Tuija Kangasmaa

Evaluation and Optimization of Novel Reconstruction Methods for Myocardial Perfusion SPECT

Myocardial perfusion imaging (MPI) is one of the most common types of SPECT studies, being highly valued for its diagnostic accuracy. However, image noise, photon attenuation, Compton scatter, collimator-detector response (CDR) and patient motion hamper the image quality of MPI. These image degrading factors have been investigated widely and the modern reconstruction-based compensation methods can greatly improve the image quality. Recently CDR compensation has attracted considerable interest, because it allows diagnostically satisfying images to be acquired in half of the acquisition time currently in use. Shorter scan times both reduce artifacts related to patient motion and increase the patient throughput. The aim of this thesis was to validate and optimize novel SPECT reconstruction and compensation techniques for use with MPI. The specific focus was on scan time reduction and on CDR compensation.
Evaluation and optimization of novel reconstruction methods for myocardial perfusion SPECT
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ABSTRACT

Myocardial perfusion imaging (MPI) is one of the most common types of SPECT studies, being highly valued for its diagnostic accuracy. However, the quality of MPI is seriously impaired by image noise, photon attenuation, Compton scatter, collimator-detector response (CDR) and patient motion. These image degrading factors have been investigated for more than three decades now and the modern reconstruction-based compensation methods can greatly improve the image quality. Recently CDR compensation has attracted considerable interest, because it allows diagnostically satisfying images to be acquired in half of the acquisition time currently in use. Shorter scan times both reduce artifacts related to patient motion and increase the patient throughput.

The utilization of modern compensation methods is not always straightforward. Their application can be time consuming and they can generate new image artifacts. The aim of this thesis was to validate and optimize novel SPECT reconstruction and compensation techniques for use with MPI. The specific focus was on scan time reduction and on CDR compensation.

In the first part of the thesis, half acquisition time imaging was studied in combination with Monte Carlo (MC)-based scatter compensation, which is a statistical technique dependent on the count level of the acquisition. The MC-based scatter compensation was not observed to hinder half acquisition time imaging. The image quality obtained with half acquisition time using CDR and MC-based scatter compensation was better than with full acquisition time and conventional reconstruction, but it did not achieve the image quality obtained with full acquisition time combined with CDR and MC-based scatter correction.

In the second part of the thesis, the MC-simulator used in the first part was developed further for simultaneous $^{201}$Tl/$^{99m}$Tc cardiac imaging. Simultaneous $^{201}$Tl/$^{99m}$Tc could also reduce the total acquisition time by half, because it allows the stress and rest scans to be performed in one single session. One problem
encountered in simultaneous $^{201}$Tl/$^{99m}$Tc is the down-scatter from $^{99m}$Tc to the $^{201}$Tl energy window. The MC-simulator was optimized for $^{201}$Tl/$^{99m}$Tc imaging. This was found to greatly improve the image quality and produce an image in less than 3 minutes.

Even with reduced scan times, some patients cannot stay still during the acquisition, which leads to artifacts that can be falsely interpreted as perfusion deficits. The third part of this thesis focused on reconstruction-based motion correction in MPI-imaging. Different motion correction methods were examined and optimized in terms of their performance and speed so that efficient motion correction could be achieved in a few minutes.

In the fourth and final part of the thesis, novel methods to reduce CDR related artefacts were developed. The CDR artefacts could be greatly reduced if CDR was used with Bayesian reconstruction methods. It was found that the best performance could be obtained with Bayesian reconstruction with an anatomical prior.

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*Medical Subject Headings: Nuclear Medicine; Heart/radionuclide imaging; Myocardium/blood supply; Tomography, Emission-Computed, Single-Photon/methods; Myocardial Perfusion Imaging/methods; Artifacts; Scattering, Radiation; Sensitivity and Specificity; Reproducibility of Results; Movement; Image Processing, Computer-Assisted/methods; Computer Simulation*

*Yleinen Suomalainen Asiasanasto: isotooppilääketiede; kuvantaminen – lääketiede; tomografia; kuvanlaatu*
Preface

This work was carried out in the Department of Oncology and the Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital during the years 2008-2009 and in the Department of Oncology, Vaasa Central Hospital during the years 2009-2014.

First of all I wish to express my deepest thanks to my principal supervisor Docent Antti Sohlberg, PhD, for the interesting research topic and the opportunity to work under his guidance. Your ability to teach and explain the theory behind reconstruction and compensation methods in such a way to make it easily understandable has helped me greatly throughout this work. I am also grateful for all the encouraging words that you gave me, especially whenever I was feeling insecure. Your endless support and patience has carried me through this work.

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I would also like to thank my supervisor Professor Jukka Jurvelin, PhD, for his valuable advice regarding the structure of this thesis as well as helping me solve the many practical questions I had towards the finishing of this thesis.

I wish to thank my co-authors of the original publications for their valuable contributions.

I offer my sincere thanks to the official reviewers Professors Brian Hutton, PhD, and Hidehiro Iida, PhD, for their valuable comments and proposals that helped to improve this thesis.
I warmly thank Dr. Ewen MacDonald for revising the language of this thesis.

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I am grateful to the personnel of the Nuclear Medicine and Radiation Therapy units in both Vaasa Central Hospital and Kuopio University Hospital for their support. In addition I would like to express my thanks to the Nuclear Medicine Department of Päijät-Häme Central Hospital for the contribution to original Publication II, as well as to the Nuclear Medicine Unit of Keski-Pohjanmaa Central Hospital for providing the phantom used in original Publication IV.

I am extremely grateful to all my colleagues in Kuopio and in Vaasa for all the help and support I have received and also for the scientific and non-scientific discussions we have shared. In particular I wish to thank Eero Kauppinen, Ph.Lic, Eini Niskanen, PhD, Juha-Pekka Niskanen, MSc, Helena Kiiiläinen, MSc, and Juha Rajala, Lic.Tech, for all the help, advice and support they have provided. Your friendship has brought me much joy and I cherish the discussions we have shared.

I owe my dearest thanks to my family and all my friends for always being there for me. I thank my parents, Irma and Pauli, for their endless love and support throughout my life. The loving and safe atmosphere that has always been present in our home has been the source of my strength. I also want to thank my siblings Tarja and Tero for their friendship and support.

Finally I wish to express my thanks to my dear spouse, Juha Perälä, for his love and encouragement as well as his endless patience with my time-consuming research projects. Thank you for being there for me.

Vaasa June 14, 2014

Tuija Kangasmaa
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<tr>
<td>AMAP</td>
<td>(Anatomical) Bowsher prior</td>
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<td>CAD</td>
<td>Coronary artery disease</td>
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<td>CDR</td>
<td>Collimator detector response</td>
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<td>CT</td>
<td>Computed tomography</td>
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<td>ECG</td>
<td>Electrocardiography</td>
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<td>FBP</td>
<td>Filtered back projection</td>
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<td>GRF</td>
<td>Geometric response function</td>
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<td>HU</td>
<td>Hounsfield’s unit</td>
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<td>IRF</td>
<td>Intrinsic response function</td>
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<td>MC</td>
<td>Monte Carlo</td>
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<td>ML-EM</td>
<td>Maximum likelihood expectation maximization</td>
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<td>MPI</td>
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<td>OSL</td>
<td>One-step-late</td>
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<td>PET</td>
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<td>SMOOTH</td>
<td>Quadratic smoothing prior</td>
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<td>SPECT</td>
<td>Single photon emission tomography</td>
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<td>SPRF</td>
<td>Septal penetration response function</td>
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<td>SSRF</td>
<td>Septal scatter response function</td>
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<td>TEW</td>
<td>Triple energy window</td>
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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on data presented in the following articles, referred to by the Roman numerals I-IV.


III Kangasmaa T S and Sohlberg A O. Optimisation of reconstruction-reprojection-based motion correction for cardiac SPECT. Ann Nucl Med. 10.1007/s12149-014-0829-6, 2014

IV Kangasmaa T, Kuikka J T and Sohlberg A. Reduction of collimator correction artefacts with Bayesian reconstruction in SPECT. Int J Mol Imaging. 630813, 2011.

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AUTHOR’S CONTRIBUTION

The publications of this thesis are original research papers on evaluation and optimization of novel SPECT reconstruction methods. The author was the main writer for all of the publications.

The author’s contribution in detail to the publications is as follows:

I  The author created the simulation phantoms, selected the patient data and undertook the reconstructions of all of the data. She analyzed the simulated data and conducted the statistical analysis for the evaluation results.

II The author created the simulation phantoms and planned the activity values and defect setting on the physical phantom. She conducted the reconstructions of all the data and analyzed the simulated and measured data.

III The author selected the patient data and planned and inserted the amount and types of motion. She conducted the reconstructions and analysis of all of the data.

IV The author planned and performed the phantom measurements and analyzed the reconstructed data.


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1 Introduction

Coronary artery disease (CAD) is the most common type of heart disease and it is also the leading cause of death in Finland; every year approximately 13,000 Finns die because of CAD [1]. The disease develops when the arteries that supply blood to the cardiac muscle become hardened and narrowed because of the growth of clusters of plaque in the inner walls of coronary arteries. This reduces the blood flow to the cardiac muscle and thus impairs the oxygen supply to the heart, leading to symptoms ranging from chest pain to a life-threatening heart attack [1].

Myocardial perfusion imaging (MPI) is one of the most common SPECT techniques; it is particularly valued for its diagnostic accuracy. MPI can be used in the diagnosis of CAD, in the evaluation of the severity and prognosis of the condition, as well as in the follow-up of invasive operations. MPI helps the clinician to come to an early diagnosis due to its high sensitivity. Since it is a noninvasive technique, it is not unpleasant for patients [2]. It has also been shown that a patient with a normal MPI study has a very low risk of suffering a myocardial infarction (<1 %), and therefore unnecessary invasive investigations can be avoided [3]. Finally the use of MPI in the diagnosis and management of CAD has been found to be cost-effective [4, 5].

