IMPLEMENTATION OF A MOTION COMPENSATION SYSTEM FOR HIGH RESOLUTION BRAIN POSITRON EMISSION TOMOGRAPHY

by

KATHERINE DINELLE

B.Sc., The University of Guelph, 2004

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE STUDIES

(Physics)

THE UNIVERSITY OF BRITISH COLUMBIA

January 2007

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ABSTRACT

In this work we implement and validate a compensation method for subject motion occurring during high resolution brain positron emission tomography (PET). Head motion is acknowledged as a significant source of resolution degradation in PET brain imaging; especially at the level of resolution, $(2.5 \text{ mm})^3$, available in the tomograph currently installed at our research centre. Several methods have been developed which are able to partially correct for this motion, however none provide the level of correction accuracy as the method implemented here.

An infrared motion tracking system was installed to collect subject motion information during PET scanning. In order to apply these measurements to the PET data, a method for aligning the two reference frames both temporally and spatially was developed. Installation of the motion tracking system allowed an in-depth analysis of typical subject motions encountered during scanning. This permitted us to motivate the need for motion correction, and to identify activities causing head motion which may be limited prior to scanning.

Motion corrections based on the acquired data were incorporated into a statistical reconstruction algorithm. First, the position and orientation of each motion impacted event was corrected back to a common reference position. Second, compensation was applied for variations in the relationship between the location of an emission event and the sensitivity of the detectors that measured it due to motion. The consideration of variations in tomograph sensitivity separates this motion correction method from those attempted previously. Experimental validation using phantom data revealed that the motion correction was able to compensate for translations ranging from a few millimeters to a few centimeters. When applied to human data, differences in

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the quantitative results for images reconstructed with and without motion correction were on the order of those changes we are attempting to study.

The motion correction algorithm was developed by a previous student in our group (A. Rahmim), while implementation and testing of the tracking system, and validation of the motion correction algorithm with phantom and human studies was completed as part of this work. Routine application of this motion correction scheme will improve the effective resolution of the tomograph, allowing improved quantification.

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GLOSSARY

ЕМ	expectation maximization
FBP	.filtered back projection
FOV	field of view
FWHM	. full width at half maximum
HRRT	. high resolution research tomograph
LM	list-mode
LM-EM	. list-mode expectation maximization
LM-OPEM	. list-mode ordinary Poisson expectation maximization
LOR	line of response
LOR-only	. reconstruction with corrections for LOR motion only
LOR+sensitivity	. reconstruction with corrections for LOR motion and
MAF	. multiple acquisition frames
MAP	. maximum a posteriori
OP-EM	ordinary Poisson expectation maximization
OS-EM	ordered subset expectation maximization
PD	Parkinson's disease
РЕТ	.positron emission tomography
РМТ	. photo-multiplier tube
PSF	. point spread function
PVE	. partial volume effect
ROI	.region of interest
SD	standard deviation
SSS	. single scatter simulation
TAC	time activity curve
UPDRS	unified Parkinson's disease rating scale

ACKNOWLEDGEMENTS

I would like to thank my supervisor Vesna Sossi for her enthusiasm and guidance during the course of my masters degree. I am also grateful for the assistance and friendship of the numerous members of our research group: Stephan Blinder, Sarah Lidstone, Kevin Cheng, Arman Rahmim, Carolyn English, Caroline Williams, Siobhan McCormick, Jess Mackenzie, Marie-Laure Camborde, Eric Vandervoort, Ken Buckley, and Tom Ruth. Finally, I would like to express heartfelt gratitude to my incredible family: Mum, Dad, Mike, Keith, Nana, Gramps, Granny and Grampa.

1 INTRODUCTION

1.1 BASIC PET THEORY

Positron emission tomography (PET) allows *in-vivo* measurements of the distribution and kinetics of chemicals of interest. The procedure begins with the injection of a chemical, tagged with a positron emitting radioisotope, which investigates a specific function in the body. The fundamental physical reaction in this process is positron emission, or β^+ decay, which occurs when a nucleus with an excess of protons decays resulting in a neutron, a positron and a neutrino (Equation 1.1). Due to the presence of the neutrino as a decay product, the positron can be emitted with a range of energies.

$$p \to n + \beta^+ + \nu_e \qquad (1.1)$$

Positron emitters, such as ¹¹C, ¹⁸F, ¹³N, and ¹⁵O, are commonly used in PET radiochemistry to form different radiotracers. For example, ¹⁸F-fluorodeoxyglucose is used to study glucose metabolism, allowing tumor detection and investigations of brain and heart function, while ¹¹C-raclopride is used to study neuro-transmitter function relevant to diseases such as Parkinson's or schizophrenia.

PET tomographs consist of numerous small scintillation crystals coupled to photomultiplier tubes (PMTs) and assembled into rings. These rings are then stacked together to form a small tunnel, or gantry, along which the study subject is inserted during scanning. The crystal rings are used to detect coincidence pairs of anti-parallel 511 keV photons that are emitted when the positron, released from the PET tracer, annihilates with a nearby electron. In order to qualify as a coincidence event the detection of both annihilation photons by the surrounding tomograph must occur within a defined coincidence timing window (on the order of nanoseconds). The location of the emission,

and therefore the PET tracer, can then be restricted to the line connecting the two crystals that detected the annihilation photons. This line is referred to as a line of response (LOR), and can be parameterized by four values: the distance of the LOR from the centre of the field of view, or radius (r), the transaxial angle of the LOR (θ), the axial position corresponding to the middle of the LOR (z), and the azimuthal angle (φ) as depicted in Figure 1.1. When numerous events are detected from a single region, the mutual intersection of their LORs will reflect the point in space from which they all originated. Using appropriate mathematical algorithms the distribution of the tracer within the subject can be reconstructed from the LOR emission data.



Figure 1.1: Definition of the LOR parameters (r, θ, z, φ) in a schematic end on view (A) and side on view (B) of the tomograph.

Thus far we have ignored two important properties of the positron emission/annihilation process, positron range and photon non-colinearity. Emission and annihilation do not take place at exactly the same location due to the kinetic energy imparted to the positron during β^+ decay. The average distance traveled by the positron before it interacts with an electron, also called the positron range, will be greater for positrons with higher average energies. This will degrade the tomograph resolution, measured as the full width at half the maximum (FWHM) of the scanner point spread function (PSF). For example, ¹⁸F has an average energy of 0.24 MeV and a range of 0.6 mm FWHM in water, while ¹⁵O is emitted with an average energy of 0.73 MeV and has a range in water of 1.6 mm FWHM [Levin, 1999]. Emission photons are

not always emitted at exactly 180° during the annihilation process. It is possible that either one or both of the interacting particles are not at rest when they meet, resulting in small deviations from colinearity based on conservation of momentum. The distribution of emission angles is Gaussian with a FWHM of 0.5° [Moses, 1997]. This results in a resolution degradation of ~0.7 mm FWHM at the centre of a 31 cm diameter gantry. Both of these issues are considered limiting factors in the resolution capabilities of PET scanners.

As well as the impact of positron range and photon non-colinearity, calculation of tomograph resolution includes information about the crystal size and the crystal decoding process. Using Equation 1.2 a reasonable estimate of the scanner resolution (FWHM, Γ) can be calculated [Moses, 1997]. In this equation: *d* is the detector width, *D* is the detector cylinder diameter with (0.0022*D*) representing the resolution degradation due to photon non-colinearity, *R* is the effective positron range, and *b* is the crystal decoding factor which is zero for a one-to-one coupling of crystal and PMT, and 2.2 otherwise.

$$\Gamma = \sqrt{(d/2)^2 + (0.0022D)^2 + R^2 + b^2} \quad (1.2)$$

1.2 PET DATA COLLECTION AND RECONSTRUCTION

1.2.1 THE HIGH RESOLUTION RESEARCH TOMOGRAPH (HRRT)

The PET scanner currently installed at our research facility is a Siemens High Resolution Research Tomograph (HRRT), a dedicated brain tomograph with a 31.2 cm radial field of view (FOV) and 25.2 cm axial FOV [Weinhard, 2002]. The resolution provided by this scanner, less than 2.4 mm FWHM, is not available from any other human size tomograph currently available [Sossi, 2005]. It was for this system that the motion correction system developed in this dissertation was designed, although it can be easily applied to other systems.

Instead of the usual circular detector ring design, the HRRT consists of 8 flat panels of crystals set in an octagonal geometry to facilitate coupling of the crystal to the PMTs (Figure 1.2). Between each of these crystal heads is a small 1.7 cm gap through which emission photons can pass undetected. Special consideration must be given to the loss of data resulting from these gaps, especially when analytical reconstruction algorithms are employed, which require uniform sampling.



Figure 1.2: A picture of the HRRT scanner from the front end with the cover off showing the octagonal ring design.

1.2.2 CORRECTIONS FOR PHYSICAL PROCESSES IN PET

To achieve a reconstructed image that best matches the true distribution of radiotracer in the scanner, we need to account for physical processes which result in discrepancies between the number of emitted and detected annihilation pairs. To ensure a uniform response of all detectors a normalization correction is applied along each LOR to account for (i) slight variations in the response characteristics of the scintillation crystals, and (ii) different incident angles of the LOR on the crystal surface which results in a varying effective efficiency. An attenuation correction is applied to account for annihilation photons that did not arrive at the detector due to the attenuating effects of the material surrounding the emission source. A correction is included for scattered events, in which one or both of the photons are scattered before arriving at the scintillation crystals; as a result the LOR assigned to these photons will be incorrect. This is achieved by calculating the scatter distribution from first principles as in the single scatter simulation (SSS) developed by Watson [Watson, 2000]. Finally, a correction is included for those coincidence detections which occur when one photon from each of two distinct annihilations reaches the detectors within the coincidence timing window. The second, undetected photon from each annihilation pair is either scattered out of the FOV, or completely attenuated by the material surrounding the emission source. These events are called random coincidences, and their distribution in the scanner can be determined by collecting events that arrive in a delayed time window, where there is zero probability that the event originated from a single, non-scattered, annihilation.

Motion can also be considered a physical process that results in an incorrect reconstructed image. In this case annihilation photons that would have been detected by one set of crystals in the case where the subject had not moved at all, will be incorrectly attributed to a different LOR because of motion. This correction will be the main focus of this work.

1.2.3 SINOGRAM-MODE DATA COLLECTION

In PET, information about a detected event can be stored either in sinogram or list-mode (LM) formats. A sinogram is a 2D histogram in which elements are specified by a radial position (r) and a projection angle (θ). By defining the number of radial positions and projection angles over which to collect data, the size of the data set is determined prior to the start of scanning. Often the number of sinogram elements corresponds to the number of possible LORs with the same azimuthal angle (ϕ). The value of each sinogram element corresponds to the number of events detected along the corresponding LOR.

The concept of a sinogram is easily understood by considering a simple 2dimensional case involving a single ring of crystals (Figure 1.3). To collect the information for a single projection angle, for example $\theta = 0^{\circ}$, we sum the events across the FOV at each radial position along the line defined by the projection angle (grey arrows in Figure 1.3A). This results in a histogram of counts versus position as depicted by the curve for $\theta = 0^{\circ}$ in Figure 1.3A. The summed value at each position is input into the sinogram at the horizontal row position corresponding to the projection angle of 0° (Figure 1.3B). The process is repeated for all projection angles ($\theta = 0^{\circ}$ to 180°) resulting in a complete sinogram image. To extend this process to 3-dimensions a sinogram will also be referenced based on its axial position and azimuthal angle.



Figure 1.3: A pictorial representation of the measurements leading to a sinogram. Figure 1.3A shows the summation across various projection angles to gain the necessary histograms, which are then condensed into a sinogram as shown in Figure 1.3B.

In older tomographs capable of recording data only in sinogram mode detected emission events are stored directly into a sinogram, therefore any additional information about the event such as the time of detection is lost. However, PET investigators are often interested in the time course of a chemical in the body, therefore a series of sinograms are collected over the course of the scan in order to recover some temporal information. The number of sinograms and the duration of data acquisition into each sinogram has to be determined prior to the start of the scan for sinogram only data collections, limiting the flexibility of the data to different types of analysis.

1.2.4 LIST-MODE DATA COLLECTION

Data collected in list-mode format record a description of each coincidence event, specifically the location of the photon detection defined by the scintillation crystals at which the annihilation photons arrived. The location of the measured LOR is written either in the form of two addresses corresponding to the scintillation crystals involved in the LOR detection, or using the four parameters (r, θ, z, φ) described in Figure 1.1. A time stamp is also written into the list-mode data stream every millisecond. By associating a detection event with the nearest time event in the list-mode file, coincidence event timing can be deduced. In subsequent discussions of event timing, it is assumed that the process of relating a coincidence event to the nearest time event has already occurred.

