Silicon Detectors for PET and SPECT

DISSERTATION

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By

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Abstract

Silicon detectors use state-of-the-art electronics to take advantage of the semiconductor properties of silicon to produce very high resolution radiation detectors. These detectors have been a fundamental part of high energy, nuclear, and astroparticle physics experiments for decades, and they hold great potential for significant gains in both PET and SPECT applications. Two separate prototype nuclear medicine imaging systems have been developed to explore this potential. Both devices take advantage of the unique properties of high resolution pixelated silicon detectors, designed and developed as part of the CIMA collaboration and built at The Ohio State University.

The first prototype is a Compton SPECT imaging system. Compton SPECT, also referred to as electronic collimation, is a fundamentally different approach to single photon imaging from standard gamma cameras. It removes the inherent coupling of spatial resolution and sensitivity in mechanically collimated systems and provides improved performance at higher energies. As a result, Compton SPECT creates opportunities for the development of new radiopharmaceuticals based on higher energy isotopes as well as opportunities to expand the use of current isotopes such as $^{131}$I due to the increased resolution and sensitivity.

The Compton SPECT prototype consists of a single high resolution silicon detector, configured in a 2D geometry, in coincidence with a standard NaI scintillator detector. Images of point sources have been taken for $^{99m}$Tc (140 keV), $^{131}$I (364 keV), and $^{124}$I (159 keV).
keV), and $^{22}$Na (511 keV), demonstrating the performance of high resolution silicon detectors in a Compton SPECT system. Filtered back projection image resolutions of 10 mm, 7.5 mm, and 6.7 mm were achieved for the three different sources respectively. The results compare well with typical SPECT resolutions of 5-15 mm and validate the claims of improved performance in Compton SPECT imaging devices at higher source energies. They also support the potential of silicon detectors to serve as the electronic collimator in these systems.

The second prototype is a high resolution PET system. By inserting a silicon PET ring inside a conventional scintillator PET ring, it has been proposed that both image resolution and system sensitivity can be increased. To investigate these claims, a partial BGO ring with clinical PET dimensions (50 cm inner diameter) has been constructed that can be used to evaluate a variety of system configurations. Initial investigations use two back-to-back high resolution silicon detectors in a 2D geometry with a small (10 cm) field of view. This configuration is used to demonstrate the potential performance of a specialized small animal imaging device for medical research applications.

Initial filtered backprojection images of a $^{22}$Na point source have shown the spatial resolution of the system to be 950 $\mu$m for the pure silicon events, 1.8 mm for the hybrid silicon-BGO events, and 7 mm for the pure BGO events. The performance is consistent with expectations and, as the first real images from this type of device, the results provide motivation to continue the investigation of the high resolution PET concept.
For my wife and parents.
I want to thank my advisors Klaus Honscheid and Harris Kagan for their guidance and support. They have lent me their wisdom and experience and given me their time and energy for the past four years. I will always keep them as role models in my career and my life. These same sentiments apply to Neal Clinthorne, who has served as a long-distance advisor and whose knowledge and expertise in nuclear medicine imaging devices have been invaluable.

I would also like to thank the members of the CIMA collaboration, who have all contributed to my dissertation work whether I have met them or not. In particular, Andrej Studen has been a great friend and colleague since I first joined the collaboration. Though we met only once, Carlos Lacasta has served as a C++ mentor through his correspondence. Sam Huh has also been a good friend and has gone out of his way on many occasions to assist me with my research.

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committed to helping me along this path.

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“AX-PET: A novel PET detector concept with full 3D reconstruction”

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Fields of Study

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Chapter 1

INTRODUCTION

Positron emission tomography (PET) and single photon emission computed tomography (SPECT) are the two fundamental imaging techniques that comprise the field of nuclear medicine. More than 16 million patients receive nuclear medicine scans each year at over 7,300 facilities nationwide [1]. Every major organ system can be imaged through nuclear medicine techniques, and there are more than 100 different imaging procedures available. These procedures are used in the diagnosis and evaluation of treatment for diseases including coronary artery disease, cancer, neurological diseases, endocrine diseases, pulmonary diseases, bone diseases, gastrointestinal diseases, and more. In addition, nuclear medicine is an important part of medical research, providing a valuable tool for the development and evaluation of new treatments.

The foundation of nuclear medicine lies in a simple concept known as the tracer principle. First developed by George de Hevesy in 1913, which earned him the Nobel Prize in Chemistry in 1943, the tracer principle is based on the observation that a radioactive nuclide is metabolized by living organisms in the same way as a stable nuclide of the same element [2]. This allows metabolic processes to be measured by introducing small amounts of radioactive substances, or tracers, into an organism and measuring the distribution of emitted radiation.

The tracer principle is not limited to elemental versions of radionuclides. In fact,
most tracers used today are chemical compounds that have been labeled, which is to say that they have had a chemical component replaced with a radionuclide. These compounds, called radiopharmaceuticals, are designed to target specific metabolic processes. A good example of this is $^{18}$F labeled fluorodeoxyglucose (FDG), used in PET imaging, which is taken up by cells at a rate proportional to glucose uptake but when it is metabolized the tracer remains trapped in the cell. Thus the concentration grows over time to reflect the rate of glucose uptake. Since tumors often have increased glucose metabolism, FDG PET scans have become a valuable tool for tumor location in cancer diagnosis and treatment.

The second basic principle of modern nuclear medicine imaging, i.e. PET and SPECT, is tomographic imaging. The most basic type of nuclear medicine imaging is planar imaging. A planar image is a projection of the source distribution into a 2D image from a single perspective, showing a flattened image through the object similar to a simple X-ray image. Many of these 2D projection images can be combined through a process called image reconstruction to form a 3D data set. Tomography (literally “slice drawing” in Greek) is the presentation of this 3D data as 2D cross sectional slices so that it can be easily visualized. With modern computing, cross sections at any angle through any portion of the data can be presented, although there are standard perspectives used in most applications.

1.1 Principles of SPECT

Single photon emission computed tomography (SPECT) utilizes radioactive isotopes that undergo a type of radioactive decay which leaves the nucleus in an excited state leading to the emission of a photon, in this context commonly called a gamma ray. The gamma rays are then detected by a device known as a gamma camera, which consists of a position sensitive radiation detector combined with a mechanical aperture known
as a collimator. Images acquired by a standard gamma camera are 2D planar images of the source distribution, similar to a simple X-ray image. The most basic SPECT imaging systems employ a gamma camera mounted on a gantry which is rotated around the patient to acquire 2D images from multiple angles. The 2D data from these images, or projections, are then combined through a tomographic reconstruction algorithm to produce a 3D data set of the source distribution.

SPECT is most frequently used for cardiac perfusion studies, which show the blood flow to areas of the heart, and provide information for the treatment of coronary artery disease and the assessment of cardiac muscle damage following a heart attack. It is also used for cerebral perfusion studies which have applications for a variety of medical conditions from psychiatric disorders and dementia to seizure disorders and cerebrovascular disease. Like most medical imaging techniques, SPECT also has many applications in oncology. Due to the low cost and versatility of the devices and more importantly the relative low cost and convenience of the isotopes used, SPECT imaging will continue to be an important medical imaging technique for the foreseeable future.

1.1.1 Collimation

In order to reconstruct images from single photon data, both an interaction position and information about the direction a photon came from must be acquired. Standard SPECT systems use a mechanical *collimator* to obtain this information. The easiest form of mechanical collimator to understand is a parallel hole collimator. A simple parallel hole collimator is nothing more than a thick slab of lead with many small holes drilled through it. A radiation detector positioned behind the collimator counts the photons that come through each hole. The number of photons detected from each hole represent a line integral of the source distribution along the line extending
from the detector back through the hole. All of these line integrals combine to form the projection image at a given angle, and many projections at different angles are combined to form a SPECT image.

There are many limitations to mechanical collimation. First and foremost is the inherent coupling of image resolution and sensitivity \[3\]. Simply put, the easiest way to increase image resolution is to decrease the size of the holes in a collimator but then less photons get through leading to a corresponding decrease in sensitivity. Collimator design has been optimized over decades to provide the best tradeoff possible and as a result modern SPECT imaging systems are essentially at the limit that mechanical collimation will allow. In addition, high energy photons penetrate matter more easily and as a result mechanically collimated systems experience reduced performance as the photon energy increases.

1.2 Principles of PET

Positron emission tomography (PET) is a type of nuclear medicine imaging that utilizes radioisotopes that undergo \textit{beta plus} ($\beta^+$) decay, which is characterized by the emission of a positron. The positron travels a short distance until it slows almost to rest and annihilates with an atomic electron, causing two 511 keV photons to be emitted in opposite directions in the rest frame of the annihilation. These back-to-back photons are then detected nearly simultaneously in a ring of radiation detectors. The positions of the interactions of the two photons in the detector ring determines a \textit{line of response} (LOR) which is the line along which the positron-electron annihilation event occurred. Many of these events are combined to form an image of the tracer distribution in the patient.

PET produces high resolution functional images of metabolic processes in the body. The most common radiotracer in PET imaging is $^{18}$F-labeled fluorodeoxyglu-
cose ($^{18}$F-FDG, or just FDG). FDG is metabolized as glucose in the body, so the
distribution of the tracer gives an indication of regional metabolic uptake of glucose.
The primary application of FDG is in clinical oncology, where it is used for the detec-
tion of tumors and metastases to aid in diagnosis as well as treatment planning and
monitoring. PET also finds applications in cardiac perfusion studies and in neurology,
including early diagnosis of Alzheimer’s disease.

Image resolution and sensitivity are generally much higher in PET than in SPECT.
The primary reason SPECT is more common is the higher cost of PET tracer pro-
duction, as well as the higher cost of PET systems. Despite the increased cost, the
number of PET systems in the U.S. has been increasing steadily for the past decade
and it is likely to continue as PET continues to become an essential diagnostic tool,
especially in oncology.

1.2.1 Positron Range

When a positron is emitted from a nucleus in beta decay, it has an initial kinetic
energy. Depending on the radionuclide, this kinetic energy can be enough that the
positron can travel a few millimeters before annihilating with an atomic electron.
The distance the positron travels before annihilating is called the positron range and
can degrade the resolution of PET images. Positron range is a factor for certain
specialized high resolution devices, such as dedicated small animal PET scanners,
and so methods to minimize its effect have been proposed including positron range
correction algorithms for image reconstruction and the use of magnetic fields [4, 5].

1.2.2 Photon Acollinearity

When the positron reaches the end of its range and finally annihilates with an atomic
electron, the two photons are not emitted at exactly 180 degrees from one another.
This is because the atomic electron has a non negligible momentum and so in order to conserve momentum the two photons will be emitted with a small variation in the angle between them. The variation in this angle will depend on the distribution of atomic electron momentums in the medium. For annihilation events in water, the acollinearity angle is a Gaussian distribution that has been measured to degrade the position resolution by 0.5 mm FWHM (full width at half maximum) for a standard full body PET scanner [6]. This effect is highly dependent on the radius of the PET scanner.

1.2.3 Timing Resolution

Unlike SPECT, which uses a mechanical collimator to determine its projections, PET uses the LORs in conjunction with the near simultaneous arrival of the annihilation photons to form projections. A PET system will have a coincidence window which sets the maximum time allowed between detected photons to accept an event. Good system timing allows this window to be small which reduces the noise caused by random events and also increases the rate the system can operate at effectively, improving image quality and reducing acquisition time. Thus the performance of a PET system is highly dependent on good timing resolution and most clinical PET systems have coincidence windows <5 ns.

1.3 Image Reconstruction

Tomography presents 3D data sets as 2D cross-sectional images. Image reconstruction is the process of creating these 3D data sets from projection images. The most basic image reconstructions produce a set of 2D images that are stacked together to form the 3D data set. These 2D images, or slices, are formed from a set of projection data.
taken at multiple angles $\phi$ around the object. The goal of the image reconstruction is to use the projections to form an estimate $\hat{f}(x, y)$ of the true source distribution $f(x, y)$ through the projection slice.

Each point of projection data can be thought of as a line integral along a line at angle $\phi$ that has a minimum distance $r$ from the center of the field of view (FOV). In real data, the value of this line integral is represented by the number of photons detected in the line determined by the corresponding detector element. Such a line is known as a line of response (LOR). A full set of projection data for a single slice is represented by a 2D histogram $p(r, \phi)$ of the values in each LOR binned by the variable $r$ and $\phi$ described above. A point source will appear as a sin curve in this histogram, so $p(r, \phi)$ is referred to as a sinogram.

The simplest way to reconstruct an image from sinogram is a simple backprojection. Essentially, for each LOR of the projection $p(r, \phi)$ the counts are divided among the pixels weighted by the amount the LOR overlaps that pixel. The sum over all LORs forms an estimate of the source distribution $\hat{f}(x, y)$. The backprojection of the projection data $p(r, \phi)$ into the source distribution estimate $\hat{f}(x, y)$ is represented mathematically as,

$$\hat{f}(x, y) = \frac{1}{N} \sum_{i=1}^{N} p(r_i, \phi_i),$$

(1.1)

where $r_i = x \cos \phi_i + y \sin \phi_i$. Simple backprojection produces poor quality images that suffer from the fact that the sampling is higher at lower spatial frequencies. The effect is observable in reconstructed images as a radial “blurring” of the images. This phenomenon is known as $1/r$ blurring and can be understood through the examination of the Fourier slice theorem, introduced in the next section. Due to this limitation of simple backprojection, more sophisticated reconstruction methods are used.
Reconstruction methods fall into two basic categories: analytical and iterative. Analytical methods, such as simple backprojection, are based on a set of mathematical and geometric assumptions and produce estimates of the source distribution that do not account for factors such as detector resolution. Iterative methods perform a series of estimates of the source distribution and attempt to improve each estimate based on the previous iteration. Factors such as detector resolution, photon attenuation, and positron range can be modeled in the method and corrections made to reduce their effects.

Depending on the application, analytical methods can be adequate and they are computationally fast, so they are still used frequently. Iterative reconstruction methods are computationally intensive, so they have become more popular as computing resources have improved. The most common analytical method, known as filtered backprojection, and the most common iterative method, known as maximum likelihood expectation maximization (MLEM), are presented here.

### 1.3.1 Filtered Backprojection

The key to the filtered backprojection algorithm is the *Fourier transform* (FT). In simple terms, a spatially varying function $f(x)$ can be represented as a summation of sine and cosine functions of different spatial frequencies $k$. This representation is known as the Fourier transform $F(k)$ of the function $f(x)$ and the computation of the Fourier transform is represented by,

$$F(k) = \mathcal{F}[f(x)]. \quad (1.2)$$

The FT is often referred to as the representation of $f(x)$ in *spatial frequency space*, or simply *k-space*, while in the context of image reconstruction the image of a source distribution is said to be in *image space* and the projection data in *projection space*.
Fourier transforms can be extended to 2D functions as well, with the FT of a 2D function given by,

$$F(k_x, k_y) = \mathcal{F}[f(x, y)],$$  \hspace{1cm} (1.3)

where $k_x$ and $k_y$ are orthogonal axes in k-space. In addition, the function in image space of a FT can be obtain through the inverse Fourier transform,

$$f(x, y) = \mathcal{F}^{-1}[F(k_x, k_y)].$$  \hspace{1cm} (1.4)

The Fourier transform becomes useful for image reconstruction in nuclear medicine by the application of the *Fourier slice theorem* which states that the FT of a 2D object along the projection angle $\phi$ is equal to the value of the FT of the object taken along a slice through the origin in k-space at the same angle $\phi$ [7]. This theorem tells us that the FT of projection data $p(r, \phi)$ can be represented as,

$$F(k_r, \phi) = \mathcal{F}[p(r, \phi)],$$  \hspace{1cm} (1.5)

where $F(k_r, \phi)$ is the value of the FT of the image at radial distance $k_r$ and angle $\phi$. The projection slice theorem thus provides the means to obtain the 2D k-space representation of an object from the projection data and reveals the origin of “$l/r$ blurring” as the sampling of the spatial frequencies falls off as $1/r$ in k-space.

Now, the steps to perform the FBP reconstruction of an image proceed as follows. First, acquire the projection data $p(r, \phi)$. Second, calculate the FT $F(k_r, \phi)$ of the projection data. Multiply the FT by a *ramp filter*, which simply scales the FT by $k_r$,

$$\hat{F}(k_r, \phi) = |k_r|F(k_r, \phi).$$  \hspace{1cm} (1.6)

Next, calculate the inverse FT of the filtered FT projections to obtain a set of filtered
projection data \( \hat{p}(r, \phi) \),

\[
\hat{p}(r, \phi) = \mathcal{F}^{-1}[\hat{F}(k_r, \phi)] = \mathcal{F}^{-1}[|k_r|F(k_r, \phi)].
\]  

Finally, perform a simple backprojection from the filtered projections,

\[
f(x, y) = \frac{1}{N} \sum_{i=1}^{N} \hat{p}(r_i, \phi_i).
\]  

For noiseless projections of a 2D image (i.e. computed projections of static images rather than measured data from real objects) and sufficient sampling, FBP reconstruction is capable of completely reproducing the original image. For real data containing noise, however, artifacts will appear in the reconstructed image. Still, due to its fast computation times and good quality images, filtered backprojection continues to play an important role in nuclear medicine imaging.