There are several detrimental image-related factors that affect the image quality of MPI; the most significant are image noise, photon attenuation, Compton scatter, collimator-detector response (CDR) and patient motion [6-8]. Image noise and CDR reduce the image quality, especially with low count density studies that are a common situation in obese patients. On the other hand photon attenuation can cause false perfusion defects in the myocardium and therefore this is likely to reduce the diagnostic accuracy of the technique [9, 10]. Compton scattering affects unfavorably on image contrast, but one also needs to take
into account the fact that scattering and attenuation are linked; as Compton scattering is usually the leading cause of photon attenuation at the energies of the radionuclides used in MPI. From a quantitative point of view, attenuation and scatter partly act in opposite directions as uncorrected attenuation reduces the detected counts and therefore the estimation of the activity distribution becomes too low, while uncorrected scatter corruption means that extra counts may be detected and thus cause an overestimation of the activity distribution [11]. Patient motion differs from the other significant artefact-generating factors because it can be often prevented with the provision of detailed instructions and careful positioning of the patient. When present however, patient motion can cause severe artefacts with false defects or distortion of the myocardium [12].

Over the years, several different approaches have been proposed to correct the artifacts created by one or more of these phenomena. These compensation approaches have often proved to be extremely useful. If one is able to compensate for attenuation, scatter and collimator response then the myocardial perfusion defect detection performance can be greatly improved [10, 13-15]. Recently CDR compensation in particular has attracted considerable attention for another reason. It has been shown that with CDR compensation it is possible to increase the image quality to the extent that diagnostically satisfying images can be acquired in a half or even a quarter of the acquisition time currently in use [16-23]. This would represent a very favorable advance as shorter acquisition times are advantageous in those patients who find it difficult to remain motionless during MPI acquisitions, reducing thus possible motion artefacts. Shorter scan times would also allow more patients to be imaged every day. The other option would be to keep the current imaging time fixed, but to reduce the injected activity to half, i.e. halving the radiation dose given to the patient which would also be a way to reduce radionuclide and radiopharmaceutical costs.

In this thesis the current state-of-the-art MPI reconstruction and compensation methods were studied and further optimised. Special attention was focussed on approaches
which could reduce the scanning time. The possible interference of different compensation methods was evaluated and new approaches were examined as ways to avoid the artefacts generated by the compensation methods.
2 SPECT reconstruction

2.1 FILTERED BACK PROJECTION (FBP)

Filtered back projection (FBP) is a fast and straightforward method for reconstruction of the acquired SPECT data. It used to be the most common reconstruction method in clinical practice. FBP can accurately calculate the inverse Radon transform that is the analytical solution of the reconstruction problem. The main problem with FBP in SPECT reconstruction is the lack of noise modelling, which leads to streak artefacts in the reconstructed images [24, 25]. In addition FBP-based reconstruction methods are not totally able to incorporate corrections for all of the physical effects that impair the SPECT image quality.

2.2 ITERATIVE RECONSTRUCTION

In comparison to analytical reconstruction methods such as FBP, iterative methods approach the reconstruction problem from a totally different perspective. Iterative reconstruction methods are based on optimizing the fit between the reconstructed image and the measured projections. The tomographic image is updated iteratively by comparing it to the measured projections, with the help of a special projector. Figure 2.1 shows the basic principle underpinning iterative reconstruction methods.

First an initial estimate is made of the object’s count distribution; e.g. this can be a uniform count level. This estimate is then converted into projections by forward projection in order to obtain an estimate of what the detector would measure given the initial object. This estimate of projections is compared with the measured projections and the ratio is used to adjust the initial estimate. This adjustment is usually being conducted after back projection of the ratios. The modified estimate becomes the
new starting point for the second iteration and the same process is repeated for multiple iterations until a final solution is reached. Usually the iterative reconstruction loop ends after a predetermined number of iterations have been completed [24, 25].

![Figure 2.1. The basic principle of iterative reconstruction methods.](image)

The advantages of iterative reconstruction algorithms are that they allow direct noise modeling, as well as inclusion of different correction methods such as attenuation and scatter correction. Iterative methods also reduce streaking artifacts and are able to handle truncated data. The main drawback with the iterative methods is their calculation time, which is considerably slower than with FBP. However, increased computer speed and previously devised acceleration techniques have allowed iterative methods to become the most common reconstruction techniques being used in clinical practice with SPECT imaging [26].
2.2.1 Maximum Likelihood Expectation Maximization (ML-EM)

The Maximum likelihood expectation maximization (ML-EM) algorithm assumes that the projection pixel values are distributed according to the Poisson distribution, which is a reasonable assumption for emission data, considering the random nature of photon emission. The use of the Poisson model also guarantees non-negativity even with low count levels [25].

With the Poisson model, the conditional probability that measured projections $P$ are acquired from the emission object $f$ can be represented as the product of probabilities for individual projection pixels:

$$L(P|f) = \frac{e^{-f}f^P}{P!} = \prod_i \exp\left[-\sum_j a_{ij}f_j\right]\left(\sum_j a_{ij}f_j\right)^{p_i} \left(p_i!\right)^{-1}, \quad (2.1)$$

where $f_j$ is the count distribution that is emitted from a voxel $j$, $p_i$ is the detected counts of the projection pixel $i$ and $a_{ij}$ is the probability that a photon emitted by voxel $j$ is detected in pixel $i$ [27, 28].

There are several methods of defining the maximum likelihood solution, but the most commonly used is the expectation maximization algorithm that is presented in equation 2.2:

$$f_{j}^{new} = \frac{f_{j}^{old} \sum_i a_{ij} \sum_k p_i}{\sum_l a_{lj} \sum_k a_{ik} f_{k}^{old}}, \quad (2.2)$$

where $f_{j}^{new}$ is the new number of counts for voxel $j$ and $f_{j}^{old}$ is the number of counts of previous iteration for voxel $j$ [27, 28]. The matrix $A$ with elements $a_{ij}$ is called a transition matrix. The transition matrix presents a model of how the radiation is emitted and interacts in a patient before being detected in the gamma camera.
The algorithm follows the same principle as shown in figure 2.1; in the algorithm, the expected projections are generated by forward projection of the estimate of the count distribution from the previous iteration using the transition matrix. The current estimate is then updated to maximize the likelihood, which is achieved by multiplication of the previous estimate after back projecting the ratio of measured and estimated projections. The compensation methods that are included in the iterative reconstruction process are inserted into the transition matrix [25].

2.2.2 Ordered Subsets Expectation Maximization (OS-EM)

An iterative reconstruction can be accelerated with block iterative methods; of them the Ordered Subsets Expectation Maximization (OS-EM) algorithm is the most common. The most significant difference between OS-EM and ML-EM is that OS-EM breaks the data up into subsets of the projections. These projection subsets are sequentially used to update the image so that the result of a previous subset is used as an initial estimate for reconstruction with the next subset. Therefore updating the image estimate in OS-EM involves less computation than in ML-EM. OS-EM can be presented as

$$f_j^{\text{new}} = \frac{f_j^{\text{old}}}{\sum_{i \in S_n} a_{ij} \sum_{i \in S_n} a_{ij}} \sum_{k} a_{ik} f_k^{\text{old}}$$

(2.3)

where $S_n$ is the number of projections in subset n with all the other parameters being the same as in equation 2.2. OS-EM has been shown to converge to an image that is nearly identical to ML-EM algorithm image, but it requires much fewer iterations and thus it is much faster [26].
2.2.3 Noise control approaches

The ML-EM algorithm aims to fit the reconstructed image to the measured projections as well as possible, but a fit to noisy projections leads to noisy image. As the number of iterations increases, the reconstructed image becomes closer to the true object distribution, but at the same time, the noise level increases. In order to control noise in SPECT images, several methods ranging from post-filtering the reconstructed image with noise-suppressing filters to Bayesian reconstruction algorithms have been described [29-34].

Bayesian methods suppress noise by incorporating prior knowledge of the reconstructed activity distribution into the reconstruction algorithm. The prior knowledge is usually simple assumptions such as the voxel value should be similar to those around it, but it can also be based on anatomical information obtained from a CT or MRI scan. With anatomical priors, the aim is to control the noise in the reconstructed image while maintaining contrast at anatomical boundaries. The prior knowledge is presented in the form of probability density functions and Bayesian methods usually try to maximize the posteriori probability density function, which is a product of the prior distribution and the likelihood [35].

The posteriori probability density function can be maximized with the one-step-late (OSL) algorithm. OSL is a practical procedure and different prior models can be easily combined into the algorithm, although OSLs convergence is not guaranteed. The OSL algorithm can be expressed as:

$$f_j^{new} = \frac{f_j^{old}}{\sum_{i \in S} a_{ij} + \beta \frac{\partial U(f^{old})}{\partial f^{old}}} \sum_{i \in S} a_{ij} \frac{p_i}{\sum_k a_{ik} f_k^{old}},$$  \hspace{1cm} (2.4)

where \( \frac{\partial U(f^{old})}{\partial f^{old}} \) is the derivative of the energy function, which defines the prior [36].

A common approach to define a Bayesian prior is to use the Gibbs distribution, which can be defined as
where \( \text{prob}[f_j] \) indicates the conditional probability for the value of the voxel \( j \) given the rest of the image, \( Z \) is a normalization constant, \( \beta \) defines the strength of the prior, and \( U \) is the energy function [37, 38]. As \( f \) meets the prior assumptions, energy function \( U(f) \) has its minimum while the prior has its maximum. \( U() \) is often computed using a potential function \( V() \), which describes the pixel differences in the neighbourhood \( N_j \):

\[
U(f, j) = \sum_{i \in N_j} w_{ji} V(f_j - f_i),
\]

(2.6)

where \( w_{ji} \) is the weight of a pixel \( i \) in the neighbourhood of pixel \( j \) [35].

### 2.3 COMPENSATIONS

#### 2.3.1 Attenuation

Attenuation occurs as some photons emitted by the radiopharmaceutical interact with tissue and other materials as they pass through the body, and are not detected. Photon attenuation is affected by the photon energy, the atomic structure and the density of the medium. Attenuation is a major problem in SPECT imaging, since it will reduce the quantitative accuracy [39, 40]. Attenuation decreases the amount of detected counts, distorting the acquired image, and it can create false-positive defects. The amount of attenuation differs depending on the tissue path-length and the type of tissue that the emitted photon encounters before it is detected [40].