The fundamental difference between sinogram and list-mode data collection, is that sinogram information is recorded for all possible LORs as defined by the scanner geometry, even when no coincidence was detected along an LOR during the course of the scan. For studies with a small number of acquired events this can prove to be a very inefficient method of storing the coincidence data when compared to the list-mode format in which only detected emission events are recorded.

It is not hard to imagine that list-mode data is better suited to the application of a motion correction scheme than sinogram data. Motion compensation will be time dependant, with the magnitude and direction of motion corrections changing over the course of the scan. The ability to correlate these corrections on an event-by-event basis is unique to the list-mode acquisition which includes timing information for each event. In addition, after the application of motion correction, an LOR may no longer correspond to the exact centre of a crystal

pair. Where list-mode data requires knowledge only of the LOR parameters (r, θ, z, φ) which are continuous, sinogram space is discrete therefore those LORs not corresponding to a physical detector pair will have to be interpolated to the nearest crystal pair reducing the accuracy of the motion correction. This is, however, expected to have a minor impact on the accuracy of the correction since sinogram bins are only 1.22 mm.

1.2.5 RECONSTRUCTION METHODS

Through the reconstruction of PET emission data our goal is to determine an image which represents as closely as possible the actual concentration distribution of the injected tracer, allowing for quantitative results. Reconstruction methods can be either analytical, which result in a single solution to the reconstruction problem (an example is filtered back projection (FBP) [Colsher, 1980]), or statistical, requiring an iterative approach to determine the image which best matches the measured data (for example the estimation maximization algorithm (EM) [Parra, 1998]). Analytical reconstruction methods are linear and much faster than statistical approaches, however they require uniform sampling, and do not allow modeling of noise processes or other effects such as detector non-uniformity, and attenuation of the emission source (Sec. 1.2.2). Statistical reconstructions are iterative, nonlinear, and require significant computing power. This approach allows flexibility in modeling characteristics of the tomograph and PET physics into the reconstruction. Knowledge about detector geometries, attenuation, photon non-colinearity and many other properties can be incorporated into the reconstructed images allowing us to account for discrepancies between the number of emitted and detected annihilation pairs. Information about subject motion can also be applied during a statistical reconstruction as will be described in Chapter 2.

1.2.6 PET DATA ANALYSIS: TIME ACTIVITY CURVES AND BINDING POTENTIALS

Prior to reconstruction PET data measured in list-mode format are often sampled into smaller data sets, or time-frames, allowing the visualization and quantification of the time course of a PET tracer within the study subject. In the case of sinogram based acquisitions this sampling is defined prior to scanning. The length of a time-frame, often referred to simply as a frame, is determined from the tracer kinetics (which define the longest frame length), and the requirement that a sufficient number of counts are collected to allow the reconstruction of a meaningful image (defining the shortest frame length). When an identical measurement is made in each frame, for example a determination of the number of counts in a region of interest (ROI), and then plotted against scan time, the resulting graph is referred to as a time activity curve (TAC). A sample TAC is shown in Figure 1.4 for a study using ¹¹Craclopride, a D₂ receptor agonist. Here the collected emission data were split into 16 frames as follows: $4\times60s$, $3\times120s$, $8\times300s$ and $1\times600s$.





The TAC approach to PET data analysis is susceptible to the effects of subject motion in the reconstructed images. This method requires the placement of ROIs in the brain in order that a measurement can be made in identical brain regions over all frames. When significant subject motion occurs from one frame to the next, the area of interest in the reconstructed image will also move. Therefore, the placement of an ROI in one frame may no longer be valid in a frame affected by the subject motion, and measurement of this ROI will yield an incorrect result. The effect of motion within a frame will also negatively impact the TAC analysis as it will act to blur the area of interest in the brain. This not only makes accurate and reproducible placement of ROIs difficult, but it also changes the distribution of counts in the image impacting the value measured in the ROI.

The end result of a PET data analysis is often a binding potential (BP), which measures the density of available receptors in the anatomy of interest [Logan, 2000]. The analysis that leads to this measurement is based on curve fitting the TAC data points. An incorrect ROI value corresponding to an erroneous point in the TAC for that data set, will cause fitting errors during analysis and ultimately impact the BP values.

1.3 MOTIVATION FOR MOTION CORRECTION

Each new generation of PET scanners is accompanied by an improvement in image resolution, from the PETT III (1976) which had a resolution of 10.35 mm FWHM [Hoffman, 1976] to the HRRT (2002) boasting a resolution of less than 2.4 mm FWHM [Wienhard, 2002]. The impact of improved resolution on image quality is easily visible as depicted with Figure 1.5 which shows images from tomographs with progressively higher resolution capabilities ($A\rightarrow C$). In order to take full advantage of these technical advances all physical causes of resolution degradation, on the order of the resolution of the scanner, must be addressed. With the arrival of the HRRT scanner the impact of subject motion on image resolution has become noticeable, while for the previous scanner installed at our center, the ECAT 953 B (FWHM = 5.8 mm), it was not a major concern [Spinks, 1992].



Figure 1.5: PET images of the human brain with scanner resolution increasing from left to right. Images are from the PETT VI (A), ECAT 953 (B), and HRRT (C).

1.3.1 MAGNITUDE OF SUBJECT MOTION

Previous studies have been carried out to investigate the magnitude of subject motion during PET scanning [Green, 1994], [Ruttimann, 1995], [Herzog, 2004]. In [Green, 1994] the authors made measurements of the amount of subject motion during a mock PET scan, and applied this information to a series of point sources located in a digital brain phantom. The study found that subject motion, limited by a thermoplastic mask restraint, resulted in a 3% degradation of their measured scanner resolution (6.0 mm FWHM). When these values were applied to an ideal case where the scanner resolution was equal to the size of the crystal elements (here the authors chose 2.5 mm square crystals) a 44% degradation in resolution was observed. These results can easily be interpreted in the context of the HRRT scanner whose measured resolution of 2.4 mm FWHM is quite similar to the intrinsic resolution of the scanner used in the study described above. It is not unreasonable to expect that this magnitude of resolution degradation (44%) will be observed in the HRRT images due to patient motion.

The impact of decreased resolution capabilities due to subject motion results in a broadening of the PSF defined by the tomograph as shown in Figure 1.6, negatively effecting our ability to uniquely resolve two adjacent sources. Due to the degraded PSF there will also be an increased partial volume effect (PVE), which occurs when the emission source is smaller than the tomograph resolution element resulting in a distribution of the activity from that source over the entire voxel, and therefore underestimating the radioactivity concentration of the source itself. An in depth analysis of subject motion using the motion acquisition system installed at our centre will further motivate the requirement that we correct for these motions (Chapter 4).



curve). The dashed curve is defined by a FWHM degraded by 44%, but composed of the same total number of counts. The arrows indicate the width at half maximum.

1.3.2 MOTION LIMITING TECHNIQUES

Currently most PET research facilities employ some system of head restraint during brain imaging. Methods include, but are not limited to: the use of a headrest lined with foam that form fits to the subject's head in conjunction with a strap placed across the forehead, fitting each subject with a custom thermoplastic mask that conforms to features such as the nose and cheekbones (Tru-Scan Imaging Inc., Annapolis, USA), or the use of a rigid mask with multiple anchor points such as those found in radiation therapy treatment centers (Orfit Industries America, NY, USA). While one would ideally choose the system providing the highest degree of motion limitation, consideration must also be given to the subject comfort, and the requirements of the scanning protocol. Based on the study protocol some PET scans may last up to 4 hours, while others require interaction of the subject with a computer screen.

The majority of research studies at our center are concerned with Parkinson's disease (PD), therefore consideration must be given to our subjects as their symptoms often include tremor, rigidity, and muscle stiffness making rigid restraint extremely uncomfortable. As a compromise, our research facility makes use of the thermoplastic mask method of subject head restraint. In this procedure a thin piece of plastic is warmed until it becomes pliable and is then formed over the subject's forehead and nose and attached at the sides of the head support. Once cooled, the mask hardens restricting subject motion, and also allowing accurate replacement of the subject in the scanner during repeat visits.

In some scanning protocols, there is a requirement for interaction between the subject and an outside stimulus, for example a computer interface. The ability to carry out these studies is limited by the small size of the scanner gantry and the thermoplastic mask as both obstruct the view of the subject. It has been determined that the use of two Velcro strap restraints, placed across the chin and forehead of the subject will allow the subject to view a small screen placed just outside the scanner gantry (Figure 1.7). With this in mind a comparison of this restraint method and the thermoplastic mask method was carried out and will be presented in Chapter 4.



Figure 1.7: Picture of a subject wearing the Velcro restraint straps.

1.4 SUMMARY

There is compelling evidence that significant subject motion occurs over the course of a routine PET scan. Due to our subject population, and the high resolving power of our scanner, the effect of subject motion is expected to be significant in the HRRT data. Therefore, the aim of this research project was to implement and evaluate a motion tracking system, and include its information into image reconstruction for scanning of the human brain on the HRRT.

Subject motion will be corrected for in the reconstructed images by inclusion of the motion data into a statistical list-mode algorithm following the method of Rahmim [Rahmim, 2004] as described in Chapter 2. Acquisition of motion data required the installation of a motion tracking device (Chapter 3), which allowed us to carry out an independent study of typical subject motion (Chapter 4). Finally the system was tested using both phantom and human data, to investigate the impact the motion correction technique would has the reconstructed HRRT images and their analysis.

2 SUBJECT MOTION AND PET DATA RECONSTRUCTION

2.1 APPLICATION OF MOTION DATA

Numerous motion compensation techniques with varying levels of complexity have been developed in conjunction with advances in tomograph resolution. The correction for subject motion during PET brain imaging is unique when compared to compensation techniques employed in PET imaging of other areas of the human body, as the types of motions observed varies greatly in different parts of the body. For example, motion compensation in the area of heart and lung imaging corrects for the motion of those organs based on determining the motion pattern associated with a subject's heartbeat and/or breathing [Klein, 1998]. Events that are collected during similar sections of the motion cycle are grouped together and reconstructed as unique images. In order to combine these images non-rigid transformations are required because both the shape and location of the subject changes due to motion. The motion correction of brain images is straightforward in comparison, because one can assume that the head is a rigid body at the level of resolution afforded by the HRRT scanner.

The simplest approach to subject motion compensation is an off-line technique requiring the realignment (or co-registration) of images obtained from each time frame. This method does not require separate knowledge of subject motion and so can be implemented without the installation of a motion tracking system. Due to motion, there may be discrepancies in subject position between frames defined by the TAC. In order to compensate for this motion, the image from each frame is realigned to a common reference eliminating any between-frame displacement. The main advantage of this technique is evident during certain image analysis procedures which require that a series of ROIs are

placed in the same anatomical position on each image across all frames. In cases where the images are not aligned, placement on each image frame is necessary in order that the same anatomy is contained in each ROI. For corregistered images the same ROIs, once placed on a single image, can be used for all image frames, significantly reducing the time cost of the analysis.

To improve the accuracy of this method the idea of frame-by-frame image realignment is retained, however frames are now delimited based on some knowledge of subject motion during the scan in addition to tracer kinetics. In this method, known as the multiple acquisition frames (MAF) motion compensation, the collection of emission data is gated such that a new frame is started each time motion above a certain threshold occurs [Picard, 1997], [Fulton, 2002]. A simple approach to motion gating is via human observation, for example the attending nuclear medicine technician takes note of times during the scan when large motions occurred and these are later used to frame the data, however this method is only applicable to list-mode data. A more sophisticated approach to motion thresholding is to use subject motion tracking hardware. In the case of list-mode data, after data collection is complete, each frame, within which no motion over the predefined threshold occurred, is reconstructed and co-registered to all other image frames. In tomographs with sinogram only capabilities, the start of a new frame is triggered in real time when motion greater than the threshold is observed. The major drawback of this method is that in cases of frequent motion necessitating the collection of a large number of frames with a small number of acquired events, the accuracy of both the reconstruction and the co-registration will suffer from low statistics. This effectively results in a lower limit on the magnitude of the motion threshold in order to ensure a reasonable number of counts are collected in each frame; therefore some within-frame motion will still be present.

Although the MAF approach requires the implementation of a motion tracking system, we are still not using the collected motion data to their full

potential. The next level of complexity in motion correction is an event driven approach where corrections are applied to each LOR based on the measured motion data. Following this scheme each LOR is transformed back to the location it would have been measured in had the subject not moved over the course of the scan. We will refer to this method as LOR-only. Most often the common reference location to which all LORs are corrected represents the location of the subject at the time of the transmission scan. The transformation for a specific LOR is determined based on the motion coordinates that most closely match the time of the coincidence event. This technique has been implemented by many research groups, and shown to compensate for motion induced blurring in the reconstructed images improving both the image quality and the TAC values [Menke, 1996], [Bloomfield, 2003], [Buhler, 2004].

