PARTIAL VOLUME EFFECT CORRECTION TECHNIQUE USING ADAPTIVE REGION GROWING TEMPLATE FOR SPECT QUANTIFICATION

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LIST OF SYMBOLS

Name	**Definition**
N_a	Number of voxels containing counts below a threshold
N_b	Number of voxels with counts above the proposed thresholds.
Nt	Total number of voxel within the drawn box
μ_a	Mean voxel counts for voxels containing counts more than a proposed threshold
μ_b	Mean voxel counts for voxels containing counts less than a proposed threshold
μ_t	Mean voxel counts within the drawn box
mCi	Millicurie
µCi	Microcurie
keV	kilo electron volts
kC/s	kilo counts per second
ml	milliliter
cm	centimeter
r^2	Coefficient of correlation
b	Strength of Correlation

LIST OF ABBREVIATIONS

Name	**Definition**
PVE	Partial Volume Effect
^{99m}Tc	Technetium-99m
A_b	Activity in Background
A_t	Activity in Target
CT	Computed Tomography
HUSM	Hospital Universiti Sains Malaysia
LEHR	Low Energy High Resolution
SPECT	Single Photon Emission Computed Tomography
SPSS	Statistical Package for the Social Sciences
T/B	Ratio of Target to Background activity concentration

TEKNIK PEMBETULAN KESAN ISIAPDU SEPARA MENGGUNAKAN KAEDAH “ADAPTIVE REGION GROWING” BERASASKAN TEMPLAT UNTUK PEGIMEJAN SPECT KUANTITATIF

ABSTRAK

Kesan isipadu separa (PVE) timbul dalam pengimejan SPECT kerana resolusi spatial terhad kamera gamma. Ini menjejaskan ketepatan kuantitatif dalam pengimejan SPECT. Kajian ini bertujuan membangun dan menilai kaedah berasaskan templat ‘adaptive region growing’ untuk mengatasi PVE dalam imej SPECT objek sasaran kecil dengan aktiviti latar belakang. Model simulasi “GEANT4 Application of Tomography Emission (GATE)” bagi kamera gamma dan pengimejan SPECT telah disahkan terlebih dulu. Imej SPECT yang mengandungi objek sasaran pelbagai saiz antara 1.44 ml hingga 10.1 ml dikelilingi oleh radioaktiviti dengan nisbah aktiviti sasaran kepada nisbah aktiviti latar belakang (T/B) sebanyak 1.25, 2.5 dan 5.0 disimulasikan dengan menggunakan simulasi model tersebut. Pembetulan PVE telah digunakan pada setiap imej SPECT simulasi. Kemudian keratan SPECT telah deperolehi menggunakan kaedah “filtered backprojection”. Kontras, keamatan imej, isipadu objek sasaran dan kepekatan aktiviti dikira dengan dan tanpa pembetulan PVE. Perbandingan keputusan kuantitatif dibuat di antara imej dengan dan tanpa pembetulan PVE. Bagi semua T/B, objek sasaran dalam imej dapat dilihat dengan lebih jelas lagi dengan pembetulan PVE. Dengan pembetulan ini juga, kontras imej bertambah baik. Untuk imej SPECT dengan aktiviti latar belakang tinggi, keamatan imej objek sasaran meningkat 40% selepas pembetulan PVE bagi saiz objek yang lebih besar daripada 6.3 ml. Untuk saiz objek kurang daripada 6.3 ml, keamatan objek sasaran meningkat sehingga 55% selepas pembetulan PVE. Persetujuan yang lebih baik diperolehi antara

isipadu simulasi dan isipadu anggaran dengan pebetulan PVE (R^2=0.3715) berbanding dengan tanpa pembetulan PVE (R^2=0.1077). Begitu juga, persetujuan yang baik antara kepekatan radioaktiviti simulasi dan kepekatan radioaktiviti anggaran telah diperolehi. Perhubungan antara aktiviti sebenar dan anggaran adalah lebih baik dengan pembetulan PVE. Sebagai kesimpulan, dengan menggunakan teknik pembetulan PVE yang dicadangkan ini ketepatan SPECT kuantitatif ditingkatkan.

PARTIAL VOLUME EFFECT CORRECTION TECHNIQUE USING ADAPTIVE REGION GROWING TEMPLATE FOR SPECT QUANTIFICATION

ABSTRACT

Partial volume effect (PVE) occurs due to limited spatial resolution of the gamma camera which degrades the quantitative accuracy in SPECT imaging. The aim of this study was to develop and evaluate the template based adaptive region growing method to correct for PVE in SPECT images of small target objects with background activities. Using a validated Geant4 Application of Tomography Emission (GATE) simulation model, SPECT images of rectangular phantom containing target objects of various sizes ranged from 1.44 ml to 10.1 ml surrounded by radioactivity with target to background activity concentration (T/B) ratio of 1.25, 2.5 and 5.0 were simulated. PVE correction was applied on each simulated SPECT data. Then the SPECT slices were reconstructed using filtered backprojection method. Image contrast, total counts, volume of target object and activity concentration were quantified using SPECT projections with and without PVE correction. The results were then compared. For all T/B, the edges of hot region of interest (ROI) were enhanced with PVE correction. Improvement in contrast of target objects were observed for SPECT images with PVE correction. For SPECT slices with high background activity (T/B=1.25), the counts in target objects increased up to 40% after PVE correction for object size larger than 6.3 ml. For object size less than 6.3 ml, the counts in target objects increased up to 55% after PVE correction. For SPECT images with low background activity, the counts in the target objects increased more than 50% after PVE correction for all target objects. The agreement between simulated volume and estimated volume of target objects with

PVE correction (R^2=0.3715) was better compared to without PVE correction (R^2=0.1077). Similarly, the agreement between simulated radioactivity concentration and estimated radioactivity concentration was better with PVE correction (R^2=0.9512) compared to without PVE correction (R^2=0.9444). In conclusion, the developed PVE correction technique improved the accuracy of SPECT quantification.