Photon attenuation can be expressed by the exponential equation:

\[
I = I_0 e^{-\int_0^L \mu(x) dx},
\]

(2.7)
where $I_0$ is the initial intensity of the radiation, and $\mu_x$ is the linear attenuation coefficient at a location $x$. The limits of integration go from the point of emission to the edge of the body, $b$. The linear attenuation coefficient describes the probability that the photon undergoes an interaction while traveling through a unit thickness of absorbing material.

There are several ways to attempt to correct the photon attenuation in SPECT data, but in order that the correction should be reliable then an attenuation map is required. The attenuation map represents the spatial distribution of linear attenuation coefficients ($\mu$ in equation 2.7) and specifically outlines the structures in the body for the region included in the SPECT image [39]. Attenuation correction is performed by incorporating attenuation in the system model during the forward- and backprojection process by modeling the path of photons according to equation 2.7.

CT-based attenuation map is currently the most commonly utilized attenuation map type nuclear medicine. CT image is well suited for this since it represents the 3D spatial distribution of attenuation coefficients in the patient [41]. However a CT image cannot be used as an attenuation map unless one has taken into account the specific characteristics of CT scan; the use of Hounsfield Units (HU) represents the CT image by tissue types rather than the measured linear attenuation coefficients [39]. The relationship between tissue type and the approximated value in HUs is relatively independent of the parameters being used to generate the CT image. HU values are defined by

$$HU(x,y) = \frac{\mu_{CT}(x,y) - \mu_W}{\mu_W} \times 1000,$$

where $HU(x,y)$ is the Hounsfield unit value of the CT scan at location $(x,y)$, $\mu_{CT}(x,y)$ is the linear attenuation coefficient at location $(x,y)$ obtained from the raw CT image and $\mu_W$ is the corresponding value of the linear attenuation coefficient in
Before a clinical CT scan can be transformed into a patient-specific attenuation map, it needs to be modified so that it is expressed in terms of the linear attenuation coefficient of the corresponding material for the energy of the radionuclide photon [25]. This is achieved by acquiring a CT scan of a phantom containing materials whose attenuation coefficients are known. HU values for these materials are then defined and the attenuation coefficient, HU value-pairs are plotted. Two lines (one for bone and one for soft tissue) are fitted to the plotted data in order to obtain the calibration equations.

In order that the attenuation correction should be reliable, the CT and SPECT slices have to be carefully aligned [42]. If the organs and tissues in the scans do not align, then this will lead to either over- or under-compensation of the SPECT data. One major challenge encountered here is the different acquisition times of the SPECT and CT scans; while SPECT acquisition can take 10-30 minutes, a CT scan is completed in a matter of seconds. For example respiratory movement during the SPECT scan leads to somewhat average position/size of the lungs in the image, but during the CT scan patient can be told to hold his/her breath. It is therefore recommended to check the alignment of the SPECT and CT data before performing the attenuation correction [42].

2.3.2 Scatter
Compton scattering is the main phenomenon which leads to scatter in SPECT scans. Coherent scatter is usually ignored since its effect is rather negligible. In Compton scattering, a photon loses energy and changes its direction after undergoing an interaction with tissue or some other matter. One consequence of Compton scattering is that the photon may be detected incorrectly on the detector or fail to be detected at all [25]. Scattering reduces the image contrast and the quantitative accuracy of the image. Scattering occurs not only in patients, but also in support structures, collimators and detector material. The scattered photon can also undergo multiple interactions.
before detection, and the emission site of the detected photon may be out with the field of view of the scanner [11].

The scatter compensation usually aims to increase the accuracy of activity quantitation and/or increase the image contrast. The scatter compensation methods can be broadly divided into two classes: energy window-based methods and reconstruction-based methods. In energy window-based methods, the scattered counts are detected by using scatter energy windows placed below and also possibly above the primary photo peak window [43, 44]. Scatter can be either subtracted from the primary peak window or preferably the scatter window data can be used in an iterative reconstruction in the forward projection process as an estimate of scatter [11].

The scatter compensation approaches that are based on iterative reconstruction can utilize the attenuation map to model the scattering in mathematical terms. The advantage of scatter modeling is its better image contrast and smaller noise level as compared to the scatter window-based methods [45]. The challenge of the reconstruction-based methods is the large calculation capabilities that they require; the scatter estimation is incorporated directly into the transition matrix in the reconstruction method’s equation, and therefore it becomes considerably larger thus slowing down the computation [46-49]. The method’s efficiency can be improved with a dual matrix approach, in which scatter is incorporated only in the forward projection step [50]. This method requires that the scatter response function is computed at each point in the attenuator for all projection views and iterations. In order to speed up the calculation time, the correction factors can be calculated only once or a few times, given that the calculated scatter component is virtually constant after the first few iterations [45]. Thus the ML-EM equation can be written as:

\[
\hat{f}_j^{\text{new}} = \frac{f_j^{\text{old}}}{\sum_i a_{ij} \sum_j a_{ij} \sum_k a_{ik} \hat{f}_k^{\text{old}}} + \hat{s},
\]

(2.9)

where \(\hat{s}\) is the scatter estimated on all projections [11, 25, 51].
2.3.3 Collimator detector response

Unlike photon attenuation and scatter, the collimator detector response (CDR) does not depend on the patient, instead it originates from collimator-detector settings and the energy of the photon. Collimation causes a point source to become distorted in the image due to the point spread function of the collimator. CDR is the primary source for specifying the resolution of a SPECT scan. In SPECT systems, CDR consists of four components: intrinsic response, geometric response, septal penetration and septal scatter. The CDR function \( d(\vec{x}, \vec{r}) \) represents the probability that radiation emitted from a point source at position \( \vec{r} \), will be detected at some point in the detector \( \vec{x} \). This can also be represented by four components:

\[
d(\vec{x}, \vec{r}) = \iint i(\vec{x}, \vec{x}') (g(\vec{x}, \vec{r}) + p(\vec{x}, \vec{r}) + s(\vec{x}, \vec{r})) d\vec{x},
\]

where \( i(\vec{x}, \vec{x}') \) is the intrinsic response function (IRF) of the gamma camera, which describes the probability that a photon emitted from a position \( \vec{x}' \) will be detected at \( \vec{x} \). Functions \( g(\vec{x}, \vec{r}), p(\vec{x}, \vec{r}) \) and \( s(\vec{x}, \vec{r}) \) refer to the geometric response function, (GRF), septal penetration response function (SPRF) and septal scatter response function (SSRF) respectively. GRF describes the probability that a photon emitted at \( \vec{r} \) will pass through the collimator hole, while SPRF and SSRF describe the probability that the same photon will pass through the septa without interacting with its material or scattering in the septa respectively, resulting in the photon being detected at \( \vec{x}' \) [25].

A common assumption is that in planes parallel to the collimator surface, the response functions are spatially invariant, and the intrinsic response is spatially invariant in the detection plane. This allows equation (2.10) to be written as:

\[
d(\vec{x}; D) = i(\vec{x}) \otimes (g(\vec{x}; D) + p(\vec{x}; D) + s(\vec{x}; D)),
\]

where \( \otimes \) denotes the convolution operation.
where $D$ is the distance between the plane of detection and the source plane [25].

IRF is the response of the gamma camera with collimators absent to a pencil beam of radiation. It can be defined by the uncertainty of the position estimation in the camera-detector system and by the scattering effects in the crystal. The scattering effects are minor for low-energy isotopes, but become relevant with medium or high energy isotopes. The uncertainty of the position estimate is defined by the noise in the signals in the photomultiplier. The noise is attributable to the two factors: statistical variation in the production and collection of scintillation photons, and the method used for the position estimation. The crystal’s efficiency in detecting photons is a function of the energy of the incident photon, the energy window in use and thickness and composition of the crystal. This can be expressed as the integral of the IRF [25].

Those detected photons that have passed through the collimator holes without interacting with the collimator septa are described by the GRF. Two factors can be used to describe the GRF in general: the GRF of a given hole in the collimator and the pattern of the holes. In the case of low energy collimators, the septal thickness is generally small in comparison to the intrinsic resolution and the aspect ratio of the collimator. This allows the use of average GRF. The averaging can be performed during the derivation of the GRF and it is equivalent to moving the collimator during acquisition [52, 53].

For parallel-hole collimators, the Fourier transform of the average GRF is related to the product of the Fourier transform of the aperture function that describes the collimator holes:

$$G(\vec{v}; D) = \mathcal{F}\{ A\left(\frac{D + L + B \vec{v}}{L} \right) \},$$

(2.12)

where $G(\vec{v}; D)$ is the 2D Fourier transform of the GRF for a source at distance $D$ from the collimator surface, $A$ is the 2D
Fourier transform of the aperture function, $L$ is the thickness of the collimator, $B$ is the distance between the back face of the collimator and the detection surface, $\varepsilon$ is the efficiency of the collimator and $\bar{v}$ is the spatial frequency [25].

Equation (2.12) shows that while the shape of the GRF remains fundamentally the same, the size of GRF is linearly related to the distance $D$, and the symmetry of the GRF is the same as for the aperture holes. GRF is thus radially symmetric only to round holes. However it has been shown that if the hole-area of a round hole and a hexagonal hole is the same, then the GRF for hexagonal holes can be approximated using the GRF for round holes [54]. This has advantages, i.e. for round holes, the spatial version of the response function can be computed analytically:

$$g(r; D) = \frac{\varepsilon}{\pi} \left( \frac{2\cos^{-1} \left| \frac{r_T}{2R} \right|}{R} \sqrt{1 - \left| \frac{r_T}{2R} \right|^2} \right),$$  \hspace{1cm} (2.13)$$

where $R$ is the collimator hole radius, $r$ is the distance between the detection plane and the intersection of the line perpendicular to the detection plane containing the source, and $r_T$ is given by:

$$r_T = r \frac{L}{D + L + B},$$  \hspace{1cm} (2.14)$$

SPRF describes those detected photons that have penetrated through the collimator septa, and SSRF is related to the photons that have scattered in the collimator septa before being detected in the detector crystal. Both of these functions are very challenging to treat theoretically, but they can be analyzed using Monte Carlo (MC) simulations [55, 56]. The effects of both SPRF and SSRF become more important with medium and high energy isotopes.

The effect of CDR in a SPECT scan is rather complex as it depends on the distance between the source and the collimator. When the compensation of CDR is included in the iterative
reconstruction algorithm, the effect of CDR is incorporated into the transition matrix. The transition matrix often becomes too large to be stored on current general purpose computers, and thus CDR modeling is often performed in a so-called on-the-fly manner during forward- and back-projections [57].

