Pinhole SPECT with Iterative Reconstruction
and the Median Root Prior

by

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in conformity with the requirements for
the degree of Master of Science

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Abstract

This thesis studies the clinical feasibility of pinhole SPECT with iterative reconstruction. The Median Root Prior (MRP), a Bayesian Maximum A Posteriori (MAP) filter, is used to reduce high frequency noise while preserving edges. The prior weight, β , is varied over the full range from zero to one.

High activity line and thyroid phantoms were imaged to study the system's abilities. A wrist was also imaged under realistic conditions to demonstrate clinical feasibility.

The iterative reconstruction with the MRP filter proved to be robust, yielding the correct geometry without serious artefacts. The average spatial resolution with a moderate amount of filtering ($\beta = 0.3$) was 6.0 ± 0.3 mm. The uniformity of hot backgrounds is better than 6% with $\beta \geq 0.1$. All cold and hot spots in the thyroid phantom were visible in all reconstructions. The wrist image, although count limited, demonstrates a clinical potential for pinhole SPECT.

Acknowledgements

Although I am usually found working alone in front of a computer, I have many people to thank for their help in this research.

My supervisor, Dr. Barry McKee, was always kind and had time to discuss my research. There were many times when we would stop to discuss current issues over tea. He has been supportive and encouraging and provided good suggestions for presenting this research at seminars and of course in this thesis. Opportunities arose to present the research at the Canadian Society of Nuclear Medicine (CSNM) and the Canadian Association of Physicists (CAP) annual meetings, and the funding was found. Barry also taught me to enjoy some time off rather than working so hard all the time.

Originally, the gamma camera, which was to be used for this research, only supported static pinhole acquisition. Thanks to Pierre Garneau, a biomedical engineer at the Ottawa Hospital, modifications were made to allow pinhole SPECT, which was essential to this work. Pierre also helped in ordering and modifying the sample holder and in answering many other questions about the camera.

The technologists at the Ottawa Hospital taught me the practical aspects of imaging. This included how to operate the camera and acquisition software and also

sample preparation. Special thanks go to Nur Jamal, the charge technologist, who found the wrist patient, got her cooperation, and made room in the camera schedule for extra imaging.

This brings us to the wrist patient who volunteered for the extra pinhole SPECT study. She was happy to support the latest research by lying on her stomach with her arm above her head, until her hand was sore with pins and needles. Her willingness and patience are much appreciated.

Dr. Michael Chamberlain, a nuclear medicine physician at the Ottawa Hospital, encouraged the clinical wrist study. Our discussions on clinical aspects of nuclear medicine, especially the wrist study, were invaluable. Dr. Chamberlain also lent his name to the submissions for the CSNM and CAP annual meetings.

The original pinhole OSEM reconstruction code was provided by Michel Defrise. Defrise leads his own team of pinhole SPECT researchers in Belgium. They are also interested in clinical uses and are investigating the effects of tilting the detector head during acquisition.

I was not considering a Master's degree until I found people who were kind enough to pay me for it. Great thanks go to NSERC especially and also Carleton University for funding my education.

My wife, Amy, has been very patient with my education. She knew when we got married that we would be moving around for years as I completed my B.Sc. My Master's has been another two years, but for the last ten months (and many, many more to come) we've been enjoying our adorable son, Adam. Now as this time comes to a close and I pursue full time employment, we are both eager to settle down.

Table of Contents

Abstract	ii
Acknowledgements	iii
Table of Contents	v
List of Tables	viii
List of Figures	ix
List of Acronyms	xi
1 Introduction	1
1.1 Introduction to Nuclear Medicine	1
1.2 Historical Context	3
1.2.1 Reconstruction Methods	3
1.2.2 Pinhole SPECT	5
1.3 Coordinate Systems and Reference Frames	7
2 Reconstruction Theory	10
2.1 Maximum Likelihood Expectation Maximization (MLEM) Reconstruc- tion	10
2.1.1 Ordered Subsets Expectation Maximization (OSEM)	14

2.2	Maximum A Posteriori (MAP) Algorithm	16
2.2.1	Median Root Prior (MRP)	18
3	Camera Calibration	21
3.1	Intrinsic Camera Response	21
3.2	Extrinsic Camera Response	22
3.2.1	On-Axis Geometrical Efficiency	23
3.2.2	Planar Variation	23
3.3	Centre of Rotation (COR) Correction	28
3.3.1	Methods	28
3.3.2	Results	31
4	Phantom Studies	34
4.1	Capillary Tubes	34
4.1.1	Methods	35
4.1.2	Results	38
4.2	Thyroid Phantom	45
4.2.1	Methods	46
4.2.2	Results	49
5	Clinical Wrist Study	57
5.1	Methods	57
5.1.1	Setup	57
5.1.2	Analysis	60
5.2	Results	60

TABLE OF CONTENTS

TABLE OF CONTENTS

6	Conclusions and Recommendations	69
6.1	Conclusions	69
6.2	Recommendations	71
A	Implementation of the MRP Algorithm	73
	References	76

List of Tables

3.1	Results of nonlinear fit of Eq. (3.3)	26
3.2	Results of the COR fitting procedure	33
4.1	Acquisition and reconstruction parameters for the capillary tubes	35
4.2	Final FWHM results of the HA line sources	43
4.3	Final FWHM results of the HT line sources	43
4.4	Final FWHM results of the VT line sources	43
4.5	Acquisition and reconstruction parameters for the Picker thyroid phantom	47
4.6	ROI sizes of the Picker thyroid phantom	48
4.7	Contrast results for the Picker thyroid phantom as a function of the MRP parameter, β	53
4.8	CoV results for the Picker thyroid phantom	55
4.9	SNR results for the Picker thyroid phantom	56
5.1	Acquisition and reconstruction parameters for the clinical wrist image	59

List of Figures

1.1	Camera and image coordinate systems	7
1.2	Definition of the transverse, coronal, and sagittal views	9
3.1	Siemens E.Cam with the pinhole collimator and sample holder	22
3.2	On-axis geometrical efficiency of a pinhole collimator	23
3.3	Off-axis geometrical efficiency of a pinhole collimator	24
3.4	Cross section of counts across the u-axis versus the angle ψ	27
3.5	The measured points and the fitted model for the COR correction	32
4.1	The three line source orientations	36
4.2	Profile of a reconstructed line source with $\beta = 0.6$ and its Gaussian fit	39
4.3	The central slice of the HT line sources with four different filter weights	40
4.4	FWHM versus iteration for two cases	42
4.5	Comparison of a Butterworth and MRP profile	45
4.6	Drawing of the Picker thyroid phantom	46
4.7	Representative slices of the Picker thyroid phantom reconstructed from a full orbit	50
4.8	Contrast versus iteration for two cases of the Picker thyroid phantom	52

4.9	CoV and SNR versus iteration for the 12 mm cold rod reconstructed over 360°	54
5.1	The static view of the patient's hands, which was requested by the physician	61
5.2	A reference image of the right hand with the bones and joints labelled	62
5.3	Transverse slices of the clinical wrist image	64
5.4	Coronal slices of the clinical wrist image	65
5.5	Sagittal slices of the clinical wrist image	66

List of Acronyms

COR Centre of Rotation

CoV Coefficient of Variation

DVS Discrete Vertex Set

FBP Filtered Back-Projection

FDK Feldkamp, Davis and Kress

FOV Field Of View

FWHM Full Width Half Maximum

MAP Maximum A Posteriori

MIP Maximum Intensity Projection

MLEM Maximum Likelihood Expectation Maximization

MRP Median Root Prior

n-D n-Dimensional

OSEM Ordered Subsets Expectation Maximization

OSL One Step Late

PET Positron Emission Tomography

ROI Region Of Interest

ROR Radius Of Rotation

SNR Signal-to-Noise Ratio

SPECT Single Photon Emission Computed Tomography

Chapter 1

Introduction

This chapter presents the context and aim of the thesis. A brief introduction to nuclear medicine and an overview of research in pinhole SPECT is provided. Additionally, the coordinate systems and reference frames are introduced in §1.3.

1.1 Introduction to Nuclear Medicine

In nuclear medicine, radioisotopes are used for the clinical diagnosis of disease. Radionuclide-labelled agents, known as radiopharmaceuticals, are designed to target specific organs. The agents are introduced into the subject, usually by injection, and travel through the body to the targeted organs. Different radiopharmaceuticals may be used to target different organs, such as the bones, the heart, and the thyroid. The emitted photons are then captured by a gamma camera to produce an image of the radioactive distribution. Thus, nuclear medicine provides functional imaging of the organ rather than anatomical imaging.

With single photon emission, the unstable nuclei emit photons of known energy

as they decay. Because the radiation is emitted isotropically, a collimator must be used to determine the direction of the captured photon. Most commonly, a parallel hole collimator is used to acquire a 1:1 image. Other collimators available include fanbeam, pinhole, and multi-pinhole, which can increase the spatial resolution of the system by focusing.

There are three basic imaging categories in nuclear medicine: planar (static), dynamic, and tomographic. Planar imaging acquires a single view, or projection, of the subject. Each pixel in the projection represents a line integral of the radioactive distribution where the line is defined by the collimation used. Dynamic imaging is a series of planar images separated in time to show temporal changes in the distribution. The images can be viewed in sequence, like a movie, to trace the path of the radiopharmaceutical. Both planar and dynamic studies use the two-dimensional (2-D) projections directly.

A tomographic study is used to construct a three-dimensional (3-D) image of the radioactive distribution. Multiple planar images are used to produce a set of projections, each with a different view of the subject. Most commonly, the projections are taken along a single orbit about the subject. The projection dataset is fed to a reconstruction algorithm, which, knowing where each projection was viewed from, attempts to reproduce the true 3-D activity distribution. This type of study is known as a SPECT study, an acronym for Single Photon Emission Computed Tomography.

1.2 Historical Context

In this section, the historical context of my thesis research is discussed. The evolution of reconstruction methods for nuclear medicine in general is presented first. The second section presents the relevant research in pinhole SPECT.

1.2.1 Reconstruction Methods

Because of time limitations, SPECT images have been reconstructed using the Filtered Back-Projection (FBP) method, which is quick. This works well for *perfect* data, but with inconsistent projections (due to noise, attenuation, etc.) it yields many artefacts, the most noticeable of which is radial streaking. With faster computers, iterative algorithms, which are more accurate and do not suffer from this streaking, have been replacing FBP.

There are two classes of iterative reconstruction algorithms for nuclear medicine. The first class contains the iterative algebraic methods, which reconstruct the image by solving a set of linear equations. Examples from this class include the Algebraic Reconstruction Technique (ART) [1, 2], the Simultaneous Iterative Reconstruction Technique (SIRT) [3], and the Iterative Least Squares Technique (ILST) [4]. The second class contains the iterative statistical reconstruction methods, which reconstruct the image by minimizing or maximizing a function. The best example from this class is the Maximum Likelihood Expectation Maximization (MLEM) [5], which maximizes a likelihood function. Good general reviews of reconstruction techniques are given by Bruyant [6] and Vandenberghe et al. [7].