CHAPTER 1

INTRODUCTION

1.1 Background of the Study

1.1.1 Quantitative SPECT

Quantitative SPECT is the ability of the Single Photon Emission Computed Tomography (SPECT) images to provide quantitative information such as the volume of the target object and activity distribution within a region of interest. Accurate SPECT quantification may assist and improve various cancer management such as staging of cancer and its therapeutic planning.

The accuracy of quantitative SPECT is influenced by attenuation, image noise and partial volume effect(PVE) (Bailey & Willowson 2013). Attenuation introduces image noise and causes inaccurate image data. Noise and PVE causes blurred edges of the target object and severely affect the segmentation procedure which is essential for SPECT quantification. Advancement in image processing techniques are necessary to minimize these factors and to optimize the accuracy of quantitative SPECT (Grimes et al. 2012).

1.1.1(a) Attenuation

The loss of intensity of a photon through absorption or scattering when it passes through or interacts with a matter is called attenuation. It expressed as a function of photon energy, and the thickness and composition of the matter. The effect of attenuation in SPECT depends on body thickness, the region of body imaged and the location of the radioactivity source.

Compton scatter is one of the possible interactions caused by attenuation. Scatter occurs when the photon interacts with a matter and transfers part of its energy to the outer shell electron and causes ejection where the photon loses energy and changes direction. Although attenuation and scatter are closely linked, the effect of correction for attenuation and scatter on image quality was applied separately (Hurton, 2002). The effect of scattering on final image for photon with higher energy (>100keV) are lesser in magnitude than attenuation (Cherry, et al., 2003).

Attenuation correction influences the accuracy of SPECT quantification (Pretorius, et al., 1991). Attenuation correction is performed by applying a correction factor based on the source depth and attenuation coefficient. The correction for attenuation can be applied on the projection profile generated by the geometric or arithmetic mean before reconstruction using an estimate of tissue thickness. Attenuation correction is simpler when applied on projection profile generated by geometric means compare to arithmetic mean (Cherry, et al., 2003). Similarly, scatter correction also results in improvement of image contrast and leads to satisfactory SPECT quantification. Mostly, during correction for attenuation, the correction for scatter was also included.

1.1.1(b) Noise

Image noise is defined as the degree of statistical variation of the counts which reduces the image quality. The image count that corresponds to noise may have no direct relation to the actual image. Non-uniform radioactivity distribution due to multiple tissue fractions is a cause of high image noise besides photon scattering, statistical variation and random electronic fluctuations.

In a clinical situation, patients with severe illness have high radioactivity uptake surrounding the target object (tumor/lesion/organ). This radioactivity uptake, which is also referred as background activity, is reported to be up to 80% of target activity in severely ill patients (Shahir 2012). In this case, the ratio of target to background activity will be 1.25 or 5:4. SPECT images with high background activity have high image noise hence reduces the image contrast. Image with poor contrast has less ability to visualize the difference in count density between the target object and background. A proper image processing technique that includes count correction method could minimize the effect of noise caused by background activity.

1.1.1(c) Partial Volume Effect

The accuracy of quantitative SPECT is rely on the accuracy of image segmentation technique used to delineate the target object. Image segmentation is often affected by several factors, one of the factors is partial volume effect (PVE). PVE causes blurred edges of the target objects and severely affect the segmentation procedure which is essential for SPECT quantification (Bailey & Willowson 2013). The phenomenon of partial volume effect (PVE) in nuclear medicine images can be well explained by Rayleigh criterion. The Rayleigh criterion is the generally accepted criterion for the minimum resolvable details of an image.

The Rayleigh criterion determines that the two point sources were distinguishable from each other, or resolved when the point sources are appear to be visually unresolved (Corle & Kino 1996). It means that the two blurry points of the same intensity can still be differentiated when the minimum of the first point source coincides with the maximum of the second. This phenomena is illustrated in Figure 1.1-1.

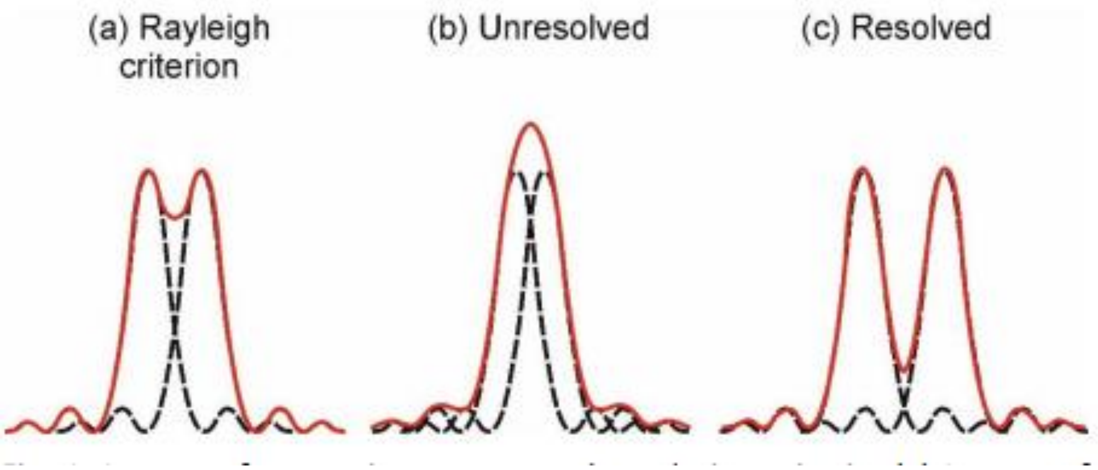

Figure 1.1-1: Images of two point sources and resolution criteria. (a) Images of two point sources that are just resolved, according to the Rayleigh criterion. (b) Images of two point sources that are not resolved. (c) Images of two point sources that are resolved. Plots adapted from article by Kallweit & Wood 1982. (Kallweit & Wood 1982)

In SPECT, the Rayleigh criterion contributes to Partial Volume Effect (PVE). As the SPECT images are formed by the count intensities obtained from the photon emitted from target object, Rayleigh criterion and PVE is explained in term of distribution of counts on pixels and how the counts corresponds to true images are resolved.