2.3.4 Motion
Patient motion during SPECT acquisition is considered to be a major cause of artefacts that can reduce the diagnostic accuracy of SPECT. There are different kinds of motion, in general they can be divided into either rigid-body motion, which can be considered as a combination of translation and rotation, e.g. movement of the patient body, or non-rigid, sometimes termed non-linear body motion that needs more complex modelling, such as respiratory movement.

There are a number of different approaches which can be used to correct the motion. For example software based methods that can be further divided into manual, semi-automatic and automatic approaches. There are also hardware based methods although these are considered as less useful in clinical practice [10, 12, 58, 58-61]. At present automatic techniques that use reconstruction-reprojection fitting are considered to be the most successful motion correction methods.

The motion compensation can be performed using reconstruction-reprojection-based algorithms. These methods try to find the displacement for each projection which minimises the difference between the measured and the reconstructed-reprojected projection. The difference is expressed with a cost function, which is at its minimum at a point where the original projection and the displaced reprojection match. The corrected data is then formed by translation of each acquired projection by its corresponding displacement value [12, 62, 63].

Motion compensation methods are not perfect and patient motion should be kept to a minimum by careful positioning, instructing the patient to avoid moving during the scan and undertaking shortest possible acquisition times that yield acceptable data quality. Respiration and organ induced motions are often unavoidable. Motion compensation methods
for these types of movements are currently an area of extensive research but none of these methods has gained widespread acceptance in the SPECT community [10, 12, 58, 59].
3 Myocardial perfusion imaging

MPI is one of the most common SPECT studies. It has achieved popularity due to its diagnostic properties in patients with coronary artery disease (CAD), which remains one of the most common causes of death in the developed countries. MPI is used in diagnosing of CAD, and in the evaluation of the severity and the prognosis of the condition, as well as in the follow-up of invasive operations. With MPI early diagnosis is possible due to its high sensitivity and since it is a noninvasive procedure, it is convenient for patients [2]. It has also been shown that a patient with a normal MPI study has a very low risk of suffering a myocardial infarction (<1 %), and therefore invasive investigations in this kind of patient can be avoided [3]. Finally the use of MPI in the diagnosis and management of CAD is cost-effective [4, 5].

The basic principle of MPI is to determine the detectable perfusion defects of the myocardium by combining the information of myocardial perfusion during exercise and rest. The diagnosis of CAD is made by detecting a relatively decreased myocardial perfusion as compared with the more normally perfused myocardium. The stress procedure can be accomplished by either exercise or pharmaceutical agents. Stress imaging is crucial, as even severe stenosis does not necessarily produce detectable blood flow defects at rest [64]. However if the stress scan is normal, then one does not need to perform the MPI at rest.

There are two radionuclides that are used for clinical MPI with SPECT; thallium ($^{201}$Tl) and technetium ($^{99m}$Tc). Both of these isotopes have their own advantages and drawbacks which are presented in table 3.1. Although the principle of MPI remains the same, the significant differences in the biokinetic
properties of the two isotopes affect the imaging protocols that are used. A major factor for choosing the protocol is the behavior of the radiopharmaceutical; does it remain fixed in the myocardium, wash out or redistribute in the myocardium over time. Thus the radiopharmaceutical affects almost every aspect of a MPI study [42, 64, 65].

Table 3.1. The properties, advantages and disadvantages of $^{201}$Tl and $^{99m}$Tc labelled radiopharmaceuticals in MPI.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>$^{201}$Tl</th>
<th>$^{99m}$Tc labelled radiopharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Properties</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Half-life</td>
<td>about 73 h</td>
<td>Half-life about 6 h</td>
</tr>
<tr>
<td>Three photon</td>
<td></td>
<td>One photon peak: 140 keV</td>
</tr>
<tr>
<td>peaks: 72,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>135 and 167 keV</td>
<td></td>
<td>One photon peak: 140 keV</td>
</tr>
<tr>
<td>3-4% of injected activity accumulates in the myocardium</td>
<td></td>
<td>1.5% of injected activity accumulates in the myocardium</td>
</tr>
<tr>
<td>Active transport through cell membrane</td>
<td></td>
<td>Passive diffusion</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personnel</td>
<td></td>
<td>Lower dose to patients</td>
</tr>
<tr>
<td>exposed to lower doses</td>
<td></td>
<td>Better image quality</td>
</tr>
<tr>
<td>Long imaging</td>
<td></td>
<td>Higher count density</td>
</tr>
<tr>
<td>period</td>
<td></td>
<td>Shorter acquisition time</td>
</tr>
<tr>
<td>Lower liver/bowel activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Redistribution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good for viability evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good linearity/high extraction fraction</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td></td>
<td>Personnel exposed to higher doses</td>
</tr>
<tr>
<td>Higher dose to patients</td>
<td></td>
<td>High splanchnic/intestinal activity</td>
</tr>
<tr>
<td>Long acquisition time</td>
<td></td>
<td>Two injections needed if rest scan has to be obtained</td>
</tr>
<tr>
<td>Low count density</td>
<td></td>
<td>Limited linearity/small extraction fraction</td>
</tr>
<tr>
<td>Poor contrast resolution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased attenuation effects</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MPI in order to collect information about left ventricle function and wall motion. Good quality gated data requires (semi)stable heart rate [42, 64-66].

In order to maximize MPI’s usefulness, the image degenerating factors, attenuation, scattering, CDR and motion, need to be taken into account. Attenuation correction is now considered a routine procedure in MPI reconstruction and it is highly recommended [42, 67]. Photon attenuation can cause false perfusion defects in the myocardium, and is therefore likely to reduce the diagnostic accuracy of the study. In female patients, attenuation artifacts appear mainly in the anterior part, the lateral part and/or in the apex of the left ventricle, whereas in male patients, attenuation artifacts are usually encountered in the inferior part of the left ventricle [6, 7, 42, 68].

In nuclear medicine imaging, scattering and attenuation are partly linked, as Compton scattering is usually the primary cause for photon attenuation. Previously the main image detrimental effect of scattering was considered to be the loss of image contrast [11]. Somewhat later it was understood that scattering also causes a complicated distortion in at least parts of the image. In MPI, this effect can cause a significant change in the counts in attenuation corrected images with a distortion that slightly increases the amount of apparent counts from apex towards the base of the heart [69].

Collimator and detector blurring reduce the resolution of the SPECT images. In MPI, this can be seen as thickened myocardial walls. Correcting the CDR in the reconstruction improves the resolution and also improves the signal-to-noise ratio [6, 7, 42]. Current resolution recovery methods have made possible the use of shorter acquisition times, which also help to reduce the motion artefacts [16, 19, 22, 70]. Figure 3.1 shows an example of the effects of compensations on the cardiac SPECT image.
Figure 3.1. An example of the effects of the compensation methods on cardiac SPECT image. Image A shows a transverse slice of a cardiac SPECT scan of a mathematical phantom reconstructed with an iterative method without any compensations. In this slice, the activity of the lungs is excessively high, and the myocardial walls are too thick. The lung activity is reduced in image B, which shows the same slice but with incorporation of attenuation correction. The myocardial wall resolution is increased in image C, as attenuation and collimator compensations have been applied. The best contrast is demonstrated in image D where attenuation, collimator response and scatter corrections have been conducted.

In MPI, motion artefacts are considered to be a major problem. Motion can occur during cardiac imaging for several reasons, i.e. body motion, respiratory movement, cardiac contraction and vertical creep. It has been shown that a 1-pixel movement during MPI is likely to cause visible motion artefacts,
but these are not always clinically important. A more than 2-pixel (>13 mm) movement however is likely to cause severe image artefacts [12, 59, 71].
4 Aims

The aim of this thesis was to validate and optimize novel SPECT reconstruction and compensation techniques for MPI. The specific focus was on obtaining a scan time reduction and on CDR compensation.

In the first part of this thesis, the effect of acquisition time reduction achieved with CDR compensation was studied in combination with the MC-based scatter compensation. MC is a statistical technique which is dependent on the noise level of the MPI study. The noise level in projections increases when acquisition time is reduced.

The MC-based scatter compensation tested in the first part was further extended to dual $^{99m}$Tc/$^{201}$Tl MPI studies in the second part of the thesis. Dual $^{99m}$Tc/$^{201}$Tl acquisition offers several advantages including the possibility to exploit the benefits of both isotopes, as well as obtaining a perfect image registration and identical physiological properties between stress and rest images. The problem in dual isotope studies is the cross-scatter between the isotopes, which seriously impairs the image quality if not compensated. The efficacy of this compensation was evaluated.

Even with reduced scan times, patient motion may still occur, leading to artefacts that can be falsely interpreted as perfusion deficits, as well as causing false distortion of the myocardium in the acquired images. The third part of this thesis focused on reconstruction-based motion correction in MPI-imaging. Different motion correction methods were studied and optimized in terms of their performance and speed.

Despite its many advantages CDR compensation can also lead to artefacts that can be falsely classified as abnormal radiopharmaceutical uptake. In the fourth and final part of this thesis, novel methods were developed in attempts to reduce the CDR compensation artefacts.
5 Materials and methods

5.1 The Effect of Monte Carlo-Based Scatter Correction on Half-Time Myocardial Perfusion SPECT Imaging (Publication I)

In the first part of the thesis, scatter corrected half-time MPI was studied with phantom modelling and patient studies. The focus was on testing the potential of a MC-based scatter correction [45] in half-time imaging. The MC-based scatter correction is performed by calculating the factor $s$ in equation 2.8 using a MC-simulator. As a statistical method, MC-based scatter compensation may increase the noise level of the reconstructed images, especially when there is a low number of counts per projection.

Three phantoms were created with the 4-dimensional NURBS-based Cardiac-Torso (4D NCAT) program obtained from the University of North Carolina [72]. One of the phantoms modelled normal perfusion and the rest had one perfusion defect each. Full- and half-time MPI studies were simulated with SIMIND Monte Carlo simulation package [73] and the data were reconstructed with the HERMES HybridRecon-Cardiology program (HERMES Medical Solutions, Stockholm, Sweden). Each phantom was reconstructed without any corrections and with attenuation, scatter and collimator response corrections.

