Evaluation of $^{18}$F-FDG PET Agent in Cardiac Gated Imaging

THESIS

Presented in Partial Fulfillment of the Requirements for the Degree Master of Science in the Graduate School of The Ohio State University

By

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2012

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Abstract

Gated cardiac imaging (GCI) is used in oncology and cardiology to improve resolution impaired by cardiac motion. Both subjects require specific imaging techniques to accurately portray the inner functionality of the human heart. Positron emission tomography (PET) is a sensitive imaging technique that details the cardiac cycle by recording the three dimensional distribution of radiotracer photon emissions. Unlike the commonly used computed tomography (CT) method which transmits source particles through the target, the PET source emits positrons from within the object, capitalizing on opposing photon emissions for anomaly detection. Within PET imaging, gated cardiac PET using an $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) source is a quantitative imaging technique which utilizes a gating technique that reduces signal blurring in the cardiac cycle. This paper evaluates $^{18}$F-FDG uptake within gated cardiac PET while developing an elementary interactive data language (IDL) program for gated cardiac PET data analysis. Digital Imaging and Communications in Medicine (DICOM) standards were used to understand PET imaging output, and DICOM conformance was used to determine the DICOM tags required for analysis. The IDL program has two objectives: to read DICOM tags integral to gated PET into the program and to develop a user interface which displays gated PET images in correct sequence. Five gated PET datasets were used to compare and verify the output of the IDL program to the output of verified and authorized EBW/LEO DICOM display workstations. Quantified results show an average...
end-diastolic volume (EDV) of 25.6 ml, average end-systolic volume (ESV) of 13.8 ml, and a left ventricle ejection fraction (EF) of 51.8 percent. Additionally, results show that the IDL program’s 1-dimensional (1D) trans-axial display matches the output from authorized workstations. In particular, the IDL program provides a graphical user interface (GUI) which facilitates visibility of gated images organized by frame and by slice, allowing the user to easily customize the axial view for further analysis. Thus, the IDL program can be utilized as a promising tool to allow multi-pharmaceutical, multi-modality medical imaging technology users to obtain information of interest utilizing an easy-to-use format.
Acknowledgments

I would like to thank Dr. Lei Cao for allowing me to work on this unique topic. Dr. Cao’s support and encouragement throughout the entire Masters career has been paramount in my growth as a student and as a professional. I also would like to thank Dr. Jun Zhang and Dr. Michael Knopp for formulating the concept and providing me the opportunity to work with their research group on such an impactful project. Additionally, I would like to thank Dr. Jun Zhang for his vision, encouragement, and constant drive for success and good results.

I would also like to express my gratitude to the research group members Katherine Binzel, Xiaoli Liu and Kristin Sullivant for their mentorship, discussion, and guidance with the software, hardware, and trouble-shooting.
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1. Introduction

Oncology requires a dynamic suite of imaging tools to reveal different forms of cancer in the human body. Each imaging technique depicts a different physical property of a sample and allows one to draw upon unique outputs. A common practice in this industry includes honing these techniques and at times simultaneously utilizing hybrid outputs from multiple techniques to better describe various features of one sample (Huang, 2012). By focusing on maximizing individual machine applicability and output, the nuclear medical imaging industry can ultimately achieve greater efficacy in overall patient diagnosis. Thus, this study will focus on application of $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) in gated cardiac imaging (GCI) with further emphasis on general software development to read and display gated cardiac positron emission tomography (PET) images.

In oncology, PET scans are used to identify and determine the extent of malignant or cancerous diseases while monitoring the effectiveness of radiological therapy for diagnosis. Additionally, in cardiology, these scans are used to detect coronary disease and myocardial perfusion (Bybel, Brunken, Shah, Wu, Turbiner, & Neumann, 2006). Under-perfused tissue can potentially benefit from revascularization if slight glucose metabolism is detected. Likewise, the absence of a metabolic signal at the site of the perfusion defect
indicates non-viable scar tissue which would not benefit from revascularization. Due to increasingly sophisticated surgical techniques and more advanced cardiovascular diseases, the demand for more accurate diagnostic tomographic imaging tools has grown with the need for better spatial and temporal resolution. (Malouf, Edwards, Tajik, & Seward, 2008)

This thesis includes a literature review on cardiac imaging techniques like PET, PET/CT, and gated cardiac PET. Also provided is literature review denoting differences between the static, dynamic, and gating imaging techniques within PET alone. Within the PET and PET/CT imaging methods, acquisition of data involves detection of collinear photons released from positron-electron annihilation. Most acquired data is translated into the form of a sinogram, but if the scanner has List-Mode capability, it can acquire time-of-flight information, or details on the time difference between the two 511 keV photons reaching collinear detectors (Dilsizian, et al., 2009). In order to comprehend these cardiac applications in oncology and their clinical relevance, one must first understand the anatomy of the heart and how it functions. One can use a technique such as the electrocardiogram (ECG) to acquire an electronic visual of the heartbeat. By understanding how gated cardiac PET/CT imaging utilizes ECG to reconstruct the scanner data into multiple gated frames, one can then discern how certain aspects of gated image reconstruction correlate to specific segments of the heartbeat. Next, the detailed understanding of the heartbeat-to-image relationship is used to describe how gated cardiac imaging data are reconstructed into an easily interpretable visual. This
understanding is needed to both complete calculations concerning cardiac performance variables and to determine the correct details required for interactive data language (IDL) software development specific to gated cardiac imaging.