Although the event-by-event motion correction technique is a vast improvement over the MAF approach, it is not completely accurate because the dependence of scanner geometry and detector sensitivity on LOR location is ignored. In terms of scanner geometry consideration must be given to LORs that move in and out of the scanner FOV, be it axially, or into gaps between detectors as is the case in the HRRT scanner (Section 1.2.1). LORs that would have been measured except that, as a result of subject motion, go undetected cannot be recovered (Figure 2.1). However, we can and should include data that were measured because of motion, for example coincidence events that fall along detector gaps after they are corrected for motion. Properly modeling detector sensitivity in these gaps will address the related image artifacts.

Consideration of tomograph sensitivity when correcting LORs for motion, for example corrections for attenuation and detector response will be influenced by motion. In order to address these additional concerns about the LOR based motion correction scheme, we chose to apply a reconstruction algorithm developed by Rahmim in [Rahmim, 2004] that not only motion corrects each LOR without discarding events corrected into detector gaps, but also models

the variations in detector sensitivity to emissions from voxels that change location with respect to the tomograph as a consequence of motion. An elaboration of this reconstruction scheme which will be referred to as LOR+sensitivity, follows.



Figure 2.1: An LOR falling along i' due to motion, cannot be recovered (left).However, an LOR i' that falls along i after motion correction should not be discarded merely because there are no physical detectors along this LOR (right).

2.2 STATISTICAL RECONSTRUCTION FORMALISM

2.2.1 MOTION COMPENSATED LIST-MODE RECONSTRUCTION

A common statistical reconstruction method for PET data is the implementation of a maximum likelihood expectation maximization (ML-EM) algorithm. In this process an estimation of the system of interest, in our case an image of the tracer distribution, and an evaluation of this estimate based on a cost function, are iterated until the cost function converges to a minimum. In order to decrease the time required for convergence, the acquired data can be distributed into n subsets, each of which is used to calculate an image estimate [Hudson, 1994]. A single iteration is complete when the algorithm has been applied once to each subset, therefore in one iteration the image estimate will be updated n times. When applied to the EM algorithm, subsets are ordered on an LOR basis, and the algorithm it is referred to as ordered subset expectation maximization (OS-EM).

The original application of the EM algorithm in the context of PET image reconstruction of sinogram data was developed by Shepp and Vardi [Shepp, 1982], and Lange and Carson [Lange, 1984] assuming a system that could be modeled with Poisson statistics. The detected emission events (also called

prompts), whose distribution we are trying to reconstruct, contain random, scattered, and true events. In order to compensate for the contamination of the true count rate, prompt data can be pre-corrected for random and scattered events via a simple subtraction, leaving only the true events. However, this solution results in true events that are no longer described by Poisson statistics, and that could take on negative values causing complications in the reconstruction process. To address these problems, random and scattered events can instead be added to the image estimate, and in this way the estimate represents the prompt count rate which follows Poisson statistics. This approach is referred to as ordinary Poisson estimation maximization, or OP-EM [Politte, 1991].

In 1998, Parra and Barrett [Parra, 1998] extended the applicability of the EM algorithm to the reconstruction of PET data in list-mode format. The difference being that when estimating the activity in a voxel during image reconstruction, the list-mode approach concerns itself only with LORs along which a coincidence was measured, instead of considering the contribution of every geometrically possible LOR as is done for sinogram data. Due to the large number of measurable LORs in the HRRT scanner (4.49×10^9) this method results in a considerable decrease in reconstruction time for data sets with a low number of acquired counts.

A formulation of the list-mode EM (LM-EM) algorithm is presented in Equation 2.1, followed by a description of the terms comprising this equation.

$$\lambda_{j}^{m+1} = \frac{\lambda_{j}^{m}}{\sum_{i=1}^{I} p_{ij}} \sum_{k=1}^{N} \frac{p_{j}(i_{k})}{\sum_{b=1}^{J} p_{b}(i_{k}) \lambda_{b}^{m}} \quad (2.1)$$



The system matrix p_{ij} gives the probability of detecting an emission from a given voxel, *j*, along a specific LOR, *i*. This matrix can be decomposed into a geometrical detection probability, g_{ij} , and an LOR weighting factor, w_i , such that $p_{ij} = g_{ij}w_i$. The weighting factor allows the incorporation of corrections for attenuation (A_i) and detector normalization (N_i) into the model of our system during the reconstruction process.

In the presence of motion the geometrical relationship between a voxel (j) and an LOR influenced by this motion (i') changes over the course of the scan based on subject position in the scanner. Herein we will denote an LOR (i) or voxel (j) influenced by motion with a prime symbol (i', j'). We also define an invertible operator L that transforms an LOR from i to i'. Explicitly this operator calculates the LOR i'_i along which an event was physically measured at a given time, based on the LOR i which would have measured it in the case of no motion. Alternately, L^{-1} provides the LOR i corresponding to an event measured along i' due to motion.

As subject motion occurs over the course of the scan the geometrical relationship becomes a function of time, $g_{i'j}^{t}$. However, prior to reconstruction each LOR is motion corrected such that $L_{i}^{-1}(i'_{i}) = i_{i=0}$ in which case the geometrical probability of detection can be written as shown in Equation 2.2 where $i = L_{i}^{-1}(i')$.

$$g_{ij}^{t} = g_{ij}^{t=0}$$
(2.2)

This concept is illustrated in Figure 2.2. Here we see that for a motion from voxel j to j', the geometric probability of detection of emissions originating from voxel j' (and also $j = M_i^{-1}(j')$) along LOR i'_1 is zero, and along LOR i'_2 is non-zero. Once a correction for this motion has been applied to each LOR, the geometric probability of detection will be conserved; detection of voxel j along

LOR i_1 is still not possible, while along LOR i_2 the probability will be non-zero.



Figure 2.2: Probability of detection for a voxel j' which is transformed to j due to motion along the measured LORs i'_1 and i'_2 (A), and along the motion corrected LORs i_1 and i_2 (B).

Corrections for attenuation (A_i) and normalization (N_i) , with respect to their application to an LOR, are also affected by subject motion. Since normalization corrections are characteristic of the crystal pairs along which a coincidence is physically detected, in the presence of motion the correct normalization factor to apply corresponds to the non-motion corrected LOR, i' (Figure 2.3).



Figure 2.3: Here LOR *i*'is measured physically at D'_1 and D'_2 due to subject motion therefore the normalization correction associated with these crystals should be applied even after the LOR has been motion corrected to *i*, and attributed to crystals D_1 and D_2 .

Alternately, the attenuation correction applied to a measured LOR, i', must be the attenuation correction corresponding to that LOR, i, once it has been motion corrected. The attenuation correction is determined from a transmission scan of the subject in a specific location and is the position that all emission LORs will be corrected to. While the attenuating material (in this case the subject's head) moves with the emission source (the radiotracer) during an emission scan, the appropriate attenuation correction for emissions from a specific location in the brain were measured at the reference position (Figure 2.4A and 2.4B).



Figure 2.4: In A an object (elliptical shaded area) will attenuate emissions along LOR i_1 with a magnitude shown by the black section of the LOR. If this is the orientation of the object during the transmission scan, then all events measured along LOR i_1 over the course of the emission scan will be corrected based on this amount of attenuating material. In B the object has moved, and an emission measured along i_1 will travel through a greater amount of material before being detected. If the attenuation correction measured in A is applied to the emission along i_1 in B, the result will be an under-correction for attenuation.

Incorporating these considerations, the system matrix in the presence of motion is given by Equation 2.3. Notice that both g_{ij} and A_i depend only on the original or motion corrected state of the subject, and therefore are not changing as a function of scan time.

$$p_{ij}^{t} = g_{ij}^{t} w_{i'} = g_{i'j}^{t} N_{i'} A_{i} = g_{ij}^{t=0} N_{i'} A_{i}$$
(2.3)

In order to build up a system matrix that represents the probability of detection over the entire course of the scan (\overline{p}_{ij}) we need to sum the contribution of the geometry, attenuation, and normalization, during each motion interval.

$$\overline{p}_{ij} = \frac{\Delta T_1}{T} g_{ij}^{t} A_{i(t_1)} N_{i'(t_1)} + \frac{\Delta T_2}{T} g_{ij}^{t_2} A_{i(t_2)} N_{i'(t_2)} + \dots + \frac{\Delta T_n}{T} g_{ij}^{t_n} A_{i(t_n)} N_{i'(t_n)}$$

$$= \frac{1}{T} g_{ij}^{t=0} A_i^{t=0} \Big[\Delta T_1 N_{i'(t_1)} + \Delta T_2 N_{i'(t_2)} + \dots + \Delta T_n N_{i'(t_n)} \Big]$$

$$= \frac{1}{T} g_{ij}^{t=0} A_i^{t=0} \sum_{t=1}^n N_{i'(t)} \Delta T_t \qquad (2.4)$$

 $T = \sum_{i=1}^{n} \Delta T_n$ n = the total # of motion intervals

Combining Equation 2.4 with the LM-EM algorithm (Equation 21.) we arrive at Equation 2.5. Here we have dropped the t=0 superscript for convenience.

$$\lambda_{j}^{m+1} = \frac{\lambda_{j}^{m}}{\frac{1}{T}\sum_{i=1}^{I} g_{ij}A_{i}\sum_{t=1}^{n} N_{i'(t)}\Delta T_{n}} \sum_{k=1}^{N} \frac{g_{j}(i_{k})}{\sum_{b=1}^{J} g_{b}(i_{k})\lambda_{b}^{m}}$$
(2.5)

The term \overline{s}_j in the motion compensated LM-EM algorithm describes the sensitivity of a voxel, *j*, in the tomograph over all motion intervals.

$$\bar{s}_{j} = \frac{1}{T} \sum_{i=1}^{I} g_{ij} A_{i} \sum_{t=1}^{n} N_{i'(t)} \Delta T_{i} \quad (2.6)$$

In order to calculate this sensitivity for a single voxel *j*, we have to perform an integration over the entire duration of the scan for each LOR *i*. This is a computationally intensive process; the number of LORs over which the integration need be done is large in the case of the HRRT scanner (4.49 billion), the scan times are often 1 hour in length, and based on our subject population who are primarily those diagnosed with a movement disorder the number of motion intervals will not be trivial. It was shown in [Rahmim, 2006] that instead of approaching this task in LOR space, the calculation can instead be completed in image space by considering corrections on a voxel level by realizing that for any motion correction applied in LOR space (L_t^{-1}), an equivalent correction can be determined in image space described by (M_t^{-1}). This "short-cut" can be implemented when the emission data are pre-corrected for attenuation, because in this case the average sensitivity matrix for a given voxel over the course of the scan can be written as:

$$\bar{s}_{j} = \frac{1}{T} \sum_{i=1}^{I} g_{ij} \sum_{t=1}^{n} N_{i}^{t} \Delta t_{t} = \sum_{t=1}^{n} s_{j} \frac{\Delta t_{t}}{T} \quad \text{for} \quad g_{ij} = g_{ij} \quad (2.7)$$

To implement Equation 2.7, we first calculate the sensitivities for each voxel s_j in the case of no motion. We then determine the voxels j' whose measured count rate contributed to j over the course of the scan due to subject motion. The sensitivities in these voxels $s_{j'}$ are then weighted by the length of time spent in that specific orientation, and summed over the course of the scan to determine the total effective sensitivity of voxel j. This significantly reduces the calculation time as the there are only 14 million voxels in an HRRT image.

2.2.2 CORRECTIONS FOR SCATTERED AND RANDOM EVENTS

Scatter and random events can be included in the motion compensated LM-EM algorithm by adding the rate of these events to the forward projected image intensity estimate resulting in an LM-OP-EM algorithm (2.8). Here \tilde{S}_i and \tilde{N}_i are the expected rate of incident scattered and random events. Recall that we are now considering attenuation pre-corrected data, therefore the scatter and random measurements must also be corrected.

$$\sum_{b=1}^{J} g_{i_k b} \lambda_b^m \to \sum g_{i_k b} \lambda_b^m + \frac{\widetilde{S}_i}{A_i} + \frac{\widetilde{R}_i}{A_i} \quad (2.8)$$

In [Rahmim, 2006] the author discusses the impact of subject motion on the estimation of scattered and random event rates. Scattered events are included using the SSS approach applied to motion corrected LOR data (Section 1.2.2). The inclusion of random events is based on the assumption that the distribution of these events is broad and therefore will not be impacted by the limited motions expected during subject scanning. Therefore we can directly apply the random distribution determined from the delayed coincidences (Section 1.2.2), with one modification. Unlike the estimated scatter distribution, the random distribution is calculated from measured data, and therefore must be extrapolated into the detector gaps present in the HRRT.
2.3 SUMMARY

Knowledge of subject motion can be included during reconstruction or as a post-processing step based on the correction accuracy required, and the available motion data. In this project the motion correction was built into an LM-OP-EM reconstruction algorithm as proposed in [Rahmim, 2006]. Corrections for motion were first applied to each LOR, and then, during the reconstruction step, the effect of motion was included in the system matrix. Corrections for random and scattered events were also included in this reconstruction. The method used to obtain measures of subject motion for inclusion via this reconstruction scheme will be discussed next.