### 1.3.2 The MLEM Algorithm

The MLEM method was first proposed in 1977 as a general prescription for developing algorithms for maximum likelihood estimation problems [8]. Shepp and Vardi were the first to use the MLEM method to adapt an algorithm for emission tomography in 1982 [9]. The MLEM algorithm for emission tomography is given by the iterative expression [10],

\[
\hat{f}_{j}^{n+1} = \sum_{j'} \hat{f}_{j'}^{n} \sum_{i} h_{ij} \sum_{k} g_{i} \hat{f}_{k}^{n}.
\]  

Here, \( \hat{f}_{j}^{n+1} \) is the new image iteration, \( \hat{f}_{j}^{n} \) is the previous image iteration, \( g_{i} \) is the measured projection data, and \( h_{ij} \) is the system matrix. The basic idea is that each progressive image iteration will be compared to the measured projection data to determine the source distribution that most probably created the measured data.
The system matrix, \( h_{ij} \), contains information on the system geometry and can also be constructed to include various system properties, such as resolution or photon attenuation, that it is desirable to make corrections for.

The process can be broken into steps. First, the projection data \( g_i \) is acquired. Then the initial image estimate (which can in principle be any random image from a constant background to an FBP of the projection data) is forward projected by the system matrix to produce an estimated set of projection data \( \hat{g}_i^n \),

\[
\hat{g}_i^n = \sum_k h_{ik} \hat{f}_k^n. \tag{1.10}
\]

Forward projection is the inverse operation of backprojection, in other words the formation of projection data from a source distribution.

Measured projection data is then divided by the estimated projection data on a pixel-by-pixel basis and backprojected by the system matrix to form a new image estimate, which is divided by the sum of the system matrix to form a correction factor \( C_j^n \),

\[
C_j^n = \frac{1}{\sum_i h_{ij} \hat{f}_i^n} \sum_i h_{ij} \frac{g_i}{\hat{g}_i^n}. \tag{1.11}
\]

This correction factor is then multiplied by the current image estimate \( \hat{f}_j^n \) to achieve the new image estimate \( \hat{f}_j^{n+1} \),

\[
\hat{f}_j^{n+1} = \hat{f}_j^n C_j^n. \tag{1.12}
\]

The iterations are repeated until a desired level of convergence is attained. Since successive iterations introduce additional variation in the images, noise in the images increases with each iteration. For this reason, the algorithm is stopped short of full convergence in most practical applications.
1.4 Overview of Dissertation

As diagnostic and research tools, there is a constant motivation to improve the technology of PET and SPECT. Since radiation detection is a fundamental part of PET and SPECT, it is natural that advances in radiation detector technology can produce significant gains in nuclear medicine imaging. Semiconductor-based radiation detectors present just such an opportunity.

This dissertation details two separate prototype nuclear medicine imaging devices designed to demonstrate potential applications for high resolution silicon detectors in PET and SPECT. The detectors used in these prototypes are high resolution pixelated silicon detectors, designed and developed for nuclear medicine applications as part of the CIMA collaboration and built at The Ohio State University.

The current chapter has served as a basic introduction to nuclear medicine, PET and SPECT in particular, and image reconstruction. It is by no means exhaustive, but gives an overview of concepts central to the remainder of the dissertation. Chapter 2 is a short review of some of the basic physics that underlies PET and SPECT, including: the modes of radioactive decay and common radionuclides utilized in PET and SPECT as well as the interactions of photons, electrons, and positrons with matter. Chapter 3 contains a discussion of silicon detector design and operation with details of the detectors used in this investigation.

Chapter 4 is a discussion of the construction and results of a prototype SPECT system. The system is based on the Compton imaging principle which removes the mechanical collimator of a standard SPECT device and replaces it with a high resolution detector. This potentially allows a Compton SPECT device to achieve higher sensitivity than a mechanically collimated device for a given image resolution, which in turn can reduce imaging times and patient doses. It should also provide higher resolution images for high energy sources, which is the property the current system
was designed to demonstrate. A more detailed explanation of the Compton imaging principle and the potential advantages it has over mechanical collimation, as well as the motivations for using silicon detectors in a Compton SPECT system, is included in the chapter.

Chapter 5 gives the details of a high resolution PET prototype based on the concept of concentric silicon and scintillator PET detector rings. Silicon detectors can provide high spatial resolution which in turn can provide high resolution PET images, however the efficiency of silicon is low compared to scintillator materials. In order to gain the benefits of both the high spatial resolution of silicon detectors and the high efficiency of scintillator detectors, the concept of placing a silicon detector ring inside of a conventional PET ring was proposed. A test bed for investigating many potential configurations of such a system has been built and initial results of a configuration that could be used for the design of a small animal PET scanner are presented in the chapter. This prototype also provides the first images showing the potential of high resolution silicon detectors used in combination with a conventional PET scanner to provide high resolution images in a small field of view, acting effectively like a “magnifier.” A probe designed for such applications will be the subject of further investigations using this system.

The final chapter draws conclusions from the investigations of the two prototypes, both on the performance of the prototypes as well as the performance of the silicon detectors in the prototype systems. It also contains general discussions about potential future endeavors in silicon detectors for PET and SPECT.
The fundamental physical processes that form the foundation of nuclear medicine can be summarized as: radioactive decay and the interaction of radiation with matter. Radioactive decay is the process that an unstable nucleus undergoes in order to release energy and drop to a more stable state. It is the energy, or radiation, released in this process that can be detected and used to reconstruct images of the source distribution of the radioactive tracer. The interaction of this radiation with matter is what allows the radiation to be detected.

For nuclear medicine applications, the most relevant decay modes are $\beta^+/\beta^-$ decay, electron capture (EC), $\gamma$ decay, isomeric transitions (IT), and internal conversion (IC). The radiation released by these decays is in the form of photons, electrons, and positrons. Thus it is the interactions of these three particles in matter that are of greatest interest in nuclear medicine.

2.1 Radionuclides for Nuclear Medicine

Naturally occurring radionuclides are generally too long lived to be of use in nuclear medicine. This is due to the fact that all short-lived radionuclides in nature have decayed long ago. As a result, all radionuclides used in modern nuclear medicine are
<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Decay Mode</th>
<th>Principle Photon Energies (keV)</th>
<th>Half-Life</th>
<th>Primary Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C</td>
<td>$\beta^+$</td>
<td>511</td>
<td>20.3 min</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>$\beta^+$</td>
<td>511</td>
<td>10.0 min</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>$\beta^+$</td>
<td>511</td>
<td>2.07 min</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>$\beta^+$</td>
<td>511</td>
<td>110 min</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{32}$P</td>
<td>$\beta^-$</td>
<td>–</td>
<td>14.3 days</td>
<td>Therapy</td>
</tr>
<tr>
<td>$^{67}$Ga</td>
<td>EC</td>
<td>93, 185, 300</td>
<td>3.26 days</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{82}$Rb</td>
<td>$\beta^+$</td>
<td>511</td>
<td>1.25 min</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{89}$Sr</td>
<td>$\beta^-$</td>
<td>–</td>
<td>50.5 days</td>
<td>Therapy</td>
</tr>
<tr>
<td>$^{99m}$Tc</td>
<td>IT</td>
<td>140</td>
<td>6.03 hrs</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{111}$In</td>
<td>EC</td>
<td>172, 247</td>
<td>2.81 days</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{123}$I</td>
<td>EC</td>
<td>159</td>
<td>13.0 hrs</td>
<td>Imaging</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>$\beta^-$</td>
<td>364</td>
<td>8.06 days</td>
<td>Imaging/Therapy</td>
</tr>
<tr>
<td>$^{153}$Sm</td>
<td>$\beta^-$</td>
<td>41, 103</td>
<td>46.7 hrs</td>
<td>Therapy</td>
</tr>
<tr>
<td>$^{186}$Re</td>
<td>$\beta^-$</td>
<td>137</td>
<td>3.8 days</td>
<td>Therapy</td>
</tr>
<tr>
<td>$^{201}$Tl</td>
<td>EC</td>
<td>68-80 X-rays</td>
<td>3.05 days</td>
<td>Imaging</td>
</tr>
</tbody>
</table>

Table 2.1: Summary of the physical properties of important radionuclides for nuclear medicine applications. (EC: electron capture, IT: isomeric transition.)

artificially produced either by nuclear fission reactors or particle accelerators. Table 2.1 lists many radionuclides important to nuclear medicine. The properties of the radionuclides in this table will be explained below.

Radionuclides for imaging applications are chosen for their characteristic radiation emissions. The desirable emissions are photons in the range of $\sim 70$ keV to 511 keV. A nucleus in an excited state can spontaneously emit a photon, historically referred to as a *gamma ray* in this context, and therefore this type of decay is generally known as *gamma decay* ($\gamma$ decay). An excited nucleus will typically have a very short half-life, so radionuclides used in nuclear medicine typically undergo another type of decay.
with a longer half-life first which leaves the nucleus in an excited state leading to \( \gamma \) decay. This can occur after \( \beta^{+/-} \) decay or electron capture. \( \beta^{+/-} \) decay is the emission of a positron/electron respectively, while electron capture is the absorption of an atomic electron into the nucleus.

\( \beta^- \) decay occurs when a neutron decays to a proton, emitting an electron and anti-neutrino along with excess energy in the process,

\[
    n \rightarrow p + e^- + \bar{\nu}_e + \text{energy}.
\] (2.1)

The emitted electron has limited imaging applications since it is not likely to escape the patient. It does have applications in therapy and for intraoperative imaging with beta probes (small detector systems designed to get close to the source during surgery to detect beta particles). The \( \beta^- \) decay can leave the nucleus in an excited state leading to \( \gamma \) decay, and this mode is referred to as \((\beta^-, \gamma)\) decay. \(^{131}\)I is the most commonly used example of \((\beta^-, \gamma)\) decay and it has both therapeutic and imaging applications.

\( \beta^+ \) decay, also known as positron emission, is the opposite of \( \beta^- \) decay, occurring when a proton is converted to a neutron, emitting a positron and neutrino in the process,

\[
    \text{energy} + p \rightarrow n + e^+ + \nu_e.
\] (2.2)

Because the rest mass of the neutron is greater than the proton, additional energy must be provided by the difference in binding energies of the nucleus before and after decay for \( \beta^+ \) decay to occur. As discussed in Section 1.2 the positron produced by beta decay will travel a few millimeters before annihilating and producing two 511 keV photons which are used for PET imaging. The most commonly used positron emitter is \(^{18}\)F, but many others can be seen in Table 2.1. Like \( \beta^- \) decay, positron
emission can be followed by $\gamma$ emission, though this is not currently utilized in nuclear medicine imaging since positron emitters are typically produced specifically for their PET applications.

Electron capture is a related process to $\beta^+$ decay. In electron capture, an inner shell electron is captured by the nucleus, converting a proton into a neutron and emitting a neutrino,

$$energy + p + e^- \rightarrow n + \nu_e.$$  \hfill (2.3)

Like positron emission, this process requires some energy from the nuclear transition to occur. The vacancy in the shell caused by EC can lead to the emission of characteristic X-rays that can be used in imaging, as in the case of $^{201}$Tl. EC can also leave the nucleus in an excited state, leading to (EC, $\gamma$) decay which is utilized in $^{111}$In and $^{123}$I.

Finally, there are metastable excited states that are differentiated from normal excited states for nuclei only in that they have a longer than usual half-life. The decay of one of these metastable states through the emission of a $\gamma$ ray is called an isomeric transition. IT is always accompanied by a chance for internal conversion in which the energy of the excited nucleus is transferred to an orbital electron instead of a $\gamma$ ray. The most widely used tracer, $^{99m}$Tc is a metastable nuclide that undergoes isomeric transition.

### 2.2 Photon Interactions

Detection of photons through their interactions with matter is the primary function of almost all nuclear medicine imaging devices. The basic interactions of photons with matter are: photoelectric absorption, coherent (Rayleigh) scattering, Compton scattering, and pair production. For the energies relevant to nuclear medicine imaging
(\sim 30 \text{ keV to } 511 \text{ keV}), only Compton scattering and photoelectric absorption are significant.

Pair production is not a significant factor for any nuclear medicine imaging device because it can only occur for photon energies above \(1022 \text{ keV} \) (i.e. \(2m_e\)). Rayleigh scattering is not a major factor in imaging applications either because the extremely low amounts of energy transferred in the process are typically below the minimum energy threshold of the detectors. Photoelectric absorption is the dominant effect in many high atomic number (\(Z\)) detector materials used in nuclear medicine, and is the dominant effect in all materials at lower energies. Compton scattering is a comparatively larger factor in low \(Z\) materials, and becomes more significant in high \(Z\) materials at the upper energy range.

2.2.1 Photoelectric Absorption

In photoelectric absorption, an incident photon is completely absorbed by an electron, freeing the electron from its bound state. In contrast to Compton scattering, photo absorption typically involves a tightly bound atomic electron. Thus the energy of the freed electron is \(E_e = E_\gamma - E_b\) where \(E_b\) is the binding energy of the electron before absorption. As electrons shift within the atomic shells to fill the vacancy left by the freed electrons, characteristic X-rays or additional electrons (known as Auger electrons) are emitted and subsequently collected by the detector such that the total initial photon energy is usually collected. The exception occurs when a characteristic X-ray is sufficiently energetic to escape the detector, in which case an \textit{escape peak} will be detected at an energy of \(E_\gamma - E_b\).

The cross section for photoelectric absorption does not have a single analytical expression over all ranges of \(Z\) and \(E\), but the dependence on atomic number \(Z\) and
incident photon energy $E_\gamma$ is approximately $[11]$, 

$$\sigma \propto \frac{Z^n}{E_\gamma^{3.5}},$$  \hspace{1cm} (2.4)

where the exponent $n$ varies between 4 and 5 depending on the value of $E_\gamma$.

### 2.2.2 Compton Scattering

Compton scattering occurs when a photon interacts with an electron, imparting some of the photon’s energy to the electron and changing the direction of motion of the photon. Compton scattering is most likely to involve loosely bound valence electrons, and thus the electron is generally treated as though it starts at rest. The wavelength of the photon before and after scattering is related to the angle of scattering by,

$$\lambda' - \lambda = \frac{h}{m_e c} (1 - \cos \theta).$$  \hspace{1cm} (2.5)

This relationship was first discovered by Arthur H. Compton in 1923 $[12, 13]$.

In 1929, Klein and Nishina derived a relativistic expression for the differential Compton scattering cross section $[14]$,

$$\frac{d\sigma}{d\Omega} = \frac{Z^2}{2} \frac{r_e^2}{\alpha (1 - \cos \theta)} \left(1 + \cos^2 \theta + \frac{\alpha^2 (1 - \cos \theta)^2}{[1 + \alpha (1 - \cos \theta)]}ight)^2,$$  \hspace{1cm} (2.6)

where $\alpha = E_\gamma/m_e c^2$ and $r_e \equiv e^2/m_e c^2 = 2.82 \times 10^{-13}$ cm is the classical electron radius. Integrating this over the solid angle yields the Compton scattering cross section, also known as the Klein-Nishina cross section,

$$\sigma = 2\pi Z r_e^2 \left[\frac{1 + \alpha}{\alpha^2} \left(2 - \frac{1 + 2\alpha}{1 + 2\alpha} - \frac{1}{\alpha} \ln(1 + 2\alpha)\right) + \frac{1}{2\alpha} \ln(1 + 2\alpha) - \frac{1 + 3\alpha}{(1 + 2\alpha)^2}\right],$$  \hspace{1cm} (2.7)

which is a function of the incident photon energy $E_\gamma$ and the atomic number $Z$ of the material.

Equations (2.5) and (2.7) assume that the initial electron is at rest when in fact the
electron will have some initial momentum. For a given initial photon energy, the uncertainty in the initial momentum of the electron causes there to be a distribution of possible final photon energies for each scattering angle. This effect is known as Doppler broadening and is discussed in more detail in Section 4.3.3.

2.2.3 Attenuation

The mass attenuation coefficient $\mu$, which gives the probability of scattering per unit mass of the target, is related to the interaction cross section by,

$$\mu = \frac{N_A}{A} \sigma,$$  \hspace{1cm} (2.8)

with $N_A$ representing Avogadro’s number and $A$ the atomic mass of the target. The total mass attenuation coefficient (neglecting coherent scattering) for a material can be thought of as the sum of components due to photoelectric absorption ($\mu_{pe}$), Compton scattering ($\mu_{cs}$), and pair production ($\mu_{pp}$),

$$\mu = \mu_{pe} + \mu_{cs} + \mu_{pp}.$$  \hspace{1cm} (2.9)

As discussed previously, photoelectric absorption varies as $\sim Z^4/E^{3.5}$ and so will be the dominant interaction in all materials at low energies and is much more significant in high Z materials. The Compton scattering cross section decreases slowly with increasing $Z$ and has a small variation in $E$ over the nuclear imaging energy range, which makes it more significant for low Z materials and at the upper end of the energy range (i.e. where photoelectric absorption is small). The contribution from pair production is zero below 1022 keV, and increases with atomic number and photon energy as $\sim Z \ln E$, making it the dominant effect at high energies but not relevant to nuclear imaging.
2.3 Electron and Positron Interactions

Electrons and positrons are not generally detected directly in nuclear medicine imaging applications because their range in matter is limited to a few mm for the energies relevant to nuclear medicine. Still, the interactions of electrons and positrons are important for a number of reasons. In PET imaging, the positron range can limit the image resolution. In semiconductors, the range of the recoil electron from photo-electric absorption or Compton scattering can place a limit on the intrinsic detector resolution. For all applications, electrons and positrons produced in the nuclear decay process can have a significant effect on the total radiation dose the patient receives.

Electrons and positrons have identical mass and equal but opposite charge. As a result, they experience essentially the same interactions as they pass through matter. The differences are due to the incident electron being indistinguishable from the electrons it interacts with and the effects are minor in nuclear medicine applications. One notable exception is that positrons will annihilate with atomic electrons near the end of their path, which is of course the basis for PET. In general, electrons and positrons will scatter through matter in a random zig-zag path, losing energy continuously as they go with infrequent large energy losses due to large angle collisions with atomic electrons.