The MLEM algorithm was introduced in 1982 by Shepp and Vardi [5]. MLEM is

a great improvement over FBP and incorporates knowledge of the Poisson counting statistics. Its drawbacks are longer reconstruction times and an increase in noise after many iterations. Almost a decade later, Green presented a modified EM algorithm based on Bayesian Maximum A Posteriori (MAP) methods [8]. This modified algorithm allowed one to penalize the noise that builds in the image as the iterations increase, by using priors. In 1994, Hudson and Larkin accelerated the original MLEM algorithm by dividing the projection data into ordered subsets [9]. This algorithm was named Ordered Subsets EM (OSEM) and accelerated convergence by a factor nearly equal to the number of subsets (typically 8). In the same year, Alenius first introduced the Median Root Prior (MRP) [10] in relation to Positron Emission Tomography (PET). Alenius and his colleagues published several other articles [11, 12, 13] which are included in his Ph.D. thesis on the topic [14]. The theory behind these techniques (MLEM, OSEM, MAP, and MRP) is covered in Chapter 2 with further details.

Without Green's modified algorithm, the standard method of controlling image noise with MLEM or OSEM is to stop the iterations before the noise builds up considerably. This simple method requires one to pick the point at which the image convergence is sufficient and the image noise is limited. Unfortunately, the best point for early stoppage is dependent on the specific image. Veklerov and Llacer's group attempted to develop statistical stopping rules [15, 16, 17], but they proved to be unsuccessful on clinical data. Therefore, in practice, a stopping point is chosen by the user and applied to all images regardless of their unique nature.

1.2.2 Pinhole SPECT

The main advantage of pinhole imaging is the higher resolution provided by the magnification. Hal O. Anger, the inventor of the gamma camera, foresaw the use of pinhole collimators for planar thyroid scans [18]. This has been extended to pinhole SPECT of the thyroid using either a full or half orbit of acquisition [19]. In these thyroid studies it was found to be beneficial to tilt the detector in order to get closer to the subject. Other applications, including the breast [20], ankle [21], and shoulder [22] have been published, often using a limited orbit (180°) due to patient anatomy. Another obvious application of pinhole SPECT is small animal research [23, 24] where features to be imaged are very small. Currently, clinical pinhole SPECT is not common outside of research, especially in North America.

A Belgian group, led by Michel Defrise, recently used OSEM for pinhole SPECT [25]. This phantom study was performed with a full orbit and without tilt. Nearly two years later, the group published again using a tilted detector and a 180° orbit [22]. This second study included phantoms as well as parathyroid and shoulder patients. Michel Defrise provided the pinhole OSEM routine used in my research.

Last year, a Finish group published twice on using MRP with pinhole SPECT [26, 27]. The first study was limited to phantom studies using MLEM, while the second used OSEM and included a small animal study.

The previous Ottawa-Carleton Institute for Physics student to study pinhole SPECT was Tanya Hewitt. Her work [28] was also done at the Ottawa Hospital, Civic Campus and studied the use of two analytic reconstruction methods. These methods were the Discrete Vertex Set (DVS) [29] and the Feldkamp, Davis and Kress (FDK) [30] algorithms. FDK is the application of FBP to converging collimators.

DVS is more flexible but still has the disadvantages of an analytic reconstruction. Her work encouraged the use of pinhole SPECT but the algorithms were seen to suffer from tail and undershoot artefacts.

During my initial literature search, I was impressed with the ability of iterative reconstruction. I could not, however, accept the solution of arbitrary early stoppage. Early stoppage precludes convergence and the rules developed to reduce the subjectiveness were shown to be ineffective for clinical data. On the other hand, MRP was shown to be both effective and simple. The algorithm could be allowed to converge without a great increase in noise, and only one parameter required adjustment.

I have therefore chosen to continue the work on pinhole SPECT at the Ottawa Hospital by studying images reconstructed with OSEM and MRP. This thesis continues to explore the clinical potential of pinhole SPECT. Unfortunately, the gamma camera used for this research could not support a tilted detector. Therefore, this thesis explores the effectiveness of OSEM-MRP under full and half orbit pinhole acquisition without tilting the detector. The abilities and characteristics of OSEM-MRP, determined here, could be transferred to any nuclear medicine SPECT image regardless of collimator.

The reconstruction theory, including MLEM, OSEM, MAP, and MRP, is presented in Chapter 2. Chapter 3 presents the camera calibrations that were performed prior to the SPECT acquisitions. The system characteristics are investigated in Chapter 4 with line source and thyroid phantoms. A wrist image demonstrates the clinical feasibility of pinhole SPECT with OSEM-MRP in Chapter 5. Finally, the conclusions and future work are contained in the last chapter.

Figure 1.1: Camera ($uv\theta$) and image (xyz) coordinate systems. The pinhole rotates about the z -axis in the xy -plane.

1.3 Coordinate Systems and Reference Frames

It is important to know how to convert from the projection coordinate system to the image coordinate system and then to the physicians' classical reference frames. Projection coordinates are 2-D and are fixed to the camera head as it rotates about the subject. The image coordinate system is 3-D and provides an absolute reference in which the patient lies and the camera rotates around. Finally the physician is interested in standard views relative to the patient.

Figure 1.1 presents the projection and image coordinate systems for this work. The image and projection coordinate systems are cartesian coordinate system labelled xyz and uv respectively. In a SPECT acquisition, the camera head rotates about the z -axis, called the axis-of-rotation. The image coordinate system is centred

in the 3-D Field Of View (FOV) such that the pinhole focus is always in the xy-plane and always the same distance from the image origin. The xy-plane is also known as the orbital plane because the pinhole orbits in this plane. The x-axis points vertically upward while the y-axis points horizontally. The angle θ represents the angle from which the camera is viewing. When the camera is directly above the subject, the pinhole is on the positive x-axis and θ is zero. As the camera rotates towards the positive y-axis θ increases.

The projection coordinate system is most easily defined at $\theta = 0^\circ$. In this position, the u-axis is parallel to the y-axis and the v-axis is parallel to the z-axis. As the camera head rotates, the v-axis is always parallel to the z-axis. The u-axis, however, rotates about the z-axis so that, for instance, at $\theta = 90^\circ$ it is parallel to the negative x-axis.

A physician is interested in standard views of the patient who may be oriented in any manner relative to the image coordinate system. There are three main orthogonal views used for tomography studies: transverse, coronal, and sagittal. Transverse slices are taken from the superior to the inferior (from the head to the feet). Coronal slices are taken from the anterior to the posterior (from the front to the back). Finally, sagittal slices are taken from the left side to the right side of the patient. For standard imaging situations, when the patient is lying on the camera couch (either prone or supine), the orientations of each view are presented in Figure 1.2. In these cases the transverse, coronal, and sagittal slices are parallel to the xy-, yz-, and xz-planes respectively.

Figure 1.2: Definition of the transverse, coronal, and sagittal views. In a), the usual patient orientation is related to the image coordinate system (with the x-axis out of the page). In b), c), and d) the coronal, transverse and sagittal views are related to the image coordinate system. Note that these views are defined in the patient frame and that the image coordinates are used here as an intermediate reference frame.

Chapter 2

Reconstruction Theory

This chapter discusses the theory required to reconstruct the tomographic images in this work. The iterative procedure used to reconstruct the 3-D distribution from the 2-D projections is discussed in §2.1. The iterative procedure is then modified in §2.2, to control image noise using Bayesian principles.

2.1 Maximum Likelihood Expectation Maximization (MLEM) Reconstruction

SPECT involves reconstructing the mean 3-D distribution of radioactivity, which we can represent as $f(x, y, z)$. The detector rotates around the object acquiring projections from many angles. These projections can be represented as $g(u, v, \theta)$. The function g is the projection of f onto the crystal as allowed by the collimator. The collimator allows one to determine the direction of the incident photon.

The challenge is to determine f given g . In the reconstruction, the functions f

and g are not continuous but discretized. g is a set of 2-D projections, each made up of 2-D picture elements or pixels. Each projection is taken from a different angle, θ . The reconstructed image, f , is a 3-D function composed of 3-D volume elements or voxels. By translating f and g into one dimensional vectors we can concisely write the relationship as $g = Af$. The matrix A represents the probability that a photon from voxel f_j is detected in pixel g_i . These probabilities depend on the imaging geometry and the type of collimation used. Shepp and Vardi first introduced the MLEM algorithm [5] to find the best estimate for f , by successive estimates.

Projection measurements are subject to variations due to the Poisson probabilistic nature of radioactive decay. As a consequence, the dataset g is a particular measurement. The best estimate for f is the mean number of disintegrations $\bar{f}$ in the image that can produce g with the highest likelihood [5, 31, 32, 33, 34]. This is found using the Poisson law that allows one to predict the probability of a measured number of photons, given the mean number of decays. Each iteration of the algorithm is divided into two steps: the expectation (E) step, where the likelihood of the estimated image producing the measured data is calculated, and the maximization (M) step, where the next estimate, having a greater likelihood of producing the measured data, is found.

The numbers of both the emitted and the detected photons are assumed to be Poisson random variables.

Let us consider the mean number of disintegrations in voxel j as $\bar{f}_j$, and the element a_{ij} of the matrix A to be the probability that pixel i detects a photon from

voxel j . The mean number of photons detected in pixel i , $\bar{g}_i$, is given by:

$$\bar{g}_i = \sum_{j=1}^J a_{ij} \bar{f}_j \quad (2.1)$$

It can be shown that the number of photons emitted for the J voxels and detected by pixel i is a Poisson variable. Thus, the probability of detecting g_i photons is:

$$P(g_i) = \frac{e^{-\bar{g}_i} \bar{g}_i^{g_i}}{g_i!} \quad (2.2)$$

The Poisson variables are independent so that the conditional probability $P(g|\bar{f})$ is the product of the individual probabilities $P(g_i)$. The likelihood function $L(\bar{f})$ is given by:

$$L(\bar{f}) = P(g|\bar{f}) = \prod_{i=1}^I P(g_i) = \prod_{i=1}^I \frac{e^{-\bar{g}_i} \bar{g}_i^{g_i}}{g_i!} \quad (2.3)$$

Taking the natural logarithm of the likelihood function, Eq. (2.3) becomes:

$$l(\bar{f}) \equiv \ln(L(\bar{f})) = \sum_{i=1}^I (-\bar{g}_i + g_i \ln(\bar{g}_i) - \ln(g_i!)) \quad (2.4)$$

and substituting for $\bar{g}_i$ using equation (2.1), we obtain:

$$l(\bar{f}) = \sum_{i=1}^I \left(-\sum_{j=1}^J a_{ij} \bar{f}_j + g_i \ln \left(\sum_{j=1}^J a_{ij} \bar{f}_j \right) - \ln(g_i!) \right) \quad (2.5)$$

This equation is of fundamental importance to the MLEM algorithm because it allows one to calculate the probability of observing a projection dataset for any image $\bar{f}$. One is searching for the image that provides the maximum probability of producing g . Therefore, the image for which $l(\bar{f})$ is maximized is considered the

best estimate of the solution.

