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Investigations in Improving Image Visualization and Quality in Positron Emission Tomography/Computed Tomography (PET/CT) Imaging

by

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ABSTRACT

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Positron Emission Tomography/Computed Tomography (PET/CT) is a widely used imaging modality for managing patients with cancer. The combination of PET and CT can provide both functional and anatomic information of disease distribution. However, despite its widespread use, it also has some limitations. One drawback is that current PET/CT scanners cannot acquire whole-body scan in a single acquisition but rather has to divide it into multiple sections due to a limitation in the extent of bed travel. The first part of this thesis focuses on developing a software tool that can display multiple PET segments as a single scan to improve the interpretation of these studies.

The second part of the thesis focuses on another limitation of PET/CT imaging, namely its low image quality. In this section, an investigation of the correlation between injected dose, patient BMI and scanner design on PET image quality is performed. The objective of this investigation is to determine the significance and extent by which these factors can impact PET image quality. The results of this work can be used as a guide to improve protocol design in an effort to generate an optimal PET image quality.
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Chapter 1

Introduction to Positron Emission Tomography/Computed Tomography (PET/CT)

Positron emission tomography (PET) is a non-invasive, diagnostic imaging technique which can measure the metabolic activity in the human body. It is clinically utilized to diagnose patients with certain conditions affecting the brain, heart, as well as to diagnose patients with certain types of cancer. PET imaging first utilized in clinical diagnosis in the early 1990s. It has the unique ability to produce functional (figure 1.1a) images, rather than those anatomical or structural images (figure 1.1b) generated by X-ray computed tomography (CT) or magnetic resonance imaging (MRI). Functional images have the ability to reveal biochemical processes within the human body, such as blood flow, receptor density and glucose metabolism, and these metabolic and biologic activities of disease always precede any anatomic evidence of the illness. Therefore PET is an important technique to image chemical or physiological processes within the body besides other anatomic imaging modalities. In PET imaging, radioactivity is first attached or tagged to a radioactive material that is intrinsic to the human body (e.g. glucose, water, and ammonia) prior to administration of the radioactive material to the patient (usually by injection or inhalation). A specially designed PET scanner monitors how the body processes this material and generates the radioactive accumulated (uptake) images. For instance, $^{18}$F labeled fluro-deoxy-glucose (FDG) is a ‘glucose analog’ that accumulates in regions having high metabolic activity such as brain, liver and malignant tumors (figure 1.1a). In this regard, accumulation of $^{18}$F-FDG by the tissue is directly related to its
metabolic state and an abnormal increase in uptake would indicate the presence of malignant tumor cells. Thus, PET has the ability to non-invasively detect functional changes in vivo with high sensitivity and specificity (1). An important additional advantage of PET imaging is its ability to quantify the amount of radioactivity taken up. This aspect is particularly important in the diagnosis, staging, and evaluation of treatment response. These advantages have enabled wide acceptance of PET imaging as a diagnostic and a research tool, with applications in oncology (2,3), neurology (4), cardiology (5), and pharmacology (6).

This chapter provides a brief introduction to the fundamentals of PET imaging, including the processes of PET data acquisition and image reconstruction. Discussion of multi-modality PET/CT imaging is also included. This chapter ends with an introduction

Figure 1.1: Example of (a) PET image and (b) CT image
to those characteristics of PET imaging that relate to image visualization and quality, the central topic of this dissertation.

1.1 PET Data Acquisition

A PET scan requires the patient to either inhale or be injected with radioactive materials that are labeled with positron emitting radio-nuclides. The most common positron-emitting nuclides are $^{18}$F, $^{15}$O, $^{13}$N and $^{11}$C, which represent the most abundant elements in the human body. These positron-emitting nuclides can be used to label many compounds as radio-pharmaceuticals such as $^{11}$CO, $^{13}$NH3, $^{15}$O-labeled water and $^{18}$F-FDG. The various radioactive labels decay by emitting positrons, the anti-particles of electrons. The most frequently used radio-pharmaceutical is $^{18}$F-FDG, and the decay equation for $^{18}$F-FDG is

$$^{18}F ightarrow ^{18}O + \beta^+ + \nu$$

(1.1)

The produced positron $\beta^+$ rapidly undergoes a unique interaction by combining with an electron $\beta^-$ from the surrounding tissue. The mass of both particles is converted by annihilation into two gamma photons, following Einstein’s mass-energy equation $E = mc^2$.

$$\beta^+ + \beta^- \rightarrow 2\gamma$$

(1.2)

Einstein’s equation shows that each gamma photon has the energy of 511 keV, and the two gamma photons are emitted in opposite directions due to the conservation of momentum.

The process of PET imaging is illustrated in figure 1.2. When annihilation between positron and electron occurs, two gamma photons are emitted simultaneously in
opposite directions, hitting two detectors within a time frame of several nanoseconds. Consequently, two detections made within such a small timing window are viewed as a 'coincidence event' resulting from this annihilation process. A line connecting the two detectors is recorded as line-of-response (LOR), which indicates that the annihilation occurred somewhere along this line. As the scanning process continues, additional coincidence events occur along each possible LOR. Data collection along each LOR is either sorted into a histogram (usually called a sinogram) according to their locations (e.g., radial distance and view angle in 2-D mode as shown in figure 1.3), or stored on an event-by-event basis known as a List-Mode acquisition. As a rough approximation, the total number of coincidence detections along a specific LOR can be considered proportional to the line integration over the underlying radioactivity
distribution. Using such a model, the sinogram constitutes a Radon transform of the original radioactivity distribution (7), which is formulated as:

\[ g(r, \theta) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} g(x, y) \delta(r - x \cos \theta - y \sin \theta) \, dx \, dy \]  

(1.3)

Figure 1.3: Mapping relationship between LOR and sinogram data in 2-D mode

Here, the Radon transform \( g(r, \theta) \) is the line integration of the image \( g(x, y) \) specified by the line parameters \((r, \theta)\), where \( r \) is the distance from the center of the field of view (FOV) to the specific line and \( \theta \) is the pitch angle of the line.

PET data can be acquired in either 2-D or 3-D mode (figure 1.4). In 2-D mode, data are collected slice by slice, which is implemented using extendable septa between adjacent slices. These septa are strips that can be extended from the PET scanner body to help stop gamma photons coming from other slices. In this regard, an accepted LOR is therefore limited in the current trans-axial planes with axially spanning of no more than two adjacent detector rings. In the 3-D whole body mode however, data is collected with these same septa retracted enabling a 3-D acquisition. Therefore LORs are not
Figure 1.4: 2-D vs. 3-D mode in PET imaging

constrained in the trans-axial planes and may span across many detector rings. 3-D acquisition provides better detection since it can accept more coincidences. However, image acquisition in 3-D mode is characterized by a greater amount of scatter than in 2-D mode, which will be discussed later in this chapter.

1.2 PET Image Reconstruction

PET image reconstruction is an inverse problem associated with PET data acquisition (i.e., formation of an estimate of the original object via analysis of the acquired image data). In PET imaging, the acquired data (the sinogram) is first reconstructed to images prior to evaluation by a physician and quantitative mathematical analysis. Previously, a filtered back-projection (FBP) algorithm having widespread use in image reconstruction (8) was used to form an image of the distribution of the radio-
activities within the body from collected sinogram data. This FBP technique is performed under the assumption that sinogram data can be modeled as a Radon transform of the original image (see previous section). Sinogram data collected at each angle are first filtered with a selected filter and then back-projected to image space (figure 1.5). The greater the number of angles projected, the better the degree to which the reconstructed images represent the original object. In a noiseless image environment, the FBP reconstruction method performs quite well, however, with noisier image conditions, the FBP reconstructed image is severely degraded. This is due to the fact that FBP is simply algorithmic and does not account for the various physical processes involved in the photon detection process.

Figure 1.5: Filtered Back-projection (FBP) reconstruction for PET imaging
Compared to FBP, statistical image reconstruction techniques have been shown to provide more accurate system models of the photon detection process and result in images of much better quality (9-11). In these statistical approaches, the PET imaging system is usually modeled as a discrete-discrete system (12) described by the following expectation function:

\[ E\{y_n\} = \sum_{n=1}^{N} H_{nm} x_m + r_n \]  

Here \( \{y_n\} \) is sinogram data vector elements representing the data acquired by the PET scanner. The vector elements \( x_m \) characterize the true patient reconstruction image and represent the amount of radioactivity inside each pixel or voxel (3-D pixel) of the model. The vector elements \( r_n \) account for noisy background incidents, including random and scatter coincidences which will be discussed later. Due to the statistical characteristic of PET imaging, \( r_n \) is usually modeled as a Poisson noise distribution. Alternatively, random and scatter events can be incorporated into (1.4) via the term \( r_n \) because of their statistical property. Finally, matrix \( H \) is called the system matrix, whose elements \( H_{nm} \) are proportional to the probability that a photon pair originating at voxel \( m \) can be detected along the LOR at \( n \). This design for the system matrix allows one to incorporate significant modeling details including physical processes such as positron range, non-collinearity, attenuation correction, detector efficiency normalization and depth of interaction. Integrating such physical detail into the system matrix description produces a model that can much better reflect the true photon detection probability (13-14).

Statistical image reconstruction is generally evaluated as an optimization problem, whereby a cost function is introduced to relate the image estimation quality to measured
data. A popular solution for this function is based on the maximum likelihood (ML) method, in which an optimal image is the one that maximizes the probability of making a detection of the data that are actually measured:

\[ X' = \arg \max_X P(Y \mid X) \]  \hspace{1cm} (1.5)

Here \( Y \) and \( X \) are the sinogram and image vector, respectively, and \( P(\cdot) \) is the Poisson likelihood function. However, ML-based image reconstruction is an ill-conditioned problem, which means that small changes in the data can cause large variations in the reconstructed image (15). A distinct characteristic of ML-based image reconstruction is that as the ML algorithm approaches a high iteration numbers, the reconstructed image becomes increasingly noisy. In this regard, the optimization of the ML cost function is usually terminated before convergence is reached. In addition, smoothing filters are usually applied to the image during or after the optimization process to suppress image noise.

As stated, iterative techniques are usually applied to solve the image reconstruction problem for ML approach. The most frequently used iterative technique is the expectation maximization (EM) algorithm (16). It has the advantage of generating a closed form updating equation:

\[ x_m^{(p+1)} = \frac{x_m^{(p)}}{\sum_i H_{ij} \sum_j H_{ij} x_j^{(p)} + r_i} \]  \hspace{1cm} (1.6)

Here, \( x_m^{(p)} \) is the value of image voxel \( m \) after the \( p-th \) iterations. A major drawback of the ML-EM algorithm, however, is its slow convergence. In order to accelerate the optimization process, evolved EM algorithm based on the concept of subsets have been developed (17-19), whereby each EM iteration is divided into a number of sub-iterations,
and each sub-iteration only reconstructs a subset of the whole acquired data (sinogram). The resultant image from one sub-iteration is then updated by the next sub-iteration. This evolution of the EM algorithm is called the Ordered-Subset Expectation Maximization (OSEM) algorithm (17-19). It conducts much faster than ML-EM algorithm while achieving similar image quality, and it is the algorithm utilized in this study..

After the image reconstruction process, the PET images are displayed on workstations so that physicians can evaluate and diagnose patients’ tumors based on $^{18}$F-FDG concentration. The whole process of PET imaging, including data acquisition, data storage and image reconstruction and display, is summarized in figure 1.6.