The MC-based scatter correction was performed with 100 000 and 1 000 000 simulated photons to study the effects of the number of simulated photons on image quality. The reconstructed data were tested by defining contrast values for lesion-to-healthy myocardium and ventricle-to-healthy myocardium, and by defining the thickness of the myocardial wall, which served as a measure for the resolution of the reconstructed image.

In the patient studies, 15 female and 15 male patients who had earlier undergone a gated rest MPI study were
randomly selected. Non-gated half- and full-time image data were created from the gated studies by adding every second or every gating frame respectively of the 16 gated frames defined. The reconstruction was performed with the HERMES HybridRecon-Cardiology program, with and without corrections. For the evaluation of the reconstructed data, four experienced nuclear medicine experts were asked to provide an individual grade assessing the image quality for every dataset on a scale from 1 to 5, with 5 being the best grade.

5.2 Monte Carlo-Based Scatter Correction in Simultaneous 201Tl/99mTc Myocardial Perfusion SPECT Reconstruction (Publication II)

Dual isotope imaging with separate or simultaneous acquisition has attracted considerable interest [44, 74-83], since it confers many advantages. While separate dual-isotope acquisition has been validated for clinical use [84, 85], there is no clear consensus on the best way to correct for the down-scatter effect of simultaneous 201Tl/99mTc imaging.

The reconstruction algorithm used in the first part of this thesis was extended into 201Tl/99mTc dual isotope reconstruction by splitting the reconstruction into three steps: 1) 99mTc reconstruction, 2) MC-based 99mTc down-scatter simulation into the 201Tl window and 3) 201Tl reconstruction incorporating the down-scatter estimate. The effect of the upper 201Tl energy peak was ignored, since only 2-4\% of 201Tl photons are detected in the 99mTc window [78]. The 99mTc reconstruction should provide a scatter-free 99mTc isotope distribution, which is then used as an input for the down-scatter-modelling from 99mTc into the 201Tl window. This down-scatter estimate is then added into the 201Tl reconstruction to the 201Tl self-scatter estimate.

The MC-simulator performance affects greatly on the time needed for the dual-isotope reconstruction. The simulator was previously accelerated by technical modifications, but the calculation time can be further reduced by optimising the number of simulated photons and the number of scatter update
iterations needed in order to obtain a good quality image. One needs to perform the optimisation separately for each of the three aforementioned steps. Both mathematical and physical cardiac phantoms were used in conducting this optimisation. All the reconstructed data were tested by defining contrast values for lesion-to-healthy myocardium and ventricle-to-healthy myocardium.

Four female and four male 4D NCAT phantoms were created to simulate different outcomes of stress-$^{201}$Tl/rest-$^{99m}$Tc dual isotope MPI, with both reversible and irreversible defects and with a hot liver in the $^{99m}$Tc data. The simulation of the projection data was generated with a MC-simulator developed in-house [86]. Noise-free projections for dual-isotope data and pure $^{201}$Tl data were created, and Poisson-noise was added after the simulations in order to create more realistic count densities for the data.

In the optimization of the dual-isotope reconstruction, the three steps were optimised separately. First, the $^{99m}$Tc reconstruction simulated data was reconstructed with different parameter combinations: Two different scatter update iterations of 2 and 10 were tested, with $10^5$ and $10^6$ simulated photons. The number of down-scatter simulated photons was held constant at $10^6$. Subsequently, the number of down-scatter simulated photons was optimised with $^{201}$Tl reconstruction with $10^5$, $10^6$ and $10^7$ down-scatter simulated photons. Scatter update iterations and the number of $^{201}$Tl scatter photons were kept constant at values 10 and $10^6$ respectively.

Finally the effect of scatter update iterations and the number of simulated photons in the $^{201}$Tl reconstruction were examined. The previously optimised $^{99m}$Tc reconstruction and down-scatter simulation parameters were exploited on the two first steps of the reconstruction. $^{201}$Tl reconstruction was optimised by comparing 2 and 10 scatter update iterations and with $10^5$ and $10^6$ simulated photons.

In order to verify the results of the simulation study, the Jaszczak phantom with a cardiac insert with fillable defects (Data Spectrum Corporation, Hillsborough, NC, USA) was used. A reversible defect in the anterior wall and an irreversible
defect in the inferior wall of the cardiac insert were inserted for the purpose of this study. Both dual-isotope data and pure $^{201}$Tl data were acquired with the same filled phantom, but the pure $^{201}$Tl data was acquired 72 hours after the dual isotope scan, when $^{99m}$Tc activity had nearly completely decayed. The projection time was increased to compensate for the decay in $^{201}$Tl activity.

The Jaszczak phantom dual isotope study was reconstructed using the parameters optimised with the simulated data. A similar contrast analysis was performed for the reconstructed data in the same way as the simulation data.

5.3 Motion Correction Optimisation for Cardiac SPECT (Publication III)

Two reconstruction-reprojection-based [12] motion correction algorithms were evaluated and optimised. The first method was the conventional algorithm that operates in the projection space. The reconstruction-reprojection method reconstructs and reprojects the original projection data in an iterative loop. The reprojected projections are considered as motion-free and the original projections are registered to them by minimizing a cost function. The horizontal and vertical translations achieved at the cost function minimum are applied to the original projections and a new iteration is started using the translated original projections. The final translations, obtained after the last iteration, are applied to the original data and the final reconstruction is run.

The second method performs the correction in image space; it is based on the ML-EM algorithm, which can be considered as a series of reprojections and backprojections. The algorithm combines motion estimation in the reprojection step by translating the image estimate before reprojection. Optimal horizontal and vertical translations are found by minimizing a cost function. The horizontal and vertical translations obtained from this registration are applied to the current image estimate.
and subsequently the ratio of original and reprojections is calculated. If the SPECT scanner has more than one detector, the motion information for each projection angle pair or group can be utilised to make the motion estimation more robust. The backprojection of the projection ratio is virtually identical to normal ML-EM, the only difference being that translations are applied during backprojection. After the motion compensated ML-EM algorithm is complete, translations are extracted and a final ML-EM reconstruction is performed using the final translations but without motion estimation.

The reconstruction-reprojection motion correction algorithm depends on the number of iterations and the cost function used for the registration. In order to optimize these two parameters, the motion correction algorithm was run with 1-20 iterations and with three different cost functions: squared difference, normalised cross correlation and mutual information.

Four patient rest MPI studies were selected that had no motion, which was verified by a nuclear medicine professional using cine, sinogram and linogram displays. Motion corrupted data was generated by adding different types of motion into the original data following the approach described by Matsumoto et al. [12]. Lateral shift, vertical shift and vertical creep motion of 25 mm were generated to gain severe motion artefacts.

For evaluation of the motion correction algorithms, the “Change”-option [87, 88] in the QPS-program (Cedars-Sinai Medical Center, Los Angeles, California) was applied. The images reconstructed from motion corrected projection data were compared to the images reconstructed from the original data without motion. The “Ischemia”-score provided by the algorithm gives the voxel-by-voxel estimation of perfusion differences between two registered scans and thus, if the motion correction worked perfectly, the “Ischemia”-score would be zero.
5.4 REDUCTION OF COLLIMATOR CORRECTION ARTEFACTS IN SPECT (PUBLICATION IV)

It has been observed that collimator response correction can generate severe Gibbs-like ringing artefacts (Figure 5.1). The collimator correction algorithm aims to recover fine details that have been lost because of the low spatial resolution of the gamma camera. The correction is not perfect, and thus can lead to over- and under-shoots near to object edges, generating the ringing artefacts [89, 90]. One possible solution to this is to use Bayesian reconstruction methods that can reduce these over- and under-shoots by favouring images whose adjacent pixel values are close to each other. In order to test these methods, two different physical phantoms and clinical data were used.

![Figure 5.1](image.png)

Figure 5.1. An example of the Gibbs-like ringing artefacts. Image A represents a reconstructed transverse slice of a phantom with active spheres with different diameters without any collimator response correction and image B shows a transverse slice with the collimator response correction. While the collimator response correction improves the image resolution, it generates an artefact that can be seen as a hole in the centre of the two largest circles, indicated by black arrows.

PTW-Freiburg’s PET/SPECT-Phantom (phantom 1), set T43004.1.008-0106 (PTW, Freiburg, Germany), which included a hot-sphere insert with six hollow glass spheres with inner, active diameters of 10, 13, 17, 22, 28, and 37 mm, though the phantom used in this study was missing the 13 mm sphere. The second phantom (phantom 2) was Veenstra Instruments’ SPECT-phantom model PS-101 (Veenstra Instruments, Joure, Netherlands) with three different inserts for image quality.
control: hot and cold lesion resolution inserts, and a linearity insert.

The reconstruction methods used in this work were based on the reconstruction engine of HERMES HybridRecon and included attenuation and detector response compensation. Three Bayesian reconstruction methods were evaluated: the quadratic smoothing prior, the median root prior and the Bowsher prior.

The quadratic smoothing prior’s penalty factor [91] was implemented in a relative form as

\[
c_j^p = \frac{1}{\sum_{i \in S_a} a_{ij} + \beta \frac{f_j^{\text{old}} - A_j}{A_j}},
\]

(5.1)

where \( A_j = \sum_{k \in N_j} w_{jk} f_k^{\text{old}} \)

\( N_j \) is the neighbourhood of voxel \( j \) and \( w_{jk} \) is the prior weight. The prior weights were defined as the inverse of the distance from the centre voxel.

The penalty factor for the median root prior can be expressed as:

\[
c_j^p = \frac{1}{\sum_{i \in S_a} a_{ij} + \beta \frac{f_j^{\text{old}} - M_j}{M_j}},
\]

(5.2)

where \( M_j \) is the median voxel value in the neighbourhood of voxel \( j \) [91].

The penalty factor of the Bowsher prior [34] is similar to the quadratic smoothing prior with the exception that the factor \( A_j \) is calculated using only \( B \)-number of voxels in the neighbourhood \( N_j \) that are most similar to the centre voxel \( j \) according to a similarity criterion. The most similar voxels were found by comparing the absolute difference in CT values [34, 92, 93].
Both phantoms were reconstructed using the OS-EM reconstruction algorithm with and without collimator response correction and using the three Bayesian reconstruction methods. In addition to the phantom studies, bone SPECT data was reconstructed with the same five algorithms to reveal the effect of the different reconstruction methods on clinical data. Bone SPECT data was used instead on myocardial perfusion SPECT data because anatomical priors work only if the CT and SPECT data resemble each other, which is the case in bone SPECT imaging.

