMAP-S and AMAP-R) to Bayesian reconstruction method without anatomical information and OSEM (Kangasmaa, Constable and Sohlberg, 2021). The primary use of Bayesian reconstruction has been considered as a noise reduction method. However post-filtered OSEM-based reconstruction has been favoured over Bayesian reconstruction, which has been criticised for seeming "patchy". The research resulted in more advantage in using Bayesian algorithms utilizing anatomical information AMAP-S and AMAP-R, compared to OSEM reconstruction method. In terms of accurate result in lesion size and shape, highest lesion standardized uptake value (SUVs), better lesion detection ability, and quantitative accuracy.

Kupitz et al., (2021) investigate the imaging protocols for quantitative and qualitative ^{99m}Tc SPECT/CT to obtain the optimize quantitative protocols. The research used two acquisitions protocols which are clinical protocol and a NEMA-oriented scan protocol and the image is reconstructed using an iterative ordered-subset expectation maximization algorithm (2D OSEM) for image reconstruction with four different parametrizations. The research explained that higher iterations improve accuracy but increase noise. For background regions, even minimal iterations are enough, as they converge quickly. Compared to scatter weighting factor (SCF) or the total number of iterations, the acquisition methodology (number of projections and time of each projection) showed a slight influence on the quantitative findings for the spheres. The best quantitative results were achieved with the object-specific SCF and a reconstruction set with 24 iterations and 10 subsets without postfiltering and the best qualitative results were

achieved with SCF with 2 iterations and 10 subsets and with postfiltering (Kupitz et al., 2021).

2.1.2 CT-Based Attenuation Correction

Image quality is reduced as a result of photon attenuation and scattering in the body, which also affects activity quantification and the relative distribution of perfusion. Attenuation correction is important in quantitative SPECT/CT imaging to improve the accuracy of SPECT/CT quantification. The CT images should be converted to a map of attenuation coefficients for the appropriate radionuclide energy and incorporated into the iterative reconstruction process (Dickson et al., 2022). Based on Luca Camoni et al., (2020), the CT scans that are for attenuation correction only (with no intended diagnostic use) should be performed at the lowest possible settings. The study suggested the using of tube voltage (70 kV -140 kV) must be adjusted according to the patient size, a low tube current (10–20 mA) together with a relatively high pitch was recommended, the slice collimation and reconstructed slice thickness should be the approximate slice thickness of SPECT or PET, a slower rotation speed (at least 1/s or less) increases the effective dose was used, and the field of view (FOV) of the protocol for attenuation correction should be the maximum diameter of the scanner (Luca Camoni et al., 2020).

Tatsuya Tsuchitani et al., (2023) investigated the quantitative values obtained when applying CT-based attenuation correction and not applying the correction using a clinical finding in patients who underwent a SPECT/CT examination of the jawbone. However, this study includes a becquerel calibration factor value in assessing the value when not applying the attenuation correction. The results were divided into two group which are no correction group and with correction group. In the no correction group, the becquerel calibration factor was underestimated in the deep region, as the deeper tissues suffer more from attenuation and fewer photons are detected. But in the superficial region,

the becquerel calibration factor was overestimated since the attenuation has less effect near the surface. Thus, without attenuation correction, the no correction group reported higher SUVs than the with correction group. This is because the overestimated of becquerel calibration factor inflated the SUV for superficial regions. In contrast, when becquerel calibration factor was obtained with the syringe method, there was no significant difference between the with correction group and no correction groups for either SUV_{max} or SUV_{peak} values (Tatsuya Tsuchitani et al., 2023). From this study, it suggested that when using phantom-based becquerel calibration factors, attenuation correction should be applied to reduce quantification bias. If the attenuation correction is not available, a syringe-based becquerel calibration factors are preferable for better accuracy, especially for superficial uptake measurements.