PVE defined as the inaccurate representation of counts in the image due to poor spatial resolution of gamma camera. PVE occurs when the count in the SPECT images spillover from one pixel to another. Spill-over in SPECT images can occur as two different scenario which spill-in and spill-out (Nyathi, Physics, et al. 2016). Spill-in of counts occurs when the minimum count of one object coincide with maximum count of neighboring object leading to overestimation of the target object. It also causes the blurred edges of target object. Spill-out effects are a result of “loss” of activity from the target object with maximum count into the background resulting in underestimation of the target object. In some cases, spill-in and spill-out occurs simultaneously which causes large quantitative errors.

One of the reasons for PVE occurrence is the limited spatial resolution of gamma camera as explained by Rayleigh Criterion. Spatial resolution is the measure of minimum distance between two points such that they can be identified separately in different pixels. It can be measured by computing full-width at half-maximum (FWHM) of gamma camera’s point spread function. The smaller the FWHM, the better the resolution of the camera. Unlike other imaging modalities such as CT and MRI, SPECT has considerably larger size of image pixels which contributes to larger FWHM. As a consequence, when imaging the target object of size less than twice the FWHM, PVE is very significant because the gamma camera is incapable of distinguishing the counts individually in each pixel. Thus, in the final acquired image, the counts belong to the individual pixels does not accurately reflect the actual activity within the target (Figure 1.1-2).

Second reason for PVE occurrence is the reconstruction techniques that lead to a spillover of counts from one pixel to another. In addition to that, reconstruction technique causes spillover of counts from on slice to another. As PVE highly depends on the resolution of SPECT system and reconstruction techniques, quantitative accuracy of SPECT is often affected.

PVE is also present in imaging the target object of size larger than FWHM, but the spillover occur only at the edges of target object. This is clearly illustrated in Figure 1.1-2 that when the target objects are smaller, the PVE becomes significant and the count profile show decreased counts per pixel and vice versa.