Positrons in nuclear medicine result from beta decay while electrons can come from nuclear emission or the ejection of atomic electrons in high energy collisions. For the relevant energy range (10 keV to 1 MeV), the deflections in particle trajectory are due mainly to elastic interactions with atomic nuclei, with rare large angle collisions with atomic electrons, while energy loss is due primarily to interactions with atomic electrons, with minor losses due to bremsstrahlung (German for “breaking radiation”).
2.3.1 Bremsstrahlung

Bremsstrahlung is radiation emitted by a charged particle as it is decelerated and deflected under the influence of the electric field produced by atomic nuclei. The cross section for bremsstrahlung $\sigma_b$ increases with higher Coulomb field strength, and thus higher atomic number $Z$ of the medium, as well as the proximity of the particle to the nucleus. It varies approximately as,

$$\sigma_b \sim Z^2 r_e^2 f(E)$$  \hspace{1cm} (2.10)

where $r_e$ is the classical electron radius, and $f(E)$ is a strongly increasing function of the initial particle energy. The resulting average energy loss per unit length is given by,

$$\left( - \frac{dE}{dx} \right)_b \sim NE\sigma_b$$ \hspace{1cm} (2.11)

where $N = \rho N_A/A$ is the atomic density of the material ($\rho$ is the density, $N_A$ is Avogadro’s number, and $A$ is the atomic mass). The energy loss due to bremsstrahlung is dominant for electrons and positrons at high energies, but it is only a minor contribution at nuclear medicine imaging energies.

2.3.2 The Bethe Equation

Most of the energy lost by charge particles in matter is due to inelastic collisions with atomic electrons. Collisions are classified as hard if they result in ionization or soft if they result in atomic excitation. Soft collisions are more likely than hard and this ratio is mostly independent of the initial energy of the incident particle. Similarly, the average energy transferred per collision is largely independent of initial energy as well. The average energy transferred is typically small and the number of atomic
electrons encountered very high, thus these collisions are generally characterized by a continuous energy loss. Because electrons and positrons have the same mass as the atomic electrons, however, they can also experience significant energy loss and large angles of deflection from a single interaction.

Electrons and positrons can emit radiation as they travel through matter in the form of Cerenkov radiation. Cerenkov radiation occurs when a charged particle travels faster than the speed of light in a medium. Radiation is emitted in a cone behind the particle forming an electromagnetic “shock wave” of polarized light.

The average energy lost per unit distance by electrons and positrons from inelastic collisions with atomic electrons and from Cerenkov radiation is given by the Bethe equation \([11]\),

\[
\frac{dE}{dx} = 4\pi r_e^2 \frac{m_e c^2}{\beta^2} N Z (A + B),
\]

where

\[
A = \ln \frac{\beta \gamma \sqrt{\gamma - 1} mc^2}{I},
\]

and

\[
B = \frac{1}{2 \gamma^2} \left[ \frac{(\gamma - 1)^3}{8} + 1 - (2\gamma^2 + 2\gamma - 1) \ln 2 \right].
\]

Here \(r_e\) is the classical electron radius, \(\gamma = (1 - \beta)^{-1/2}\), \(\beta = v/c\), \(N = \rho N_A / A\) is the atomic number density (\(\rho\) is the density, \(N_A\) is Avogadro’s number, and \(A\) is the atomic mass), \(Z\) the atomic number, and \(I\) is the mean excitation potential of the medium in eV.

Figure 2.1(a) shows the energy loss of electrons per unit length \(dE/dx\) as a function of energy due to inelastic collisions and bremsstrahlung in lead and water. It is apparent from the plot that bremsstrahlung is a minor factor for nuclear medicine.
Figure 2.1: (a) Energy loss per unit length $dE/dx$ for beta particles as a function of kinetic energy due to inelastic collisions and Bremsstrahlung radiation in water and lead. (b) $dE/dx$ as a function of penetration depth (exhibiting the characteristic Bragg peak). Images from [15].

imaging applications. The graph also shows that the energy loss due to inelastic collisions increases at lower energies. This leads to a greater fraction of the particle’s energy being deposited towards the end of its path, as can be seen in Figure 2.1(b) which shows $dE/dx$ as a function of penetration depth for electrons. The characteristic peak in this curve is known as the Bragg peak and is exploited in external beam radiation therapy using heavy charged particles.

There are some details of the Bethe formula that are worth pointing out. The values for the mean excitation potentials are obtained from tabulated values [16]. Equation 2.14 actually has a slightly different form for electrons and positrons due to the incident electrons and atomic electrons being indistinguishable particles. The difference has no effect on the overall behavior of the energy loss, but is a small effect that is typically included in detailed Monte Carlo simulations. In addition, the Bethe formula in Equation 2.12 neglects the interaction of the electric fields between atoms that is significant in liquids and solids. Thus a density correction must be made to the Bethe formula to account for a net reduction in the electric field that occurs in
dense materials \cite{17, 18}. The overall result is a weakening of the effective electric field seen by the incident particle, so that the energy loss in dense materials is less than what is predicted by the uncorrected Bethe formula and the effect is strongest for highly relativistic particles.

2.3.3 Knock-on Electrons

As already discussed, hard inelastic collisions result in ionization. The escaped electron can have enough energy to cause ionizations on its own, in which case it is referred to as a knock-on electron or delta ray. An approximation of the probability per unit length for an incident electron or positron with $\beta = v/c$ to cause the emission of a knock-on electron with energy $E_\delta$ is given by \cite{15},

$$P(E_\delta) = \frac{2\pi r_e^2 m_e N}{\beta^2} \frac{1}{E_\delta^2}, \quad (2.15)$$

where $N$ is the electron density of the medium. The average number of knock-on electrons $N_\delta$ created with energy greater than $\epsilon$ per unit length is then given by,

$$N_\delta(E_\delta > \epsilon) = \frac{2\pi r_e^2 m_e N}{\beta^2} \frac{1}{\epsilon}. \quad (2.16)$$

The production of knock-on electrons contributes to the spread of the energy deposited by the particle over a diffuse “cloud” around the initial particle track.

2.3.4 Molière’s Theory of Multiple Scattering

Electrons and positrons will interact with the Coulomb forces of atomic nuclei as they travel through matter. The much larger mass of the nuclei dictates that these Coulomb collisions will be elastic, however the deflection of the incident particle will still be significant. Electrons and positrons often experience multiple elastic scattering events and these events are the primary cause for the zig-zag path of electrons and
positrons through matter. Thus while multiple Coulomb collisions will not result in significant energy loss, they can have an important impact on the range of the particles.

Molière’s theory of multiple scattering, as described by Bethe, provides an accurate model for electrons and positrons in the energy range relevant to nuclear medicine imaging [19]. For cases where the expected number of independent collisions with atomic nuclei is greater than 20, the probability for an incident electron or positron with momentum $p$ and velocity $v$ to be scattered by angle $\theta$ after traveling through thickness $t$ of a material with atomic number $Z$ and atomic density $N$ is given by [15],

$$f(\theta)d\theta = \lambda d\lambda \int_0^{\infty} ydy J_0(\lambda y) \exp \left[ \frac{y^2}{4}(-b + \ln \frac{y^2}{4}) \right], \quad (2.17)$$

where $y$ is a dummy variable, $\lambda = \theta/\chi_c$, $J_0$ is the zeroth order Bessel function, and $b$ is derived from,

$$e^b = \frac{\chi_c^2}{1.167\chi_a^2}. \quad (2.18)$$

The quantity $e^b$ is an estimate of the number of scattering interactions $\Omega_0$ in thickness $t$, while $\chi_c$ represents the minimum possible scattering angle,

$$\chi_c^2 = \frac{4\pi Nte^4Z(Z+1)}{(pv)^2}, \quad (2.19)$$

and $\chi_a$ characterizes the screening angle and is approximated as,

$$\chi_a^2 = \chi_0^2(1.13 + 3.76\alpha^2), \quad (2.20)$$

with $\chi_0$ representing the critical scatter angle below which nuclear effects create differences from the Rutherford scattering law,

$$\chi_0 = \frac{\lambda'}{0.885a_0Z^{-1/3}}. \quad (2.21)$$
The other quantities used are $\alpha = Z e^2 / h \nu$, the de Broglie wavelength of the electron $\lambda' = h/p$, Planck’s constant $h$, and the Bohr radius $a_0$. A detailed discussion of the conditions under which Molière’s theory is applicable, as well as numerical methods for generating $f(\theta)$ can be found in [20].

2.3.5 Range

The range of an electron or positron in a medium is defined as the maximum distance it penetrates before losing all of its energy. Due to the highly stochastic nature of the energy loss and deflection of electrons and positrons as they travel through matter, the range and path length as calculated from an integration of $dE/dx$ will be very different. In general, the total distance the particle traverses is much greater than the range and there can be very large variations in the range between individual particles. Tabulated values of electron and positron ranges in various materials can be found in [16].

The absorption of a monoenergetic beam of electrons or positrons is well represented by an exponential. Since in beta decay there is a continuous spectrum of possible energies, the absorption of beta particles from a beta emitting radionuclide as a function of depth is also well approximated by an exponential,

$$I = I_0 e^{-\mu x},$$

(2.22)

where $I$ is the beta intensity after a thickness $x$ of the absorber, $I_0$ is the initial intensity, and $\mu$ is the beta absorption coefficient which is a function of both the material and the maximum, or endpoint, energy of the beta decay.
A metal is characterized by an energy band that is always partially filled and partially empty, creating an excess of free charge and thus making them highly conductive. An insulator, on the other hand, has a characteristic gap, referred to as the band gap, in its energy band structure around the Fermi level. This means that the lower band, called the valence band, is usually full while the upper, or conduction, band is usually empty. The size of the band gap determines how difficult it is to free charges from the valence band into the conduction band. Thus insulators are typically poor conductors. As the size of the band gap decreases, however, the conductivity of an insulator increases. An insulator with a band gap $\lesssim 4$ eV is typically classified as a semiconductor. Since conductivity of a material varies with temperature, materials that are semiconducting at room temperature can become insulating at low temperatures, while materials that are insulating at room temperature can become semiconducting at higher temperatures.

Silicon is the foundation of all microelectronic devices precisely because it is a natural semiconductor at room temperatures. This is also the reason it is the most widely used material for solid-state photodetectors. Technology crossover from microelectronics has greatly aided in the development and reduced the production costs of silicon photodetectors. In addition, the photolithography techniques developed
for the microelectronics industry have enabled the construction of silicon detectors with extremely small structures, making their position resolutions unparalleled among photodetectors.

Table 3.1 provides a comparison of some properties of common photodetector materials relevant to nuclear medicine. The mean electrons created per MeV demonstrates the inherent energy resolution advantage of semiconductor materials over PMT-based scintillator detectors. Among semiconductors, silicon is preferred as a detector material for its relative low cost and ability to operate effectively at room temperature. The primary drawback of silicon is its comparatively low efficiency for detecting photons in the energy range relevant to nuclear medicine (characterized by the linear attenuation coefficient in Table 3.1). In addition, the increased performance of solid-state detectors comes at the cost of increased electronics requirements, which adds additional cost and complexity compared to scintillation detectors. These issues are reduced as the technology continues to advance.

### 3.1 Sensor

As a photon travels through silicon, it will typically interact with an electron, imparting some or all of its energy to the electron. The energy transferred in this interaction is usually enough to free the bound electron from the valence band. The freed electron will then deposit its energy in the silicon, freeing additional electrons in the process. Each electron freed in this manner leaves a vacancy in the valence band, commonly referred to as a hole and conceptually treated as a positive charge carrier. This process of freeing electrons from the valence band and thus creating electron-hole pairs continues until all of the energy transferred to the initial electron by the photon is deposited in the silicon. Since the total number of electron-hole pairs created is proportional to the energy transferred, collecting the charge generated by this process
<table>
<thead>
<tr>
<th>Property</th>
<th>LSO</th>
<th>BGO</th>
<th>NaI(Tl)</th>
<th>Si</th>
<th>Ge</th>
<th>CZT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective atomic number</td>
<td>66</td>
<td>75</td>
<td>51</td>
<td>14</td>
<td>32</td>
<td>50</td>
</tr>
<tr>
<td>Density (g cm(^{-3}))</td>
<td>7.40</td>
<td>7.13</td>
<td>3.67</td>
<td>2.33</td>
<td>5.32</td>
<td>5.80</td>
</tr>
<tr>
<td>Linear attenuation coefficient (cm(^{-1}))</td>
<td>0.87</td>
<td>0.96</td>
<td>0.34</td>
<td>0.20</td>
<td>0.43</td>
<td>0.53</td>
</tr>
<tr>
<td>Photoelectric fraction</td>
<td>0.32</td>
<td>0.41</td>
<td>0.17</td>
<td>0.002</td>
<td>0.04</td>
<td>0.17</td>
</tr>
<tr>
<td>Compton fraction</td>
<td>0.63</td>
<td>0.54</td>
<td>0.79</td>
<td>0.99</td>
<td>0.93</td>
<td>0.79</td>
</tr>
<tr>
<td>Mean electrons created per MeV(^*)</td>
<td>4,400</td>
<td>1,200</td>
<td>7,600</td>
<td>2.8\times10^5</td>
<td>3.4\times10^5</td>
<td>2.0\times10^5</td>
</tr>
</tbody>
</table>

Table 3.1: Properties of photodetector materials used in nuclear medicine. Data from [11, 21, 22]. Attenuation and interaction fractions are for 511 keV photons. \(^*\)A PMT quantum efficiency of 20% is assumed for LSO, BGO, and NaI(Tl).

Figure 3.1: Schematic showing the basic principles of a PIN photodiode for use as a photodetector.
makes it possible to measure the energy transferred by the photon-electron interaction. In order to collect this charge, a silicon detector is manufactured to operate as a photodiode (see Figure [3.1]).

Semiconductors are intentionally manufactured with impurities in order to introduce desired properties into the material. This process is referred to as doping. The two basic types of doping are known as p-type and n-type doping. In n-type doping, donor atoms which have weakly bound valence electrons are introduced into the lattice thus adding extra electrons to the valence band. Similarly, p-type doping introduces acceptor atoms which add extra holes to the valence band.

When a p-doped and an n-doped region are put together the extra electrons in the n-doped region will diffuse into the p-doped region creating anions and leaving behind cations. Thus a net negative charge will build in the p-doped region and a net positive charge will build in the n-doped region. The electric field produced by these net charges will grow until it becomes strong enough to prevent any charges from flowing between the two regions. At this point a high resistance region devoid of excess charge carriers, known as the depletion region, will have built up at the pn-junction. When a photon interaction occurs within the depletion region, the resulting electron-hole pairs will be attracted to the n-doped and p-doped regions respectively. The generated current can then be collected by electrodes attached to the p and n-doped regions.

For applications as a photodetector, it is useful to increase the thickness of the depletion region to create a larger volume where photons can be detected. This can be achieved by placing a larger undoped (intrinsic) region of silicon between the p and n regions and applying a reverse bias voltage across the diode in order to deplete the intrinsic region of excess charge carriers. Since the basic structure is a sandwich of p-type, intrinsic-type, and n-type regions, this device is called a PIN diode.
practice, the intrinsic layer is actually a lightly n-doped region sandwiched between heavily p-doped \((p^+\)) and n-doped \((n^+\)) regions to create a \(p^+nn^+\) diode. The light n-doping in the bulk layer helps mask defects in the silicon. A schematic of the basic design can be seen in Figure 3.1.

The thickness \(d\) of the depletion region in a \(p^+nn^+\) silicon photodiode is a function of the reverse bias voltage \(V\) and the dopant concentration \(N_d\) in the n region,

\[
d = \sqrt{\frac{2\epsilon\epsilon_0 V}{eN_d}},
\]

where \(\epsilon\) is the dielectric constant of silicon, \(\epsilon_0\) is the permittivity of free space, and \(e\) is the charge of the electron.

The resistivity \(\rho\) of the bulk n-region of the diode is determined by the donor concentration \(N_d\),

\[
\rho = \frac{1}{N_d\mu_e\epsilon_0},
\]

where \(\mu_e\) is the electron mobility in silicon (1350 \(cm^2/Vs\) at room temperature).

### 3.1.1 Position Resolution

The physical limit on the position resolution of a silicon detector is determined by the size of the electron-hole cloud created by the photon interaction. The initial electron will have the greatest initial energy and therefore the greatest total range. Figure 3.2 shows the range of electrons in silicon as a function of the initial kinetic energy. The energy range of photons relevant to this study is 140 keV to 511 keV. For these energies in silicon, the photon is not likely to be absorbed and transfer all of its energy to the electron, but rather Compton scatter imparting a portion of its energy. The maximum energy transferred by the scattering is known as the *Compton edge* and is
a function of the initial photon energy $E_\gamma$,

$$E_{e}^{\text{max}} = \frac{E_\gamma}{1 + \frac{m_e c^2}{2 E_\gamma}}.$$  \hfill (3.3)

This energy will determine the maximum range of the electron, and therefore the limit on spatial resolution, for a given source.

Table 3.2 shows the principle photon energy, Compton edge, and expected maximum electron range in silicon for a range of isotopes used in nuclear medicine. From this data it can be seen that the largest electron range in silicon for nuclear medicine applications is approximately 0.55 mm. For a silicon detector with elements larger than the electron range the position resolution will primarily be determined by the detector element size. Thus the error on the position in a sensor with detector element size $s$ will be due to the geometric uncertainty, which is given by the variance,
\[
\sigma^2 = \int_{-s/2}^{s/2} \frac{x^2}{s} \, dx = \frac{s^2}{12}.
\] (3.4)

Thus the root means square (rms) resolution due to the geometric uncertainty is simply \( \sigma = s/\sqrt{12} \).