It can be shown that there is only one maximum for $l(\bar{f})$ [33]. This maximum is found when the derivative of $l(\bar{f})$ is zero:

$$\frac{\partial l(\bar{f})}{\partial \bar{f}_j} = -\sum_{i=1}^I a_{ij} + \sum_{i=1}^I \frac{g_i}{\sum_{j'=1}^J a_{ij'} \bar{f}_{j'}} a_{ij} = 0 \quad (2.6)$$

One can then multiply all of equation (2.6) by $\bar{f}_j$ and rearrange to arrive at:

$$\bar{f}_j = \frac{\bar{f}_j}{\sum_{i=1}^I a_{ij}} \sum_{i=1}^I \frac{g_i}{\sum_{j'=1}^J a_{ij'} \bar{f}_{j'}} a_{ij} \quad (2.7)$$

This leads to the iterative scheme of the MLEM algorithm as described by Lange and Carson [32]:

$$\bar{f}_j^{(k+1)} = \frac{\bar{f}_j^{(k)}}{\sum_{i=1}^I a_{ij}} \sum_{i=1}^I \frac{g_i}{\sum_{j'=1}^J a_{ij'} \bar{f}_{j'}^{(k)}} a_{ij} = \frac{\bar{f}_j^{(k)} c_j^{L(k)}}{\sum_{i=1}^I a_{ij}} \quad (2.8)$$

where the likelihood coefficient, $c_j^{L(k)}$, is defined by the right hand equation.

The EM algorithm can be seen as a series of projections and backprojections [8]. The factor $g_i/(\sum_{j'=1}^J a_{ij'} \bar{f}_{j'}^{(k)})$ is the ratio of the measured number of counts to the current estimate of the mean number of counts in pixel i . The backprojection of this ratio for voxel j is represented by the likelihood coefficient $c_j^{L(k)}$. Equation (2.8) can be extended to the whole image and interpreted as:

$$\text{Image}^{(k+1)} = \text{Image}^{(k)} \times \text{Normalized Backprojection of} \left(\frac{\text{Measured Projections}}{\text{Projections of Image}^{(k)}} \right) \quad (2.9)$$

Thus, at each iteration k , a current image estimate is available. (The initial esti-

mate is usually a uniform object.) Using a system model, one simulates projections of the estimate. The measured projections are compared with the simulated projections and the ratio is used to modify the current image estimate, which becomes the new estimate for iteration $k + 1$. This process is repeated many times as the MLEM algorithm slowly converges to the *best* estimate.

In addition, the detail of the system used to perform the reconstruction can be modified. This allows for many effects (e.g. collimator blurring) to be accounted for with proper programming by incorporating them in the system model, and the probability matrix A .

2.1.1 Ordered Subsets Expectation Maximization (OSEM)

Ordered Subsets Expectation Maximization (OSEM) was proposed by Hudson and Larkin [9] to accelerate the MLEM reconstruction algorithm. With OSEM, the projection dataset is divided into smaller subsets. The MLEM algorithm is then applied to each subset in order as a subiteration. A full iteration is complete when each subset has been used to update the image estimate. The use of subsets accelerates the convergence by updating the estimate more often, and can provide an acceleration nearly equal to the number of subsets used when compared to standard MLEM [9, 35]. OSEM, therefore, is able to considerably reduce the computing time needed for reconstruction.

The choice and order of the subsets is important for optimization. The projections in each subset are chosen to be evenly spaced about the orbit. In this way the subsets are interleaved and each samples the full range of views to update the image. The subsets should be processed in an order which introduces the most new infor-

mation at each step. For example, given 128 projections, one might divide it into 8 subsets each containing 16 projections. The first subset would contain projections 1, 9, 17, ..., 121, the second would contain projections 2, 10, 18, ..., 122, etc. For optimal acceleration the subsets should be processed in the order: 1, 5, 3, 7, 2, 6, 4, 8 [36]. This choice and order of subsets would provide the greatest acceleration with 8 subsets.

It is unreasonable to increase the number of subsets too much because the projection sampling in each subset would become too sparse. In the example above, if one were to use 64 subsets each update would be based on two opposing projections. A single subset would not adequately represent the full set of projections. Each update would attempt to produce the projection pair, which would be significantly different from the last or the next pair. In this way, each update would significantly change the image and the last subset processed would have a larger effect on the final image. This effect would be seen in streaking pointing towards the final subset views.

There is a large amount of variability in the number of subsets used in the literature. Hudson and Larkin originally suggested opposing pairs or triplets for a three-headed system [9] although they admitted that the last subset would have a larger effect on the final image. On the conservative side, Alenius and Ruotsalainen suggested only 2 or 4 subsets with 256 projections [11]. Generally, investigators are more liberal, interested in utilizing the acceleration more fully [22, 25, 27, 35]. For this thesis, image quality was more important than acceleration. 16 projections per subset were chosen for the phantom studies (§4) to produce either 4 or 8 subsets. No acceleration was used for the clinical wrist image (§5) since there were only 32 low count projections available.

2.2 Maximum A Posteriori (MAP) Algorithm

The Maximum Likelihood Expectation Maximization (MLEM) iterative algorithm is based on the Poisson statistics of the photon counting problem. This algorithm works to produce the image that has the highest likelihood of producing the measured data. For a Poisson distribution, the mean provides the largest probability. Thus, in the best fit, all of the simulated and measured projections would match exactly. The projections, however, contain counting noise, which is then transferred to the image during the maximization process. As the iterations increase, and the algorithm continues to converge, one can see a type of checkerboard noise pattern of artificial high and low spikes emerging in the image [37, 38]. These noisy images do not represent the real distribution although they may yield projections that closely match the measurements. The MLEM algorithm must therefore be modified to prevent this artefact in the image.

The first and simplest measure is to limit the number of iterations. This prevents the reconstruction from reaching convergence and often leaves the image biased towards the initial estimate. The initial estimate is normally a uniform image so that early stoppage may be biased towards a flat smooth image. It is known that the higher frequency information develops in later iterations so that early stoppage may obstruct the viewing of fine details [39]. The best point at which to stop depends on one's interest and is dependent on the specific circumstances. The point chosen at which to stop iterating is usually an empirical *rule of thumb* although Veklerov and Llacer have tried to develop statistical stopping rules [15, 16, 17]. Unfortunately, these statistical stopping rules only appeared to work on simulations and were not robust enough to handle clinical data [15].

Early stoppage is less than ideal, but it is still used by many due to its simplicity. Usually early stoppage is combined with pre- and/or post-filtering. By prefiltering the projection data, one reduces the counting noise and thereby reduces the noise built up in the image. The image can also be post-filtered after reconstruction to try to remove the built up noise. At the Ottawa Hospital, Civic Campus, where this research was performed, the current clinical practice is 4 iterations with 8 subsets followed by a Butterworth filter. In these cases, the MLEM algorithm must be stopped arbitrarily before convergence to limit the noise.

Current image reconstruction research is exploring alternatives to early stoppage of the MLEM algorithm. A Bayesian approach is used to allow a modified algorithm to converge. One can modify the standard MLEM algorithm by using a Maximum A Posteriori (MAP) approach. This approach uses an energy function to modify the update values of the image. If one derives the energy function from a smooth distribution, any rough sections developing in the image will be penalized and will be less likely to appear in the final image. The MAP approach allows one to iterate to convergence while maintaining a limited amount of noise in the image.

Green introduced a modified MLEM algorithm [8] based on the Bayesian MAP approach. The One Step Late (OSL) algorithm is described by:

$$\bar{f}_j^{(k+1)} = \frac{\bar{f}_j^{(k)}}{\sum_{i=1}^I a_{ij} + \beta \frac{\partial}{\partial \bar{f}_j} U(\bar{f}_j^{(k)})} \sum_{i=1}^I \frac{g_i}{\sum_{j'=1}^J a_{ij'} \bar{f}_{j'}^{(k)}} a_{ij} = \bar{f}_j^{(k)} c_j^{L(k)} c_j^{P(k)} \quad (2.10)$$

where $\frac{\partial}{\partial \bar{f}_j} U(\bar{f}_j^{(k)})$ (the prior term) is the derivative of an energy function, U , and is chosen to enforce smoothing and β is a value chosen to modulate the importance of the prior. The OSL approach gets its name from the fact that the last estimate is

used in the energy function rather than the current estimate. With the simplifying assumption that $\sum_{i=1}^I a_{ij} = 1$ [5], the penalty coefficient becomes:

$$c_j^{P(k)} = \frac{1}{1 + \beta \frac{\partial}{\partial f_j} U(\bar{f}_j^{(k)})} \quad (2.11)$$

The penalty coefficient is close to unity if the current image meets the prior assumptions at j . Large values of the derivative imply that the image deviates from the prior assumption.

A remark must be made that the denominator may become negative. In this case, the voxel value may become negative which is nonphysical and defeats one of the benefits of MLEM reconstruction. The energy function and the weight of the prior, β , must be chosen carefully to provide proper smoothing and noise control. Gibbs priors have been used [40, 41], and others have been suggested [42].

2.2.1 Median Root Prior (MRP)

Within a SPECT image, one expects areas of uniform or slowly changing activity as well as abrupt changes at the edge of a target organ. It is a challenge to smooth an image where appropriate without blurring edges. If anatomic information is available (e.g. from CT or MRI), then one may limit smoothing to areas of the same anatomic volume as the voxel of interest. In practice, this is difficult, and often laborious, as the separate images must be coregistered and the edges within SPECT and CT or MRI may be different [43, 44]. Others have introduced priors with an edge height parameter [34, 40, 41] so that large differences in activity are not smoothed but assumed to be edges. This approach begins to fail if the noise amplitude is of the

same order as the edge heights. The setting of the height parameter is often sensitive and requires fine tuning for different images [34].

The Median Root Prior (MRP) algorithm was first introduced by Alenius [10] for Positron Emission Tomography (PET), to smooth while preserving edges. Any image that is locally monotonic is invariant under the median filter and is called a root image [45]. The MRP algorithm favours any locally monotonic image. The final image, however, is generally not a root image.

The penalty coefficient for MRP is calculated as:

$$c_j^{P(k)} = \frac{1}{1 + \beta \frac{\bar{f}_j^{(k)} - M_j}{M_j}} \quad (2.12)$$

where $\lambda_b^{(k)}$ is the current voxel, M_b is the median value of the neighbourhood, and β is the weight of the prior.

Unfortunately, due to the nonlinear nature of the median operator it is difficult to compare MRP's penalty coefficient with Eq. (2.11). Although the prior is difficult to work with analytically, Alenius has compared it qualitatively with the Gaussian prior [14]. The Gaussian distribution is considered the most conservative assumption when little is known about a distribution. The law of large numbers also states that the combination of many errors leads to a Gaussian distribution.

Equation (2.12) is simple and only depends on one parameter, β . This weight can vary from zero to one, or from no filtering to a true median filter respectively. Previous studies [11, 14, 26] have shown that the algorithm is robust and is not overly sensitive to the choice of β . Because the median filter naturally preserves edges without smoothing, there is no need for additional edge height parameters.