3 MOTION TRACKING SYSTEM

Several systems exist which allow real-time collection of motion data, both translation and rotation, of a moving subject. These systems have previously found use in areas such as gait analysis and motion capture for the development of computer animations [Sadeghi, 2004], [Welch, 2002]. The basis of these technologies is the interaction of a series of small markers with a receiver, often through infrared (Advanced Real-Time Tracking, A.R.T. GmbH, Germany) or magnetic pulses (Flock of Birds, Ascension Technology Corporation, USA).

When choosing a tracking system appropriate for use with the HRRT scanner, consideration was given to the scanner geometry and current scanning protocols, and to the experiences of other members of the PET community involved in motion correction. The measurement of, and correction for, subject motion had already been achieved at other PET centers for lower resolution scanners, using a variety of motion collection and compensation methods [Menke, 1996], [Bloomfield, 2003], though none with the same level of sophistication in the reconstruction algorithm as that presented here. Motion correction solutions were also under investigation by Siemens who manufactured the HRRT scanner. The majority of research groups chose a Polaris infrared tracking system developed by Northern Digital Incorporated (NDI, Ontario, Canada), a decision supported by Siemens who now provide a next generation Polaris tracking system, the Polaris Vicra, to all HRRT users. The merits of the Polaris system are its high precision tracking capabilities (\pm 0.35 mm RMS error as measured by the manufacturer), functionality in a limited field of view such as the one defined by the long, narrow gantry of the HRRT, and affordability.

3.1 HARDWARE ISSUES

3.1.1 System Setup and Tool Design

The Polaris system consists of an infrared emitter/receiver that determines the position and orientation of a group of retro-reflective spheres. These spheres are mounted via small screws to a rigid surface in a well known geometry, allowing the Polaris system to recognize and track the tool while it is within the tracking volume (FOV) of the system (Appendix A). The tool originally shipped with the Polaris system was not designed with the application of subject motion tracking in mind and was therefore too large and bulky to be attached comfortably to a subject. A new tool that better reflected its intended use in a subject motion tracking system was designed and manufactured in house, with constraints placed on size and weight.

When designing the new Polaris tool two specific geometric constraints, defined by the manufacturer, had to be observed: (i) the distance between any two markers could not be less than 50.00 mm, and (ii) the distance between any two markers had to differ in length by at least 5.00 mm for all possible pairs of markers. For example, if we design a tool with three markers (A, B, and C), and begin by setting the distance AB equal to 50.00 mm, then given constraint (ii), neither BC or CA can be less than 55.00 mm. If we then set BC equal to 55.00 mm, CA must be 60.00 mm or greater in order that all possible segment lengths (AB, BC, CA) differ by the requisite 5.00 mm.

The Polaris emitter/receiver was placed at the rear of the HRRT scanner and aligned both vertically and horizontally with the centre of the scanner gantry, in order to track a tool placed at the top of the subject's head (Figure 3.1). By projecting the line of sight of the Polaris emitter/receiver along the HRRT gantry it was determined that the tracking area of the Polaris in the scanner at the expected location of the tool was only 165.20 mm in diameter, resulting in further size limitations on the tracking tool (Appendix A). In order for the

Polaris receiver to track any tool, at least three marker spheres must be reflecting infrared pulses at any time. With the limited field of view in the HRRT, it was assumed highly probable that one of the markers would stray outside the tracking volume. As a result a tool design incorporating four marker spheres was implemented in order to decrease the chance that the entire tool would become "lost" to the Polaris system.



Figure 3.1: A schematic (A) and picture (B) of the setup of the Polaris system for motion tracking during human brain scanning.

A tool design meeting all of the aforementioned requirements is shown in Figure 3.2, and is the schematic after which the tool was manufactured. The markers were mounted on a thin acrylic plate with inter-marker spacing as shown. An inter-marker distance tolerance of ± 0.05 mm was enforced during production of the tool as required by the Polaris manufacturer. The spheres were attached to the plate using plastic pegs, instead of the metal pegs

originally supplied with the Polaris system, for purposes of localization of the spheres in a transmission image (Section 3.2.2). With this modification the sphere can be distinguished from the supporting tool plate in the transmission images (Figure 3.3).

After completing the tool, its engineering data were used to create a file that uniquely characterized its geometry, and would be used by the Polaris receiver during tracking to both identify the tool and determine its position and orientation.



Figure 3.2: Polaris tracking tool design for use in the HRRT. Inter-marker distances are labeled.



plastic screw (B).

3.1.2 TOOL ATTACHMENT

A major difficulty of motion tracking is devising a method of rigid attachment between the tracking probe and the subject's body. For motion correction on the HRRT scanner we are only interested in measuring motions of the head. The solution to this problem must be comfortable for the patient, compatible with the use of a thermoplastic mask currently employed to restrain motion, and fit inside the narrow HRRT gantry (310 mm in diameter). Methods previously suggested for this purpose are: (i) the use of elastics to attach the four corners of the tool to the thermoplastic mask [Lopresti, 1999], (ii) attaching the tool to a pair of ski goggles worn by the subject during tracking [Buhler, 2004], and (iii) attachment to a cap worn by the subject [Fulton, 2002], [Bloomfield, 2003]. Method (i) does not meet the requirement of rigid attachment between the tool and subject, for example rotational motions will not be accurately represented by motion of the tracking tool. Method (ii) does not meet the space limitations imposed by the scanner gantry. Therefore the decision was made to use method (iii) for motion tracking was made as it achieves all of the goals identified above.

In practice, the tracking tool was attached using Velcro strips to a surf cap commonly worn by scuba divers (Henderson Microprene Tropic Cap, NJ, USA). This cap is made of thin neoprene therefore it stretches snugly to fit each subject, and also has a chin strap which further prevents any motion of the cap independent of the subject's head (see Figure 3.4). Four different sizes of cap were available increasing the probability that a satisfactory fit could be found for each subject.



Figure 3.4: Picture of a subject wearing a thermoplastic mask and the motion tracking system from the front (A), and back (B) of the scanner.

Incorporation of the cap and tracking tool into the routine of everyday scanning went smoothly. The microprene cap was specifically developed for divers in hot climates and therefore did not result in the subjects feeling overly warm while wearing it. The cap fit easily and comfortably under the thermoplastic mask, and after ~25 scans there have been no major complaints of discomfort from study subjects. Finally, the caps can be easily washed after each use with a cleaning agent designed for neoprene materials, addressing any hygiene concerns.

All of the methods discussed for attachment of the tracking tool assume a direct correspondence between tool and head motions. However, this level of attachment cannot be guaranteed without physically securing the spheres to the subject's head which is too invasive for the purposes of this study. Visual observations of subject motion during routine scanning correlated well with motions measured by the Polaris, leading us to believe that the cap is reflecting actual subject motion.

3.2 SOFTWARE ISSUES

3.2.1 POLARIS OUTPUT

During subject scanning, motion data are collected during the 6 minute transmission scan through to the end of the emission scan. The output from the Polaris system is a quaternion (q_0, q_x, q_y, q_z) which defines the orientation of the tracking tool, a position (p_x, p_y, p_z) defining the translation of the tool, and an associated time stamp [Altman, 1986]. As it is collected, data are written to file in binary format in order to decrease the physical size of the data set. Motion data are collected at 20 Hz, and later averaged into a single measurement per second which helps to decrease the noise in the data. Figure 3.5 shows the variation in the measured position of the tracking tool in a single static position

over a period of two minutes prior to averaging. The standard deviation of the measured position over the time interval was ± 0.05 mm.



From the quaternion and translation information we can define a matrix $M_{Polaris}^{T}$, that allows us to calculate the location and orientation of any point in the Polaris frame of reference that is rigidly attached to the tracking tool (Equation 3.1). Application of this matrix to the coordinate (0,0,0) will tell us the location of the centre of the Polaris tool in the scanner frame of reference.

$$M_{Polaris}^{t} = \begin{bmatrix} q_{0}^{2} + q_{x}^{2} - q_{y}^{2} - q_{z}^{2} & 2(q_{x}q_{y} + q_{0}q_{z}) & 2(q_{x}q_{z} + q_{0}q_{y}) & p_{x} \\ 2(q_{y}q_{x} + q_{0}q_{z}) & q_{0}^{2} - q_{x}^{2} + q_{y}^{2} - q_{z}^{2} & 2(q_{y}q_{z} - q_{0}q_{x}) & p_{y} \\ 2(q_{z}q_{x} - q_{0}q_{y}) & 2(q_{z}q_{y} + q_{0}q_{x}) & q_{0}^{2} - q_{x}^{2} - q_{y}^{2} + q_{z}^{2} & p_{z} \\ 0 & 0 & 0 & 1 \end{bmatrix}$$
(3.1)

3.2.2 REGISTRATION OF THE POLARIS AND TOMOGRAPH DATA IN TIME

In order to apply the appropriate motion correction, which is changing over the course of the scan, the Polaris motion information had to be correlated in time with the events acquired by the tomograph. As discussed previously the HRRT data are collected in list-mode format such that each coincidence event can be associated with a timing event to the nearest millisecond. In the case of the Polaris data each motion event is written out with the time in milliseconds at which it was measured. A common time server services both the Polaris motion and HRRT acquisition computers ensuring that time alignment can be achieved by correlating the timing information in both data sets.

3.2.3 SPATIAL REGISTRATION OF THE POLARIS AND HRRT FRAMES

Application of the translations and rotations measured by the Polaris system to correct for motions in the tomograph frame of reference requires spatial registration of the two frames. To determine the transform that converts Polaris coordinates into HRRT coordinates ($T_{Polaris \rightarrow HRRT}$) a simultaneous measurement of the location of an object is recorded with both systems. Two methods have been previously suggested by other research groups. The first involves the use of small positron emitting radioactive point sources fixed in a known orientation with respect to the Polaris tool [Fulton, 2002]. Simultaneous measurement occurs by recording Polaris motion information in conjunction with an emission scan. After reconstruction of the emission data the location of the point source within the scanner can be determined from the emission image and coupled with the motion information recorded during the emission scan. Alternately, the tomograph position measurement can be determined from a transmission image of the Polaris tool [Buhler, 2004]. All four of the Polaris tracking spheres are easily visible in a reconstructed transmission image therefore their positions in the HRRT reference frame can be determined, and paired with the Polaris tracking information collected during the transmission scan.

The use of small radioactive point sources requires the handling of highly concentrated amounts of activity during source preparation in order that enough activity is transferred to the source to produce a reasonable image. This method also requires that the point source is precisely placed on the Polaris tool in a known position with respect to the tracking spheres. The use of the

transmission image to determine the position measurement in the tomograph reference frame alleviates the need to handle radioactivity and accurately position the radioactive source with respect to the tool centre. In either case the calibration of the two frames of reference must be completed only when the Polaris tracking system is moved with respect to the tomograph, which can be minimized by rigidly fixing the system to a shelf or the back of the scanner. Based on these challenges, the method employing transmission scans of the Polaris tool was chosen for implementation.

In this method paired coordinates were acquired by placing the Polaris tool in the scanner gantry with the spheres visible to the tracking system. A 10 minute transmission scan of the tool was collected while its position was measured with the Polaris system. The process was repeated a total of four times with the tool placed in different orientations and gantry locations for each. Measurements of the tool location, other than with the Polaris receiver and the tomograph, were not made. The collection of multiple paired data sets decreased the impact of errors introduced during the determination of the sphere positions on the final transformation. Sixteen paired coordinates were therefore collected, as each tool position resulted in four sets of coordinates, one for each sphere.

Each transmission image was reconstructed using a maximum *a posteriori* transmission (map-TR) statistical reconstruction algorithm [Nuyts, 2001]. Segmentation of the data was not applied to the image because, during analysis, the spheres and marker plate have to be visually distinguishable in the image. If a segmentation had been applied all similar materials (both the tracking spheres and plate are plastic) in the image would take on the same value. Each image was imported into Matlab (The Mathworks Inc., Massachusetts, USA) where a series of analysis steps were applied to determine the location of the spheres. First each sphere in the transmission image was isolated. The spheres appeared as hot spots in a projection image along the z-axis and therefore could

easily be found by searching for maximum voxels in the image. Any section of the remaining image clearly belonging to the tool plate was removed so that it did not interfere with the 3D Gaussian fit used to determine the marker location.