2.2 Calibration Factor

Calibration factor (CF) is a value to convert from counts to activity concentration to analyse the SPECT/CT quantification. Based on International Atomic Energy Agency, 2014, calibration factor can be divided into two components which are sensitivity of collimator and detector, and a protocol specific factors. However, CF in terms of sensitivity is commonly used due to easily measured and can be calibrated frequently. The gamma camera CF depends on the type of collimator, camera spatial resolution, camera sensitivity, peak and scatter acquisition windows and reconstruction algorithms (Raskin et al., 2023). The precision of the CF, relating the reconstructed counts from the scanner to activity measured in a radioactive calibrator which the readings should be traceable to a primary reference, is undoubtedly a key component of quantitative SPECT/CT. Errors in this CF will lead to systematic bias in quantitative values derived from the images (Dickson et al., 2022).

According to Mehrotra et al., (2023), a study of CF measured using same acquisition protocol and parameter for SPECT/CT quantitative scanned at three points similar to the patient was conducted. This study used two set of phantoms with different parameters set in terms of activity, weight, and volume of the phantom. In SET-I study; 370 MBq and 6.09 L volume were used and in SET-II study, 399.23 MBq, 6.06 L volume were used. The study showed a constant CF measurement at three point similar for a week. However, the changes of protocol caused a decrease of CF due to the activity was not uniformly distributed in the phantom. The findings of this study clearly imply that the CF is also dependent on the image acquisition methodology and should be constant across all time points for both patient and phantom image acquisitions. A precise activity measurement and meticulous preparation to ensure uniform activity distribution within the phantom are critical to enhancing the accuracy of the calibration factor in quantitative activity assessment. It is recommended to acquire the reconstruction images and apply corrections for degrading factors in the same way as it is performed in the patient studies at different time points (Mehrotra et al., 2023). Figure 2.2 represent the comparison of CFs obtained from different experiments (SET-I study and SET-II study) with the same phantom and SPECT/CT. The authors conclude the SET-II study confirm that consistency in acquisition protocol and uniform radiotracer distribution are critical for ensuring stable and reproducible CF measurements across different time points and SPECT/CT systems.