One should also note that the penalty is always positive and therefore will not introduce nonphysical negative voxel values.

MRP is simple, effective, and easily implemented. The implementation of the MRP algorithm for this work is presented in Appendix A.

Chapter 3

Camera Calibration

All experiments in this thesis were performed using a Siemens E.Cam nuclear medicine camera. The camera with the pinhole collimator and sample holder is shown in Figure 3.1. In order to properly reconstruct tomographic images there are three calibration steps that must be performed. These steps are the intrinsic flood correction (§3.1), the extrinsic flood correction (§3.2), and the Centre Of Rotation (COR) correction (§3.3).

3.1 Intrinsic Camera Response

One must compensate for the sensitivity variations in the crystal and photomultiplier tubes of the camera head. The camera performance is measured daily and updated monthly by the nuclear medicine technologists. This is measured by imaging a point source without any collimators on the camera. The measurement is compared to the ideal response and a correction table for each head is calculated by the camera software. The correction table is then applied to every acquisition automatically to

Figure 3.1: Siemens E.Cam with the pinhole collimator and sample holder.

compensate for nonuniformities in the crystal and photomultiplier tubes.

3.2 Extrinsic Camera Response

To properly reconstruct relative activities across the FOV, the response of the camera with the pinhole collimator must be known. This extrinsic response describes how efficient or sensitive the pinhole collimator is at collecting photons from any direction in the FOV. This response is related to A , the probability of a photon from voxel f_j being detected in pixel g_i , as discussed in §2.1. The extrinsic camera response is measured after a correction for the intrinsic camera response has been applied.

Figure 3.2: On-axis geometrical efficiency of a pinhole collimator.

3.2.1 On-Axis Geometrical Efficiency

A radioactive object emits radiation isotropically over 4π steradians. At a distance b , the fluence is proportional to $1/4\pi b^2$. The area of the pinhole aperture is πr^2 (see Figure 3.2). The ratio of these two quantities represents the on-axis geometrical efficiency:

$$\epsilon_{on-axis} \simeq \frac{\pi r^2}{4\pi b^2} = \frac{r^2}{4b^2} \quad (3.1)$$

Equation (3.1) is an approximation, which only holds for $r \ll b$. For the studies in this research, r is 2 mm, while b is a minimum of 4 cm, and therefore $r \ll b$ is always met. Being proportional to $1/b^2$, the sensitivity and image intensity decrease quickly as the object to aperture distance increases.

3.2.2 Planar Variation

The discussion in §3.2.1 was limited to an object on-axis. The result of (3.1) must therefore be modified to account for activity anywhere in the FOV.

Let us consider a point off-axis as shown in Figure 3.3. The distance R , from the

Figure 3.3: Off-axis geometrical efficiency of a pinhole collimator.

pinhole to a point off-axis, is greater than b by a factor of $1/\cos \psi$. Additionally, the aperture will no longer appear circular but rather will appear reduced in one dimension by a factor of $\cos \psi$. The final expression demonstrates a dependence on $\cos^3 \psi$:

$$\epsilon \simeq \frac{r(r \cos \psi)}{4R^2} = \frac{r^2 \cos^3 \psi}{4b^2} \quad (3.2)$$

The geometrical efficiency of a real pinhole collimator is not ideal. The collimator is made from a thick lead cone and a Tungsten pinhole insert. The thick lead cone can be considered a perfect absorber of 140 keV photons as can much of the insert. The pinhole insert, however, becomes very thin at the edge of the aperture and therefore some photons scatter off of, or pass through the thin edge. Tungsten is used to reduce these effects because of its higher density and greater attenuation. The remaining effects are compensated for by modifying the power to which $\cos \psi$

is raised.

Methods

A flood source was used to measure the planar variation in the geometrical efficiency. The source was a disc (44 mm inner radius, 50 mm outer radius, 8 mm inner height, 14 mm outer height, filling port on the circumference) filled with Tc-99m, which emits 140 keV photons. The disc was positioned parallel to the detector and close to the aperture. This geometry provides a uniform source that fills the entire FOV. It also ensures that the edges of the flood source are not in the FOV.

A high statistics measurement with 130 million total counts was acquired to reduce the Poisson counting noise. The angle ψ was determined for each pixel along the u-axis. The outer 5 percent of the data was ignored to avoid edge effects where the cone meets the crystal. The static acquisition was acquired with 2.4 mm pixels, and provided 82 usable points along the u-axis. Because of the circular symmetry, the negative and positive u-axis values provide 2 measurements of each angle. A single line through the projection center was used to more evenly sample the response versus angle. If every pixel were used, there would be much more weight given to larger angles near the edge whereas the region of greatest interest for pinhole imaging is in the centre.

The data were fit to the following equation:

$$y = m \cos^x \psi \quad (3.3)$$

where y is the pixel value, m is the amplitude, and x is the power we wish to

Parameter	Value	Uncertainty
m	22796	26
x	3.32	0.024

Table 3.1: Results of nonlinear fit of Eq. (3.3). The coefficient of correlation is 0.73.

determine. The amplitude depends on the total number of counts acquired for the measurement. The first approximation of m and x was found by performing a linear least squares fit with equal uncertainties. This is possible by taking the logarithm of (3.3):

$$\log y = \log m + x \log(\cos \psi) \quad (3.4)$$

The results from the linear fit were then used as the initial estimate for a nonlinear fit using the Marquardt minimization procedure [46]. Routines for performing these fits were taken from the source code provided with Brandt's textbook [47]. The proper Poisson errors were used for weighting this final fit.

Results

The results are presented in Table 3.1 and Figure 3.4. The result of $x = 3.32 \pm 0.024$ demonstrates that the effect of scatter and attenuation from the aperture should be accounted for in the reconstruction. This is a 10% difference in the power from $x = 3$, which Eqn. (3.2) implied for a perfect aperture. The result also agrees well with previous results from Jaszczak's group [48, 49] who reported experimental and calculated results of $x = 3.3$ and 3.8 using three different models. There are still deviations between the data and the fitted curve because the model is an approximation.

Figure 3.4: Cross section of counts across the u-axis versus the angle ψ after application of the intrinsic camera response correction. The line is the result of the nonlinear fit of Eq. (3.3).

3.3 Centre of Rotation (COR) Correction

A COR correction must be performed in order to determine the camera acquisition geometry. The camera geometry is used during reconstruction for proper forward- and back-projection. If the geometry is not known well, the projection and image data will be incorrectly mapped to each other. A poor COR correction will result in improper geometry and poor quality in the reconstructed image.

3.3.1 Methods

A tomographic acquisition of two point sources was used to calculate the camera geometry. An ideal model of the camera, which is described below, was built in Microsoft [®] Excel 2000 to calculate projected locations of simulated point sources. The projection data from the two sources were then fit with the ideal model to determine the camera parameters.

The two point sources were made using aluminum zeolite molecular sieve beads less than 2 mm in diameter. A single drop of Tc-99m was added to each bead while trying to make the activity as high as possible. One bead began with an initial activity of 174 MBq and the other with 109 MBq. The beads were wrapped in tape and affixed to the phantom holder 75 mm apart. The camera was set to position the points in the yz-plane. The Radius Of Rotation (ROR) was set to approximately 10 cm, measured from the axis-of-rotation (z-axis) to the pinhole focal point. Starting at θ equals zero degrees, 32 projections covering 360 degrees were acquired for 50 seconds each. This setup provided an average of 690,000 counts per projection to locate the centre of mass for each point.

The magnification provided by a pinhole imaging system is well known. Using the notation from Fig. 3.2 (p. 23), the magnification is calculated as:

$$mag = \frac{a}{b} \quad (3.5)$$

where a is the focal length and b is the ROR. The pinhole collimator has a measured focal length of 197 mm, so that a 10 cm ROR would provide a magnification of approximately two.

The ideal camera model calculates the projection of a point source based on camera parameters. An ideal point source located at (x, y, z) is projected through an ideal pinhole to determine the detector position (u, v) . The detector position will change depending on the ROR, focal length, camera angle θ , and the point source location. As the detector rotates around a stationary point, the projected points trace an ellipse.

I used Excel's solver from the analysis toolpak to search for the best fit. The relevant options were set as follows: precision= 10^{-6} ; tolerance= 10^{-4} ; estimates: quadratic; derivatives: central; and search: conjugate. The point source separation of 75 mm was incorporated to constrain the source locations. Thus, the magnification can be determined based on the known point source separation and measurements of the projection data. In addition, I incorporated the measured focal length. Therefore, the model could fit the magnification and thereby determine the ROR according to Eq. (3.5).

For each of the $M = 32$ projections, at detector angle θ_m , the measured centroids $(\hat{C}_{U_{m_i}}, \hat{C}_{V_{m_i}})$ of each point source must be determined. The centroids are calculated

as:

$$\hat{C}_{U_{m_i}} = \frac{\sum_k \sum_j D_{U_j} P(\theta_m, D_{U_j}, D_{V_k})}{\sum_k \sum_j P(\theta_m, D_{U_j}, D_{V_k})} \quad (3.6)$$

$$\hat{C}_{V_{m_i}} = \frac{\sum_k \sum_j D_{V_k} P(\theta_m, D_{U_j}, D_{V_k})}{\sum_k \sum_j P(\theta_m, D_{U_j}, D_{V_k})} \quad (3.7)$$

where $P(\theta_m, D_{U_j}, D_{V_k})$ are the intensities of projection m at pixel location (j, k) . D_{U_j} and D_{V_k} denote the pixel locations in the uv coordinate system. The first point source, $i = 1$, is located in negative z and therefore is projected onto positive v . For the second point source the situation is reversed. Thus, for a 256X256 projection matrix we consider 256X128 pixels for each point. For $i = 1$, $j = 1, \dots, 256$ and $k = 129, \dots, 256$, while for $i = 2$, $j = 1, \dots, 256$ and $k = 1, \dots, 128$.