This project requires the master’s candidate to learn and understand gated PET/CT imaging, its applications in cardiac analysis, and culminates with the development of an elementary IDL code which assists in gated cardiac PET data analysis. As part of a larger parent project at The Ohio State University, there is a need to incorporate an IDL program that allows for simple reading and display of gated cardiac PET images into the parent suite of programs. This individual IDL program discerns numerical data stored in output PET files, and quickly provides a visual pertinent to operators of the imaging technology based on validation via registered workstations and via adherence to Digital Imaging and Communications in Medicine (DICOM) standard. Validation is required due to the standardized electronic output which medical imaging machines are required to incorporate, making output across various medical imaging machines more uniform.
2. Background

2.1 PET and PET/CT

For studies involving oncology, neurology and cardiology, two commonly used medical imaging methods include computerized tomography (CT) and positron emission tomography (PET). While the CT measures X-ray attenuation within the tested range, PET uses radiotracers to observe functional data regarding specific physiological processes including and similar to $^{18}$F-FDG uptake (Carney, 2007). Additionally, these two imaging techniques have also been combined in a procedure called PET/CT, which gives both physiological and anatomic information combined in one output along with properties of interest including cardiac data and standard uptake value (SUV), or measure of the activity concentration ratio within a patient (Boellaard, et al., 2009). Cardiac data will be discussed further in detail in section 4 below, and a general equation for SUV is shown below in Equation 1.

$$SUV = \frac{\text{decay corrected dose/ml of tumor}}{\text{injected dose/patient weight in grams}}$$

(1) (Mawlawi, 2011)
CT utilizes X-ray views from a sequence of angles to create cross-sectional images of inner bodily tissue. CT is commonly utilized when one needs to diagnose muscle or bone disorders, or it is used when one wants to detect and monitor diseases and conditions like cancer, heart disease, tumors, infections, blood clots, or internal bleeding. The most important contribution CT gives to hybrid PET/CT systems includes the attenuation correction (AC) data the CT provides. Due to coincidence detection in PET which will be elaborated upon below, there is an increased likelihood of photon attenuation within the human body due to random and scatter events (Schwaiger, Zeigler, & Nekolla, 2005). Random and scatter events in PET will be defined in the PET section below.

During the procedure, the portion of the body to be scanned is placed on a table in the doughnut-shaped gantry ring containing the 120 kev x-ray tube and detectors shown below in Figure 1. During the scan, the table will move a short distance in a few seconds through the rotating gantry, and each rotation of the gantry will yield many images called “slices”. (Culpeper Regional Hospital Medical Imaging Center, 2012) (Mayo Clinic, 1998-2012). This study will not focus on CT scan procedures specifically; however the CT applicability and compatibility in PET/CT scanning will be briefly addressed as a useful area of future work.
PET is a non-invasive quantitative imaging technique which presents physiological processes by displaying the distribution of radiopharmaceutical tracers throughout the body. Shown below in Figure 2 is a visual describing the process used during PET scanning. First, tracers like $^{18}$F-FDG listed below in...
Table 1 are to be injected at a site contralateral to the site of concern (Delbeke, et al., 2006). These tracers then accumulate in targeted tissue during a 45-90 minute “uptake time” time frame mostly due to enhanced glucose metabolism within cancerous tissue. The radioisotopes in the tracer then emit a positron when they decay, and this positron annihilates an electron to produce a “line of response (LOR)” denoted by two collinear gamma rays emitted in opposite (180 degree) directions as shown in Figure 2 below.

Figure 2 – Positron Emission Description (Kinehan, 2006)
Table 1 – PET Tracer Examples and Uses (Bybel, Brunken, Shah, Wu, Turbiner, & Neumann, 2006)

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Example Use</th>
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<td>$^{18}$F-FDG</td>
<td>Glucose Metabolism</td>
</tr>
<tr>
<td>$^{18}$F Fluoride</td>
<td>Cell Proliferation &amp; Bone Imaging</td>
</tr>
<tr>
<td>$^{11}$C Methionine</td>
<td>Amino Acid Metabolism</td>
</tr>
<tr>
<td>$^{11}$C Tyrosine</td>
<td>Amino Acid Transport</td>
</tr>
<tr>
<td>$^{124}$I</td>
<td>Thyroid Metabolism</td>
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The PET scanner detects these paired scintillation events called “coincidence events” using a 360 degree gantry shown below in Figure 3. Three basic categories of coincidence events that can be detected by the scanner are visualized below in Figure 4. The first and most important is a “true coincidence” event, where both photons emitted from the annihilation event are detected at the same time, and neither undergoes any interaction before being detected. Next, a “scattered coincidence” event is detected when one or potentially both photons undergo Compton scattering, resulting in a lower energy photon emitted at an angle away from the true coincidence event, an incorrect LOR and additional noise to the overall signal. Lastly, a “random coincidence” event occurs when two photons originating from different positron annihilations are detected within the coincidence time window of 6 nanoseconds on a plausible LOR. Both scatter and random
events are dependent upon the volume of the subject being imaged, and concurrently how much energy is attenuated within the subject (Badawi, 1999).

Figure 3 - PET scan basic setup (Tavernier, 2011)
Within 15-45 minutes (for a skull to mid-thigh image acquisition) the data can be acquired and then later reconstructed into a three-dimensional (3-D) image of tracer distribution. For more specific regions of interest and higher image quality, imaging acquisition time may be prolonged to acquire more counts. (Delbeke, et al., 2006) It is important to note that PET corrects for attenuation in organ tissue, and this aspect of PET results in acceptable spatial resolution after reconstruction. (Bybel, Brunken, Shah, Wu, Turbiner, & Neumann, 2006) (Tavernier, 2011)

PET/CT is the combined display of functional and physiological information given by a device with both a CT scanner and PET scanner on one table. (Delbeke, et al., 2006) Such integration provides details on the precise size and localization of lesions on PET scans while combining the anatomical location information given by CT scans.
While the protocol for PET/CT scans is very similar to that of solely CT or PET alone, one sequential difference intrinsic to PET/CT involves first CT data acquisition typically in the initial 30 seconds, followed by the PET scan lasting 15-45 minutes afterwards (Virginia, 2006). The same protocol depicting CT and PET scan major processes mentioned above are still executed in order. Then, once data acquisition is complete, reconstruction and fusion (or overlay) of both PET and CT images can occur.

2.2 Gated PET

Gating is defined as a technique used to provide clear and improved visualizations through image segmentation in the presence of bodily movement during both the cardiac and respiratory cycle. Gating within PET is primarily necessary to reduce blurring caused by respiratory or cardiac motion in medical imaging, in order to avoid the unnecessary irradiation of any healthy tissue surrounding the region of interest. In order to do so, one must accurately be able to track the movement of the body and note how regions of interest change in size and shape with each type of movement. Most PET imaging requires correction for both respiratory and cardiac movement, as both cycles affect the imaging sequence in a different way. Motion from either cycle must be corrected for either by the machine during the scan or more commonly afterwards during image
reconstruction. This study focuses primarily on the cardiac cycle and the gating techniques used to properly segment the process into viewable sections. In the next section, gating within the cardiac cycle will be further addressed.