Figure 1.6: The process of PET imaging
1.3 PET/CT Multi-modality Imaging

Although PET imaging has great advantages as a functional imaging modality, it has limitations especially when dealing with acquisition related to anatomy such as lesion localization and tumor volume measurement. This limitation is due to its relatively low image resolution and corresponding high image noise level when compared to other anatomical imaging modalities such as CT and MRI. In this regard, functional images provided by PET and anatomical images provided by CT or MRI are usually presented together to facilitate both diagnosis and treatment planning.

Figure 1.7: Images generated in a PET/CT for the same patient. (a) CT, (b) PET, (c) Fused PET/CT.
Figure 1.7 shows an example of the PET/CT multi-modality imaging, where the PET image, CT image and fused PET/CT image are all displayed to provide both functional and anatomical information. The assumption in this evaluation is that the PET image is properly aligned with the CT image, thereby a lesion identified on the PET image can be accurately localized on the CT image. However, if the patient needs to be transported between different scanners, a change in the external pose as well as internal organ displacement could occur between the two imaging procedures. In this regard, an extra image registration process is often required to align the images acquired from different imaging sessions with each other (20). This adds to the complexity of the imaging protocol and also reduces the reliability of the overall approach.

To solve this difficulty, the PET/CT scanner has been introduced as an alternative to the dedicated PET scanner. In current PET/CT scanner implementations, the PET scanner is integrated with a multi-slice CT scanner. Consequently, the patient can receive both PET and CT scan within the same imaging session without any transportation between different scanners (figure 1.8). This minimizes patient motion between the PET and CT scans, and facilitates better co-registration between the acquired PET and CT images. In addition, the CT image acquired in a PET/CT imaging session can also be used to correct the PET data for attenuation (21).

Nowadays, individual PET scanners are rarely made by major medical imaging equipment manufacturers, while integrated PET/CT scanners are usually supplied. The success of PET/CT multi-modality scanners has motivated the exploration of other integrated imaging techniques, such as the single photon emission computed tomography SPECT/CT imaging (22) and PET/MRI imaging (23).
1.4 PET Detector Material

The detector material used in a PET scanner is an important factor in determining its sensitivity and performance. Because of the relatively high energy of the 511 keV annihilation photons, PET scanners use dense high-Z scintillation detectors arranged in rings around the scanned object (24,25). These systems not only provide high detection
efficiency but they allow the simultaneous collection of data for all projection angles with a completely stationary set of detectors.

Current PET scanners utilize scintillation crystals coupled to photomultiplier tubes (PMTs) as detectors (26,27). The signals from the PMTs are processed using pulse mode (the signals from each interaction are processed separately from those of other interactions) to create signals that identifying the position, deposited energy, and time of each interaction. Specifically, the energy signal is used for energy discrimination to reduce mispositioned events due to scatter, whereas the time signal is used for coincidence detection.

In early PET scanners, each scintillation crystal was coupled to a single PMT, which became increasingly costly and impractical to pack smaller and smaller PMTs into each detector ring. Modern designs couple larger crystals to more than one PMT (figure 1.9). The relative magnitudes of the PMT signals coupled to a single crystal are used to determine the position of the interaction in the crystal, as in a scintillation camera (28).

Figure 1.9: Design of PET detectors: scintillator coupled to PMTs
Each detector material exhibits a characteristic dead time that is related to the time required to process individual detected events. The pulses produced by a radiation detector have a finite time duration, so that if a second pulse occurs before the first has disappeared, the two pulses will overlap to form a single distorted pulse. In this regard, the second pulse does not produce a detectable output signal and is lost. Scintillators themselves are energy-sensitive detectors. The overlap mentioned above usually occurs in the pulse amplifier, causing baseline shift and pulse pileup. Shifted or overlapped pulse amplitudes may fall outside the selected analyzer window, thus resulting in a loss of valid events. Such losses are called dead time losses. The shorter the dead time, the smaller the dead time losses. Scintillation systems usually have dead times are the order of 0.1-1 μsec.

The scintillation material should emit light promptly to permit true coincident interactions to be distinguished from random coincidences and to minimize dead-time count losses at high interaction rates. To maximize counting efficiency, the detector material must have a high linear attenuation coefficient for 511 keV photons. Most PET systems today use crystals of bismuth germinate (Bi₄Ge₃O₁₂, abbreviated BGO) (29,30). The light output of BGO is only 12% to 14% of that of NaI(Tl), but its greater density and average atomic number give it a much higher efficiency in detecting 511 keV annihilation photons (31). Light is emitted rather slowly from BGO (decay constant of 300 nsec), which contributes to dead-time count losses and random coincidences at high interaction rates. Several new inorganic scintillators are being investigated as possible replacements for BGO. Three of the most promising of these are lutetium oxyorthosilicate (Lu₂SiO₅, abbreviated LSO) (32), lutetium yttrium orthosilicate (Lu₁.₈Y₀.₂SiO₅, abbreviated LYSO) (33,34), and gadolinium oxyorthosilicate (Gd₂SiO₅,
abbreviated GSO) (35). Their attenuation properties are nearly as favorable as those of BGO and their much faster light emission produces better performance at high interaction rates, especially in reducing dead-time effects and in discriminating between true and random coincidences. Their higher conversion efficiencies may produce improved intrinsic spatial resolution and scatter rejection. The properties of BGO, LSO(Ce), LYSO(Ce), and GSO(Ce) are contrasted with those of NaI(Tl) in table 1.1.

Table 1.1: Properties of several scintillators in PET scanner

<table>
<thead>
<tr>
<th>Material</th>
<th>Density</th>
<th>Atomic Number (Z)</th>
<th>Attenuation coefficient 511 keV (cm⁻¹)</th>
<th>Photo Fraction (%)</th>
<th>Light Output (photons/MeV)</th>
<th>Decay Time (nsec)</th>
<th>λ (nm)</th>
<th>Energy Resolution (% FWHM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BGO</td>
<td>7.1</td>
<td>75</td>
<td>0.95</td>
<td>40</td>
<td>9000</td>
<td>300</td>
<td>480</td>
<td>12</td>
</tr>
<tr>
<td>GSO</td>
<td>6.7</td>
<td>59</td>
<td>0.70</td>
<td>25</td>
<td>8000</td>
<td>60</td>
<td>440</td>
<td>9</td>
</tr>
<tr>
<td>LSO</td>
<td>7.4</td>
<td>66</td>
<td>0.88</td>
<td>32</td>
<td>30000</td>
<td>40</td>
<td>420</td>
<td>10</td>
</tr>
<tr>
<td>LYSO</td>
<td>7.1</td>
<td>65</td>
<td>0.83</td>
<td>30</td>
<td>29000</td>
<td>42</td>
<td>420</td>
<td>10</td>
</tr>
<tr>
<td>NaI(Tl)</td>
<td>3.7</td>
<td>51</td>
<td>0.34</td>
<td>17</td>
<td>41000</td>
<td>230</td>
<td>410</td>
<td>8</td>
</tr>
</tbody>
</table>

* Data come from (36,37)
1.5 PET Counting Efficiency

Although PET imaging has been widely used for tumor diagnosis and staging, this imaging modality suffers from a relatively low image quality with respect to other modalities such as CT (figure 1.1). The low image quality in PET image is mainly due to the high noise content, which arises from the relatively low counting efficiency of the scanner as well as the acquisition of scatter and random coincidences during the imaging process.

![Figure 1.10: Three kinds of coincidences: (a) True, (b) Scatter and (c) Random](image)

Scatter

When two single events happen within the duration of the coincidence window of the PET scanner, they are recorded as a “coincidence”. Figure 1.10 illustrates three kinds of coincidence events that PET scanners accept: true events, scatter events, and random events. Scatter coincidences occur when one or both of the photons from an annihilation event outside the sensitive volume for true coincidence events undergoes scattering and is
detected in a detector instead of the one that would be appropriate for a true coincidence event (figure 1.10(b)). The fraction of scatter coincidences is dependent on the total amount of material that is scattering and therefore is less in head with respect to body part. In clinical studies, the scatter-to-true coincidence ratio ranges from 0.2 to 0.5 for brain imaging and from 0.4 to 2 for abdominal imaging. Scatter coincidences provide false localization of the annihilation, and lead to a broad distribution of mispositioned events. Since scatter coincidences are real coincidences, reducing the activity administered to the patient, reducing the time window, or using a scintillator with faster light emission does not reduce the scatter coincidence fraction. The energy discrimination window of the PET scanner reject some events that the deposited energy differs significantly from 511 keV, thus reduce the effect of scatter coincidences (38-40). However, some annihilation photons that are not scattering by patient interact with the detectors by Compton scattering, depositing less energy than 511 keV. An energy discrimination window that encompasses only the photopeak rejects these valid interactions as well as photons that have scattered in the patient. Moreover, the relatively low conversion efficiency produces poor energy resolution, limiting the ability of energy discrimination to reject scatter. Generally speaking, there are two main approaches used for scatter correction in PET currently. The first approach uses information from the original scatter-contaminated image and transmission image to derive the correction (41,42). The transmission image reflects the attenuation coefficient of the tissue. At 511 keV, virtually all attenuation is due to Compton scatter. Using these two images and computer modeling with some simplifying assumptions, it is possible to derive an estimate of the distribution of scattered events and their contribution to individual profiles. The estimated contribution
of scattered radiation then is subtracted from the total projections and the reconstruction is repeated with the scatter-corrected data. This method works well when all the sources of radioactivity that could lead to scatter are contained within the FOV of the scanner. When large amounts of activity lie just outside the FOV of the scanner, problems can arise. Also this approach is that it is computationally intensive. A second method for scatter correction is based on an examination of projection profiles immediately outside the object \((43,44)\). Based on the premise that scatter is a low frequency phenomenon with little structure, data from the tails of the projections can be extrapolated by simple smoothly varying functions across the entire projection. Both Gaussian and cosine functions can be used for this purpose. The extrapolated scatter distribution then is subtracted from the projection profiles prior to image reconstruction. This method is rapid, and it accounts for scatter from radioactivity outside the FOV because it involves a direct measurement of scatter levels. However, it can only approximate the true scatter distribution and, in situations where the scatter distribution is complex, or when the object fills the whole FOV with no portion of the profile to examine outside the object, the technique may result in significant errors. These can range from a few percent for brain imaging to tens of percent at the heart-lung interface. In summary, scatter correction is very difficult and upon searching the current literature we find that it still is.

**Random**

Random coincidences occur when annihilation photons from two different and unrelated positron annihilation events are detected in two different detectors, within the coincidence timing window, and recorded as a single coincidence event (figure 1.10(c)).
In actual PET scanners, the ratio of random-to-true coincidence counting rates typically ranges from about 0.1 to 0.2 for brain imaging to greater than 1 for applications where large amounts of activity may be nearby, but outside the true coincidence volume of the scanner. Random coincidences actually add a relatively uniform background on the reconstructed image, suppressing contrast and distorting the relationship between image intensity and the actual amount of activity in the image. One approach to correct for random coincidences is the delayed window method (45,46). An estimation of the random coincidence rate is first obtained by delaying the coincidence timing window by a time that is much greater than its width. For example, with a timing window of 12 nanoseconds, the delayed window can be 64 nanoseconds. With this amount of time delay, only events that have arrival times separated between 64 and 76 nanoseconds are accepted. Therefore no true or scattered prompt coincidences will be detected in the delayed window. However, the rate of random coincidences will be the same in the delayed and undelayed windows because the rate at which uncorrelated photons strike the detector is the same for both windows. In this regard, the delayed window approach provides an estimation of the number of random coincidence events. This number is then subtracted from the total number of coincidence events for the detector pair. The other approach for correcting random coincidences is the singles rate method (47). The rate of random coincidences between any pair of detectors is calculated as:

\[ R_{\text{random}} = 2\tau S_1 S_2 \]  

(1.7)

where \( \tau \) is the coincidence time window, \( S_1 \) and \( S_2 \) are the actual count rates of the detectors, which are often called singles rates. The time window is the time interval following an interaction in a single detector in which an interaction in the other detector
is considered to be a coincidence. However, there is a limit of the smallest extent the time window can be. If the time window is set too short, some true coincidences are also rejected because of imprecision in the interaction timing. Scintillation materials that are able to emit light fast permit the use of shorter time windows and therefore can better discriminate between true and random coincidences. The number of random coincidences calculated by equation 1.7 is then subtracted from the number of true plus random coincidences. However, even if corrections are made, random coincidences could still cause an increase in the statistical noise level of the image.