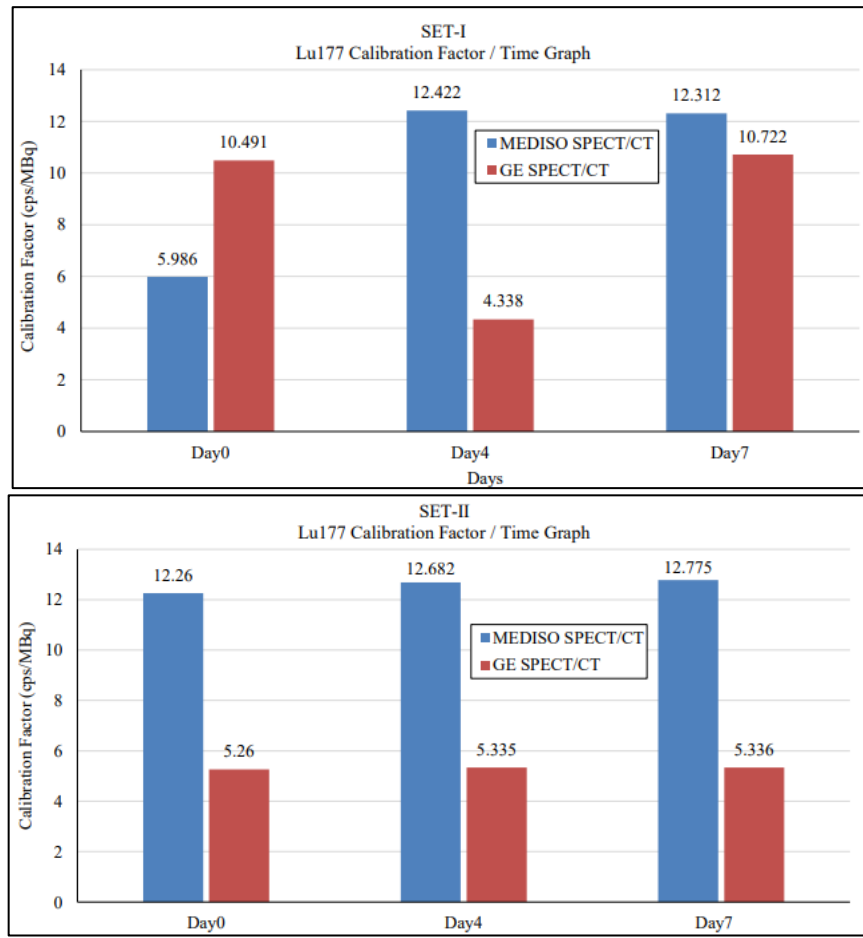


Figure 2.2: Analyses of calibration factor for each SPECT/CT in the SET-I and SET-II study (Mehrotra et al., 2023).

Another study by Mohd Akmal Masud et al., (2023) investigated the effect of absolute CF of different dimensions in quantitative SPECT/CT. The study stated that there is no significant variation in regards of CF calculation observed across different count rates (cps) within each sphere. However, sensitivity exhibited an increasing trend with larger matrix sizes. This indicates that smaller pixel sizes enhance the sensitivity of count collection per pixel, resulting in higher pixel count values. The CF does not change because the counts collected in the Digital Imaging and Communications in Medicine (DICOM) information are the same detector (Mohd Akmal Masud et al., 2023). Nevertheless, this study used Iodine-131 (^{131}I) for the scanning, the results of the investigation show that ^{131}I still required the recovery coefficient to achieve approximately actual activity in the lesion. It is due to energy level of $^{99\text{m}}\text{Tc}$ which is 140

keV compared to ^{131}I , 364 keV where $^{99\text{m}}\text{Tc}$ is more sensitive than ^{131}I . Remarkably, the studied SPECT/CT detector is much more sensitive to gamma rays ranging between 120 and 140 keV (Mohd Akmal Masud et al., 2023). Figure 2.3 present the bar chart of CF and sensitivity of SPECT. The study resulted that there were no significant changes in the ^{131}I CF for different cps in every sphere.

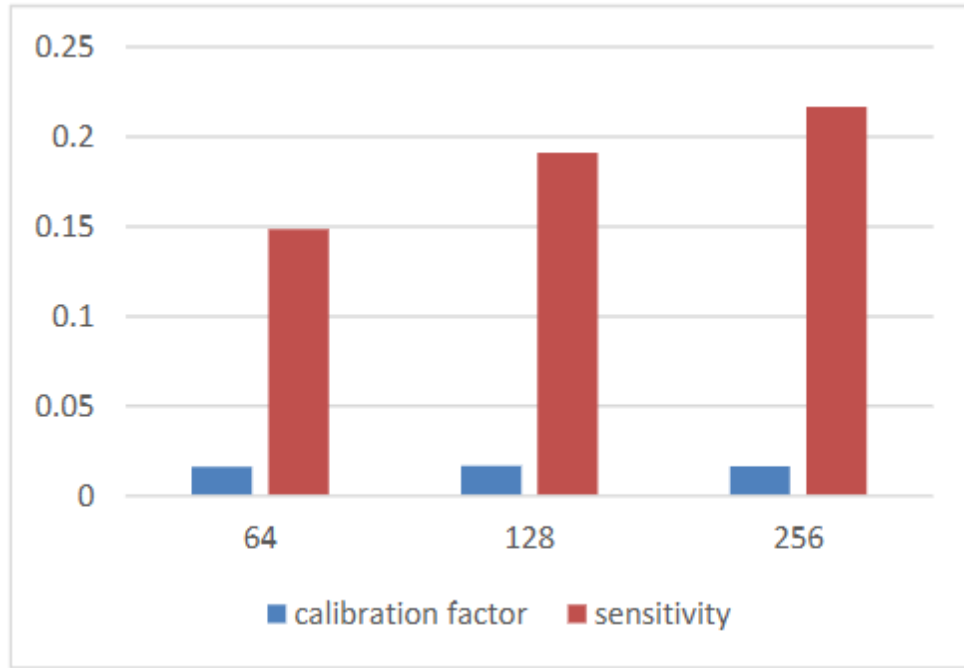


Figure 2.3: The calibration factor and sensitivity of the SPECT based on increasing matrix size (Mohd Akmal Masud et al., 2023).