The Chi squared (χ^2) function minimized in the Excel solution is given by:

$$\chi^2 = \sum_m \sum_{i=1}^2 \left\{ \frac{[\hat{C}_{U_{m_i}} - C_{U_{m_i}}]^2}{\sigma_{C_{U_{m_i}}}^2} + \frac{[\hat{C}_{V_{m_i}} - C_{V_{m_i}}]^2}{\sigma_{C_{V_{m_i}}}^2} \right\} \quad (3.8)$$

where $C_{U_{m_i}}$ and $C_{V_{m_i}}$ are the modelled ellipse points for each projection m and each point source i . Therefore, the function fits both ellipses simultaneously. The errors in the denominator are the variances which can be expressed as [50]:

$$\begin{aligned}
\sigma_{C_{U_m}}^2 = & \left\{ \left[\sum_k \sum_j D_{U_j}^2 P(\theta_m, D_{U_m}, D_{V_k}) \right] \left[\sum_k \sum_j P(\theta_m, D_{U_m}, D_{V_k}) \right]^2 \right. \\
& - \left. \left[\sum_k \sum_j D_{U_j} P(\theta_m, D_{U_m}, D_{V_k}) \right]^2 \left[\sum_k \sum_j P(\theta_m, D_{U_m}, D_{V_k}) \right] \right\} \\
& \times \left[\sum_k \sum_j P(\theta_m, D_{U_m}, D_{V_k}) \right]^{-4} \quad (3.9)
\end{aligned}$$

$$\begin{aligned}
\sigma_{C_{V_m}}^2 = & \left\{ \left[\sum_k \sum_j D_{V_k}^2 P(\theta_m, D_{U_m}, D_{V_k}) \right] \left[\sum_k \sum_j P(\theta_m, D_{U_m}, D_{V_k}) \right]^2 \right. \\
& - \left. \left[\sum_k \sum_j D_{V_k} P(\theta_m, D_{U_m}, D_{V_k}) \right]^2 \left[\sum_k \sum_j P(\theta_m, D_{U_m}, D_{V_k}) \right] \right\} \\
& \times \left[\sum_k \sum_j P(\theta_m, D_{U_m}, D_{V_k}) \right]^{-4} \quad (3.10)
\end{aligned}$$

3.3.2 Results

The results from Excel's solver are presented in Table 3.2. The ROR, which is difficult to measure, was determined to be 109 mm. The extremely large χ^2 value results from the very small uncertainties used, $\sigma_{C_{U_m}}^2$ and $\sigma_{C_{V_m}}^2$, which were calculated from the high count acquisition. There are other uncertainties in the camera position that are not considered in the calculation. This method provided us with some non-uniform weighting which reflects the different accuracies due to counts.

Figure 3.5 demonstrates that the final solution is a good approximation of the measured ellipses. The fact that the fit is not perfect tells us that the actual geometry

Figure 3.5: The measured points and the fitted model for the COR correction.

Parameter	Result
$x1$ [mm]	-1.7
$y1$ [mm]	21.1
$z1$ [mm]	-32.3
$x2$ [mm]	-3.1
$y2$ [mm]	-23.9
ROR [mm]	108.7
χ^2	1.56×10^{10}
$\Sigma(\Delta u^2 + \Delta v^2)$	291

Table 3.2: Results of the COR fitting procedure. The separation between the two point sources was known to be 75 mm and was used to calculate $z2$. The focal length was measured and set to 197 mm allowing the ROR to vary and adjust the magnification. There were 58 degrees of freedom in the model.

is not ideal as it was modeled to be. This may be due to the camera head tilting slightly during acquisition.

For all of the SPECT studies the camera was set to the same ROR. Therefore the ROR determined by the COR correction was used for all following reconstructions. Using this ROR provides a magnification factor of 1.81 for the studies. The reconstructed SPECT studies in §4 and §5 are well focused and the correct size. Thus, the calculated COR correction was deemed to be sufficient for reconstruction purposes.

Chapter 4

Phantom Studies

In this chapter, phantom studies are presented that examine the system characteristics. The reconstructed spatial resolution is measured with line sources in §4.1. Contrast, Signal-to-Noise Ratio (SNR), and the Coefficient of Variation (CoV) are measured in §4.2 using a Picker thyroid phantom. Within each section the methods and results of the phantom study will be discussed.

4.1 Capillary Tubes

Capillary tubes were used as line sources to measure the reconstructed spatial resolution.

Acquisition Parameters	
Object	Capillary Tubes
Orientations	HA, HT, VT
Activity	79 and 86 MBq
ROR	10.9 cm
Pixel Size	2.4 mm
Rotation	360°
Projections	128
Timing	10 s/proj

Reconstruction Parameters		
orbit	360°	180°
voxel size	1 mm	1 mm
subsets	8	4
iterations	20	40

Table 4.1: Acquisition and reconstruction parameters for the capillary tubes. The central and outer capillaries were filled with 79 and 86 MBq respectively. The orientations are defined in Figure 4.1.

4.1.1 Methods

Setup

Fisherbrand® micro-hematocrit capillary tubes were used to measure the system resolution. The tubes have an inner diameter of 1.1 to 1.2 mm and a wall thickness of 0.2 mm. The tubes were filled with approximately 70 mm of activity and sealed at each end using Critoseal®, a vinyl plastic putty. With these dimensions, the capillary tubes closely approximate line sources.

The capillary tubes were filled with high concentrations of Tc-99m to provide high count, low noise projections. The camera was set to 2.4 mm pixels to provide high spatial sampling and 128 views were taken to provide high angular sampling. Further acquisition and reconstruction parameters are provided in Table 4.1.

Figure 4.1: The three line source orientations: Horizontal Axial (HA), Horizontal Transverse (HT), and Vertical Transverse (VT). The central source (passing through the origin) was filled with 79 MBq and the outer source with 86 MBq. The camera rotates about the z-axis in the xy-plane.

The capillary tubes were sequentially imaged in three orientations to measure the resolution along each axis. Two capillary tubes were placed parallel to each other but separated by 3 cm. One was centred in the FOV and the other offset to measure any positional dependency. Both sources were entirely in view for all projections so that all activity was within the 3-D FOV. The sources were placed in the horizontal and vertical transverse (yz and xy) planes as shown in Figure 4.1.

Analysis

The projection data used for reconstruction were either 360° or 180° . In the case of a half orbit, the projections used were a subset of the original data acquired. Thus, there are 128 projections available to reconstruct a full orbit but only 64 projections available to reconstruct the half orbit image. In each case, there were 16 projections per subset.

The 64 projections used for 180° reconstruction were chosen to be either $\theta = -90^\circ$

to $+90^\circ$ or $\theta = 180^\circ$ to 360° . The choice for each case was determined based on the best sampling of the outer line source. In case HA, the projections were taken from 180° to 360° because the outer source was closest to 270° . In case HT, the projections were taken from -90° to $+90^\circ$ because this allowed equal sampling of each end of the outer source. In case VT, the projections were taken from -90° to $+90^\circ$ because the outer source was closest to 0° .

The MRP prior weight, β , which adjusts the degree of filtering, was varied from zero to one in increments of 0.1 to sample the full range. In addition, a comparison with the traditional Butterworth post-reconstruction filter was performed. Early stoppage and post-reconstruction Butterworth filtering is the standard procedure at the Ottawa Hospital, Civic Campus. Following this procedure, the unfiltered image, $\beta = 0.0$, was stopped after an equivalent of only 32 standard iterations. The standard procedure of 8 subsets with 4 iterations was used for full-orbit reconstruction, while 4 subsets with 8 iterations was used for half-orbit reconstructions. A Butterworth filter with a cut-off frequency of 2.8 cycles/cm and order 5 was then applied within the Hermes software suite (Nuclear Diagnostics, Stockholm, Sweden). The cut-off frequency was chosen as the maximum frequency used clinically (1.4 cycles/cm) multiplied by two for the approximate zoom factor of the pinhole acquisition geometry. The equation used to define the Butterworth filter in the frequency domain is given by [51]:

$$H(\omega) = \frac{1}{1 + \left(\frac{\omega}{\omega_c}\right)^{2A}} \quad (4.1)$$

where ω_c is the cutoff frequency and A is the order.

The resolution was measured using the Full Width at Half Maximum (FWHM).

A single slice in the plane of the line sources was used for the measurements. The slice was selected to provide the maximum activity and represent the central axis of the capillary tubes. Within the slice, four rows along the length of the sources were averaged to provide a one-dimensional profile across the capillaries. Three neighbouring profiles were used to determine an average measurement and a standard deviation to represent the error. The FWHM was measured directly using linear interpolation of the points at half of the maximum profile value.

Investigators often use a Gaussian fit of their profiles to measure the FWHM [25, 26, 28]. A Gaussian fit of the data was attempted but abandoned because of the poor fit of the Gaussian distribution with the MRP profiles. The poor fit is due to the nature of the median operator, which works to lower the peak value to that of its neighbours while preserving the profile edges. Especially when β becomes large, the profile becomes more rectangular than Gaussian. In this case, the Gaussian fit overestimates the maximum and therefore underestimates the FWHM. An example profile showing the poor fit of the Gaussian distribution is presented in Figure 4.2.

4.1.2 Results

Let us begin with a qualitative look at the reconstructed images. Figure 4.3 shows the central slice of the HT case for four different filter weights as an example. The line sources were well focused and in the proper geometry in the reconstructed images. The unfiltered case suffers from a great deal of noise as expected, and therefore the colour scale is expanded. The MRP filter maintains the same average concentrations without the severe noise spikes, providing a much more uniform reconstruction.

The FWHM was measured after every full iteration for the full range of β in

Figure 4.2: Profile of a reconstructed line source with $\beta = 0.6$ and its Gaussian fit. The voxels are 1 mm in size.

increments of 0.1. The quantitative results are presented in this section for $\beta = 0.0$, 0.1, 0.3, 0.6, and 1.0. These values were found to be representative and provides a more concise presentation. The reconstruction dynamics are discussed and example cases of the FWHM dependence on iteration are presented in Figure 4.4. The final results for each case are presented in Tables 4.2, 4.3, and 4.4. We will first discuss the MRP reconstructions and then consider the Butterworth comparison.

It was found that the FWHM values could behave unpredictably in the early iterations. The FWHM could start smaller, quickly rise and level at a constant value or begin very close to the final value. Figure 4.4a presents a case where the FWHM first rises and then falls to its final value. As another example, when both line sources were placed in the orbital plane, case VT, the sources were often superimposed in the projection data. During the initial reconstruction estimates,

Figure 4.3: The central slice of the HT line sources with four different filter weights. The colour scale indicates the relative reconstructed radioactive concentration.

the backprojection process would blur the activity across the orbital plane and thus the resolution would begin very poor. As the iterations increase, the sources become better separated and focused and the resolution improves. This behaviour can be seen in Figure 4.4b.

In some cases of no filtering, $\beta = 0$, the error bars grow larger as the image converges (Fig. 4.4). This is an indication that the variation of the FWHM along the line source is increasing, due to the increase in checkerboard noise as the iterations continue. Increasing the filter weight a moderate amount controls the noise significantly as evidenced by the smaller errors seen in Figure 4.4 and Tables 4.2, 4.3, and 4.4 for all non-zero values of β .

For the early stoppage technique, unpredictability in the early iterations can result in greater variability in image quality depending on the stopping point. One is searching for a balance between relative convergence and the checkerboard noise which is building. For practicality and image throughput, the same stopping point is usually used for each image without considering that each image is unique. Consider Figure 4.4 again, and note the different shapes and errors of the unfiltered curves. Differences such as these make it difficult to choose the best early stopping point for each image. The standard stopping point is likely not the best choice for a particular image.

The final results of the FWHM measurements are presented in Tables 4.2, 4.3, and 4.4. Considering the MRP results, increasing the prior weight, β , generally degrades the resolution as expected. Looking at all of the cases, increasing β from 0.1 to 1.0 results in an average loss of resolution of only 8%. The individual losses vary considerably from 0.2—21% with the standard deviation being 6%.

Figure 4.4: FWHM versus iteration for two cases: a) outer HT line source reconstructed over 180° b) outer VT line source reconstructed over 360° . In the 180° case, there are 40 iterations with 4 subsets to compare with the 20 iterations of 8 subsets in the 360° case. These are equivalent to 160 standard iterations. Results from the Butterworth filter, applied after early stopping, are shown as a constant across all iterations.