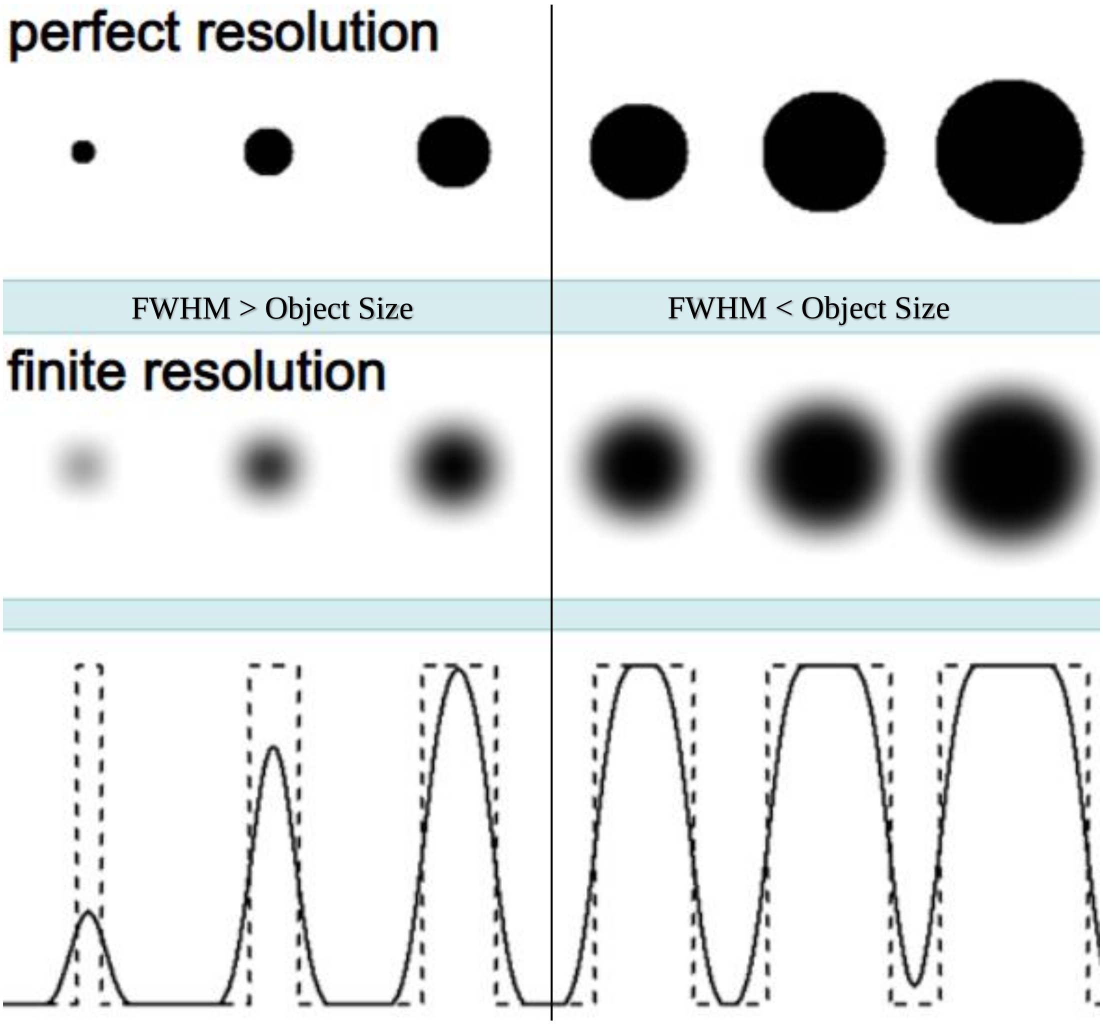

Figure 1.1-2: Partial volume effect

PVE occurs during image acquisition and processing which is nearly impossible to prevent. However, correction techniques can be applied on SPECT images during image processing in order to eliminate the distortions caused. Therefore, advancement in image processing techniques are necessary to correct PVE on SPECT images and optimize the accuracy of quantitative SPECT (Grimes et al. 2012). Therefore a correction of partial volume effect should be done based on gamma camera resolution and image processing techniques.

Various studies have suggested that correction for partial volume effect may improve the delectability of functional volumes in SPECT imaging (Itti et al. 1997; Kato et al. 2012; Kato et al. 2008; Pretorius & King 2009; Pretorius et al. 1998; Shcherbinin et al. 2013; Soret et al. 2006). Over the years, a range of different correction techniques for PVE with various approaches was developed such as image enhancement techniques, image domain correction techniques, projection-based correction, corrections for non-uniform regions, correction for tissue fraction and correction for dynamic data (Erlandsson et al. 2012). It is believed that not one single technique that would be optimal in all imaging conditions. Specific techniques for each kind of SPECT studies are necessary to achieve optimum quantification. A comprehensive review on PVE correction techniques is presented in Chapter 2.

1.1.2 Simulation of SPECT images

Monte Carlo (MC) simulation is a numerical calculation method that has been used extensively in Nuclear Medicine to solve problems that are difficult to study by experimental or analytical approach (Ljungberg, Strand, & King, 1998). Several type of MC simulation codes are available for simulation of SPECT studies which includes EGS4, MCNP, ITS, and GEANT, SIMIND, PETSIM and SIMSET. Every code has its own advantages and disadvantages in SPECT simulation. No code can be considered as gold standard for SPECT simulation since all MC codes also present weakness besides valuable features. Therefore, a suitable MC code must be chosen carefully in respect to their function of application. A detailed review on dedicated codes for SPECT simulation is presented in chapter 2.

In present study, Geant4 Application of Tomography Emission (GATE) is used to simulate SPECT images. GATE is considered as a good option to simulate SPECT and Planar images due to the proven high modularity (Aguiar et al. 2012; Könik et al. 2012; Min-Jae et al. 2009; Nguyen & Pham 2016; Strulab et al. 2003). It is proven effective for simulation of system definition and performance which provides many details in developing a realistic simulation model of gamma camera (Taheri et al. 2017).

GATE simulation package could perform realistic SPECT simulation and provides rich information that facilitate development of novel image processing algorithms to solve various issues arises in SPECT imaging such as noise, attenuation and partial volume effect. As mentioned in previous section, attenuation and noise occur during image acquisition and processing which is nearly impossible to prevent. Therefore, attenuation and noise must be taken into account during simulation of SPECT images.

1.2 Problem Statement and Rationale of the Study

Partial volume effect (PVE) is one of the factors that limit the accuracy of volume and activity quantification in SPECT. Various studies have proposed methods for PVE correction to improve SPECT quantification (Shcherbinin et al. 2013) . There were 2 major drawbacks among these PVE correction methods.

Firstly, most of the available methods of PVE corrections are based on anatomical knowledge obtained from other modalities such as CT which causes extra radiation exposure to patients. Second, the available PVE correction methods are less accurate for SPECT images with poor contrast. In actual clinical settings, SPECT images of patients with severe illness are degraded by high radioactivity uptake in the background of target object. The magnitude of background activity could be up to 80% of target activity, hence severely degrades the contrast of image (Syahir 2012). To date, PVE correction method that is not anatomical based and also proven accurate for images with high background activity are not available either for clinical or experimental purpose.

Present study was initiated to tackle the abovementioned drawbacks of currently available PVE correction methods. Therefore, an adaptive region growing template-based PVE correction was developed to provide following features:

- ✓ The method is not based on prior anatomical knowledge that obtained from other imaging modality. This was achieved by using region growing method for image segmentation of target.
- ✓ The method is applicable over severely degraded SPECT images. This can be achieved by creating templates based on voxel-wise count analysis and these templates will be applied on raw image before reconstruction.
- ✓ Unlike other existing template-based correction method which uses average ROI and background values to create template, the present method utilizes perimeter of the ROI to define values correspond to target and background. Therefore, high definition edges of ROI of small object can be obtained after the correction being applied.
- ✓ Inexpensive and easy to implement using developed software by transferring the data from SPECT processing system to personal computer.

1.3 Aim and Objectives of the Study

1.3.1 Aim

To develop and to evaluate a partial volume effect correction technique that does not require prior anatomical information applicable for SPECT images with high background activities.

1.3.2 Specific Objectives

- To simulate planar and SPECT images of phantom containing hot/cold spot of various sizes and background activities using validated GATE simulation model of gamma camera
- To develop an algorithm for PVE correction technique using adaptive region growing template
- To evaluate the PVE correction method for quantification of volume of target objects and activity concentrations

1.4 Justification of the Study

It is well known that cancer diagnosed at an early stage allows more effective treatment and could help patient to fight cancer. SPECT is one of the diagnostic tools that effectively diagnose cancer. The discovery of Technetium-99m leads to a major development in cancer imaging by SPECT which provides metabolic and functional information. SPECT's advantage on visualizing functional volume leads to better visualization of cancerous cells. SPECT is proven effective for many cancer diagnostic studies such as lymphoscintigraphy, bone imaging, octreotide scintigraphy, and prostate cancer localization(Ammar et al. 2017; Elisei et al. 2017; Alavi 2011; Guezennec et al. 2017; Goffin et al. 2017). SPECT is also a simpler technique for quantification of tumor volume and may replace other imaging modalities such as CT and MRI which provide only anatomical information.