**Noise equivalent count rate (NECR)**

One method to assess the image quality in PET imaging is to calculate the noise equivalent count rate (NECR) in the resultant image. This metric has been suggested as a good indicator of image quality since it takes into account the effects of scatter, random and true coincidences in its evaluation (48-50). NECR was defined by Strother et al. (48) as:

$$\text{NECR} = \frac{T^2}{T + S + kR}$$

(1.8)

where $T$, $S$ and $R$ are the true, scatter and random count rates, respectively. Factor $k$ is defined as 1 or 2 depending on the randoms correction method. The delayed window correction method makes $k$ equal to 2, whereas the singles rate correction method makes $k$ equal to 1. According to the definition of NECR and equation 1.8, all factors that affect the relative counting rate of true, scatter and random coincidences can finally impact NECR response. In this regard, NECR is affected by factors such as the injected dose of radioactive materials to the patient, scan time post-injection, and scanner type, etc.
1.6 PET/CT Image Visualization

The display of PET/CT images can be manipulated in a number of ways to aid in interpretation. This includes changing from a linear gray scale to a color scale or to a nonlinear gray scale like logarithmic scale. One of the most commonly used methods is to change the range of pixel values displayed, which is known as changing window and level (51). The definition of window and level are shown in figure 1.11, whereby level designates the center of the range of values mapped to grayscale and window designates the extent of the range to either side of the level. Therefore, the range mapped is (level-window/2) to (level+window/2). For a positive window value, regions less than (level-window/2) are clamped to black and regions greater than (level+window/2) are clamped to white. Regions at level are 50% gray. Generally speaking, if greater contrast is desired in one region of an image, the full brightness range of the display device can be used to display only the range of pixel values found within that region. This increases the

![Figure 1.11: Window and level](image-url)
displayed contrast in the selected area, but other parts of the image may have diminished contrast as a result (i.e., the counts per pixel may be beyond the upper or lower range of the selected gray-scale window). Figure 1.12 shows several commonly used window and level values in displaying CT image. Figure 1.12 (a) is the original image with no correction for window and level, (b) is a standard setting on workstation, (c) is the ‘Lung’ preset level showing details in lung tissue, and (d) is the ‘Bone’ setting displaying details in bone structure.

Figure 1.11: Four different window and level settings for CT images
Tomographic nuclear medicine data that consists of a 3-D volume can be displayed in three conventional views: transaxial, coronal and sagittal (52), as shown in figure 1.13. Often it is useful to display all three views simultaneously on the screen. Typically, a point within the three orthogonal images that pass through that point are displayed. As the cursor is moved, the transaxial, coronal, and sagittal images are updated. This is an efficient way of navigating through a large 3-D dataset. The dataset also can be resliced at an arbitrary orientation to provide oblique views. This is useful for objects whose line of symmetry does not fall naturally along one of the perpendicular axes of the 3-D volume.

(a) (b) (c)

Figure 1.13: Three views of PET image: (a) coronal; (b) transaxial and (c) sagittal
1.7 PET Image Quantification

As previously stated, an important additional advantage of PET imaging is its ability to quantify the amount of radioactivity taken up. This radioactivity value is directly related to the extent of malignancy of the tumor. The direct unit of the pixels in a reconstructed PET image is Bq/cc, however, this value can vary with patient weight, injected dose, scan time post injection, etc. One approach to standardize this value to a more universal indicator of radio uptake is to calculate the Standardized Uptake Value (SUV) (53):

$$SUV = \frac{\text{Uptake Value}}{\text{Injected Dose / Patient Weight}}$$  \hspace{1cm} (1.9)

where uptake value is the real pixel value from the reconstructed image, in a unit of Bq/ml; injected dose has the unit of Bq, and patient weight calculates as gram. Therefore, SUV is often in the unit of g/ml. SUV is a universal quantity that can help to distinguish between benign and malignant lesions. For example, an SUV below 2.5 determines a benign tissue, SUV between 2.5 and 4 is indeterminate, and 4 and above SUV is signal of malignant lesions.

1.8 Forward to the Thesis

This thesis composed of two main topics. Chapter 2 mainly deals with the PET/CT image visualization. One drawback in current PET/CT scanners is that it cannot acquire whole-body scan in a single acquisition but rather has to divide it into multiple sections due to a limitation in the extent of bed travel. Chapter 2 focuses on developing a software tool that can display multiple PET segments as a single scan to improve the
interpretation of these studies. It leads to more efficient readings of patient images since one image rather than two needs to be reviewed. Chapter 3 investigates PET image qualities using different values for imaging parameters. The aim of this project is to determine which imaging parameters strongly impact PET image quality. Results of this section provide a preliminary guide as how to enhance PET image quality, as well as how image quality might be equalized among different patient and imaging environments. Moreover, the results of this work can be used as a guide to improve protocol design in an effort to generate an optimal PET image quality. Possible further extensions are discussed in chapter 4.
Chapter 2

A Software Tool for Stitching Two PET/CT Body Images into a Single Image

2.1 Background and Motivation

In PET/CT imaging, some patients require the acquisition protocol of the whole body scan, which means from head to toe. For example, whole body protocol and melanoma protocol both require a whole body patient scan. Among them, patients require whole body protocols account for about 4% of the total patients who have PET/CT scans in The University of Texas MD Anderson Cancer Center. This number is 20% for melanoma patients. Therefore, there are significant numbers of patients who require whole body PET/CT scans. However currently, a majority of PET/CT scanners cannot support a single whole body scan due to a limit on the extent of their bed travel. PET/CT scanners available at The University of Texas MD Anderson Cancer Center are GE Discovery STE and GE Discovery RX PET/CT scanners (62,63). Both scanners have an axial field of view (FOV) covers 15.7 cm and the maximum FOV number of 10. Therefore, they both have a limit bed travel length around 150cm. In such cases, a whole body PET/CT scan has to be divided into two segments, an upper body segment and a lower body segment. It means that a patient should first lie on the scanner couch with a head-in protocol and scan the upper body part, and then lie on the scanner couch with head-out protocol to scan the lower body part, as illustrated in the cartoon of figure 2.1. The patient who has a whole body PET/CT scan, likewise has two separate images (figure 2.2). It is difficult to view this images as a single whole body scan.
Figure 2.1: (a) Upper body segment and (b) Lower body segment

Figure 2.2: (a) Upper body image and (b) Lower body image
Our objective is to develop a software tool that can stitch the two body images into a single whole body image, thus facilitating interpretation. There are several advantages to this technique. First, it improves the efficiency of reading PET/CT scans, since only a single image set needs to be loaded rather than two. Secondly, the stitched study facilitates the comparison of a patient’s current and prior scans in a single session, rather than having to compare two separate paired segments. Finally, a patient’s whole body image can be rendered, thereby providing the radiologist with the ability to generate whole body images or movies for educational and demonstration purposes.

2.2 Mathematical Model

According to current PET/CT imaging protocols, images of upper part and lower part have an overlap region to eliminate any possible anatomical truncation. This overlap section facilitates the stitching of the two body segments to one another, shown in figure 2.3. The bisection of the two body segments usually occurs at the level of the lower

Figure 2.3: Stitch two body images into a single image according to overlap region
extremities (legs) and the stitching was performed according to the information available in this region of leg overlap. A preliminary assumption is that patient's leg is a rigid object and that movement of a rigid object is determined by the movement of three points within that object. Since the three points may not lie on a line, three independent markers are needed within the overlap region for the stitching.

![Figure 2.4: Illustration of stitching method](image)

Our mathematical model for stitching is shown in figure 2.4, where the upper segment (left in figure) contains three fiducial markers (A1, B1, C1) placed within the overlap region of the two segments. Similarly, the lower segment (right in figure) contains the same three markers (A2, B2, C2) in the overlap region. Arbitrary points X and Y are also shown in the upper and lower segments relative to the respective markers. In the lower segment, the position of the patient's leg may be different than in the upper segment thus displacing the markers (new position A2, B2, C2). Knowing the voxel positions of X, (A1, B1, C1) and (A2, B2, C2), one can solve for the voxel position of Y based on the assumption that the leg is a rigid body and the relative position of the
fiducial markers remains unchanged. Thus, three equations can be written according to
the geometric relationships:

\[
\begin{align*}
(A_1 - B_1) \cdot (X - B_1) &= (A_2 - B_2) \cdot (Y - B_2) \\
(C_1 - B_1) \cdot (X - B_1) &= (C_2 - B_2) \cdot (Y - B_2) \\
(A_1 - B_1) \times (C_1 - B_1) \cdot (X - B_1) &= (A_2 - B_2) \times (C_2 - B_2) \cdot (Y - B_2)
\end{align*}
\] (2.1)

Here, each point is represented by a vector that has three coordinates. The first equation
states that the relative positional relationships among A1, B1, and X remain the same as
the relative positions among A2, B2, and Y. Similarly, the second equation states that the
relative positions among C1, B1, and X remain the same as the relative positions among
C2, B2, and Y. The third equation shows the volume of the pyramid A1, B1, C1, and X is
equal to the volume of the pyramid A2, B2, C2, and Y. With this set of three equations in
three unknowns (the coordinates of vector Y), equation 2.1 can be rewritten in a matrix
vector product format as equation 2.2. Carefully examining the first part of the r.h.s of
equation 2.2, we can see that it is a 3 by 3 matrix. If A2, B2, and C2 happen to lie along
the same line, the module of this matrix is 0, which means the equation has infinite
solutions. Therefore, an important premise is that the three markers can never lie on the
same line as indicated by the inequality given in equation 2.3. Therefore, (Y - B_2) exists
and is unique; thereby Y exists and is unique. Now the value at point X has been
successfully obtained in figure 2.4. The values of other points can be obtained in an
analogous manner.

\[
\begin{bmatrix}
(A_1 - B_1) \cdot (X - B_1) \\
(C_1 - B_1) \cdot (X - B_1) \\
(A_1 - B_1) \times (C_1 - B_1) \cdot (X - B_1)
\end{bmatrix}
= \begin{bmatrix}
(A_2 - B_2)^T \\
(C_2 - B_2)^T \\
(A_2 - B_2)^T \times (C_2 - B_2)^T
\end{bmatrix}
\cdot (Y - B_2)
\] (2.2)
In selecting the locations of the fiducial markers, different approaches can be taken. Since our patient have both a PET image and a CT image taken, we may select marker locations according to the leg structure displayed in the CT image. However, it is not accurate since legs structure looks similar. We can also select based on PET images, but PET images are too noisy. The preferred method in placing fiducial markers is to attach radio-opaque markers (BB) in the overlap region of each leg (3 BBs for each leg). The BBs positions were placed in the overlap section of both CT segments.