The analysis was performed for phantom 1 by taking profiles through the active spheres and calculating contrast values for the four largest spheres. The images of phantom 2 and the clinical data were only evaluated visually.
6 Results

6.1 THE EFFECT OF MONTE CARLO-BASED SCATTER CORRECTION ON HALF-TIME MYOCARDIAL PERFUSION SPECT IMAGING (PUBLICATION I)

The results for phantom analyses in Table 6.1 reveal that the contrast values are highest for the corrected slices. The corrected half-time slices also produced higher contrast values than the uncorrected full-time slices. The myocardium wall thickness (i.e. the resolution) was better for the corrected data and furthermore it was not dependent on the acquisition time.

Table 6.1. The contrast values for the phantoms. The first column shows the dataset type, i.e. full- or half-time and the second column shows the position of the defect. The contrast values are given in percentage for uncorrected slices (NC) and corrected slices with 0.1 million and 1.0 simulated photons (0.1 million/1.0 million).

<table>
<thead>
<tr>
<th>Counts</th>
<th>Defect</th>
<th>Healthy wall vs. defect (%)</th>
<th>Healthy wall vs. ventricle (%)</th>
<th>Myocardial wall thickness (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NC</td>
<td>C</td>
<td>NC</td>
</tr>
<tr>
<td>HALF-TIME</td>
<td>anterior wall</td>
<td>12.0</td>
<td>24.7/30.2</td>
<td>90.3</td>
</tr>
<tr>
<td>FULL-TIME</td>
<td></td>
<td>13.8</td>
<td>28.6/27.5</td>
<td>92.1</td>
</tr>
<tr>
<td>HALF-TIME</td>
<td>inferior wall</td>
<td>27.5</td>
<td>30.5/30.3</td>
<td>92.2</td>
</tr>
<tr>
<td>FULL-TIME</td>
<td></td>
<td>27.6</td>
<td>33.3/33.1</td>
<td>92.2</td>
</tr>
</tbody>
</table>

The number of simulated counts in scatter correction had only a minor effect on the contrast and resolution values. Figure 6.1 shows example slices of the phantom data, where it is apparent that the defect is more visible in the corrected slices and the myocardium wall is thinner than in the uncorrected slices.
Figure 6.1. An example of the reconstructed slices in the phantom study. The upper row shows the corrected short axis slices and the lower row has the uncorrected slices of the phantom with an anterior defect.

The results for the patient data evaluation are presented in Table 6.2. The results support the phantom analysis as the corrected full-time slices were scored with the highest grades, while the uncorrected half-time slices had the lowest average grade. In addition the corrected half-time slices were again graded better than the uncorrected full-time slices. The statistical significance of the results was tested with SPSS 17.0 program (SPSS Inc., an IBM Company, Chicago, Illinois) by using the paired Wilcoxon sign test. All the results had p-values lower than 0.002. Figure 6.2 shows an example of the reconstructed slices.

Table 6.2. The results for the patient data evaluation. The table shows the average grades given for the uncorrected (NC) and corrected (C) slices in terms of image quality and the standard deviation (SD) of the grades.

<table>
<thead>
<tr>
<th></th>
<th>FULL-TIME</th>
<th></th>
<th>HALF-TIME</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NC</td>
<td>C</td>
<td>NC</td>
<td>C</td>
</tr>
<tr>
<td>Average grade</td>
<td>3.73</td>
<td>4.36</td>
<td>3.57</td>
<td>4.07</td>
</tr>
<tr>
<td>SD</td>
<td>0.40</td>
<td>0.56</td>
<td>0.53</td>
<td>0.68</td>
</tr>
</tbody>
</table>
Figure 6.2. An example of the reconstructed slices from the patient study. The upper row shows the corrected short axis slices and the lower row displays the uncorrected slices.

6.2 MONTE CARLO-BASED SCATTER CORRECTION IN SIMULTANEOUS $^{201}$TL/$^{99}$Tc MYOCARDIAL PERFUSION SPECT RECONSTRUCTION (PUBLICATION II)

The results for optimisation of the $^{99}$Tc reconstruction indicated that 2 scatter update iterations and $10^5$ simulated photons produce virtually identical images as compared to reconstruction with 10 scatter update iterations and $10^6$ simulated photons (Table 6.3).

Table 6.3. The contrast values for the $^{99}$Tc optimization. In this table, myocardium vs. defect and myocardium vs. left ventricle (LV) contrasts are presented for the $^{99}$Tc optimisation.

<table>
<thead>
<tr>
<th>Number of simulated photons in $^{99}$Tc reconstruction</th>
<th>Number of down-scatter simulated photons</th>
<th>Number of scatter update iterations</th>
<th>Myocardium vs. defect contrast</th>
<th>Myocardium vs. LV contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10^5$</td>
<td>$10^6$</td>
<td>2</td>
<td>0.74</td>
<td>0.97</td>
</tr>
<tr>
<td>$10^5$</td>
<td>$10^6$</td>
<td>10</td>
<td>0.73</td>
<td>0.97</td>
</tr>
<tr>
<td>$10^6$</td>
<td>$10^6$</td>
<td>2</td>
<td>0.73</td>
<td>0.97</td>
</tr>
<tr>
<td>$10^6$</td>
<td>$10^6$</td>
<td>10</td>
<td>0.73</td>
<td>0.97</td>
</tr>
</tbody>
</table>

The results for the down-scatter simulation optimisation demonstrated that $10^6$ simulated down-scatter photons provided
contrasts and down-scatter projections that were nearly identical to the $10^7$ simulated down-scatter photons. For the $^{201}$Tl reconstruction two scatter update iterations and $10^5$ simulated photons are sufficient in order to obtain good quality results (Table 6.4).

**Table 6.4.** The contrast values for the $^{201}$Tl optimization. In this table, myocardium vs. defect and myocardium vs. left ventricle (LV) contrasts are presented for the $^{201}$Tl reconstruction optimisation.

<table>
<thead>
<tr>
<th>Number of simulated photons</th>
<th>Number of down-scatter simulated photons</th>
<th>Number of scatter update iterations</th>
<th>Myocardium vs. defect contrast</th>
<th>Myocardium vs. LV contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10^5$</td>
<td>$10^6$</td>
<td>2</td>
<td>0.68</td>
<td>0.89</td>
</tr>
<tr>
<td>$10^5$</td>
<td>$10^6$</td>
<td>10</td>
<td>0.67</td>
<td>0.89</td>
</tr>
<tr>
<td>$10^6$</td>
<td>$10^6$</td>
<td>2</td>
<td>0.67</td>
<td>0.89</td>
</tr>
<tr>
<td>$10^6$</td>
<td>$10^6$</td>
<td>10</td>
<td>0.68</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Optimised and non-optimised reconstructions were compared to reconstructions from dual isotope data without down-scatter correction ("uncorrected") and pure $^{201}$Tl data with the simulated phantoms (Table 6.5, and Figure 6.3). The uncorrected and non-optimised reconstructions were performed with 10 scatter update iterations and $10^6$ simulated photons for the $^{99m}$Tc and $^{201}$Tl reconstructions and $10^7$ simulated down-scatter photons. At this point, the $^{99m}$Tc images were not studied.

The results indicated that optimised parameters provided contrast values that were equivalent to the values obtained with the non-optimised parameters, but requiring a significantly shorter reconstruction time. The down-scatter effect was not fully compensated as can be observed by comparing the contrast values of the dual-isotope and pure $^{201}$Tl reconstructions. However, the contrasts for the corrected data were better than for the uncorrected data.
Table 6.5. Contrast evaluation with NCAT phantoms. The table shows myocardium vs. defect and myocardium vs. left ventricle (LV) contrasts for uncorrected, optimised and non-optimised $^{201}$TI/$^{99m}$Tc reconstruction and for pure $^{201}$TI reconstruction. The results were obtained using all the Monte Carlo simulated NCAT phantoms, and the contrasts are average values of the corresponding female and male phantoms. Only $^{201}$TI reconstruction results are shown.

<table>
<thead>
<tr>
<th>Defect</th>
<th>Reconstruction</th>
<th>Myocardium vs. defect contrast</th>
<th>Myocardium vs. LV contrast</th>
<th>Reconstruction time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANT</td>
<td>Uncorrected</td>
<td>0.57</td>
<td>0.86</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Optimised</td>
<td>0.62</td>
<td>0.91</td>
<td>&lt;3</td>
</tr>
<tr>
<td></td>
<td>Non-optimised</td>
<td>0.61</td>
<td>0.91</td>
<td>&lt;13</td>
</tr>
<tr>
<td></td>
<td>Pure $^{201}$TI</td>
<td>0.71</td>
<td>0.96</td>
<td>&lt;1</td>
</tr>
<tr>
<td>INF</td>
<td>Uncorrected</td>
<td>0.65</td>
<td>0.90</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Optimised</td>
<td>0.80</td>
<td>0.94</td>
<td>&lt;3</td>
</tr>
<tr>
<td></td>
<td>Non-optimised</td>
<td>0.81</td>
<td>0.94</td>
<td>&lt;13</td>
</tr>
<tr>
<td></td>
<td>Pure $^{201}$TI</td>
<td>0.90</td>
<td>0.97</td>
<td>&lt;1</td>
</tr>
<tr>
<td>SEPT</td>
<td>Uncorrected</td>
<td>0.51</td>
<td>0.90</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Optimised</td>
<td>0.70</td>
<td>0.96</td>
<td>&lt;3</td>
</tr>
<tr>
<td></td>
<td>Non-optimised</td>
<td>0.67</td>
<td>0.95</td>
<td>&lt;13</td>
</tr>
<tr>
<td></td>
<td>Pure $^{201}$TI</td>
<td>0.64</td>
<td>0.97</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Figure 6.3. Example $^{201}$TI short-axis slices of the NCAT phantoms. Picture A refers to the uncorrected $^{99m}$Tc/$^{201}$TI reconstruction result, B shows the optimised result, a non-optimised result is shown in picture C and a reconstruction from pure $^{201}$TI data in D.