HA	Central		Outer	
Filter	360°	180°	360°	180°
$\beta = 0.0$	6.01 ± 0.22	5.70 ± 0.13	5.40 ± 0.05	5.89 ± 0.15
$\beta = 0.1$	5.93 ± 0.06	6.18 ± 0.04	5.48 ± 0.02	5.74 ± 0.03
$\beta = 0.3$	6.08 ± 0.04	6.26 ± 0.01	5.54 ± 0.01	5.76 ± 0.02
$\beta = 0.6$	6.18 ± 0.02	6.30 ± 0.01	5.55 ± 0.01	5.76 ± 0.02
$\beta = 1.0$	6.26 ± 0.02	6.34 ± 0.02	5.59 ± 0.01	5.78 ± 0.03
Butterworth	6.18 ± 0.03	6.15 ± 0.02	5.696 ± 0.002	5.81 ± 0.01

Table 4.2: Final FWHM results of the HA line sources as a function of the MRP parameter, β , and for the Butterworth filter applied after early stoppage. The FWHM values are measured in mm.

HT	Central		Outer	
Filter	360°	180°	360°	180°
$\beta = 0.0$	5.76 ± 0.17	5.14 ± 0.39	5.62 ± 0.21	5.18 ± 0.27
$\beta = 0.1$	5.92 ± 0.05	5.73 ± 0.14	5.70 ± 0.06	5.74 ± 0.08
$\beta = 0.3$	6.12 ± 0.04	6.01 ± 0.19	5.68 ± 0.03	5.86 ± 0.01
$\beta = 0.6$	6.27 ± 0.04	6.19 ± 0.12	5.68 ± 0.04	5.89 ± 0.05
$\beta = 1.0$	6.35 ± 0.05	6.27 ± 0.04	5.71 ± 0.04	5.94 ± 0.07
Butterworth	5.964 ± 0.001	5.86 ± 0.02	5.76 ± 0.02	6.03 ± 0.03

Table 4.3: Final FWHM results of the HT line sources as a function of the MRP parameter, β , and for the Butterworth filter applied after early stoppage. The FWHM values are measured in mm.

VT	Central		Outer	
Filter	360°	180°	360°	180°
$\beta = 0.0$	6.13 ± 0.24	5.24 ± 0.27	4.91 ± 0.20	5.13 ± 0.16
$\beta = 0.1$	6.22 ± 0.23	6.07 ± 0.32	5.56 ± 0.05	5.42 ± 0.05
$\beta = 0.3$	6.42 ± 0.13	6.28 ± 0.21	5.87 ± 0.03	5.75 ± 0.02
$\beta = 0.6$	6.70 ± 0.11	6.34 ± 0.13	6.16 ± 0.05	5.95 ± 0.04
$\beta = 1.0$	7.00 ± 0.10	6.47 ± 0.12	6.36 ± 0.04	6.13 ± 0.03
Butterworth	6.61 ± 0.03	6.72 ± 0.15	6.22 ± 0.01	5.98 ± 0.01

Table 4.4: Final FWHM results of the VT line sources as a function of the MRP parameter, β , and for the Butterworth filter applied after early stoppage. The FWHM values are measured in mm.

The FWHM results of the Butterworth cases are often worse but with smaller errors than the MRP results. The loss of resolution is due to the edges of the profiles being smoothed and broadened rather than preserved. A comparison of the Butterworth and MRP ($\beta = 1.0$) profiles is given in Figure 4.5. The broadening has a large impact on the base of the peak, for example at the Full Width Tenth Maximum (FWTM). On the other hand the peak activity is reduced with MRP due to the lower activity on each side. The smoothing effect of the Butterworth filter can also be seen in the smaller errors, which represent more uniformity along the length of the sources. Variability in image convergence with early stoppage can be seen in the variation of the Butterworth measurements: in most cases the resolution is the worst, but on occasions one is fortunate and it is quite good. The Butterworth filter also introduces ringing that is not measured in the FWHM but can produce undesirable artefacts in an image.

The outer line source is often better focused than the central line source. The magnification and resolution of the pinhole system degrades as objects are farther away. In addition, the sensitivity is reduced according to the inverse square law as the distance increases. The outer line source is sometimes further and sometimes closer to the pinhole as the orbit is acquired. This leads to varying magnification and resolution as well as sensitivity of the source in the projections. The reconstruction algorithm searches for the best fit to the Poisson data and naturally lends more weight to the higher count projection pixels. As a result, the highly magnified, high count projections of the outer source receive more weighting, resulting in a more focused reconstruction.

The MRP algorithm provides good noise control and does not severely degrade

Figure 4.5: Comparison of a Butterworth and MRP ($\beta = 1.0$) profile. The voxels are 1 mm in size.

resolution. When compared with the standard Butterworth filter, it does very well and allows the image to converge without a large increase in noise. In addition, it does not introduce any ringing artefacts.

4.2 Thyroid Phantom

The Picker 3602 thyroid phantom was used to measure contrast, Signal-to-Noise Ratio (SNR), and the Coefficient of Variation (CoV). The phantom is a standard used in planar and SPECT imaging, especially in pinhole SPECT. There are three cold rods measuring 12, 9, and 6 mm in diameter as well as an 11 mm hot rod. These rods represent cold and hot nodules that may be found in the thyroid. The phantom has a single filling port and is filled with a uniform concentration of activity. Plastic

Figure 4.6: Drawing of the Picker thyroid phantom. The left lobe contains two cold rods with 6 and 12 mm diameters. The right lobe contains a 9 mm diameter cold rod and an 11 mm diameter hot rod. The right lobe has a cold plastic background in the lower half where the hot rod is defined and a hot background in the upper half where the 9 mm cold rod is defined.

rods in empty regions of the phantom produce the cold regions whereas the hot rod is a hole in a plastic background. In this way, the activity is either on or off. A drawing of the phantom is provided in Figure 4.6.

4.2.1 Methods

Setup

The thyroid phantom was filled with 550 MBq and centred in the horizontal plane. This orientation of the thyroid phantom represents the standard orientation of a patient's thyroid in a clinical situation. The camera was set to acquire 128 views at 15 seconds per projection. The total imaging time was nearly 38 minutes and too long to be clinically feasible. In addition, the activity is much greater than one

Acquisition Parameters	
Object	Thyroid Phantom
Orientation	Horizontal
Activity	550 MBq
ROR	10.9 cm
Pixel Size	2.4 mm
Rotation	360°
Projections	128
Timing	15 s/proj

Reconstruction Parameters		
orbit	360°	180°
voxel size	1 mm	1 mm
subsets	8	4
iterations	40	80

Table 4.5: Acquisition and reconstruction parameters for the Picker thyroid phantom.

would expect in a normal patient. The higher count projections were acquired to accurately measure the system's ability rather than the clinical feasibility. The full set of acquisition and reconstruction parameters are listed in Table 4.5

Analysis

The data were reconstructed using 1 mm voxels and β was varied from zero to one. The range of projection data provided for reconstruction was either 360° or 180°. Clinically, one can only acquire slightly less than a half orbit because the cone of the pinhole collimator is limited by the subject's shoulders. In the case of the half orbit reconstruction, the 64 projections were taken from -90° to +90° mimicking the clinical situation.

Rod Size and Type	12 mm Cold	9 mm Cold	6 mm Cold	11 mm Hot
Rod ROI	$4 \times 4 \times 1$	$3 \times 3 \times 1$	$2 \times 2 \times 1$	$4 \times 4 \times 1$
Background ROI	$8 \times 8 \times 1$	$6 \times 6 \times 1$	$4 \times 4 \times 1$	$7 \times 7 \times 1$

Table 4.6: Rod and background ROI sizes (in mm or voxels) used to calculate contrast and SNR. The hot and cold backgrounds of the 12 mm cold and 11 mm hot rods respectively were also used to calculate the CoV.

Contrast and SNR were calculated for all four rods using the following formulae:

$$c = \frac{|\mu_r - \mu_b|}{\mu_b} \quad (4.2)$$

$$SNR = \frac{|\mu_r - \mu_b|}{\sqrt{\sigma_r^2 + \sigma_b^2}} \quad (4.3)$$

where μ and σ are the mean and standard deviation of a Region Of Interest (ROI), and where the subscripts r and b represent rod and background respectively.

The ROIs for each rod and its respective background were taken from the same coronal slice. Because of the phantom geometry, these slices could not be the same for every rod. For example, the 9 mm cold rod and its background is only defined in the upper coronal slices while the 11 mm hot rod and its background is only defined in the lower coronal slices. The background ROI sizes were chosen to be the largest square to fit inside the rod's diameter. The rod ROI sizes were chosen to be approximately one quarter the size and therefore fit easily inside the rod. These ROI sizes are listed in Table 4.6. Both the rod and its respective background were taken from the same lobe of the thyroid phantom. The background ROIs were selected from the uniform portions between the pair of rods in each lobe.

In addition to contrast and SNR, the CoV was measured for both a cold and hot

background. The ROIs chosen for this measurement were the largest background areas, which were provided by the background ROIs of the 12 mm cold and 11 mm hot rods. The CoV was calculated as the standard deviation over the mean:

$$CoV = \frac{\sigma_b}{\mu_b} \quad (4.4)$$

where the notation is the same as in Eqn. 4.2 and 4.3.

4.2.2 Results

Representative slices of the reconstructed thyroid phantom are shown in Figure 4.7 for a qualitative comparison. An upper and lower coronal slice are presented for three different filter weights ($\beta = 0.0, 0.3$, and 0.6). The iterative reconstruction provides excellent contrast that is well maintained with MRP. Filtering is also seen to greatly improve the uniformity and thereby the SNR.

The quantitative results from the Picker thyroid phantom will be presented in a similar manner as in §4.1.2. Again, $\beta = 0.0, 0.1, 0.3, 0.6$, and 1.0 will be used to sample the full range of prior weights. Example cases of the reconstruction dynamics are presented in Figures 4.8 and 4.9. The final results for each rod for both the full and half orbit reconstructions are presented in Tables 4.7, 4.8, and 4.9.

In every reconstruction, all of the cold rods are visible. For the cold rods, the contrast quickly reached a constant level with any amount of filtering. In the unfiltered reconstruction the contrast for the 9 and 6 mm cold rods was initially the best but then began to fall as the noise in the image increased. Overall, the best contrast for the cold rods was achieved after approximately forty standard iterations (i.e. 4

Figure 4.7: Representative slices of the Picker thyroid phantom reconstructed from a full orbit. The rows present three different filter weights ($\beta = 0.0, 0.3$, and 0.6). The columns show an upper coronal slice where the 9 mm cold rod is defined and a lower coronal slice where the 11 mm hot rod is defined.

subsets and 10 iterations for 180° or 8 subsets and 5 iterations for 360°).