### 3.1.2 Timing Resolution

The inherent timing resolution in silicon is dependent on the time it takes to collect the electron-hole pairs. Collection time will vary based on the depth of the interaction which determines how far the electrons and holes must travel before being collected by the electrodes. Electrons and holes travel at different rates through silicon and their rates are dependent on their mobility in silicon and the strength of the electric field. Since the magnitude of the electric field varies over the thickness of the detector, the basic expressions for the velocities of electrons and holes in silicon are a function

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Principle Photon Energy (keV)</th>
<th>Compton Edge (keV)</th>
<th>Electron Range (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{99m}\text{Tc})</td>
<td>140.5</td>
<td>49.8</td>
<td>0.024</td>
</tr>
<tr>
<td>(^{111}\text{In})</td>
<td>245.4</td>
<td>120.2</td>
<td>0.11</td>
</tr>
<tr>
<td>(^{131}\text{I})</td>
<td>364.5</td>
<td>214.3</td>
<td>0.29</td>
</tr>
<tr>
<td>(^{113m}\text{In})</td>
<td>391.7</td>
<td>237.1</td>
<td>0.31</td>
</tr>
<tr>
<td>(^{18}\text{F})</td>
<td>511</td>
<td>340.7</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Table 3.2: Electron range in silicon for some common isotopes in nuclear medicine applications.
of the electric field $E(x)$,

$$v_e = \mu_e E(x), \quad (3.5)$$

$$v_h = \mu_h E(x), \quad (3.6)$$

where $\mu_e$ and $\mu_h$ are the electron and hole mobility in silicon respectively.

The mobility of the electrons and holes in silicon at room temperature (300 K) are 1350 $cm^2/Vs$ and 480 $cm^2/Vs$ respectively [11]. With the origin defined as the pn-junction, the magnitude of the electric field in the depletion region is given by,

$$E(x) = \frac{V}{w} - \frac{eN_d}{\epsilon\epsilon_0} \left( \frac{w}{2} - x \right), \quad (3.7)$$

where $V$ is the reverse bias voltage and $w$ is the thickness of the detector.

From Equations \ref{3.5}–\ref{3.7} the total collection times for electrons and holes as a function of interaction depth $x$ are given by,

$$t_e(x) = \frac{\epsilon\epsilon_0}{e\mu_e N_d} \ln \left( \frac{3 + V/V_{FD}}{1 + V/V_{FD} + 2x/w} \right), \quad (3.8)$$

$$t_h(x) = \frac{\epsilon\epsilon_0}{e\mu_h N_d} \ln \left( \frac{1 + V/V_{FD}}{1 + V/V_{FD} - 2x/w} \right), \quad (3.9)$$

with $V_{FD}$ representing the full depletion voltage. Figure 3.3 shows charge collection times as a function of interaction depth assuming a 1.0 mm thick detector at full depletion voltage and a bulk resistivity of 20 kΩ cm.

Increasing the reverse bias voltage will reduce the collection time, however there is a limit to the voltage that can be applied before the diode breaks down and damage is potentially caused to the semiconductor, the electrodes, and the read-out electronics [11]. In addition, the drift velocities given in Equations \ref{3.5} and \ref{3.6} are approximations that are only valid for a range of electric field strengths. The actual drift
velocities will eventually reach a maximum that can not be increased regardless of the electric field strength [23].

### 3.1.3 Energy Resolution

The intrinsic energy resolution of a photodetector is determined by the statistical fluctuations in the number of charge carriers created per unit of deposited energy. Because the number of charge carriers per unit of energy deposited in a semiconductor based detector is two orders of magnitude greater than in a traditional scintillator-PMT system (see Table 3.1), the intrinsic energy resolution of solid state detectors is superior to scintillator-PMT based detectors. This is a result of the fact that the statistical fluctuation in a Poisson process is directly related to the square root of the number of detected events,

$$\sigma_N = \sqrt{N_E} = \sqrt{E/\eta}. \quad (3.10)$$
Thus the variance in the number of charges, $\sigma_N$, is equal to the square root of the average number of charge pairs, $N_E$, created for energy $E$ deposited in the detector, with the average being equal to the deposited energy $E$ divided by the average energy $\eta$ required to free a charge carrier.

This simple Poisson model actually overestimates the variance in a semiconductor because the creation of each charge carrying electron-hole pair is not an independent event. The variance is dependent on the total history of the recoil electron’s path as it scatters through the crystal and loses energy through the creation of electron-hole pairs and lattice excitations \[24\]. A correction factor, termed the Fano factor, is introduced to the variance calculation \[25\],

$$\sigma_N = \sqrt{FN_E}, \quad (3.11)$$

$$F = \frac{\sigma_N^2}{N_E}. \quad (3.12)$$

Values of the Fano factor measured for silicon vary from 0.084 to 0.16 \[11\].

Table 3.3 shows computed values of the mean and variance of created charge pairs for selected initial recoil electron energies, assuming a Fano factor of 0.1 and an average energy of 3.6 eV required to create electron-hole pairs in silicon. Rough estimates of the corresponding average current (I) and variation in the current ($\Delta I$) are given assuming collection times $\tau$ of 200 ns (close to the $p^+$ side) and 30 ns (close to the $n^+$ side). In practice, the inherent energy resolution of semiconductor detectors is rarely an issue as the resolution will be dominated by the front-end electronics.

## 3.1.4 Photon Attenuation

Figure 3.4 shows the mass attenuation coefficient of silicon as a function of initial photon energy. For the energies relevant to nuclear medicine ($\sim$30 keV to 511 keV), it is apparent that Compton scattering is the dominant process in silicon. Photoelectric
Table 3.3: Computed values of the mean and variance of created charge pairs as well as the resulting peak currents and their variance. $E_e$ is the scattered electron energy, $N(E_e) = E_e/\eta$ is the mean electron-hole pairs created (assuming an average energy for creating pairs in silicon of $\eta = 3.6$ eV) and $\sigma_N$ is the variance in the number of pairs created. Rough estimates of the average current ($I$) and variation in the current ($\Delta I$) are given assuming collection times $\tau$ of 200 ns (close to the $p^+$ side) and 30 ns (close to the $n^+$ side).

<table>
<thead>
<tr>
<th>$E_e$ (keV)</th>
<th>$N(E_e)$</th>
<th>$\sigma_N$</th>
<th>$\tau = 200$ ns</th>
<th>$\tau = 30$ ns</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>8300</td>
<td>29</td>
<td>13</td>
<td>46</td>
</tr>
<tr>
<td>100</td>
<td>28000</td>
<td>53</td>
<td>44</td>
<td>298</td>
</tr>
<tr>
<td>200</td>
<td>56000</td>
<td>75</td>
<td>90</td>
<td>597</td>
</tr>
<tr>
<td>340</td>
<td>94000</td>
<td>97</td>
<td>150</td>
<td>1003</td>
</tr>
</tbody>
</table>

Figure 3.4: Photon attenuation in silicon as a function of energy from 1 keV to 10 MeV. Data from [26].
absorption has a negligible effect at higher energies in silicon, but can be seen at the lower energies of the nuclear medicine range. The implications for applications in nuclear medicine are that silicon will have an overall lower efficiency than other detector materials but a much higher fraction of Compton scattering events (see Table 3.1).

3.2 Front-End Electronics

A PIN silicon detector does not have any inherent charge amplification. Whatever charge is produced by the photon interaction is the charge collected by the electrodes. Accurate measurement of this charge requires front-end electronics that convert the measured charge into an amplified voltage signal. This is typically achieved through the use of a charge sensitive preamplifier which feeds into a CR-RC pulse shaper.
3.2.1 Preamplifier

In a charge sensitive preamplifier the charge from the electrodes is collected and converted to a voltage by a capacitor ($C_p$). The input capacitance of this circuit is $C_{\text{in}} = AC_p + C_d$, where $A$ is the open-loop gain of the operational amplifier (op-amp). Thus a charge $Q$ on the capacitor produces an output voltage $V_p = -Q/C_{\text{in}}$. To allow the charge on the capacitor to dissipate over time, making the preamplifier ready for subsequent events, a resistor $R_p$ is placed in parallel with $C_p$. As a result, the output of the preamplifier for a charge impulse, i.e. $I(t) = Q\delta(t)$, is given by,

$$V_p(t) = \begin{cases} 0 & : \ t < 0 \\ -\frac{Q}{C_p}e^{-t/\tau_p} & : \ t > 0 \end{cases},$$

(3.13)

where $\tau_p = R_pC_p$ is the time constant, or relaxation time, of the preamplifier. Since the output is inversely proportional to $C_p$, smaller capacitance values yield larger gains. Therefore $C_p$ is selected to provide the desired gain, usually as small as possible without introducing extra noise, and then $R_p$ is selected to provide a sufficiently small recovery time without introducing excessive noise. Typical values for $\tau_p$ are on the order of tens of microseconds, which is insufficient for high-rate applications. To improve the recovery time of the signal a subsequent pulse shaping circuit is used.

3.2.2 Shaper

The output of the preamplifier (preamp) is fed into the shaper. Figure 3.6 shows a schematic of a shaper commonly used in semiconductor detectors. This shaper is composed of a CR differentiator, also known as a low-pass filter, that feeds into a voltage-sensitive amplifier followed by an RC integrator, or a high-pass filter that feeds into a second voltage-sensitive amplifier. The combined circuit is known as a CR-RC shaper and its purpose is to produce a fast, well-shaped pulse.
It is typical to make the time constants of the CR and RC circuits equal. If we approximate the output of the preamp as a step function with amplitude $V_p = Q/C_p$, the output voltage of the shaper is given by,

$$V_{\text{out}} = \frac{Q}{C_p} \frac{t}{\tau_s} e^{t/\tau_s},$$

(3.14)

with $\tau_s = R_s C_s$ the common timing constant of the CR and RC filters. From this equation we can see that the output of the shaper reaches its peak value at $t = \tau_s$. In reality, the input to the shaper from the preamp is not a step function and, as a result, the tail of the pulse undershoots the baseline voltage. The severity of the undershoot is related to the ratio of the timing constant of the shaper to the timing constant of the preamp, with the pulse shape approaching the expression in Equation 3.14 for $\tau_s \ll \tau_p$.

### 3.2.3 Noise

Noise in the front-end electronics is a critical factor in the operation of silicon detectors. The sources of noise in the front-end electronics of a silicon detector are generally categorized as current noise, voltage noise, and $1/f$ noise. Figure 3.7 shows a diagram of a circuit showing the basic sources of current and voltage noise in the
front-end electronics of most silicon detector systems.

Fluctuations in the leakage current of a silicon detector due to electron emission statistics produce a current noise source, $i_{nd}$, which is often referred to as shot noise after Walter Schottky who developed the basic theory explaining it \[27\]. The magnitude of the shot noise is given by,

$$i_{nd}^2 = 2eI_d,$$

(3.15)

where $e$ is the electron charge and $I_d$ is the current from the detector bias.

Resistors introduce noise due to thermal fluctuations, which can be either current or voltage noise. This type of noise is known as Johnson noise, or sometimes Johnson-Nyquist noise, after John Johnson, who first discovered it, and Harry Nyquist, who first explained it \[28, 29\]. Typically resistors in series with the signal are modeled as voltage noise while resistors parallel to the input are modeled as current noise. Therefore the resistor on the bias voltage, $i_{nb}$, is shown as a current noise source, while the noise of any series resistance in the circuit is included as a voltage noise.
source, \( e_{ns} \),
\[
i_{nb}^2 = \frac{4kT}{R_b}, \tag{3.16}
\]
\[
e_{ns}^2 = 4kTR_s, \tag{3.17}
\]
with \( k \) the Boltzmann constant and \( T \) the temperature.

Electronic noise from the amplifier and pulse shaping electronics can be modeled as a combination of current and voltage sources \( e_{na} \) and \( i_{na} \). An analytical expression for the magnitudes of these noise sources is dependent on the amplifier electronics and the corresponding current gating, and thus is device specific. Typical values of \( e_{na} \) and \( i_{na} \) are on the order of \( \text{nV/}\sqrt{\text{Hz}} \) and \( \text{pA/}\sqrt{\text{Hz}} \) respectively [30].

Both the shot noise and the Johnson noise, as well as the voltage and current noise from the amplifier, are \textit{white} noise sources, meaning that their spectral power densities \( dP_n/df \propto di_{na}^2/df \propto de_{ns}^2/df \) are all constant. In other words, their magnitudes are frequency independent. In addition to this white noise, there are also \textit{pink} noise sources whose magnitudes vary with frequency as \( 1/f \),
\[
e_{nf}^2 = \frac{A_f}{f}, \tag{3.18}
\]
with the coefficient \( A_f \) being device specific and typically in the range \( 10^{-10}-10^{-12} \text{V}^2 \) [30]. Pink noise can result from power fluctuations such as those resulting from trapping and detrapping processes in resistors, dielectrics, and semiconductors. In addition to the pink noise, there is a fraction of the current noise that flows through the detector capacitance, producing a frequency-dependent voltage noise,
\[
e_{nd} = \frac{i_n}{\omega C_d}. \tag{3.19}
\]

All of these noise contributions are added in quadrature, with the total noise at the shaper output being equal to the integral over the full system bandwidth. The
noise is assumed to be random, and thus is expected to have a Gaussian distribution.

### 3.2.4 Energy Resolution

Since the energy deposited in a silicon detector is converted to charge, the system noise is commonly characterized by the detector signal that will produce a signal-to-noise ratio (SNR) of one. This parameter is known as the equivalent noise charge (ENC), $Q_n$, and the basic expression for capacitive sensors is given by [31],

$$Q_n^2 = i_n^2 F_i T_s + e_n^2 F_v C^2 T_s + F_v f A f C^2,$$

(3.20)

where $C$ is the sum of capacitances parallel to the input, the form factors $F_i$, $F_v$, and $F_v f$ are determined by the shape of the pulse produced by the shaper, and $T_s$ is the characteristic time of the circuit (e.g. peaking time of a semi-Gaussian shaper). Values of these form factors for a wide variety of pulse shapes can be found in [32, 33].

From Equation (3.20), we see that the contribution of the noise current, $i_n$, is proportional to the characteristic time $T_s$, while the noise voltage contribution, $e_n$, is inversely proportional to the characteristic time, and the 1/f noise is independent of the characteristic time. The result is that for a given system, there will be an optimal characteristic time $T_s$ where the total noise is at a minimum. This will occur when the current and voltage noise contributions are equal. Increasing the characteristic time above the optimal value will result in greater voltage noise, while decreasing it below optimum will result in greater current noise. The 1/f noise will cause an offset that flattens out the minimum. These effects are illustrated in Figure 3.8.
3.2.5 Timing Resolution

For optimizing timing resolution, the slope-to-noise ratio becomes an important factor as well as the signal-to-noise ratio. The timing noise, or *jitter*, is given by \[ \sigma_t = \frac{\sigma_n}{(dS/dt)_{S_{\text{thr}}}} \approx \frac{t_r}{S/N}, \] (3.21)

where \( \sigma_n \) is the rms noise, the time derivative of the signal \( S \) is evaluated at the trigger threshold level \( S_{\text{thr}} \), and \( t_r \) is the rise time of the signal. Rise times of a series of cascaded amplifiers will add in quadrature. From this, we can see that reducing the rise time, \( t_r \), or improving the signal-to-noise ratio, \( S/N \), will improve the jitter.

Time-walk (i.e. variation in trigger time by pulse-height) can be corrected in hardware or software \[35\]. Variation in timing due to depth of interaction is a concern in thicker detectors. Over-biasing the detector will improve timing for most systems, up to the tolerance level of the detector.
3.3 Our Detectors

The detectors used in the current investigations use 1.0 mm thick silicon sensors with 512 1.4 mm x 1.4 mm pads manufactured by SINTEF \[36\]. Pads are read out by 128 channel application specific integrated circuits (ASICs) designed and developed by Gamma-Medica Ideas \[37\]. The sensor and ASICS are all mounted on a custom printed circuit board (PCB) called a hybrid which routes the signals between the front-end electronics and the rest of the data acquisition system. Hybrids used in this investigation have all been designed and developed at The Ohio State University (OSU). All detectors used in this study were also assembled and tested at OSU. Figure 3.9 shows an assembled detector consisting of a 512 pad sensor and four VATAGP3 version ASICs mounted on a single-sided hybrid. Figure 3.10
Figure 3.10: (a) Top view of a double-sided 512 pad detector read out by VATAGP7 version ASICs. (b) Side view of the same detector.

shows a detector consisting of two 512 pad sensors mounted backplane-to-backplane on a double-sided hybrid. Each sensor is read out by four VATAGP7 version ASICs. These detectors are designed to test applications which require close stacking of the silicon.

### 3.3.1 Sensor

All of the detectors in this investigation use the same 1.0 mm thick 512 pad detectors from SINTEF. Figure 3.11(a) shows the layout of a 1.0 mm thick silicon wafer containing a variety of sensor designs for imaging applications. Figure 3.11(b) shows a detail of the layout for the 512 pad sensors. Individual pads are 1.4 mm x 1.4 mm and the 512 pads are arranged in a 32 x 16 array for a total pad area of 4.48 cm².
Figure 3.11: (a) Layout of a silicon wafer containing a variety of sensor designs for imaging applications. (b) Detail of the layout for a 512 pad sensor.
Figure 3.12: Diagram of a cross section through three pads of a 512 pad detector.

x 2.22 cm. The perimeter of the sensor is surrounded by a grounded guard ring to
counteract edge effects. The total sensor size is 2.59 cm x 4.76 cm.