2.3 Gated Cardiac PET

In order to understand how information in gated cardiac PET is obtained, one must first understand the basic workings of the heart with particular focus on the larger left ventricle muscle. Next, after learning the anatomy of the heart, one must also understand one of the most commonly recognized technologies, the ECG, used to gather information from a heartbeat in order to properly correlate the movement of the left ventricle and the output of the ECG during image acquisition. By correlating the electrical signals obtained from the ECG along with the data acquired from the gated cardiac PET after reconstruction, one can arrange and extract data from the PET scan, then compare the acquired data to expected values to see how far they deviate from normal values. The particular data being compared includes variables such as End-Systolic Volume (ESV), End-Diastolic Volume (EDV), and Left Ventricle Ejection Fraction (LVEF), which will be elaborated on further in Section 4.
2.3.1 Anatomy of the heart

The heart, whose cross-section is shown below in Figure 5, is an organ needed to transport nutrients to the rest of the body using a system of pumps and valves (McConahy, 2007). The major chambers of the heart pertinent to this project are the right atrium, right ventricle, left atrium, and left ventricle. One ventricle pumps blood to become oxygenated, and the other pumps blood to the rest of the body. One primary characteristic of such cardiac pump cells is contractility, or the ability for a muscle to contract in response to certain stimulus. In response to electrical stimulus (which will be touched upon in section 2.3.2), when cardiac cells shorten, a muscular contraction is caused forcing blood into the next chamber (Johnson, 2007). The entire circulation system and electrical conduction system related to it are also of interest but will only be mentioned in a passing note for conceptual clarity.
The atria are smaller than the ventricles and provide a chamber to receive blood returning from the circulation system to be passed to the ventricles. The ventricles’ primary purpose is to receive blood from the atria and pump it through arteries to other sections of the body (McConahy, 2007). If the heart has a problem, the left ventricle is first considered for any potential weaknesses with contractility, or ability for a muscle to contract in response to certain electrical stimulus.
The flow of blood through the body places particular importance on left ventricular function, as the left ventricle is tasked to pump blood out to the entire body. Shown below in Figure 6 are the pulmonary and systemic circuits. The pulmonary circuit begins with oxygen depleted blood entering the right atrium. Next, the blood is pumped by the right ventricle through the pulmonary arteries as shown in Figure 6 below into the lungs. The blood is then oxygenated and sent to the left atrium through pulmonary veins. This particular system is a low-pressure system because relative to the systemic circuit, the pulmonary circuit only requires blood to be transported a short distance.

The systemic circuit begins when the oxygen rich blood is pumped into the left ventricle from the left atrium. The left ventricle then pumps the blood through the aorta to the remaining parts of the body. Finally, after being depleted of oxygen, blood is sent back to the right atrium to begin the cycle again. This systemic cycle requires a larger pressure system to handle the increased distance that blood must flow, so the strength of the larger left ventricle becomes necessary to handle the higher pressure system. A simplified and more detailed flowchart depicting blood flow through the pulmonary and systemic circuit is shown below in Figure 7.
Figure 6 – Diagram of systemic and pulmonary circulation systems (Silverthorn, 2000)
2.3.2 Electrocardiogram

By definition, an ECG is a measurement of the electrical activity of the heart over some period of time logging information from one end-diastole to the next end-diastole shown below in Figure 8. This is recorded by a device requiring electrodes attached to the outer surface of the skin (Yale Medical Group, 2012). Based on the cardiac cycle, the ECG produces a wave called the R-R interval, indicating the electrical signals output from one cardiac cycle or one heartbeat. This R-R interval contains major waves labeled
P, Q, R, S, and T waves as shown in Figure 8 below. Certain intervals consisting of a combination of waves further indicate particular events in the cardiac cycle. In Figure 8 below, electrical stimulation of the atria causes blood to be pumped to the ventricles, shown as the low amplitude P-wave in green. Next, the QRS complex indicates that the ventricles are electrically stimulated to pump blood out. After the QRS complex, ventricular repolarization is depicted during the time from the end of ventricle contraction to the beginning of the T wave. The T wave indicates the recovery period for the ventricles. A visual of blood flow during one ECG wave can be depicted in Figure 9 below (University of Pennsylvania, 2012) (Yale Medical Group, 2012).
Figure 8 – QRS complex example (University of Pennsylvania, 2012)

Figure 9 - Functionality of the heart (Agur & Dalley, 2008)
2.3.3 Acquisition

Each CT, PET, or PET/CT imaging technique has a unique process to follow to acquire imaging data; however, there are some similarities between each process. The scanners used in this project have list-mode acquisition capacity. This means the scanners have the ability to store temporal time-of-detection information along with the spatial coordinates and energy for all detected events (Rahmim, Tang, & Zaidi, 2009). In each of these techniques, one of the most important initial steps for any PET/CT sequence (static PET, dynamic PET, or gated PET) is to always begin by obtaining a scout view, also called topogram. This allows the administrator to obtain a whole body field of view (FOV). The FOV provides the operator details on what scanning boundaries are required (whole-body, chest, cardiac, or brain scans) and is the first step to determining which areas of the subject to focus on. Then, for each PET/CT sequence, the CT scan is acquired to obtain anatomical data from the patient which can then aid in attenuation correction of a PET scan based on the FOV.

PET scans can attribute production of a lower amount of detected coincidence events to attenuation in the body or due to scatter outside the FOV (Rector and Visitors of the University of Virginia, 2006). Attenuation is a particularly large problem in these PET scans because the required simultaneous detection of collinear photons results in much longer acquisition time than that of the CT scan, introducing far more noise into the
acquired images. Attenuation correction data acquired from the initial CT scan is particularly useful to PET/CT imaging because it provides tissue and anatomic differentiation data at a high imaging speed (Wechalekar, Sharma, & Cook, 2005). When the CT scan’s high imaging speed and anatomical differentiation data is combined with the PET scan’s functional imaging capacity, the result is a combined technique that provides clearer images than CT or PET alone can generate. However, if these images are misaligned, imaging artifacts may appear, forming regions of interest in the incorrect location. Thus, in addition to attenuation correction, proper patient alignment is required for PET/CT to display accurately.