A determination of the accuracy that could be expected from fitting Gaussian curves to transmission data was carried out using a Jaszczac phantom. This phantom is a large water filled cylinder containing a series of thin solid plastic rods running the length of the phantom. The known cold rod diameters were 4.8, 6.4, 7.9, 9.5, 11.1, and 12.7 mm as shown in Figure 3.6. The internal spacing between like rods in a single section was equal to twice their diameter, or 9.6, 12.8, 15.8, 19.0, 22.2, and 25.4 mm respectively. The Jaszczac phantom (I.D. = 21.6 cm) was placed in the HRRT scanner and a 6 minute transmission scan was obtained. Reconstruction was completed using the map-TR algorithm [Nuyts, 2001]. The position and FWHM of each cold rod, in each plane, was determined using a 2D Gaussian fitting program written in Matlab. Results were then averaged over the axial extent of the phantom (50 planes). Inter-rod distances were calculated from the measured rod centres and compared to the known phantom specifications. The most relevant result was for rods with a diameter of 11.1 mm as they are closest in size to the reflective spheres used in Polaris tracking (d = 11.81 mm). The mean distance calculated between these spheres was 22.08 mm, compared to the known value of 22.2 mm, with a standard deviation of 0.51 mm. As the tracking accuracy is at best ± 0.35 mm, and the motions we expect to correct for are those > 1.0 mm, this ability to determine positions in the transmission scan is acceptable for our purposes.



Figure 3.6: A schematic of the Jaszczac phantom (A), and the corresponding transmission image (B).

Once each set of paired coordinates had been measured, the corresponding transformation was determined by applying Horn's "Closed form solution of absolute orientation using unit quaternions" [Horn, 1987]. This method uses a least squares approach to minimize the difference between the measured scanner coordinates and the calculated scanner coordinates determined by application of the transform to the measured Polaris coordinates. This transform $(T_{Polaris \rightarrow HRRT})$ can then be used to convert each Polaris coordinate into the tomograph reference frame as shown in Equations 3.2 and 3.3. The residual error after applying the transform to the Polaris coordinates and comparing to the measured scanner coordinates was on the order of 0.6 mm in the transaxial directions and 0.8 mm in the axial direction. These values were deemed acceptable because: (i) the error is mainly a reflection of our ability to measure the paired coordinates which is not perfect, as opposed to an error in the ability of the transform to convert from one reference frame to the next, (ii) we are correcting for motions greater than 1.0 mm, and (iii) the accuracy of the transform can be improved with multiple measurements as the overall error associated with measuring the paired coordinates will decrease. The possibility of acquiring large paired coordinate data sets for the determination of $T_{Polaris \rightarrow HRRT}$ becomes feasible once the position of the Polaris receiver is rigidly

fixed with respect to the scanner. The time cost of collecting and analyzing a large number of paired data sets is not practical with the current setup, as there is no guarantee that the relationship between the Polaris and tomograph has not changed between scanning days and must therefore be repeated. As an upgraded Polaris reciever was expected in the near future it was not deemed worthwhile to rigidly fix the current Polaris receiver in the interim, therefore a limited number of paired coordinates were collected for each calibration in the interest of time.

$$P_{HRRT} = T_{Polaris \to HRRT} \times P_{Polaris}$$
(3.2)
$$\begin{bmatrix} P_x \\ P_y \\ P_z \\ 1 \end{bmatrix}_{HRRT} = \begin{bmatrix} R_{11} & R_{12} & R_{13} & T_x \\ R_{21} & R_{22} & R_{23} & T_y \\ R_{31} & R_{32} & R_{33} & T_z \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} P_x \\ P_y \\ P_z \\ 1 \end{bmatrix}_{Polaris}$$
(3.3)

3.3 MOTION CORRECTION OF LINES OF RESPONSE AND VOXELS

In order to apply a motion correction based on the collected Polaris data, the transformation that corrects each tomograph LOR for motion must be calculated $(T'_{EM\to TX})$. Each LOR must be transformed back to the position it would have been recorded in had no subject motion occurred after the start of the transmission scan. In reality we correct back to the *average* position of the subject during the transmission scan. This is because motion correction of the transmission data has not yet been implemented therefore the transmission image will be an average over any motion that occurs within it.

The matrix defining the location of the Polaris tool during the transmission scan is calculated from the quaternion and translation measurements averaged over the course of the scan $(M_{Polaris}^{TX})$. This matrix is then transformed into the HRRT frame of reference (M_{HRRT}^{TX}) using the transform $T_{Polaris \rightarrow HRRT}$ defined in Section 3.2.2. We are now prepared to determine the transformations that

convert positions measured during the emission scan back to this reference position for each motion interval defined by the Polaris data.

It is now required that we determine the motion intervals Δt during which a unique motion correction will be applied to the emission data. This is accomplished by applying certain thresholds to the motion data; we require a change in position at the approximate centre of the subjects head (100 mm from the tracking tool along the long axis of the scanner) from one interval to the next of 1.5 mm along any coordinate direction, and that the motion interval is at least 30 seconds in length. With these thresholds applied we correct motions that are on the order of, or greater than, the scanner resolution and avoid correcting for very short motions that will have little impact on the resulting images. For each motion interval Δt , the average translation and quaternion of the tracking tool during the interval is determined, and the matrix representing the average measurement ($M_{Polaris}^{EM(\Delta t)}$) is prepared (Equation 3.1). Again we transform this matrix into the scanner frame of reference using $T_{Polaris \to HRRT}$ to arrive at $M_{HRRT}^{EM(\Delta t)}$.

We can now determine the location of any object rigidly attached to the Polaris tool during the transmission scan using M_{HRRT}^{TX} , or during any of the motion intervals Δt with $M_{HRRT}^{EM(\Delta t)}$. Therefore we can also determine the transform which describes a motion from the reference transmission scan position to some other location during the emission scan using Equation 3.4.

$$M_{TX \to EM}^{\Delta t} = M_{HRRT}^{EM(\Delta t)} \times \left(M_{HRRT}^{TX}\right)^{-1} \quad (3.4)$$

This process of determining the motion correction matrix is repeated for all determined motion intervals. In order to correct an LOR measured during a motion interval Δt in the emission scan, we apply the inverse transform, $M_{EM \to TX}^{\Delta t} = \left(M_{TX \to EM}^{\Delta t}\right)^{-1}.$

We are now prepared to apply these coordinate transformations during image reconstruction, as described in the Chapter 2. In order to correct each LOR we will have to convert from our LOR coordinates $(r, \theta, z_{LOR}, \varphi)$ to LOR endpoint coordinates (x_1, y_1, z_1) and (x_2, y_2, z_2) because the transform $M_{EM \to TX}^{\Delta t}$ was developed for application to Cartesian coordinates. To achieve this conversion we apply Equation 3.5 whose derivations can be found in Appendix B.

$$\begin{pmatrix} x \\ y \\ z \end{pmatrix} = \begin{pmatrix} -r\sin\theta \mp \sqrt{R^2 - r^2}\cos\theta \\ r\cos\theta \mp \sqrt{R^2 - r^2}\sin\theta \\ z_{LOR} \mp \frac{1}{2}\sqrt{\Delta x^2 + \Delta y^2}\tan\varphi \end{pmatrix}$$
(3.5)

After determining the LOR endpoints, we apply the corresponding transform, $M_{EM\to TX}^{\Delta t}$, to convert each of the coordinates, $(x_1, y_1, z_1)_{HRRT}$ and $(x_2, y_2, z_2)_{HRRT}$, back to the transmission reference position. A conversion back to the LOR parameterization, as described by Equation 3.6, completes the process, resulting in motion corrected LORs that can now be reconstructed.

$$\begin{pmatrix} r \\ \theta \\ z_{LOR} \\ \varphi \end{pmatrix} = \begin{pmatrix} y_1 \cos \theta - x_1 \sin \theta \\ \arctan\left(\frac{\Delta y}{\Delta x}\right) \\ z_1 + \left(\frac{-x_1 \Delta x - y_1 \Delta y}{\Delta x^2 + \Delta y^2}\right) \Delta z \\ \arctan\left(\frac{\Delta z}{\sqrt{\Delta x^2 + \Delta y^2}}\right) \end{pmatrix}$$
(3.6)

Recall that the motion correction technique implemented in Chapter 2 also corrects for motion via the sensitivity matrix \bar{s}_j , which requires the ability to determine the motions of a voxel over the course of the scan. This is substantially easier, than for the LOR case, as we can simply apply the motion correction transform, $M_{EM\to TX}^{\Delta i}$, directly to the Cartesian voxel coordinates in the HRRT reference frame.

3.4 SUMMARY

A motion tracking system, for use with the HRRT scanner has been implemented. This system tracks a tool that was designed specifically for purposes of subject motion tracking requiring a rigid attachment of the tool to the subject's head. A method was developed for the calibration of the scanner reference frame and the tracking system reference frame in which the motion measurements were made. After calibration of the measured motion data the process used to apply this data in the LM-EM reconstruction, on both an LOR and voxel basis, was defined. A motion tracking system is now in place that not only allows the investigation of subject motion types and magnitudes (Chapter 4), but also the inclusion of these motions within the reconstruction framework (Chapter 5).

4 AN INVESTIGATION OF SUBJECT MOTION

Every correction for motion will have some degree of negative impact on the reconstructed image, at the very least there is some uncertainty in the motion tracking; therefore we would like to limit motion as much as possible prior to implementing a motion correction technique. In practice complete subject immobilization is an unrealistic goal unless sedation is applied, which is clearly not desirable; nevertheless some limitations to motion can be employed, such as the use of the thermoplastic mask described in Section 1.3.2. Application of a severe head restraint is not possible since it would lead to unbearable discomfort for the majority of subjects. Another possibility is to avoid situations that encourage subject motion, for example minimizing interactions with the scanning personnel.

In order to address this second issue an investigation of subject motion under typical brain scanning conditions was carried out [Dinelle, 2006] using the Polaris motion tracking system implemented in Chapter 3. We propose to use the collected motion data in two ways. First, to correlate various commonly occurring events, for example speaking to a nurse, with the magnitude of motion they induce in an attempt to identify avoidable situations that unnecessarily lead to significant motion. Second, to establish how these typical motions affect various regions of the brain; for example, the impact of head rotations on the displacement of these regions will differ depending on their distance from the centre of rotation. This information will aid in a determination of the impact of motion on the accuracy (and noise) of the associated TACs.

Some likely sources of motion were identified prior to this study based on the scanning protocol. Interactions occurring between the subject and the

attending nurse/scanning staff while ensuring subject comfort were generally not restricted and often involved the readjustment of the subject's limbs. Due to time constraints relating to the delivery of the radio-tracer, the subject's intra-venous (IV) needle was prepared during the transmission scan. Finally, as part of the investigation protocol, 40 minutes into the emission scan a physician evaluated the subject's symptoms using a modified version (no head or neck observations) of the Unified Parkinson's Disease Rating Scale (UPDRS) requiring the subject to speak and move both their arms and legs [Fahn, 1987].

4.1 METHODS

4.1.1 DATA COLLECTION

Subject motion was investigated under typical scanning conditions for two patient populations: healthy controls (n = 3) and subjects suffering from movement disorders, specifically PD (n = 8). In addition to the Polaris motion data an observer kept a record of visible subject movements during each scan. By pairing the measured and observed motion information, the magnitude of different motion during a variety of activities was determined.

Each subject underwent both a transmission scan and a one hour emission scan. Often the emission scan did not begin immediately after the end of the transmission scan. Due to the relatively quick decay of PET radiotracers, the subject must be fully prepared for the emission scan to start as soon as the tracer arrives, however due to the complicated radiotracer synthesis process the delivery time of the tracer can only be estimated. As a result, a period of 15 to 30 minutes often elapses between the end of the transmission scan and the start of the emission scan while waiting for the delivery of the tracer.

Data were obtained for the PD group by tracking motion during a regular scanning session as part of a study already being carried out in our centre. In the case of the healthy group, data were collected using volunteers placed in a mock scanning situation. All aspects of the PD study were replicated for the

healthy subjects except for the injection of a radioactive tracer during the emission scan. Two sets of data were collected for the healthy controls in order to compare two different types of head restraint: the thermoplastic mask currently in use, and a system of Velcro straps placed over the chin and forehead and attached to the scanner bed. This allowed a determination of the impact changing the subject restraint system would have on motion and the quality of the reconstructed images.

4.1.2 DATA ANALYSIS

The transmission image for each scan was reconstructed and used to locate three brain regions, cerebellum, occipital cortex, and striatum, over which regions of interest (ROIs) are commonly placed. This method of ROI placement, on the transmission as opposed to emission images, was chosen because emission images were unavailable for the healthy subjects. The motion information, measured at the center of the Polaris tracking tool, was used to calculate the displacement of the center of each ROI. The new ROI coordinates were then compared to the average position of that same ROI during the transmission scan. ROI rotations were determined using the same reference, the average orientation of the plate during the transmission scan, but were calculated only once for each measured motion as the plate and subject's head were assumed to be a rigid body. For each ROI location the displacement data were plotted against scan time.