Figure 3.12 shows a schematic representation of a cross section through the sensor.
The bulk of the detector volume is composed of high-purity, lightly $n$-doped silicon.
Photolithography followed by etching and dopant implantation is used to form the
$p^+$ implants. The entire back side is implanted to form the $n^+$ layer. Metal contacts
are formed by deposition and a polymide insulation layer is applied.

The electrodes consist of two metal layers connected by a metal via through the 10
$\mu$m thick polymide layer. Metal layer 1 is DC-coupled to the $p^+$ implant. The second
layer forms the readout lines that route the charge collected to the edge of the detector
where the bonding pads are located for connection to the front-end electronics. Wire
bonds attached by ultrasonic welding connect each bonding pad to an ASIC channel.

3.3.2 ASICs

Figure 3.13 is a block diagram of the readout electronics for the first and last channel
of an ASIC in the VATAGP series. Each chip has 128 identical readout channels.
Figure 3.13: Example block schematic of the electronic circuits used to trigger and shape the signal for the first and last of 128 channels in the VATAGP family of ASICs.
arranged in parallel. Each channel has a charge sensitive preamplifier which amplifies and sums the charges collected by the connected electrode. The resulting output is routed into the fast shaper, which is used for trigger generation, and the slow shaper, which is used for an accurate measurement of the pulse to determine the energy.

The fast shaper is a CR-RC circuit which has been optimized to produce a fast (150 ns) rise-time for trigger generation. The output of the fast shaper is fed into a leading-edge discriminator which generates the trigger signal if an externally supplied threshold voltage is exceeded. The slow shaper is optimized to provide an accurate measurement of the energy deposited in the connected pad. In order to allow time for the preamplifier to collect all of the charge generated by an interaction, the characteristic time $\tau$ ($2 \mu$s) of the slow shaper is much greater than in the fast shaper. The slow shaper signal is monitored by a sample and hold circuit which stores the peak voltage to be read out.

Figure 3.14 is a schematic of the signal generation process in a readout cycle of a VATAGP chip. The readout cycle is initiated by a photon interaction in the silicon that gives rise to a small current pulse (line 1). This pulse is collected and amplified by the charge-sensitive preamplifier (line 2). The output of the preamplifier is routed into both the slow shaper (line 3) and the fast shaper (line 4). When the signal from the fast shaper exceeds the threshold voltage of the discriminator, the trigger pulse (TA) is generated. The trigger pulse leaves the VATAGP chip and is processed by external electronics. Typically, the external electronics will generate a delay late trigger signal (DLT, not shown) to prevent any additional triggers in the chip while external logic decides whether or not to read out the channels.

Once the external logic has decided to read out the channels, the external electronics generate a series of signals to initiate the readout cycle. A sample and hold signal (SH) is generated to coincide with the peak of the slow shaper signal. The
Figure 3.14: Schematic of the signal generation process in a VATAGP readout cycle. Image from [38].
sample and hold circuit samples the value of the slow shaper at the rising edge of
the SH signal and holds this value while the SH signal is high. If the channel values
are to be read out, external electronics will generate a signal (SHIFT-IN), which ini-
tiates the channel readout, and a clock (CLK) that shifts the readout from channel
to channel causing the value stored in each channel’s sample-and-hold buffer to be
sent out on the analog output signal (OUTP). There are in fact two multiplexers
per channel which store the sampled value and therefore two parallel readouts which
occur simultaneously in reverse order with respect to channel readout. Thus there
are two analog outputs per readout cycle, dubbed UP and DOWN.

Once the readout cycle is complete for all 128 channels on a chip, the chip will
generate a signal (SHIFT-OUT) which is routed to the SHIFT-IN signal of the next
chip in line, thus initiating its readout cycle. Thus the sample and hold circuit values
of all in-line chips is output onto a single analog signal which is then digitized by
external electronics. An external reset signal causes the DLT and SH signals to go
low, which prepares the chip to trigger again.

The VATAGP chips have three basic readout modes: serial, sparse, and sparse
plus adjacent. Serial mode is the most basic mode of operation. All channels in the
chip are clocked out onto the analog output. In sparse mode, only the channel which
generated the trigger is clocked out, along with the address of the channel. Similarly,
in sparse plus adjacent, the triggered channel is read out along with a specified number
of subsequent channels in the readout line.

VATAGP3

To configure a VATAGP chip for operation, there are digital settings that must be
configured, consisting of a series of bits collectively referred to as the control regis-
ter. For a VATAGP3 version chip, the control register determines the readout mode,
channel mask, test mask, threshold DAC values, and various chip operation parameters including calibration settings and signal polarities. Setting a bit in the channel mask disables triggers from the corresponding channel. When the test bit is set in the control register, the chip enters a test mode which allows charge to be injected directly into the channel specified in the test mask. This mode of operation is used for testing chip functions independently from the sensor. The threshold DAC (data-to-analog converter) values are three bits wide and determine an offset of the trigger threshold voltage for each channel so that adjustments can be made to account for gain variations between channels.

In addition to the digital settings, there are a number of analog parameters which are determined by externally supplied DC reference voltages, referred to as biases. Important biases for VATAGP3 operation include \(v_{fp}\) (voltage for preamplifier), \(v_{fsf}\) (voltage for fast shaper), \(v_{fss}\) (voltage for slow shaper), and \(mb_{ias}\) (master bias). The feedback resistor value of the preamplifier can be tuned through \(v_{fp}\). Similarly, the shaping time of the fast and slow shaper can be adjusted with \(v_{fsf}\) and \(v_{fss}\) respectively. Finally, \(mb_{ias}\) is used as a reference for a number of chip parameters, including the voltage step for the threshold DAC.

**VATAGP7**

The VATAGP7 ASIC is latest installment in the VATAGP family. Updates to the VATAGP design in this new model focus on improving the overall functionality of the calibration settings and optimizing the signal shaping for improved timing while trying to minimize the resulting loss in energy resolution. Changes from the VATAGP3 design include:

- Slow shaper intrinsic shaping time reduced from 3 \(\mu\)s to 500 ns.
- Fast shaper intrinsic shaping time reduced from 150 ns to 50 ns.
• Gain stage on fast shaper removed.

• Ability to turn off fast shaper slew rate compensation added.

• Per-channel threshold DAC values increased from 3 to 4 bits for finer control. Thresholds may now be varied independently for each channel.

• Channels can accept positive or negative polarity signals.

• Can produce an internally generated calibration pulse with amplitude set by a DAC.

• Pads added for DLT/DLTb lines above and below chip to allow daisy-chaining between chips.

Chip operating voltages have changed, and many biases have reversed polarity, but the design remains consistent enough with the VATAGP3 schematics that the same data acquisition system can be used with minimal modification.

3.3.3 Data Acquisition

The ultimate goal of the data acquisition system is to store the data from the photon interactions in the silicon detector on a computer for processing. Custom electronics and software have been built to accomplish this. Beyond the sensor, ASICs, and hybrid already discussed, there are three custom electronic boards and a custom data acquisition software package that handle the readout of the silicon detectors. Figure 3.15 shows a simple diagram of the components. In order from the front-end electronics to the computer, the components are: transition card, intermediate board, VME board, data acquisition software. All of the custom electronic boards used in this setup were built at The Ohio State University.
The role of the transition card is to separate the analog and digital signals being transferred between the front-end electronics and the intermediate board and it also provides easier access and control to the signals. It features many jumpers and potentiometers that are used to fine tune the system, but do not alter the basic function so they will not be discussed here. The intermediate board is the primary interface to the front-end electronics. It provides the external voltages and signals that the VATAGP chip requires and provides an interface for the VME board. The primary functions of the VME board is to provide an interface via VMEbus (VERSAmodule Eurocard bus, ANSI/IEEE 1014-1987) between the intermediate board and the desktop computer, which runs the data acquisition software, and to control the VATAGP readout sequence (refer to Figure 3.14).

The intermediate board provides an internal/external trigger mode jumper. In internal trigger mode, the intermediate board immediately passes any trigger generated
by the front-end electronics to the VME board, which then initiates the readout cycle. In external trigger mode, the intermediate board routes an external trigger signal to the VME board to initiate the readout cycle. The intermediate board also provides an output of the VATAGP trigger which can be used to form coincidences with triggers from other detectors, which can then be fed back to the intermediate board via the external trigger. The intermediate board generates the DLT signal which prevents additional triggers after an initial trigger until a reset signal is received. A jumper provides the option to disable the generation of the DLT signal, allowing all triggers to pass through, in which case the detector can be used as a radiation counter.

The VME board provides an interface between the intermediate board and (via the VMEbus interface and a desktop PC) the data acquisition software. When the VME board receives a trigger from the intermediate board, it provides the delayed sample and hold signal and the shift-in signal and clock for the readout cycle. The intermediate board routes these signals to the VATAGP chip, amplifies the output and routes it back to the VME board where it is digitized by a 12 bit ADC and stored in a FIFO to be read out by the software over the VMEbus.

The data acquisition software interacts with the VME board, writes the data to digital storage, and provides a real-time online analysis for data monitoring. Software controlled system settings include: channel mask, test mask, threshold DAC, threshold voltage, and readout mode.

3.3.4 Data Processing

Data acquired from the custom data acquisition system designed for the VATAGP-based silicon is stored as a set of 32 bit integers, one for each channel in the readout. Since the output signals of the VATAGP chips is digitized by two 12 bit ADCs, the digitized values of the two analog signals are stored as the first 12 bits of the top and
bottom halves of the 32 bit integers. These 12 bit values represent the peak values of the slow shaper from the front-end electronics. In order to extract the energy of the photon interaction, this raw data must be processed.

For imaging, the goal of the silicon data processing is to reduce the raw data from a single trigger, termed an *event*, to an energy value and a position. For the 1.4 mm x 1.4 mm pitch of the detectors used in this study, only a small fraction of events will deposit energy in more than one pad (see Table 3.2), so in this investigation the position of an event is determined by the channel that generated the trigger. In sparse and sparse-adjacent modes, the channel is acquired as part of the readout, but in serial mode it is determined as part of the process of determining the energy of the event. For determining the energy of an event, the raw data from each channel is characterized by four values: the pedestal, noise, signal, and gain.

**Pedestals and Noise**

The output from each channel has an average baseline voltage offset which can be measured for all channels in an event that did not collect charge from an interaction. The average of the baseline values of a channel are called the *pedestal*, while the
variation in the baseline is referred to as the noise.

In serial mode, there is presumably only one channel that has triggered and all other channels are at their baseline values. A simple average over a few thousand events should establish very good values for pedestals and noise. In sparse-adjacent, there will be fewer channels at their baseline values in each event, so a proportionately larger number of events must be processed to determine an accurate value for the pedestals. An advantage to sparse-adjacent is that the channel which generated the trigger is known, so the other channels in the readout can be assumed to be at baseline value, with the possible exception of the channel directly adjacent to the triggered channel. Obviously, in sparse mode only the triggered channel is read out, so no pedestals can be calculated and therefore pedestals from another run must be used. In general, sparse mode is used for applications where an energy calculation is unnecessary.

Generally, the variation in the pedestals over time is small, so it is possible to calculate pedestals for a detector and use these pedestals in subsequent runs. However, the baseline can vary if the voltages supplied to the chips change, therefore it is preferable to calculate pedestals for every run. In order to account for potential variations of the baseline within a single run, it is also possible to use a running average and running variance calculation to determine running values for the pedestals and noise.

Signal

Once pedestals have been calculated, the signal is simply the raw data value in each channel with the corresponding pedestal subtracted. In sparse and sparse-adjacent, the channel that triggered is known and the signal value from this channel is the signal for the event. For serial readout mode, however, the pedestals must be subtracted.
from every channel and then a $5\sigma$ cut on the signal value is made (i.e. we look for a signal value that is more than five times the corresponding noise) to determine which channel triggered. Events with no signals above the $5\sigma$ cut or with more than one channel above the cut are generally discarded. Multiple scatter events could potentially have some applications, but in the current detectors there is no way to distinguish the order of events, so it is difficult to extract useful data from these events. If a running pedestal calculation is being performed, then any channel determined to have a trigger would not be included in the calculation.

**Gains**

The peak value of the slow shaper is generally seen to be linear with the charge collected, and therefore with the energy of the photon interaction. Thus there is a simple slope that relates the pedestal subtracted signal to the energy of an event which is generally known as the *gain*. There is a variation in gain from channel to channel, so gains must be calculated for every channel.

In order to calculate the gains, the energy of the interaction must be known. For our silicon detectors, the 59.5 keV photopeak of $^{241}$Am provides a good reference for determining the gains, since there is an appreciable photo absorption cross section at
that energy. For sources used in medical imaging, however, the cross section for photo absorption is small in silicon, only a small portion of events will be in the photopeak. Thus, to achieve a good estimate of the gain in every channel, a large number of events would have be collected. Since imaging applications require coincidences, the event rate is inherently lower than when acquiring single events in silicon. These factors make it necessary to perform specific calibration runs to determine the gains, and so we call these runs *gain runs*.

During the processing of a gain run, a histogram of the signals is made. The threshold in a gain run is set higher than necessary in order to insure that the principal peak in the signal histogram in every channel will be the 59.5 keV photopeak. Thus determining the gain is as simple as determining the maximum bin value in the histogram and dividing by 59.5. The gains for every channel are then stored in a file, which is used on subsequent runs. With the gain determined, the energy of each event is simply the signal of the triggered channel divided by its gain.
3.3.5 Performance

As discussed in Section 3.1.1, the position resolution is dominated by detector geometry. Thus the inherent rms position resolution of our detectors, given the detector element size of 1.4 mm x 1.4 mm x 1.0 mm, is approximately 0.4 mm x 0.4 mm x 0.29 mm. A small fraction of events will deposit energy in more than one pad and the energies from each pad could be used to determine the position with more precision for these events. However, the fraction is very small and only serial readout mode provides enough information to make the additional processing useful, so these events are not accounted for in the data processing of these detectors and the inherent geometric resolution is assumed for all events.

As discussed in Section 3.3.2, the current investigations involve systems based on two different versions of the VATAGP ASIC. One of the primary goals of the updated VATAGP7 version ASIC was to improve timing resolution and rate capability. The natural tradeoff was energy resolution, as the shaping times were reduced and the S/N decreased. Figure 3.19 shows a comparison of the energy spectrum of $^{241}$Am for a VATAGP3 and a VATAGP7 based detector, both using the same 512 pad sensor design. As the spectra show, the VATAGP3 has an energy resolution of $\sim 1.6$ keV FWHM, while the VATAGP7 detector resolution is $\sim 2.4$ keV FWHM. Thus the VATAGP7 detector has lost about 50\% in FWHM energy resolution compared to the VATAGP3 system.

The energy resolutions from these spectra are obtained by a Gaussian fit to the 59.5 keV photopeak of $^{241}$Am. For a Gaussian distribution, the FWHM is related to the standard deviation by,

$$FWHM = 2\sqrt{2\ln 2} \sigma \approx 2.35482 \sigma.$$  \hspace{1cm} (3.22)

Detailed investigations of the timing properties of these detectors can be found
in [39] for the VATAGP3 based detectors and [40] for VATAGP7 based detectors. In both cases, the timing of the system is found to be dominated by the time walk due to pulse height variations of the signal used by the leading edge discriminator of the VATAGP trigger electronics. This time walk has been measured at up to $\sim 150$ ns depending on the threshold value and the energy of the interaction in silicon. Additional time variation is seen to result from the depth of interaction, which is due to both the difference in electron and hole mobilities as well as variation in the electric field over the depth of the sensor. An investigation of these issues for our detectors can be found in [41] and general remedies for these issues are discussed in [35].

The result of these factors for the purposes of the current investigations is that timing is not optimal, and therefore the rates have been limited to compensate. Since actual timing performance is dependent on threshold values and event energies, the actual timing performance of the system varies by application.
The conventional gamma cameras used in modern SPECT systems employ photon absorbing collimators to form the 2D projection images of the source distribution. While essential to the design of a standard gamma camera, the collimator inherently couples the spatial resolution and the sensitivity of the device in an inverse relationship. In principle, higher resolution can be achieved by simply reducing the size of the holes in the collimator, but then fewer photons will be detected and the sensitivity is decreased.

In addition, higher energy photons penetrate matter more easily, requiring a thicker collimator to shield the detector. However, increasing collimator thickness also reduces sensitivity so conventional SPECT systems suffer decreased performance with higher energy sources such as $^{131}$I. This also limits the development and use of radionuclides for SPECT imaging with energies much above 300 keV. These limitations can be potentially overcome through a radically different single photon imaging technique known as Compton SPECT.

The Compton SPECT imaging technique removes the inherent coupling between sensitivity and resolution found in conventional systems by replacing the mechanical collimator with a position sensitive detector in which the incident photons Compton scatter and continue on to be absorbed by a position sensitive second detector. The
tracer distribution is then reconstructed from the energies and positions in the two detectors. Thus the spatial resolution is tied to the performance of the two detectors and the physics of Compton scattering while the sensitivity depends primarily on the system geometry and the probabilities of interaction in the two detectors.

Because of this, a Compton SPECT imaging device has the potential for much higher sensitivity at a given image quality when compared to a conventional system. This provides the opportunity to reduce patient doses, reduce collection time, or improve performance for time-sensitive functional imaging. In addition, Compton SPECT imaging has increased performance at higher energies, which makes Compton camera systems particularly attractive for imaging higher-energy sources such as $^{131}$I and could potentially open the door to new radiopharmaceuticals based on higher energy sources (see Table 4.1). There are also many isotopes currently being investigated for potential radiation therapy applications which emit high energy photons, thus a Compton Camera could provide images for designing and monitoring treatment with these isotopes.