Although SPECT is an established diagnostic imaging technique, the data derived from SPECT is not sufficient for staging and therapeutic planning for cancer due to the limitation of SPECT images that includes partial volume effect (PVE) (Bailey & Willowson 2014; Groshar et al. 1997; Mezzenga et al. 2017; Schmitt et al. 2018). During early stage of cancer, the cancerous cells are smaller in size and difficult to identify due to partial volume effect (PVE). PVE must be corrected effectively and efficiently in order to obtain accurate quantification of cancer cells. The method of PVE correction must also be easy to apply on image to reduce image processing time.

Various approaches for PVE correction exist. One of the major issues of existing PVE correction method is their dependence on prior anatomical knowledge obtained from CT or MRI for image segmentation. Another issue is the limitation of the methods over region with non-uniform radioactivity distribution. Therefore present study was initiated to develop a correction method for partial volume effect that fulfills the abovementioned requirement which helps effective and fast diagnosis of cancer at early stage.

1.5 Outline of Thesis

This thesis consists of 6 chapters. The current chapter presents the theoretical background of quantitative SPECT, PVE occurrence in SPECT images and the principles of volume estimation using SPECT imaging. The section also discusses the influence of partial volume effect and noise on the accuracy of quantitative SPECT. The problem statement and rationale of the study, the aim and objective of the research, and the scope of the present study are also discussed here. The second chapter presents a concise review of the published literature related to the PVE correction technique and the challenges of developing accurate PVE correction techniques.

The material and methods of the experiments were reported comprehensively in Chapter 3 and 4. The experimental design of SPECT simulation used in present study illustrated in Figure 1.5-1. Monte Carlo simulation of SPECT images was carried out using GEANT4 Application of Tomography Emission (GATE). A validation of GATE simulation of Siemens e.cam Signature Series single head gamma camera was carried out prior to the simulation of SPECT data. The complete methods of validation and the results were documented comprehensively in Appendix A.

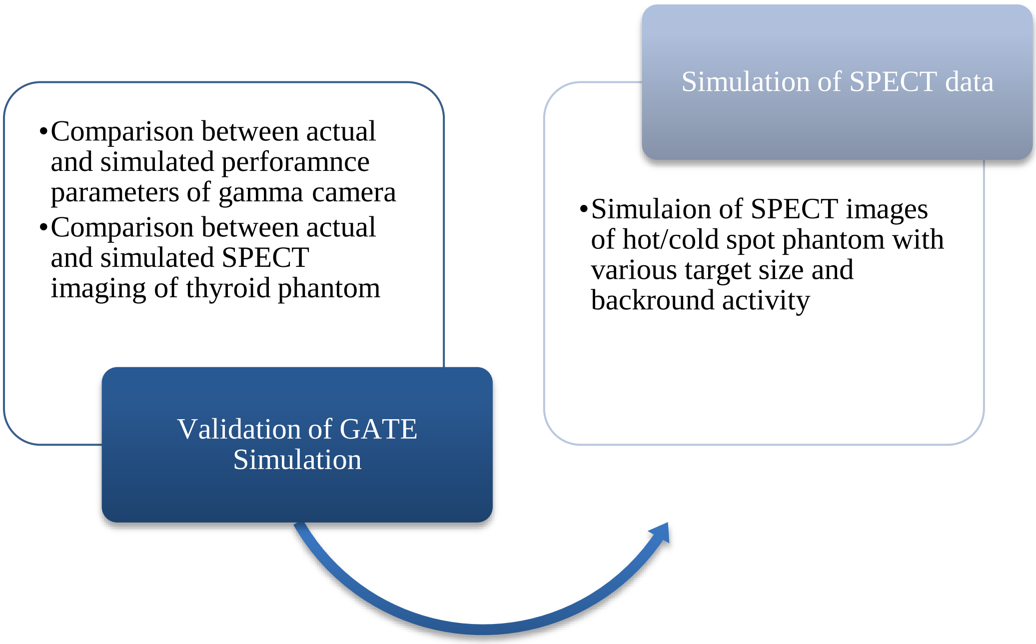

Figure 1.5-1: The experimental design of the simulation of SPECT images

After the SPECT data were simulated, the development and evaluation of PVE correction technique was carried out. The experimental design of the development and evaluation of PVE correction technique is explained in Figure 1.5-2. The development of PVE correction technique is presented in Chapter 3. An algorithm that incorporates image segmentation and count adjustments was developed to correct for PVE. The theoretical construct of the PVE correction technique and methods underpinning are demonstrated in detail in this chapter.