One reason to attach BBs to patient body is that BBs pixel value in the CT image is significantly higher than the pixel values of surrounding tissues. The pixel value in the CT image, $CT(x,y)$, is determined by the following expression:

$$CT(x,y) = 1000 \frac{\mu(x,y) - \mu_{\text{water}}}{\mu_{\text{water}}}$$

(2.4)

where $\mu(x,y)$ is the attenuation coefficient of the $(x,y)$ pixel, $\mu_{\text{water}}$ is the attenuation coefficient of water, and $CT(x,y)$ is the CT number (or Hounsfield unit) that ends up in the final clinical CT image. The value of $\mu_{\text{water}}$ is about 0.195 for the x-ray beam energies typically used in CT scanning. This normalization results in CT numbers ranging from about -1000 to +3000, where -1000 corresponds to air, soft tissues range from -300 to -100, water is 0, and dense bone and areas filled with contrast agent range up to +3000. In this regard, the pixel value for BBs is above 3000 and is easily calculated from the CT image (figure 2.5). Hence the stitching operation is performed using information from
BBs positions in two CT image segments. PET images are stitched afterwards by transferring BBs position information from the CT to PET images.

![Figure 2.5: A typical CT image in transaxial FOV showing two legs with a BB](image)

### 2.3 Computer Simulation

A computer simulation was performed based on the above mathematical model to help establish its validity. In addition, the accuracy of both the structure and image pixel value were examined based on this model.

An original image was generated using MATLAB (figure 2.6). This image represents ‘a true whole body image’. Three dots have been placed in the top semicircular part of the image (see arrows). These are the three markers needed in the stitching process. Two different sizes of spheres are placed in the lower part of figure 2.6. These represent tumors of 25mm and 10mm in diameter, respectively. These two sizes of
spheres can facilitate the comparison of the pixel values in each sphere in the original and stitched images. There are three letters ‘PET’ placed at the bottom of figure 2.6, to evaluate the precision of the structure in the stitched image. The image background intensity was set to a value of 5, whereas the value within the three markers was set at 20. The two sizes of tumors were assigned an intensity value of 10, while the three letters ‘PET’ had a value of 15. Finally, Poisson noise was added to simulate a more realistic (noisy) imaging environment.

Figure 2.6: Simulated original image

Based on the original image in figure 2.6, two image segments were further generated: an upper segment and a lower segment, as shown in figure 2.7. The three markers were shown in the overlap region of both segments. In the lower segment, the image was rotated by 40 degrees clockwise to simulate possible patient movement between the two segments.

A program implementing the stitching algorithm discussed earlier (section 2.2) was generated in MATLAB and applied to the two segments in figure 2.7. The stitched image is shown in figure 2.8, where the part above the yellow line was obtained from the
figure 2.7 (a), the upper segment; and the part below the yellow line was stitched from figure 2.7 (b), the lower segment.

Figure 2.7: (a) Upper segment and (b) lower segment

Figure 2.8: Stitched image from figure 2.7
Visualization of figures 2.6 and 2.8 shows that the original and stitched images look very similar. To further verify the accuracy of the pixel value, a line profile was plotted along the large and small spheres in both figures 2.6 and 2.8 and the results are shown in figure 2.9. This figure shows that the original and stitched image pixel values agree very well. Evaluation of structure accuracy was performed by comparing the relative positions of the three letters ‘PET’ in both original (figure 2.6) and stitched (figure 2.8) images. The results are shown in figure 2.10, where the positions of the structure between original and stitched image are within 1 pixel, which equivalent to 2 mm in the actual clinical situation.

In summary, the results of our computer simulations verified the the stitching approaches derived from the mathematical model. They also provided an evaluation of the accuracy of both the structure and the pixel value via a quantitative comparison of the original and stitched images in the presence of Poisson noise (figures 2.9 and 2.10).

![Figure 2.9: Line profiles of the (a) large and (b) small spheres in both original (figure 2.6) and stitched (figure 2.8) image](image-url)
2.4 Phantom Study

Our mathematical model and computer simulations both showed encouraging results regarding the image stitching method. However, they are based on ideal conditions and hence cannot represent the actual clinical situation. In this regard, a phantom study represents a closer approximation to the actual clinical environment. A phantom is a physical model of the imaging problem, often consisting of a plastic or glass container with precisely positioned interior structures (figure 2.11). Elements of the

Figure 2.11: (a) IEC phantom; (b) ACR phantom
phantom can be injected with radioactive materials that serve as radioactive sources within the phantom. The phantom can then be placed on the PET/CT scanner couch to simulate a patient. Data is taken with the PET/CT scanner.

There are three objectives for this phantom study. The first objective is to validate the decay correction between two segments. The radioactive material injected to the patients decays according to the fundamental decay equation:

$$A_t = A_0 e^{-\lambda t}$$  \hspace{1cm} (2.4)

where $A_0$ is the initial activity, $A_t$ is the activity at time $t$, $\lambda$ is decay constant and it is related with the material's physical half-life $T_{1/2}$ by

$$\lambda = \frac{\ln 2}{T_{1/2}} = \frac{0.693}{T_{1/2}}$$  \hspace{1cm} (2.5)

PET scans often take several or even tens of minutes, hence material decay occurs simultaneously during the scan. PET/CT scanners have the ability to correct for the decay of each scan to the beginning time of that scan. However, for patients whose scan is divided into an upper segment and a lower segment, the decay correction of the scanner corrects each segment to its own beginning time. Consequently, activity concentration at the initial time will differ in the two scans, and this can cause activity value error in the stitched image. The solution to this problem is to correct the decay of the lower segment to the beginning time activity concentration of the upper scan before stitching them into a whole body image. A MATLAB program was written for this evaluation. The accuracy of this correction method was then investigated in our phantom studies where the activity of the species injected into the phantom is known.
The second objective of the phantom study is to simulate the patient’s two legs. Bisection of the upper segment and the lower segment usually occurs at the level of the lower extremities. Therefore, stitching is concerned with attaching the lower legs to their upper equivalents. Since between upper and lower scans, the patient may have moved their legs in a different way, splitting the lower segment into two leg parts is essential for accurate stitching. Consequently, the program should have the ability to first split the two legs, followed by a second stage of leg by leg stitching.

The final objective of the phantom study is concerned with adapting the stitched images to Digital Imaging and Communications in Medicine (DICOM) format, which facilitates the display of the images by current GE or Siemens PET/CT workstations. A single DICOM file contains both a header (which stores information about the patient's name, the type of scan, image dimensions, etc), as well as the image data (which can contain information in three dimensions) so that the image can never be separated from the header information by mistake. Since a header contains all the information regarding each scan, some parameters in the DICOM header might require editing so that the stitched image might appear as a single scan rather than two separate scans.

It is essential to choose a proper phantom for meeting the requirements of all three objectives. Generally speaking, a phantom needs to be sealed, and it must be able to represent both patient legs. The IEC and ACR phantoms shown in figure 2.11 are too large for this study, since two such phantoms cannot be placed in parallel on the scanner couch. Finally, it was decided to use two coke bottles to represent the legs (figure 2.12). Each bottle had a cross-section diameter of about 10cm so that the bottles could easily be placed in parallel on the scanner couch (width 40cm).
Three BBs were attached on each bottle at the planned overlap section before two scans. The activity concentration of the material filling each bottle was 0.09uCi/cc. The bottles underwent a 3 minute scan, which represented the upper segment scan. After the first scan, the position of the bottles was changed by rotating and shifting the bottles. A wait period of 30 minutes followed after which a second scan of 3 minutes duration was taken. With this wait period, there was a significant decay in activity concentration, since the half life of the radioactive tracer $^{18}$F is 109 minutes.

Figure 2.12: Coke phantom

Figure 2.13 shows the original PET and CT images of the two segments. A clear shift in position was imposed between the two scans. The flow chart of the stitching program is shown in figure 2.14. The program first splits the two bottles in the lower segment image, and then stitches each bottle respectively to its upper equivalent according to the BBs positions. Figure 2.15 shows the final stitched PET and CT images of the bottles.
Figure 2.13: (a) CT images of the two scans; (b) PET images of the two scans

Figure 2.14: Flow chart of the stitch program: First split the bottles and then stitch.
Figure 2.15: Stitched (a) CT and (b) PET images

Visual inspection of Figure 2.15 shows a quite accurate stitching in structure. A further investigation was conducted to evaluate whether the decay correction in the stitched PET image has been properly manipulated. Specifically, a line profile of activity was taken along each slice of the stitched PET image, where in each slice, the activity was the average of that from 50 randomly selected pixels. Figure 2.16 shows the result where the x axis is the slice number and the y axis is activity concentration in units of Bq/cc. The black line represents the actual injected activity concentration, and the slice numbers after 40 are stitched slices. Blue and red represent the left and right bottle, respectively. We can see that after decay correction, the activity variation of the stitched slices is within 5% of the true activity, which verifies that the decay correction was conducted properly.
A final challenge for the phantom study was to display the final stitched image in DICOM format on GE or Siemens PET/CT workstations. These workstations only accept DICOM format images, and hence a translation of each slice of the stitched image into a single DICOM image is essential. This simple translation however is more complicated than it seems. Specifically, a more comprehensive modification of the DICOM header is first necessary to help the workstations recognize the images as a single scan rather than two separate scans. After several experiments, we found it necessary to modify 5 distinct parameters in the DICOM header, before the resultant stitched DICOM images can be displayed properly. The parameters are:

- **SliceLocation**: which indicates the location of the current slice in the PET/CT scanner. Within a single scan, this parameter changes continuously from the first to last slice. However, a discontinuity is encountered between two different scans. Consequently, a change in the ‘SliceLocation’ of the lower segment is required to make it follow the trend in the upper segment.

![Figure 2.16: The activity concentration of each slice in the stitched PET](image)
• **InstanceNumber**: which shows the order of the current slice in the whole scan. Analogous to the change made for ‘SliceLocation’, the sequence of slice numbers of the second sequence must be brought into registry with that of the first segment.

• **ImageIndex**: a parameter whose order refers to either a head-in or head-out imaging protocol. If it changes from the first to last as ‘InstanceNumber’, it represents a head-out protocol. If it changes from the last to the first slice, it represents a head-in protocol. ‘ImageIndex’ also exhibits a discontinuity between two segments and registry between two segments should follow in a continuous manner.

• **NumberOfSlices**: which shows the total slice number in a single scan. This number has to be edited to the sum of the upper and lower segment slices.

• **RescaleSlope**: this scaling parameter is used for data compression, in that the real value is compressed into a 16 bit integer (range from 0 to 65535) after dividing it by this parameter. ‘RescaleSlope’ needs to be edited, because manual decay correction has been applied to the lower segment so that its real value has been changed.

### 2.5 Patient Studies

The above mathematical model, simulation and phantom studies all provided encouraging results. Hence, the approach was applied to data from patient studies.

Six whole body PET/CT scans were acquired on a GE DSTE or DRX PET/CT scanners in two body segments. Bisection of the two body segments all occurred at the level of the lower extremities (legs). An overlap region was selected to eliminate any possible anatomical truncation. Three BBs were attached to each leg in the overlap region of both body segments to facilitate this stitching. Our stitching program calculated the
relative positions of the BBs on the 2 segments of the CT image set and generated a rigid transformation that matched the BBs between the two segments and merged the two segments into a single whole body image. This process was facilitated by splitting the lower segment into two leg parts as discussed previously. The same transformation was then applied to the PET image set. Decay correction was applied to the second segment to compensate for the difference in scan time between the segments. A single DICOM whole body PET/CT image set was then generated and displayed for interpretation on GE and Siemens workstations.