Further analysis was applied in order to determine the impact of motion on the TACs. The amount of motion that occurred during each TAC frame was calculated by averaging measured ROI translations over the time intervals dictated by the TAC analysis, thus determining a mean displacement during that frame and an associated standard deviation (SD). A TAC was calculated for one PD subject, and a comparison was made to the corresponding tracked and visually observed motions.

4.2 RESULTS

4.2.1 COMMON MOTION TYPES

Several different kinds of motion were visually observed and tracked. These included continuous or drifting type motions, motions occurring about a mean position, and large motions that resulted in a sustained change in position. All three types of motion were present in both the healthy and PD subject data. Measured drift type motions resulted in considerable accumulated displacements over the entire course of the scan. Long drift motions measured throughout the healthy subject scans correlated to the subject falling asleep, whereas for PD subjects these motions often reflected the commonly observed tendency to pull to one side. Examples of this type of motion for both subject types are shown in Figure 4.1. Here the healthy subject drifted 2 mm over the course of the scan, and did not undertake any large rotations of the head represented in the small deviation in displacement measured in different regions of the brain. Drifting motions up to 13 mm were observed for the PD subject shown in Figure 4.1, as well as large head rotations leading to the discrepancies in translation between the different ROIs. At the start of the emission scan no translation had occurred between the emission and transmission scans for the healthy subject, however a large translation (up to 9 mm) had occurred in the case of the PD subject, thus the observed initial offset.



Figure 4.1: Healthy (lower curves) and PD (upper curves) subject long drift type motions for three regions of interest in the brain.

4.2.2 MOTION EXHIBITED BY HEALTHY SUBJECTS

Typical motion data acquired during a healthy subject scan are shown in Figure 4.2. Here we can see the correlation between the visually observed motions (labeled) and the tracked motions (plotted). Activities observed during this scan were: talking, which resulted in displacements up to 1 mm and rotations up to 1.5° , the UPDRS evaluation, with displacements up to 2 mm and rotations up to 1.25° , and motion caused by the subject pushing their head vertically back into the headrest to relieve pressure from the mask on the bridge of their nose, 1 mm maximum displacement and 1.5° maximum rotation. All of these motions occurred about a mean position, however a drift motion from 0 mm to 2 mm over the entire course of the scan was also observed along the axial (z) direction for this subject. As the scan progressed, the degree of rotation of the subject's head increased, effecting the measured displacements of the ROIs. In the vertical (y) direction (at t = 50 minutes) displacement of the region placed in the cerebellum was 1.6 mm, twice what was observed in the occipital cortex region (0.8 mm).



Figure 4.2: Translations made by a healthy volunteer wearing a thermoplastic mask restraint, along the horizontal (A), vertical (B) and axial (C) directions. Corresponding rotations about all three axis are shown in D. Translations of 0 mm represent no displacement between the emission and transmission scans.

Similar motions were observed throughout the other healthy subject scans. Long drift motions were on the order of 2.5 mm in magnitude and typically observed along the z-axis. Movement occurring about a mean position attributed to talking was at most 1.5 mm, while the result of participation in the UPDRS evaluation was a displacement of up to 3 mm.

4.2.3 MOTION EXHIBITED BY PD SUBJECTS

A representative PD subject motion data set is presented in Figure 4.3. Motions both visually observed and tracked included tracer injection (up to 3.5 mm), being woken up from sleep (up to 1.5 mm), and the UPDRS evaluation (up to 2 mm). Rotation type motions were small (on the order of 0.5°) throughout the scan, therefore large deviations in position were not observed between the various brain regions studied.



Figure 4.3: Translations made by a PD subject wearing a thermoplastic mask restraint, along the horizontal (A), vertical (B), and axial (C) axes. Corresponding rotations about all three axes are shown in D.

Long drift motions did not occur for this specific subject, however they were present in several other PD data sets. In one case, drifts of up to 6 mm were measured for ROIs placed in the striatal region, and up to 15 mm in the occipital cortex region (Figure 4.1). In the remaining seven PD scans, motion

related to the UPDRS evaluation caused displacements of up to 8 mm to occur about a mean position. Less common motions resulting in long term changes in position included using a bedpan, which resulted in head motions up to 20 mm (Figure 4.4A shows a less serious case), removing a bolster from under the subject's legs (up to 2.5 mm) and moving the legs from a flat to a knees up position (up to 2.5 mm) (Fig 4.4B).



Figure 4.4: Translations measured during PD subject scanning. Motion along the axial direction during the use of a bedpan is shown in A. Subject motion along the vertical direction during a series of leg motions and the UPDRS evaluation is shown in B.

As expected, PD subjects exhibited greater translations and rotations during scanning than the healthy subjects. Figure 4.5 shows the mean motion magnitude \pm SD, measured in the striatum for one healthy and one PD subject. Not only were the overall displacements made by the PD subject greater than those made by the healthy subject (5.2 mm maximum displacement versus 2.4 mm), but the variation in position during each frame measured as the SD was much greater (1.6 mm versus 0.3 mm).



4.2.4 PRE-EMISSION SCAN MOTIONS

Positional discrepancies may occur between transmission and emission data due to motions accumulated during the transmission scan, or between the transmission and emission scans. Movement during the six-minute transmission scan is of particular concern, as the motion correction scheme has not yet been extended to include these data. Under the current scanning protocol, no limits were placed on interactions between the subject and attending nurse/scanning staff during the transmission scan. Often this time was used to reassure the subject verbally, prepare their IV, and take their blood pressure. As a result, PD subjects moved about their mean transmission scan position in the range of ± 3.0 mm. When a more concerted effort was made to limit subject motion during transmission scanning, the range of motions decreased to ± 1.5 mm. An extreme example of mismatch between the transmission and emission scans was observed for the PD subject presented in Figure 4.1.

4.2.5 MOTION AND SUBJECT RESTRAINT

When comparing the thermoplastic mask to a Velcro restraint system an increase in mean subject displacement of less than 1.0 mm was observed due to use of the less restrictive system, as shown in Figure 4.6. Although there was only a small increase in mean displacement, the SD of the motion with the Velcro restraint was much greater than for the thermoplastic mask (1.8 mm maximum SD versus 0.2 mm). This effect was especially evident in times of induced subject motion, such as during the UPDRS evaluation which occurred between 35 and 45 minutes. The long drift motions discussed previously were not observed for scans completed with the Velcro restraint system. Instead the trend was for slightly larger motions to occur about a mean position with no bias towards a specific direction.



Figure 4.6: Mean \pm SD of healthy subject motion measured in the striatum with a thermoplastic mask (\blacktriangle) and Velcro restraint (\blacksquare).

4.2.6 SUBJECT MOTION AND TAC ANALYSIS

The magnitude of translation due to rotation varied depending on the area of the brain being evaluated. Rotations of only a few degrees resulted in the displacement of various brain regions of interest of up to 4 mm (Figures 4.2D and 4.3D). Rotations about both the horizontal (x) and vertical (y) axes had the greatest affect on displacement of the region in the cerebellum. The largest displacements caused by rotations about the long (z) axis were observed in the occipital cortex region. This information is relevant when estimating the contribution of different ROIs to noise during the determination of biologically relevant parameters.

An obvious effect of motion can be seen in the TAC for the subject data shown in Figure 4.7. The majority of the motion during the scan was limited to a single frame, from 25 to 30 minutes. By examining the TAC for the striatum corresponding to this subject, it is obvious that the unusual dip in the curve relates exactly to the occurrence of the large motion.



Figure 4.7: PD subject displacement in the striatum along the x, y, and z axes during a 1 hour emission scan with the corresponding striatal TAC overlaid.

4.3 DISCUSSION

As expected an increase in subject motion was observed between the healthy and PD subjects (Figure 4.5). This is not surprising as the symptoms of PD include not only tremor, but muscle stiffness, joint rigidity and sometimes pain. Other differences between the subject groups that may have contributed to the increase in motion included age, the PD subjects were older in all cases, and familiarity with the scanner as the healthy controls were chosen from within our research group. While the use of a more rigid restraint system would help to reduce these motions for both subject types, this method would be far too restrictive for subjects with movement disorders. Increased discomfort may induce tremor which often worsens in stressful situations. In this case, we feel that we have reached the limit of physical restraint based on concerns for subject comfort, without which the success of the scan may be jeopardized.

The use of a Velcro restraint system may prove to be one method for improving subject comfort, while only minimally impacting the amount of subject motion. The major difference observed between the two systems was the presence of long drift type motions when using the thermoplastic mask, as opposed to larger magnitude motions occurring about a mean position observed with the Velcro system. As a result the Velcro case is more likely to contribute to overall image blurring as opposed to systematic artifacts that would be introduced by the mask type motion. A clear advantage of the Velcro system is the fact that the subject could easily see out of the scanner, decreasing the risk of claustrophobia and allowing studies requiring the patient to view an external screen.

Our observed data emphasize the need to carefully plan the schedule of events during scanning in order to decrease the amount of subject motion. Movements observed during the transmission scan, and between the transmission and emission scans were, in several cases, larger than the resolution of the scanner (Figures 4.2 and 4.3). During the transmission scan, movement was detected mainly due to the insertion of the subject's IV. In subsequent studies this measured motion was minimized by fully preparing the subject for their emission scan prior to the beginning of the transmission scan (inserting IV, providing pillows and blankets), and strictly limiting interaction with the subject during the scanning process. This reduced the mean transmission scan motion from ± 3.0 mm to ± 1.5 mm. The impact of motion can also be reduced by starting the emission scan immediately after the transmission scan, thereby decreasing the chance of large displacements occurring between scans. This would be especially beneficial in cases where subjects exhibit long drift type motions, as the mismatch increases continuously over the course of the scan.

Some observed motions, such as large leg readjustments or the use of a bedpan, will be unavoidable in subsequent scans as they were required in order to ensure the subject's comfort. Awareness of the magnitude of head displacement corresponding to these motions allows those attending the subject to encourage communication, and impress the importance of making any discomfort they may be feeling known prior to the start of scanning. Understanding that these motions will impact the reconstructed images, a record should be kept whenever they occur, especially in cases where a motion correction technique will not be employed.

4.4 SUMMARY

Motion data obtained with the Polaris system provided a useful tool for investigating the types and magnitudes of subject motions occurring under typical scanning circumstances. Based on the subjects studied here, movements ranged from 1 to 20 mm in magnitude. A variety of motion types were observed including movements that resulted in a sustained change in

position, long drift motions that resulted in a large accumulated displacement over time, and frequent short duration motions about a mean position. Application of the Velcro restraint system did not result in a large increase in measured motion for the limited dataset of healthy volunteers studied here. The effect of motion on different brain regions showed a positional dependence due to rotational motions with variations between regions of a few millimeters. This measurement provided motion related information on the accuracy that can be expected in TACs for different brain regions.

Although the implementation of a motion correction scheme will allow for compensation of these motions, the optimal images will always be obtained when no motion is present. Methods identified to reduce the impact of subject motion include decreasing the amount of interaction between the nurse/scanning staff and subject during scanning, and decreasing the time between the transmission and emission scans. An increased awareness of the effect each task has on subject motion can be used to motivate limitations on these motions.

5 EXPERIMENTAL VALIDATION OF THE MOTION CORRECTION METHOD

Evaluation of the motion correction scheme was carried out for three levels of emission source complexity: a line source, a contrast phantom, and a set of four human scans. In the first two cases we ensured that the algorithm was implemented properly. Using a simple line source, to which discrete motions were applied, the setup of the Polaris acquisition system and the implementation of LOR-only corrections in the reconstruction were tested. An extended object, specifically an elliptical phantom with small hot and cold inserts, was used to check the efficacy of the LOR+sensitivity method compared to the cases of no motion correction and LOR-only motion correction (Chapter 2). In the third case we investigate the performance of the implemented motion compensation scheme for human data, as motion correction will eventually become routine in the processing of our HRRT PET data at our research centre.

5.1 MEASUREMENT OF A MOVING LINE SOURCE

5.1.1 **METHOD**

Approximately 1 mCi of ¹⁸F was placed into a long thin plastic tube with a total volume of 5 ml. The tubing and Polaris tracking tool were then rigidly affixed to a small piece of Styrofoam so that motion of the line source could be measured throughout the experiment. The whole setup was placed into the centre of the HRRT gantry. A 5 minute transmission scan was acquired prior to emission scanning, followed by a 10 minute emission scan of the source in a stationary position. After collecting this baseline information, two more 10 minute emission scans were carried out during which discrete motions were applied to the source at 5.0 minutes and 7.5 minutes into the scan. In both cases

the motions built upon one another; the motion applied at t = 5.0 min was maintained when the second motion was applied at t = 7.5 min. In the first experiment translational motions of 2 mm and 4 mm in magnitude were applied along the long axis of the scanner. In the second experiment a rotation of ~10° about the vertical axis was applied, followed by a translation of 3 mm also along the vertical axis. Reconstruction of the emission data was completed using the LOR-only motion correction. In this experiment we were only concerned with demonstrating that the implementation of the LOR-only algorithm was correct.