In this study, both PET and CT scans are located in the same machine and the software is also co-registered or motion-corrected between imaging techniques. Thus, the attenuation correction data can be assumed to have no misalignment because both CT and PET scans are in the same FOV. If the CT and PET machines are located in different locations and scan at different points in time, the possibility of misalignment would be very high due to patient movement.

Following the relatively quick CT scan, the PET scan is performed with procedures denoted below, varying according to the type of PET scan being performed.

For PET acquisition, the system tracks overall counts at any given time, so data acquired spans over the entire FOV and over the entire 10 minute scanning period.
Certain acquisition parameters can be considered to optimize image quality, including acquisition/imaging mode (Static, Dynamic, or Gated), scan duration per bed position, uptake time period, and 18F-FDG dose (Boellaard, Standards for PET Image Acquisition and Quantitative Data Analysis, 2009).

Within PET scanning, two general approaches for data acquisition are used depending on if the scanner has list-mode capacity or not. The first method is called frame-mode (conventional) acquisition and has been routinely used in dynamic and gated PET scanning. The second is list-mode acquisition as defined earlier, used predominantly in static PET capable of utilizing TOF mentioned earlier. This study did not utilize TOF during gated cardiac imaging, thus the main focus will reside with conventional acquisition. In conventional PET acquisition, a set of sinograms encompassing the entire length of the scan is obtained, and depending on the imaging mode (Static, Dynamic, or Gated), that data is binned accordingly during reconstruction. An example of a sinogram, which houses distance and angular data is shown below in Figure 10. This conventional acquisition method allows PET to be traditionally used for gross tracer uptake (Saha, 2010).
For imaging accuracy, prior to reconstruction one must check for any acquisition errors in instrumentation, patient motion, soft-tissue attenuation artifacts, severe arrhythmia, or any errors in reconstruction filter choice or cutoff limit. This will prevent severe error propagation from compromising the output (Paul & Nabi, 2004).

2.3.4 Reconstruction

The data acquired from PET scanners must be reconstructed into cross-sectional images. For either CT or PET, reconstructed tomographic information provides images of functional information from many medical applications. Current reconstruction methods are divided into two types of approaches: analytical and iterative. Analytical
reconstruction methods allow for a direct mathematical solution for forming an image, and iterative reconstruction methods, based on a more accurate definition of the imaging process, utilize a more complex mathematical solution using multiple steps or iterations to arrive at an image (Alessio & Kinahan, PET Image Reconstruction). This project utilizes the iterative reconstruction method, so analytical reconstruction methods will be briefly touched upon, and iterative reconstruction methods will be further elaborated upon for clarity.

Analytical reconstruction methods are further divided into two-dimensional (2-D) and three-dimensional (3-D) subsections. The 2-D methods currently in use include the 2-D central section theorem, backprojection, backprojection-filtering, filtered-backprojection, and regularization. The 3-D methods include a three-dimensional reprojection algorithm (3DRP) and rebinning methods.

Iterative reconstruction methods contain five basic components. First, a description of the form of the image is required, either in pixels for 2-D image elements or voxels/blobs for 3-D image elements. Second, a system model relating the image to the data is required. The model can include detector response, corrections for data, or other data like efficiencies. Third, a statistical model describing how each measurement behaves around its mean is required. This relates the actual measurement values to expected measurement values, usually present in Gaussian or Poisson distributions and histograms derived from ECG signal data. Fourth, an objective function that defines a
governing principle for determining the optimal image is required. One of the most common functions is the maximum likelihood statistical estimation method. Fifth, a method for maximizing the governing principle is required. Most routinely used is the Expectation Maximization (EM) method and its variant the Ordered Subset Expectation Maximization (OSEM) method. Other methods for maximizing the governing principle, such as Maximum A Posteriori (MAP), Penalized Weight Least Squares (PWLS), and Generalized EM, can be used as well (Alessio, Introduction to PET Image Reconstruction, 2007) (Alessio & Kinahan, PET Image Reconstruction). These methods help remove data originating from arrhythmic heartbeats that unexpectedly occur, eliminating beats that may be too fast or too slow from being considered in the normal heartbeat average.

For static PET reconstruction, if all detected events throughout the 10 minute scanning period are used for reconstruction, the operator has one frame encompassing the entire 180 mm FOV.

Next, for dynamic PET reconstruction, if the counts acquired for the entire FOV are split into time segments, 2 minute time segments for example, then for the 10 minute scanning period, dynamic PET reconstruction would bin the counts into five-two minute frames, and data would be binned according to the chronological order encountered while binning. If one 10 minute frame is chosen for dynamic PET reconstruction, the results would be the same output from static PET reconstruction.
Lastly, for gated PET reconstruction, the ECG cardiac data shown in Figure 11 must be incorporated. As stated earlier, the RR signal is intrinsic to one heartbeat. Over the course of the entire scan, hundreds, potentially thousands of heartbeats are registered, each approximated at one beat per second on average. First, the operator uses data from the preliminary ten minute image to determine the length of the cardiac cycle. Next, a range of acceptable beats is specified by determining the mean R-R interval value and what percent (or tolerance) deviation from this interval is acceptable to be considered a normal heartbeat. Any cardiac cycles shorter or longer than this range will be rejected, preventing arrhythmic heartbeats from being included in the dataset. The RR interval is then split into eight equal-length frames per cardiac cycle, which is considered satisfactory based on routine practice and data is binned according to the phase it correlates to within the RR interval (Paul & Nabi, 2004). This differs from dynamic and static PET reconstruction because gated PET reconstruction is based on ECG signal, and not a sequential time-frame. A more generalized visualization of cardiac cycle framing or binning can be seen below in Figure 12.
Figure 11 – Principle of ECG-gated acquisition (Paul & Nabi, 2004)
2.3.5 Clinical Relevance / Applications

PET/CT applications are primarily used in detection of early stage malignancies within oncology and cardiology. Some general clinical advantages of using PET/CT include advances in localization, sensitivity, and specificity when correcting for attenuation effects (Wechalekar, Sharma, & Cook, 2005). By utilizing a combination of both techniques, many issues involving improper diagnosis can be mitigated and when compared to PET with standard attenuation-correction alone, PET/CT is 25-30 percent faster, allowing for a more comfortable examination and increased patient throughput (von Schultess, Steinert, & Hany, 2006). Finally, this study focuses on $^{18}$F-FDG uptake in gated cardiac imaging, but PET/CT is currently used in numerous other applications.
beyond the scope of this paper. These applications will be mentioned briefly to showcase PET/CT versatility and breadth of application.