PET images before and after stitching are shown in figure 2.17 for one patient. Fused PET/CT images of the same patient are shown in figure 2.18. Figure 2.18 (c) does

Figure 2.17: PET images of upper (a) and lower (b) segment of a patient; (c) stitched whole body PET image
not show the complete sagittal image of the patient (feet missing). The reason is that it is only one slice in sagittal view, and this slice is not an exact slice to show whole body. A change to another slice number could ensure the display of whole body.

Figure 2.18: PET/CT fused images of upper (a) and lower (b) segment of a patient; (c) stitched whole body PET/CT fused image

The results of the PET images of another patient (before and after image stitching) are shown in figure 2.19. The fused PET/CT images of this patient are shown in figure 2.20.
Figure 2.19: PET images of upper (a) and lower (b) segment of a patient; (c) stitched whole body PET image
Figure 2.20: PET/CT fused images of upper (a) and lower (b) segment of a patient; (c) stitched whole body PET/CT fused image

The patient figures shown in figure 2.17-2.20 were directly extracted from the GE advanced workstations, which also has the capability to generate a Maximum Intensity Projection (MIP). MIP is a computer visualization method for 3D data that projects in the visualization plane, those voxels with maximum intensity that fall in the way of parallel rays traced from the viewpoint to the plane of projection. To improve the sense of 3D, animations are often rendered using several MIP frames, wherein the viewpoint is changed slightly from one point to another, thus creating the illusion of rotation. This
visualization technique aids the viewer in finding the relative 3D positions of object components. Figure 2.21 shows 4 MIP views of the stitched PET image of a patient.

Figure 2.21: Four views from the MIP of a patient
2.6 Software Generation

Our stitching program has been tested and verified by the above mentioned simulation, phantom study and patient studies. However, at this point, it is a single program rather than a powerful software tool. To better facilitate its usage by physicians and technologists, generation of a user-friendly software is the final step in the design process. This was accomplished by designing a graphical user interface (GUI), which allows program users to interact with programs in a more straightforward manner, particularly in using images rather than simply typing text commands. A GUI utilizes graphical icons and visual indicators rather than text-based interfaces, and actions are usually implemented using direct manipulation of graphical elements. Ideally, this software should be contained in a universally executable file that has the ability to run on any computer.

![Flow chart of the stitching software](image)

**Figure 2.22: Flow chart of the stitching software**
The flow chart of the software progress is shown in figure 2.22. There are a total of 5 steps in the stitching process, whereby decay correction and DICOM header modification are embedded in steps 3 and 4 respectively.

A prototype of this software tool is currently available and its interface is shown in figure 2.23. There are three buttons on the left labeled ‘Read DICOM’, ‘Stitch’, and ‘Write DICOM’. As the user approaches the GUI, he should first load the original two segments of patient PET/CT data to the software by clicking ‘Read DICOM’. The browse window pops up for the user to choose a single patient folder, as shown in figure 2.24. A waiting bar lets the user track how much of the patient data has been loaded (figure 2.25). Upon successfully loading the data, the user has to make a decision to save the loaded patient data or directly go to the stitching process. When the stitching process begins, a pop-up window tells the user to select 6 BBs in the CT image (figure 2.26). The user can scroll the slider bar to browse each slice from either of the three points of view (Transaxial, Coronal, Sagittal) from the three buttons, respectively (on the right), until a BB is found (figure 2.27). Window and level adjustment on the right of the interface can be used to change the relative brightness and contrast of the CT image to facilitate the search for BBs. To accurately select the BB, the user can employ ‘zoom in’ to enlarge the area of the image containing the BB (figure 2.28). A simple click on the BB by the mouse stores the BB’s position and the textbox at the bottom right shows how many BBs have been selected. Stitching begins after all the BBs have been selected and a waiting bar shows its progress (figure 2.29). The stitched DICOM image set begins to write out after stitching is finished (figure 2.30), and the user can browse a position to save this image set, thus completing the task.
GUI software for PET/CT image stitching

Read DICOM

Stitch

Write DICOM

Figure 2.23: Software interface

Figure 2.24: Browse patient data
GUI software for PET/CT image stitching

Figure 2.25: Loading patient images

Figure 2.26: Select BBs
GUI software for PET/CT image stitching

**Figure 2.27:** Scroll the image to find BBs

**Figure 2.28:** Zoom in the position around the BB
GUI software for PET/CT image stitching

Axial View, Slice 38

Read DICOM

Stitch

Write DICOM

Figure 2.29: The stitching progress

Axial
Coronal
Sagittal

Window 2000
Level 0

Select BB
have selected 6 BBs

420 421 422 423 424 425 426 427 428 429

Figure 2.30: The stitched image is generated
We have demonstrated the software tool’s ability to merge the two body segments and output the images in a format that is compatible with our current PET/CT display workstations. Two executable versions of this software tool have been generated for Windows (*.exe) and Linux (*.bin) operating systems, respectively. This software tool continues to be evaluated by our radiologists to assess its impact on the efficiency of image interpretation. The initial results on the 6 patients tested have been encouraging.

2.7 Possible Improvement

The ability of the software tool to stitch two body segments into a single whole body image set has been demonstrated in our patient studies. However, there are still some further discussions and possible improvements that can be envisioned.

The current stitching algorithm in this software is based on solving the matrix equation in equation 2.2. To find the value of a voxel \( \overline{X} \), we have to solve equation 2.2 to find the position of the corresponding voxel \( \overline{Y} \). However, although the three coordinates of \( \overline{X} \) are integer numbers, the corresponding coordinates of \( \overline{Y} \) are probably not. Consequently, the value at position \( \overline{Y} \) needs to be interpolated from the surrounding integer voxels. Candidate interpolation methods are nearest interpolation, linear interpolation, spline interpolation and cubic interpolation. Our software uses linear interpolation to balance image quality and operating speed. One significant effect of using interpolation is that it results in image blurring, as shown in figure 2.15(b). A horizontal boundary can be clearly seen in figure 2.15(b) below which the image is more blurred than the top part. This blurring effect is equivalent to applying a low pass filter to the original image data. Although blurring is unavoidable in interpolation, there are other
techniques that can be used to equalize the extent of blurring in both segments. This equalization is facilitated by the fact that all clinical PET images are subjected to post-filtering after reconstruction. In this regard, we may consider applying post-filtering only to the upper segment, leaving the lower segment image as it is. During the stitching process, low pass filtering was in effect added to the lower segment image via the interpolation process. Therefore, both segments go through only one blurring process. Adopting this approach tends to equalize the blurring effect in the stitched image, thus increasing image quality.

Besides the blurring caused by interpolation, pixel value is also impacted by this approach. The maximum SUV is often used as an indicator of the tumor diagnosis, whereby SUV > 4g/ml is usually be characterized as a malignant tumor. Blurring has the effect of smoothing the image and hence decreases the maximum SUV of a certain region. Consequently, there may be some voxels that changed value from greater than 4g/ml to less than 4g/ml. If this is the case, a potentially false diagnosis might occur. Thus, we propose further evaluations of how blurring affects the SUV value.

The current software requires the user to manually select BBs. Recalling that 6 BBs are attached to the patient legs and the BBs appear in both the upper and lower segments, one has to click 12 times to select all the BBs in two segments. This approach can be made more convenient, if software can be designed to automatically distinguish BBs in the CT image. The main difficulty involved in this automation process, is that some patients have metals implanted in their legs, such as the patient shown in figure 2.20, where one can see that the patient’s knees have a very high tissue density. Actually there are metals implanted there. The value of the BBs and the metal are relatively the
same in the CT image so that using a simple threshold to identify BB would include the metal as well. However, there are at least two techniques that could lead to automatic selection. First solution is to select BB base on the size of the area. BB and implanted metal have different sizes although they appear to have the same value. The BB only shows in several continuous pixels, while the metal occupies a much larger area. The factor of size may help to segment BB from the implanted metal. A second solution is to select based on a specific position of the body. BBs are attached to the patient skin whereas metal is implanted into the patient body. Thus, one can search only on the surface of the patient leg, where the boundary between the patient and air may help automatically select BBs rather than other objects.

A more advanced approach with respect to automatic selection is to employ image registration, which would not use BBs, and yet would allow stitching of the segments. The 2-D image registration is common in camera technology. Many brands of camera have the ability to ‘stitch’ several pictures with overlap regions. However, the PET/CT images are 3-D images and 3-D registration is far more complicated than the 2-D registration especially for the low resolution PET image. Therefore, deeper investigation of this subject is required for development of an automatic image registration technique for use in stitching PET/CT images.

This software tool is primarily developed for nuclear medicine PET/CT imaging. However, other imaging modalities such as single photon emission computed tomography / computed tomography (SPECT/CT), gamma camera planar imaging, CT, and magnetic resonance imaging (MRI) may encounter the same problem. A reasonable modification of this software may widen its application to other imaging modalities.
Moreover, we can envision the development of a more general software that would be compatible for all types of imaging modalities in the future.

Finally, two versions of this software are available currently for the Windows and Linux operating systems, respectively. It is encouraging to consider generation of other versions that could serve other operating systems (e.g. Mac, Solaris).
Chapter 3

PET Image Quality Variance as described by NECR and noise for different Inject Dose, BMI and Scanner Type

Positron Emission Tomography (PET) imaging using fluorine-18 fluorodeoxyglucose ($^{18}$F-FDG) has been widely used for the diagnosis, staging and monitoring of patients with a wide variety of tumors (54). However, despite its widespread use, this imaging modality has been characterized by a relatively low image quality largely due to the high noise content in the resultant image. This noisy characteristic partially arises from the relatively low counting efficiency of the scanner as well as the acquisition of random and scatter coincidences during the imaging process. One method to assess the image quality in PET imaging is to calculate the corresponding noise equivalent count rate (NECR) in the reconstructed image. This metric has been suggested as a good indicator of image quality since it takes into account the effects of scatter, random and true coincidences for its calculation (48-50). Other parameters that affect the NECR and hence image quality include injected dose, scan time post-injection, patient weight and scanner design. These factors impact NECR through their influence on the measured randoms, trues and scatter events.

This chapter investigates how PET image quality is affected by different imaging parameters. One objective is to evaluate which of these factors has an impact on PET image quality and by how much. The results of this project will provide a preliminary guide as to how PET image quality might be improved or even equalized among different factors.
3.1 Overview of NECR studies in PET imaging

Several research groups have investigated the relationship between NECR and injected dose in an effort to improve PET image quality (55-57). The majority of these investigations however were based on phantom studies and suggested that the relationship between NECR and injected dose (derived from phantom data) can be extrapolated to real patients using different models. However, the main drawback of such an approach is that phantom data does not represent a true patient habitus. In this regard, the derived relationship between injected dose and NECR can not be extrapolated to patient studies without sustaining large errors. These drawbacks were further examined in a simulation study that compared the NECR of a NEMA NU 2-2001 count rate phantom to three anthropomorphic models that were derived from 3 different patients having 3 different weights (small, medium, large), while simulating different tissue activity concentration (57). The result of this study revealed a big difference in peak NECR between the NEMA phantom and the anthropomorphic models, demonstrating the limitation of using such a phantom to predict the NECR in patients.