Figure 4.8a shows the contrast versus iteration for the 9 mm cold rod in the 180° reconstruction. One can see the filtered measurements quickly reaching a stable value while the unfiltered reconstruction begins to fall due to noise in the image. This has an even greater effect in the 6 mm cases where noise can have a larger effect on the mean in a smaller ROI.

In the case of the 11 mm hot rod, the contrast is defined between zero and infinity because ideally the cold background would have zero activity. Figure 4.8b shows the contrast versus iteration for the hot rod in the full orbit reconstruction. The most apparent feature is that the contrast is still rising for all prior weights. Because of this trend, the thyroid phantom was reconstructed with twice as many iterations as the line source to determine whether the result would reach a constant. It was found that the mean background continued to decrease very slowly as the iterations continued. Although, this decrease has a large effect on the contrast because of the small denominator, it has little or no visual effect on the image. Thus, it was not felt necessary to continue for even further iterations.

The final contrast results presented in Table 4.7 are very encouraging. The 12 and 9 mm cold rod cases provide contrasts between 0.85 and a perfect 1.0. The 6 mm cold rod still faired quite well for all cases with an average contrast of 0.5. This means that the smallest rod did not reach zero activity but did manage to reach half of the background activity. In this case, MRP again did a good job of controlling the noise which otherwise degraded the contrast in the unfiltered image significantly.

The contrast measured for the hot rod was sufficient to easily identify it. The

Figure 4.8: Contrast versus iteration for two cases of the Picker thyroid phantom: a) the 9 mm cold rod reconstructed over 180° b) the 11 mm hot rod reconstructed over 360°.

	12 mm Cold		9 mm Cold		6 mm Cold		11 mm Hot	
β	360°	180°	360°	180°	360°	180°	360°	180°
0.0	0.999	1.000	0.888	0.969	0.421	0.510	23.4	11.2
0.1	0.990	0.998	0.891	0.953	0.553	0.561	20.2	9.37
0.3	0.978	0.984	0.882	0.932	0.522	0.537	21.1	9.05
0.6	0.969	0.970	0.873	0.922	0.481	0.501	20.6	8.68
1.0	0.963	0.960	0.866	0.911	0.449	0.487	19.1	8.43

Table 4.7: Contrast results for the Picker thyroid phantom as a function of the MRP parameter, β .

results from the 180° reconstructions showed contrasts of slightly less than half of their 360° counterparts. This reduction in contrast is due to the fact that the hot rod was not sampled optimally in the half orbit. It was mentioned earlier that the hot rod is only defined in the lower coronal slices. The half orbit chosen to reconstruct the thyroid phantom began at -90° and proceeded around the front to +90° as it would be done in a patient situation. This orbit provides better sampling of the upper coronal slices than the lower slices. As a consequence, the activity is less focused in the lower coronal slices and so the hot rod does not reach the same activity while the background is reconstructed with a higher activity. Both of these effects lower the contrast measurement.

On the other hand, the cold rods do not show this trend. The 12 and 6 mm cold rods which were measured in a central coronal slice produce similar results for both the full and half orbit reconstructions. The 9 mm cold rod which is only defined in the upper coronal slices actually produces slightly better results in the 180° reconstruction.

Let us now consider the interplay between the CoV and SNR dynamics. Plots of the CoV and SNR for the 12 mm cold rod are shown in Figure 4.9 and are

Figure 4.9: CoV and SNR versus iteration for the 12 mm cold rod reconstructed over 360°.

	12 mm Cold		9 mm Cold		6 mm Cold		11 mm Hot	
β	360°	180°	360°	180°	360°	180°	360°	180°
0.0	0.227	0.269	0.312	0.297	0.192	0.221	0.72	0.75
0.1	0.049	0.055	0.029	0.040	0.024	0.031	0.23	0.20
0.3	0.027	0.033	0.018	0.024	0.013	0.017	0.21	0.19
0.6	0.023	0.025	0.014	0.019	0.012	0.014	0.21	0.15
1.0	0.020	0.022	0.013	0.016	0.011	0.014	0.15	0.10

Table 4.8: CoV results for the Picker thyroid phantom.

representative of the trends found in all the rods. In the unfiltered case, $\beta = 0.0$, the checkerboard noise begins to enter and the noise level continues to rise as the CoV increases. After our long reconstruction, the noise is still increasing. This would be an obvious argument for early stoppage were it not for priors like MRP. Adding the MRP filter controls the noise extremely well. Even with $\beta = 0.1$, the noise is much better controlled although still rising slightly in this particular case.

The control of noise in the image clearly affects the SNR. As the noise increases, the denominator increases and SNR is reduced. This is clearly visible for $\beta = 0.0$ in Figure 4.9. For $\beta = 0.3, 0.6$, and 1.0 , there are clear jumps in the SNR making the graph choppy. This is primarily due to changes in σ_b , which dominates the denominator, and which produces corresponding changes visible in the CoV. Several other cases also showed this jumpy behaviour while others were smooth.

Table 4.8 presents the final CoV results for each case. Even the smallest amount of filtering, ($\beta = 0.1$), has a large effect in controlling the otherwise increasing noise. Increasing β has the obvious effect of further controlling the noise and lowering the CoV. We note that the CoV for the 11 mm hot rod is considerably larger than for the cold rods. This is because the CoV is taken from a cold (rather than hot) background where there is more counting noise in the projections.

	12 mm Cold		9 mm Cold		6 mm Cold		11 mm Hot	
β	360°	180°	360°	180°	360°	180°	360°	180°
0.0	4.4	3.7	2.6	3.2	1.6	1.8	4.1	3.9
0.1	19.9	18.0	15.6	21.1	17.6	11.5	34.7	20.9
0.3	34.2	29.4	20.8	32.6	39.6	22.8	36.4	21.0
0.6	38.2	36.7	24.1	39.6	36.5	28.0	35.1	19.8
1.0	44.3	41.2	24.3	37.9	42.4	33.4	38.4	21.0

Table 4.9: SNR results for the Picker thyroid phantom.

The final SNR values (Table 4.9) of the filtered reconstructions are sufficient for detecting even the smallest rod. The final values of the unfiltered reconstructions on the other hand are much lower. These small ratios are due to the increasing noise levels in the unfiltered images.

Chapter 5

Clinical Wrist Study

A pinhole SPECT acquisition was taken of a patient's wrist bones to demonstrate clinical feasibility. Bone imaging in nuclear medicine is commonly done using Tc-99m labelled medronate di-phosphate (MDP). The MDP tracer is injected into the blood stream and over a period of a few hours is taken up preferentially in the bones, particularly in areas of increased blood supply. Regions of increased uptake, known as hot spots, are generally active sites of bone or joint pathology (bone injury, infection, tumor, etc.).

5.1 Methods

5.1.1 Setup

The patient was a 57 year old woman who was injected with 792 MBq of MDP. The injection was given in order to acquire bone flow, bone blood pools and whole body bone images as part of a routine clinically indicated study. Afterwards, the

physician requested a static image of her wrists with a parallel hole collimator. At this point, four hours after injection, the pinhole SPECT image of her left wrist was taken. The additional pinhole SPECT imaging was performed with the patient's informed consent. This study did not subject her to any radiation exposure other than that which was incurred for the clinically indicated study.

The image represents clinically realistic conditions, and the conditions were not optimized for quality. 792 MBq is within the range of activity administered for bone studies. 32 projections were acquired over a full orbit with 30 seconds per projection. The total imaging time including camera movement was 18 minutes 30 seconds. The maximum time for a SPECT acquisition is considered to be 20 to 30 minutes before it becomes too uncomfortable for the patient. The delay time at which to acquire a bone image must balance the target to background ratio and the radioactive decay rate. As MDP is taken up, it is locked in the bone while the background tracer left in the blood washes out, so the target to background ratio improves with time. The optimal delay is two to three hours after injection when the target to background ratio is good and less activity has decayed away. By four hours, 37% of the initial Tc-99m activity has decayed away. In addition, the uptake is highest in growing bones and therefore younger patients. The realistic acquisition time and activity together with the longer delay period and patient age provided a less than optimal acquisition.

The patient was positioned in such a way as to allow the wrist to be in the pinhole FOV, while the patient's head and body are out of the camera's way as it rotates. Having the patient lie prone on the bed with their arm above their head allowed the patient to be fully supported and fairly comfortable.

Acquisition Parameters	
Object	Left Wrist
Orientation	Palm Down
Injection	792 MBq MDP
Injection Time	4 Hrs Prior
ROR	10.8 cm
Pixel Size	2.4 (4.8) mm
Rotation	360°
Projections	32
Timing	30 s/proj
Total Counts	55,000

Reconstruction Parameters	
orbit	360°
voxel size	2 mm
subsets	1
iterations	100
β	1.0

Table 5.1: Acquisition and reconstruction parameters for the clinical wrist image. The projection data was acquired with 2.4 mm pixels but it was resampled to 4.8 mm pixels before reconstruction to reduce counting noise.

The camera was set to a 10.8 cm ROR, which differs from the COR acquisition by only 1 mm. This difference was due to time pressures during positioning and is not significant. The projections were acquired at the highest resolution with 2.4 mm pixels but were later resampled to 4.8 mm pixels to reduce the counting noise. Correspondingly, the voxel size was increased to 2 mm, which also increases the filter neighbourhood in the spatial domain. Further acquisition and reconstruction parameters are presented in Table 5.1.

5.1.2 Analysis

The reconstructed image was analyzed qualitatively to determine whether clinical pinhole SPECT of the bones in the wrist will be useful. Therefore, the images were studied to determine whether they provide more clinically useful information than conventional planar imaging.

The individual transverse, coronal and sagittal slices were viewed. In addition a rotating Maximum Intensity Projection (MIP) movie was also very useful in analysis. Unfortunately the MIP movie cannot be meaningfully reproduced here but has been presented in the past [52, 53]. The reconstructed image was also compared to the (parallel hole) static view of the patient's hands, shown in Figure 5.1, which was requested by the physician. References such as the one presented in Figure 5.2 (author unknown) were very useful in identifying features in the image.

5.2 Results

In general, the reconstructed image is noisy due to the low count projections. The total number of counts in the projection data is similar to the number of counts in a single parallel hole projection of a bone SPECT of the chest. The reconstructed concentrations are small and noise in the background is therefore more evident. Due to the high level of noise, the projection data were resampled and the voxel edge size was doubled as mentioned in §5.1.1. In addition, a median filter was applied at every update ($\beta = 1.0$) for maximum filtering. Despite the noise, there are identifiable features and clinical utility in the reconstructed image.

Figures 5.3, 5.4, and 5.5 show the transverse, coronal and sagittal slices respec-

Figure 5.1: The static view of the patient's hands, which was requested by the physician. The spot of activity on the right edge indicates the right hand. The image was acquired with a parallel hole collimator.

Figure 5.2: A reference image of the right hand with the bones and joints labelled.

tively. In these figures, the first frame provides a perpendicular reference view with lines defining the slice limits. The following frames are single slices and are labeled in the upper left corner. The label provides the orientation and slice number of the frame. For example, the label T:40 found in the second frame of Fig. 5.3 identifies the frame as transverse slice number 40. Slices are numbered left to right and from bottom to top in a Cartesian manner. The frame labels will be used during discussion of the results.