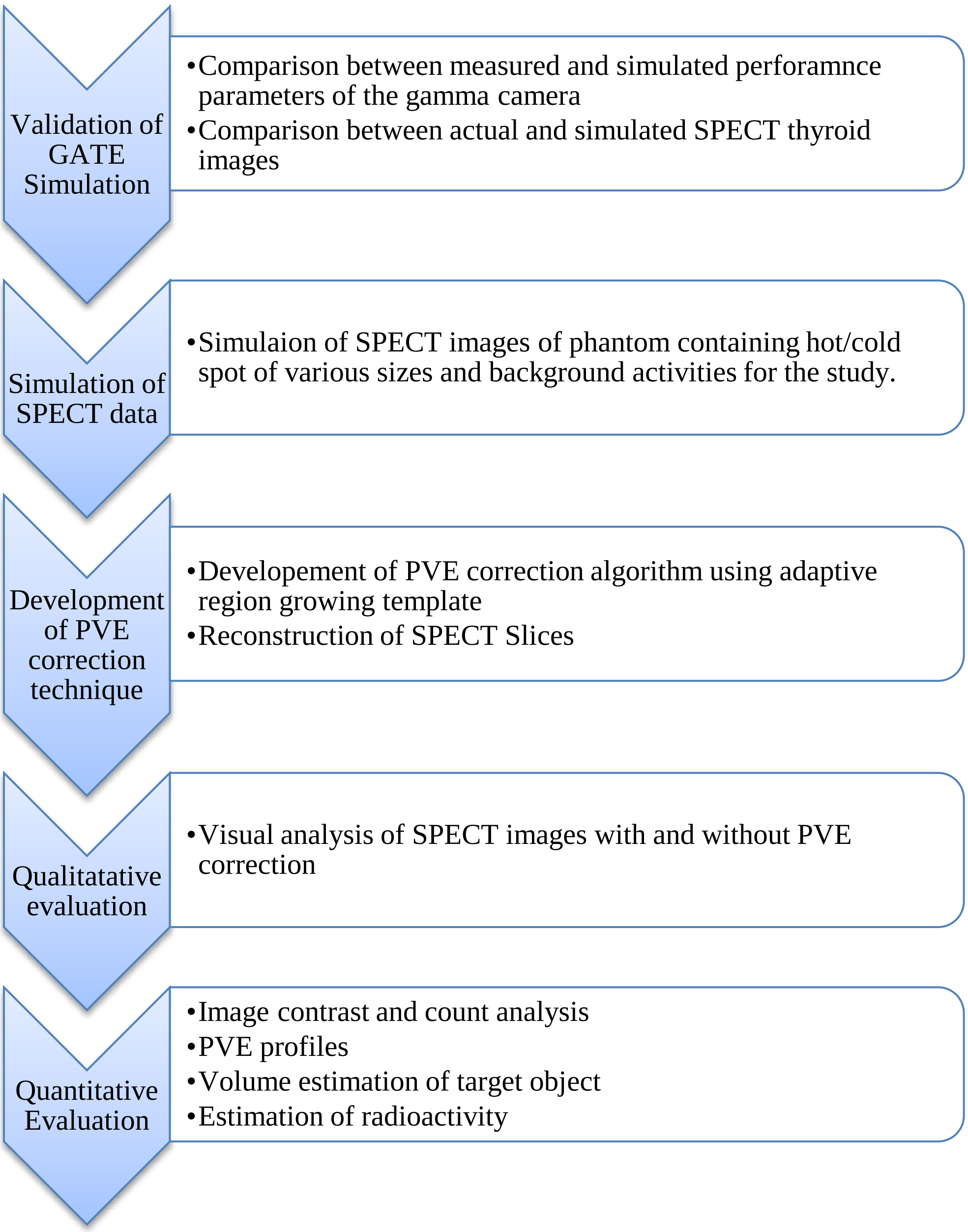

Figure 1.5-2: The experimental design of the study

The developed PVE correction method is evaluated quantitatively in chapter 4 using simulated planar and SPECT images containing target objects with various sizes and various ratio of background activity. SPECT and PLANAR images that resemble actual clinical situation such as poor contrast and high background radioactivity was acquired using a validated GATE simulation model. The comprehensive report on

GATE simulation is presented in Appendix A. Quantitative measurements such as volume and activity estimation of target objects were carried out to assess the accuracy of the PVE correction method.

The results of the quantitative evaluation of the developed PVE correction method is presented and discussed in Chapter 4. The effectiveness as well as the limitation of the developed technique was concluded in Chapter 6. Future development and potential further work from this research are also recommended.

CHAPTER 2

LITERATURE REVIEW

2.1 Monte Carlo Simulation

2.1.1 Simulation Software

Monte Carlo (MC) simulation is a numerical calculation method based on repeated random sampling and probability that has been used extensively in Nuclear Medicine to solve problems that are difficult to study by experimental or analytical approach (Ljungberg, Strand, & King, 1998). Several type of MC simulation codes were developed for simulating variety of SPECT studies particularly to improve SPECT quantification. Two types of MC simulation codes can be used for simulation. One of the types is the general purpose codes which simulate particles transportation which developed for high energy physics. Another type of MC code is “dedicated codes” that designed specifically for particular imaging system such SPECT or PET. EGS4, MCNP, ITS, and GEANT are some of the general purpose MC simulation codes available for Nuclear Medicine simulation whereas SIMIND, PETSIM and SIMSET are some of the available dedicated codes with free access (Buvat & Castiglioni, 2002; Lazaro et al., 2004; Ljungberg & Strand, 1989). However, no code can be considered as gold standard for SPECT simulation since all MC codes also present weakness besides valuable features. Therefore, a suitable MC code must be chosen carefully in respect to their function of application.

Geant4 Application for Transmission Emission (GATE) is a dedicated MC simulation program designed to answer specific needs of Nuclear Medicine applications, i.e., SPECT (Lee, Sanghyeb ; Gregor, Jens ; Osborne 2013; Min-Jae et al. 2009; Staelens et al. 2003a; Anon n.d.; Strulab et al. 2003; Lazaro et al. 2004; Jan et al. 2004; Mikeli et al. 2009; Vieira et al. 2014; Rodrigues et al. 2007).