More recently, real patient data rather than phantom studies were utilized to correlate image quality with different injected doses per unit weight (58-61). An optimal injected dose of 8 MBq/kg or greater was suggested (58), since 90% of patient images with this weight normalized injected dose were classified as having 'good' quality by 2 different human observers. This optimal injected dose, however, was shown by Watson et al., Lartizien et al. and Danna et al. to be wasteful for heavy patients (59-61). In these three papers, the optimal dose used to reach the peak NECR was found to be independent
of patient weight, thereby indicating that poorer image quality in heavier patients could not be overcome by increasing dose in proportion to patient weight. In all of these papers (59-61), the patients NECR curves were derived by extrapolating phantom data using different models. Data extrapolation was primarily used due to the difficulty in generating the true NECR curve for each patient since that would require injecting and imaging the patient multiple times, with different amounts of radiotracer activity concentration.

An opportunity presented itself when our clinic switched PET data acquisition mode from 2D to 3D, while gradually reducing the injected dose from an average of 629MBq for 2D to an average of 370MBq in 3D mode. Specifically, a population study could be conducted on the behavior of NECR as a function of patient BMI, injected dose and scanner type. Our objective was to investigate how NECR and noise change with different injected dose, BMI and scanner design, while relying on only patient studies and without any consideration of phantom data. We hypothesized that such a study should capture the true interrelationships between these factors without any modulating effects, and hence could be used to support or refute previously published results derived from phantom data. Our patient studies were selected from two different PET/CT scanner designs, one based on BGO detectors and the other on LYSO detectors. The setup and preparation of the patient studies is described in section 3.2 and their results are shown in section 3.3. Further considerations are discussed in section 3.4.
3.2 Materials and methods

PET/CT Scanners

A GE Discovery STE (DSTE) and a Discovery RX (DRX) PET/CT scanner (GE Healthcare, Waukesha, Wisconsin, USA) were used for the patient studies in this paper. The PET gantries of the two scanners consist of 24 rings of 560 and 630 detector crystals per ring, respectively. The detector material of the PET component in the DSTE scanner is BGO while in the DRX scanner, the detector is made of LYSO. In both scanners, the PET component has a trans-axial FOV of 70 cm and a 15.7 cm axial extent. The DSTE is composed of 70 detector blocks per ring and each consisting of a 6×8 detector elements. The DRX has the same design except each detector block is composed of a 6×9 detector elements. The DRX scanner can achieve an axial and trans-axial resolution of 4.8 mm and 5.1 mm (measured as full-width half maximum (FWHM)), respectively, while in the DSTE scanner these resolutions are 5.1 mm and 5.4 mm. The scanners have retractable septa and can operate in both 2-D and 3-D modes. The energy window is 425-650 keV in 3D mode for both scanners while the coincident window width is 9.6 and 5.8 ns for the DSTE and DRX respectively.

The CT component of the two PET/CT scanners has a 50 cm trans-axial FOV and can acquire images with slice thickness ranging between 1.25 and 20.0 mm. The tube current is variable between 10 and 440 mA, and the tube voltage is variable between 80 and 140 KVp, in increments of 20 kVp. The description and performance characteristics of the two PET/CT scanners have been published in (62) and (63). All acquired data were corrected for attenuation, random, scatter and dead time and reconstructed using the OSEM algorithm. The standard reconstruction protocol for DRX scanner is OSEM with 2
iterations and 21 subsets, whereas with the DSTE scanner, the standard protocol is OSEM with 2 iterations and 28 subsets.

**Patient Studies**

A total of 180 patients (90 male, 90 female, mean age 55±13 years) divided into 2 groups of 90 patients per scanner model were selected in this investigation. All patients had a 3D PET/CT scan at The University of Texas MD Anderson Cancer Center between December 2007 and February 2008. The 2 scanner models investigated were the GE DSTE and GE DRX. Each group of 90 patients were further divided into 9 subgroups according to 3 BMI ranges (20-25, 25-30, >30kg/m²) and 3 injected dose (ID) ranges (296-444, 444-555, >555MBq), which amounts to 8-12, 12-15, >15mCi, respectively. This gives a total of 10 patients in each BMI & ID subgroup. Each subgroup was matched for gender and age variance. Table 3.1 shows the patient demographics. None of the selected patients had a liver lesion.

<table>
<thead>
<tr>
<th>Demographic</th>
<th>DSTE</th>
<th>DRX</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Male (%)</td>
<td>45 (50)</td>
<td>45 (50)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.2±4.5</td>
<td>27.7±5.8</td>
</tr>
<tr>
<td>Lymphoma (%)</td>
<td>22 (24)</td>
<td>25 (28)</td>
</tr>
<tr>
<td>Lung cancer (%)</td>
<td>19 (21)</td>
<td>17 (19)</td>
</tr>
<tr>
<td>Breast cancer (%)</td>
<td>13 (14)</td>
<td>12 (13)</td>
</tr>
<tr>
<td>Melanoma (%)</td>
<td>4 (4)</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Other cancer (%)</td>
<td>32 (36)</td>
<td>28 (31)</td>
</tr>
</tbody>
</table>
All patients fasted for at least 4 hours prior to being injected with $^{18}$F-FDG. Imaging started 78±17 min post injection, during which the patients were allowed to lie comfortably on a reclining chair. For each patient, a whole-body PET scan following a CT scan was conducted while the CT data was used for attenuation correction. PET data were acquired in 3D mode, using a protocol of 3 minutes per bed position (1 patient with 2 min, 2 patients with 210 sec, and 7 patients with 4 min per bed position). After data acquisition, images were reconstructed using OSEM (DRX: 2 iterations, 21 subsets; DSTE: 2 iterations, 28 subsets) and a post-reconstruction filter (6 mm) was applied.

**Data Analysis**

Two parameters were calculated for each patient; the NECR of the bed position covering the patient liver and the noise content in a fixed size ROI drawn in the liver. The liver was used in both cases since it represents the largest organ that is characterized by a relatively high but uniform activity concentration. NECR was defined by Strother et al. (48) as:

$$NECR = \frac{T^2}{T + S + kR}$$  \hspace{1cm} (3.1)

where $T$, $S$ and $R$ are the true, scatter and random count rates, respectively. The factor $k$ equals to 1 or 2 depending on the randoms correction method. In this investigation $k$ was set to 1 since randoms were calculated based on singles measurement. The prompt rate defined as $P = T + S + R$ can be used to represent the denominator of equation (3.1). The directly measurable counting rate is $T + S (= P - R)$ and the scatter fraction (sf) is defined as:

$$sf = \frac{S}{S + T}$$  \hspace{1cm} (3.2)
Therefore, trues can be computed from \( T = (P - R)(1 - sf) \). Finally the equation of NECR can be rewritten as:

\[
NECR = \frac{(P - R)^2 \times (1 - sf)^2}{P}
\]  

(3.3)

where \( P, R \) and \( sf \) are the prompts rate, randoms rate and scatter fraction, respectively. All of the necessary parameters to calculate NECR in equation (3.3) are recorded in the patient’s raw data, which can be obtained from the scanner. Noise on the other hand, was determined as the standard deviation of a fixed size VOI drawn in the liver of each patient. In some cases, the liver of a patient covered two bed frames depending on patient positioning. In those cases, the final NECR was calculated as the average of the two NECR values for each bed position.

The NECR and noise values for each patient were then averaged for each subgroup. A comparison of patient NECR and noise between scanners was then performed using a t-test while keeping the same BMI and ID. To assess the effect of different BMI (same ID & scanner) as well as different ID (same BMI & scanner) on NECR and noise in the liver, an ANOVA test was performed. For both tests (t-test and ANOVA test), a \( p \) value below 0.05 was considered significant.

3.3 Results

The relationships between the NECR and ID for each BMI range are shown in figure 3.1 (a) and (b) for the DSTE and DRX scanner, respectively. The figures clearly show that NECR decreases on average by 40\% and 42\% with increasing BMI from 20-25 to >30kg/m\(^2\) for the DSTE and DRX scanners. On the other hand, NECR for the same
BMI does not change much with ID. The average NECR changes by only 1% and 4% for the DSTE and DRX scanners when increasing ID from 296-444 to >555MBq. The same effect is found for both scanners except that NECR values are higher for the DRX scanner compared to the DSTE scanner. Tables 3.2, 3.3 and 3.4 show the results of

![Figure 3.1](image.png)

Figure 3.1: NECR response versus ID for different BMI ranges: (a) DSTE scanner, and (b) DRX scanner

statistical tests conducted on the data shown in figure 3.1. Table 3.2 shows that there exists a statistically significant difference between two scanners for each BMI & ID subgroup. On the other hand, table 3.3 shows that no statistically significant difference exists by changing ID for all BMI & scanner subgroups. Finally table 3.4 shows that there is a statistically significant difference for different BMI but same ID & scanner design.
Table 3.2: T-test results of NECR between two scanners for each BMI & ID subgroup

<table>
<thead>
<tr>
<th>BMI (kg/m^2)</th>
<th>20-25</th>
<th>25-30</th>
<th>&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>296-444</td>
<td>0.00004</td>
<td>0.00019</td>
<td>0.00003</td>
</tr>
<tr>
<td>444-555</td>
<td>0.00013</td>
<td>0.00010</td>
<td>0.00028</td>
</tr>
<tr>
<td>&gt;555</td>
<td>0.00005</td>
<td>0.00000</td>
<td>0.00019</td>
</tr>
</tbody>
</table>

Table 3.3: ANOVA test results of NECR among different ID for each BMI and scanner subgroup

<table>
<thead>
<tr>
<th>BMI (kg/m^2)</th>
<th>Scanner</th>
<th>20-25</th>
<th>25-30</th>
<th>&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DSTE</td>
<td>0.296</td>
<td>0.723</td>
<td>0.603</td>
</tr>
<tr>
<td></td>
<td>DRX</td>
<td>0.949</td>
<td>0.307</td>
<td>0.124</td>
</tr>
</tbody>
</table>

Table 3.4: ANOVA test results of NECR among different BMI for each ID and scanner subgroup

<table>
<thead>
<tr>
<th>Dose (MBq)</th>
<th>Scanner</th>
<th>296-444</th>
<th>444-555</th>
<th>&gt;555</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DSTE</td>
<td>1.72E-05</td>
<td>1.80E-04</td>
<td>1.61E-08</td>
</tr>
<tr>
<td></td>
<td>DRX</td>
<td>1.22E-05</td>
<td>5.47E-08</td>
<td>3.04E-05</td>
</tr>
</tbody>
</table>

Figure 3.2 shows a scatter plot of the same data shown in figure 3.1. Each dot in the figure represents a single patient. Figure 3.2(a) shows more clearly that NECR value
does not greatly vary with different ID, while figure 3.2(b) shows that NECR decreases with the increasing patient BMI.

![Graph](image)

Figure 3.2: (a) NECR responses to different ID, and (b) NECR responses to different BMI

The results of noise in the liver for all patients are shown by figure 3.3. As expected, noise increases with increasing BMI. The average noise increases by 44% and 42% for the DSTE and DRX scanners when increasing BMI from 20-25 to >30kg/m². Furthermore, noise for the same BMI range also changes with ID. The average noise decreases 13% for both scanners when increasing ID from 296-444 to >555MBq. The same effect is found for both scanners. Tables 3.5, 3.6 and 3.7 show the results of statistical tests for the data presented in figure 3.3. Table 3.5 shows that there is no statistically significant difference between the two scanners for each BMI & ID subgroup.
Figure 3.3: Noise versus ID for different patient BMI: (a) the DSTE scanner, and (b) the DRX scanner

Table 3.6 also shows that there is no statistically significant difference between ID for each BMI & scanner subgroup (except for the subgroup of BMI>30kg/m² in the DSTE scanner). Finally table 3.7 shows that there is a statistically significant difference between the different BMI for each ID & scanner design subgroup.