Advances in localization capacity include the ability to anatomically locate a lesion using $^{18}\text{F}$-FDG metabolism when other organs or tissue are nearby. Without the anatomical registration of the CT scan, areas of the body with complex anatomical structures surrounding the region of interest will be more difficult to interpret. By utilizing an integrated PET/CT system, problems with patient repositioning and anatomic changes can be overcome. This integrated PET/CT system will become very applicable in radiotherapy planning by providing anatomical CT data along with the PET information, allowing accurately registered functional information to be applied (Wechalekar, Sharma, & Cook, 2005).

Improvements in sensitivity from PET imaging to PET/CT combination imaging also allow for more frequent upstaging of patients in cancer treatment. Determination of the correct stage of cancer is of paramount importance when deciding which level of treatment is necessary. In low-grade uptake situations where a malignant tumor could be overlooked with PET alone, PET/CT combinations allow for CT characteristics to also be fused with the PET to lower the likelihood of overlooking the mass. It is this combination that accounts for times when solely PET or CT analysis would fail to correctly diagnose the disease (Wechalekar, Sharma, & Cook, 2005).
In addition to improvements in localization and sensitivity, PET/CT hybrid imaging has increased the procedures specificity for disease diagnosis. Specificity denotes how well a diagnostic technology detects one disease over others which are closely related, minimizing false diagnoses. This increase in specificity lowers the number of required diagnostic scans when using just PET or CT, and also improves the diagnostic accuracy (Wechalekar, Sharma, & Cook, 2005).

Lastly, the scope of this paper only encompasses the PET/CT gated cardiac imaging application in cardiology, but clinical applications for PET/CT are still listed to provide broad information concerning where PET/CT is currently applied, and potentially where it can be applied in the future. The PET/CT technique is shifting beyond cancer staging and diagnosis and into the therapy response monitoring / radiation treatment planning realm (Oyen & Chiti). In oncology alone, current applications include head, neck, lung, breast, and prostate cancer detection, in addition to digestive track, lymphoma, and neuroendocrine tumors. While the technique can be used to pinpoint infections and inflammation, two other major applications include cardiology and neurology. Applications in cardiology have been discussed earlier in terms of advancements in localization, sensitivity, and specificity. The applications in neurology include diagnosis for brain disorders including dementia, mobility disorders, epilepsy, and brain tumors (Oyen & Chiti).
2.4 DICOM and DICOM Conformance

From the National Electrical Manufacturers Association (NEMA), one of the main purposes of the DICOM standard is to facilitate the interoperability of medical imaging equipment through defining certain specifications. These specifications include protocols for network communications and syntax/semantics used for commands and exchangeable information within these protocols (National Electrical Manufacturers Association, 2008). The DICOM standard pertains to the sub-division of health informatics called medical informatics, which enables effective collection of medical data using technology tools to develop medical knowledge (University of Illinois at Chicago, 2011). In the future, these protocols must be advanced to help enhance exchange of digital information between medical imaging devices and other systems, and such protocols will have to be improved to address other areas of medical informatics (National Electrical Manufacturers Association, 2008).

This project requires use of imaging workstations and specific implementations of the DICOM standard throughout all levels of software development. This adherence to the DICOM standard is called “DICOM conformance” and is a critical part of a program wishing to retain digital image application interoperability. Thus, the use of modality-specific modules for gated cardiac PET is necessary to retrieve the correct data based on DICOM conformance. DICOM tags specific to this project are determined and applied according to DICOM conformance and will allow the program generated by this project
to potentially be utilized across multiple GCI machines which follow the DICOM standard.
3. Methodology and Approach

3.1 PET/CT system

The long-term purpose of the gated cardiac PET is to determine if drug-induced increases in left ventricular contractility affects cardiac FDG uptake and/or left ventricular morphology by utilizing PET/CT imaging. The subject details and protocol for actual PET/CT acquisition and reconstruction are listed below. The procedure for analysis and validation is listed along with sequence of events for software development. Due to the proprietary nature of the software and project itself, actual program code will not be included in the appendix; however, detailed description concerning the program’s main operations will be included.

3.1.1 Acquisition

This study selects a dog to undergo the gated cardiac 18F-FDG PET/CT procedure. The procedure utilizes a mobile Gemini TF 64 PET/CT system (WCI-BMI & Philips Healthcare) to perform the PET/CT scans.
Prior to scanning, the proctor ensures the dog is well positioned and stabilized on the table (head-in). Instruments of anesthesia, IV injection, and ECG are set up and enabled. A CT scout is performed to define the cardiac FOV, followed by a cardiac CT scan to be used for PET attenuation correction. The dog was administrated an 18F-FDG activity of 0.3 mCi/kg, and cycles of 10-minute gated cardiac PET scans were repeated after the administration.

3.1.2 Reconstruction

After acquisition is completed, iterative reconstructions with attenuation and scatter corrections are performed based on gated cardiac PET list-mode data. Eight phases containing 45 axial slices per phase and 4 mm thick slices are generated with isotropic voxel resolution and a 144 by 144 matrix.

PET images are then imported to the Extended Brilliance Workspace (EBW) and Syngo e.soft workstations for review and quantitative data assessment. Values of clinical relevance such as heart rate, end-diastolic volume (EDV), end-systolic volume (ESV), and left ventricular ejection fraction (LVEF) are calculated from the gated cardiac PET data.
3.2 Workstations

3.2.1 EBW and LEO

This study uses two stations to validate some of the visual results of this study. The primary workstation used for validation is the EBW mentioned earlier and the secondary workstation made by Siemens is called the Leonardo (LEO) workstation. By generating the base code first, and checking the results on both the EBW and LEO stations, one can confirm the visual results from the unregistered program with the visual output from the registered machines.