A similar comparison between the uncorrected, optimised and non-optimised reconstructions as described
above was performed with the physical phantom data (Table 6.6, and Figure 6.4). These results agree with the findings of the simulation study, although the difference between the contrasts of the uncorrected and the corrected data is less than the difference in the phantom study.

**Table 6.6.** Contrast evaluation with the physical phantom. The table shows myocardium vs. defect and myocardium vs. left ventricle (LV) contrasts for uncorrected, optimised and non-optimised ²⁰¹Tl/⁹⁹mTc reconstruction and for pure ²⁰¹Tl reconstruction. The results were obtained using the Jaszczak phantom with a cardiac insert. Only ²⁰¹Tl reconstruction results are shown.

<table>
<thead>
<tr>
<th>Defect</th>
<th>Reconstruction</th>
<th>Myocardium vs. defect contrast</th>
<th>Myocardium vs. LV contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANT</td>
<td>Uncorrected</td>
<td>0.56</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>Optimised</td>
<td>0.60</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>Non-optimised</td>
<td>0.59</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>Pure Tl-201</td>
<td>0.72</td>
<td>0.87</td>
</tr>
<tr>
<td>INF</td>
<td>Uncorrected</td>
<td>0.43</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>Optimised</td>
<td>0.46</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>Non-optimised</td>
<td>0.48</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>Pure Tl-201</td>
<td>0.65</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Figure 6.4. Example ²⁰¹Tl short-axis slices of the Jaszczak phantom with the cardiac insert. Picture A refers to the uncorrected ⁹⁹mTc/²⁰¹Tl reconstruction result, B shows the optimised result, a non-optimised result is shown in picture C and a reconstruction from pure ²⁰¹Tl data in D.
6.3 Motion Correction Optimisation for Cardiac SPECT (Publication III)

The results of the comparison between motion corrected and motion-free studies for each motion (lateral shift, vertical shift, and vertical creep) for Method 1 indicated that three iterations were sufficient to obtain good quality correction for all three types of motions. The ischemia scores for Method 1 obtained with three iterations and the corresponding scores for Method 2 are presented in Figure 6.5. This reveals that the mutual information cost function is clearly the best cost function for both motion correction methods.

![Figure 6.5. Ischemia scores for Method 1 and Method 2 for every motion and cost function studied.](image)

Figure 6.6 shows an example of short axis slices of the original motion-free data, motion-corrupted data reconstructed with Methods 1 and 2 and uncorrected motion-corrupted data for all three motions. The figures illustrate that both Method 1 and Method 2 provide good quality images.
Figure 6.6. Example of short axis slices reconstructed from: motion free data (row 1), motion corrupt data with motion correction Method 1 (row 2), motion corrupt data with motion correction Method 2 (row 3) and motion corrupt data without motion correction (row 4). Image A corresponds to lateral shift motion, B corresponds to vertical shift motion and C corresponds to vertical creep motion.

In clinical practice, the time needed to conduct the reconstructions is a relevant feature of an algorithm. The average time for Method 1 reconstruction with three motion correction iterations followed by the final reconstruction was 6 minutes. However, method 2 took three hours to complete the reconstruction, though this value should be considered as only indicative, as Method 2 was not fully optimised for speed in this study.

6.4 REDUCTION OF COLLIMATOR CORRECTION ARTEFACTS IN SPECT (PUBLICATION IV)

The most important finding is shown in Figure 6.7. The example slices of phantom 1 as well as profiles for the largest sphere combined with the theoretical profile of the sphere are shown. The OS-EM reconstruction with collimator correction produced the ring-like artefact, which is highly visible in the largest
sphere and clearly apparent in the profile. The artefact is well compensated with the Bayesian methods, but there is slightly lower image resolution with the median root prior and smoothing prior than can be achieved with OS-EM with collimator correction. The Bowsher prior is close to the true shape, but a more distinct "halo" can be seen around the hot spheres than is present with the other of the reconstruction algorithms.
Figure 6.7. A representative slice taken from the PTW-Freiburg’s PET/SPECT phantom with the hot-sphere insert reconstructed with the five methods studied, and also the equivalent CT slice. The plotted profiles are shown for the largest sphere (black line) with the corresponding theoretical profile (grey line) scaled to the reconstructed image’s maximum value. From left to right (upper row): OS-EM without collimator correction (OS-EM NORR), OS-EM reconstruction with collimator correction (OS-EM RR), and Median root prior (MRP). Lower row: Quadratic smoothing prior (SMOOTH), Bowsher prior (AMAP) and low-dose CT slice, which has been re-sampled to the SPECT image size. The black arrow marks the location of the missing sphere.
The contrast value analysis (Table 6.7) agrees with the observations stated above, i.e. the median root prior and smoothing prior were inferior to OS-EM with collimator correction, the Bowsher prior achieved the highest overall contrast values. It is also apparent that collimator correction increases the contrasts, as the OS-EM without the correction has the lowest resolution. The visual evaluation of phantom 2 supports these findings (results are shown in the original publication 4).

Table 6.7. Contrast values of the 4 largest spheres for the five different reconstruction methods: OS-EM without collimator correction (OS-EM NORR), OS-EM reconstruction with collimator correction (OS-EM RR), Median root prior (MRP), Quadratic smoothing prior (SMOOTH) and Bowsher prior (AMAP).

<table>
<thead>
<tr>
<th>Sphere</th>
<th>OS-EM NORR</th>
<th>OS-EM RR</th>
<th>MRP</th>
<th>SMOOTH</th>
<th>AMAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sphere 1</td>
<td>0.741</td>
<td>0.888</td>
<td>0.871</td>
<td>0.810</td>
<td>0.910</td>
</tr>
<tr>
<td>Sphere 2</td>
<td>0.691</td>
<td>0.849</td>
<td>0.817</td>
<td>0.776</td>
<td>0.898</td>
</tr>
<tr>
<td>Sphere 3</td>
<td>0.595</td>
<td>0.802</td>
<td>0.768</td>
<td>0.701</td>
<td>0.802</td>
</tr>
<tr>
<td>Sphere 4</td>
<td>0.519</td>
<td>0.782</td>
<td>0.702</td>
<td>0.620</td>
<td>0.742</td>
</tr>
</tbody>
</table>

Figure 6.8. shows example slices of the bone SPECT reconstruction. Again the visual evaluation is in favour of the findings reported above.
Figure 6.8. Example sagittal slices of the clinical bone SPECT reconstructed with the five different algorithms. From left to right (upper row): OSEM without collimator correction (OSEM NORR), OSEM with collimator correction (OSEM RR), Median root prior (MRP). Lower row: Quadratic smoothing prior (SMOOTH), Bowsher prior (AMAP) and low-dose CT slice, which has been re-sampled to SPECT image size.


7 Discussion

7.1 The Effect of Monte Carlo-Based Scatter Correction on Half-Time Myocardial Perfusion SPECT Imaging (Publication I)

In the first part of this thesis, full and half-time myocardial perfusion SPECT acquisitions were compared when attenuation and MC-based scatter correction were applied. The best image quality was achieved with the corrected datasets, and the corrected half-time data displayed a better image quality than the uncorrected full-time slices, though they failed to achieve the image quality of the corrected full-time slices.

These findings agree with prior studies [14, 17, 20, 22, 94-97] conducted using new reconstruction algorithms with shortened acquisitions, although most of the prior studies have concentrated only on collimator correction, without attenuation or scatter compensations. In order to achieve the best possible lesion detection performance, all the corrections should be included in the reconstruction process. Therefore half-time imaging should also be evaluated with all the corrections.

MC-based scatter correction is more generic and accurate than the widely used triple-energy-window (TEW) method, and it can model even highly non-uniform medium such as the thorax. The problem with MC-based scatter correction is the possible increase in image noise if the number of simulated counts is too small [98], though this problem was not present in this study, as can be seen in Table 6.1.

The transition from conventional to new reconstruction techniques with state-of-the-art corrections is not straightforward for all nuclear medicine practitioners. At the time of the patient study evaluation, the new reconstruction method had not yet been incorporated into the clinical routine in Kuopio University Hospital, where this study was conducted. This lack of experience is probably reflected in the results. The
SD-values in Table 6.2 are higher for the corrected data than for the uncorrected data possibly a reflection of some uncertainty in reporting the corrected slices. Therefore an adjustment period might be recommended before the new reconstruction methods are implemented into clinical practice.

The patient data obtained in the first part of this thesis was generated from the full-time gated data. This might have affected the image quality as non-gated data can have better image quality than perfusion data that has been obtained by summing the gating frames. On the other hand, by using the same data to obtain both full- and half-time images does make the physical properties of the images exactly the same, reducing the possible difference e.g. in the appearance of motion artefacts or bowel activity.

The advantages of shortened acquisition are undeniable, but half-time imaging should not be attempted without properly testing this technique with the scanners and reconstruction methods in use. In this study, the corrected half-time images produced better image quality than the uncorrected full-time images, but failed to achieve the image quality of the corrected full-time reconstruction. Therefore the diagnostic accuracy of the half-time images might be lower than can be obtained with the full-time images. This needs to be considered, i.e. can we really sacrifice the better image quality achieved with the new correction methods simply to achieve a shorter acquisition time or lower dose?

An alternative to the shortened acquisition time might be the use of high sensitivity collimators, instead of the commonly used high-resolution collimators. The resolution loss of the high sensitivity collimators can be compensated by collimator correction, providing a higher image quality than the high-resolution collimators with equal acquisition time or equal image quality with shortened acquisition time. Preliminary results obtained with high sensitivity collimators appear to be rather promising [99-101].
The possible increase in patient throughput and the reduction of patient discomfort are only of the two advantages conferred by the simultaneous dual-isotope MPI. The protocol also provides perfect alignment and identical physiological conditions between stress and rest images, which may provide additional information to the physician.

In this study, the reconstruction algorithm presented in the previous publication was extended and optimised for dual isotope $^{201}$Tl/$^{99m}$Tc studies in terms of reconstruction speed. Two scatter update iterations and $10^5$ simulated photons for the $^{99m}$Tc and $^{201}$Tl reconstructions (Table 6.3) and $10^6$ simulated down-scatter photons (Table 6.4) were found to provide accurate results with clinically acceptable reconstruction times. The reconstruction time was reduced by approximately 75% with the parameter optimisation (Tables 6.5 and 6.4).