The first frame of Figure 5.3 provides a summed coronal reference view where we can identify several interesting features. There are two hot spots in the wrist, a small one to the left and a much larger one around the carpo-metacarpal joint of the thumb. One can also see the edge of the FOV where the image edge is rounded at the top and bottom. The edge of the FOV contains artefacts of increased activity. This artefact is due to activity outside the FOV which was only seen in some projections but must be accounted for in the OSEM reconstruction. This extra activity is reconstructed at the periphery of the image while activity levels in the central FOV are largely unaffected. Therefore, hot spots at the periphery should be ignored.

The transverse slices presented in Figure 5.3 are useful in identifying individual bones. Frames T:29–27 provide excellent examples of the ability to distinguish and identify bones in the wrist. In T:24–23, the pisiform bone can be seen protruding down towards the palm. One can easily identify the large hot spot where the thumb joins the wrist proper (T:35–31).

The coronal slices provide a familiar view of the wrist (Fig. 5.4). These slices show the general shape of the hand so that one can easily identify features and get one's bearings. The frames move from the back of the hand (C:44) towards the palm

Figure 5.3: Transverse slices of the clinical wrist image. The upper left frame is a summed coronal reference view, with lines showing the range of transverse slices being displayed.

Figure 5.4: Coronal slices of the clinical wrist image. The upper left frame is a summed transverse reference view, with lines showing the range of coronal slices being displayed.

Figure 5.5: Sagittal slices of the clinical wrist image. The upper left frame is a summed transverse reference view, with lines showing the range of sagittal slices being displayed.

(C:26). On the way, we pass through the metacarpals of the four fingers centered on C:36 and the thumb metacarpal in C:33–29. It becomes obvious that the two hot spots are both forwards in the wrist, near the palm of the hand. This identifies one hot spot as the pisiform rather than the triquetral which is directly above.

Less useful are the sagittal slices presented in Figure 5.5. It is still possible to see separate bones in certain frames (e.g. S:33), however, it is more difficult to determine where a slice is located in the subject. The left to right location of features in the image is more easily determined in the other views. The artefacts around the edge of the image are also more prevalent and distracting.

The MIP movie, which cannot be presented here, was also a very useful presentation of the image. As it rotates, it produces a 3-D illusion presenting the highest activity features seen from each direction. This allows the user to quickly identify the hot spots and their locations in the subject. In this form, one can filter the rotating image visually to ignore background activity outside the subject. On the other hand, the peripheral artefact is more distracting as the fingers blur together and may appear to be bent into a claw hand.

The MIP movie should only be considered a quick visual tool and does not represent the full data. The activity levels are also weighted in the image according to depth and so the representation is not accurate. As such, one should always view the slices that represent the actual reconstructed data.

Overall, one should be pleased with this very first clinical attempt of pinhole SPECT at the Ottawa Hospital. Although the projections are count poor, details of individual bones and other features can be seen in the wrist. The peripheral artefact is felt to be tolerable and does not affect the central area of interest.

The 3-D reconstructed image provides depth information unavailable from the parallel hole static view. This allows one to identify the one hot spot as the pisiform rather than the triquetral. These bones are superimposed in the static view and therefore cannot be distinguished. The pinhole SPECT image also provides greater resolution, with its magnification, than the parallel hole image.

For clinical use, the delay after injection should be optimized for greater activity. In addition, the ROR could be reduced to focus more tightly on the wrist. Reducing the ROR would also increase the magnification and resolution as well as increase the sensitivity, which would reduce the noise.

Chapter 6

Conclusions and Recommendations

The results of this study are encouraging for clinical pinhole SPECT. This chapter presents the conclusions and recommendations arising from the research.

6.1 Conclusions

The OSEM reconstruction algorithm produces quality images with few artefacts. The 3-D activity distribution is correctly recovered from the 2-D projection data set. It also provides excellent resolution and contrast. As the iterations increase, however, the checkerboard noise pattern emerges, quickly degrading image quality.

The early stoppage technique attempts to take advantage of OSEM's benefits while limiting the noise. It may seem reasonable to stop the reconstruction before SNR and uniformity suffer greatly. Unfortunately, the ideal stopping point depends on the particular image and the properties that one is looking for. It is also known that high frequency details appear later. In addition, it is obvious that early stoppage precludes convergence and may result in a bias towards the initial uniform estimate.

MRP penalizes local non-monotonicity in the image at every update. The prior increases uniformity by controlling the emerging noise in the OSEM reconstruction. Limiting the noise allows one to reach convergence and avoid the potential problems of early stoppage.

Line sources were used to measure the system resolution by measuring the FWHM. It was also shown that the edges are preserved (§4.1.2), however, the MRP filter tends to flatten sharp features in the image. The average spatial resolution, with a moderate amount of filtering ($\beta = 0.3$), was 6.0 ± 0.3 mm. The resolution depends on β and degrades slightly with increasing filtering. MRP was seen to provide better and more consistent results than the standard Butterworth filter applied after early stoppage. The Butterworth filter also introduces undesirable ringing in the image, which is not present with MRP.

Image quality was measured quantitatively using the Picker thyroid phantom. It was found that OSEM provides excellent contrast, especially for the larger rods. Even the smallest rod (6 mm) was visible in all images with an average contrast of 0.5. The unfiltered images suffered from poor uniformity and had an average SNR of 3.2. The use of MRP decreased the CoV, and consequently improved the SNR, each by an order of magnitude.

Incomplete sampling of the projection data set, using 180° acquisition, still provided good image quality. Objects closer to the pinhole were better focused, benefiting from increased magnification. The contrast and SNR, however, were noticeably reduced for the 11 mm hot rod, because it was outside of the ideal sampling region. Uniformity in the images was unaffected by a half orbit reconstruction. Therefore, when using an incomplete orbit it is important to sufficiently sample the feature of

interest.

The wrist image demonstrated the clinical feasibility of pinhole SPECT with OSEM-MRP. With the pinhole magnification, one is able to identify individual wrist bones and locate abnormal tracer uptake in the image. A 3-D SPECT image also provides more information than static projections can. Therefore, despite the low count data acquired, the reconstructed image is clinically useful.

The one major artefact encountered was due to activity outside the 3-D FOV. This activity, which may be seen in some but not all projections produces inconsistencies in the data. The extra counts are reconstructed on the periphery of the image as hot spots or a halo. This artefact is not considered serious because the central volume, in which one is interested, is unaffected.

6.2 Recommendations

I recommend that further clinical studies be done with pinhole SPECT. In addition to wrists, the ankles and knees, etc. could benefit as they are not currently well imaged by nuclear medicine. Due to the small ROR and large cone involved in pinhole SPECT it is difficult to support the patient in the FOV. Further studies will require a better arrangement for positioning and supporting patient extremities.

Current commercial packages support iterative reconstruction, but depend on early stoppage and pre- or post-filtering. In the clinic the early stoppage point is chosen arbitrarily and for practicality cannot be optimized for each image. The use of MRP should be added to commercial packages so that clinicians can benefit from this filter in all their SPECT studies.

Finally, the pinhole collimator used in this research did not use the full camera head available in acquiring projections. I believe that pinhole SPECT may benefit from a larger acceptance angle. A larger acceptance angle will increase the 3-D FOV for a given ROR. If the ROR is then reduced, one may produce a 3-D FOV equal to the original size. The reduction of the ROR, however, will increase the sensitivity and magnification. Thus, the resulting image would suffer from less noise and have an improved resolution.

The negative side to modifying the collimator in this way is that its size will increase. Already, the cone size can make patient positioning difficult for certain studies such as the thyroid. Enlarging the cone may aggravate this problem although not likely for extremities such as the wrist and ankle. The present pinhole collimator is quite heavy (74.3 kg) but has been designed for higher energies (I-131). A specialized design for Tc-99m tomography could be wider but less heavy.

Appendix A

Implementation of the MRP Algorithm

Implementation of the MRP algorithm was done by the author in C on a Unix platform. The algorithm was then integrated into the pinhole OSEM code provided by M. Defrise, which was also written in C. Various modifications of the pinhole OSEM routines were made to accomodate MRP as well as to increase its efficiency.

The median filter was originally intended for 1- and 2-D data. MRP was originally developed for 2-D transmission and emission imaging. Pinhole SPECT, however, requires full 3-D reconstruction due to the divergent ray geometry. Thus, for Pinhole SPECT the MRP algorithm must be modified to use a 3-D neighbourhood. In this work, a $3 \times 3 \times 3$ voxel neighbourhood is used. This modification has been previously introduced for 3-D PET [54] and pinhole SPECT [26, 27].

Because the calculation of the median of 27 values was going to be very frequent, several functions were tested for speed. The function chosen was *Quickselect* from

Devillard [55], but with the array size hard coded to 27. *Quickselect* in turn is based on the *Select* function from Numerical Recipes in C [56]

If a voxel contains zero activity it will remain zero because the update factors are multiplicative (Eq. (2.10)). Many of the voxels in the reconstruction space are outside the 3-D pinhole FOV, and will be forced to zero since one or more projections cannot see the voxel. If a voxel concentration becomes very small (10^{-12}) during reconstruction, the voxel is considered to be approximately zero and is no longer updated, saving time during reconstruction.

This approach also works to prevent underflows, which produce voxels of zero activity. Voxels of zero activity can produce problems for the MRP algorithm. If the median of a neighbourhood is zero, Eq. (2.12) results in a division by zero. Thus, if a voxel does become zero it is reset to 10^{-32} to prevent division by zero. Additionally, this voxel is no longer updated as 10^{-32} is less than 10^{-12} , the limit imposed for approximately zero.

Another significant time savings was to store the normalization factors in memory rather than on disk. These normalization factors are the summed backprojection of the planar variation for each projection in the subset. The normalization factors require 4 bytes per voxel per subset so that $100 \times 100 \times 100$ voxels with 8 subsets requires 30.5 MB. Memory was readily available to store these factors and the reconstruction benefited from the faster access times.

The relative increase in time required to reconstruct with MRP versus without MRP depends on the number of active voxels being updated. Within the first few subiterations most of the voxels that are outside the FOV are no longer being updated. If the FOV then contains large volumes with no activity, these voxels also

will no longer be updated. Every voxel is considered in the projection and backprojection steps, however, so that those procedures are not accelerated. The relative increase in time required for MRP varied between 18 and 25 percent. Therefore the additional time required for the MRP algorithm is reasonable.

The total time required for reconstruction using OSEM-MRP depends of course on the sampling of the projection and image data. The phantom studies were acquired with high spatial and angular sampling, providing 128 projections each with 256×256 pixels. The reconstructed phantom images contained $100 \times 100 \times 100$ voxels. Under these circumstances one standard iteration using MRP took approximately 135 seconds. On the other hand, the clinical study used 32 projections of 128×128 pixels to reconstruct an image containing $64 \times 64 \times 64$ voxels. A standard iteration for this study took approximately 5.4 seconds so that the total reconstruction time for the image was 9 minutes. These timings were performed on a 300 MHz Pentium II processor without any competing processes.

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