With the potential benefits of Compton SPECT come significant technical challenges [42]. For a conventional gamma camera the technical requirements of the detector and electronics are relatively low and have been met sufficiently for decades. A Compton camera has much greater demands on the technology, requiring both very good spatial resolution and very good energy resolution in the scatter detector (also referred to as an electronic collimator). Good spatial resolution is also generally desirable in the absorption detector, with the specific requirements depending on the system geometry. The replacement of the mechanical collimator also puts very high rate of data acquisition (DAQ) demands on the absorption detector. In order to see the potential gains in efficiency created by the electronic collimation, the scatter detector will also need to have high efficiency and DAQ rate capabilities.
<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-Life</th>
<th>Gamma Energy (keV)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc</td>
<td>6.01 hours</td>
<td>140.5</td>
<td>89</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>8.02 days</td>
<td>364.5</td>
<td>81.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>637.0</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>284.3</td>
<td>6.1</td>
</tr>
<tr>
<td>$^{111}$In</td>
<td>2.8 days</td>
<td>245.4</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>171.3</td>
<td>90</td>
</tr>
<tr>
<td>$^{113m}$In</td>
<td>1.66 hours</td>
<td>391.7</td>
<td>64.2</td>
</tr>
</tbody>
</table>

Table 4.1: Potential isotopes for Compton SPECT imaging.

4.1 Experimental Goals

Previous investigations by CIMA into Compton camera devices using silicon detectors have provided proof of principle evidence for the feasibility of our detectors in Compton SPECT applications [39]. The goal of this investigation is to characterize the performance of a new prototype over the energy range relevant to SPECT and demonstrate the improved performance of the device at higher source energies. For SPECT applications, the relevant energy range extends from the photopeak of $^{201}$Tl (70 keV) to the positron annihilation energy (511 keV). Three sources in this range have been imaged: $^{99m}$Tc (140 keV), $^{131}$I (364 keV), and $^{22}$Na (511 keV). A simulation of the prototype has also been developed in order to help understand the effects of the intrinsic detector resolutions on the image resolution and how the effects vary with source energy.
4.2 History

The first gamma camera was invented by Hal Anger in 1957 [43]. It consisted of 7 photomultiplier tubes attached to a NaI scintillating crystal and shielded by a lead pinhole aperture. Most modern gamma cameras are derived from this device, and as a result gamma cameras that use mechanical apertures are often referred to as Anger cameras.

The Compton imaging technique was first proposed for imaging solar neutrons, first by Pinkau in 1966 and then independently by White in 1968 [44, 45]. Potential gamma-ray astronomy applications were proposed in 1973 by Schönenfelder et al, leading to the Imaging Compton Telescope (COMPTEL), first described in 1984, which launched with the Compton Gamma Ray Observatory (CGRO) in 1991 [46, 47].

Application of Compton imaging to nuclear medicine was first described in 1974 by Todd et al. [48]. During the 1980s, Manbir Singh along with others published numerous analytical and experimental results on a Compton camera designed for SPECT which consisted of a pixelated germanium scatter detector in coincidence with a NaI scintillator second detector [42, 49]. The germanium scatter detector was later used at the University of Michigan in a Compton camera that utilized a “ring” geometry [50].

More recently, investigations at the University of Michigan, including work as part of CIMA, were conducted using a ring geometry and a pixelated silicon scatter detector [51, 39]. The current investigation is a progression of this work, utilizing a pixelated silicon scatter detector but employing a more conventional geometry.
4.3 Principles

In order to reconstruct an image of a source distribution from the emitted radiation, it is necessary to ascertain not only the position of a detected photon but also the direction it came from. A standard gamma camera uses a lead collimator to achieve this by limiting the direction incident photons can approach the detector. In Compton SPECT, however, a pair of detectors are used in coincidence and the physics of Compton kinematics is used to determine the possible directions the photon came from.

When a photon travels through matter, it can interact with that matter in many ways. One possible interaction is known as Compton scattering and occurs when the photon interacts with an electron, imparting some of the photon’s energy to the electron and changing the direction of motion of the photon. The angle between the photon’s direction of travel after Compton scattering and its direction before the scatter is related to the amount of energy transferred to the electron. Thus, if the energy of the electron is known, this angle can be calculated. By constructing a set of detectors, the first of which is designed to Compton scatter the photon and the second of which is designed to absorb the photon, the initial direction of the photon
can then be restricted to lie on the surface of a cone [48]. This cone has its apex at the point of the Compton scatter in the first detector, it’s axis along the line between the point of interaction in the first detector and the point of interaction in the second detector, and it’s angle is equal to the angle of the Compton scatter (see Figure 4.1). A device which takes advantage of this technique is referred to as a Compton camera and when such a device is utilized to create tomographic images the technique can be aptly called Compton SPECT.

4.3.1 Compton Kinematics

The physical principles on which the Compton SPECT concept are founded began with the first quantum theory of the scattering of X-rays in matter by Arthur H. Compton in 1923 [12, 13]. He proposed a model based on quantized light particles.
scattering off of atomic electrons. By assuming light was composed of particles with energy and momentum proportional to the frequency of the light and applying conservation of energy and momentum to the photon–electron system, he derived an expression relating the change in wavelength of the light before and after scattering to the scattering angle

$$\lambda' - \lambda = \frac{h}{m_e c} (1 - \cos \theta).$$  \hspace{1cm} (4.1)

For a Compton SPECT device, the kinetic energy of the recoil electron is detected in the scatter detector and the goal is to use the Compton kinematics to determine the scatter angle. Thus it is useful to use an alternate expression which relates the scatter angle to the kinetic energy of the recoil electron. Using conservation of energy,

$$E_\gamma + E_e = E_{\gamma'} + E_{e'},$$

where the electron is assumed to initially be at rest, so the energies before and after scattering are given by,

$$E_e = m_e c^2$$

and

$$E_e^2 = (m_e c^2)^2 + (p_e c)^2,$$

which upon substitution yields

$$E_\gamma + m_e c^2 = E_{\gamma'} + \sqrt{(m_e c^2)^2 + (p_e c)^2}$$

and solving for $p_e^2 c^2$ results in

$$p_e^2 c^2 = (E_\gamma + m_e c^2 - E_{\gamma'})^2 - m_e^2 c^4.$$  \hspace{1cm} (4.2)

Now using conservation of momentum,

$$p_\gamma = p_{\gamma'} + p_e$$
then solving for $p_{\epsilon'}$ and taking the dot product with itself

$$p_{\epsilon'}^2 = p_{\epsilon'} \cdot p_{\epsilon'} = (p_\gamma - p_{\gamma'}) \cdot (p_\gamma - p_{\gamma'}) = p_\gamma^2 + p_{\gamma'}^2 - 2p_\gamma p_{\gamma'} \cos \theta.$$ 

Finally, multiply by $c^2$ and using $p_\gamma c = E_\gamma$ gives

$$p_{\epsilon'}^2 c^2 = E_\gamma^2 + E_{\gamma'}^2 - 2E_\gamma E_{\gamma'} \cos \theta.$$ 

If we combine (4.2) and (4.3) we find

$$(E_\gamma + m_e c^2 - E_{\gamma'})^2 - m_e^2 c^4 = E_\gamma^2 + E_{\gamma'}^2 - 2E_\gamma E_{\gamma'} \cos \theta$$

$$2E_\gamma m_e c^2 - 2E_{\gamma'} m_e c^2 = 2E_\gamma E_{\gamma'} (1 - \cos \theta)$$

$$m_e c^2 (E_\gamma - E_{\gamma'}) = E_\gamma E_{\gamma'} (1 - \cos \theta).$$

Now using conservation of energy to substitute $E_\gamma - E_{\gamma'} = E_{\epsilon'} - E_\epsilon$ and similarly $E_{\gamma'} = E_\gamma + E_e - E_{\epsilon'}$ we find

$$m_e c^2 (E_{\epsilon'} - E_\epsilon) = E_\gamma (E_\gamma + E_e - E_{\epsilon'}) (1 - \cos \theta).$$

Since we can express the energy deposited in the scatter detector by the recoil electron as the difference of the final and initial electron energies $E_{\epsilon'} - E_\epsilon \rightarrow E_\epsilon$, solving for $\cos \theta$ leaves the final expression relating the scattering angle to the initial photon energy and the energy $E_\epsilon$ deposited by the recoil electron

$$\cos \theta = 1 - \frac{m_e c^2 E_\epsilon}{E_\gamma (E_\gamma - E_\epsilon)}.$$  

(4.4)

### 4.3.2 Detector Resolutions

From Equation (4.4) we can derive an expression relating the uncertainty in the scatter angle based on the uncertainty in the energy deposited by the recoil electron (i.e. the
scatter detector resolution),
\[
\sigma_\theta = \frac{m_e c^2 \sigma_{E_e}}{\sin \theta (E_\gamma - E_e)^2}.
\]

Using Equation 4.4 and some algebra this expression can be rewritten solely in terms of the incident photon energy \(E_\gamma\) and the scatter angle \(\theta\),
\[
\sigma_\theta = \frac{m_e c^2 \sigma_{E_e}}{\sin \theta E_\gamma^2} \left( 1 + \frac{E_\gamma}{m_e c^2} (1 - \cos \theta) \right)^2.
\] (4.5)

This relationship reveals many of the important properties of the Compton imaging technique. First, that the angular resolution improves roughly as \(1/E_\gamma^2\). It also shows that the resolution has a heavy dependence on the scatter angle. The uncertainty in the scatter angle diverges at 0 and 180 degrees, with a minimum somewhere between. In addition, a range of scatter angles which provide high resolution can be identified and this range widens with higher photon energy.

While Equations 4.4 and 4.5 provide a good understanding of the dependence of the image resolution on the energy resolution of the scatter detector, the image resolution will also depend on the spatial resolution of both detectors and the system geometry. Ordonez et al. have described a detailed algorithm for determining the effects of spatial resolution and geometry on image resolution for a Compton system [52].

In general, high spatial resolution will be required for the scatter detector in any geometry. The requirements on the spatial resolution of the second detector will vary by detector geometry, but high resolution in the second detector will also generally be a requirement for achieving good image resolution. Spatial resolution and geometric effects do not improve with increasing energy so they will be an important factor regardless of the isotope being imaged.
4.3.3 Doppler Broadening

Equation 4.4 predicts a unique scattering angle for a given incident photon energy and recoil electron energy. This is based on the assumption that the recoil electron is initially unbound and at rest. In any experiment involving photons Compton scattering within matter the electron will in fact have an initial momentum drawn from a statistical distribution that depends on the material, with higher momentums encountered in materials with higher atomic numbers \((Z)\). The result is that for any given scattering angle there are in fact a distribution of possible final energies for the gamma ray. This phenomenon is known as *Doppler broadening* and represents a fundamental uncertainty in the Compton scattering angle for Compton imaging. It was first recognized by Ordonez et al. that Doppler broadening represents a potential physical limit on the resolution of a Compton camera for nuclear medicine imaging \[53\].

In 1975, Roland Ribberfors was the first to describe a relativistic treatment of Compton scattering that accounted for the distribution of momentums of bound electrons \[54\]. He derived an expression for the relativistic double differential cross section for Compton scattering for an incident photon of energy \(E_\gamma\) to Compton scatter at angle \(\theta\) with final energy \(E_\gamma'\) \[55\],

\[
\frac{d^2\sigma}{d\Omega dE_{\gamma'}} = \frac{mr_0^2 E_{\gamma'}}{2E_\gamma [E_\gamma^2 + E_{\gamma'}^2 - 2E_\gamma E_{\gamma'} \cos \theta]^{1/2}} \left( \frac{E_\gamma}{E_{\gamma'}} + \frac{E_{\gamma'}}{E_\gamma} - \sin^2 \theta \right) J(p_z). \tag{4.6}
\]

The \(J(p_z)\) term is known as the *Compton profile* and is the pre-collision momentum distribution of the electron and in general is a function of the orbital level, the atomic number of the atom, and the binding effects of the neighboring atoms. In practice, \(J(p_z)\) can be obtained from tabulated values of the Hartree-Fock Compton profiles for atomic Doppler broadening as well as measured values for crystalline Doppler broadening \[56\, 57\].
Qualitatively, it is easy to see that the effects of Doppler broadening on image resolution will diminish with increasing photon energy. Since the Compton profiles remain unchanged, the relative uncertainty must decrease as the incident photon energy increases. The uncertainty due to Doppler broadening can exceed the uncertainty due to the energy resolution of the scatter detector, so the choice of scattering material becomes a key consideration in constructing a Compton imaging device. Lower $Z$ materials will have narrower Compton profiles, and thus relatively smaller effects of Doppler broadening.

Clinthorne $et$ $al.$ have performed a detailed study of the effects of Doppler broadening on image variance and spatial resolution in a Compton imaging system for various potential scatter detector materials [58]. Their study shows that the effects of Doppler broadening are significant at 140 keV, and that silicon has more favorable Doppler broadening properties at this energy than other potential detector materials such as Germanium and Neon.

4.3.4 Silicon for Compton SPECT

High resolution silicon pad detectors have many properties that make them a good choice for the scattering detector in a Compton SPECT system. As the semiconducting element with the lowest atomic number, silicon detectors have the lowest angular uncertainty due to Doppler broadening among semiconductor based detectors. The energy resolution of these detectors can be very good, potentially good enough to provide system resolutions competitive with traditional SPECT systems at 140 keV even without cooling. Since pad sizes of $\sim 1$ mm are typical, silicon detectors provide good intrinsic spatial resolution, which is important for the scattering detector at all energies. Finally, silicon has a very high ratio of Compton scattering to total scattering cross section which is important for achieving high system sensitivity.
The primary challenges presented by silicon pad detectors for Compton imaging are due to the low attenuation coefficient of silicon. Due to the low attenuation, the thickness of silicon required to achieve an equivalent efficiency in the scattering detector will have to be higher than for other materials such as Germanium. The thickness of silicon pad detectors is limited to less than 1 mm in order to achieve acceptable timing resolution for Compton SPECT, so the attenuation problem must be addressed by stacking multiple layers of silicon pad detectors. This greatly increases the required number of readout channels, and thus increases the cost and complexity of the system.

4.4 Experimental Setup

A prototype Compton SPECT camera system has been built to quantify the benefits over conventional SPECT systems as a function of source energy. The system consists of a high resolution, 512 pad silicon first detector in coincidence with a NaI scintillator second detector. The silicon detector is a 1.0 mm thick, 4.5 cm x 2.2 cm rectangular wafer with 1.4 mm x 1.4 mm pads read out via four VATAGP3 ASICs [37]. The 1.4 mm by 1.4 mm pads result in an intrinsic rms spatial resolution of 0.4 mm x 0.4 mm x 0.29 mm in the first detector. This detector has been measured to have an energy resolution of 1.6 keV FWHM in the current system at the 59.5 keV photopeak of $^{241}$Am.

The second detector is a clinical gamma camera with the mechanical collimator removed and the read-out electronics replaced. It consists of a 46 cm x 56 cm x .9525 cm continuous NaI crystal and 55 photomultiplier tubes (PMTs). The phototubes are primarily Hamamatsu Photonics R6233-02 8-stage PMTs, with 6 smaller model R6231-03 tubes on the perimeter [59]. Measured resolutions in the second detector are 5.6 mm FWHM spatial resolution and 23 keV FWHM energy resolution for the
Figure 4.3: Diagram and images of the “single-slice” geometry used in the Compton SPECT prototype.

140 keV photopeak of $^{99m}$Tc.

In order to alleviate some of the technical challenges of a fully 3D Compton SPECT system, we have chosen to take the data for this investigation using a 2D “single-slice” arrangement that effectively reduces the source region visible to the scattering detector to a plane. The sources are collimated through a 1.0 mm slit, while the scatter detector is oriented parallel to the plane of this slit so that the collimated photons pass through the 2.2 cm dimension of the detector (see Figure 4.3). This geometry reduces the count rate on the second detector, increases the effective sensitivity of the scatter detector, and simplifies image reconstruction while still allowing the performance of the system as a function of source energy to be evaluated.

### 4.4.1 Detector Calibration and Performance

The initial second detector calibration was carried out using a pinhole collimated $^{99m}$Tc source mounted on an electric stage. The source was panned across the face of
Figure 4.4: An image of the second detector position calibration process.

the detector in a 1 cm x 1 cm grid to perform a sensitivity calibration of the second
detector, as seen in Figure 4.4. A hit map from the full calibration run can be seen
in Figure 4.5(a). Energy resolution and gain calibration of the second detector was
obtained from $^{99m}$Tc flood runs, and an example spectrum can be seen in Figure
4.5(b). The flood runs were performed with an uncollimated $^{99m}$Tc source positioned
$\sim 60$ cm from the detector.

Calibration of the silicon detector primarily consisted of gain calibration runs using
a $^{241}$Am source. A hit map and energy spectrum from one of these gain calibration
runs can be seen in Figure 4.6. In order to reconstruct the Compton events, an
accurate measurement of the silicon position relative to the second detector was also
necessary. This was achieved using the same electric stage used for the second detector
sensitivity calibration. A slit collimated $^{99m}$Tc source was panned across the front of
the detector in the horizontal and vertical directions in 1.0 mm steps and the count
rate in the silicon detector was used to determine the position of the edges of the
silicon detector.

The trigger from the silicon scatter detector was used to create a coincidence
Figure 4.5: (a) Hit map from the 1 cm x 1 cm second detector position calibration run. (b) $^{99m}$Tc energy spectrum.

Figure 4.6: (a) The hit map in silicon from a $^{241}$Am source. (b) The resulting energy spectrum and measured energy resolution.
window for the sum of the triggers from the amplifiers for the PMTs. A coincidence spectrum for the system can be seen in Figure 4.7. Due to the limited geometry, count rates were not an issue in either detector. Thus, the system was not optimized for timing resolution and a generous timing window of 300 ns was selected to maximize the coincidence rate.