The greatest challenge with the reconstruction algorithm is that the $^{99m}$Tc/$^{201}$Tl cross-talk was not fully compensated as can be seen in Tables 6.5 and 6.6, where pure $^{201}$Tl data achieved higher contrast values than the down-scatter compensated data. Currently the algorithm only compensates for patient scatter, but neglects the lead X-ray emissions, which occur when $^{99m}$Tc photons hit the collimator. These X-rays are emitted at the $^{201}$Tl energy level and they contaminate the $^{201}$Tl data. The inclusion of the correction of the lead X-rays in the reconstruction does improve image quality [76] but it also prolongs the execution time extensively as well as making the reconstruction algorithm implementation more challenging.

This study had some limitations. Only MC-simulated projection data and physical phantoms were used, without any clinical studies. In order to compensate for the lack of real patient data, the phantoms used were realistic and the activity levels mimicked clinically meaningful values. It is anticipated that the optimised reconstruction method studied works well also with patient data, but a large number of patient studies will
still be required to validate our method and the entire $^{201}$Tl/$^{99m}$Tc dual isotope SPECT.

**7.3 Motion Correction Optimisation for Cardiac SPECT (Publication III)**

Despite their widespread use in clinical practice, reconstruction-reprojection-based motion correction methods have not been fully optimised as for their free parameters. In this study, the aim was to optimise number of motion correction iterations for two different reconstruction-reprojection-based motion correction algorithms, as well as to find the type of cost function which would yield the best correction results.

The mutual information cost function was in general superior to the other cost functions for both correction methods (Figure 6.5). The mutual information cost function is not directly based on pixel-by-pixel differences in the projection counts, and thus is unlike the two other studied cost functions, instead it is based on the differences in the histograms of the projection images. The projection counts in the reprojections are distorted due to the lack of attenuation modelling, which might reduce the effectiveness of cost-functions which work on pixel-by-pixel differences. If attenuation would have been modelled it is possible that the performance of the cost-functions might have been different. The problem with attenuation modelling is the possible misalignment of the SPECT image and the attenuation map, which is expected to be worse on studies where there is movement already in the projection data. The longer calculation time reduces the practicality of Method 2 despite the slightly better overall performance. On the other hand, even though it was not exploited in this study, Method 2 can correct for all rigid motion shifts and rotations, making it more versatile than Method 1. At present motion correction algorithms that operate in the reconstruction space are currently the only alternative capable of correcting for non-rigid motion, such as breathing or cardiac contraction.
There are a few caveats also with this study. The small number of patients might influence the reliability of the results, although the trend of the results was obvious. The added motion was relatively large in order to test the methods with meaningful artefacts. During a myocardial perfusion, SPECT acquisition 1-pixel movement is likely to evoke visible motion artefacts, but these are not always clinically important. A more than 2-pixel (>13 mm) movement however is likely to cause severe image artefacts [12, 59, 71]. Any method that succeeds in correcting severe motion artefacts is likely to work well also with smaller movements.

7.4 REDUCTION OF COLLIMATOR CORRECTION ARTEFACTS IN SPECT (PUBLICATION IV)

The benefits of collimator correction are clear, but collimator correction can also have undesirable effects on the reconstructed image, called ringing artefacts (Figure 5.1). In the final part of this thesis, the effects of three Bayesian reconstruction methods on SPECT collimator correction artefacts were studied. The penalties of these reconstruction methods can be considered to belong to three different categories: simple smoothing penalty, edge-preserving penalty and anatomically set penalty. These methods are all easy to use and can be implemented with only minor modifications needed to the OS-EM algorithm.

The most common penalty is the quadratic smoothing prior. Those voxel values that differ substantially in a near neighbourhood are penalised and thus it provides smooth images. This same feature also reduces the collimator correction related ring-like artefacts. The high edges and deep valleys are penalised during the reconstruction, producing images with less ring-like artefacts and with very low noise level as can be seen from Figure 6.7. Unfortunately the images may well become overly smoothed as real edges are also penalised.

The median root prior is an edge-preserving penalty that penalises images which are not locally monotonic. This
behaviour allows the median root prior to pass edges without a penalty, but still to reduce noise effectively. Median root prior can produce images whose resolution is better than the resolution of images reconstructed with the smoothing prior (Figure 6.7). The problem with this method is that it cannot always totally separate the false edges generated by the collimator correction from real edges. If a too low Bayesian weight is used, faint collimator correction artefacts may be seen.

The Bowsher prior is an anatomically set penalty. It tries to restrict smoothing into those anatomical regions whose voxel values in the anatomical image are similar. This behaviour provides good collimator correction artefact reduction (Figure 6.7), but if the voxel size is large in comparison to the details in the data, the details in reconstructed images may become blocky, lowering the performance of the prior.

The hot-sphere phantom was used for this study, because the large activity difference between the sphere and background demonstrates the collimator correction artefact very easily. However, the hot-sphere phantoms in general should be used with care; it has been shown that cold walls surrounding an active core can lead to overestimation of the volume of the core [102]. However, it was found that the wall effect does not apply when there is no background activity, as was the set-up of the phantom measurements in this study. This effect was demonstrated with phantom measurements, and the authors concluded that their findings do not apply to patient imaging.

The clinical effects of the collimator correction artefacts are unknown. The possible effects of the artefacts on lesion detection or quantitative accuracy have currently not been evaluated. In addition, the lower resolution of the smoothing prior or the median root prior might decompensate for the gain provided by the lack of collimator correction artefacts. Nonetheless, it is still important to acknowledge that collimator correction is not artefact-free and the possible existence the artefacts should be borne in mind when evaluating SPECT images reconstructed using standard OS-EM algorithms.
7.5 MEETING THE AIMS AND FUTURE ASPECTS

The work done during this thesis was divided into four individual parts. These parts, however, share a common goal: reduction of MPI SPECT acquisition time. The first two parts focused on testing the CDR and scatter compensation in half-time imaging. The acquisition time reduction was accomplished in the first part by simply halving the imaging time, whereas in the second part the acquisition time was reduced by imaging the stress and rest parts at the same time. The third part of the study focused on patient motion, which is a by-product of long acquisition times. In the fourth part, the possible artefacts associated with the CDR compensation methods were studied.

The clinical usefulness of the methods presented in this thesis is not yet fully known. The methods developed and tested here have been implemented as a part of a commercial SPECT reconstruction package which is used worldwide. The clinical feedback from users of the software package in the next few years will no doubt be the best measure of the success of this work.

Shortening of acquisition time has attracted a huge amount of interest. The introduction of cardiac imaging specific scanners [103-105] and special collimators [106] are only two examples of this interest.

The dual isotope imaging can be used to shorten MPI acquisition time, but it can also provide additional information, such as the viability of the myocardium or myocardial innervation if $^{123}$I-MIBG is used instead of $^{201}$Tl. Apart from their use in cardiac imaging, dual isotope techniques are also utilized in other SPECT studies, such as parathyroid imaging. The same approaches for compensating the cross-talk are also relevant for these studies.

The techniques used to minimize or correct motion are closely related to shorter acquisition times as already mentioned. Although rigid body motion can be efficiently corrected with reconstruction-reprojection methods, there still substantial substantive issues such as motion-induced by breathing and
heartbeat. Cardiac and breathing motion correction is currently a hot topic in SPECT and especially in PET imaging.

Although the collimator compensation-induced artefacts are often seen on phantom imaging, they have not been widely studied or discussed. Their existence or impacts in clinical practice remain unknown and thus they should be better investigated. In oncological imaging, these artefacts might become relevant, as tumours with necrotic cores can be seen as objects with active walls and an inactive centre. In some cases the information of a necrotic core might affect the radiation therapy planning. Another example is internal dosimetry, where the distorted activity distributions exert direct effects on the dose distributions. The Bayesian compensation methods, especially when used with anatomical priors, could provide specific information about the activity boundaries, as well as reducing the boundary-related artefacts. It will be interesting to determine whether reconstruction methods applying anatomical information will become more popular now that PET/MRI scanners are a reality.
8 Conclusions

In this thesis, the current state-of-the-art MPI reconstruction and compensation methods were studied and further optimised. A special focus was on approaches which could reduce the scanning time. The possible interference of different compensation methods was evaluated and new approaches to avoid the artefacts generated by the compensation methods were devised.

The main observations of this thesis can be summarised as follows:

- Half-time MPI with attenuation and MC-based scatter correction produced images of superior quality when compared to full time imaging with standard reconstruction. One hundred thousand simulated photons in the MC-based scatter correction did not add noise to the reconstructed images even with half scanning time, but provided a good quality correction.

- Two scatter update iterations and $10^5$ simulated photons for the $^{99m}$Tc and $^{201}$Tl reconstructions and $10^6$ simulated down-scatter photons were sufficient to obtain good quality images in the dual $^{99m}$Tc/$^{201}$Tl reconstruction. In order to fully compensate for the down-scatter effect in the reconstructed images, lead X-ray emissions need to be taken into account.

- The traditional reconstruction-reprojection-based motion compensation method, with three update iterations and mutual information cost function, is a good option for rapid motion correction in clinical myocardial perfusion SPECT.

- All the three Bayesian reconstruction methods studied reduced the collimator correction artefacts. The Bowsher prior achieved a reduction without
evoking adverse effects on reconstructed resolution or on the contrast.

- The MPI technique can benefit greatly by incorporation of modern correction algorithms.
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Myocardial perfusion imaging (MPI) is one of the most common types of SPECT studies, being highly valued for its diagnostic accuracy. However, image noise, photon attenuation, Compton scatter, collimator-detector response (CDR) and patient motion hamper the image quality of MPI. These image degrading factors have been investigated widely and the modern reconstruction-based compensation methods can greatly improve the image quality. Recently CDR compensation has attracted considerable interest, because it allows diagnostically satisfying images to be acquired in half of the acquisition time currently in use. Shorter scan times both reduce artifacts related to patient motion and increase the patient throughput. The aim of this thesis was to validate and optimize novel SPECT reconstruction and compensation techniques for use with MPI. The specific focus was on scan time reduction and on CDR compensation.