To use the EBW, one needs the DICOM files output from the PET/CT scan. By utilizing the Fusion Viewer function, one can obtain the correct gated PET images used to validate the IDL program. This validation is necessary to move forward and develop further functionality beyond just reading and displaying gated pet images using the IDL software language. Details on software development are listed in section 3.3 below.

3.3 Software development

Software development must first begin with the brainstorming stage. Prior to any personal contact with the IDL program, the anatomy of the heart, PET imaging, gated imaging, and GCI details and understanding must be acquired. By understanding the
processes in GCI, and what type of results can be expected, one can better sift through the large amount of information given by the DICOM output files when determining what information is necessary and what unnecessary information can be removed from the base code to increase computing speed. When first approaching the IDL language, one first studies example encoding files and help files, and then creates a software program that can read and display gated pet images properly and in the correct order.

3.3.1 IDL Program overview

One of the major tasks of this project requires creation of a program that can read DICOM data and properly display gated PET results correctly, organized both by slice and by frame. First, a function must be written to load the files in and select data. Next, the base structure is created, and encoded to sort the data correctly. Following sorting, the actual display must be created and resized to proper viewing size. Then, specific button functions are defined, and then the actual main interface of the program is defined. Finally, the entire program can be compiled and executed, providing the requested gated PET display.

3.3.2 IDL Program Details

This IDL program has many different and unique functions and encodings within the entire program. Due to the proprietary nature of the software, actual code cannot be
published at this time. Thus, this next section will describe the major requirements necessary within the code that should give the reader a good idea as to what has been incorporated into this particular code. In-depth description of what function each code cluster represents is detailed below. A visual representing the major functions of the program is shown below in Figure 13.

![IDL Program Workflow Diagram](image)

**Figure 13 – IDL Program Workflow**

First a function for loading files into the program was written. The code first prompted the user to pick a file path, and within this file path, the ability for both multiple file selection and a filter for just DICOM files (denoted with a .dcm after the file name) were incorporated. Next, the number of total DICOM images selected was
determined and saved for later use as a counter. Following this count, a container object for all respective DICOM tag values necessary to the program was created. A command to obtain the DICOM tag value for each DICOM image selected was created. The particular tags which indicate the number of frames, number of slices, original size of the image and pixel location, as well as the proper ordering of images via trigger time and image index were stored within this container. This allowed for all pertinent information to be made available in one location to be accessed later on in the program.

Next, all information obtained from the selected DICOM files must be stored in an area that can be accessed and organized well. A base array including the above mentioned tags for one file was created, and then the base array was replicated depending on the total number of DICOM files selected. This ensured the base array was large enough to fill with data from all PET files selected.

Subsequently, once the data was stored in one area, one had to sort the data so it could be displayed correctly in the future. Before sorting, for all the files selected by the user, each new file required a unique container to hold each unique set of DICOM data per file. Thus, for each file, a new object container was created to hold the filepath and the indicators for slice and frame that once sorted, would allow the images to display in the proper order. Afterwards, a new array was created which included the sorted data by trigger time; however the data still needed some manipulation. At first, the raw data was
presented as a string, so to prevent sorting issues the data had to be set to a numeric integer type.

After sorting by trigger time (or by frames), a new loop was required that could sort the data by slice after having been sorted by frame. Since the built-in commands within the program could only sort all data files by one criterion within a structure at one given time instead of within one select group, the second sort was more complex. Thus, after having sorted by frame, a loop that considered each image index value in the prior-sorted frame was created for the purpose of sorting by the image value within only one frame or gate. The image index value was particularly important because within each gating frame, the index values denoted the correct order of slices. By compiling a code capable of sorting both by frame and by slice, the program could obtain image data in the correct order to be used during image display.

Next, although the image data had been sorted, the new sorted image data still must be placed into a new array before its image values and corresponding pixel values can be associated with the frame and time. In a similar loop mentioned above, for each individual frame and slice, a new four variable array was required. First, all image data elements required a placeholder before data could be populated, so a new array container was created which held the x and y-value pixel values, frame, and slice number, and this array’s initial values were set to zero. Second, for all frames and corresponding slices per frame, a new object container associated with each sorted DICOM image filepath from
the prior sorted array was created. This container held the sorted pixel data corresponding with each file. Next, a new array containing both x-value and y-value pixel data was defined and all pixel values were acquired and assigned to the new array for each file in the sorted filepath.

Lastly, before ending the function to load files into the program, a resizing of the original image was required for better viewing aesthetics. This particular encoding required that the resized values must be integral multiples of the original dimension. Thus, the code was fixed so each image that was read into the program, regardless of its original size, was first changed into an integral value, and then resized by some multiple of such integral. Using this technique ensured proper resizing while allowing for any image to be properly resized despite the image’s original size. Finally, the sorted and resized array was passed out of the function back into the main program, signifying the final result of the function.

Next, a function to display the images properly was created by calling the user value labeled “widget_status” defined in the main program. This widget_status structure will be further elaborated upon in the main program after functions and events are defined. When using the IDLgrImage object (this will also be elaborated on in the main program), the data values of some images may have exceeded the range of 0 to 255, and the type of image produced may have contained discontinuities. Using a scaling
technique, all image values were set to properly scale within the range mentioned above to ensure good contrast within the image.

After major functions were defined, the program events which characterized the action to be performed when a user manipulated a widget were defined. First, user values in the widget_status structure mentioned earlier were retrieved. Next, routines which were executed when a widget event was called were created one by one depending on the number of widgets defined on the application interface. This particular program required four widgets total: one button for importing files into the program, a slider for displaying PET images by frame, another slider for displaying PET images by slice, and finally a button to exit out of the application.

The first button for importing files specified the starting working directory where files may be located. After choosing the directory for DICOM images, a pointer which called one particular user value related to loading files was called. The last command for the import button called the display function mentioned earlier.

The second button was a slider created to facilitate the switch between different frames of the gated PET images. The user value pertaining to frames was called, and the maximum value for frame count was determined by referring to the frame placeholder in the four dimensional sorted array mentioned earlier. After the frame was called, the display function was called again to ensure proper frame display.
The third button was a slider created to facilitate the switch between different slices of different frames of the gated PET images. First, the user value pertaining to slices was obtained, and the maximum value for slice count was determined by referring to the slice placeholder in the four dimensional sorted array mentioned earlier. Then, after the requested slice was called, the display function was requested to allow for proper slice display.