### 4.5 Simulation

A simulation of this detector geometry has been developed using EGS5 [60]. The simulation generates photons of a specified energy and a custom routine determines the initial position based on a user-defined source distribution and applies a rotation transformation as necessary to simulate the rotation of the camera/source. Then the incident direction of the photon is determined randomly within the bounds that it is incident upon the front plane (closest to the source distribution) of the silicon. This limitation helps reduce computation time without affecting the validity of the simulation.

Once the initial photon position and direction are determined, the EGS5 code handles the particle transport. All events in which a Compton interaction occurs in
the silicon and is followed by an interaction in the NaI are output to a data file in the same format as the processed data from the real system. Timing resolutions of the system are not accounted for, and no attempt has been made to simulate random coincidences or singles rates in either detector. Thus, this is a highly idealized simulation, however the simulation of the Compton events does account for all major physics effects. EGS5 has routines to handle the Compton kinematics in the silicon scatter detector and the options to include Doppler broadening and photon polarization have been enabled. The individual energy and position resolutions of the detectors were not included in the simulations but were added independently to the data before image reconstruction so that their effects on the reconstructed image resolution could be studied.

4.6 2D Reconstruction

The Compton imaging method uses the positions in the 1st and 2nd detector along with knowledge of the kinematics of the Compton scattering in the 1st detector to determine a probability region for the origin of the gamma ray. As described in Section 4.3 this region takes the shape of a cone. When this cone is backprojected through a slit, the region is effectively reduced to two lines in the plane of the slit. One of these lines passes through the source while the other is a vestige of the measurement process (see Figure 4.8). The vestigial line is frequently outside the field of view, reducing its effect on image quality for this investigation.

When the entire field-of-view is measured in this manner it is akin to a standard tomographic measurement using line integrals, of course with the addition of the “extra” line. Thus an algorithm similar to a standard filtered backprojection can be used. For details on the method of filtered backprojection, see Section 1.3.1.

The “extra” lines in this method are assumed to add randomly to a uniform
Figure 4.8: Images demonstrating the backprojection of events in the 2D reconstruction method. All events shown were collected at the same rotation angle. The images show backprojected lines from (a) a single event, (b) two events, (c) many events, and (d) all events collected at a single angle.

background when backprojected. Since the ramp filter noted above has zero response at DC, a backprojected and filtered uniform background should disappear (except for noise). This assumption is not strictly true and as a result the reconstructed points display some tail-like distortions. However, one advantage of using this method over a more accurate, but more complicated, iterative reconstruction algorithm is that no “resolution recovery” is performed making the resolutions of the reconstructed images reasonable figures of merit for the system.
4.7 Images

The energies relevant to SPECT imaging range from 70 keV to 511 keV; from the photopeak of $^{201}$Tl to the positron annihilation energy. To explore the performance of the prototype system, three sources in this range have been imaged: $^{99m}$Tc (140 keV), $^{131}$I (364 keV), $^{22}$Na (511 keV). Data for each of the real images were acquired by stepping a point source through 6 degree rotational steps via an electric stage. 2,000 events were acquired at each step and the source was stepped through 360 degrees 10 times, for a total of 1.2 million events per image.

The simulated data were generated using the same parameters of 6 degree steps and 2,000 events per step, however the source was only stepped through a single 360 degree turn for a total of 120,000 events per image. Measured detector resolutions from the real system were added before reconstruction to produce images which demonstrate the effects of the individual detector resolutions on the reconstructed image. For each source imaged with the real system, three simulated images were generated. The first is a pure reconstruction of the simulated data, demonstrating only the inherent physics effects without accounting for detector resolutions. The second incorporates the energy and position resolution of the silicon scatter detector, with the energy resolution being the dominant effect of the two on the resulting image quality. The last simulated image in each set incorporates the energy and position resolution of the silicon as well as the position resolution of the second detector (energy in the second detector is not used in the current reconstruction).

4.7.1 Images at 140 keV

A reconstructed image of a 1 mm diameter $^{99m}$Tc source can be seen in Figure 4.9(a). Figure 4.9(b) shows that the resolution of this image is 10 mm FWHM, which is
consistent with the performance of the previous prototype for $^{99m}$Tc \[39\].

Looking at the simulated images (Figures 4.10 to 4.12) it is apparent that the first detector has the greater impact on the image resolution at this energy. This is expected since at lower scatter energies the uncertainty in the recoil electron energy results in a comparatively larger angular uncertainty and a corresponding increase in its impact on the reconstructed image resolution.

4.7.2 Images at 364 keV

The image of a 1 mm diameter $^{131}$I source in Figure 4.13 shows distortions due to a mechanical problem with the rotating stage which caused the source to slip along the polar direction. However, the resolution of the image along the radial direction should not be affected and shows the FWHM resolution of the system at 364 keV to be approximately 7.5 mm. This is a significant improvement over the 140 keV resolution of 10 mm.

Simulations at this energy (Figures 4.14 to 4.16) show that the relative effects on the image resolution due to the individual detector performance has reversed its relationship. At 364 keV, the position resolution of the second detector is a comparatively larger factor than the energy resolution in the first detector for the values of the current system. This verifies the prediction that the effects on image resolution from the electronic noise in the scatter detector fall off quickly with incident photon energy.

4.7.3 Images at 511 keV

A reconstructed image of a 1.5 mm diameter $^{22}$Na source is shown in Figure 4.17. The FWHM resolution of this image is 6.7 mm, showing continued improvement over the 364 keV image. This demonstrates that the current system exhibits the improvement
Figure 4.9: Real image of a 1 mm $^{99m}$Tc source and a histogram showing the FWHM resolution.

Figure 4.10: Simulated image of a 140 keV point source with no detector resolution added and a histogram showing the FWHM resolution.
Figure 4.11: Simulated image of a 140 keV point source with 1st detector resolution added and a histogram showing the FWHM resolution.

Figure 4.12: Simulated image of a 140 keV point source with 1st and 2nd detector resolutions added and a histogram showing the FWHM resolution.
Figure 4.13: Real image of a 1 mm $^{131}$I source and a histogram showing the FWHM resolution. The image shows distortions caused by a malfunction of the gantry used to rotate the source.

Figure 4.14: Simulated image of a 364 keV point source with no detector resolution added and a histogram showing the FWHM resolution.
Figure 4.15: Simulated image of a 364 keV point source with 1st detector resolution added and a histogram showing the FWHM resolution.

Figure 4.16: Simulated image of a 364 keV point source with 1st and 2nd detector resolutions added and a histogram showing the FWHM resolution.
in image resolution predicted for the Compton SPECT imaging technique at higher energies.

The simulations at 511 keV (Figures 4.18 to 4.20) show that while the position resolution of the second detector continues to be a larger factor than the energy resolution in the scatter detector, the effects of both detector resolutions are diminished at higher energies.
Figure 4.17: Real image of a 1.5 mm $^{22}$Na source and a histogram showing the FWHM resolution.

Figure 4.18: Simulated image of a 511 keV point source with no detector resolution added and a histogram showing the FWHM resolution.
Figure 4.19: Simulated image of a 511 keV point source with 1st detector resolution added and a histogram showing the FWHM resolution.

Figure 4.20: Simulated image of a 511 keV point source with 1st and 2nd detector resolutions added and a histogram showing the FWHM resolution.
Figure 4.21: Graph of measured and simulated image resolutions as a function of source energy for the Compton SPECT prototype

4.8 Summary

The current experimental setup has successfully demonstrated the improved performance of a Compton SPECT imaging system with increasing source energy. A graph of the results for the measured and simulated image resolutions as a function of source energy can be seen in Figure 4.21. The observed behavior is precisely the opposite of traditional SPECT systems, and is promising evidence of the potential for Compton SPECT to provide improved resolution for radiotracers such as $^{131}$I and $^{18}$F.

Simulations indicate that improving the spatial resolution in the second detector would likely provide the greatest gain in image resolution across the energy range investigated. The 1.6 keV energy resolution of the silicon detector is likely already adequate for gamma sources from 364 keV to 511 keV, but significant gains in image resolution at 140 keV would be achieved with improved energy resolution. The comparative poor performance of the simulated image at 140 keV is not fully understood.
at this time, further investigations will be conducted and a new simulation will likely be designed in GEANT 4 for comparison.

The system geometry used in this investigation greatly reduced some of the technical challenges faced by a full 3D Compton SPECT geometry. First, the reconstruction was simplified to the point where a relatively simple filtered backprojection algorithm could be used. For a fully 3D system, a more complicated iterative method would be required. Second, the effective thickness of the silicon the incident photons passed through was increased from 1.0 mm to 2.2 cm, greatly increasing the probability of interaction without increasing the complexity of the electronic readout. Finally, the singles rate in the second detector was significantly reduced, simultaneously alleviating the problems of event pile up in the second detector and inadequate timing resolution in the silicon detector. A discussion of potential solutions to these problems as well as proposed future investigations into fully 3D Compton SPECT imaging systems can be found in Section 6.3.
The functional images produced by PET can provide vital information on the development and progression of tumors as well as the effectiveness of new pharmaceuticals for cancer treatment. Brain imaging with PET also presents a valuable opportunity for research. Finally, the development of reporter genes that produce proteins capable of “trapping” positron-labeled compounds has made PET an exciting new tool for genetic research.

Much of the research in these areas involves preclinical trials with small animals, particularly rats and mice. By imaging the animals rather than dissecting them, much fewer animals are required for a given study which can significantly reduce the cost. In addition, by imaging the same animal multiple times rather than dissecting many different animals, variations due to interanimal differences can be reduced. The much (> 200 times) smaller anatomies of these animals compared to humans has created the need for very high resolution PET scanners designed specifically for small animal imaging.

Reconstructed image resolution of 1-2 mm FWHM at the center of the field of view (FOV) is typical of current dedicated small animal pet scanners, however the estimated resolution limit for $^{18}$F of 0.5-0.75 mm has not yet been achieved in a commercial system [61]. Current commercial systems employ technologies ranging
In order to achieve the desired submillimeter resolution, the inherent resolution of the radiation detectors must be greatly increased from systems designed for human imaging. Unfortunately, the solution is not as simple as scaling the detector element size of standard PET systems down to millimeter scales. As the element size is reduced in a segmented scintillator crystal, inter-crystal scatter and uncertainty in the depth of interaction (DOI) become limiting factors (see Figure 5.1). This is due to the fact that while the axial and transverse element size can be easily reduced, the radial thickness cannot be reduced without adversely affecting the system sensitivity.

The effects of inter-crystal scatter on position resolution in BGO and LSO scintillator detectors has been investigated by Shao and Cherry [66]. Various strategies
for determining the crystal where the initial interaction occurred have been proposed in order to combat this problem \cite{67, 68}.

There have also been many strategies proposed for reducing the depth of interaction uncertainty. One strategy takes advantage of the variation in light patterns between separate crystal layers to provide DOI information \cite{69}. Other strategies have been proposed where the crystals are attached to photomultipliers at both ends, allowing the ratio in the signals to be used to determine DOI \cite{70, 71}. It has also been suggested that crystal doping that varies with crystal depth can be used along with pulse-shape discrimination to help determine DOI \cite{72}.

Another strategy to combat the inter-crystal scatter and DOI uncertainty characteristic of scintillator devices is to use solid-state detectors. The high three-dimensional spatial resolution of solid-state detectors eliminates the DOI uncertainty and also provides information that can be used to counteract inter-detector scatter issues \cite{73}. Sensitivity in a solid-state PET system is achieved by stacking multiple layers of detectors until the desired efficiency is achieved. The major drawback of this approach is the additional cost and complexity incurred by the increase in readout channels.

As discussed in Chapter 3, silicon has many advantages as a choice for solid-state detector material, particularly maturity of the technology and room temperature operation, however the major drawback is low attenuation. To offset the low attenuation, a hybrid system consisting of concentric scintillator and silicon rings has been proposed \cite{74, 75}. This system would combine the very high resolution of the inner silicon detector ring with the high efficiency of the outer scintillator ring to create a hybrid PET system with both high sensitivity and submillimeter spatial resolution. In order to reduce costs, the inner silicon ring could also be designed as an insert to be placed inside a clinical full-body human PET scanner.
5.1 Experimental Goals

Previous investigations by CIMA into high resolution PET devices using silicon detectors have shown that a system using our silicon detectors can achieve submillimeter resolution \[76\]. The experimental setup in those investigations was limited to a slit geometry using two VATAGP3 silicon detectors edge-on in coincidence with a pair of BGO detectors at 90 degree angles to the silicon detectors (see Figure 5.2) in order to investigate the use of Compton kinematics to improve the noise equivalent count rate in the silicon \[77\].

The goal of the current investigation is to develop a new experimental setup that can be used to test the dual-ring PET design. In this new setup, BGO detectors adapted from a clinical PET scanner are used to construct a partial scintillator ring. For the initial investigations, this partial BGO ring is used in conjunction with a pair of VATAGP7 silicon detectors arranged in the edge-on geometry of the previous experiments. The results of this investigation will provide the first images produced
by a dual silicon-scintillator ring PET device. The initial images will be of $^{22}\text{Na}$ point sources.

In addition, this system will serve as the base for additional stages of investigation which incorporate additional silicon detectors to more closely approximate the envisioned design of the inner silicon ring. It will also serve as the base for additional investigations into related applications (for a discussion of these applications, see Section 6.4). As a secondary objective, this system will be the first to fully utilize the new VATAGP7 based detectors and so will provide valuable information about their performance, in particular we will characterize any improved timing properties over the VATAGP3 detectors.

## 5.2 Principles

Figure 5.3 shows a rough diagram of the concept behind the high resolution PET scanner using concentric scintillator and silicon rings. Three types of PET events are possible. The first occurs when both photons are detected in silicon (Si-Si). This is a very high resolution event, but also has low sensitivity since the detection efficiency is low in the silicon ring. The second possible PET event occurs when both photons are detected in the conventional scintillator ring (Scintillator-Scintillator). This is a low resolution event, but has high sensitivity due to the thickness and high stopping power of the scintillator material. Finally, “hybrid” PET events where one photon is detected in the silicon and the other is detected in the scintillator ring are also allowed (Si-Scintillator). These events have high spatial resolution, since the silicon ring is closer to the FOV and thus will dominate the resolution, and they have moderate sensitivity.

In addition to the three types of PET events, it is important to recognize that additional information is provided by photons which Compton scatter in the silicon
Figure 5.3: Diagram of the dual ring PET concept and the three potential types of PET coincidences. In order of highest resolution to lowest (and lowest sensitivity to highest), they are: standard PET events in the silicon ring, hybrid events between the silicon and conventional ring, and standard PET events in the conventional ring. Nearly all silicon interactions are Compton scatters followed by the absorption of the photon in the scintillator ring.
and then continue on to be absorbed in the scintillator ring. Nearly all silicon events will be Compton scatters, so in order to perform energy discrimination on the events to reduce the effects of random coincidences and photons that have scattered in the object, the summed energy from the silicon ring and the scintillator ring must be used. While at low count rates it is possible to run the silicon ring as an independent PET scanner, at high count rates the system design assumes that only silicon events that coincide with a subsequent absorption event in the scintillator ring will be accepted. Since the scintillator ring has high efficiency, this should not have a serious impact on the sensitivity of silicon events \[75\].

Compton scattering events can also be reconstructed themselves to either provide additional selection criteria for accepting PET events or to be reconstructed themselves. The principles of imaging using Compton kinematics are discussed in more detail in Section 4.3. Compton imaging can also be used as the sole operation mode for the system, in which case the system would be capable of single photon imaging. The current investigation will not encompass these aspects of the system, but they will be explored in future investigations with the current prototype.

5.3 Experimental Setup

To demonstrate the potential performance of a dual ring PET system based on our current silicon detectors, we have constructed a partial ring setup. Figure 5.4 shows the basic geometry of the system. A partial scintillator ring is in coincidence with a partial inner silicon ring. The structure of the outer scintillator ring will be fixed, while the inner silicon ring will first be represented by a pair of edge-on detectors in a slice geometry and then will be scaled up gradually with additional detectors to more closely approximate the envisioned inner ring. This system is able to approximate a full ring by rotating the source.
Figure 5.4: Diagram of the partial ring setup with rotating source to simulate a full ring.

Figure 5.5: Image of the high resolution PET partial ring setup during final assembly.
Figure 5.6: Image of a single BGO detector with the shielding removed. The BGO crystal is segmented into a 4 x 8 array and read out by four PMTs.

Figure 5.5 is a picture of the actual setup during the final stages of assembly. The partial scintillator ring is composed of 24 (12 on each side) BGO detector modules harvested from a CTI 931 PET scanner. An individual BGO module with the shielding removed can be seen in Figure 5.6. The total scintillator block size is 5.3 cm x 4.9 cm x 3 cm and it is segmented into a 4 x 8 array of 12.5 mm x 5.25 mm x 30 mm crystals. Each module has four Hamamatsu R2497 PMTs [59]. The inner diameter of the ring is 50 cm, a standard size for full body human imaging. Thus this setup will evaluate the potential performance of an inner silicon ring designed to be inserted into a clinical PET scanner.

Figure 5.7 shows a close up view of the silicon detectors. These detectors are double-sided silicon detectors using 2.59 cm x 4.76 cm and 1 mm thick sensors composed of 512 pads at 1.4 mm pixel pitch, all read out by four VATAGP7 ASICs. A detailed view of these detectors can be seen in Figure 3.10 and a full description can
be found in Section 3.3. For the current investigation the detectors are aligned in the edge-on view shown, with approximately 14 cm between them. Only the top two detectors on each side will be used in this geometry.