5.1.2 RESULTS

When compared to the reconstructed image of the stationary 10 minute reference scan (Figure 5.1A), degradation due to the applied motions can clearly be observed in the translated and translated/rotated images when these data are not corrected for motion (Figures 5.1B and 5.1C). The images shown here are projections of all data along the y-axis into the xz-plane, resulting in a top-down view of the source in the tomograph.



Figure 5.1: Reconstructed images of the line source in the *xz*-plane for the static emission data (A), the translated data (B), and the combined rotation and translation data (C), for 1.21875 mm/pixel.

Application of the LOR-only correction to the motion effected emission data resulted in images without motion artifacts. Specifically, no blurring of the source due to the motion was visible. The motion corrected images appeared to be identical to the reference image with only random noise remaining between the baseline static image and either of the motion corrected images (Figure 5.2).



Figure 5.2: Reconstructed images of the line source for the static emission data (A), the motion corrected translated data (B), and the motion corrected rotated and translated data (C).

5.1.3 CONCLUSION

Based on the results of this experiment we conclude that both the calibration and LOR-only motion correction have been implemented correctly in the image reconstruction step. Inclusion of the LOR+sensitivity motion compensation in the reconstruction algorithm will be investigated in the following sections.

5.2 MOTION CORRECTION OF A CONTRAST PHANTOM

5.2.1 **Method**

The body of an elliptical phantom was filled with radioactive water; the total volume of water in the phantom was 3187 ml mixed with 0.74 mCi of ¹⁸F in a negligible volume (activity corrected to emission scan start time). Two small water filled spheres were supported inside the phantom with thin pieces of tubing that extended from the sphere to the phantom wall. In one of the small spheres (volume = 31.42 ml) 0.35 mCi of ¹⁸F was added, resulting in a calculated hot to background activity ratio of 4.77. The second spherical insert contained a volume of 13.42 ml of water and no radioactivity.

The phantom was supported in the centre of the scanner gantry with the long axis of the ellipse oriented along the vertical scanner axis to best represent the shape of a human brain. A 5 minute transmission scan of the phantom was measured pre-emission. Over the course of a 28 minute emission scan the phantom was moved through a series of discrete positions by application of a number of translations and rotations as described in Table 5.1. Emission data were reconstructed via three methods: with no motion correction applied, with LOR-only correction, and with the LOR+sensitivity corrections. The data acquired in the moved positions were reconstructed together over the entire 28 minute scan duration to emphasize possible image motion artifacts. In addition, two minute data subsets from the "rest" condition (frame 1) and frames 3, 8, 10 and 12 were reconstructed separately to allow a contrast versus noise evaluation (Table 5.1).

Frame	Time (min)	Direction of applied motion.		
		X (mm)	Y (mm)	Z (mm)
1	0-2	0	0	0
2	2-4	0	+5°	· 0
. 3	4-6	0	-5°	. 0
4.	6-8	, 0	0.	. +3°.
5	.8-10	0	0	+6°
6	10-12	0	0	+9°
7	12-14	+5°	0.	0
8	14-16	+15°	0	0
9	16-18	0	0	+10
10	18-20	0	+10	+10
11	20-22	0	+10	+20
12	22-24	0	+20	+20
13	. 24-26	0	+20	+30
14	26-28	0	+30	+30

Table 5.1: Contrast phantom	positions during a	a 28 minute emission scan m	easured
relative to the location	of the phantom d	luring the transmission scan	•

After image reconstruction hot:background and cold:background contrast ratios were determined from the reconstructed images. These values were used to quantitatively compare the two motion correction methods employed during

reconstruction. The cold contrast (C_{cold}) was determined by comparing the average number of counts in ROIs placed in the cold and background regions.

$$C_{cold} = \left(1 - \frac{\text{mean counts in cold region}}{\text{mean counts in background region}}\right) \times 100\% \quad (5.1)$$

The contrast between the hot sphere (C_{hot}) and the background was calculated using ROIs placed in the hot and background areas of the image (Equation 5.2). Here we incorporate the known hot/background ratio (4.77) into the measure of our ability to determine the contrast recovery between two regions in the image.

$$C_{hot} = \left(\frac{\left(\frac{\text{mean counts in hot region}}{\text{mean counts in background region}}\right) - 1}{\text{known hot to background ratio (4.77)}}\right) \times 100\%$$
(5.2)

Hot and cold contrast values were plotted against the percentage noise (mean/SD) measured in a large background region. To achieve different levels of noise in the image, the number of iterations completed during reconstruction with the LM-OPEM algorithm was varied. High numbers of iterations are known to increase both the contrast recovery and the noise in the image.

5.2.2 RESULTS

A comparison of the reconstructed images for the three levels of motion compensation are shown in Figure 5.3 for a representative transaxial and coronal slice. The effect of the motion is clearly visible in the non-motion corrected case (A), where both the hot and cold regions are smeared across the coronal images while variation across these regions is evident in the transaxial image. In the images reconstructed with the LOR-only corrections applied (B), the hot and cold regions have been corrected to a single location, however the impact of neglecting corrections for the LOR sensitivity is apparent in the star shaped (transaxial) and line (coronal) artifacts in the image. Neither of these artifacts are present in Figure 5.3C where reconstruction was completed with the LOR+sensitivity correction.



Figure 5.3: Transaxial (top) and coronal slices (bottom) through an elliptical phantom with hot and cold spheres reconstructed without motion correction (A), with LOR-only (B), and with LOR+sensitivity correction applied (C) for the entire data set.

The hot and cold contrast versus noise values were significantly improved by inclusion of detector sensitivity information into the motion correction. In this Figure 5.4 we see the contrast versus noise values for a subset of the collected motion data (frames 1, 3, 8, 10 and 12). Variations in the amount of noise in the images was achieved by varying the number of iterations completed during reconstruction. The reference case (solid line) was calculated for an image reconstructed from only the first two minutes of the collected emission data, during which the phantom had not yet been moved from the reference transmission scan position. Four other 2 minute emission images were reconstructed using both motion compensation methods (Table 5.1). These were frames 3 (\bigcirc), 8 (\blacksquare), 10 (\diamondsuit) and 12 (\triangleleft). In Figure 5.4 little difference in the contrast/noise ratios between the reference image (—) and any of the motion effected images reconstructed with LOR+sensitivity corrections (- - -). However, a worsening of the contrast/noise values was observed for the LOR only corrections (|||), related to the magnitude of the motion in the frame. The contrast/noise ratio was worst, when compared to the reference position, for the motion of +20 mm along both y and z axis (frame 12, \triangleleft), and the best for the -5° rotation about the y axis (frame 3, \bigcirc).



Figure 5.4: Cold (left) and hot (right) contrast versus noise ratios for a number of motion types reconstructed with (- - -) and without (| | |) compensation for variations in LOR sensitivity due to these motions.

5.2.3 CONCLUSION

Application of LOR+sensitivity corrections during image reconstruction resulted in improved image quality compared to those images reconstructed with the simple LOR-only correction. The hot and cold contrast versus noise values measured in the LOR+sensitivity corrected images showed improved contrast recovery, equal to that measured in the no-motion reference case.
Reconstructions completed with the LOR+sensitivity motion corrections showed superior performance in contrast recovery when compared with the results from the LOR-only corrected images.

5.3 MOTION CORRECTION OF HUMAN DATA

5.3.1 **Method**

Motion data was collected using the Polaris system over the course of four subject scans in conjunction with a study of PD subjects being done by other researchers in our group. Each subjects scanned underwent a 6 minute transmission scan, followed by a one hour emission scan using ¹¹C-raclopride, a D_2 receptor agonist. Reconstruction of the PET data was completed without motion correction, with the LOR-only method, and with the LOR+sensitivity method. Images of the reconstructed data were investigated to determine if the impact of the reconstruction methods could be visually observed.

In order to quantify the impact that the motion correction scheme had on the images, a typical PET data analysis procedure was applied to each reconstructed subject data set. In this analysis a series of circular ROIs were placed by hand over the striatum on images of the subject's brain. One set of ROIs was placed on each striatum (left and right), with each set composed of four ROIs covering the caudate (1 ROI) and putamen (3 ROIs). Average values in each ROI were recorded across 12 image planes (14.6 mm). A reference ROI was placed in the cerebellum extending across 5 planes (6.09 mm). A Logan analysis was then applied to the data which calculated the binding potential (BP) of the tracer in a given ROI [Logan, 2000]. BP values from data reconstructed with and without motion correction were compared by calculation of a percent difference between the various cases. Results for the four ROIs placed on a single striatum were plotted in order to visualize the gradient across these ROIs. Values in neighboring ROIs placed within in the same structure were not expected to exhibit significant changes.

5.3.2 **R**ESULTS

As in the case of the elliptical phantom, a significant effect of ignoring the need to correct for changes in sensitivity due to motion can be observed in a reconstructed human subject image (Figure 5.5). Here a transaxial slice through the brain is shown with the striatum clearly visible. At first glance the difference between the uncorrected, and LOR+sensitivity corrected images is not as striking as it was in the phantom study.

An obvious change was observed in the measured BP values between the LOR-only images and the LOR+sensitivity images. A comparison of the BP values for each ROI (left and right, 1 caudate and 3 putamen) is given in Table 5.2. Differences between the BP values ranged from 0.1% to 39.6%. This magnitude of variation in the results of the image analysis is significant as it is on the order of the changes we are attempting to study using the ¹¹C-raclopride tracer (12-18% difference between a baseline and intervention) [Tedroff, 1996], [Fuente-Fernandez, 2004].

Region in Striatum	Percent Difference in Analysis							
	scan 1		scan 2		scan 3		scan 4	
	right	left	right	left	right	left	right	left
Caudate	17.4	24.0	6.5	7.4	0.1	7.2	2.2	9.9
putamen 1	20.6	20.6	7.4	2.7	0.9	13.0	4.5	7.0
putamen 2	19.0	22.5	13.0	13.2	11.6	4.1	4.2	27.0
putamen 3	28.5	36.4	5.3	9.5	20.1	14.9	1.3	39.6

 Table 5.2 : A comparison of the analysis of realigned and motion corrected human PET data.

Plots of the BP values for each ROI in the right striatum are shown in Figure 5.6. We see that the gradient between ROIs is less in the non-motion corrected and the LOR+sensitivity corrected cases, than in the LOR-only motion correction case. Based on our knowledge of biology, abrupt changes in BP values between neighboring ROIs can not be physical as it would mean

there was a substantially different uptake between two contiguous areas of the same anatomical structure. Therefore was can classify many of the BP values measured in the LOR-only images as incorrect due to the dissimilarity from one ROI to the next. In all of the studies analyzed an increase was observed in the BP values calculated on the sensitivity motion corrected images as compared to the non-motion corrected values.





5.3.3 CONCLUSION

Differences were observed in both the reconstructed images, and in the BP values determined from ROIs placed on the striatum in the reconstructed images. The LOR-only motion compensation method is clearly a poor choice for reconstruction of emission data effected by subject motion. Serious image artifacts as well as non-uniform BP values in a single anatomical region were observed for these images. The LOR+sensitivity motion correction method resulted in an overall increase in BP compared to the non-motion corrected case. The distribution of BP values is less uniform over ROIs placed in a single

striatum in the LOR-only case compared to the other types of reconstructed images. Thus far we have proven that the LOR+sensitivity reconstruction is functioning properly, however more subject data sets must now be analyzed in order to determine the impact of this method.

5.4 SUMMARY

The motion correction method implemented in this project was applied to a line source, a phantom, and also to human data. In the case of the line source we observed that both the calibration of the Polaris and HRRT reference frames, and the LOR-only event motion compensation technique, have been correctly implemented in the reconstruction framework. Using a contrast phantom improvement of the LOR+sensitivity motion correction over the LORonly motion correction was clearly demonstrated, both in the reconstructed images, and in their calculated contrast/noise ratios. Finally, application of the motion compensation scheme to a set of human scans in which a typical data analysis was completed resulted in variations of up to 40% in the BP values measured in images reconstructed with and without motion correction. An improvement of the sensitivity motion correction over the LOR only correction was obvious in both the reconstructed images, and the calculated BP values. A difference between the non-motion corrected data and the sensitivity motion corrected data was also observed, however further investigation is required to ensure that the change is an improvement, resulting in a more accurate estimation of the true tracer distribution.