A study was proposed to validate a new calibration method using the lesion-to-background counts/voxel ratio and the lesion volume as varying parameters for determination of the camera CFs (Raskin et al., 2023). The CFs was calculated using conventional method and sphere-to-background counts/voxel ratio (SBVR) method. Small VOIs are more prone to background effects and partial volume effects (PVE), leading to higher quantification errors using the conventional method. SBVR correction method significantly reduced the quantification errors, achieving <10% error for small spheres even at shorter acquisition times. As a result, the SBVR method offers a simple, accurate, and practical solution for improving SPECT/CT quantification. It effectively

compensates for background and PVE, particularly in small lesions and non-uniform backgrounds. Nevertheless, the authors proposed a few limitations regarding the study which are only the three largest spheres were used in the calibration process, lack of larger spheres in the calibration phantom, and the influence of the geometry on CF values were neglect (Raskin et al., 2023).

2.3 Partial Volume Effects (PVE)

PVE in SPECT/CT is a phenomenon where the limited spatial resolution of the imaging system leads to an apparent underestimation of activity concentration in small or low-contrast objects. PVE causes significant underestimation of activity in small lesions and overestimation in surrounding tissues, thereby affecting the accuracy of quantitative SPECT/CT imaging, especially in clinical applications such as tumour dosimetry and radionuclide therapy. The poor spatial resolution results in a “blurring” of the object below a certain size relative to resolution volume known as the PVE (Marquis, Willowson and Bailey, 2023). Based on International Commission on Radiation Unit (ICRU) Reports 96. and IAEA Human Health Reports No. 9, PVEs can also affect larger objects because of count spill-in and spill-out at the edges of the object. Many studies propose that collimator-detector-response could reduce the PVE. However, this way did not result in fully resolution recovery. PVC methods have been proposed by many researchers to improve the SPECT/CT quantification accuracy.

According to Marquis, Willowson and Bailey, (2023), a study was proposed to investigate the impact of the PVE on clinical imaging in PET and SPECT/CT with current state-of-the-art instrumentation and the implications that this has for radionuclide dosimetry estimates. The PVE’s visual impact for the two distinct spatial resolution values under two different conditions where the radionuclide concentration in the spheres is kept

constant in the first condition, while it is varied in the second condition to provide a constant reconstructed quantitative response. The impact of PVE in SPECT/CT showed poorer resolution while PET showed higher resolution resulting in minor effect. At such poor resolution, accurate quantification of radiopharmaceutical uptake is only possible in large organs, not in smaller tumors or tissues, unless additional image corrections are applied. Figure 2.4 showed the visual impact of the PVE for the two different spatial resolution values under two different conditions: in the first condition the concentration of the radionuclide in the spheres is held constant, while in the second condition the concentration of the radionuclide in the spheres is varied to give a constant reconstructed quantitative response, equivalent to $SUV_{max}=10$ (Marquis, Willowson and Bailey, 2023).