Table 3.5: T-test results of noise between two scanners for each BMI and ID subgroup
Table 3.6: ANOVA test results of noise among different ID for each BMI and scanner subgroup

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>20-25</th>
<th>25-30</th>
<th>&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSTE</td>
<td>0.6377</td>
<td>0.4884</td>
<td>0.0053</td>
</tr>
<tr>
<td>DRX</td>
<td>0.3714</td>
<td>0.0727</td>
<td>0.1333</td>
</tr>
</tbody>
</table>

Table 3.7: ANOVA test results of noise among different BMI for each ID and scanner subgroup

<table>
<thead>
<tr>
<th>Dose(MBq)</th>
<th>296-444</th>
<th>444-555</th>
<th>&gt;555</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSTE</td>
<td>3.18E-05</td>
<td>1.81E-04</td>
<td>0.0076</td>
</tr>
<tr>
<td>DRX</td>
<td>1.80E-04</td>
<td>8.58E-04</td>
<td>0.0246</td>
</tr>
</tbody>
</table>

3.4 Discussion of the results

The aim of this work was to investigate the effects of injected dose, BMI and scanner design on NECR and noise in PET images. The major difference of our work with respect to previously published studies on NECR (58-61) is that our findings are based on patient data only, rather than extrapolation from phantom or simulation studies. In this regard, our results can be used to validate whether extrapolated phantom data are applicable for patient studies. Furthermore, our investigation covered relationships between different types of PET scanner (BGO and LYSO), whereas all previous studies were conducted using a single scanner with either LSO or BGO detectors. Finally, our
investigation included a noise evaluation in addition to NECR. Such an evaluation provides a more comprehensive assessment of scanner performance, since image noise is more frequently used as an indicator of image quality.

The investigation of NECR for the various conditions was performed on bed frames covering the liver of all patients. The reason to choose this bed position is that the liver is the largest organ with a relatively uniform and constant radiotracer uptake (65). The choice of the liver bed positions was consistent among all patients to mitigate the variations of NECR with different body sections, as described by Watson et al. (59). In order to obtain the noise in the liver for all the patients without any confounding factors, none of the selected patients had a liver lesion.

Both figure 3.1 and figure 3.2 show that the NECR value for the DRX PET/CT scanner is substantially higher than the DSTE scanner. The difference in NECR between the two scanners is statistically significant as shown in table 3.2. This result is expected according to the performance measurements of LYSO and BGO-based PET/CT scanners (62-64), which shows that the peak NECR is higher for the DRX when compared to the DSTE scanner. This difference is mainly due to the faster decay time of LYSO detectors which leads to a decrease in dead time. Therefore, a narrower coincidence timing window is utilized in the DRX scanner (5.8 ns) compared to the DSTE scanner (9.6 ns) to reduce the random coincidences, and hence results in a higher NECR value. However, when comparing the noise performance of the two scanners, Table 3.5 shows no significant difference between the two scanners for each BMI & ID subgroup. Therefore, although the two scanners have significant difference in NECR measurements, the noise content in the images are almost the same. This finding is somewhat counterintuitive since usually a
scanner with a higher NECR measurement should result in a lower image noise. However, our results show otherwise. Combining these two findings together, one can infer that the DRX scanner can generate better image quality than the DSTE scanner (higher NECR, same noise) for the same imaging conditions.

Figure 3.1 and figure 3.2(a) also show that decreasing dose will not affect the NECR value and hence the resultant image quality. This is similar to the observation by Watson et al. (59) which can be further verified by the ANOVA results in table 3.3, which shows no statistically significant difference in NECR among ID >555, 444-555 and 296-444 MBq for each BMI and scanner type. This finding suggests that for patients with certain BMI and scanner model, the ID has minimal impact on the image quality. Consequently, ID can be decreased from >555 to 296-444 MBq in the clinic without affecting image quality. Such an approach will result in a reduction of patient exposure as well as radionuclide cost. A decrease in ID from an average of 629MBq to an average of 370MBq will result in a total effective dose reduction of 7.77mSv (0.77rem).

A comparison of figures 3.2(a) and (b) shows that although the NECR remains relatively the same for different ID, the NECR decreases with increasing patient BMI. Table 3.4 shows this decrease is statistically significant among the different BMI for each ID and scanner type. This finding is further demonstrated in figure 3.4 which shows data fitting curves corresponding to the results in figure 3.2(b). The curves clearly show the nonlinear relationship between NECR and BMI. NECR decreases faster at smaller BMI values than at larger value. Such a characteristic has been previously reported by Danna et al. (61). Combining this information with that about the performance of NECR with ID suggests that poorer image quality in larger patients can not be overcome by injecting
more doses. Improvement of image quality in this patient group can possibly be achieved by increasing the scan duration as suggested by Watson et al. (59) and Masuda et al. (65).

Our noise measurement shows that this metric behaves similarly to NECR with respect to the effects of ID and BMI conditions. The results in table 3.6 show that no significant difference was found for all subgroup in the DRX scanner. The only

![Image](image.png)

**Figure 3.4:** NECR responses to different patient BMI for (a) the DSTE scanner, (b) the DRX scanner
statistically significant difference was found for the subgroup of BMI>30 in the DSTE scanner. The finding suggests that ID does not affect image noise level, except for obese patients (BMI>30) that were scanned in the DSTE scanner. In this regard, although decreasing ID will not affect NECR in obese patients (BMI>30) scanned in the DSTE scanner, it will however increase image noise. Thus increasing ID might be utilized in this patient subgroup and scanner model to improve image quality.

Finally our ANOVA results in table 3.7 show a statistically significant difference in noise among different BMI for each ID and scanner subgroup. Combining this result with the one in figure 3.3, that larger BMI has larger noise level, we conclude that image noise increases significantly with increasing BMI. This result is consistent with the relationship between NCER and BMI whereby NECR decreases with higher BMI. Therefore large patients will not only result in significantly lower NECR, but also significantly higher noise as well, both of which contribute to poorer image quality.

In summary, there are three significant findings in our study. First our results which are based on patient data only supports the finding of previous studies \((59,61)\) with regard to the NECR behaviors which were based on phantom data. Furthermore, the LYSO and BGO-based scanners have almost the same noise content in the resultant images although they have a significant difference in NECR values. Sometimes vendors may recommend LYSO-type scanners based on their higher NECR characteristics. However, our results indicate that this aspect has little impact on image quality as described by noise measurement when compared to BGO systems. Finally, the subgroup of BMI>30kg/m\(^2\) scanned on BGO systems such as the DSTE scanner seems to benefit when injecting a greater dose. The noise significantly decreases with increasing ID for
this subgroup while all other subgroups have similar NECR and noise characteristics with different ID.

The main limitation of our study is that we do not have a prior knowledge of the parameter settings that will result in the optimal image quality represented by the peak NECR value. In this regard, our comparison of NECR among each subgroup may be biased as we may compare some patients/subgroups that reached peak NECR with others that did not. The information of peak NECR requires a full shape of NECR curve by injecting different doses to the same patient which is not feasible in the clinic. However, the remarkable feature of the NECR curve for varying injected dose is its relatively flat plateau whereby small variations around the peak NECR are shown to have quite a large

![NEC curves](image.png)

Figure 3.5: NEC curves corresponding to a representative central frame (abdomen) for three patients (under-weight: BMI=16.16kg/m^2, normal-weight: BMI=20.76kg/m^2, over-weight: BMI=26.42kg/m^2) as a function of the activity at the acquisition time

* Data come from (61)
range of activities (59,61). The patients in this study had activity concentrations at acquisition time that ranged from 181 to 467 MBq. According to the NECR curve in figure 3.5, this activity range leads to a 90% of the peak NECR for each patient. In this regard, we can assume that our results are not biased since such an injected activity range will result in 90-100% of the peak NECR. This assumption can be further verified by the results in figure 3.2. Figure 3.2(a) shows that the NECR remains at the same level for different ID for both scanners suggesting that the injected dose range is actually in the plateau range of the NECR curve. Recall that NECR first increases rapidly with increasing injected dose before it reaches a plateau over a wide range of injected dose. There is still some dispersion in the patient NECR in figure 3.2, and this is likely due to the variations in physiologic and radiotracer biodistribution among the patients.
Chapter 4

Discussion and Extension

4.1 PET Image Quality

Chapter 3 described an investigation of how NECR and noise are affected by factors such as injected dose, BMI and scanner type in the PET images. Indeed, NECR and noise are two major parameters that affect image quality, but there are additional factors that should also be considered. There continues to be a strong interest in the field, to find new approaches that can increase PET image quality as much as possible. Scanner design is one of these most important factors. The major PET/CT manufacturers have devoted considerable resources for the production of better PET/CT scanners that have the ability to more accurately acquire images of the radiotracer distribution in the human body. The last 30 years have seen considerable advances in PET technology and instrumentation, and the two scanners used in chapter 3 serve as excellent examples of the high level of development in PET/CT scanners. The GE DSTE PET/CT was first exhibited at the 2005 Society of Nuclear Medicine (SNM) Conference in Toronto. It is characterized by its high sensitivity, resolution and count-rate performance, and its powerful processing & acquisition capabilities make it the ideal system for growing procedure demands in neurology and cardiology, without sacrificing the requirements of a premier oncology system. The GE DRX scanner was introduced less than a year later than the DSTE PET/CT scanner. The major difference of these scanners is the detector material. DSTE uses BGO detectors whereas DRX uses LYSO detectors. LYSO detectors have a faster decay time than BGO detectors, and hence less dead time. In this
regard, the DRX scanner needs a narrower coincidence timing window compared to the DSTE scanner to reduce the number of random coincidences. Our studies in chapter 3 clearly showed that there is a higher NECR value in the DRX scanner compared to the DSTE scanner. In this regard, the DRX scanner can generate better image quality than the DSTE scanner for the same imaging conditions.

While changing the detector material is one approach to improvement in scanner performance and image quality, upgrading software design of the scanner is yet another method of improving image quality. The time of flight (TOF) PET/CT scanner is such an improvement nowadays. In a PET scan when a positron collides with an electron, two gamma rays are generated in the annihilation process. The TOF PET scanner has the ability to detect the time difference (which is very small) between the two gamma rays, hence the scanner can pinpoint the original location of the positron-electron annihilation in the corresponding LOR. TOF makes it possible for point of origination of annihilation to be more accurately predicted, which leads to more accurate imaging. Improved event localization reduces noise in image data, and results in higher image quality, shorter imaging times, and lower dose administration to the patient.

The idea of using TOF information was originally proposed in the early stages of PET scanner development (66,67), and the first TOF PET systems were developed in the 1980s (68–71). These early systems used cesium fluoride (CsF) or barium fluoride (BaF2) scintillators and were capable of meeting the high-count-rate demands of research brain and heart studies with short-lived isotopes. However, they could not match either the spatial resolution or the sensitivity of conventional PET scanners with BGO scintillators. By the early 1990s, these early TOF scanners were retired from use—just before whole-
body oncology studies with $^{18}\text{F-FDG}$ became common for the clinical diagnosis and staging of cancer. TOF PET is particularly advantageous for whole-body imaging because the theoretical improvement with TOF is predicted to increase with the size of the patient. The promise of TOF for clinical PET is that it has the potential to improve the image quality in heavy patients, precisely where it is needed most.