6 SUMMARY, FUTURE WORK, AND CONCLUSIONS

6.1 FUTURE WORK

6.1.1 SUBJECT MOTION DATA ACQUISITION SYSTEM

A next generation Polaris system, the Polaris Vicra has been received by our research group. Its implementation will allow improved tracking accuracy (from ± 0.35 mm to ± 0.25 RMS error), and also an extended FOV inside the HRRT gantry due to the small extent of the Vicra emitter/receiver. Another advantage of the small size of the Vicra is that it can be mounted to the back of the tomograph, with the result that the two coordinate reference frames (Polaris and HRRT) are rigidly fixed with respect to one another, and therefore calibration of the two frames will be required only when a major event occurs to upset this relationship, for example scanner maintenance. Each subject scan will allow us to verify the current calibration, as the Polaris tool will show up in the subject's transmission scan. This allows the determination of a set of paired coordinates on which the transform can be tested.

An alternate method of subject restraint may be necessary, either for studies requiring a visual stimulus external to the scanner, or to allow the use of a video motion capture tracking system that requires an unobstructed view of the subject's facial features. Using the Polaris system studies of the impact different restraint types have on the magnitude of measured motion can be performed as discussed in Chapter 4. The study of the Velcro strap restraint system will be extended to include a greater number of healthy subjects, and also to subjects diagnosed with PD. As every correction has some error associated with it, we would like to choose a system that minimizes motion as much as possible while still allowing the subject to see out of the scanner.

Another method of subject restraint which achieves this goal is the use of a thermoplastic band across the subject's forehead.

We will also undertake an investigation into the assumed rigid attachment of the Polaris tool, worn on a swim cap, to the subject's head. One approach will be to scan a subject wearing the cap and tracking tool in an MRI scanner which provides better anatomical and timing resolution than that provided by an HRRT transmission scan. Ideally we will be able to resolve both the tool and the brain in the images, and determine if their relationship changes over time.

6.1.2 THE MOTION CORRECTION ALGORITHM

In Chapter 5 differences in the results of an image analysis were observed between images reconstructed with the LOR+sensitivity motion correction algorithm and those reconstructed without motion correction. We must now demonstrate that this brings the results of our image analysis closer to the true case. Applied to phantom data the LOR+sensitivity motion correction algorithm was able to successfully restore the motion impacted images such that they reproduced the static reference image. However, the capabilities of the algorithm are more difficult to show when the true tracer distribution is unknown as in the case of human data. One possibility is to compare differences between images reconstructed with and without a less involved motion correction algorithm, for example a frame by frame realignment, to determine if the same trends are observed between these data sets as in the LOR+sensitivity versus non-motion corrected case.

Based on the collected Polaris motion data, the magnitude of subject motion is known to vary significantly from subject to subject, and even for one subject during the same scan. In cases where the subject does not move substantially over the course of the scan, or makes one large motion which is sustained for the remainder of the scan, the use of a MAF approach may be an acceptable method of accounting for motion. This method is less computationally intense

as it does not require numerous small motion correction steps as in the LOR+sensitivity method introduced in Chapter 2. Of course, there will still be many cases where large, frequent, motions occur over the course of the scan requiring the more accurate LOR+sensitivity motion correction approach presented in this paper. The possibility of tailoring the motion correction process to each individual scan, and possibly to each frame, should be investigated in order to decrease the time cost of each reconstruction, and to simplify the process wherever possible.

6.2 CONCLUSION

With the installation of a high resolution PET tomograph, the HRRT, subject motion became a significant source of error in the reconstructed images and their subsequent analysis. In this work, a system for measuring and correcting for these motions was implemented. Subject motion information was recorded using a Polaris acquisition system, which was correlated both temporally and spatially to the PET system. Using this system, relevant information about PD subject motion during a typical PET study was obtained. Motions in the range 1 mm to 20 mm were observed in the PD subject studies, which are significant when compared to the resolution capabilities of the HRRT (2.4 mm FWHM). The motion data were incorporated into an LM-OPEM reconstruction algorithm, which included corrections for both LOR position, and changes in sensitivity due to the position of the LOR with respect to the scanner. The system was applied to a motion impacted line source, contrast phantom, and PD subject data. Improvements were observed in the LOR+sensitivity case when compared to the commonly implemented LORonly motion correction. Changes were also evident in the reconstructed images and the results of their analysis, between the non-motion corrected and LOR+sensitivity motion compensated approaches. With the implementation of this motion correction scheme we are able to eliminate a source of resolution

degradation in the HRRT images. This brings us one step closer to achieving the maximum image resolution possible from the tomograph.

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APPENDIX

A POLARIS MEASUREMENT VOLUME IN THE HRRT GANTRY

The field of view available for tracking within the HRRT gantry can be calculated by projecting the line of sight of the Polaris down the length of the scanner. If we set the center of the Polaris as (0,0) then $\mathbf{A} = (0,25)$, $\mathbf{B} = (\mathbf{D}, 12.6)$, $\mathbf{C} = (\mathbf{D}+63 \text{ cm}, \mathbf{R})$, where \mathbf{D} is the distance from the back of the tomograph to the Polaris, and \mathbf{R} is the radius of the field of view (Figure A.1). The line \mathbf{AB} is parallel to line \mathbf{BC} where $\mathbf{AB} = (\mathbf{D}, -12.4 \text{ cm})$, $\mathbf{BC} = (63 \text{ cm}, R-12.6 \text{ cm})$. Then we have the relationship:

$$\frac{-12.4cm}{D} = \frac{R - 12.6cm}{63cm} \quad (A.1)$$
$$\therefore R = \left[\frac{(-12.4cm)(63cm)}{D}\right] + 12.6cm \quad (A.2)$$

Under normal circumstances the Polaris field of view extends from 140 cm to 240 cm from the Polaris unit (Figure A.2). If we consider these two distances the minimum radial FOV in the scanner is R(140 cm, D=77 cm) = 2.45 cm and the maximum is R(240 cm, D=177 cm) = 8.19 cm. In order not to be at the extreme edge of this field of view, we positioned the Polaris emitter/receiver at 180 cm from the back of the gantry, resulting in a measurement diameter of 16.52 cm which falls within the calibrated volume.



Figure A.1: Geometry for the Polaris field of view in the HRRT gantry.



Figure A.2: The Polaris field of view and calibrated volume.

B DERIVATION OF COORDINATE TRANSFORMATIONS

B.1 CONVERSION FROM LOR COORDINATES (R, θ , ZLOR, φ) TO ENDPOINTS (X, Y, Z)_{1,2}

We want to show that the following relationship is true.

$$\begin{pmatrix} x \\ y \\ z \end{pmatrix}_{1,2} = \begin{pmatrix} -r\sin\theta \mp \sqrt{R^2 - r^2}\cos\theta \\ r\cos\theta \mp \sqrt{R^2 - r^2}\sin\theta \\ z_{LOR} \mp \frac{1}{2}\sqrt{\Delta x^2 + \Delta y^2}\tan\varphi \end{pmatrix}$$
(B.1)

The values for (x_1, y_1) and (x_2, y_2) can be determined via geometrical consideration of the LOR in the xy-plane as depicted in Figure B.1. Here the LOR, which makes an angle θ with the x-axis, is encircled by a crystal ring of radius *R*. An enlargement of this configuration is also shown in Figure B.1, in which it can be see that the location of (x_1, y_1) is a combination of the x (or y) components of the shaded triangles (B.2).

$$x_1 = -A_x - B_x$$
 $y_1 = -A_y + B_y$ (B.2)

Throughout this discussion we will employ the sum/difference trigonometric identities, namely:

$$\sin(\alpha \pm \beta) = \sin(\alpha)\cos(\beta) \pm \sin(\beta)\cos(\alpha)$$
(B.3)

$$\cos(\alpha \pm \beta) = \cos(\alpha)\cos(\beta) \mp \sin(\alpha)\sin(\beta) \qquad (B.4)$$

From the triangle \triangle the equations for A_x and A_y can be written as follows:

$$A_x = r\cos(\theta - \pi/2) = r\sin(\theta) \qquad A_y = r\sin(\theta - \pi/2) = -r\cos(\theta) \qquad (B.5)$$

From the triangle \triangle the equations for Bx and By can be written as shown below.

$$B_x = \sqrt{R^2 - r^2} \sin(\theta + \pi/2) = \sqrt{R^2 - r^2} \cos(\theta)$$
 (B.6)

$$B_{y} = \sqrt{R^{2} - r^{2}} \cos(\theta + \pi/2) = -\sqrt{R^{2} - r^{2}} \sin(\theta) \quad (B.7)$$

Finally, combining A and B we arrive at the endpoint equations for, namely:

$$x_{1} = -A_{x} - B_{x} = -r\sin(\theta) - \sqrt{R^{2} - r^{2}\cos(\theta)}$$
(B.8)
$$y_{1} = A_{y} - B_{y} = r\cos(\theta) - \sqrt{R^{2} - r^{2}}\sin(\theta)$$
(B.8)



Figure B.1: Schematic of an LOR in the xy-plane with definitions in coordinate systems. An enlargement of the central section is shown on the right.

It can easily be shown that the second set of endpoints (x_2,y_2) can be determinted through substitution of A and B into the following set of equations:

$$x_2 = -A_x + B_x$$
 $y_2 = -A_y - B_y$ (B.9)

In order to determine the relationship between $z_{1,2}$ and the LOR coordinates, a side on view of the tomograph is employed as shown in Figure B.2. From the triangle delimited by the LOR, the line Δz , and the line $(\Delta x^2 + \Delta y^2)^{1/2}$ we can write a relationship relating the cartesian coordinates to the angle φ (*B.10*).

$$\tan \varphi = \frac{\Delta z}{\sqrt{\Delta x^2 + \Delta y^2}} \qquad (B.10)$$

To find the position of the endpoint coordinate z_1 , the above equation is first solved for Δz . Since z_{LOR} denotes the z coordinate of the middle of the LOR, we subtract half of the length Δz from z_{LOR} to get to z_1 .

$$z_{1,2} = z_{LOR} \pm \frac{1}{2} \Delta z = z_{LOR} \mp \frac{1}{2} \sqrt{\Delta x^2 + \Delta y^2} \tan(\varphi)$$
 (B.11)



Figure B.2: Side on view of the tomograph gantry with coordinates labeled in both systems.

B.2 CONVERSION FROM ENDPOINTS $(X,Y,Z)_{1,2}$ TO LOR COORDINATES $(R, \theta, Z_{LOR}, \varphi)$

After applying a motion correction to the LOR endpoints, a conversion back to the LOR coordinate system is required in order to continue with the reconstruction. In this case we use the following relationships:

$$\begin{pmatrix} r \\ \theta \\ z_{LOR} \\ \varphi \end{pmatrix} = \begin{pmatrix} y_1 \cos \theta - x_1 \sin \theta \\ \arctan\left(\frac{\Delta y}{\Delta x}\right) \\ z_1 + \left(\frac{-x_1 \Delta x - y_1 \Delta y}{\Delta x^2 + \Delta y^2}\right) \Delta z \\ \arctan\left(\frac{\Delta z}{\sqrt{\Delta x^2 + \Delta y^2}}\right) \end{pmatrix}$$
(B.12)

To derive the equation for θ we return to Figure B.1 from which we can write Equation B.13. This equation can be rearranged to find the the equation for θ in Equation B.12.

$$\tan(\theta + 90^{\circ}) = \frac{\cos(\theta)}{-\sin(\theta)} = \frac{\Delta x}{-\Delta y}$$
(B.13)

The determination of z_{LOR} requires careful consideration. We begin by parameterizing the line between two points (x_1, y_1, z_1) and (x_2, y_2, z_2) , with $\Delta x = (x_2-x_1)$, $\Delta y = (y_2-y_1)$, $\Delta z = (z_2-z_1)$.

 $(x_1, y_1, z_1) + t(\Delta x, \Delta y, \Delta z)$ (B.14)

We need to find the point on this line at which the distance from the point on the line to the z axis is minimized, this is our definition of z. The location of this point will be the

location of the line at which is is closest to the origin of the x-y plane. For a cylindrical geometry, such as we have with the PET tomograph, $x^2 + y^2 = R$ (a constant radius), therefore we will minimize $x^2 + y^2$ with respect to the parameter t.

$$\frac{\partial}{\partial t} \left((x_1 + t \cdot \Delta x)^2 + (y_1 + t \cdot \Delta y)^2 \right) = 0$$
 (B.15)

Which results in the following value of *t*:

$$t = \frac{-(x_1 \cdot \Delta x + y_1 \cdot \Delta y)}{(\Delta x^2 + \Delta y^2)} \qquad (B.16)$$

Substitution of the minimized t into our original parametric equation gives z_{LOR} to be:

$$z_{LOR} = z_1 - \frac{x_1 \cdot \Delta x + y_1 \cdot \Delta y}{\left(\Delta x^2 + \Delta y^2\right)}$$
(B.17)

The determination of φ come from a simple rearrangement of Equation B.10.