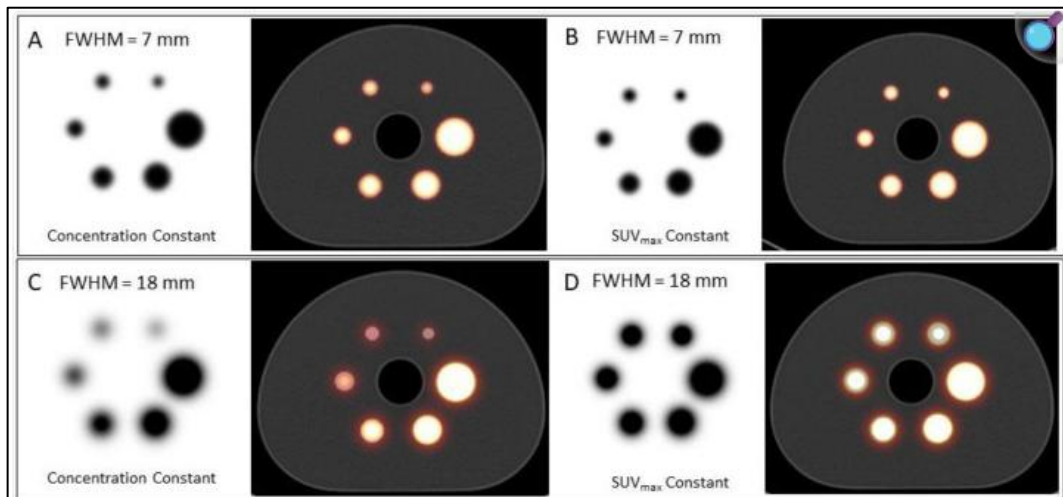


Figure 2.4: Demonstration of the impact of the partial volume effect for two different spatial resolution values (7 and 18 mm FWHM) in the IEC Body Phantom. A and C are the image from PET while B and D are the images from SPECT imaging (Marquis, Willowson and Bailey, 2023).

While whole organ absorbed dosimetry estimates are, in general, relatively unaffected by the PVE due to the organ sizes usually being far greater than the spatial resolution value, smaller lesions and areas of abnormality are significantly impacted (Marquis, Willowson and Bailey, 2023). The PVE severely limits the accuracy of radiopharmaceutical uptake quantification in small lesions when using current SPECT/CT systems where it poses a major challenge for accurate dosimetry in

radionuclide therapy, particularly when quantifying activity in small tumors. Improved spatial resolution, correction techniques, or recovery coefficient models are necessary to ensure meaningful and reliable dose estimates.

2.3.1 Recovery Coefficients

The RCs is a key metric used in quantitative SPECT/CT imaging to correct for PVE. Due to limited spatial resolution, small or low-contrast structures in SPECT/CT are subject to underestimation of radioactivity. RCs are employed to correct the measured activity by relating it to the true activity concentration, typically as a function of object size or volume. One of the most practical and widely used PVCs in radionuclide therapy dosimetry applications is based on using volume-dependent RCs from phantom measurements to correct the patient's mean target activity for PVEs (Sgouros et al., 2021). The ratio between the apparent activity concentrations to the true activity concentration is known as recovery coefficient (Mohd Yusof et al., 2020).

Based on Keamogetswe Ramonaheng, Staden and Hanlie du Raan, (2021) study, they aimed to investigate the effect of two CFs to the RC and SPECT/CT quantification accuracy. The CF geometries investigated were a radioactive-sphere surrounded by non-radioactive water and a cylindrical phantom uniformly filled with radioactive water. Two RCs were generated from sphere and cylindrical phantom. Similar trends in quantification errors were seen for all phantoms using both CF-RC combinations. For the small sphere, applying PVC caused a slight overestimation of activity due to mismatch from the actual RC and fitted RC function. Without PVC, the sphere-CF produced smaller errors for spheres than the cylinder-CF, likely due to better geometric match between the CF and the object. Quantification accuracy varied based on whether the sphere-CF or cylinder-CF was used, depending on the phantom geometry. Therefore, it is important to note both the geometry and the delineation method used for the CF, RCs, and object of interest

(Keamogetswe Ramonaheng, Staden and Hanlie du Raan, 2021). As the result, applying the RCs indicates a PVC reduced the quantification errors.