The final button was a program exit button used to exit the program when the user was finished. First, the event checked to see if there are still any pointers, objects, variables or elements still in use. If there were variables still in use, the variables were released from program use, and the top-level widget within a hierarchy of widgets was killed. Finally, if the user pressed the exit button, the aforementioned widget_status user value input variable was relocated, leaving the input variable undefined.

Finally after the major functions and events were defined, the main program was called. In the main program, the foundation of the interface was developed, and any major program boundaries, buttons, windows, and objects were defined. The interface was then realized, and all events were managed accordingly.

First, the screen size was obtained, and the base window width and length value was defined. To form the base graphical user interface (GUI) foundation, a base widget
was created and defined to populate any buttons in a column format. Next, a button for importing and opening files was created on the main foundation. The program then drew a window for image display on the main foundation below the import button using the base window width and length defined earlier. This window was set to use IDL object graphics instead of IDL direct graphics to let the program know graphic objects must be drawn instead of using static visualizations of direct graphics. Below the graphics window, a label was created on the foundation indicating the display contains only the transaxial plane of view. Below the label, the slider to maneuver between frames was generated, setting the size equivalent to the width of the current foundation window and requiring events be generated continuously while the slider was dragged. Likewise, after the frame slider, the slider to maneuver between slices was created on the main foundation, maintaining the same size and slider event generation requirements as the frame slider. The last of the required buttons was generated on the foundation below the slice slider as an exit button to terminate the program after the user was done viewing images.

After the required buttons were formed on the foundation interface, next to be defined were the objects which will be used in the object-oriented program. First, the color scheme for the gated PET images was created by placing a new palette of colors into an object container. Additionally, the red temperature color scheme was added to the color container to simulate a more realistic human image. Next, an atomic graphic object was created using the color palette generated earlier, and was set so one could see
through the foreground image to the background when the image was generated. Additionally, the image was set to be generated from top to bottom due to a default inversion of the DICOM image. This graphic object required a container to be placed in, so a model object container was then created to allow multiple graphical items placed inside to be rotated or scaled accordingly. This model also required a rectangular area in which graphics were drawn, and so a viewing object container was created to hold the model object, which held the palette information objects. This viewing container specified the bounds in the x and y directions of the view volume (NASA, 2007) Lastly, a container was created which held the palette object, atomic graphic object, model object, and view object in one location to facilitate grouping of IDL objects and which allowed for ease of movement or destruction of IDL objects within the container.

Finally, once the foundation interface, buttons and objects were defined, the interface must be realized before being used. Thus, the program was tasked to realize the interface and image display windows. After realizing the interface, the user value widget_status was created to define the placeholders, pointers, event handles, and buttons that would be called by the events mentioned earlier. Once this structure was defined, the program was set to store the user value to be called in specific events. Lastly, the program called an event handling procedure called XMANAGER to manage events originating from the main interface (NASA, 2007).
4. Results

4.1 Quantification

Results from gated PET trials include quantified data encompassing varying values of key parameters within the RR cycle including EDV, ESV, and LVEF values. Also, visualizations of the varying volumes throughout the cardiac cycle as well as the visual GUI program output are listed below.

In Figure 14 and Figure 15 below (and in Figure 34 through Figure 36 in Appendix A) graphical output from each gating frame in the RR cycle can be observed. On the LV volume curve shown in Figure 14 and Figure 15 below, one can see maximum and minimum values are recorded. The highest volumetric point on the volume curve (maximum value on the y-axis) denotes the greatest left ventricle volume at any point in the cardiac cycle, or EDV. The lowest volumetric point on the volume curve (minimum value on the y-axis) denotes the lowest left ventricle volume within the same cardiac cycle, or ESV.

The ejection fraction (EF) or LVEF listed on the volume curve is calculated using Equation (2) shown below.
\[
LVEF(\text{or} \ EF) = \frac{\text{Stroke Volume}}{EDV} = \frac{(EDV - ESV)}{EDV}
\] (2)

Figure 14 – [GA-N_CTAC] C-gated-FDG-01 Volume Curve
Shown in Table 2 below are values obtained from the gated PET canine test. Run 1 and 2 data are highlighted to denote a difference between experimental conditions than present in run 3, 4, and 5. Brief analysis is provided below, but detailed analysis of this experimental difference conflicts with proprietary agreements and lies beyond the scope of this project. Most noticeable is the EF value change from 26% in run 2 to 76% in run 3, denoting an induced change in patient condition. If further data analysis is required, principal investigators Dr. Michael Knopp and Dr. Jun Zhang may be contacted at The Ohio State University Wright Center of Innovation for Biomedical Imaging (WCI-BMI).
Table 2 – Reconstructed Gated PET Data

<table>
<thead>
<tr>
<th>Canine Subject gated PET Results</th>
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<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>EDV [ml]</td>
</tr>
<tr>
<td>ESV [ml]</td>
</tr>
<tr>
<td>EF [%]</td>
</tr>
</tbody>
</table>

In Table 3 below, canine values from another study state EDV ranges from 42.1-116.0 ml, ESV ranges from 15.1-63.4 ml, and LVEF ranges from 33.4-67.3% (Gueret, Meerbaum, Wyatt, Uchiyama, Lang, & Corday, 1980). The results listed in Table 3 differ slightly from Table 2, however technological advances since 1980 as well as differences in technologies, detector sensitivity, dog type, and imaging type account for such variability. Visuals for the left ventricle (LV) volume curve in Figure 14 and Figure 15 show the gating method has properly segmented the heartbeat into regions capable of analysis.