GATE is a free simulation software developed by the international OpenGATE collaboration(Anon n.d.). Validation of each GATE simulation must be carried out in order to determine the effectiveness and reliability of the simulation model to reproduce approximately same results as the actual gamma camera. Literatures on such validation of simulation model for several commercial gamma cameras are published by many researchers. For instance, simulation of Trionix TRIAD SPECT Camera(Min-Jae et al. 2009) is validated in term of energy spectrum and resolution, the system sensitivity, and the spatial resolution. A good agreement is found between actual and simulated gamma camera with roughly 5% of error. Siemens Inveon SPECT imaging platform(Lee, Sanghyeb ; Gregor, Jens ; Osborne 2013) is simulated and validated in term of energy spectrum and resolution, the system sensitivity, scatter fraction, integral uniformity and reconstructed image signal to noise ratio. Approximately ±5% of agreement between simulated and actual data was reported. A GATE simulation of IASA (Institute of Accelerating Systems & Applications) scintillation camera is validated by comparing point spread function, energy spectra, sensitivities, scatter fractions and image of a capillary phantom with corresponding experimental data. The study demonstrated the capability of GATE for simulation of original detector design. A simulation of Siemens E-cam Dual Head gamma camera(Rodrigues et al. 2007) using GEANT4 is validated by performing experimental characterization in terms of energy resolution, sensitivity, spatial resolution, linearity and imaging evaluation of thyroid and Polymethylmethacrylate (PMMA) phantom. In addition to these literatures, validation of DST-XLI(Autret et al. 2005), Millennium VG(Autret et al. 2005), and 2 other standard gamma(Staelens et al. 2003b; Assié et al. 2005) camera are also published.

SIMIND Monte Carlo simulation program, which is also established for SPECT with low-energy photons. This program was originally designed for the calibration of whole-body counters, eventually evolved to simulate gamma cameras. It is now available in Fortran-90 and can be freely downloaded from http://www.radfys.lu.se/simind and run on major computer platforms. The program can simulate non-uniform attenuation from voxel-based phantoms and includes several types of variance reduction techniques. Transmission SPECT images can also be simulated. The literatures shows that the SIMIND MC Code can be used with confidence to simulate SPECT/CT gamma camera (Ejeh et al. 2019; Taghi et al. 2009)

Monte Carlo N-Particle code, version 5 (MCNP5) is a general purpose Monte Carlo code and it can be used for the design of imaging systems. It accounts for all the interaction types: photoelectric absorption, Compton scattering, coherent scattering, and pair production. Furthermore, important features make MCNP very versatile and easy for complicated geometry structures. MCNP also demonstrated the flexibility and accuracy to simulate the basic features of SIEMENS Symbia T SPECT Camera and exemplified its potential benefits in protocol optimization and in system design (Dong et al. 2019)

The comparison of GATE, SIMIND and MCNP5 shows differences of the codes that would be considered more in a typical simulation with their respective pros and cons. SIMIND is the most flexible and user-friendly code to define a SPECT system, however limited in the system definition and performance in some cases. Based on the literatures, the best way of performing a process of simulation and validation a SPECT system is utilizing the SIMIND. SIMIND also less complex compared to MCNP5. One of the biggest drawbacks of MCNP is its limited ability to simulate the optical photons however it can calculate the spectrum broadening using user defined parameters. Furthermore, MCNPX cannot repeat the simulation for 64 projections automatically and this means that for each projection the rotation parameters should be changed manually. In comparison with other Mont Carlo simulation toolkits and codes, MCNPX is a frequently-used code by novices providing a more convenient approach for simulation.

In summary, GATE provides so many details in a more accessible manner whereas it needs rationally more time and hardware facilities to run a simulation. Compared with SIMIND, MCNPX shows more complexities but easier handling than GATE. GATE could be a reliable tool for developing the procedure in more details after validation of a gamma camera simulation (Taheri et al. 2017).

2.2 Partial Volume Effect

For a smaller object that only partially fills a resolution-volume element, the sum of the intensities of all the pixels that correspond to that object still reflects the total amount of activity within it. This effect is called Partial volume effect (PVE)(Cherry et al. 2003; Rosenthal et al. 1995). PVE is highly depends on the "resolution volume" of a SPECT system. It degrades the quantitative accuracy of SPECT by affecting the accuracy of the image segmentation process. Thus correction of partial volume effect should be done during image processing to improve the accuracy of SPECT quantification(Bailey & Willowson 2013).

2.2.1 Correction for PVE

Correction for partial volume effect improves the detectability of functional volumes in SPECT imaging by improving image contrast and definition of target object. (Ritt et al. 2011; Itti et al. 1997; Kato et al. 2008; Kato et al. 2012; Pretorius & King 2009; Pretorius et al. 1998; Shcherbinin et al. 2013; Soret et al. 2006) Over the years, a range of different correction techniques for PVE with various approaches was developed such as image enhancement techniques, image domain correction techniques, projection-based correction, corrections for non-uniform regions, correction for tissue fraction and correction for dynamic data (Erlandsson et al. 2012). The correction methods such as template-projection-reconstruction using a filling fraction(Pretorius & King 2009), adaptive template-based method (Shcherbinin et al. 2013), and iterative correction (Erlandsson et al. 2012) has a reliable outcome but highly depend on anatomical information from CT and MRI images. Not one single technique that would be optimal in all imaging conditions especially for SPECT images that are often affected by noise due to high background activity.

Background activity highly influences the accuracy of SPECT quantification, algorithm for PVE corrections that based on background activity may improve the quantitative accuracy of SPECT imaging. Studies evaluating accuracy of PVE correction on image with high background activity or non-uniform regions are very limited(Itti et al. 1997; Pretorius & King 2009). Most of the PVE correction methods in SPECT are only practical for uniform regions (Erlandsson et al. 2012; Itti et al. 1997; Kato et al. 2012; Kato et al. 2008; Pretorius et al. 1998; Shcherbinin et al. 2013; Soret et al. 2006). As phantom studies may not accurately represent clinical situation, a simulation of SPECT images can be useful in such situations.