Steffie M. B. et al., (2020) investigated the quantitative accuracy and inter-system variability of RCs that were determined using phantom experiments and the effects of lesion volume and reconstruction algorithm on RC. The smallest sphere had poor visibility and unreliable recovery coefficient values due to low contrast and PVE. Larger spheres also showed lower RCs in some systems, especially with vendor-neutral reconstruction due to Gibbs artifacts affecting the delineation. Thus, reducing the Gibbs artifacts may improve the quantification accuracy. Furthermore, by using standard reconstruction as recommended by the vendor, the RC increase as the sphere diameter increase. It is most likely the outcome of the reconstruction of resolution recovery algorithm. However, the RCs rapidly decrease as the sphere diameter decrease. This study's purpose to compare the RCs between the system. Hence, the results could be used to work towards a normalization between centers and systems (Steffie M. B. et al., 2020). This study serves as an important step towards a vendor independent standard for absolute quantification in SPECT/CT.

A study by Leube et al., (2024) investigate the impact of sphere positioning in the NEMA SPECT/CT Phantom on RCs determined by ^{177}Lu SPECT/CT. A set of six RCs was determined for both configurations and both SPECT/CT reconstructions. The RC is defined as the SPECT-based total activity in the sphere divided by the nominal activity within the sphere (Leube et al., 2024). From the study, for the reconstruction without resolution modelling, highest RCs occurred when spheres were located at the top of the phantom and lowest RC occurred for sphere laterally at the bottom. However, for the reconstruction with resolution modelling, the result showed fixed positions for highest and lowest RC for spheres where highest recovery coefficient occurred at the centrally

position spheres while lowest RC occurred at the spheres at the top. Smallest RCs tended to appear when large spheres were adjacent where it is likely due to spill-out effects from large neighbouring volumes. Therefore, the best spatial resolution is expected at the top of the phantom, as for this position the partial volume effect is smallest, resulting in the largest RCs (Leube et al., 2024). This study demonstrates that the RCs are significantly impacted by the spherical location. In order to facilitate image processing and harmonisation across many sites, the sphere positioning should be taken into account in any potential future accreditation process for quantitative SPECT/CT. Figure 2.5 present the schematic diagram of the workflow used to generate the dataset used in this study.

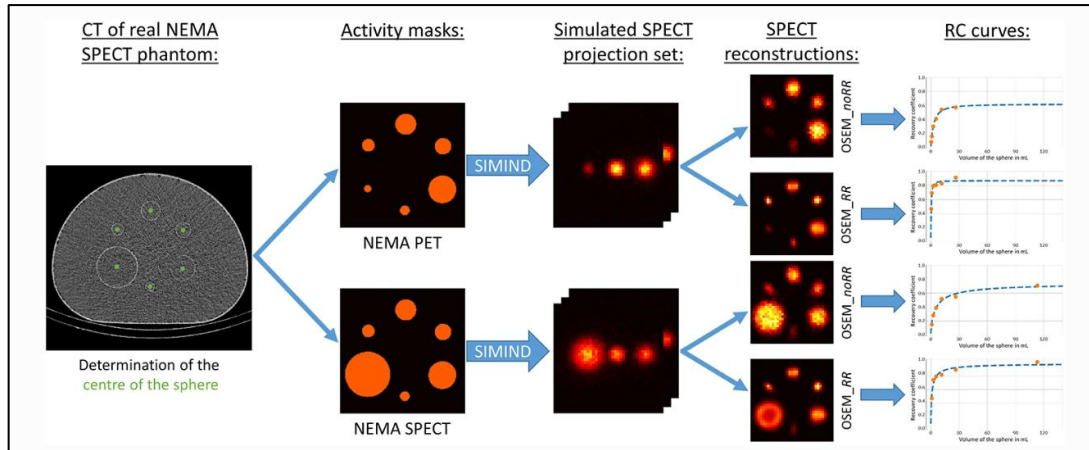


Figure 2.5 A schematic overview of the generation of the dataset utilized in this study of the position dependence of RCs in ^{177}Lu -SPECT/CT reconstructions – phantom simulations and measurements (Leube et al., 2024).