The major reason why TOF is making a resurgence in PET today is the development of new scintillators that combine fast time decay with high light output and high stopping power (25,72). The advantage of scintillators such as LSO and LYSO is that they have desirable properties for PET without TOF, so their very good time resolution should further enhance good performance. In contrast, CsF and BaF$_2$ have very good time resolution, but their low light output limits the detector design choices for light sharing and decoding crystals. Older TOF scanners used with these scintillators generally had low sensitivity resulting from a poor packing fraction and poor spatial resolution (10-15 mm), since the crystals were large in cross-section. It is common today in conventional PET scanners to use smaller crystals with encoding schemes for crystal identification to achieve spatial resolutions of 4-6 mm. Although modern clinical scanners all have spatial resolutions in this range, the encoding ratio (number of crystals to number of photomultiplier tubes [PMTs]) depends on the light output of the crystal, so BGO is typically configured with a lower encoding ratio than LSO or LYSO. For TOF PET a high encoding ratio is desirable because this reduces the number of PMTs in the system. This is of practical importance, since: (1) a TOF PET system cannot use the same PMTs as a conventional PET scanner, and (2) fast PMTs tend to be more expensive due
to the more complicated plano-concave photocathode design that is used to achieve the shorter transit time spread and faster rise time required in TOF measurements.

Besides the improvements in scanner material and software design discussed above, other improvements have also been made in detectors, hardware, and image processing that impact both image quality and accuracy of quantification. Some of these achievements are: (a) the evolution from 2-D systems with septa to 3-D systems with larger axial fields of view for improved sensitivity, and (b) the transition from analytic filtered back projection reconstruction algorithms to fully 3D iterative techniques with data corrections included in the system model for improved image quality and quantification.

### 4.2 PET Image Quality Equalization

Although there are efforts that to increase PET image quality in general, image quality for different patients has a large variation. Our studies in chapter 3 revealed that for patients with different BMI, the resultant PET images have large differences in noise content (figure 3.3). Figure 4.1 shows PET images of two patients with different BMI, where the patient with lower BMI has a better image with less noise than the patient with larger BMI. Since image qualities between patients of different BMI have a large variance, there is continuing interest in generating methods that provide similar image quality for all patients, to eliminate confounding factors that may influence the reading of patient images.
Figure 4.1: PET images of two patients with BMI of (a) 20.3 kg/m\(^2\), (b) 32.6 kg/m\(^2\); both with injected dose of 10mCi

One may think it logical to equalize image noise in large BMI patients by injecting a larger dose. However, according to our results in chapter 3, especially the results shown in figure 3.3, dose has minimal effects on resultant PET image noise. Another factor that could affect PET image noise is scan duration, since increasing scan duration results in a greater number of radioactive counts in the resultant image, hence less noise in the image. To investigate the relationship of image noise and scan duration, we conducted phantom studies. Specifically, a NEMA/IEC phantom (figure 4.2) was scanned on a GE DRX PET/CT scanner. The activity concentration injected into the phantom background was 3900 Bq/cc and the sphere to background ratio was set to 7:1.
PET data was acquired in 3D for 3 minutes using LIST mode and then rebinned into 11 different scan durations (5, 10sec, 20 to 180 sec with 20 sec interval). All PET images were reconstructed using OSEM (2 iterations 21 subsets). Noise in each image was calculated as the standard deviation of 60 randomly selected pixels in the background. Figure 4.3 shows the relationship between image noise and scan duration.
Another investigation of noise vs. scan duration was conducted using patient data. A total of 50 patients were imaged on a GE DRX PET/CT scanner in 3D mode. These patients were divided into 5 BMI ranges: <20, 20-25, 25-30, 30-35 and >35kg/m², resulting in 10 patients/subgroup. For all patients, the bed position covering the liver was acquired for 5 minutes using LIST mode and then rebinned into 10 different scan durations ranging from 30sec to 5min with a 30sec interval. All PET images were reconstructed using 3D OSEM (2 iterations 21 subsets) using 6mm post filter. For each patient, image noise was derived from the standard deviation of a VOI drawn in the liver and normalized by injected dose and patient weight. The results were then averaged for all 10 patients in each BMI range and scan durations. Figure 4.4 shows the results of noise vs. scan duration for each patient subgroup.

Figure 4.4: Noise in the liver vs. scan duration for each BMI subgroup
Both figures 4.3 and 4.4 show that image noise decreases with increasing scan duration. In this regard, increasing scan duration is a proper approach for decreasing image noise in obese patients, and hence it can be used to achieve better equalization of image noise. However, more investigations are needed to evaluate exactly how much increased scan duration is required to equalize patients with large BMI relative to the patients with small BMI. This can be achieved by scanning patients with different BMI for multiple durations, and curve fitting the relationship between image noise and scan duration to determine a range of times where image noise would be equalized.

Although increasing scan duration is a feasible approach to equalize image noise among patients with different BMI, patients with very large BMI may require a very long scan duration. The standard scan duration for PET imaging in MD Anderson Cancer Center is 3 minutes per bed frame. A whole body scan always takes up 5 to 8 bed frames, so that the average patient requires about 20 minutes for a whole body scan. If equalization of image noise requires an obese patient to scan for 10 minutes per bed frame, this patient will spend about one hour in the PET/CT scanner. Such a long scan duration is not feasible since it would lead to increased dosage, patient inconvenience and lower throughput.

An alternative approach for equalizing image noise while maintaining standard scan duration is to add post filters to the reconstructed PET images. Filters with larger Full Width Half Maximum (FWHM) result in greater image smoothing and less image noise. A study of image noise with different post filter widths was conducted using patient data. A total of 50 patients were imaged on a GE DRX PET/CT scanner. These patients were divided into 5 BMI ranges: <20, 20-25, 25-30, 30-35 and >35kg/m$^2$. 
resulting in 10 patients/subgroup. PET images of the bed position covering patient liver were acquired in 3D for 3 minutes. All PET images were reconstructed using 3D OSEM (2 iterations 21 subsets). Gaussian post filters of 4 to 10mm FWHM with a 2mm interval were applied to each patient data. Noise was determined as the standard deviation of a fixed size VOI drawn in the liver and was normalized by injected dose and patient weight to have a unit of g/ml. Noise in the liver was calculated at each filter width for each patient. The average noise for 10 patients in each BMI range was calculated for different filter width. Figure 4.5 shows the results of image noises affected by filter width for patients with different BMI ranges. We can see that noise decreases with increasing filter width for all BMI ranges. Therefore, increasing post filter width is also a feasible method to decrease noise in obese patients and achieve noise equalization.

![Figure 4.5: Noise vs. post filter width for different BMI subgroup](image)

Although increasing filter width can improve throughput and patient convenience compared to increasing scan duration, increasing filter width will result in a decrease in
image resolution. In this regard, detailed structures or small tumors may not be detected on a low resolution image generated by a large width filter. According to the advantages and disadvantages of changing scan duration and post filter width, we may combine these two approaches together to increase scan duration and filter width together for obese patients. Such an approach can remain a moderate resolution, while not scanning for a very long time. The relationship among image noise, scan duration and filter width can be displayed by a 3-D surface curve as shown in figure 4.6. Figure 4.6 shows the average noise in the liver for 10 patients with BMI between 25 and 30 kg/m$^2$, while changing scan durations and filter widths. The same image noise can be achieved by multiple combinations of scan duration and filter width with varying resolution degradation. As to choose which combination of scan duration and filter width in clinic to balance the tradeoff of these two factors, more investigations are required to be conducted.

Figure 4.6: Noise in the liver for different filter widths and scan durations: an average of 10 patients of BMI 25-30 kg/m$^2$. 
Chapter 5

Summary and Conclusion

5.1 Brief Summary

This thesis focuses on several topics related to the improvement in image visualization and image quality achieved using the Positron Emission Tomography/Computed Tomography (PET/CT) imaging modality.

Chapter 1 contains an introduction to the PET/CT imaging modality, including the physical foundations of PET imaging, the processes of PET data acquisition, PET image reconstruction approaches and multi-modality PET/CT imaging. Several aspects related to PET image visualization and image quality were also introduced, which provided the background information for the investigations conducted in chapters 2 and 3.

Chapter 2 describes a novel software tool for improving PET/CT image visualization. In PET imaging, some protocols require the acquisition of whole body scans, which means from head to toe. This requirement is not supported by some current commercially available scanners due to a limit on the extent of the bed travel. In such cases, a whole body scan has to be divided into two segments with no ability to merge them before they are reviewed by radiologists for clinical interpretation. A novel software tool is developed in this chapter to stitch the two PET/CT body segments into a single image while incorporating all necessary data correction. The output result can then be displayed on the current PET/CT display workstations for radiologist review and interpretation. This software will lead to more efficient readings of patient images since one image set rather than two needs to be reviewed.
Chapter 3, on the other hand, investigates the topic of PET image quality with different imaging parameters. The PET image qualities are represented by noise equivalent count rate (NECR) and image noise. Several imaging parameters investigated are injected dose, patient BMI and PET/CT scanner design. This chapter demonstrates how NECR and noise in PET images are affected by injected dose, BMI and scanner type. The results of this investigation provide a foundation for determining which factors impact PET image quality and by how much. The results presented provide a preliminary guide as how to increase PET image quality or even equalize PET image quality among different factors.

Chapter 4 is the discussion and extension mainly focused on the results in Chapter 3. The results in Chapter 3 show that patients with larger BMIs consistently generate poorer images compared to patients with smaller BMIs. Chapter 4 proposes several possible approaches for equalizing image quality between obese and normal patients, and preliminary results are shown for different approaches. Finally, accurate quantification in PET images is also proposed as a ‘normalization’ among patients with different imaging and reconstruction parameters.

5.2 Contributions of this Thesis

For the software introduced in chapter 2, the contributions are:

- the mathematical model is derived for image stitching process.
- a Matlab program is generated based on the mathematical model.
- the validity and feasibility of this Matlab program is tested by conducting simulation study, phantom study and patient studies.
• the Matlab program is incorporated into a user-friendly GUI software tool.
• two versions of this software is generated for Windows and Linux operation system respectively.

For the investigations in chapter 3, the contributions are:

• 180 patients in the large pool of patient list are selected according to the preset injected dose range, BMI range and scanner type.
• NECR for each patient is calculated by extracting the information in the PET/CT scanner system
• the noise in the liver for each patient is calculated using a written Matlab program.
• corresponding t-test and ANOVA test is conducted to compare the NECR and noise from different patient subgroups.
• all the results are incorporated to summarize the conclusion.

5.3 Conclusion

The PET/CT image stitching software developed in chapter 2 has the capability to:

• allow the stitching of two body segments to generate a whole body PET/CT scan.
• correct for radioactive decay between the two body segments.
• output a DICOM image set that can be tested on two different PET/CT display workstations (GE –AW, and SIEMENS E-SOFT).
The advantages of this software are:

- improves efficiency of reading PET/CT scans since only a single image set needs to be loaded rather than two.
- facilitates comparison of a patient’s current and prior scans in a single session rather than having to compare two separate paired segments.
- allows rendering of a patient’s whole body (head to toe) image, thus improving the effectiveness of interpreting the study.
- Provides radiologist with the ability to generate whole body images/movies for educational and demonstrational purposes.

The investigation of image quality with different parameters in chapter 3 indicates:

- the GE DRX PET/CT scanner has high NECR, but similar noise characteristics compared to the GE DSTE PET/CT scanner.
- patients with larger BMI consistently generate poorer image quality, as measured by noise and NECR metrics and this drawback can not be overcome by injecting more dose.
- dose reduction from 555 to 296-444 MBq has minimal impact on image quality independent of patient BMI and the scanner type.
- a reduction in dose is feasible, since it decreases patient exposure as well as radionuclide cost.
Bibliography


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77. Etchebehere EC, Macapinlac HA, Gonem M et al. Qualitative and quantitative comparison between images obtained with filtered back projection and iterative