### 5.3.1 Data Acquisition

The data acquisition system for this prototype is much more complex than any of our previous investigations. In order to manage the coincidence logic and acquire detailed timing information on events, a CAEN V1495 FPGA VME board has been employed [78]. The custom firmware programmed in VHDL effectively implements all of the coincidence logic and provides time-to-digital converter (TDC) functionality. Figure 5.8 shows a block diagram of the DAQ hardware for the partial ring setup.

Each BGO module is connected to a custom amplifier board that includes a constant fraction discriminator on the sum of all four PMTs for trigger generation. The
silicon trigger for each detector is output as a NIM signal by the respective intermediate board (see Section 3.3.3 for a more detailed discussion of the silicon readout electronics). All 24 BGO triggers and both silicon triggers are NIM signals and pass through custom NIM to LVDS converter boards that include 20 ns digital delays used for aligning the BGO triggers. The LVDS signals are then routed to the CAEN V1495 FPGA board for coincidence processing.

If the FPGA firmware determines that a coincidence has occurred it will generate a trigger for the appropriate silicon modules. A trigger is sent to the three CAEN V785 peak sensing ADCs to acquire the PMT signals for all coincidences so that Compton events can be identified in data processing. The silicon electronics require a reset signal if they are not read out, so the FPGA will also generate a silicon reset if the coincidence window passes without a coincidence. Output signals from the V1495
for silicon are on the LVDS channels, so the signals pass through a custom 32 channel
LVDS to NIM converter en route to the silicon electronics.

The CAEN V1495 has a 40 MHz clock, which provides a period (25 ns) that is too
long for the timing constraints of a PET system. Fortunately, the FPGA has a phase
lock loop (PLL) that allows for up to a five times multiplier, providing reliable timing
operations up to 5 ns. All of the input trigger signals to the FPGA are synchronized
to the PLL clock. Expected rates are low enough that the BGO triggers on each side
are combined to form a single delayed trigger. The delay and width of this signal are
configurable via software through the VME interface. Each silicon detector has its
own delayed trigger signal, also with configurable width.

Figure 5.9 shows an approximate schematic of the signal processing for a single
silicon interaction with no coincidence in BGO or silicon, thus requiring a reset to
be sent to the detector, followed by a BGO-BGO coincidence which then generates
a BGO output gate on the NIM output. At this point additional coincidences would
be blocked, and a VME register bit will be set to let the DAQ software know a
coincidence has occurred. Another register contains the coincidence bits that indicate
which signals caused the coincidences. Once the data has been read from all relevant
VME modules, a reset signal will be sent to the FPGA allowing coincidence detection
to resume.

In addition to the coincidence processing, all input triggers (including individual
BGO channels) in the FPGA are given a time stamp based on a 5 ns global counter.
The timestamps are read out at each coincidence and then reset. Offline processing
can take advantage of the timestamps to identify Compton events, which are not
directly detected by the coincidence logic.
Figure 5.9: Approximate schematic of the coincidence signal processing in the FPGA firmware.
5.3.2 System Calibration

The first step in calibrating the BGO ring was to adjust the gains on the individual BGO modules. Since each module is composed of four PMTs and the crystals are not isolated so light sharing across PMTs can occur, the PMTs within an individual module need to have equivalent gains in order for the trigger on the sum of the four PMTs to have good timing. The four corner crystals are isolated such that all the light in each corner crystal is collected by a single PMT. In order to assure that only interactions in the corner crystal are being counted, coincidences between the BGO module and a small NaI crystal positioned opposite the corner crystal are counted from a $^{22}$Na source. Gains are adjusted until all four corner crystals have equal count rates.

The next set of BGO calibrations are carried out by placing a $^{22}$Na source in the center of the FOV and a “flood” run is acquired. Coincidence logic within the FPGA is set to be a simple logic OR between all triggers, so that single interactions in all modules are accepted. The $^{22}$Na spectrum of a single module is used to determine an appropriate threshold for that module, then the thresholds of all other modules are adjusted until all modules have equivalent count rates. At this point, $^{22}$Na spectra are acquired in all modules in order to obtain the gain of each module.

Positions are calculated with a simple centroid method and the positions from the flood run are used to map calculated positions to individual crystals. The position of the assigned crystal is used to determine the LOR for reconstruction. Figure 5.10 shows an example of the crystal assignment in one of the BGO modules.

The final step is to align the triggers of all BGO modules. This is again achieved by placing a $^{22}$Na source in the center of the FOV and operating the ring in coincidence mode. The trigger times are adjusted using the 20 ns delays on the NIM to LVDS converter board. The first module on one side is chosen as a reference and assigned a
delay of 10 ns. The coincidence timing between this module and the module directly across from it is adjusted to peak at zero. Then the second module in line on the opposite side is also adjusted to the first reference module. This third module is then used as the reference for the module adjacent to the original reference and the pattern repeated until all triggers are aligned.

Silicon detector calibration begins first by mechanically aligning the positions of the detectors using the translation stages on which they are mounted. The detectors are then leveled using a laser level mounted to the optical table as reference. Finally, a $^{241}\text{Am}$ source is placed inside a slit collimator at the center of the FOV and the detectors are slowly adjusted to maximize the count rate. Gain calibration of the silicon detectors follows the process detailed in Section 3.3.4. The timing of the silicon detectors is adjusted using the programmable delay in the FPGA coincidence logic.
Figure 5.11: Gain adjusted $^{22}\text{Na}$ spectra in (a) the left side and (b) the right side of the BGO ring from flood runs.

5.3.3 System Performance

Figures 5.11(a) and (b) show the energy resolutions (~26% FWHM) of the two halves of the BGO ring from a flood run. Energy resolution in the BGO ring is used primarily for event selection, to help reduce the effects of random coincidences and scattered photons. Figures 5.12(a) and (b) show the energy resolutions of the silicon detectors (~2.17 keV FWHM) from $^{241}\text{Am}$ gain runs. Energy resolution in the silicon is more critical since it can be used to provide additional information through the reconstruction of Compton kinematics. The energy of Compton scattering events can also be added to a coincident absorption event in the BGO ring for event selection, but the summed energy resolution will be dominated by the BGO detector performance.

Figures 5.13(a)-(c) show the coincidence timing spectra from the three different types of PET events in the partial ring high resolution PET system. As the plots show, the BGO-BGO events display a reasonable PET timing resolution of 11 ns FWHM. Si-BGO events feature a much poorer timing resolution of 46 ns FWHM, which is dominated by the silicon timing. Si-Si events of course show the lowest timing resolution of 84 ns, which is consistent with the previous prototype [76].
Figure 5.12: Gain adjusted $^{241}\text{Am}$ spectra in the (a) left and (b) right silicon detectors.

Figure 5.13: Coincidence timing spectra from (a) BGO-BGO events, (b) Si-BGO events, and (c) Si-Si events.
Figure 5.14: Plot of the significant time walk still present in the VATAGP7 chips.

Figure 5.14 shows, the timing in silicon is still dominated by the time walk, so without time walk compensation the new VATAGP7 chips do not have improved timing performance over the VATAGP3 chips.

5.4 Images

Initial images are of slit collimated $^{22}$Na sources. The primary motivation of the slit is to reduce the singles rate from axially extended sources. This is not particularly relevant for the point sources used here, but the slit collimator also serves to axially collimate projections of the source onto the BGO detectors, which helps define the geometry for Si-BGO and BGO-BGO events. Sources are rotated through 360° to compensate for any asymmetry in the partial ring setup, particularly in the alignment of the two silicon detectors.

5.4.1 Point Source and Resolutions

The first set of images are of a 0.25 mm diameter $^{22}$Na source, which is small enough to be an equivalent point source for the system. These first images were reconstructed using a simple filtered backprojection (see Section 1.3.1) and the FWHM resolution
was measured through the center of the point spread function along the x and y directions. Figures 5.15 through 5.17 show the reconstructed images from Si-Si coincidences, Si-BGO coincidences, and BGO-BGO coincidences respectively.

The FWHM of the Si-Si events was measured to be 1.0 mm in the x direction and 0.8 mm in the y direction. This is consistent with the performance of the previous prototype, which was measured to have 980 µm FWHM resolution at the center of the FOV \cite{76}. FWHM resolution for the hybrid Si-BGO events is 1.8 mm in the x direction and 1.9 mm in the y direction. The previous prototype did not include the outer PET ring, so no direct comparison can be made, however this resolution is on the same order as some dedicated small animal PET systems and is in line with expectations for these high resolution, moderate sensitivity events. Finally, the FWHM of the BGO ring alone is \(~8.5\) mm which is also in line with expected performance.

These filtered backprojection images are a good measure of system performance and serve to show that the system is working as expected. The ultimate goal is to use an MLEM reconstruction that combines all of the separate event types into a single high quality image. This reconstruction is in development. For an introduction of the MLEM algorithm, refer to Section 1.3.2.

5.4.2 Multiple Point Sources

Figure 5.18 shows an FBP image of three $^{22}$Na point sources spaced approximately 2.0 mm apart from center-to-center. The image is actually reconstructed from three separate data runs collected with a single 0.25 mm point source moved by 2.0 mm between each run. Data from all three runs was combined and reconstructed together.

An MLEM reconstruction for Si-Si events of a dual point source consisting of two 0.25 mm diameter $^{22}$Na point sources separated by 1.5 mm from center to center can
Figure 5.15: $^{22}\text{Na}$ point source data from Si-Si events (a) sinogram, (b) FBP image, (c) x and y profiles of the PSF.
Figure 5.16: $^{22}$Na point source data from Si-BGO events (a) sinogram, (b) FBP image, (c) x and y profiles of the PSF.
Figure 5.17: $^{22}\text{Na}$ point source data from BGO-BGO events (a) sinogram, (b) FBP image, (c) x and y profiles of the PSF.
Figure 5.18: FBP reconstruction of three $^{22}$Na point sources separated by 2.0 mm center to center.

Figure 5.19: MLEM reconstruction of two $^{22}$Na point sources separated by 1.5 mm center to center.
be seen in Figure 5.19. The two sources are clearly resolved, demonstrating the high position resolution of the PET events in the silicon detectors.

5.5 Summary

The current high resolution PET system has been shown to be operating with expected spatial resolution for the small FOV configuration. Spatial resolution of images reconstructed with Si-Si events are consistent with previous results and the Si-BGO and BGO-BGO resolutions are consistent with expectations. Timing resolution of the system is also consistent with the previous system.

Now that the system is confirmed to be performing well, the immediate goal will be to reconstruct images from the combined data of all three coincidence types using an MLEM method. These reconstructions will represent the first real images from a high resolution PET device designed around the concept of concentric silicon-scintillator PET rings. Additional images of more complicated phantoms will be acquired to further demonstrate the system’s capabilities.

The reconstruction of the combined Si-Si, Si-BGO, and BGO-BGO events is the first demonstration of this kind. In particular, the Si-BGO events show that a high resolution silicon detector can be combined with a relatively poor resolution detector to produce high quality images in a narrow field of view. This concept is not only important to the small animal PET design but also to the concept of a “PET probe.” The idea behind the PET probe is to place a high resolution detector close to a region of interest interest in a patient and use the probe in conjunction with a standard PET system to achieve high resolution images of a small FOV, just as we have done with the Si-BGO events in the current prototype. In this way, the PET probe would act like a “magnifier.”

The current small FOV configuration of the system is just the first of many in-
vestigations planned for the partial ring setup. A discussion of future investigations, including investigations into the PET probe, can be found in Section 6.4.
Chapter 6

Conclusions

The objective of the dissertation was to explore potential applications for high resolution silicon detectors in PET and SPECT. Two prototypes were developed that demonstrate the performance of our current detectors in high performance applications. The results of these investigations provide promising evidence of the feasibility of high resolution silicon detectors for both Compton SPECT and high resolution PET systems. They also help quantify and qualify the remaining technical challenges for developing full-scale devices.

6.1 Compton SPECT

The “single-slice” Compton SPECT prototype was built to assess the performance of a Compton SPECT imaging system based on a design similar to a standard gamma camera. The prototype consisted of a single high resolution silicon detector, configured in a 2D geometry, in coincidence with a standard NaI scintillator detector which had been harvested from a standard SPECT system. Point source images were taken with the prototype for $^{99m}$Tc, $^{131}$I, and $^{22}$Na to demonstrate the performance over a wide range of energies (140 keV, 364 keV, and 511 keV). Filtered back projection image resolutions of 10 mm, 7.5 mm, and 6.7 mm were achieved for the three sources respectively. These images clearly demonstrate the improved performance of the sys-
tem with increasing energy which is a key motivation in the development of Compton SPECT systems. The results represent the most promising evidence so far for the feasibility of our detectors, and pixelated silicon detectors in general, for Compton SPECT applications.

A simulation of the prototype was also developed using EGS5. The simulated images showed good overall agreement with the performance of the prototype, with the exception of the 140 keV images. By incorporating the effects of the scatter detector and the absorber independently, insight into the technical limitations of the system was obtained. It was apparent that for the image resolution, the primary contribution to image degradation was the position resolution of the second detector, with the energy resolution of silicon being a major contribution at 140 keV, a lesser contribution at 364 keV, and perhaps only a minor contribution at 511 keV. The effects of the silicon energy resolution are not surprising since it has previously been suggested that an energy resolution below 1 keV is desirable for imaging 99mTc. The timing resolution and rate capabilities of both detectors were poor, well below what would be required for clinical operation, which was a primary motivation for the 2D geometry along with the low efficiency of silicon.

6.2 High Resolution PET

A partial PET ring composed of BGO detectors has been built to serve as a testbed for many PET applications. The first application chosen is a small FOV high resolution PET prototype for small animal imaging that is a natural progression of previous investigations which established the very high resolution PET images achievable with our silicon detectors. Combining the high efficiency outer ring with the high resolution inner ring has been proposed as a solution for a submillimeter resolution small animal PET scanner with high sensitivity. This prototype is the first to fully test this concept.
with the simultaneous acquisition of standard PET events in each ring and hybrid PET events between the two rings. The first images from the system are promising and a full analysis of the system performance will hopefully provide strong motivation to continue progress towards a full-scale device.

This prototype also served as the first proving ground for the new iteration of the VATAGP ASICs. The new version, VATAGP7, was specifically designed to sacrifice a small amount of energy resolution for increased timing resolution. Performance of the new detectors, based on the same sensors and hybrids with only the ASICs updated, has shown that the energy resolution has gone from $\sim1.5$ keV to $\sim2.5$ keV. This provides ample performance for pure PET applications, but is clearly insufficient for Compton SPECT imaging. It should still provide adequate performance for using Compton kinematics to increase the noise equivalent count rate in high resolution PET.

Unfortunately, the VATAGP7 continues to employ a leading edge discriminator for trigger generation, so the time walk continues to dominate the timing performance and a large coincidence window is employed in order to maximize the sensitivity of silicon events. The new custom coincidence system includes a TDC implementation, so it is possible to correct for the time walk in the data processing and the timing performance of the system with time walk removed will be analyzed.

6.3 Future SPECT

Future Compton SPECT efforts will fall along two lines: additional investigations with our current silicon detectors and investigations into new scatter detectors.

Despite the poor timing of our current silicon detectors, the excellent spatial resolution and high energy resolution still present many avenues for investigation. 2D images of more complicated sources is the simplest extension. It had been intended
to image complicated sources with the “single-slice” system, but the demolition of
the lab space force the system to be dismantled prematurely. The construction of
a new system employing a second detector with increased spatial resolution could
demonstrate higher resolution images. The new partial BGO ring built for the high
resolution PET prototype is a promising candidate.

The next logical extension is to use multiple stacks of detectors. Again, the new
partial ring setup with its FPGA-based coincidence system would make the design of
such a system much easier than the comparatively simple “single-slice” system. Full
3D images of a complex source distribution would be an important step in validating
Compton SPECT imaging.

Improvements in detector performance are ultimately needed in order to continue
to advance Compton SPECT imaging as a viable modality. Continuing to take ad-
vantage of advances in detector technology will be essential, especially in development
of the scatter detector for which the ultimate goal is high timing resolution and very
high energy resolution, and ideally a high Compton scattering cross section. Silicon
pixel detectors remain a leading contender for this role.

6.4 Future PET

Only the very first images of this system have been reconstructed. Images of more
complicated sources are planned, and incorporation of Compton kinematics into the
image reconstruction is a priority. The 2D geometry continues to be useful for in-
creasing the efficiency of the silicon detectors, however the system is already designed
to run with two silicon detectors operating on each side. If the detectors were ori-
ented face-on instead of edge-on, even with two detectors on each side the efficiency
of coincidence events would be reduced by two orders of magnitude. With the timing
performance and dead time in the current system, this would make image acquisition,
especially with short-lived sources, problematic to say the least.

The partial BGO ring and associated data acquisition system provides great opportunities for further applications. Likely the first application once the current high resolution PET efforts are concluded will be first images with the silicon PET insert probe [79]. The silicon PET insert probe is a small stack of 1.0 mm thick pixel detectors with 1.0 mm pitch designed to be positioned close to a region of interest in order to provide high resolution images within a very select FOV. It could potentially be used to drastically improve image resolution for tumors that have already been located to provide greater detail for treatment planning.

Just as for future SPECT applications, improvements in detector performance will ultimately be required to make these PET applications viable. For small animal PET applications, 1.4 mm pixel pitch is likely not adequate. 1.0 mm pixels or smaller (perhaps as small as 0.3 mm) would be preferred in order to bring the intrinsic resolution of the silicon ring down to the limits imposed by the $^{18}$F positron range and photon acollinearity [80]. The timing resolution in the silicon detectors still needs to be addressed, and it seems the design of a new readout chip with pulse-height correction is the likely remedy. Moving to thinner sensors may also be necessary, since it is known that good timing is achievable in silicon sensors with 300 µm thickness.
Bibliography