CHAPTER 3

MATERIALS AND METHODS

3.1 Materials

The study was conducted in the department of Nuclear Medicine, Radiotherapy and Oncology, Hospital Pakar Universiti Sains Malaysia (HPUSM), Kubang Kerian, Kelantan. The materials and apparatus used is GE Discovery NM/CT 670 Pro SPECT/CT, NEMA 2012/IEC 2008 phantom, ^{99m}Tc pertechnetate source, 5 cm diameter of fillable sphere and petri dish, 25-cc syringe and plastic tube to insert the source inside the phantom, well-type ionization chamber dose calibrator: AtomlabTM 500 to measure the activity of ^{99m}Tc , Xeleris workstation for image registration and reconstruction and finally Q Metrix software to yield the counts and activity concentration of the spheres and background.

3.1.1 Discovery NM/CT 670 Pro SPECT/CT



Figure 3.1: Discovery NM/CT 670 Pro SPCT/CT

The GE Discovery NM/CT 670 Pro as shown in Figure 3.1 is a hybrid SPECT/CT imaging system that combines a high-performance Optima CT540 CT system with a dual-detector, integrated nuclear imaging system. The Optima CT540 has a short-geometry, 16-slice CT design. This imaging system's SPECT-optimized design and advanced Elite NXT detector technology provide exceptional image quality. Additionally, it offers remote PC and PACS processing and review solutions along with sophisticated, integrated Xeleris workstation clinical applications. Furthermore, it allows a dose reduction system without compromising image quality, enabled in both CT and NM scans.

3.1.2 NEMA 2007 / IEC 2008 Phantom



Figure 3.2: NEMA 2007 IEC / 2008 Phantom

The phantom used is NEMA (National Electrical Manufacturers Association) 2007 / IEC (International Electrotechnical Commission) 2008 phantom as shown in Figure 3.2 is a standardized phantom used for evaluating the performance of PET scanners. The phantom indicates human body where it consists of a body phantom, a lung inserts and an insert with six spheres with various sizes which are 10 mm, 13 mm, 17 mm, 22 mm, 28 mm, and 37 mm. The volume of empty cylinder is 9.7 litre, the outside diameter of cylindrical insert is 51 mm and the cylindrical length is 180 mm (Mirion,

2025). It can be used as a simulation of whole-body imaging using PET and camera-based coincidence imaging techniques including SPECT (Sirona Complete Care, 2024). The phantom helps assess the overall performance of the SPECT system, including its ability to create clear images.

3.1.3 Technetium-99m (^{99m}Tc)

^{99m}Tc is a radionuclide agent used for this study. It is a Food and Drug Administration (FDA) approved agent that are used for diagnostic imaging across various human organs, encompassing critical areas (Kane et al., 2024). Technetium can exist in a variety of valence states, ranging from -1 to $+7$. When eluted from an alumina column generator, ^{99m}Tc is present primarily as heptavalent ($+7$) pertechnetate (TcO_4^-). In the preparation of radiopharmaceuticals, ^{99m}Tc pertechnetate can be reduced from $+7$ to a lower valence state, usually $+4$, to permit the labelling of various chelates (Sciencedirect.com, 2025). ^{99m}Tc is one of the most widely used radionuclides in nuclear medicine. The half-life of the radionuclide is short which is 6 hours. Thus, it is suitable to be used because it does not remain in the body or the environment for long (US EPA, 2015).

3.1.4 Syringe and Plastic Tube



Figure 3.3: A 25-cc syringes and plastic tube

Figure 3.3 shown a 25-cc syringe and a plastic tube used in this study. 50-cc volume of syringe was also used during phantom preparation. It was used to inject the