Table 3 - Cardiac Assessment Values for Canines, n=sample set (Gueret, Meerbaum, Wyatt, Uchiyama, Lang, & Corday, 1980)

<table>
<thead>
<tr>
<th>Canine (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-Diastolic Volume (EDV)</td>
</tr>
<tr>
<td>End-Systolic Volume (ESV)</td>
</tr>
<tr>
<td>Ejection Fraction (EF)</td>
</tr>
</tbody>
</table>
4.1 Visualization

The output of the main IDL program must be validated by a registered standards system before it can continue to grow. To verify the accuracy of the IDL program output with the EBW system output, three frames, each with three slices per frame, were produced and compared. Frames 1, 2, and 3 from the [GA-N_CTAC] C-02-gated-FDG-01 test were chosen, along with Slice 1, 15, and 33. In Figure 16 through Figure 18, the IDL program output of frame 1, slices 1, 15, and 33 is shown. These visually correlate with the output from the EBW machine for corresponding frame 1, slices 1, 15, and 33 shown below in Figure 19 through Figure 21. Currently, only the visual output from IDL program can be compared and validated by the EBW machine. Improvements to the program, including further data to be collected and displayed, will be discussed below in Section 5 and 6.
Figure 16 - IDL Image output, Frame 1, Slice 1
Figure 17 - IDL Image output, Frame 1, Slice 15
Figure 18 - IDL Image output, Frame 1, Slice 33
Figure 19 – EBW Output, Frame 1, Slice 1
Further comparison between IDL and EBW outputs can be seen in Appendix A, Figure 22 through Figure 33 for Frame 2 and 3, both outputting images for slices 1, 15, and 33.
5. Discussion and Conclusions

Results from this evaluation include an understanding of gated PET/CT imaging, its application towards cardiac analysis, and the development of an elementary IDL program for gated PET data analysis. In this analysis, the major products include the elementary program itself followed by an actual gated PET analysis for a canine patient. Ultimately, these two products must be improved before moving on to prolonged clinical use.

Currently, the resulting program is capable of reading and displaying gated cardiac images. The resulting images have been visually validated by the EBW workstation, but the program is still relatively basic in nature. Ultimately, the program should at least include capacity to adjust the view to show the short axis, capacity to gather more information from additional gated cardiac PET DICOM tags, capacity to display sagittal and coronal views, and ability to automatically calculate and determine EDV, ESV, LVEF, and contractility. Each of these additional properties will add to program versatility and eventually add to suite versatility if released with other software within one package. Another requirement is that the program be optimized for most efficient processor use. While the time to load each photograph varies only slightly, the initial time for image output is currently too slow for commercial use. By optimizing the
loops, syntax, and overall command execution sequence, the program will be able to produce results much quicker than possible in the original program.

Next, concerning the actual results from this study, one may recall this study utilizes data acquired from a canine patient. Traditionally, equipment for imaging is designed for human patient use. Thus, using medical imaging hardware based on a human template to image a canine introduces a large level of variation into the final product. To remedy this problem, modifications are necessary when switching between human and canine anatomy. These modifications may not yet be optimized, so resulting images may not yet properly depict the most correct information. Thus, a better understanding of the inherent differences between human and non-human imaging requirements is necessary to mitigate variation between results. To obtain a better understanding of those differences, more human clinical trial data are necessary to incorporate human imaging data into the evaluation of $^{18}$F-FDG PET agent.

Throughout this project, the principal advisors expected a scope of work involving comprehension of gated PET/CT imaging, its applications in cardiac analysis and if possible, development of an elementary IDL programming for gated cardiac PET data analysis. It was also expected that medical imaging specific concepts such as $^{18}$F-FDG, PET, CT, PET/CT, DICOM, gated PET, cardiac anatomy, IDL programming, basic knowledge of PET reconstruction, gated cardiac PET data quantification, and experience with vendor workstations would encompass the $^{18}$F-FDG PET agent evaluation.
Future Work

The IDL program which can currently read and display gated cardiac PET images has many improvements that could take place. As discussed in section 5, the software needs to be expanded based on the vendor workstation requirements and additional functionality must be included to make the program much more robust. Also, further understanding of how PET can be optimized for different patient types is necessary for PET/CT vendors. More time and data is necessary for the vendors to determine if data is acceptable or accurate using such modifications. The culmination of this individualized project satisfies the project requirements via development of an elementary IDL program ready for optimization, and comprehension of gated PET/CT imaging and how it applies to cardiac analysis. Details concerning the synthesis of this individualized project within the parent project that Dr. Michael Knopp and Dr. Jun Zhang are working on are currently proprietary.
7. References


http://depts.washington.edu/nucmed/IRL/pet_intro/intro_src/section2.html#fig5


http://academic.cuesta.edu/fjohnson/powerpoint_pdf/anatomyelectrophysiologyheart.pdf


http://www.eastpennsd.org/teacherpages/pikewil/


http://www.fda.gov/Radiation-EmittingProducts/RadiationEmittingProductsandProcedures/MedicalImaging/MedicalX-Rays/ucm115317.htm

University of Illinois at Chicago. (2011). What is medical Informatics. Retrieved June 18, 2012, from Health Informatics and Health Information Management:
http://healthinformatics.uic.edu/what-is-medical-informatics/


http://www.yalemedicalgroup.org/stw/Page.asp?PageID=STW022866
Appendix A: Additional IDL Output Files

Displayed below in Figure 22 through Figure 33 are comparisons for Frames 2 and 3, slices 1, 15, and 33, between IDL output and EBW output. Then, Figure 34 through Figure 36 depicts the remaining resulting FDG volume curves for the FDG-03, FDG-04, and FDG-05 tests.
Figure 22 – IDL Image output, Frame 2, Slice 1
Figure 23 – IDL Image output, Frame 2, Slice 15
Figure 24 – IDL Image Output, Frame 2, Slice 33
Figure 25 – IDL Image Output, Frame 3, Slice 1
Figure 26 – IDL Image Output, Frame 3, Slice 15
Figure 27 - IDL Image Output, Frame 3, Slice 33
Figure 28 – EBW Output, Frame 2, Slice 1
Figure 29 – EBW Output, Frame 2, Slice 15
Figure 30 – EBW Output, Frame 2, Slice 33
Figure 31 – EBW Output, Frame 3, Slice 1
Figure 32 – EBW Output, Frame 3, Slice 15
Figure 33 – EBW Output, Frame 3, Slice 33
Figure 34 – [GA-N_CTAC] C-gated-FDG-03 Volume Curve
Figure 35 – [GA-N_CTAC] C-gated-FDG-04 Volume Curve
Figure 36 – [GA-N_CTAC] C-gated-FDG-05 Volume Curve