2.2.2 PVE Correction using Reconstruction Methods

Accuracy in SPECT quantification is achievable by advancement in image processing. Image processing includes reconstruction, image filtering as well as correction methods. Some of the PVE correction was done along with image reconstruction.

A study reported a new developed PVC method for SPECT, that works in combination with OSEM reconstruction where the correction was applied in the projection domain at each iteration of OSEM (Erlandsson et al. 2011). The developed correction is explained in Equation 2.2-1.

$$\boldsymbol{\varphi}^k = \frac{F(a^k)}{F_R(a^k)}$$

Equation 2.2-1

$\boldsymbol{\varphi}^k$ is the set of PV correction factors for k iteration index, FR and F represent the forward projection operator with and without resolution modelling(R), respectively. The $a^k$is a piece-wise constant image where each voxel-value is equal to the corresponding regional mean value, therefore, an average pixel value of the regin of interest were used for normalization. The developed method, OSEM-PVC, were evaluated with simulated phantom data and brain SPECT imaging of healthy volunteers. The results shows that the OSEM-PVC image has a similar contrast as the conventionally reconstructed image but improved structural definition. However, the evaluation over the original contrast of image and contrast after PVE correction shows that images with poor contrast has less improvement over contrast and definition of structures.

Another study published earlier compared the effects of applying PVE correction during and after reconstruction in SPECT imaging (Livieratos et al. 2009).

For during reconstruction PVE correction procedure, the image processing system of the gamma camera, called as PHILIPS ASTONISHTM was used. For after-reconstruction, a post-reconstruction deconvolution algorithm was used. Iterative deconvolution using the Lucy-Richardson and Van-Cittert algorithms were used as the post-processing algorithms. These algorithms were intended to eliminate the noise observed in deconvolution methods. The article concluded that post-reconstruction PVE correction showed similar or slightly better quantitative accuracy compared to during-reconstruction (PHILIPS ASTONISHTM) PVE correction. To date, PVE correction technique that applied on raw SPECT images before reconstruction is not reported.

Poor spatial resolution of gamma camera is the major cause of partial volume effect. Hence, studies were carried out to correct partial volume effect with 3D modelling of spatial resolution in iterative reconstruction to improve accuracy of activity quantification (Pretorius et al. 1998). The iterative reconstruction algorithms investigated were maximum-likelihood expectation-maximization (MLEM), MLEM with ordered subset acceleration (ML-OS), and MLEM with acceleration by the rescaled-block-iterative technique (ML-RBI). The accuracy of methods was measured in term of the central count ratio (CCR) which is the average count in the central voxel of the sphere and the total count ratio (TCR) which is the recovery of total counts in the spheres (activity recovery). Fraction of the voxel volume occupied by the sphere is determined using Equation 2.2-2.

$$\mathrm{WF}\ (i,j) = \frac{\text{true counts}\big(\text{voxel}(i,j\,)\big)}{\text{true counts}(\text{voxel}(i,j\,))\ \text{true maximum counts in sphere}}$$

Equation 2.2-2

The correction method was assessed for simulated image data without background, and with a 20% uniform background added. The results provides much valuable input for future development of PVE correction based on 3D modelling spatial resolution. The most noteworthy finding was the addition of background has a significance influence on the convergence rate and noise properties of iterative techniques.

2.2.3 Template-based PVE correction

In a SPECT phantom experiment, two methods to generate templates for template-based partial volume effect correction were introduced (Shcherbinin et al. 2013). The first method creates an image-based template using a data derived from reconstructed images using conventional OSEM method which includes CT-based attenuation map and Gaussian model of resolution loss. The mean ROI values and pixel values correspond to background in the conventional images was used to create template for target region and background region respectively. The second method, called adaptive template, uses the average activity concentrations in the ROI and background and the probability of photon emitted from any voxel belonging to the ROI and the background, respectively. CT-based attenuation map is also used for this method. The phantom with various size and activity with the lowest ratio of target to background activity of 2.3 was used.

The results shows that image-based PVE correction resulted in consistent but relatively weak PVE compensation. The adaptive template based PVE correction method resulted in a selective (accuracies for only 19 ROIs were improved) but considerably better compensation than image-based PVE correction. One of the limitation of the study was the phantoms used here has uniform radioactivity distributions. The author suggested to further studies with numerical phantoms which might have both irregular shapes and non-uniform activity distributions.

2.2.4 Anatomical-based PVE correction

Many original article on PVE correction method that uses aid of other imaging techniques such as CT and MRI are published over the years. A reconstruction based correction method uses MRI for segmentation of region of interest (Erlandsson et al. 2011). The advantage of using MRI based segmentation are ability to achieve higher contrast. However the accuracy of the method can be affected by errors in the MRI-to-SPECT co-registration and in the MRI segmentation/parcelation procedure.

Another study reported a template projection – reconstruction method Partial-Volume Correction in SPECT application to 177 Lu radionuclide therapy(Brolin & Ljungberg 2011). Evaluation of the method using SIMIND simulation of XCAT phantom shows that the PVC reduced the error in kidney activity concentration from approximately -20 % to -1 % with templates acquired from the true organ configuration. However more realistic situation in term of activity distribution is warranted.

2.2.5 Other PVE correction methods

A recent study introduced a cost effective and non-anatomical based PVE correction method (Nyathi, Sithole, et al. 2016). The method was carried out using a freely available software called, ImageJ for planar images acquired using Jaszczak phantom that filled with activity free water. The method successfully recovers the image counts that are responsible for underestimation of image counts for target objects less than 2- 3 times the FWHM of the imaging system. However, the effectiveness of the proposed method was not addressed for images with presence of background activity and degraded by image noise.